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THE EFFECT OF GOLD NANOPARTICLES ON RADIATION DOSE DISTRIBUTION IN BREAST CANCER USING MONTE CARLO SIMULATION

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The simulation model for MCNP5 code was used to study the effect of the gold nanoparticle (AuNPs) in cancer breast samples. The dose rate distribution of AuNPs in water and breast phantom was calculated using MCNP5 code. For inhomogeneities, cone cells were designed to calculate dose distribution around Ir-192 source in breast and inhomogeneous medium that includes gold nanoparticles at different concentration. Both barometers, the track length energy deposition tally (F6) and pulse height tally (*F8), were used. The result indicated that the F6 is better than *F8 for radiation dose calculation. Angular doses distribution in water was compared with data published for tally F6 and*F8 with the different percentage range of 0.0136 to 0.3019% for tally F6 at the average angle of 5˚and 175˚respectively. For *F8 tally, different percentage range of -0.0014 to 0.8253 % was obtained at an average angle of 75˚and 5˚ respectively. For breast phantom, the result of the F6 tally with the *F8 tally was compared. The difference in calculations between the two tallies in the angular anisotropic distribution was found to be in the range from 0.0514 to 0.4596% at the average angle of 15 ˚ and 175 ˚ respectively. The obtained results showed that the AuNP dose increases when the concentration increases up to ten percent (100 mg/ml), and then decreases for concentration higher than ten percent. The concentration of AuNPs greater than ten percent is not recommended. The results indicated that tally F6 is a good tool to calculate the effect of inhomogeneities due to breast cancer on brachytherapy.

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1. Introduction

Cancer and the problems associated with it are considered as the leading healthcare problem in the world [1]. Therefore, it is important that researchers focus on the reasons underlinying the prevalence of cancer. Indeed, studies are increasingly focused on understanding the pathogenic mechanisms of breast compositions, which decrease with efficiency of cells [2, 3]. The cancer is considered as abnormal cells [4]. The major challenge in cancer treatment is to restore cell composition. However, cancer cell changes, cell compositions variations, and other factors are probably relevant pathogenic factors of the disease [4]. Moreover, cancers are of many

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types; they are agreeing into abnormal cells which growths uncontrolled group's diseases characterized and spread if the spread is not controlled, the result can be death [5]. Cancers are caused by different factors; some are internal such as inherited genetic mutations, immune conditions and hormones, while others are external such as tobacco, unhealthy diet, and contagious organisms [5]. These factors can act in sequence or together to result to cancer. Cancer causes deaths more than AIDS as reported worldwide, and it has been published that one out of seven deaths is caused by cancer [6]. Breast tumors are the most causes of death among women in the world [6]. Women breasts are composed of glandular tissues and adipose tissues [7]. Cancer cells are categorized into different types. The cancer treatments and development vary significantly with the type of cancer. In the past years, more attention and progress have been made towards the treatment and understanding of the earlier proposed reasons of cancer [8]. Among different cancer treatments, radiation-therapy or radiotherapy remains an important modality used in cancer treatment. The dawn of radiotherapy started soon after the discovery of X-rays by the German/Dutch physicist, Wilhelm Conrad Röntgen, in 1895. At the dawn of radiotherapy, only low photon energies were achievable. Radiation dose is used as a physical agent to cure cancer cells. The ion radiation (electrically charged particles) deposits energy when it passes through the cancer cells. However, this ion radiation deposited energy in cancer cells can cure cancer cells.

The role of the gold nanoparticles in common radiotherapy practices has been studied extensively by using Monte Carlo simulations and experimental measurements [9]. The results of most of the studies in cancer cells confirmed an increase of the radiation absorbed doses to various cancer cells as a result of the existence of gold nanoparticles [10].

However, the results are still controversial regarding the interaction mechanism of ionizing radiation with the cancer cells. Several studies have investigated the administration of the higher doses [7-10], which include the dimension of nanoparticles, high molar concentrations, and lower energies of the photons or gamma rays. Moreover, many attempts have been made to derive a dose measurement that appropriately quantifies the energy absorbed by the radiosensitive tissue in the breast [11-13].

The Monte Carlo N-Particle-Version 5 (MCNP5) code was used to investigate the dose distribution near an Iriduim-192 brachytherapy source (Ir-192) [13, 14]. The MCNP5 codes are extensively performed to calculate brachytherapy sources dosimetric parameters [15]. This code simulates electrons, neutrons, and photons in a wide field of energy through a stochastic process based on physical and statistical principles of the radiative transfer and particle interaction [15]. The MCNP5 code gives an answer by simulating individual particles, tallying the results, and inferring the average conduct of particles in a physical system from the simulated particles using the central limited theorem [16]. Recently, gold nanoparticles conjugated with radionuclide were developed as a brachytherapy novel form [14]. Gold nanoparticles can be aided through physical distribution in homogenizing dose of radiolabeled AuNP [10]. Nanotechnology is extensively used to manufacture product ranging from consumerism, electronics, and biomedical devices. Due to their ratio of large surface to its volume, Nano-scale semiconductor and metal particles are at the center of many applications. Although nanoparticles are widely and frequently used, their effect on cells is still the subject of intense research. Many reports have indicated that such nanoparticles have physical properties that allow them to invade into the skin and other organs in unusual ways [18].

In this study, the simulation and validation of AuNPs for dose enhancement capability was presented. Furthermore, the analysis of the nanoparticles influence on the dose rate distribution on water and breast tissue has been performed to verify a good tool for dose calculation. Moreover, MCNP5 was performed to simulate the Ir-192 brachytherapy source with typical homogeneous and inhomogeneous (extremely irregular) phantoms. This is done by using two deferent baronets (the track length energy deposition tally (F6) and pulse height tally (*F8)) and making comparison between them which is the best to calculate dose distribution. In homogeneities medium, an effect was performed using water, breast tissue and air; whereas for inhomogeneous medium, in addition to water, breast tissue and air, the nanoparticles were added.

2. Material and methods

2.1. Materials

The breast phantom consists of 100% fibro-glandular tissue. Elements composition and density were taken from the reference [3]. Table 1 shows a comparison of the elements composition and density (ρ) of the water and the breast tissue.

Table 1. Elements composition and density (ρ) for water and breast tissue.

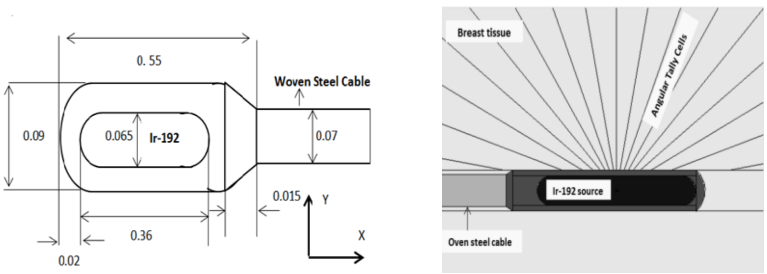
Materials	Elements composition as a percentage (weight fraction)								density
	H	C	N	O	Na	S	Cl	P	$\rho(g/cm^3)$
Water	11.11			88.89					1.00
Breast tissue	10.6	33.2	3.0	52.7	0.1	0.2	0.1	0.1	1.020

Gold nanoparticles at different concentrations of 5 at.%, 7 at.%, 10 at.%, 15 at.%, and 30 at.% were chosen and mixed with water or breast tissue by weight percentage. As the density of water or breast tissue changes, the concentration also changes. This was defined on material card in MCNP5.

2.2. Methods

The simulation setup is typically a brachytherapy device, defined by MCNP5. The MCNP code input file consists of three cards, i.e. surface card, cell card, and data card.

The cells are applied to define the part of geometry. Also, the material content of physical space and surface cards define the boundary of cells. The Ir-192 brachytherapy device used in this application has been designed by Siebert [19] as shown in Fig. 1(a). The device content Ir-192 (ρ=22.42 g·cm^{-3}) core cylinder with radius 0.0325 cm is geometrically centered at the origin. The core is surrounded by a stainless steel cylinder with a radius of 0.045 cm and a spherical half-plug of 0.061 cm at one end. It is closed at two ends by half spheres of equal radius to give a total length of 0.36 cm. The other end is a cone connected to the woven steel cable to give the steel envelope a maximum length of 0.45 cm. The cable and capsule are usually chosen from steel with different densities. A 5 cm radius sphere filled with pure water (ρ=1.00g·cm^{-3}) surrounds the device which is a boundary of the problem. The dose was determined from ten-degree increments from 0° which is the x-axis through the center of the device along the woven steel cable up to 180° as shown in Fig. 1 (b).



(a) (b)

Fig. 1. (a) Internal construction and dimensions of Ir-192 brachytherapy device geometry. (b) Side view of MCNP5 brachytherapy model. It illustrates the angular tally cells as wedges of a sphere cut at 10^o increments in Breast tissue.

The volume of the wedges was calculated and the data were inserted manually for the tallies in the anisotropic dose determination process. The cell mass can be calculated from MCNP program data by multiplying the density of the material within the cell times the cell's volume [16]. The MCNP5 simulation code can be used to evaluate the radiation transport through a stochastic process based on the physical and statistical principles of radiative transfer and particle interaction. A number of particles of 5×10^8 were traced to perform the simulation for the estimation of nanoparticles effect on the dose distribution. For nanoparticles effect study, the dose was firstly calculated without nanoparticles and within the regular conical wedges (volume cells) around the source of water. The breast tissue (ρ=1.02g·cm^{-3}) phantom was replaced by water and the dose was then calculated at the same cells around the source.

2.2.1 Source Specifications

The source contains a cylinder with two half spherical caps at the ends, which were all included in the same cell description. In this work, a high-dose brachytherapy device is used. The brachytherapy is a medical procedure in which a radioactive source is put within a body cavity or tumor (interstitial), or in close proximity to a tumor (intercavitary) [17]. This brachytherapy device uses a gamma source, ^{192}Ir, to deliver a high dose-rate in the near-field (defined to be < 5 cm by the author of the problem, Dr. Robert Price) to surrounding water. The dose is calculated for both radial and anisotropic distributions using MCNP 5 code. This process usually releases a gamma photon with an average energy of 0.38 MeV (max 1.06 MeV).This source was defined as a cylindrical source with a radius equals to the radius of the ^{192}Ir. The extent was defined as the distance from outer caps to the cylinder center by including cell 1 in the source definition card (SDEF card). Only source points sampled within cell 1 were used, which makes the source geometry appropriate for the source with two half spherical end caps. This description, therefore, gives a uniform distribution of source points within a cylinder as well as within cell 1 that is inside this cylinder [16].

2.2.2. Tally specifications

The radial dose distribution was limited by placing cylinders about the ^{192}Ir core and steel encapsulation in 0.5 cm increments up to the 5 cm radius sphere. The anisotropic dose distribution was originally set up for ten-degree increments up to 180^{o}. The variance of the variance (VOV) fluctuated, indicating a high weight/low probability event to be sampled. Both F6 and *F8 tallies were used in the anisotropic and radial dose determinations. The F6 tallies results is MeV g^{-1}, and is then converted into Gray (Gy) by tally multiplier card. The *F8 tallies, which give results in MeV, were later converted to Gy by dividing it by the mass within the cell and multiplying it by 1.602×10^{-10} to change the units from MeV g^{-1} to J kg^{-1}. The cell mass was specified by multiplying the material density in the cell by the cell volume. The obtained results of the F6 and * F8 tallies were used and compared with the published data.

2.3. Dose enhancement calculation

After distribution, the AuNPs and the tumors will be united given their size and the dose enhancement factor (DEF) for AuNPs, which can be calculated using the MC method.

The relationship between AuNPs and tissues in the MC studies was reported elsewhere [21-23]. Several authors reported AuNP and DEFs for the Ir-192 brachytherapy source [21]. Different DEFs for the same size of AuNP showed that DEF varied significantly in gold nanoparticles in terms of concentration and simulation configuration [21]. In a regular distribution, photon interactions in the tumor have different forms [21]. Throughout this work, a new algorithm of MCNP 5 was introduced to create the semi-random distribution of NP in the tissue. The DEF for AuNPs with different concentrations was calculated for gamma-ray source (Ir-192).

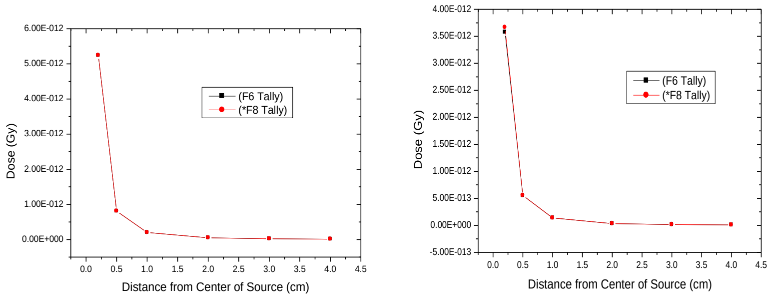
The dose distributions in the sample were calculated with and without gold nanoparticles.

For this study, AuNPs doses of 5%, 7%, 10%, 15% and 30% (1% =10mg/ml) were applied to samples. However, Monte Carlo calculations are presented to calculate the DEF [23]. The DEF is defined similar to other radiobiological ratios and is given by:

$$DEF = \frac{absorbed\ dose\ with\ NPs}{absorbed\ dose\ without\ NPs} \quad (1)$$

3. Result and discussion

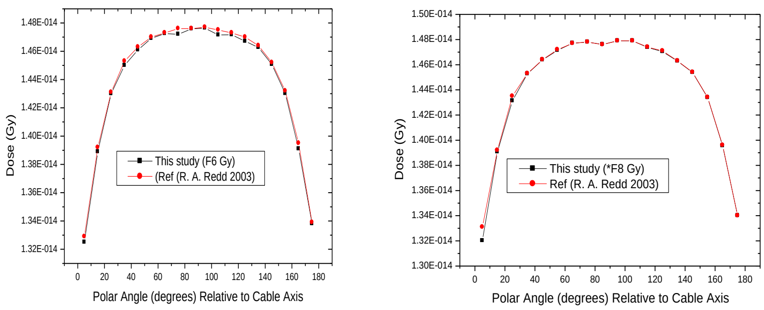
The radius and angular anisotropic dose distributions were estimated with each result normalized to one source particle (photon). For homogeneous water and breast, the phantom performed an assurance quality on the simulation. Fig. 2 (a) shows the graph of the radius dose distribution for water, while Fig. 2 (b) shows breast phantom, both without AuNPs, comparison tally F6 track length energy deposition with pulse height tally *F8.



(a) *(b)*

*Fig. 2. A comparison between the tally F6 and tally *F8 for radius dose distribution function for (Ir-192) brachytherapy (a) In water and (b) in breast tissue both without AuNPs.*

A comparison between tallies F6 and *F8 results is shown in Fig. 2. The percent-difference in the radius anisotropic dose distribution between F6 and *F8 results are maximum of 7.8159$\times 10^{-01}$ % at a radius of 1 cm and a minimum of 7.6435$\times 10^{-04}$ % at the radius of 4 cm in water. For breast phantom, the maximum difference was 2.4958$\times 10^{-00}$% at radius value of 0.2 cm and the minimum difference was 2.5580$\times 10^{-01}$% at radius value of 4cm. However, both have a very small associated significant standard deviation. Angular dose distribution for Ir-192 brachytherapy device in water was compared with a similar data from reference [24]. This comparison was for tally F6 and *F8 after converting from MeV g^{-1} to J kg^{-1} (Gy). The result was in a good agreement for both tally as shown in Fig. 3(a) for tally F6 and (b) for tally *F8.



(a) *(b)*

*Fig. 3. Anisotropy functions of different angular dose distribution for Ir-192 brachytherapy in water. A comparison between (a) result of tally F6 and (b) tally *F8 with previous work.*

Fig. 4 shows an angular dose distribution for Ir-192 brachytherapy source in breast phantom. The result of F6 tally (Track length estimate of energy deposition) and tally *F8 (energy distribution of pulses created in a detector) were compared after converting from MeV g^{-1} to J kg^{-1} (Gy). The result was quite in agreement with the maximum percent difference of 0.4596 % at average angle 175 ° and minimum percent difference of 0.0514 % at average angle 15°.

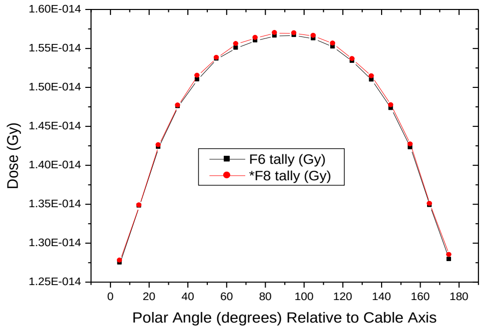
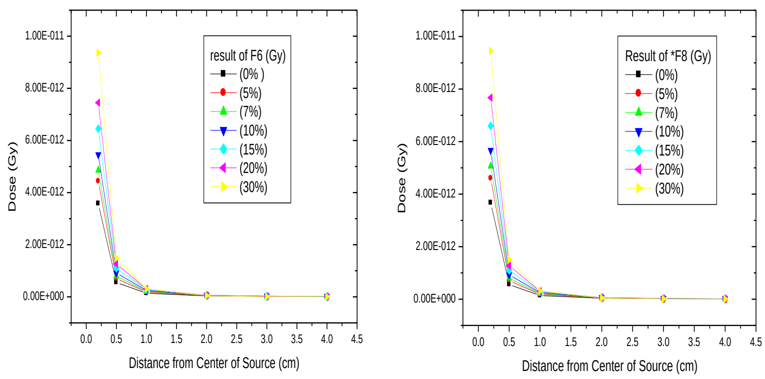


*Fig. 4. Angular dose distribution for Ir-192 brachytherapy device in breast phantom tally F6 compared with *F8 after converting from MeV g^{-1} to J. kg^{-1} (Gy).*

3.1. Effect of AuNPs

Gold nanoparticles have considerable interest attracted for a range of biomedical applications. Within these studies, some are focused on the DEF of AuNPs in radiation therapy of cancer. Clinically, AuNP is being applied as a good radio-sensitizer. In combination with radiotherapy, the effective radio-sensitization depends on factors such as energy of the photon, AuNPs concentration, and the location within the cell [25]. There are some studies which indicated energy dependencies of DEF, while others have studied the AuNP size effect in association with photon energy [25]. However, in some aspects of AuNP-based radiotherapy, the results of recent studies do not seem to be very conclusive. Fig. 5 (a) and (b) demonstrates the result of tally F6 and *F8.

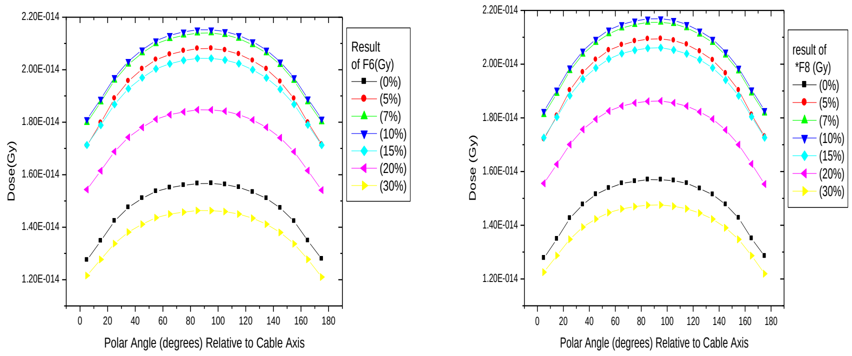
The obtained results of the dose distribution as a function of radius and the effect of AuNPs were in good agreement with the experimental data.



(a) *(b)*

*Fig. 5. The comparison between six difference concentrations as function of radius anisotropic dose distribution for Ir-192 brachytherapy in breast phantom, (a) F6 tally and (b) tally *F8 (Gy).*

Fig. 6 (a) and (b) showed the comparison between F6 and *F8 tally. The results are in a good agreement with the dose distribution as a function of average angle. Furthermore, the effect of nanoparticles on the dose distribution was also observed.



(a) *(b)*

*Fig. 6. A comparison between six difference concentrations of AuNPs for angular anisotropic dose distribution of Ir-192 brachytherapy source in breast phantom (a) tally F6 and (b) tally *F8.*

3.2. Dose enhancement factor (DEF)

High dose rate (HDR) brachytherapy with Ir-192 brachytherapy source was simulated for breast phantom to calculate DEF of AuNPs. Six concentrations were simulated to obtain the dose rate constant for radius dose functions and the angular dose functions. The values of F6 tally and *F8 tally ware compared. Moreover, the dose enhancement factor of a distance from the center of the source, for F6 and *F8, was illustrated in Fig. 7 (a). The results are in a good agreement for almost all points. Additionally, the dose enhancement factor of an angular dose, for F6 and *F8, is given in Fig. 7 (b). It also shows a good agreement for all points.

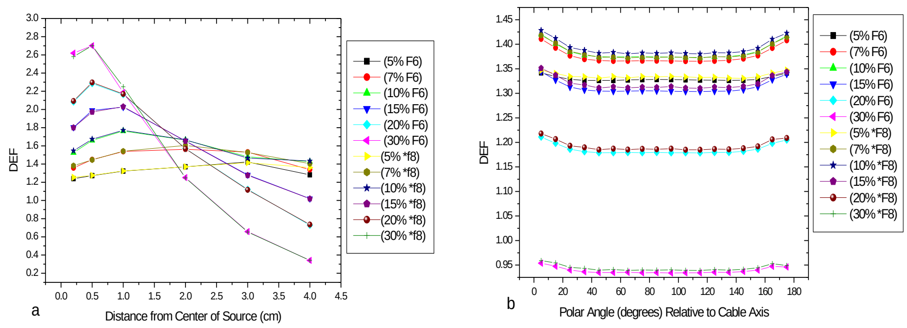


*Fig. 7. (a) Dose enhancements factor (DEF) for radius dose distribution in breast phantom. Result of F6 tally and *F8 tally compared for several concentrations of AuNPs (5, 7,10,15,20 and 30%). (b) Dose enhancements factor (DEF) for angular dose distribution in breast phantom. Result of F6 tally and *F8 tally compared for several concentrations of AuNPs (5, 7, 10, 15, 20, and 30%).*

4. Conclusions

This work simulates a satisfactory condition using the Ir-192 geometry. Gold nanoparticles enhanced radiation therapy and the effect of nanoparticles was investigated in dose parameters associated with treating breast cancer. The results of the study indicated that MCNP5 code is a powerful method for obtaining dosimetry parameters and for verifying the measurement data brachytherapy. The increasing of the concentration of AuNPs up to 100 mg/ml increased DEF. Radiation therapy has unique features that are rarely deformed.

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