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Boron neutron capture therapy design calculation of a 3H(p,n) reaction based BSA for brain cancer setup

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Technical Report

Abstract

Purpose: Boron neutron capture therapy (BNCT) is a promising technique for the treatment of malignant disease targeting organs of the human body. Monte Carlo simulations were carried out to calculate optimum design parameters of an accelerator based beam shaping assembly (BSA) for BNCT of brain cancer setup. **Methods:** Epithermal beam of neutrons were obtained through moderation of fast neutrons from $^3H(p,n)$ reaction in a high density polyethylene moderator and a graphite reflector. The dimensions of the moderator and the reflector were optimized through optimization of epithermal / fast neutron intensity ratio as a function of geometric parameters of the setup. **Results:** The results of our calculation showed the capability of our setup to treat the tumor within 4 cm of the head surface. The calculated peak therapeutic ratio for the setup was found to be 2.15. **Conclusion:** With further improvement in the polyethylene moderator design and brain phantom irradiation arrangement, the setup capabilities can be improved to reach further deep-seated tumor.

Keywords: BNCT; Brain Phantom; $^3H(p,n)$ Reaction; Polyethylene Moderator and Graphite Reflector; Beam Shaping Assembly; Monte Carlo simulations

Introduction

Boron neutron capture therapy (BNCT) is a binary radiation therapy modality proposed as an alternative treatment for brain tumors.[1-9] The two major components of the therapy are a stable isotope ^{10}B of boron that can be concentrated preferentially in tumor cells and a beam of low energy neutrons.[2-3, 8] Initially the BNCT treatment was proposed using the thermal neutrons beams. Due to low penetrating power of thermal neutrons it was necessary to open the human scalp and irradiate the tumor with the thermal neutron beam. Later it was proposed to use the epithermal neutron beam, which has enough penetrating power to reach the deep-seated tumor in the brain without opening the scalp.[2, 8]

There are several techniques to produce epithermal beams of neutrons either using nuclear reactors[1, 6] or a particle accelerator as a neutron source.[2-5, 7-9] Epithermal beams of neutrons from nuclear reactors have been tested to treat patients with a glioblastom multiforme, and intracranial metastatic and subcutaneous melanoma.[1, 6] The accelerator based neutron sources have certain advantages over reactor based neutron sources such as low gamma ray background associated with neutrons, low cost, ease of placing an accelerator in or near hospitals etc.

An accelerator based beam shaping assembly (BSA) used in BNCT utilizes fast neutron producing nuclear reaction along with a moderator-reflector combination to produce desired features of the neutron beam. It is desired to improve the quantity and the quality of neutron beams for BNCT treatment by choosing a suitable nuclear reaction in conjunction with an appropriate moderator-reflector combination. Some of the nuclear reactions which are tested to produce epithermal neutron beams for BNCT are: $^{13}C(d,n)$ [4] and ^7Li (p, n).[2-5, 7-9] ^7Li (p, n) reaction is commonly used in conjunction with different types of moderator-reflector combinations e.g. light water (H_2O) moderator and Alumina (Al_2O_3) reflector[2]; D_2O moderator and lead reflector[8] and BeO moderator and Li_2CO_3 reflector[9] etc. to produce epithermal neutron beams.

In this study ^3H (p, n) reaction[10, 11] was tested for its application to produce epithermal neutrons beam for BNCT application. ^3H (p, n) reaction is similar to ^7Li (p, n) reaction but with slightly higher neutron energy than those from ^7Li (p, n) reaction.[12] The neutrons from ^3H (p, n) reaction have keV energies, and are moderated in a high density polyethylene moderator and then are collimated to a brain phantom containing boron concentrated tissues. This paper describes the

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design calculation of the moderator assembly and ultimate dose in the brain phantom.

Methods and Materials

BNCT geometry

The geometry of the $^3H(p,n)$ reaction based BNCT setup is shown in **Figure 1**. It mainly consists of a $^3H(p,n)$ point source located inside a cylindrical polyethylene moderator. A graphite reflector is built around the moderator to enhance the epithermal neutron yield. A double truncated cylindrical collimator was used to collimate the epithermal neutron beam from the moderator to the tumor location in the brain phantom.[13] The collimator was made of paraffin and lithium carbonate mixed in equal weight fractions. The BNCT setup geometry was optimized by calculating the epithermal, thermal and fast neutron intensities as a function of moderator size, reflector size and source position inside the moderator. The neutron dose in the boron carrying tumor in the brain phantom was calculated. Due to its high hydrogen concentration and easy machining properties, high-density polyethylene was chosen as the moderator material. The number of particles used in this study was 1E09; this number of histories gave 1.34% of uncertainty.

Neutron energy spectrum from $^3H(p,n)$ reaction

$^3H(p,n)$ reaction near the reaction threshold was used to produce fast neutrons. The neutrons from the $^3H(p,n)$ reaction near the reaction threshold are emitted in a forward cone with a maximum energy ranging up to few hundred keV.[10, 11] The neutrons are not mono-energetic and they have an energy distribution of Maxwellian type and the experimental angular distribution data can be fitted with an analytical function of type: $Ee^{-E/kT}$. The best fit is obtained for neutrons produced by a proton beam with energy 80 keV above the reaction threshold. The experimental neutron spectrum has a 91% overlap with a Maxwellian distribution for kT=52 keV and the neutrons are emitted within an angular cone of ± 60° with respect to the proton beam axis.[11] The neutron energy spectrum, used in this study, was generated using a built-in neutron source function of the MCNP4B2 code for an evaporation energy spectrum of the type: $Ee^{(-E/a)}$ with a = 0.052 MeV.[14, 15]

Brain phantom

The human brain and its surrounding structures were modeled using the MCNP transport code. The data used to model human brain and its surrounding structures were taken from reference.[10] As shown in **Figure 2**, the brain is assumed to be an ellipsoid with axes 132, 172 and 115 mm respectively; and is surrounded by a skull of thickness 9 mm, and a scalp consisting of soft tissue (3 mm) and skin (2 mm). The elemental compositions of the material present in the cranium are listed in the **Table 1**. The data were taken from ICRU-44.[16] The dose was evaluated in volume segments around the central axis of the neutron beam. The dose profiles were obtained by extrapolating to the central axis. The boron concentrations in different parts of the phantom are listed in the **Table 2**.

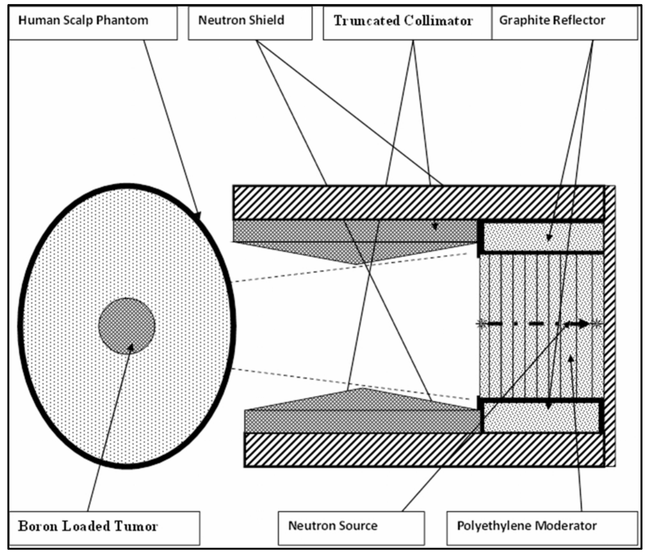

FIG. 1: Schematic of accelerator-based BNCT setup.

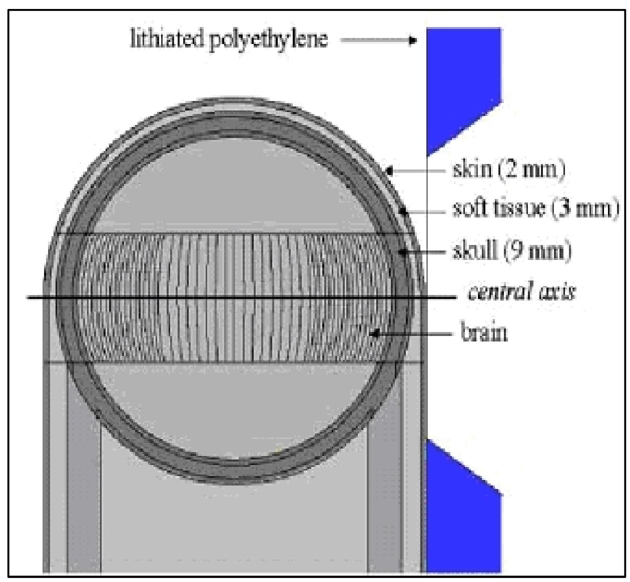

FIG. 2: Schematic of the brain phantom used for dose calculations.

TABLE 1: Elemental composition of brain and skull Phantom taken from IRCU [7].

Phantom part	Boron concentration(μg/g)
Skin	15
Tissue under skin	10
Skull	–
Normal brain tissue	10
Tumor brain tissue	35

TABLE 2: Boron Concentration in Brain.

Parameters	Values
Moderator thickness (cm)	9 cm
Source position (cm)	4 cm from the modera-end facing brain phantom
Moderator outer radius (cm)	4
Graphite side reflector thickness	2-3
γ-ray Pb side shielding thickness	0.5
γ-ray Pb front shielding thickness (cm)	0.2
Neutrons side shielding thickness (cm)	0.5-1.0 cm

The therapeutic efficacy of neutron beams for our BNCT setup were calculated through its figures-of –Merit i.e. Advantage depth (AD), Advantage ratio (AR), and Peak therapeutic ratio.[1] The AD indicates the penetrability of the neutron beam while AR gives the tumor dose relative to surrounding healthy tissue dose; and the peak therapeutic ratio gives maximum tumor dose / maximum healthy tissue dose ratio.[2] The advantage depth is defined as the depth in a phantom at which point the tumor dose rate equals the maximum healthy tissue dose rate. Any tumor mass located beyond the AD receives less than the maximum healthy tissue dose, thus reducing any treatment "advantage." The advantage ratio is defined as the ratio of the areas under the dose rate curves for tumor and healthy tissue along the phantom centerline from the surface to the advantage depth[2]:

$$AR = \frac{\int_0^{AD} D_{tumor}(z)dz}{\int_0^{AD} D_{tissue}(z)dz}$$

Where, $D_{tumor}(z)$ and $D_{tissue}(z)$ are the doses to tumor and healthy tissue, respectively, along the centerline (z-axis) of the phantom.[2] Finally, the advantage depth dose rate is defined as the tumor dose rate at the advantage depth, which is equal to the maximum healthy tissue dose rate. In all dosimeteric calculations of biological systems, dose components should be weighted with appropriate relative biological effectiveness (RBE) factors.

The following RBE values are used for the dose components in these BNCT simulations: fast neutron, 3.2; thermal neutron, 3.2; ^{10}B in healthy tissue, 1.35; ^{10}B in tumor, 3.8; photon, 1.0 photon.[2] Currently, these RBE values are being used in clinical BNCT trials at the Massachusetts Institute of Technology (MIT) and Brookhaven National Laboratory (BNL) along with the pharmaceutical borono-phenylalanine (BPA) as the boron delivery compound. Dosimeteric conversion factors and ^{10}B concentrations followed generally accepted standards when using BPA for brain glioma's.[2] Any adjustment of these RBE values will change all three figures of merit defined above, and inter-comparisons of the results presented here with published results for other neutron beams must take this into account. It should be noted that tumor and healthy tissue boron RBE values are unlikely to differ between reactor and near-threshold beams, since they are primarily determined by the distribution of the boron compound within cells.[17]

However, the neutron RBE values for near-threshold beams may differ appreciably from those for reactor beams, because the neutron energy spectra of reactor and near-threshold beams differ. Since RBE values for near threshold neutron energy spectra of have not been determined, the RBE values given above are considered at this point a "best guess" and are used for comparison purposes only.

Results and Discussion

BNCT setup geometry optimization

The BNCT setup geometry was optimized by calculating epithermal, thermal and fast neutron intensities as a function of moderator length and radius, reflector size and source position inside the moderator. For all moderator lengths, the epithermal neutron yield increases initially with increasing distance of the source from the moderator-end facing the brain phantom and then decreases rapidly. As shown in the **Figure 3**, the maximum yield of the epithermal neutrons has been observed for the source position at a distance of 0.75 cm from the moderator-end facing the brain phantom. The fast neutron intensity decreases very rapidly with increasing source distance inside the moderator. This is clearly shown in **Figure 4**, which represents epithermal and fast neutron yield as a function of source position inside 2-14 cm long polyethylene moderators.

In the **Figures 3 and 4** each curve terminates at maximum length of corresponding moderator. For all moderator lengths, the maximum value of epithermal/ fast neutron yield ratio was observed for a source position at a distance of 4 cm from the moderator end facing the brain phantom. **Figure 5** represents epithermal/fast neutron yield ratio and epithermal /thermal neutron yield ratio plotted as a function of 3-15 cm long moderators. Both ratios show almost constant values for moderator lengths in excess of 9 cm. Therefore, a 9 cm long moderator with a neutron source located at a distance of 4 cm from the moderator end was chosen to be an optimum moderator length. Similarly, for moderator-radius optimization, an epithermal/fast and epithermal/thermal neutrons intensities ratios were calculated as a function of the moderator radius. As shown in **Figure 6**, the optimum value of the two ratios can be achieved with a moderator having 4 cm radius.

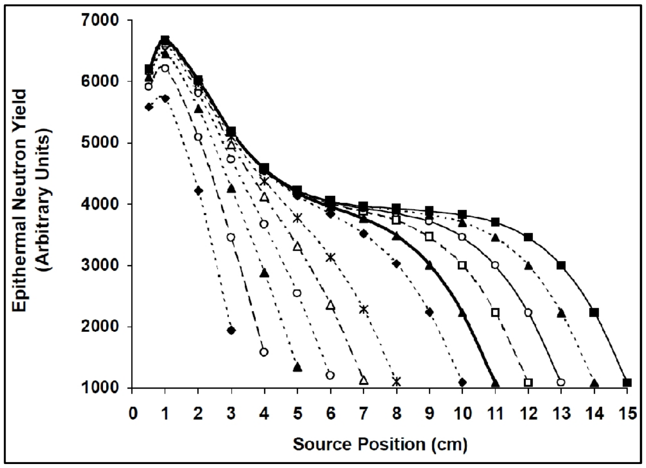

FIG. 3: Epithermal neutron yield as a function of source position inside a 2-14 cm long polyethylene moderator. Each curve terminates at maximum length of corresponding moderator.

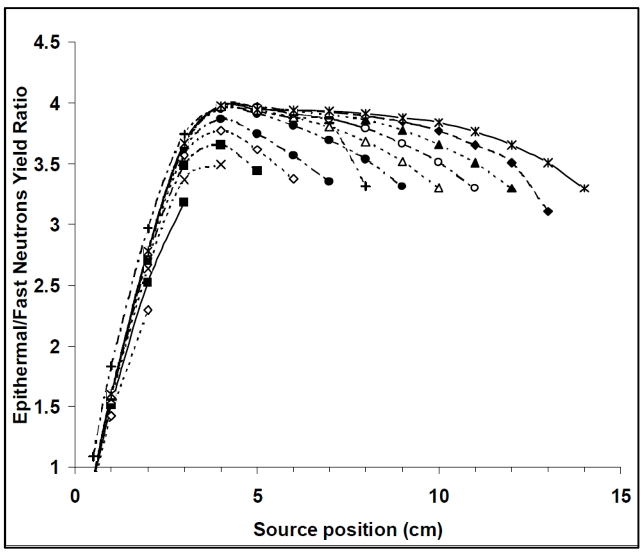

FIG. 4: Epithermal/ Fast neutrons yield ratio plotted as a function of source position inside a 2-14 cm long moderators. Each curve terminates at maximum length of corresponding moderator.

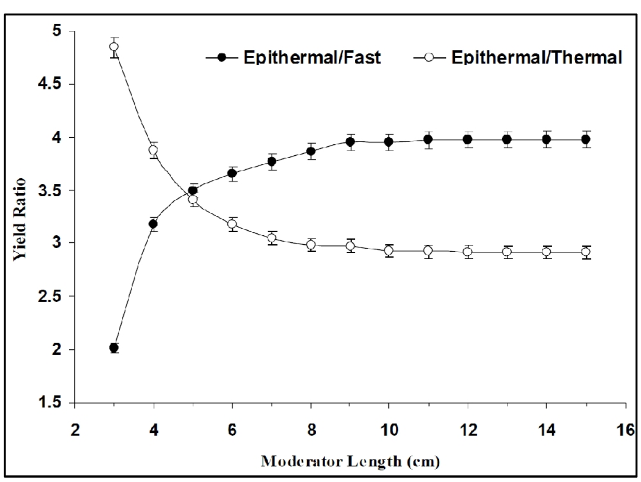

FIG. 5: Optimum Epithermal/fast and epithermal /thermal neutrons ratio plotted as a function of 3-15 cm long moderators.

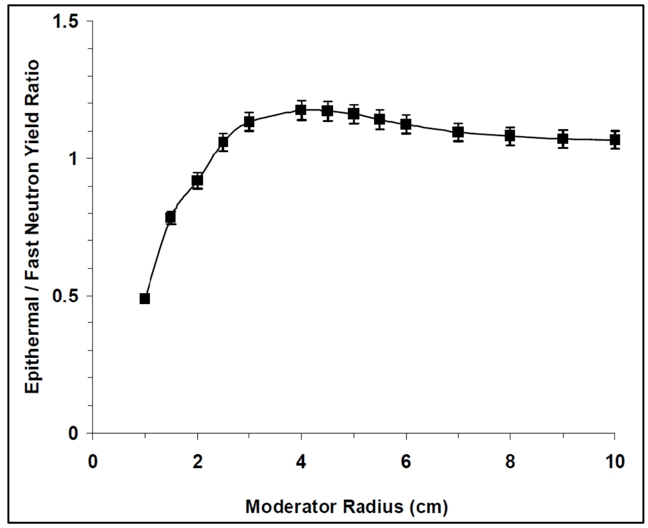

FIG. 6: Optimum Epithermal/fast neutrons ratio plotted as a function of moderator radius.

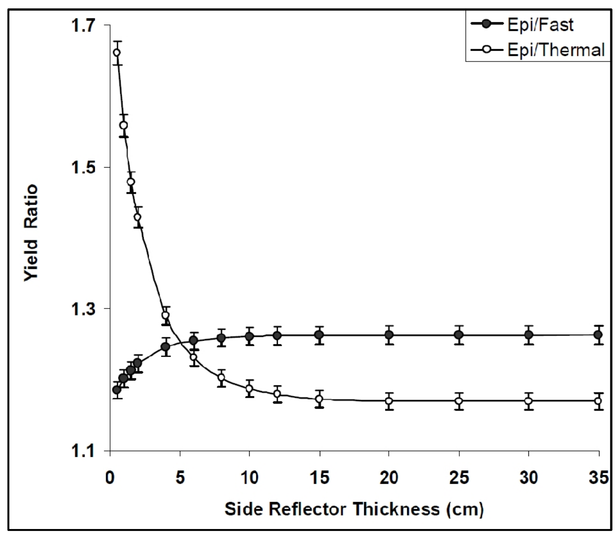

FIG. 7: Optimum Epithermal/fast and epithermal /thermal neutrons ratio plotted as a function of side graphite reflector thickness.

The reflector thickness was then optimized using the ratios of epithermal/fast and epithermal/thermal neutron intensities calculated as a function of graphite reflector thickness. Since the reflector increases the intensity of thermal neutrons, the epithermal/thermal ratio decreases rapidly with increasing reflector collar. As a compromise between the two ratios, as shown in **Figure 7**, 2-3 cm thick graphite reflector was found to be optimum. Neutron shielding using Paraffin and Li_2CO_3 and gamma ray lead shielding was built around the moderator and its cylindrical graphite reflector to minimize the dose at the brain phantom outside the field of treatment.

The neutron intensity was found to be reduced by 50% after using 5 mm thickness of the paraffin absorber. The γ-rays are attenuated by only 5% in the same thickness of the paraffin. In order to reduce the gamma ray dose at the brain phantom location, a 5 mm thick lead shielding was inserted at the exit of the moderator assembly. The length of the neutron collimator was assumed to be 2-3 times the neutrons mean free path. The collimator length used in the simulation was 50 cm. The optimum values of the geometry parameters of the BSA are listed in **Table 3**.

TABLE 3: Optimum values of the design parameters of the accelerator based BNCT setup.

Mat.	Z/A	I(eV)	Density	Brain phantom composition in weight fraction given in term of atomic number Z										
				Z=1	Z=6	Z=7	Z=8	Z=11	Z=12	Z=15	Z=16	Z=17	Z=19	Z=20
Skin	0.54975	74.9	1.000	0.1011	0.111	0.026	0.762							
Soft Tissue	0.54996	74.7	1.06	0.102	0.143	0.034	0.708	0.002	-	0.003	0.003	0.002	0.003	
Skull	0.51478	112.0	1.92	0.034	0.155	0.042	0.435	0.001	0.002	0.103	0.003			0.225
Brain	0.55239	73.9	1.04	0.107	0.145	0.022	0.712	0.002	-	0.004	0.002	0.003	0.003	

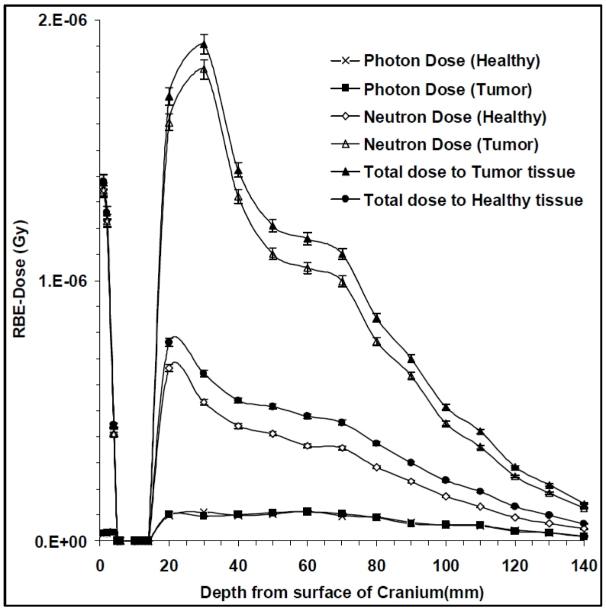

FIG. 8: Calculated neutron, boron and photon dose in tumor, and healthy tissues at different depth of cranium.

TABLE 4: Comparison of figure of merit of various BNCT setups.

Exp-Design	Reaction	Moderator/Reflector	RBE-AD	RBE-ADDR
YZSK [8]	$^{7}Li(p,n)$	D_2O/Pb	8.5	4.1
WBGG[9]	$^{7}Li(p,n)$	BeO/Li_2CO_3	9.2	5.0
LZKHH[2]	$^{7}Li(p,n)$	H_2O/Al_2O_3	5.9	4.8
Present study	$^{3}H(p,n)$	Polyethylene/Graphite	4	

Dose calculations in a brain phantom

Figure 8 shows the calculated neutron and photon doses in the tumor and healthy tissues at different depth of the cranium. The neutron dose is almost zero at the location of the skin, soft tissue and skull that has almost no Boron uptake. The neutron dose increases as the depth in brain tissue increases, it reaches a maximum and then decreases. At the depth of maximum neutron dose in the tumor tissue, the neutron dose to healthy tissue is about half of that of the tumor tissue.[18] The photon dose calculated in the phantom does not include the gamma ray dose associated with $^{3}H(p, n)$ reaction. It only includes gamma rays from the moderator setup and the phantom itself. The value of advantage depth AD (RBE-AD) obtained in our study is 4 cm. The value of advantage ratio (AR) was found to be 1.92. The Peak therapeutic ratio calculated was found to be 2.15. The results obtained in the present study are listed in **Table 4** along with the results quoted for other accelerator-based facilities in reference.[2]

The values of RBE-AD and AR are very specific to set up design parameters such as moderator material, reflector material, and irradiation setup of brain phantom. As shown in **Table 4**, the YZSK [8] and WBGG [9] designs have superior RBE-ADs, and therefore can treat deeper tumor than the near-threshold design. RBE-ADDR (advantage depth dose rates) values are listed in **Table 4**. The RBE-AR from LZKHH [2], YZSK and WBGG studies are comparable. The three setups use different moderator/reflector combinations and geometries. The LZKHH setup has an annulus of D_2O for neutron shielding. In WBGG design, the patient head is placed inside the inner radius of the D_2O shield. The YZSK design uses a $D_2O/^6Li$ neutron shield surrounding the reflector. The LZKHH design utilizes Li (p, n) reaction while YZSK design uses Li (p, n) reaction with 2.5 MeV protons to produce neutrons. Our design which uses ^3H(p, n) reaction at the threshold energy gives result closer to LZKHH design. Replacing the moderator with more appropriate one and choosing more effective irradiation arrangement of the brain phantom, can improve RBE-AD and AR. of our setup.

Conclusion

A systematic study has been carried out to design an accelerator based BNCT setup using ^3H(p, n) reaction near threshold. In the calculation the moderator, reflector and collimators size was optimized. Finally neutron dose was calculated at a tumor location in a brain phantom. Results of our calculation showed the capability of our setup to treat the tumor within 4 cm of the head surface. With further improvement in the design and brain sample irradiation arrangement, the setup capabilities can be improved to reach deeper seated tumor.

Conflict of interest

The authors declare that they have no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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