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Beam Neutron Optimization for Boron Neutron Capture Therapy (BNCT) facility

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ABSTRACT

This work aims to focus on beam shaping assembly (BSA)'s design and optimization for boron neutron capture therapy (BNCT) facility based on a proton accelerator. The BSA optimization is simulated by MCNP Monte Carlo code. The output neutron beam characteristics are compared to that recommended by the international atomic energy agency (IAEA).

The dose components that contributed to the absorbed dose are simulated using MCNP code based on the neutron interactions mode and boron concentration values taking into account the relative biological effectiveness (RBE) factors. The total effective dose in brain tumor and healthy tissues for different values of ^{10}B concentration are compered to calculate the therapeutic gain (TG). The results indicated that the healthy tissues at the skin surface, skull and beyond the tumor receive the lowest radiation dose. TG may be used as a fast evaluation of the impact of varying ^{10}B concentrations on the therapeutic outcome, and treatment optimization.

1- INTRODUCTION

The boron neutron capture therapy (BNCT) is an efficient form of radiotherapy that allows for higher radiation doses to the tumor while avoiding most healthy tissues. This procedure is a treatment of malignant tumor such as head, neck and brain cancers.

Overall, BNCT is a binary system that takes advantage of boron-10 nuclear reaction when absorbing a thermal neutron, cancer-specific boron delivery agents and boron's special neutron capture characteristics to cause radiation damage enclosed within the cancer cell with the least amount of harmful effect to the surrounding tissues which is a the main advantage of BNCT over conventional radiotherapies [1].

The ability to selectively deliver boron to tumor cells rather than healthy cells is crucial for treatment effectiveness; in general, neutron production and irradiation process stay the most affecting parameters on treatment success. BNCT neutron beam should have high beam purity to reduce gamma ray and fast neutron contamination, and have highly beam intensity to ensure the delivery of appropriate neutron dose. Also the irradiation room is desired to be well-shielded with patient viewing, communication and control system reliability to ensure the patient receives the prescribed dose, without any unintentional exposure [2].

Since BNCT requires a neutron source, nuclear reactors, which provide readily available neutron beams, have traditionally been the preferred application for this technology [3-5]. However, the installation of a reactor in a general hospital poses significant challenges because of its enormous size and the exceptionally highly costs associated with its installation and maintenance [6-9]. Furthermore, the scheduling of treatments based on patient needs is constrained by the inherent difficulty of starting or stopping a nuclear reactor.

Nowadays, accelerator-based BNCT (AB-BNCT) research is being actively pursued as a substitute for reactor-based BNCT with its limitations. An accelerator facility is generally simpler in design and operation compared to nuclear reactors. It does not

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require the complex systems and safety measures needed to control a nuclear chain reaction, and has offer a greater advantage in terms of accident risk compared to nuclear reactors. In AB-BNCT, the neutron beam quality is an important parameter determining treatment success. It is determined by the beam shaping, the neutron energy, and the relative intensity of secondary radiation. Many researches have investigated the accelerator-based epithermal neutron sources aiming to be installed in side or near the hospital instead of a conventional reactor-based neutron source [10-11].

The major components of an AB-BNCT [1] are: (1) proton beam accelerator, (2) proton beam target, that act as the proton-to-neutron converter, (3) a beam shaping assembly (BSA), and (4) the resulting neutron beam lines that lead to instrument stations for clinical work. There is still opportunity to improve the final neutron yield by cleverly designing of BSA, composed of a moderator, reflector, gamma and neutron filters [10].

Although some previous studies [11-14] perform their designs with different ideas, not all of their results are in compliance with all IAEA' recommendations. Lee CL et. al. [11] and Suharyana et. al. [13] use single materials a moderator like aluminum fluoride while Jacob et. al. [12] and R. Avagyan et. al. [14] employed combinations of multiple materials as a moderate. The total volume of BSA design plays an important role in applicability of implementation of the attached treatment unit. Some various design approaches for BSA [12-16] are ranged in BSA lengths are between 52 to 109 cm, the later which may be considered as in large size.

The aim of this study is to design a suitable neutron beam for AB-BNCT system, both in terms of energy and flux, using BSA based on the recommended values of the International Atomic Energy Agency (IAEA), using Monte Carlo simulation in order to facilitate that system's application in medical centers. A simulation of the dose components that contributed to the absorbed dose based on the neutron interactions modes and values of boron-10 concentration values is done. The total effective dose in brain tumor and healthy tissues is calculated taking into account the RBE factors, and different values of ^{10}B concentration to determine the therapeutic gain (TG).

2- THEORETICAL ASPECTS

2-1 BNCT Facility

Boron compounds are injected into tumor cells, followed by thermal neutron irradiation, inducing the ^{10}B (n, α) ^{7}Li nuclear reaction

$$^{10}B + n_{th} \rightarrow ^{11}B \rightarrow ^{7}Li\ (1.01\ MeV) + ^{4}He\ (1.78\ MeV)\ (6.3\%)$$

$$^{10}B + n_{th} \rightarrow ^{11}B \rightarrow ^{7}Li\ (0.84\ MeV) + ^{4}He\ (1.47\ MeV) + \gamma(0.48\ MeV)\ (93.7\%) \quad \textbf{(1)}$$

Both ^{7}Li nuclei and α particles deposit their energies along their very short paths, which are comparable to the size of cells. As a result, cancer cells are destroyed with high accuracy without harming healthy tissues [17, 18].

Different studies have identified the optimal boron agent drug [1, 18 - 19] with high selectivity for cancer cells. It exhibits high tumor uptake, maintains ^{10}B concentrations in cancer cells during irradiation of the neutron, rapidly clears from healthy tissues and blood after irradiation of the neutron, and has low toxicity while meeting international pharmaceutical requirements for human use. The advancement of compact accelerator-based neutron source (CANS) technology has led to a resurgence of BNCT as a viable cancer treatment. The CANS technology as BNCT potential cancer treatment is generates neutrons by bombarding a light element target, as beryllium or lithium, with low-energy protons, as in the reactions of ^{9}Be (p, n) ^{9}B and ^{7}Li (p, n) ^{7}Be [11, 18]. In general, the fast neutrons generated by this way should to be moderated by BSA to be used for BNCT treatment.

The functions of BSA are as follows: firstly slowing down fast neutrons (> 10 keV) to epithermal neutrons (0.5 eV−10 keV) or thermal neutrons (< 0.5 eV) and secondly reduce the fast neutron, thermal neutron and γ ray component as much as possible, and finally collimate neutron beam. By other meaning BSA design aids in generating thermal neutron for treating superficial lesions and epithermal neutron for treating deep ones [18].

IAEA's recommendations for BNCT neutron beam quality are outlined in IAEA-TECDOC-1223 [20]. Table 1 showcases desired values for neutron beam flux, gamma ray dose ratio, and doses of the fast neutrons for BNCT tumor treatments.

Table (1): IAEA's recommendations for BNCT neutron beam characterizations [20]

Specified BNCT Parameter	Recommended values
Epithermal neutron flux	$> 5 \times 10^8$ n/cm^{2}s
The ratio between the thermal flux to the epithermal flux	< 0.05
Gamma ray dose / epithermal neutron	1 to 13 x 10^{-13} GY cm^2/n$_{epithermal}$
Fast neutron dose / epithermal neutron	2.5 to 13 x 10^{-13} GY cm^2/n$_{epithermal}$
Current /Flux ratio	> 0.7

Beam Shape Assembly Design

BSA design is mainly focus on generating epithermal neutrons and eliminating components of fast, thermal neutrons and also gamma components. This is done to be in compatible with the recommendations of IAEA using specific materials which have essential roles in reflect moderate and filter the high energy neutrons to lower energies. The BSA material composition designed as the following:

Reflector

The reflector material is the first part in the design that should be used to reflect and redirect the scattered high energy neutrons back into the beam and used as a collimator for neutrons. Reflector materials at the firstly it should have a low absorption cross section to minimize neutron absorption and maximize reflection. Secondly, it should exhibit a high elastic scattering cross section, particularly for epithermal energies, in order to efficiently redirect the neutrons. Lastly, it should have a substantial mass number to minimize energy loss during each elastic collision. For typical epithermal BNCT systems, lead is commonly used as the BSA reflector material due to its favorable properties in fulfilling these requirements [12 -16, 21].

Moderator

The moderator materials typically a hydrogenous substance which can slows down the high-energy neutrons through elastic collisions, converting them to epithermal and thermal neutrons. It should have a high removal cross section at high neutron energies, a low scattering cross section at the epithermal energy range, minimal radioactive neutron, gamma captures and the absence of substantial gamma ray production through inelastic scattering. In order to execute the ideal moderation characteristics; some distinct materials and various combinations of them were considered such as Fluental, Al_2O_3, CF_2, MgF_2, D_2O, TiF_3, ^7LiF, BeD_2, AlF_3, BeO_2, CaF_2. [12, 17]

Neutron and gamma filters

To achieve a neutron beam characteristic that is appropriate for BNCT beam, it is necessary to incorporate filters for fast, thermal neutrons, and gamma rays. The fast neutron filter enhances the $f_{epithermal}/f_{fast}$ ratio without significantly reducing the $f_{epithermal}$ component, for instance, by utilizing materials like Nickel (Ni). For filtering thermal neutrons, materials with a highly absorption cross-section for thermal energy, like cadmium (Cd) or lithium (Li), are suitable options that do not absorb a significant portion of epithermal neutrons. Gamma ray filters are typically made from lead or bismuth. Lead (Pb) is an excellent filter for gamma rays, but it significantly diminishes the intensity of epithermal neutrons. On the other hand, bismuth (Bi) is a preferable choice for using at BNCT because it effectively attenuates photons without significantly absorbing epithermal neutrons to a large extent [22-24].

2-2 Neutron interactions and dose calculation

In BNCT, the absorbed dose in healthy tissues is influenced by neutron scattering and neutron capture reactions in the brain, the contribution of neutron scattering to the secondary dose on healthy tissues as it thermalizes through tissues. The total absorbed dose in tissue, in BNCT, can be calculated by the following equations:

$$D_T = D_B + D_n + D_p + D_\gamma \qquad \textbf{(2)}$$

Each component part of the total absorbed dose is associated with different nuclear reactions:

1. The boron dose D_B, is due to ^{10}B (n, α) ^7Li reaction.
2. The neutron dose D_N, is due to ^1H (n, n')^1H reaction.
3. The Proton dose D_P, is due to ^{14}N (n, p)^{14}C reaction.
4. The gamma dose D_γ, is due to ^1H (n, γ) ^2H reaction and the residual gamma due to ^{10}B neutron capture reaction ^{10}B (n, γ) ^7Li.

These doses are calculated based on the ionization energy released by the particles involved in the respective reactions.

The biological dose can be calculated using RBE factors involves considering the different biological effectiveness of each component. This is obtained by multiplying the values of absorbed dose component by the associated RBE weighting factor; as following [25-28]:

$$D = w_c * D_B + w_n * D_n + w_p * D_p + w_\gamma * D_\gamma \quad \textbf{(3)}$$

were: w_c, w_n, w_p, w_γ are the relative biological effectiveness weighting factor for boron, neutron, proton and gamma respectively. The research in biological dose in the BNCT community is still an active field.

3 – MATERIALS AND METHODS

3-1 Beam Shape Assembly Design

In this work neutron beam is produced from interaction of accelerated protons with 0.6 cm thick beryllium target (100% abundance of ^{9}Be) which used as the converter in accelerator – based boron neutron capture therapy (AB_BNCT) facility. The total neutron yield of the ^{9}Be (p, n) ^{9}B is 2.81×10^{14} n/sr.s.mA.Mev. The initial spectral energy distribution for the emitted neutrons as shown in figure (1) is considered from that measured by M. A. Lone et al. [29] and incorporated into code input.

The BSA design is simulated using MCNP5 code as a tool that simulates the transport probability of neutrons, photons, and electrons as well as their interactions, including fission, scattering, and absorption reaction [30]. The Fast neutrons beam generated by an accelerator-based BNCT (AB-BNCT) is transformed to a high epithermal neutron flux using the new BSA design configuration that can also reduce background radiation (thermal, fast neutron and γ -rays).

The materials configuration for BSA design is selected depending on their interaction with neutron. Different configuration designs are simulated by MCNP5 code to obtain the most suitable design to meet therapeutic requirements and verify the IAEA recommendation values as mentioned in table 1.

For the proposed BSA configuration design simulation investigates various materials for different purposes; Pb and Bi are investigated as reflector and gamma filter materials. Also, calcium fluoride (CaF_2), Magnesium Fluoride (MgF_2), aluminum (Al), aluminum oxide (Al_2O_3), heavy water (D_2O) and lithium fluoride (LiF) are studied as moderator materials while Cd and Ni are examined as neutron filter materials. These materials are assessed through numerous simulations with varying thicknesses and configurations to optimize the design of BSA.

3-2 Head model and dose calculation

The head model is performed based on spherical cancer tumor with 4.1 cm radius existing in the front center of the brain at a distance of 0.9 cm from the skull. The dose distribution investigation on the head model is including the skin, skull, health brain cells and brain cancer tumor.

Neutron flux for different energy groups, neutron and gamma dose are tallied with histories of $10^7 – 10^8$ particles considering the human head with a brain tumor are simulated using the material elemental compositions and densities that recommended by ICRU-^{46} [31] which illustrated at Table 2.

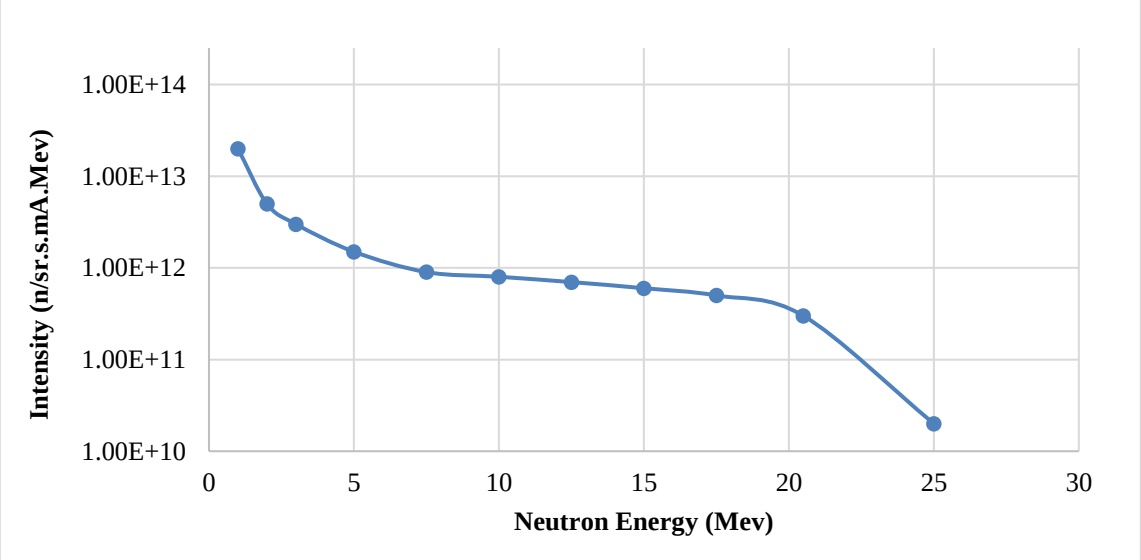

Fig. (1): The initial spectral energy distribution for the emitted neutrons in (AB_BNCT) facility [29]

Table (2): Materials elemental compositions used for head phantom in simulation [31]

Tissue	Density (gm/cm^3)	H	C	N	O	Na	Mg	P	S	Cl	K	Ca
Skin	1.12	10	20.4	4.2	64.5	0.2	-	0.1	0.2	0.3	0.1	-
Skull (Bone)	1.935	5	21.2	4	43.5	0.1	0.2	8.1	0.3	-	-	17.6
Brain	1.04	10.7	14.5	2.2	71.2	0.2	-	0.4	0.2	0.3	0.3	-

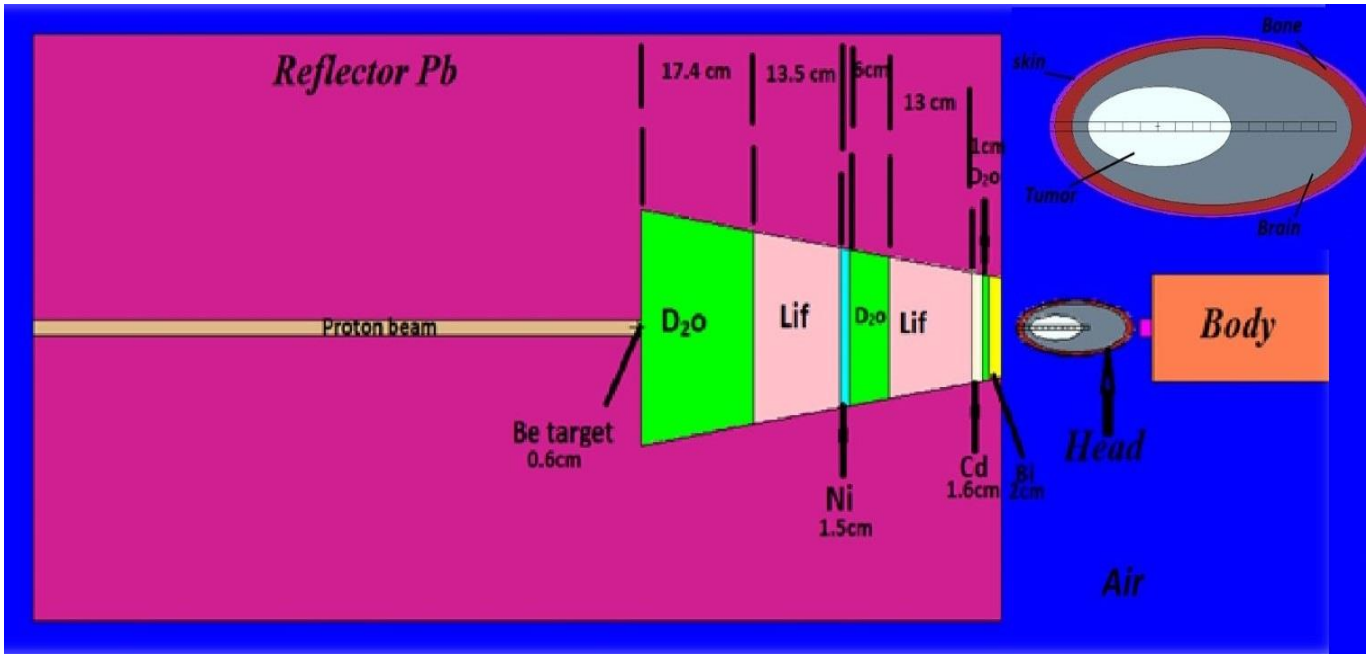

Fig. (2): final BSA model geometry configuration design and a human head model.

The boron concentrations injected in tumor cells and healthy tissues are assumed to be at a ratio of 4:1 [32, 33], ranging from 10 ppm to 80 ppm. The total effective doses at the brain tumor and healthy tissue are calculated using simulated dose results as missioned in equation (3) and relative biological effectiveness (RBE) factors illustrated in table 3 [25, 34].

Table (3): RBE factors used for different dose components

Tissue	Tumor	healthy tissue
w_c	3.8	1.32
w_p	3.2	3.2
w_n	3.2	3.2
w_x	1	1

The calculation of the total effective dose in brain tumors and healthy tissues is essential in BNCT to determine the therapeutic gain (TG). TG calculation involves assessing the effective dose delivered to the tumor cells divided by the maximum effective dose delivered to healthy tissues [35], for different values of ^{10}B concentration through the head phantom based on the specific geometry and position of the cancer target.

4 – RESULTS AND DISCUSSION

4-1 Beam Shape Assembly Design

Different simulations with MCNP5 code used various materials and arrangements to optimize neutron beam quality and satisfy IAEA recommendation. Figure (2) shows the final BSA model design and human head model configuration.

Figure (2) indicates that for the BSA configuration design, Pb is selected as a reflector material because it is suitable for a highly elastic scattering cross section for epithermal energies, while bismuth is found a better choice as a gamma filter compared to lead. These results are in compatible with some study [20, 36]. D_2O, LiF are selected as a moderator material to ensure increasing of epithermal neutron flux, followed

by Ni is a fast neutron filter; to reduces the fast component flux, and Cd as thermal neutron filter because it with large absorption cross section in thermal energy rate Also it is in consist with some studies [12, 20, 37].

The neutron source energy spectrum is obtained from BSA performed simulation model is 1.18 x 10^9, 2.17 x 10^8 and 4.16195 x 10^8 n/cm^{2}s for flux of epithermal, thermal and fast neutron respectively, with estimated uncertainty values are generally reliable confidence in the Monte Carlo results [38]. The results of the BSA model are instigated and compared with the neutron beam criteria that recommended by the IAEA to ensure beam therapy quality, and it is illustrated in table 4. BSA model results are compatible with IAEA' recommendations and the thermal ratio may be more suitable to treat superficial tumors as mentioned by Guangru Li et.al. [39].

4-2 Head model and dose calculation

The results of head irradiation simulation model before ^{10}B injection are shown in the next figure which illustrates the relation between neutron flux components, and gamma ray flux along head depth for normal and tumor cells. Figure (3) illustrate that, the higher thermal flux is in tumor cells at depth 4.2 cm is 2.12 x 10^9 n/cm^{2}s, and epithermal and fast flux decreases along the head depth due to continuous slowing down inside the tumor cell tissues.

Table (4): Comparison between the resulted BNCT neutron beam characteristics and the neutron beam criteria recommended by IAEA.

BNCT neutron beam characteristics	$\emptyset_{epi}$ (n/cm^{2}s)	$\emptyset_{Th}/\emptyset_{epi}$	$\frac{D_F}{\emptyset_{epi}}$ (GY cm^2/n$_{epithermal}$)	$\frac{D_\gamma}{\emptyset_{epi}}$ (GY cm^2/n$_{epithermal}$)
IAEA recommendation	> 5 x 10^8 n/cm^{2}s	< 0.05	1 to 13 x 10^{-13}	2.5 to 13 x 10^{-13}
BSA Model Results	1.18 x 10^9	0.18	7.08 x 10^{-13}	1.89 x 10^{-13}

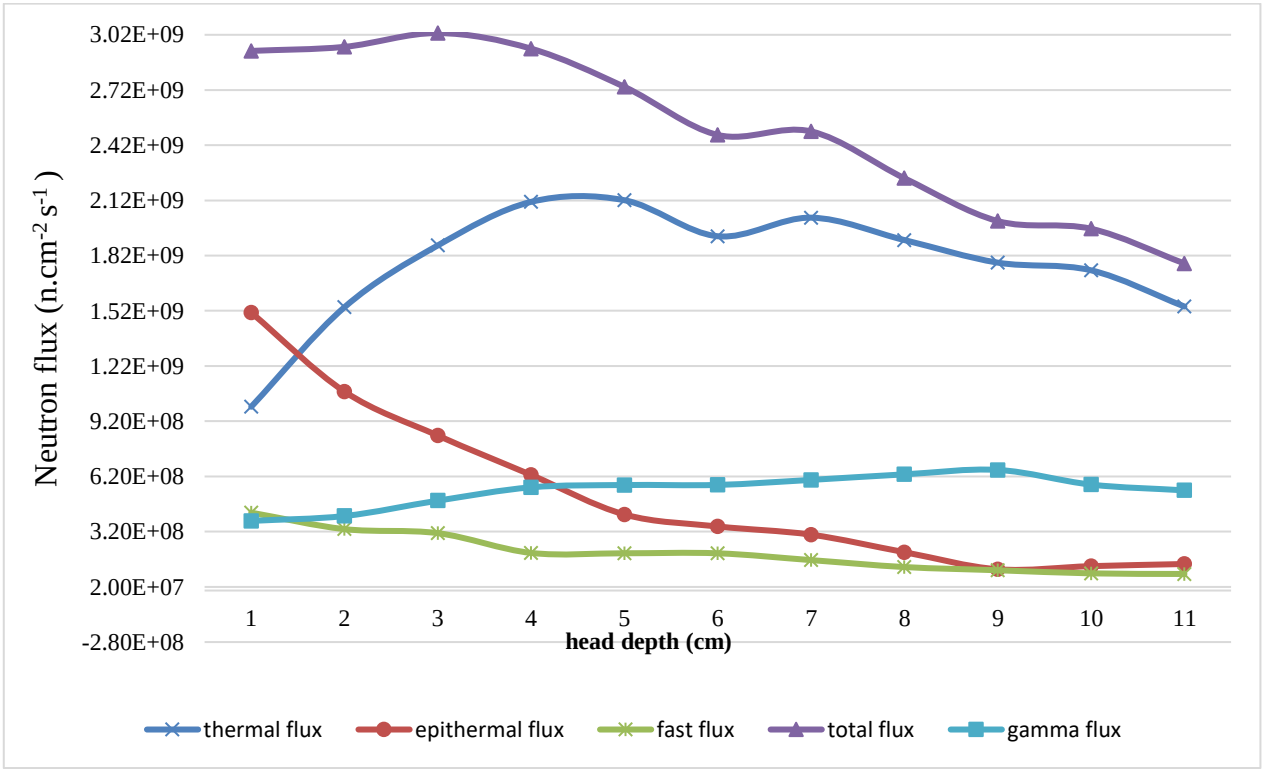

Fig. (3): Neutron flux and gamma flux distributions along the head depth before ^{10}B injection.

The biological dose rate released to normal and tumor tissues is calculated at different ^{10}B concentration (10 – 80) mg/kg. Figure (4) shows the results of the total biological doses (D_T) at ^{10}B concentrations from 10 to 80 mg/kg. The results indicate that biological dose is increasing with ^{10}B concentration increase. The boron dose is the most effected component on the total biological dose is inside the tumor. Proton and gamma doses decrease along the head depth. The healthy tissues beyond the tumor receive the lowest radiation dose. The highest dose at healthy cells in front of the tumor is at skin surface and the lowest one at the skull due to high dense. The results indicate that biological dose rate peaks is at 4.2 cm in the tumor where the boron dose is maximum.

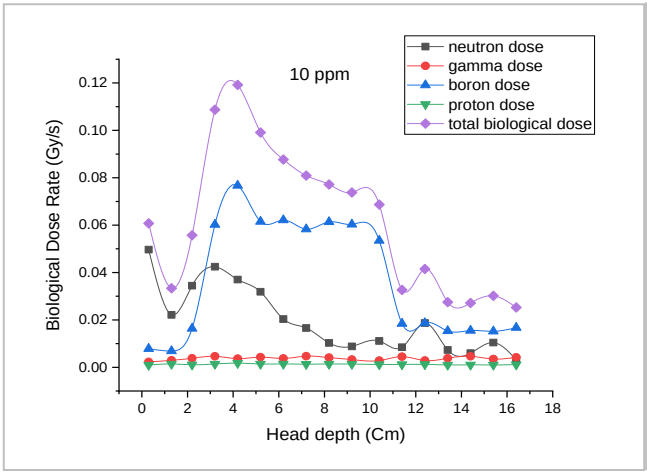

Fig. (4-a): The D_T for 10 mg/kg^{10}B conc.

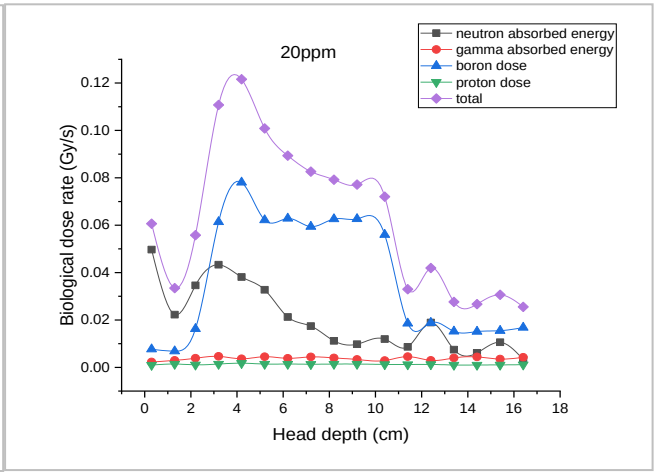

Fig. (4-b): The D_T for 20 mg/kg^{10}B conc.

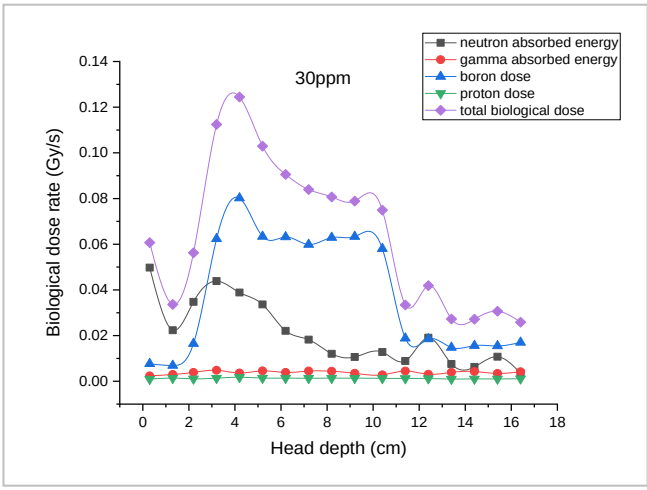

Fig. (4-c): The D_T for 30 mg/kg^{10}B conc.

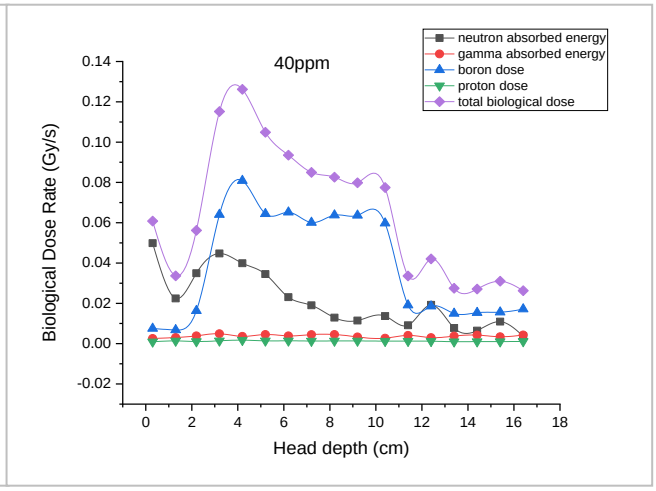

Fig. (4-d): The D_T for 40 mg/kg^{10}B conc.

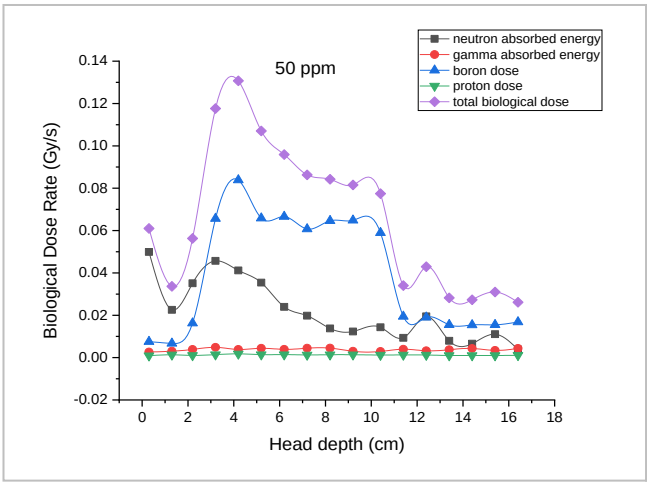

Fig. (4-e): The D_T for 50 mg/kg^{10}B conc.

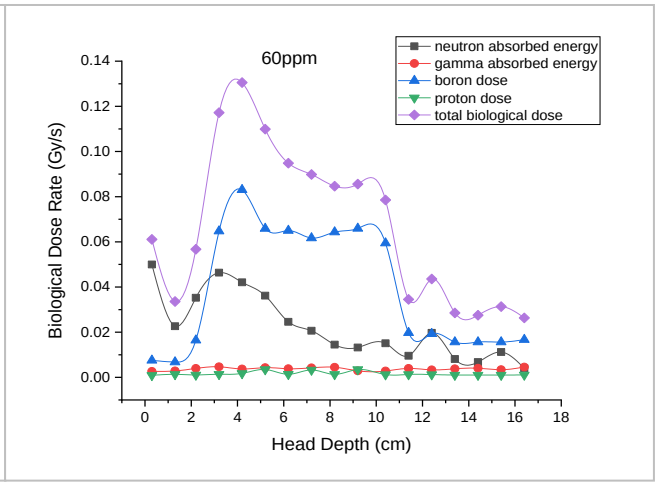

Fig. (4-f): The D_T for 60 mg/kg^{10}B conc.

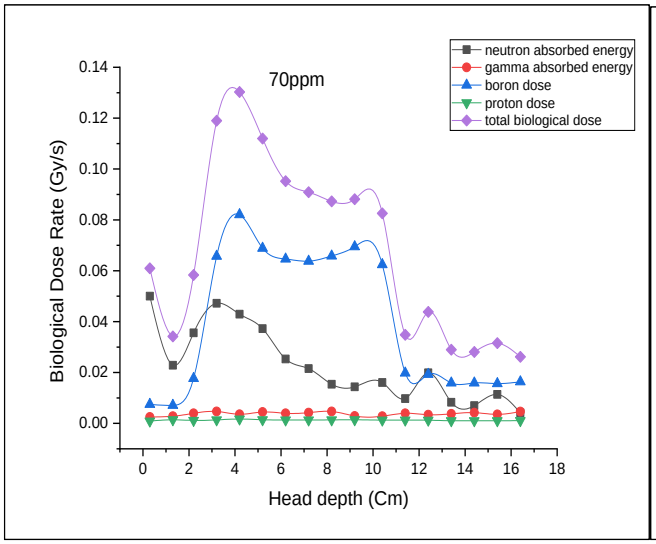

Fig. (4-g): The D_T for 70 mg/kg ^{10}B conc.

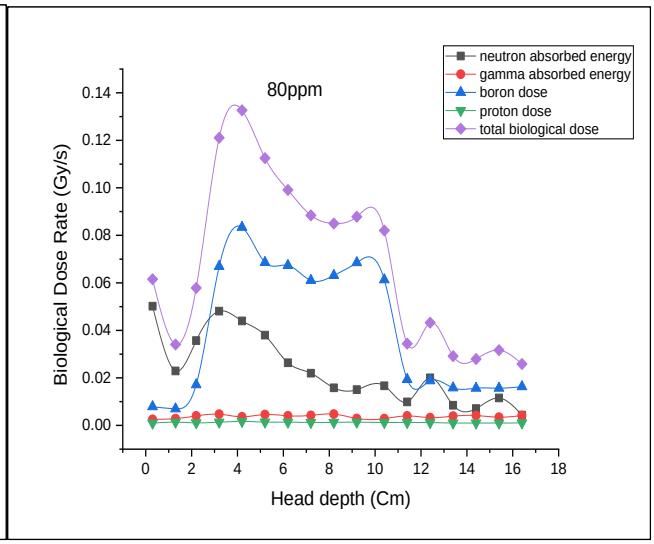

Fig. (4-h): The D_T for 80 mg/kg ^{10}B conc.

Fig. (4): The total biological dose rate values and its components along the head depth for various injected ^{10}B concentrations

The results of therapeutic gain (TG) calculation for different values of ^{10}B concentration through the head phantom are illustrated at figure (5). The results show that TG is increased with ^{10}B concentration.

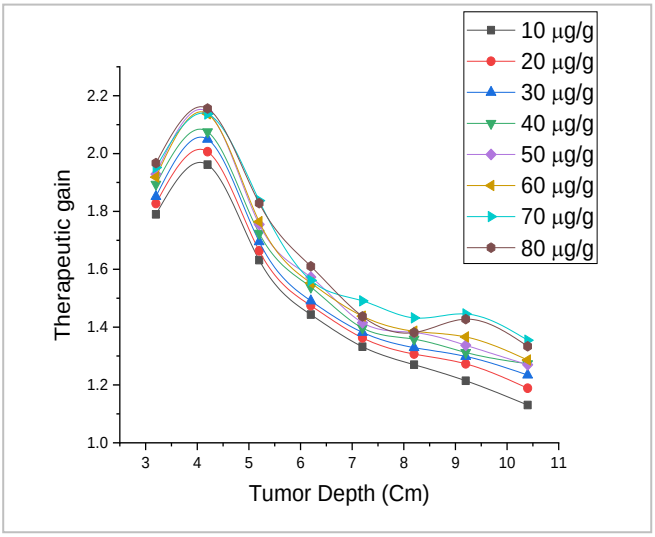

Fig. (5): Therapeutic gain versus different head depths for various injected ^{10}B concentrations.

Values of TG have the same trend from ^{10}B concentration 10 to 60 mg/kg and there is a change in its value after that. This indication means TG calculation is crucial for evaluating the impact of varying ^{10}B concentrations on the therapeutic outcome, and treatment strategies optimization, while the impact on surrounding healthy tissues will be minimized. The value of TG at ^{10}B concentration 80 mg/kg may be more suitable due to higher biological dose rate and highest TG which may in agreement with some previous study [28].

CONCLUSION

The proposed BSA model geometry configuration gave a BNCT neutron beam characteristics are in compatible with the neutron beam criteria recommended by the IAEA. The ratio of thermal neutron flux to the epithermal neutron flux founded may be more suitable to treat superficial tumors. The proposed head model illustrate that the higher thermal flux is in tumor cells, and epithermal and fast flux decreases along the head depth due to continuous slowing down inside the tumor cell tissues. The biological dose is increasing with ^{10}B concentration increase. And the total biological dose is mainly depending on the boron dose component. The healthy tissues at the skin surface, skull and beyond the tumor receive the lowest radiation dose. TG may be used as a fast evaluation of the impact of varying ^{10}B concentrations on the therapeutic outcome, and treatment optimization.

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