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Fluka Monte Carlo for Validating Low-Energy Neutron Capture Therapy Tissue with Boron and Gadolinium

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ABSTRACT

Research Gap: Neutron Capture Therapy (NCT) represents a cutting-edge neutron-therapy technique for tumor treatment, but there is a gap in understanding the optimization of neutron dose deposition in tumor cells, particularly in tissues enriched with boron and gadolinium. Research Objective: This study aims to evaluate the dose deposited by thermal neutrons in adipose tissues enriched with boron and gadolinium, utilizing the Monte Carlo Fluka code. Research Methodology: The research employs Fluka, an open source Monte Carlo simulations to assess thermal neutron dose deposition in tissues. The focus is on boron and gadolinium-enriched tissues to understand their impact on neutron dose optimization. Results: Findings affirm the advantages of boron and gadolinium in enhancing neutron dose deposition within tissues. Fluka simulations demonstrate the strategic utilization of neutron properties, showcasing the potential for improved tumor management. The study highlights gadolinium's attractiveness, suggesting its promising application in clinical settings.

INTRODUCTION

Neutron, which was discovered in 1932, was introduced into the treatment of cancers soon after its discovery. Known for its high biological effects, neutron therapy has been proven to be very effective in the treatment of antibiotic-resistant tumors, particularly the treatment of salivary gland tumors and many others. The neutrons used are obtained by irradiation of a dense target by a proton beam or by nuclear power. The emitted neutrons have an energy between a few electronvolts (eV) and several Mega electronvolts (MeV), allowing them to be classified into relativistic neutrons, having an energy E_n > 20 MeV, fast neutrons with 10 keV less than E_n and E_n less than or equal to 20 MeV, thermal and epithermal neutrons that have an average energy more than 10 KeV. The beginning of this therapy marked for a long time by the use fast and relativistic neutrons from certain centers. Over the past few decades, this technique for treating tumors is experiencing a rebound with the use of slow or thermal neutrons whose interaction with certain nuclides, such as boron (B) and gadolinium (Gd), will channel the neutron dose deposit into tumor cells and thus exploit the relative favorable biological effectiveness of neutrons [1]. This is known under the term neutron capture therapy (NCT), and will be the subject of this study. The Monte Carlo code Fluka was used to check the dose deposition of neutrons in the tumor cells enriched in boron and gadolinium atom.

METHODOLOGY

NCT consists of introducing nuclides within the tumor cell range comprising an atomic nucleus of ^{10}B and ^{157}Gd. These nuclides have a very large thermal neutron capture cross section, which will cause either a fragmentation of the nucleus, i.e. the emission of numerous Auger electrons or conversions (low-energy electron) which will create a very strong local dose deposit. The thermal neutrons used come from the impact of proton beams with energies between 2 and 30 MeV on a

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target, such as solid and liquid beryllium and lithium, shaped by an accelerator. Figure 1 represent of energy profile of the epithermal neutron beam, defined by the moderator [2].

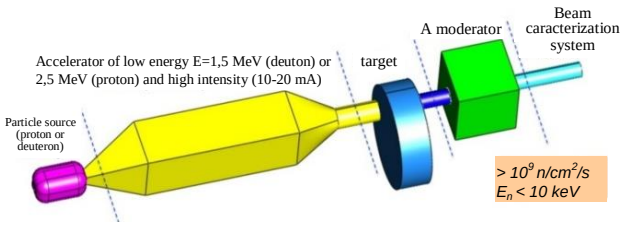

Fig. 1 Energy profile of the epithermal neutron beam, defined by the moderator [3].

The energy sought is between 0.1 and 10 KeV. This treatment modality is already available in several countries around the world, namely: Budker Institute, Russia [4]; IPPE-Obninsk, Russia [5], Birmingham University, UK [6]; KURRI, Japan [7]; Legnaro INFN, Italy [8]; Tsukuba University, Japan [9]; and CNEA [10]. The neutrons are directed towards cancer cells enriched with boron or gadolinium, and give a localized dose deposition by various reactions. In this study, we used the Fluka Monte Carlo code to evaluate and compare the dose deposited by thermal neutrons in a cancer cell, both enriched and not enriched with boron and gadolinium. The Monte Carlo Fluka code was used to model a simple geometry formed by two spheres. The first sphere has a central coordinate at (0.0.0) and a radius of 100 cm. The second sphere has the same coordinates at (0.0.0) with a radius of 10 cm. Between these two spheres, there is an adipose tissue in a parallelepiped shape with the following coordinate: X_{min}=-2.5 cm; X_{max}=2.5 cm; Y_{min}=-2.5cm; Y_{max}=2.5 cm; Z_{min}=0; and Z_{max}=5 cm. This tissue was irradiated by a 10 keV neutron beam emitted at the point (0.0.0) in the direction of the Z-axis. The objective of the study being to show the impact of boron and gadolinium on the dose deposition thermal neutrons in the therapeutic context of oncology. Initially, we irradiated normal adipose tissue, then we enriched the tissue with boron and gadolinium at various contents.

The region bounded by the two spheres is called blackhole, which aims to terminate any particle entering the absorption zone. A second region is defined between our adipose tissue and the second sphere called vacuum from which neutron beams towards the cell to be irradiated. The results obtained from the irradiation of adipose tissue with a thermal neutron beam of intensity 10 keV are shown in Fig. 3. The dose deposition measured using the Monte code Carlo shows a classic deposition as in the case of irradiation of tissues by photons and fast neutrons. It is marked by a more or less high entry dose. The maximum dose is deposited almost at the entrance to the adipose tissue followed by an exponential decrease over the rest of the course. The total dose thus released by thermal neutrons appears low given the neutron beam energy. Figure 2 represents our study geometry prepared using the Fluka code [11].

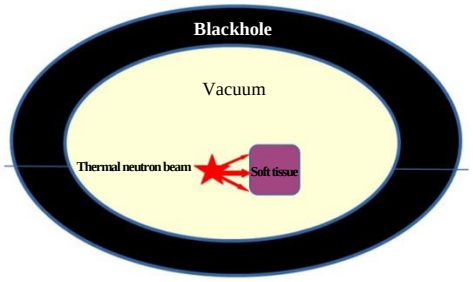

Fig. **2** Geometry of study modelled with Flair.

RESULTS AND DISCUSSION

The results obtained from adipose tissue irradiation with a thermal neutron beam with intensity of 10 keV are shown in Fig. 3. Dose deposition measured using Monte Carlo shows a classic deposition as in the case of irradiation of tissues by photons and fast neutrons. It is marked by a more or less high entry dose. The maximum dose is deposited almost at the surface to the adipose tissue, followed by an exponential decrease over the rest of the cell. The total dose exposed by the thermal neutrons appears to be low given the neutron beam energy.

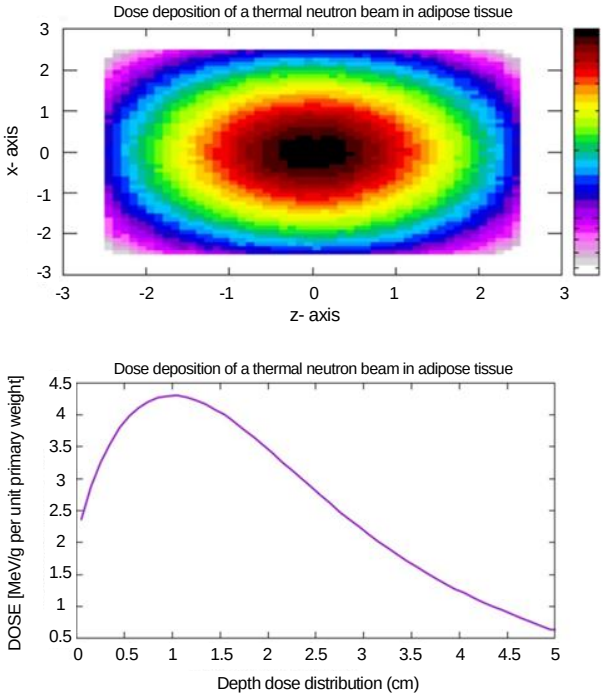

Fig. 3. Dose deposition of a thermal neutron beam in adipose tissue of (5x5x5) cm^3.

Irradiation of the same cells under the same conditions, but enriched with boron gives the results as shown in Fig. 4. On this dose deposition curve we observe a strong increase in dose profile deposited in the boron-enriched adipose tissues. This dose deposit is comparable to that of the International Atomic Energy Agency standard [12]. The presence of boron in adipose tissue results in a high concentration of localized dose deposition compared to boron-free tissues. This dose increase would be a consequence of a secondary reaction between neutrons and boron. Boron has a very large neutron capture cross section. The neutron capture by ^{10}B will transmute it into an unstable nucleus of ^{11}B. This instability would thus cause the fragmentation of ^{11}B responsible for the production of numerous auger electrons [3] and short range heavy particles such as helium (^{4}He), lithium (^{7}Li) and gamma rays [13] and [7]. All of these secondary particles resulting from neutron capture would therefore be responsible for this strong localized dose deposition.

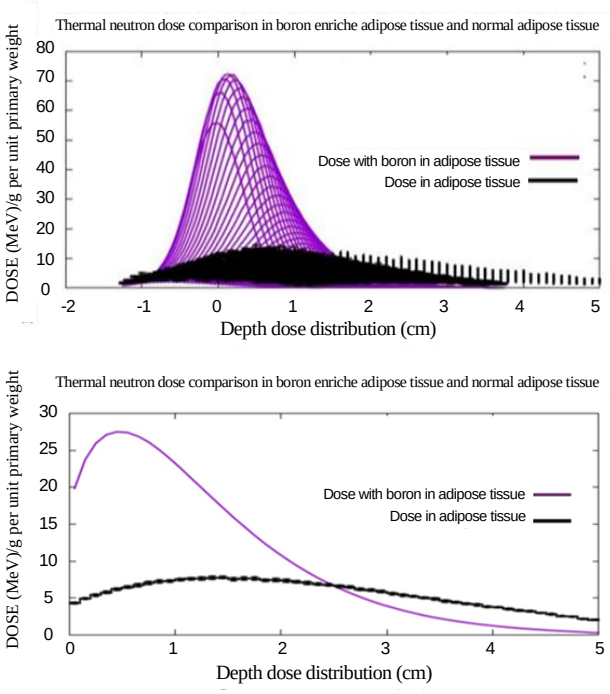

Fig. 4. Dose deposited by a thermal neutron beam in adipose tissue enriched in boron and boron-free adipose tissue.

The enrichment of adipose tissues with gadolinium gives the dose deposition as shown in Fig. 5. Dose deposited by thermal neutrons in the presence of gadolinium is similar to that observed in the case of boron. There is a significant increase in the dose administered to the tumor. This increase is the result of secondary reactions resulting from neutron capture by the gadolinium. Indeed, neutron capture would form an unstable nucleus of ^{158}Gd that by disintegration causes the emission of gamma rays, X-rays, conversion electrons, and auger electrons.

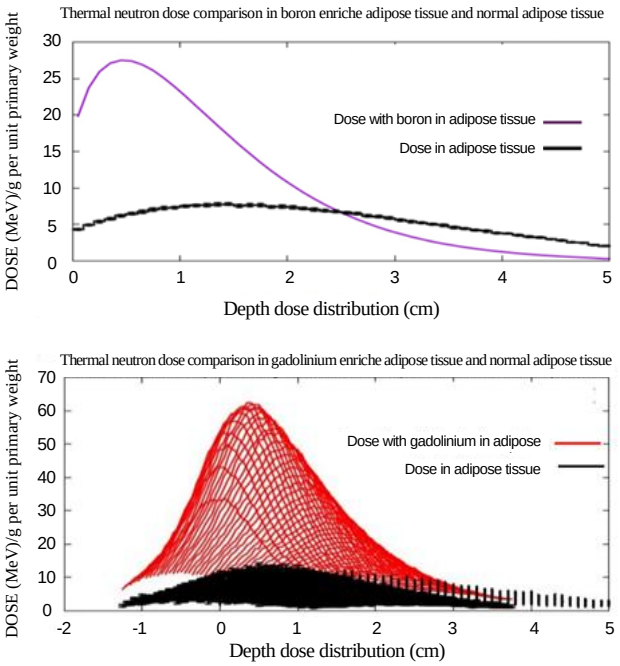

Fig. 5. Dose deposited by a thermal neutron beam in adipose tissue enriched in gadolinium and adipose tissue without gadolinium.

Figure 6 is the comparison of thermal neutron dose deposition in tissue enriched with boron and gadolinium. The results obtained by simulation show that in the presence of boron in the cells, the dose given by thermal neutrons is greater, more localized, and less diffuse than that of gadolinium. The difference in dose deposition observed in the two cases is the result of particles emitted during the reaction of the decay of the unstable nucleus. The ^{11}B released heavy charged particles with a short range, i.e., alpha particles, helium lithium, and gamma rays, unlike ^{158}Gd which only emitted gamma rays, X-rays, and electrons. Secondary gadolinium reaction by products have low linear energy transfer (LET) and induce modest radiobiological damage, with the exception of high LET auger electrons that induce double-strand DNA break. However, compared to boron, the utilization of gadolinium is easier because of its natural abundance of 15.7 % and its efficiency in terms of neutron capture. In addition to these advantages, gadolinium is an agent of contrast used in magnetic resonance imaging (MRI) which accumulates in the tumors and not in the surrounding healthy tissues. Therefore, it is easier to introduce into the tumor tissues. Figure 7 illustrates the dose deposition of a thermal neutron beam in adipose tissue enriched in boron. The tissue has been enriched in various proportions, from 0.1 and 0.005 ppm. The results obtained with the Fluka code show a variation in the dose deposition in adipose tissue. The results show an increase in dose deposition depending on the boron content. The higher the boron content, the greater the dose deposited by thermal neutrons.

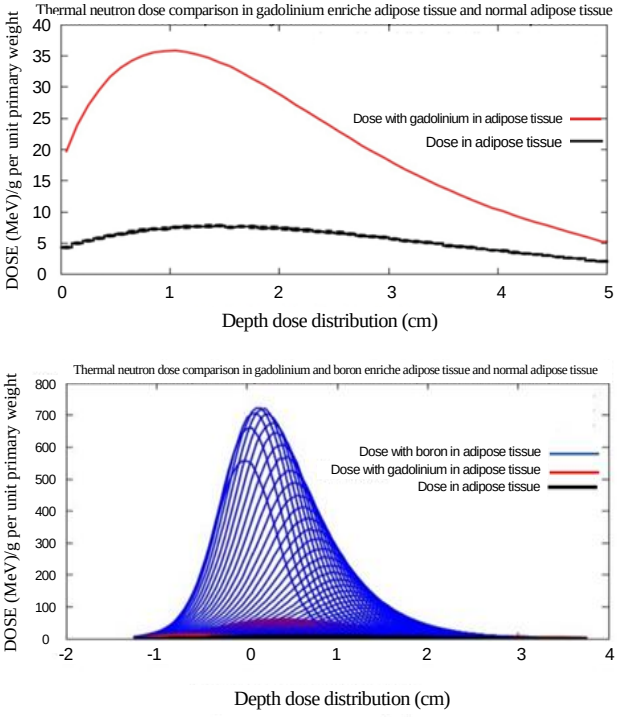

Fig. 6 Comparison of dose deposited by a thermal neutron beam in tissue adipose enriched with gadolinium and boron.

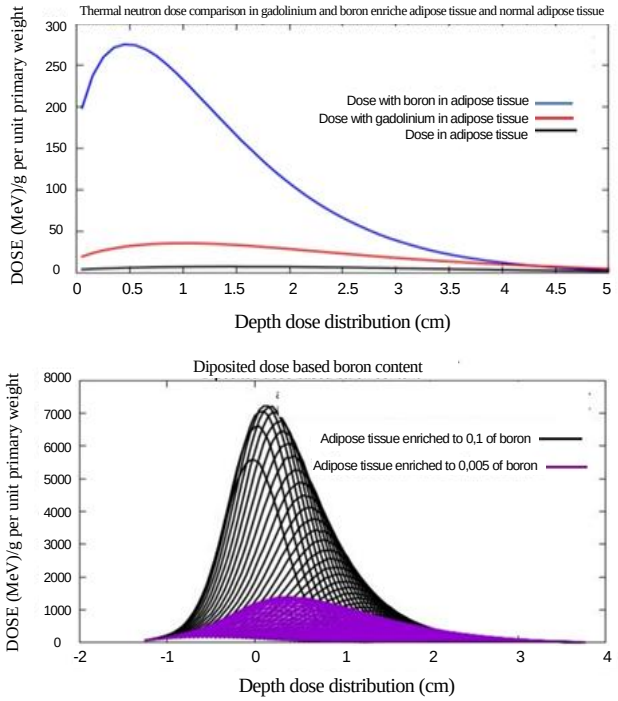

Fig. 7. Comparison of dose deposited by a thermal neutron beam in tissue adipose enriched with boron and variable content.

The variation in the gadolinium content is the same as in the case of boron. The results presented in Fig. 8 are obtained with a gadolinium content of 0.1 and 0.005 ppm. However, the results obtained in both cases show a difference. With boron, the drop in content leads to a clear and very significant drop in the dose deposited (nearly 1/5 of a dose). Unlike gadolinium, the energy lost by reducing the gadolinium content is not too large.

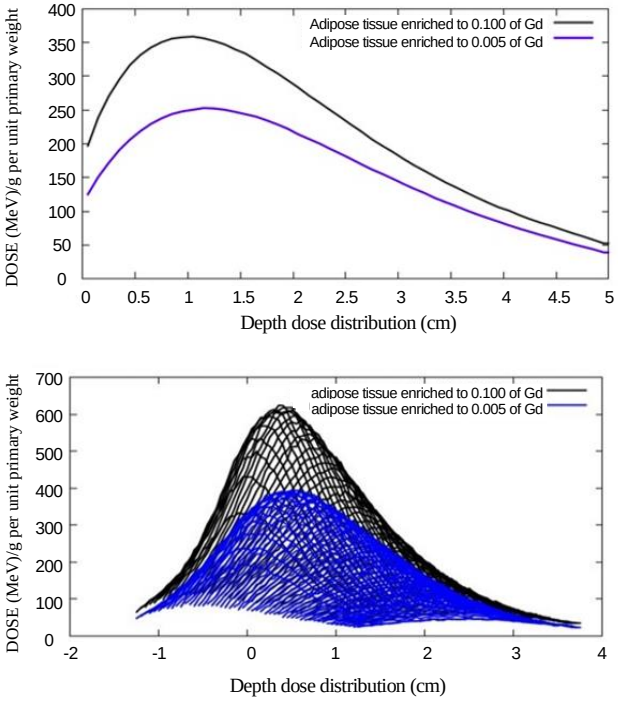

Fig. 8. Comparison of dose deposited by a thermal neutron beam in tissue adipose enriched with gadolinium variable content.

The results obtained from irradiating adipose tissue with a thermal neutron beam of 10 keV intensity, as shown in Fig. 3, reveal a dose distribution that has captured our attention. Contrary to what might have been anticipated, the dose distribution closely resembles that observed when tissues are irradiated with photons and fast neutrons. It exhibits a peak dose more or less pronounced at the tissue entry point, followed by an exponential decrease as neutrons penetrate deeper. The total dose delivered by thermal neutrons appears relatively low given the energy of the neutron beam, suggesting that improvements are needed to enhance the effectiveness of this irradiation method.

However, the results of irradiating the same cells under similar conditions but enriched with boron (as shown in Fig. 4) display a notable shift. A significant increase in the dose distribution is observed in boron-enriched adipose tissues, which is comparable to the standards set by the International Atomic Energy Agency. This substantial dose increase is attributed to a secondary reaction between neutrons and boron, leading to effective neutron capture by ^{10}B. This capture results in the formation of an unstable nucleus of ^{11}B, triggering the fragmentation of ^{11}B and the release of numerous Auger electrons, heavy particles with short range such as helium (^{4}He), lithium (^{7}Li), and gamma rays. These secondary particles resulting from neutron capture are responsible for the significant localized dose increase, which may offer an advantage in specifically targeting tumors. Regarding the

enrichment of adipose tissues with gadolinium (depicted in Fig. 5), the results exhibit a dose distribution similar to that obtained with boron.

This is due to the secondary reactions resulting from neutron capture by gadolinium, which produces an unstable nucleus of ^{158}Gd. The subsequent decay of ^{158}Gd generates gamma rays, X-rays, conversion electrons, and Auger electrons, contributing to a significant increase in the dose delivered to the tumor. The fact that gadolinium is readily available in natural abundance, efficient in terms of neutron capture, and commonly used as a contrast agent in MRI to specifically target tumors makes it a promising choice for targeted irradiation.

The direct comparison between boron and gadolinium (as presented in Fig. 6) reveals that the presence of boron in cells induces a higher, more localized, and less diffuse dose than that of gadolinium.

This difference is attributed to the particles emitted during the decay of unstable nuclei, with boron emitting heavy particles with a short range, while gadolinium primarily emits gamma rays, X-rays, and low-energy electrons. This distinction is crucial to consider when designing treatment strategies, as it can influence the biological effects on target and surrounding tissues. The FLUKA code is a program that can also handle the dose deposition profile of carbon and helium ions in a water phantom for research purposes [14].

Finally, the analysis of variations in the concentration of boron and gadolinium in adipose tissues (as presented in Figs. 7 and 8) demonstrates that the dose delivered by thermal neutrons increases proportionally with the concentration of these elements. However, it is crucial to note that reducing the boron concentration leads to a significant reduction in the delivered dose, while reducing the gadolinium concentration has a less pronounced impact. These observations suggest that adjusting the concentration of boron or gadolinium may be a means of modulating the delivered dose to meet specific treatment needs.

CONCLUSION

The results obtained by Fluka simulation of thermal neutron dose deposition in tissues in the presence of boron and gadolinium shows that the advantages of neutrons such as LET and EBR of these neutral particles can be used differently to improve the management of tumor. However, the case of gadolinium seems more attractive given that it is already used in magnetic resonance imaging to increase the natural contrast of tumors.

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AUTHOR CONTRIBUTION

T. E. Bakolia, A. Didi and R. Sebihi A. equally contributed as the main contributors of this paper. All authors read and approved the final version of the paper.

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