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Evaluating Epithermal Neutron Energy Levels for Optimized Neutron Capture in Cancer Therapy

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ABSTRACT

Neutron flux is a measure of neutron radiation intensity and a crucial parameter, as it determines the availability of neutrons required to initiate the boron-neutron capture reaction (BNCT). Epithermal neutron energies, ranging from 1 eV to 10 keV, are recommended for BNCT. However, at the upper limit of this range, the neutron flux decreases, which is undesirable for treatment. In this research, neutron flux in soft tissue was evaluated using PHITS (a Monte Carlo simulation) to optimize neutron capture. The phantom consists of soft tissue with a 30-ppm concentration of Boron-10 and is irradiated with neutron energies of 5 keV, 6 keV, 7 keV, and 8 keV to minimize the absorbed dose to the skin while maximizing the dose at greater depths within the phantom. The simulation demonstrates that neutron interactions occur throughout the target, from the surface to its depth, with substantial neutron capture within the target volume. Among the four tested energies, 7 keV yields the highest neutron flux, making it the most effective for generating thermal neutrons. This aligns well with the goal of BNCT, which aims to facilitate efficient neutron capture by Boron-10 while minimizing the production of fast neutrons and unwanted gamma radiation.

Keywords: *Boron Neutron Capture Therapy, Epithermal Neutron, Monte Carlo simulation, Neutron Flux, PHITS.*

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1 Introduction

Neutron flux is a measurable indicator of neutron radiation intensity, defined by the rate of neutron flow in Boron Neutron Capture Therapy (BNCT). BNCT is an advanced form of particle therapy that operates at the cellular level, targeting and treating cancerous cells with high precision (Mai et al. 2023, Kavitaa et al. 2016). The process involves incorporating Boron-10 atoms into tumor cells using boron delivery agents. The most accessible tumor area is then exposed to a neutron field, initiating the Boron-Neutron Capture Reaction (BNCR). In BNCR, a Boron-10 atom captures a thermal neutron, forming radioactive Boron-11, which subsequently fragments into an alpha particle (^{4}He) and a Lithium-7 (^{7}Li) nucleus, releasing a significant amount of energy that destroys the tumor cells.

Effective neutron capture depends on the boron uptake within the target volume and the neutron flux. Since the probability of neutron capture by Boron-10 increases exponentially at lower neutron energies, the presence of thermal neutrons at the tumor site is crucial to maximizing neutron capture and improving treatment efficacy (Marine et al. 2023). Additionally, therapy effectiveness is directly influenced by neutron flux—the higher the neutron flux, the greater the neutron capture, leading to optimized tumor treatment (Bisceglie et al. 1999).

Neutron flux is a crucial parameter as it determines the number of neutrons available in a given region for the Boron-Neutron Capture Reaction (BNCR). In BNCT applications, since neutrons are thermalized and absorbed at shallow depths in tissues, incident neutrons with energies

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higher than thermal levels are required for the treatment of deep-seated tumors (Gayratulla et al. 2024; Marine et al. 2023).

Epithermal neutrons, with an energy range of 0.5 eV to 10 keV, play a vital role in BNCT. They can penetrate deep into biological tissues, gradually losing energy and thermalizing near the tumor site. This process enables precise targeting of cancer cells while minimizing unnecessary radiation exposure to surrounding healthy tissues, thereby enhancing the safety and efficacy of the treatment (Bavarnegin et al. 2017, Ian et al. 2021).

This study aims to determine the relationship between neutron flux and the energy of the incident neutron beam. By evaluating and comparing neutron flux at different epithermal neutron energy levels, the study seeks to identify the optimal neutron energy for maximizing neutron capture within the target volume. Ultimately, the research focuses on enhancing and optimizing neutron capture, which plays a critical role in BNCT.

2 Materials and Methods

The [T-track] tally in PHITS was used to track and measure neutron flux within the phantom region. This tally calculates flux based on the track length of neutrons within a specified region. As neutrons pass through, the tally records their track length and normalizes it by the region's volume and the total number of source particles. PHITS then provides detailed flux data for each mesh within the region, enabling precise analysis.

According to Marziyeh et al. (2016), optimizing neutron capture in tissue at a depth of 6 cm to 8 cm requires balancing therapeutic gain with the constraint of keeping the surface dose within permissible limits to determine the optimal neutron beam energy (Bisceglie et al. 2000, Marziyeh et al. 2016, Herve et al. 2021). The imposed dose limit restricts neutron energies to a range of 1 eV to less than 8 keV.

Thus, the optimal neutron beam energy should fall within this range to maximize therapeutic gain while ensuring the surface dose remains within safe limits. To examine the effects of different neutron energies within this range, the following neutron energies were selected: 5 keV, 6 keV, 7 keV, and 8 keV, based on the study by Marziyeh et al. (2016).

3 Results and Discussions

The neutron flux values after irradiation with four different epithermal neutron energy levels are shown in Table 3. At 5 keV, 6 keV, and 7 keV, the neutron flux originates from the surface and penetrates into the phantom, as illustrated in Figure 2. However, when the neutron energy is set to 8 keV, the neutron flux suddenly decreases.

It is observed that at all energy levels, neutron flux penetrates from the surface throughout the entire volume of the target phantom, as shown in Figure 2. This indicates that neutron irradiation effectively covers the entire target volume, ensuring uniform exposure of the boron-containing tissue.

Figure 2 demonstrates the suitability of the epithermal neutron energy range from 5 keV to just below 7 keV, based on its penetration and thermalization properties. Neutrons within this energy range travel deeper into tissues before slowing down and thermalizing at an optimal depth, enhancing neutron flux within the target phantom (Kabirian et al. 2014).

For neutron energies beyond 8 keV, neutron toxicity gradually increases due to thermalization in tissues and energy transfer via elastic scattering on hydrogen nuclei, which contributes to a secondary dose to healthy tissues (Marine et al. 2021, Satoshi et al. 2021). This finding aligns with the studies of Marine et al. (2021) and Kabirian et al. (2014), which investigated neutron irradiation of a Snyder head phantom using neutron energies ranging from 10 eV to 10 keV. Their results indicate that an optimal balance between penetration and therapeutic effect is achieved when neutron energy remains below 10 keV.

Figure 3 illustrates the distribution of neutron flux as a function of depth within the phantom. The highest neutron flux is observed at a depth of 2–4 cm, which is attributed to the thermalization of epithermal neutrons as they lose energy through scattering interactions with the material.

When neutrons penetrate the body, they interact with tissues, particularly hydrogen, oxygen, nitrogen, and boron, causing a gradual loss of energy. This attenuation process results in a decrease in neutron flux with increasing depth, meaning that fewer neutrons reach deeper tissues compared to shallower ones (Kiragga & Brazovskiy 2024). However, the rate at which neutron flux decreases with depth depends on factors such as

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Table 1. Chemical composition of ICRU soft tissue and Borono-phenylalanine in mass fraction per gram.

	C	H	N	O	B
ICRU soft tissue	0.101	0.111	0.026	0.762	-
Borono-phenylalanine	0.517	0.057	0.067	0.306	0.051

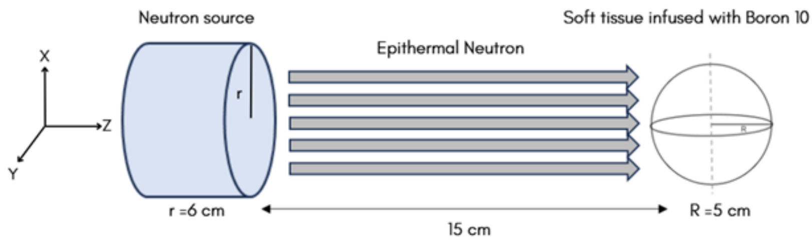

Figure 1. Schematic diagram of simulation set-up:10B infused spherical phantom and mono-energetic neutron source

Table 2. Neutron flux in soft tissue of different neutron energies.

Energy	Fluence (n cm-2 per source)
5 keV	3.2632×10^{-3}
6 keV	3.5649×10^{-3}
7 keV	3.9624×10^{-3}
8 keV	3.3652×10^{-3}

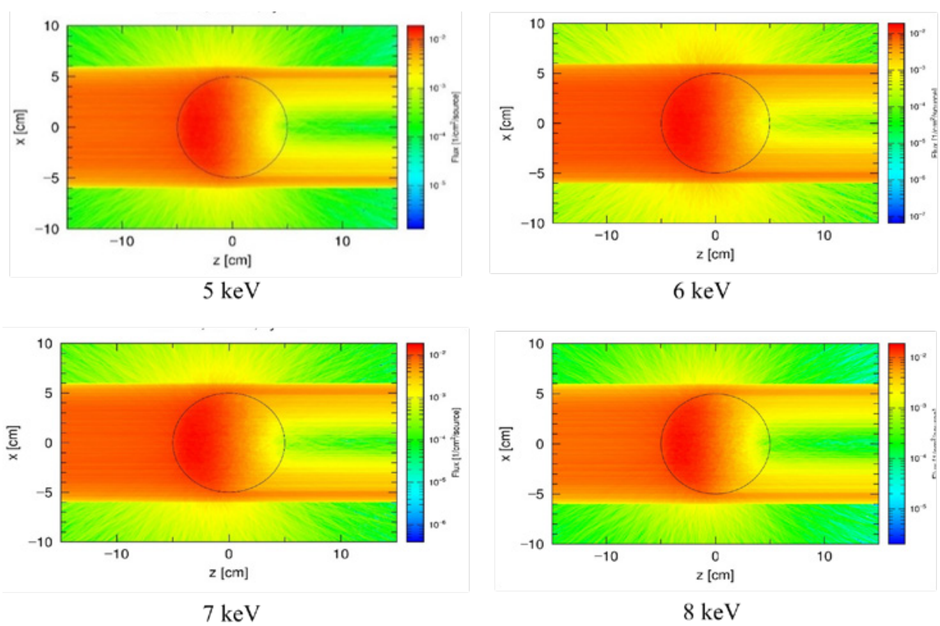

Figure 2. Neutron flux track of 5 keV, 6 keV, 7 keV and 8 keV of neutron energy.

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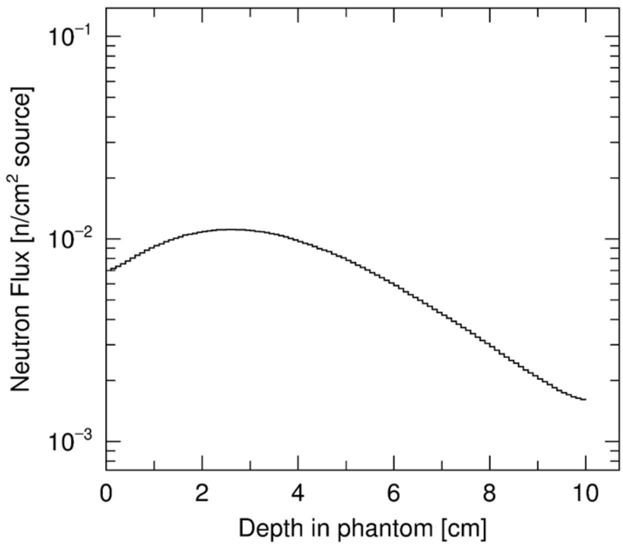

Figure 3. Neutron flux at the depth of the phantom

initial neutron energy, tissue composition, and the presence of neutron absorbers like boron, which plays a crucial role in BNCT (El Shazly et al. 2013, Kry et al. 2009).

For shallow tumors, lower-energy neutrons are preferred, as higher-energy neutrons may penetrate too deeply, reducing their effectiveness in treating surface layers. In contrast, deeper tumors require higher-energy neutrons to ensure sufficient flux at greater depths (Satoshi et al. 2021). The ideal neutron energy and flux for any given depth must achieve a balance between penetration and interaction with tissue, maximizing therapeutic effectiveness while minimizing damage to surrounding healthy tissue.

4 Summary and Conclusion

The simulation shows that, as the energy of neutrons increases from 5 keV to 7 keV, the neutron flux also increases. However, upon setting the energy to 8 keV, there is a noticeable decrease in neutron flux, which could consequently result in reduction of neutron capture. In conclusion, it is suggested that the ideal epithermal neutron energy for effectively treating deep-seated tumors lies within the energy of 7 keV since it exhibits the highest neutron flux in the range of 5 keV to 7 keV. This energy shows significance in achieving optimize neutron capture within the target volume and minimizing damage to skin and healthy cells.

To refine this initial assessment, further investigation is recommended. Researchers should employ additional figures of merit, such as advantage depth and therapeutic gain, to comprehensively evaluate the treatment's efficacy. By systematically analyzing various factors that influence therapeutic outcomes, scientists can enhance the precision of neutron energy selection, ultimately improving treatment effectiveness and patient safety.

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6 Declaration of Generative AI and AI-Assisted Technologies in the Writing Process

The authors declare that generative artificial intelligence (AI) and/or AI-assisted technologies were used during the preparation of this manuscript solely to assist with grammar improvement and language editing. All content was critically reviewed and revised by the authors, who take full responsibility for the accuracy, originality, and integrity of the work. No generative AI tool was used to create scientific content, data, results, interpretations, or conclusions.

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