Size dependence of GNPs dose enhancement effects in cancer treatment –Geant4 and MCNP code

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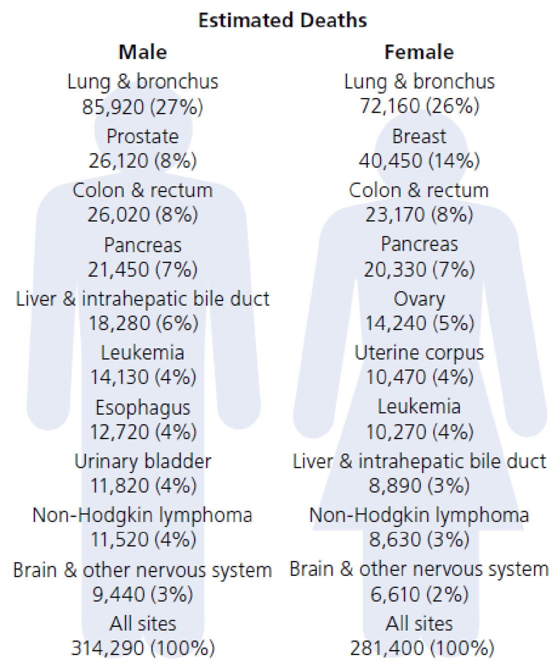
Cancer

Cancer is a disease characterized by an uncontrolled growth and spread of abnormal cells. Cancer may be caused by external factors such as tobacco or alcohol use and an unhealthy diet, Also it can be caused by internal factors such as inherited genetic anomalies. Worldwide, one in seven deaths is due to cancer; it is the second leading cause of mortality in developed countries and the third cause of death in developing countries.



Leading Sites of New Cancer Deaths – 2016 Estimates

TREAETMENT

Treatments include radiotherapy, surgery, chemotherapy, hormone therapy, immune therapy and targeted therapy. Radiotherapy is one the main methods of cancer treatment. Almost half of the patients diagnosed with cancer undergo radiotherapy during their treatment period. In spite of modern radiotherapy techniques to deliver a homogeneous therapeutic dose throughout the target tumor volume, one of the main challenges faced by radiotherapy is to deliver a lethal dose to the tumor volume while minimizing the damage to surrounding healthy tissues.

RADIOSENSITIZER

Radiosensitization is a technique developed to radiosensitize the tumor region specifically to radiation effects. A radiosensitizer is an agent used to make tumor cells more sensitive to radiotherapy. An ideal radiosensitizing agent must be tumor cell specific, persistent during treatment and biocompatible. Among other kinds of radiosensitizing agents, high atomic number (high-Z) radiosensitizers benefit from the increased photoelectric cross-section resulting in the production of low energy auger and photoelectrons which causes a more localized dose enhancement.

GOLD NANOPARTICLES

In recent years, GNPs have been used widely as radiosensitizers due to their unique properties such as high atomic number, biocompatibility, inertness and the possibility of surface modification and conjugation with tumor targeting moieties. In vivo studies have shown that GNPs accumulate preferentially in the tumor region relying on the enhanced permeation and retention effect of the leaky tumor vasculature. Since gold has a higher mass energy absorption coefficient compared to soft tissue, it absorbs substantially more energy per unit mass than soft tissue which increases the local dose absorption when only a small amount of GNPs are delivered in tumor region. In a Monte Carlo study it was reported that GNP size is not an important factor while another study by Geant code showed that GNPs with larger diameters contribute more dose to the surrounding tissue. Due to these contradictions and importance of factors affecting radiosensitization including GNPs size and concentration, this study was conducted to further elucidate the mentioned obscurity; thus the aim of this study was to report the optimum size and concentration of GNPs to deliver the highest dose in the tumor.

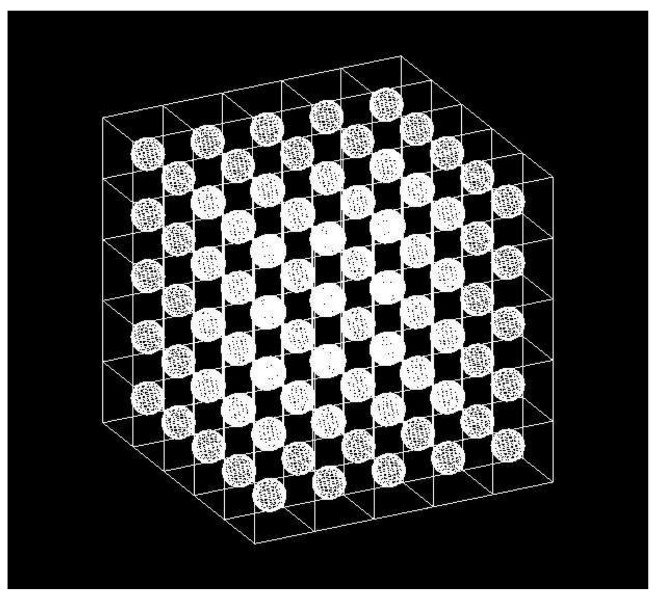
MONTE CARLO STUDY (MCNP and Geant4)

This work was carried out with MCNP and Geant4 codes. The 10x10x10 cm3 cubic water phantom and a tumor region with a size of 1x1x1 cm3 were simulated. Factors such as different concentrations and GNP sizes were implemented into the simulation, so as to obtain the optimum results, specifying the maximum absorbed dose within the tumor while sparing healthy tissue. In a certain concentration, different sizes of GNPs including 30, 50, 70 and 100 nm were defined within the tumor and the absorbed dose by the GNPs-loaded tumor were calculated for different sizes. Similarly, the absorbed dose was calculated for different concentrations of 7, 10, 18 and 30 (mg Au/ gram of tumor) in a certain size of GNPs. The absorbed dose in the presence of GNPs with the aforementioned sizes and concentrations was estimated for different concentrations and sizes of GNPs.

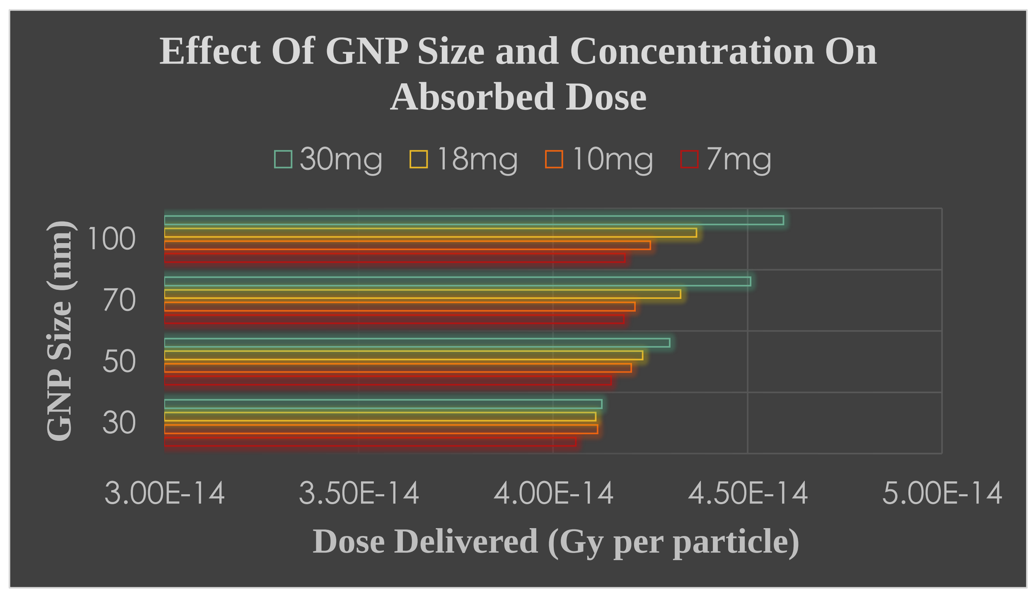
RESULTS

The calculations were performed for different GNPs sizes and concentrations and a comparison is made between them for both MCNP and Geant4 codes. In a certain diameter of GNPs the higher concentration made more increase in absorbed dose by the tumor. In a certain concentration, higher size of GNPs made higher absorbed dose by the tumor. Although simulations with Geant4 code much better showed the importance of GNPs size, which can be attributed to the comprehensive cross sections and database libraries regarding the enhanced photoelectric effect in the presence of GNPs.

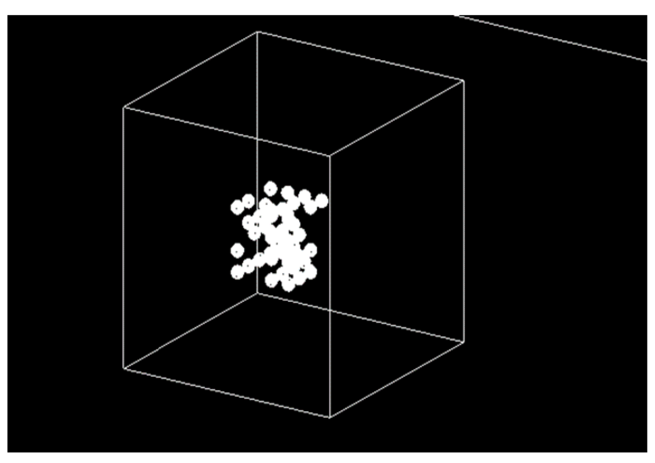
SIMULATION



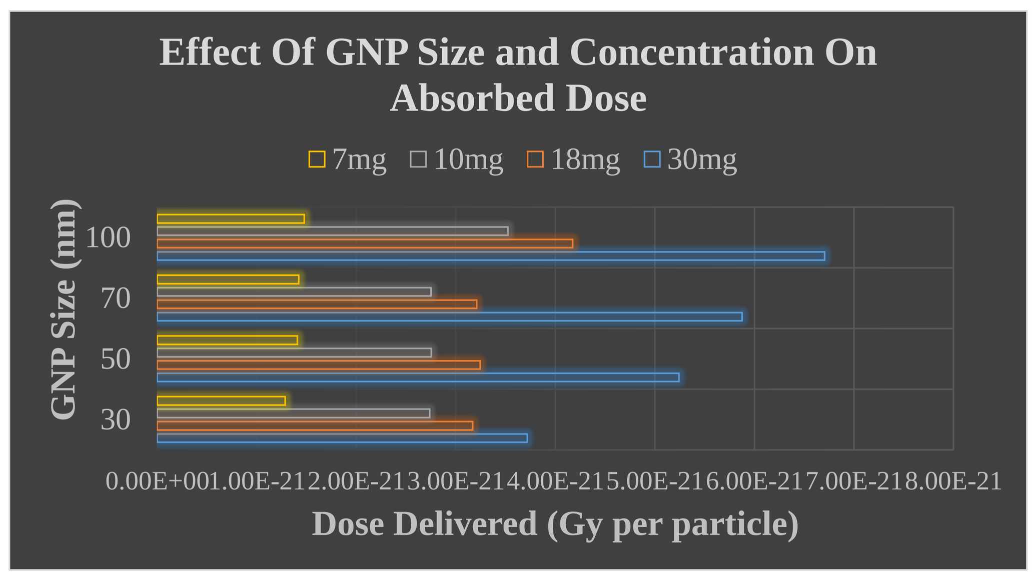
Schematic representation of cubic tumor loaded with GNPs (MCNP code)



Effect of GNPs size and concentration on absorbed dose (Simulations done with MCNP code)



GNPs accumulated in a volume inside tumor (Geant4 code)



Effect of GNPs size and concentration on absorbed dose (Simulations done with Geant4 code)

CONCLUSION

Size and Concentration are two key factors affecting GNPs radiosensitization. Based on the current study with two Monte Carlo codes (MCNP and Geant4) it is shown that in a certain concentration, GNPs with higher dimensions contribute more dose to the tumor area; while in a fix size, higher concentration of GNPs in the tumor region causes a remarkable increase in the dose delivered. The difference between two Monte Carlo codes becomes evident especially in determining the optimum GNP size, where the effect of higher GNP diameters can be better observed with Geant4. Given the fact that therapeutic applications of GNPs in acquiring the proper dose enhancement have demanded much attention in recent years, defining the proper size and concentration would be considered extremely vital for pre-treatment plans.

SUPPORTS

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