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Original Article

Simulation of the BNCT of Brain Tumors Using MCNP Code: Beam Designing and Dose Evaluation

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Abstract

Introduction
BNCT is an effective method to destroy brain tumoral cells while sparing the healthy tissues. The recommended flux for epithermal neutrons is 10^9 n/cm^{2}s, which has the most effectiveness on deep-seated tumors. In this paper, it is indicated that using D-T neutron source and optimizing of Beam Shaping Assembly (BSA) leads to treating brain tumors in a reasonable time where all IAEA recommended criteria are met.

Materials and Methods
The proposed BSA based on a D-T neutron generator consists of a neutron multiplier system, moderators, reflector, and collimator. The simulated Snyder head phantom is used to evaluate dose profiles in tissues due to the irradiation of designed beam. Monte Carlo Code, MCNP-4C, was used in order to perform these calculations.

Results
The neutron beam associated with the designed and optimized BSA has an adequate epithermal flux at the beam port and neutron and gamma contaminations are removed as much as possible. Moreover, it was showed that increasing J/Φ, as a measure of beam directionality, leads to improvement of beam performance and survival of healthy tissues surrounding the tumor.

Conclusion
According to the simulation results, the proposed system based on D-T neutron source, which is suitable for in-hospital installations, satisfies all in-air parameters. Moreover, depth-dose curves investigate proper performance of designed beam in tissues. The results are comparable with the performances of other facilities.

Keywords: Beam Designing, BNCT, Brain Tumors, Dose Evaluation, MCNP-4C Code

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1. Introduction

The cell is the basic structural and functional unit of all living organisms. As the smallest unit of a living body, it is often called the building block of life. In normal cells, the processes of cell division are controlled while in cancer cells, they no longer respond to the signals that control the cellular growth and death. In other words, a tumor is a part of a tissue that is abnormally growing. Glioblastoma Multiforme (GBM) is the most common and most aggressive malignanant brain tumor involving star-shaped glial cells, which provide support and protection for nervous system. GBM, which is classified as grade IV tumors, shows rapid tumor growth and commonly spreads to the nearby healthy tissue. Despite the improvements made in theraputical techniques such as surgery, chemotherapy, and radiotherapy, these techniques have been rarely effective [1].

As a form of radiation therapy, Boron Neutron Capture Therapy (BNCT) is used to eradicate the brain tumors which are hard to remove with surgical methods. The concept of this method, which benefits from high Linear Energy Transfer (LET) particles to destroy cancer cells, was initially proposed by Gordon L. Locher in 1936, four years after the discovery of neutrons by Chadwick. In this binary therapy, ^{10}B compounds -stable isotopes of boron with large absorption cross section for thermal neutrons- are administered in tumor cells. Following to irradiation of the target regions by neutron beam, the particles which are generated in the process of nuclear reaction between ^{10}B and thermal neutrons release their energy to destroy tumor cells. Therefore, there are two key steps that BNCT relies on:

In the first step, a boron carrier drug such as Boronophenylalanine (BPA) and Borocaptate Sodium (BSH) is administered to the patient. These ^{10}B-enriched drugs are called tumor-seeking.

In the next step, tumor area is subjected to the neutron irradiation. After a thermal neutron capture, the excited ^{11}B nucleus immediately fissions into an alpha particle and lithium recoil nucleus via one of the following reactions [2]:

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

$$^{10}B+n_{th}\rightarrow{}^{4}He(1.78MeV)+{}^{7}Li(1.01MeV) \quad (6.3\ \%) \quad (2)$$

The high LET emitted particles deposit their energy in a range of about 10 μm, which is of the same order of cell diameter [3, 4**].** Occurring the fundamental BNCT reaction close to the cell nucleus increases the probability of DNA breaking, which leads to the cancer cell death without damaging normal ones.

Two different neutron beams are commonly used in BNCT: the thermal neutron beam which limits the treatment to shallow tumors, such as skin melanoma and Gliblastoma Multiforme associated with craniotomy, and the harder epithermal neutron beam which reaches the thermal energy range after passing through tissues. As the latter can penetrate deeper into tissues due to its high energy, it has been suggested for treating the deep-seated tumors [5].

The designed beam for BNCT should encompass suitable “quality” and “intensity”. It is evaluated with two sets of International Atomic Energy Agency (IAEA) recommended values: in-air and in-phantom parameters [6]. The widely accepted in-air parameters to assess the designed beam quality and intensity before reaching the tissue are presented in Table 1. In this table, Φ_{epi}, $\Phi_{thermal}$, and J are epithermal neutron flux, thermal neutron flux, and surface current, respectively. Moreover, $\dot{D}_{fn}$ and $\dot{D}_{\gamma}$ stand for dose rates due to the fast neutrons and gamma rays.

Although the in-air parameters provide a convenient way to evaluate beam performance at the beam port, beam performance in a phantom is the ultimate measure to assess the designed beam. The in-phantom parameters, which reflect therapeutic effects of designed beam in tissues, serve the latter purpose. These parameters are related to the different dose

profiles due to the irradiated beam in phantom, which may be simulated or constructed.

Table 1. BNCT in-air recommended values and corresponding neutron energy limits [6].

BNCT in-air Parameters	Limit
$\Phi_{epi}(n/cm^2s)$	$>10^9$
$\Phi_{epi}/\Phi_{thermal}$	>100
$\dot{D}_{fn}/\Phi_{epi}(Gycm^2)$	$<2\times10^{-13}$
$\dot{D}_{\gamma}/\Phi_{epi}(Gycm^2)$	$<2\times10^{-13}$
J/Φ	>0.7
Fast Energy Group	E>10 keV
Epithermal Energy Group	1 eV≤E≤10 keV
Thermal Energy Group	E<1 eV

As mentioned earlier, one of the key factors for success in BNCT is irradiation of an appropriate neutron beam to the tumor area. The neutron flux should be large enough so that the therapy can be established in a reasonable time. As a result, utilizing a suitable neutron source is very important. Nowadays, nuclear reactors are the only neutron sources which are capable of providing adequate intensity of neutron beam for BNCT [7]. Recently, many researches have tried to develop alternative compact size neutron sources which are more suitable for in-hospital treatments due to their compact size, high safety, low setup and installation cost, and high social acceptability. As an example, neutron generators based on D-T fusion reaction satisfy all of the above requirements [8]. The monoenergetic neutrons emitted from this reaction have energies of 14.1 MeV.

This article deals with design and optimizing a beam shaping assembly based on D-T neutron source -which yields 10^{14} n/s- and dose evaluation due to the designed beam in a simulated head phantom. The Monte Carlo code, MCNP-4C [9], was used in order to perform all simulations and dose evaluations.

2. Materials and Methods

1.2. Design and Optimization of BSA

As it is showed in Table 1, the minimum desirable beam intensity for BNCT should be 10^9 epithermal neutrons per cm^2 per second. Epithermal neutrons slow down to the desired thermal energy required for BNCT reactions while passing through tissues. On the other hand, as emitted neutrons from D-T source belong to the fast energy range, they cannot be used directly for this therapy method. In order to make them available for treating deep tumors, an epithermal neutron spectrum is required. This involves design of a Beam Shaping Assembly (BSA) consisting of different cells such as moderator, reflector, collimator, and filters to moderate neutrons to the desired epithermal energy range and guide them toward the patient. The BSA dimensions and materials should be optimized in a way that the resultant beam carries the least amount of neutron and gamma contamination.

Slowing down fast neutrons produced by D-T reaction toward the epithermal energy range by means of interaction of neutrons with BSA materials, leads to the reduction of the neutron flux at the beam port. It is due to the neutron capture, neutron escape from the system, and $\Phi\sim1/r^2$ law [10]. Therefore, it is crucial to use some methods to increase the number of neutrons at the end of BSA. In this work, fissile materials are utilized as neutron multiplier in order to avoid loss of neutron flux [10,11]. The most suitable materials are investigated through a careful analysis of simulation results to be used as moderators, filters, reflector, and collimator.

The variation of beam divergence is measured by calculating J/Φ, which is a convenient measure of beam directionality. It takes a maximum value of one for a parallel beam and decreases when beam becomes more isotropic [12]. As it is showed in Table 1, this ratio should be greater than 0.7 [6]. The results show that a higher beam convergence leads to a minor damage to healthy tissue surrounding the tumor. In our work, additional attempts have been made in order to increase beam convergence by means of adding different thicknesses of LiF layer to the configuration, while J/Φ has already been satisfied for proposed BSA. Such a calculation enables us to discuss beam directionality on in-tissue beam performance.

In the next subsections, a simulated Snyder head phantom [13] is used to examine designed beam performance in phantom and to evaluate dose distribution in tumor and healthy tissue. The in-phantom parameters are calculated and the results are compared with two other facilities.

2.2. Dose Evaluation

The beam derived from a BSA, contains all three energy groups of neutrons and also gamma rays generated from capture and elastic interactions with BSA materials. When such mixed spectrum impinges on tissues, four principal physical dose components need to be considered. These are as follows:

Fast neutron dose (D_{fn}), also called "hydrogen dose" is due to the proton recoil generated from $^{1}H(n,n')^{1}H$ interaction [14]. As recoiled proton locally deposits its energy, the mentioned dose component reaches its maximum value in the skin and shallow tissue, and then decreases exponentially. Clearly, the reduction of D_{fn} leads to the reduction of damage to the skin.

Thermal neutron dose (D_N), is a dose produced by the thermal neutron capture from $^{14}N(n,p)^{14}C$ reaction. Generated particles from such a reaction, i.e., 600 keV protons and recoiled ^{14}C nucleus, are responsible for thermal neutron dose in tissues [14,15].

Boron dose (D_B), is caused by thermal neutron capture from $^{10}B(n,\alpha)^{7}Li$ reaction.

Gamma dose (D_γ), which is a combination of dose from incident photon to the patient due to the BSA, and dose from photons which is induced by neutron capture reactions in tissues. As an example for the latter, $^{1}H(n,\gamma)^{2}H$ emits 2.2 MeV photons.

In order to take into account relative biological effects, the four physical dose components should be multiplied by an appropriate "weighting factor". The total dose, denoted by D_T, is defined as follows:

$$D_T=w_{fn}.D_{fn}+w_N.D_N+CBE.D_B+w_\gamma.D_\gamma \qquad (3)$$

Where w_{fn}, w_N, CBE (Compound Biological Effectiveness), and w_γ stand for weighting factor related to the fast neutron dose, thermal neutron dose, boron dose, and gamma dose, respectively. In this study, we used 3.2 for w_{fn} and w_N, and 1 for w_γ [8,12,15].

Obviously, the calculation of total dose depends on boron concentration in tissues. In our simulation, the boron concentration in tumor is assumed to be 40 ppm. Moreover, CBE values and boron concentration in different head tissues are summarized in Table 2 which are the same values observed for intravenous infusion of BPA [16]. According to the data in this table, the CBE factor and boron concentration for skin are different from other healthy tissues.

Table 2. Assumptions used for CBE and boron concentration based on BPA intravenous infusion for various head tissues [17].

Tissue	CBE Factor	Boron Concentration
Blood	-	Measured Directly
Scalp/Skin	2.5	1.5 Times Blood
Brain	1.35	1 Times Blood
Tumor	3.8	3.5 Times Blood

3.2. In-phantom Parameters

Although in-air parameters present a convenient way to measure beam performance at the beam exit window, in-phantom parameters investigate the beam effect on patient body. These parameters are the ultimate measures for evaluating designed beam and are determined considering the treatment limitations such as maximum allowable dose to healthy tissue. If a beam indicates convenient performance in tissues, the designed system is suitable enough to treat the tumors. As the most accepted in-phantom criteria, Advantage Depth (AD), Advantage Ratio (AR), Therapeutic Depth (TD), AD Dose Rate (ADDR), and Treatment Time (TT) are defined as follows:

AD is the depth in phantom which the total therapeutic dose in tumor equals the maximum dose to healthy tissue. The therapeutic dose is sum of the total background dose and boron dose in tumor. AD indicates the depth of effective beam penetration [12,16].

Table 3. Elemental compositions of materials used in simulated head phantom [19].

	Density (g cm^{-3})	weight percent (%)										
		H	C	N	O	Na	P	Cl	K	S	Mg	Ca
Brain	1.04	10.7	14.5	2.2	71.2	0.2	0.4	0.3	0.3	0.2	-	-
Skull	1.61	5.0	21.2	4.0	43.5	0.1	8.1	-	-	0.3	0.2	17.6
Skin	1.09	10.0	20.4	4.2	64.5	0.2	0.1	0.3	0.1	0.2	-	-

AR is the ratio of total therapeutic dose in tumor to the total normal tissue dose over a given depth (usually from the surface to AD) [11,16]. TD defines the depth which the tumor dose falls below twice the maximum dose to healthy tissue [18]. ADDR is the maximum delivered dose rate to the healthy tissue [12,16,18]. Considering that the maximum allowable dose to healthy tissue is 12.5 Gy [8,10], TT can be estimated. As ADDR decreases, TT will increase. On the other hand, considering patient condition, the designed beam intensity should be large enough that treatment time remains in a reasonable limit. In BNCT, treatment time can extend up to one hour [6].

In this paper, the Snyder's head model [13] is simulated using MCNP-4C code. This phantom contains skin, skull, and brain which are simulated by the following equations:

$$\text{Brain: } (\frac{x}{6})^2+(\frac{y}{9})^2+(\frac{z-1}{6.5})^2=1 \quad (4)$$

$$\text{Skull: } (\frac{x}{6.8})^2+(\frac{y}{9.8})^2+(\frac{z}{8.3})^2=1 \quad (5)$$

$$\text{Skin: } (\frac{x}{7.3})^2+(\frac{y}{10.3})^2+(\frac{z}{8.8})^2=1 \quad (6)$$

The elemental composition and densities of materials in the models are listed in Table 3. Using this head model, depth dose distribution in tissues is evaluated and the in-phantom parameters are calculated. In order to investigate the effect of tumor position on delivered dose to phantom, four different tumor positions (from surface to the center) are suggested.

3. Results

Since the neutron beam intensity at the beam port closely relates to the BSA materials and their dimensions, appropriate optimization of BSA is important. Such an optimization process was previously performed by authors and the results were reported [11]. According to these results, fissile materials such as natural uranium are appropriate choice to be utilized as the first BSA cell. As a result, the number of neutrons will increase. Increasing the number of neutrons using multiplier system depends on radius of uranium sphere. Therefore, uranium sphere of 14 cm radius was selected as neutron multiplier. This geometry increases the number of neutrons emitted from D-T neutron source more than 2.8 times [11]. As the next cells, different materials have been investigated and their geometry was optimized in order to moderate this amplified neutrons to the epithermal energy range. The best geometry is made of 17 cm Al and 36 cm Fluental (mixture of 69% AlF_3, 30% metallic aluminum, and 1% LiF) as moderators, 4 cm Fe as fast neutron filter, and 2.6 cm Bi as gamma filter. Moreover, Pb was used in order to avoid neutron escape before reaching the patient and to decrease the BSA exit window to a flat circular surface of 6 cm radius. Figure 1 shows our proposed BSA. The neutron beam related to such a BSA satisfies IAEA recommended parameters which are presented in Table 1.

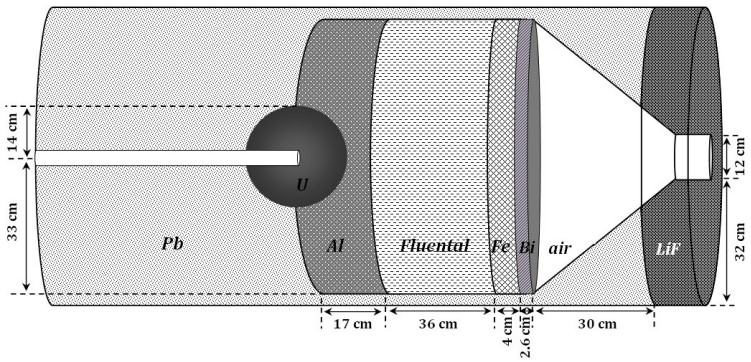

Figure 1. Designed BSA: Natural uranium as neutron multiplier, Al and Fluental as moderators, Fe as fast neutron filter, Bi as gamma filter, and Pb as reflector and collimator. LiF thickness in configurations (a), (b), and (c) are 0, 4, and 7 cm, respectively.

Table 4. BNCT in-air parameters of three designed BSAs with different thicknesses of LiF. For all configurations, recommended IAEA criteria have been met.

In-air parameters \ Configuration	Configuration (a)	Configuration (b)	Configuration (c)
LiF Thickness (cm)	0	4	7
Φ_{epi} (n/cm^{2}s)	3.54×10^{9}	2.05×10^{9}	1.40×10^{9}
$\Phi_{epi}/\Phi_{thermal}$	116.9	130.4	137.3
$\dot{D}_{fn}/\Phi_{epi}(Gycm^2)$	5.003×10^{-14}	7.155×10^{-14}	8.212×10^{-14}
$\dot{D}_{\gamma}/\Phi_{epi}(Gycm^2)$	1.131×10^{-13}	1.495×10^{-13}	1.916×10^{-13}
J/Φ	0.76	0.83	0.87

As Figure 1 shows, two different thicknesses of LiF are added to the designed system to remove large angle neutrons and make beam converge: 4 cm and 7 cm that are named as configuration (b) and configuration (c), respectively. In-air parameters calculated for three proposed configurations are given in Table 4. In our MCNP simulations, the number of particles emitted from neutron source was considered so large that the statistical uncertainties are less than 1%. Neutron and gamma fluxes were calculated using F4 tally and corresponding dose values were determined using fluence to KERMA conversion factors reported in ICRU 63 [20]. Moreover, J (surface current) was calculated using F1 tally.

In Figure 3, neutron spectrums related to the designed BSAs are compared with the proposed configuration of Ref. [8]. Figure 4 shows the calculated total neutron flux at 1 cm in front of three proposed configurations for different vertical distances.

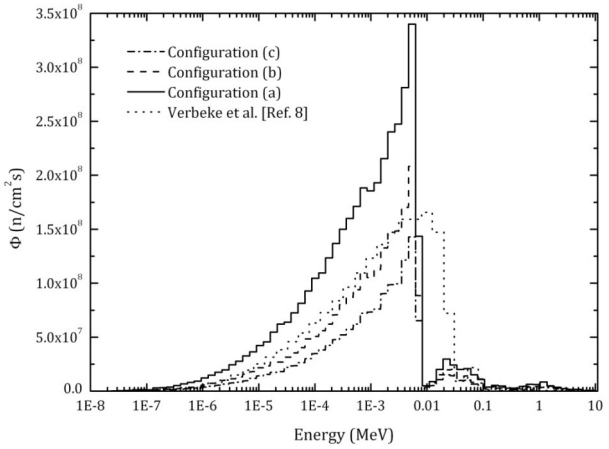

Figure 2. Neutron spectrum calculated at the beam port of three designed BSAs and the proposed configuration of Ref. [8].

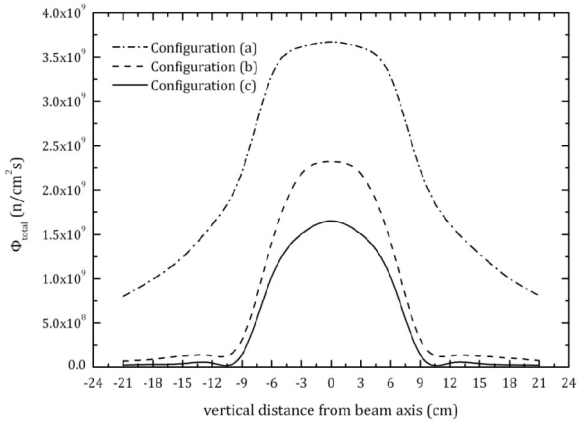

Figure 3. Total neutron flux calculated at 1 cm from beam port of configurations (a), (b), and (c) versus different vertical distances.

Figure 4 shows depth-dose curves due to the designed beam irradiation to the simulated head phantom. Moreover, Table 5 presents a comparison between calculated in-phantom parameters due to our designed BSAs and proposed configurations based on FiR1 and THOR reactors.

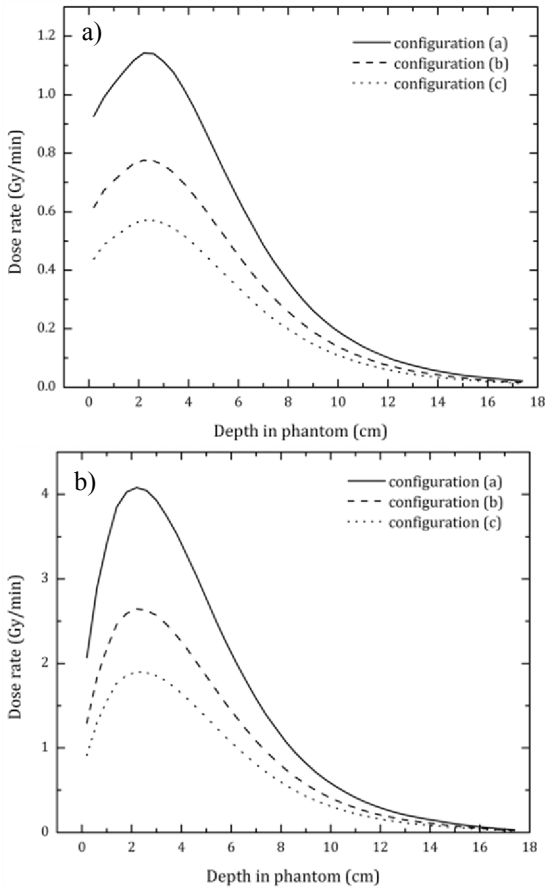

Figure 4. Total delivered dose rate to the a) healthy tissue and b) tumor, due to the beams related to the configurations (a), (b), and (c) for different depths in simulated head phantom.

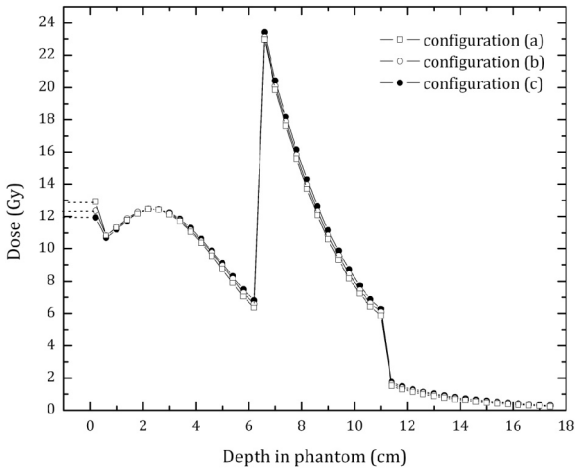

Figure 5. Total delivered dose to different depths in the simulated head phantom due to the designed beams related to three proposed configurations.

Calculated total dose (due to the thermal neutron dose, fast neutron dose, boron dose, and gamma dose) for different depths of phantom during the treatment time are shown in Figure 5.

Figure 6 shows a three-dimensional view of energy distribution in phantom due to the irradiated beam related to the configuration (c) for four different tumor positions in head. As can be seen, only one quarter of the simulated phantom are shown in these figures. In such a presentation, the central parts of phantom and tumor are observable. Red and blue colors are representative for maximum and minimum deposited energy, respectively. The maximum delivered dose to the tumor in treatment time for four mentioned positions of tumor are given in Table 6.

Table 5. In-phantom parameters evaluated for our designed BSAs and proposed BSAs based on FiR1 and THOR reactors.

In-phantom Parameters / Configuration	ADDR (cGy/min)	TT (min)	AD (cm)	TD (cm)	AR
Configuration (a)	114.23	10.94	8.05	5.71	3.33
Configuration (b)	77.56	16.11	8.07	5.69	3.19
Configuration (c)	57.02	21.91	8.11	5.72	3.13
THOR	50	25	8.9	5.6	-
FiR1	45	30	9.0	5.8	-

Table 6. Maximum delivered dose to the tumor for four different tumor position that are shown in figure 6.

Tumor Position	Distance from Tumor Center to the Phantom Surface (cm)	Maximum Delivered Dose to the Tumor in TT (Gy)
I	3.6	42.57
II	5.2	48.90
III	6.8	39.12
IV	8.8	23.42

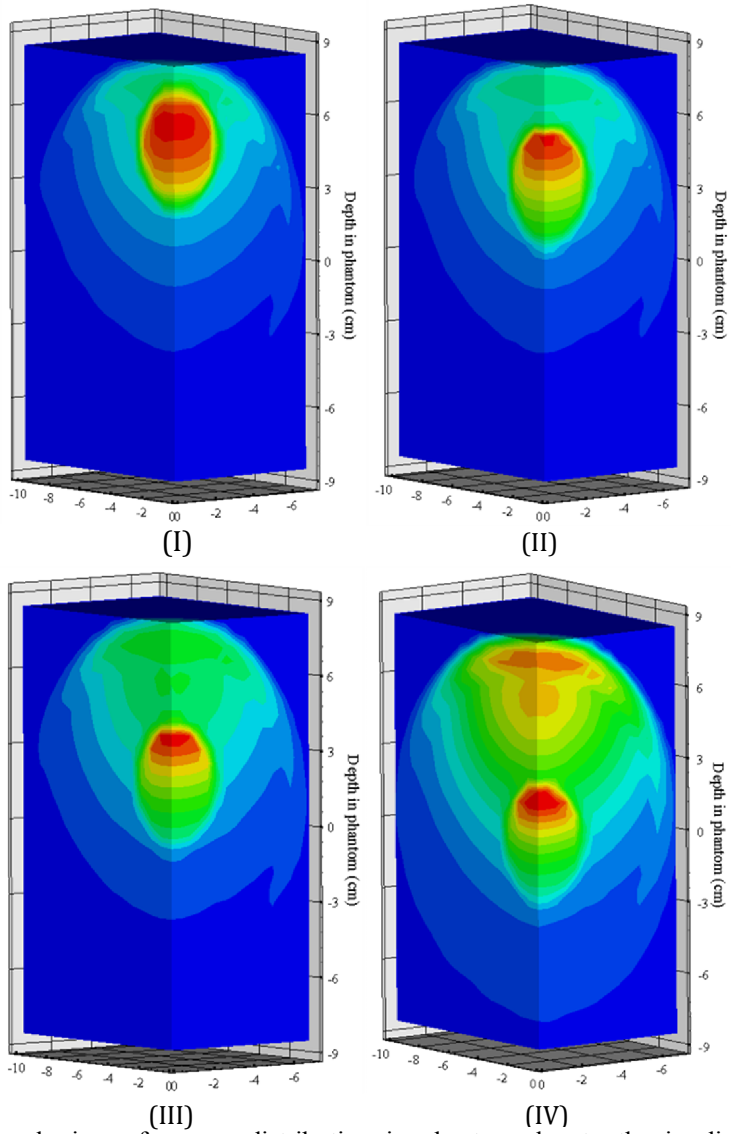

Figure 6. Three-dimensional view of energy distribution in phantom due to the irradiated beam related to the configuration (c) for four different tumor positions in the head. Red and blue colors are representative for maximum and minimum deposited energy, respectively.

4. Discussion

The MCNP modeling of Beam Shaping Assembly based on D-T neutron source is potentially able to provide a proper epithermal neutron output. Although all IAEA recommended criteria are satisfied, significant additional efforts are focused on the upgrading beam directionality to improve the quality of therapy. Simulation results show that adding 7 cm LiF to the BSA materials leads to increasing J/Φ considerably and removes large angle neutrons. In other words, by using this cell, forward oriented neutrons will pass through a cylinder with radius of 6 cm and large angle ones, which damage healthy tissue surrounding the tumor, will absorbed by LiF layer before reaching the patient. Although, neutron spectrums related to all proposed configurations belong to the desired epithermal energy range and fast and thermal neutron contaminations are removed as much as possible (see Figure 2). Figure 3 shows a considerable decrease in total neutron flux outside the beam port (-6 cm to 6 cm) for collimated beam. As an example, evaluated total neutron flux at 9 cm from beam axis of configuration (a) (J/Φ=0.76) is 2.2×10^{9} n/cm^2, while for configuration (c) (J/Φ=0.87) decreases to 1.4×10^{8} n/cm^2.

As Table 5 presents, the in-phantom parameters for three proposed configurations are pretty much the same, except for the treatment time. The results indicate that a higher neutron flux reduces the treatment time. As Figure 5 shows, in spite of the fact that evaluated TT due to the three designed beams are different, total delivered dose to phantom during treatment time are the same. Besides, the maximum delivered dose to skin due to the irradiated beam related to configuration (a), which is more intense and divergent than two other configurations, is higher than permissible value. Actually, although a higher J/Φ (i.e., better collimation) is obtained at the cost of beam intensity, the total delivered dose to tumor during treatment time is the same for all proposed configurations.

Figure 6 shows a three-dimensional view of energy deposition in simulated phantom for different tumor positions due to the irradiated beam related to configuration (c). According to the results, for the second tumor position presented in Table 6, tumor receives the highest dose in comparison with the others, while healthy tissues are survived.

5. Conclusion

In the presented paper, a study is carried out using MCNP code to design an optimal BSA based on D-T neutron generator. This system produces a suitable neutron beam for treating the deep-seated brain tumors in the context of BNCT. The results show that D-T neutron generator is a proper choice for in-hospital treatments due to the compact size, low cost, and ease of use. The resultant beam due to the optimal proposed BSA based on such a neutron source establishes an acceptable agreement between beam quality and beam intensity. Furthermore, biological dose evaluation in the simulated head phantom shows that designed beam is effective to treat deep-seated brain tumors in a reasonable time and improves treatment conditions. The calculations related to the determination of delivered dose to the simulated head phantom for four different tumor positions reveal that the proposed BSA is appropriate not only for treating deep-seated brain tumors, but also can be used for BNCT of tumors that are located at the central parts of the head.

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