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An Epithermal Neutron Beam Design for BNCT Using $^{2}H(d,n)^{3}He$ Reaction

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Abstract

A feasibility study was performed to design an epithermal neutron beam for BNCT using the neutron of 2.45 MeV on the average produced from $^{2}H(d,n)^{3}He$ reaction induced by plasma focus in the z-pinch instead of the conventional accelerator-based $^{3}H(d,n)^{4}He$ neutron generator. Flux and spectrum were analyzed to use these neutrons as the neutron source for BNCT. Neutronic characteristics of several candidate materials in this neutron source were investigated using MCNP code, and ^{7}LiF, 40%Al + 60%AlF_3, and Pb were determined as moderator, filter, and reflector in an epithermal neutron beam design for BNCT, respectively. The skin-skull-brain ellipsoidal phantom, which consists of homogeneous regions of skin-, bone-, or brain-equivalent material, was used in order to assess the dosimetric effect in brain. An epithermal neutron beam design for BNCT was proposed by the repeated work with MCNP runs, and the dosimetric properties (AD, AR, ADDR, and Dose Components) calculated within the phantom showed that the neutron beam designed in this work is effective in tumor therapy. If the neutron source flux is high enough using the z-pinch plasma, BNCT using the neutron source produced from $^{2}H(d,n)^{3}He$ reaction will be very feasible.

Key Words : *BNCT, NCT, $^{2}H(d,n)^{3}He$ reaction, epithermal neutron, beam design, MCNP*

1. Introduction

Although today's standard treatments such as surgery, radiation therapy, and chemotherapy have successfully cured many kinds of cancers, there are still many treatment failures. The promise of a new experimental cancer therapy with some indication of its potential efficacy has led many scientists from around the world to work on an approach called boron neutron capture therapy (BNCT) [1]. BNCT has the potential to be a very effective treatment of brain tumors, or especially other untreatable and deep-seated tumors such as glioma. This therapy can selectively kill tumor cells minimizing the damage of healthy tissues, based on the physiological characteristic of brain cells known as the Blood-Brain Barrier (BBB) and the boron-neutron interaction that produces an alpha particle and a lithium ion by thermal neutron irradiation in brain cells following the administration of a suitable boronated agent. The emphasis has been on the use of epithermal neutron beams to produce the required thermal neutron flux at brain depth because these higher energy neutrons can penetrate deeper into the brain volume before slowing to thermal energy.

One of the important characteristics of the neutron source for BNCT is flux. This must be large enough so that therapy procedures can be concluded in a reasonable time. The common neutron sources currently available for potential use in BNCT are research/medical reactor, accelerator, and californium-252. The largest neutron source is a nuclear reactor. Since reactors are capable of delivering higher neutron flux levels to the patient than other neutron sources, BNCT studies using reactors as a neutron source have been performed most actively all over the world and some countries including the U.S. and Japan introduced good treatment results as well as conducted clinical trials using reactors. However, because the construction of new reactors for BNCT leads to financial problem, spatial restriction, approval issue, etc., it is not easy to equip a hospital with the reactor providing BNCT facilities. Although the proton accelerators as an alternative neutron source to reactor have been actively being pursued for the last ten years, no clinically usable neutron beam based on an accelerator source has yet been developed and research into the development of such a source is currently underway by a number of investigators. The use in BNCT of californium-252, that is a self-fissioning isotope, is being investigated conceptually in that the application of assemblies containing subcritical quantities of a fissile material can improve relatively low neutron flux density The low production rate (<1 g/year in the U.S.) and short half-life (2.65 year) makes, however, widespread use of californium-252 for BNCT unlikely.

Recently, the high energy neutron produced from $^2H(d,n)^3He$ (D-D) or $^3H(d,n)^4He$ (D-T) reaction is interesting as a new neutron source for BNCT [2]. The D-T reaction neutron generation device using one-body accelerator has been developed and spread, but it requires a high cost and has the drawback that the high energy neutron of about 14.1 MeV on the average produced from this fusion reaction makes it more difficult moderating and shielding. While the energy of neutron produced from the D-D reaction is lower as about 2.45 MeV on the average, this reaction cannot give sufficient neutron flux by only ion accelerator because the reaction rate is less than 1/100 of the D-T reaction rate. However, if it is possible to develop a small size pulse neutron generator which can produce high flux neutron using the z-pinch plasma D-D reaction rather than ion accelerator, the application to BNCT neutron source will be of most interesting because of the relatively low energy nature and the small size expected to be achieved.

The purpose of this study is to evaluate the feasibility of an epithermal neutron beam design for BNCT using neutrons produced from the D-D reaction induced by plasma focus in the z-pinch.

2. Backgound and Rationale

2.1. Boron Neutron Capture Therapy

The focus of radiation therapy is to irradiate cancer with dose as much as possible while to irradiate healthy tissue below threshold dose and it is just the same with the therapy using neutron. The principle of neutron capture therapy (NCT) is that neutron irradiation following the administration of a compound absorbing neutron well and concentrating on cancer cell leads the compound within cancer to absorb neutrons and the radiation from the reaction kills cancer cell. Especially, BNCT uses boron compound which has nontoxicity, selective assimilation into tumor cell, and activation by thermal neutron, and can selectively kill tumor cells as inducing (n,α) reaction between boron and neutron. The neutron capture reaction with boron that allows BNCT is as follows:

$$^{10}B + n \rightarrow {}^{11}B^* \rightarrow \begin{cases} {}^{7}Li(1.01\ MeV) + \alpha(1.78MeV) & (6.3\%) \\ {}^{7}Li(0.84\ MeV) + \alpha(1.47MeV) + \gamma(0.48MeV) & (93.7\%) \end{cases} \quad (1)$$

^{10}B has (n,α) cross section of 3837 b for thermal neutron. This is much higher than the neutron absorption cross sections of other elements in brain, which are typically much less than 1 b. In the reaction, $^{10}B(n,\alpha)^{7}Li$, the ^{10}B atom becomes ^{11}B atom in the excited state for a very short time (~ 10^{-12} seconds) by thermal neutron capture and the ^{11}B atom then fissions producing an alpha particle, and a recoiling ^{7}Li ion, and gamma ray in 93.7 % of the reaction. Because the charged particles with an average total kinetic energy of 2.339 MeV have a range in tissue of 5μm (^{7}Li) and 9 μm (α), which is less than or comparable to a cell diameter, the entire energy can be absorbed in a cell or in a cell and its nearest neighbors, depending on the location of the ^{10}B in the cell. Consequently, the DNAs of tumor cells are damaged selectively by the energetic alpha particles and ^{7}Li fission products. To provide a significant therapeutic effect, the boron must have a high concentration in the tumor, and the neutron beam at the tumor position must consist primarily of low energy neutrons that will readily interact with the boron.

2.2. Specific Dosimetric Considerations

In general, three dosimetric properties or figures of merits have been used to facilitate neutron beam quality evaluation and to describe the performance of NCT beams. These include the advantage depth (AD), the advantage ratio (AR), and the advantage depth dose rate (ADDR), which were developed by the MIT/BIDMC BNCT group and used at the beam design workshop held at MIT [3]. The AD is useful for evaluating the ability of a neutron beam to treat deep-seated tumors. The AD provides a measure of the maximum useful depth for therapeutic benefit and is defined in two ways: the minimum AD and the maximum AD. The minimum AD is the maximum depth in the phantom at which the delivered dose to a tumor containing ^{10}B is greater than the maximum dose to healthy brain tissue anywhere in the phantom when healthy tissue contains ^{10}B. The maximum AD is similarly defined as the maximum depth in the phantom at which the delivered dose to a tumor is greater than the maximum background dose to healthy brain tissue. Beyond these depths, the tumor would be expected to receive a smaller dose than the maximum delivered to healthy tissue. To provide therapy to a tumor at any part of the patient' s brain, the ADs must be equal or close to half the thickness of the head, which is about 7 to 9 cm. The AR is a ratio of the dose to the tumor over the dose to the tissue, integrated from the phantom surface to the maximum AD. The AR is a measure of the beam' s ability to minimize integral dose to healthy tissue while effectively treating the tumor. Therefore, it is desirable to keep this ratio as high as possible. The ADDR is the dose rate at the maximum AD and was developed primarily as a clinically meaningful neutron beam intensity criterion for neutron beam design studies. In addition, the dose rate to a tumor located at a depth of the midline in the brain phantom is also evaluated. Because a useful beam should also be able to deliver sufficient dose to tumor at brain center and within a reasonable time, the intensity of the dose rate at brain center becomes an important design criterion.

The tumor dose composition is routinely divided into a high LET component, from fast neutrons and $^{14}N(n,p)^{14}C$ reactions of thermal neutrons; a low LET component, primarily from gamma rays; and a boron-induced dose component, from thermal neutron reactions. Therefore, the boron dose must be as high as possible to treat tumors effectively and the high LET as low as possible to minimize damage of healthy tissue.

3. Neutron Source

The neutron yield for plasma in pulse mode such as plasma focus can be predicted by experimental data which have indicated a scaling law for neutron yield per pulse, Y, as a function of capacitor energy, E. This scaling law for the D-D reaction may be written approximately as

$$Y = 10E^{2}, \tag{2}$$

where E is in joules and appears to be approximately followed over the whole range of energy over which data is available, i.e., 1 kJ to 1 MJ [4]. Since the plasma discharge energy is the capacitor energy, if high performance capacitors (C = 1 μF, V_{max} = 50 kV) currently available are used in Marx Bank Generator (MBG), the neutron yield can be increased. Therefore, a capacitor of C = 1 μF and V_{max} = 1 MV is available in the case of 20 step MBG and E is calculated as the following

$$E = \frac{1}{2}CV^{2} = \frac{1}{2}\left(10^{-6}\right)\left(10^{6}\right)^{2} = 5 \times 10^{5} J. \tag{3}$$

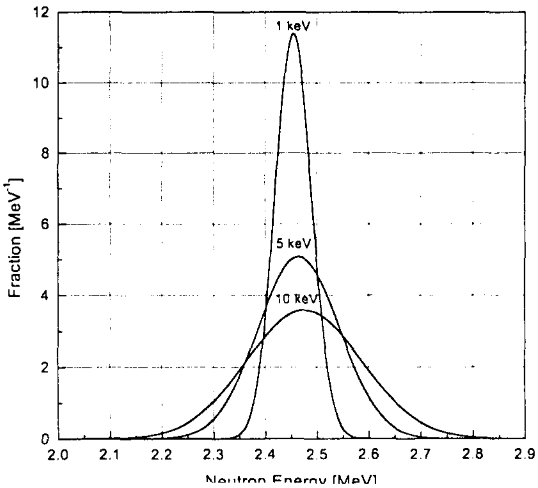

Fig. 1. Neutron Energy Spectra of $^{2}H(d, n)^{3}He$ Reaction as Ion Temperature

The neutron yield rate is then 2.5×10^{12} neutrons/shot by Eq. (2). Consequently, the neutron flux density at distance of 50 cm from the reaction focus is about 1.0×10^{11} neutrons/cm^{2} · sec if repeating the shots in high frequency of 1 kHz by use of switches like Thyratron. In this study, it was assumed that the flux of neutron source is 1.0×10^{11} neutrons/cm^{2} · sec based on the above results and the neutrons are emitted monodirectionally across a 2 cm diameter flat circular surface.

The D-D reactions produce neutrons of about 2.45 MeV on the average with Gaussian spectrum. Figure 1 shows neutron spectra for some temperatures of ion in the D-D reaction. The neutron energy spectrum for the D-D reaction was modeled as the Gaussian fusion energy spectrum using coefficients recommended in the Monte Carlo N-Particle (MCNP) code [5] manual and it was assumed that the ion temperature is 1 keV since it is available to plasma focus in the z-pinch.

The repeated D-D reactions in high frequency such as 1 kHz lead to increase the number of the reaction products, i.e., ^{3}H or ^{3}He, and therefore

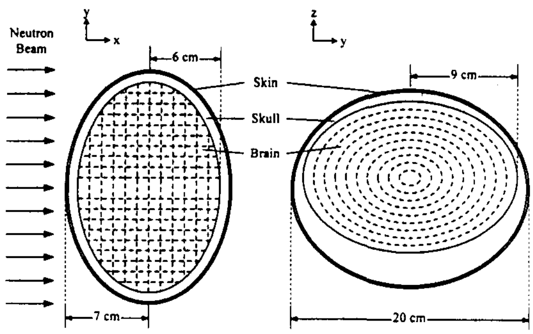

Fig. 2. Schematic Illustration of the Skin-Skull-Brain Ellipsoidal Phantom Modeled by MCNP

the concomitant reactions of the products interfere the D-D reactions. Especially, one reaction, D-T reaction, emits the high energy neutrons of about 14.1 MeV on the average and the other reaction, D-^{3}He reaction which emits protons, decreases the D-D reaction rate as the competitive reaction. However, both are not remarkable because the densities of products in the reaction volume are much less than that of deuterium. This study dose not, therefore, consider the interference of the concomitant reactions.

4. Epithermal Neutron Beam Design

The neutron energy must be favorable for BNCT to design an acceptable neutron beam. Fast neutrons increase the dose to the healthy tissues at the surface, i.e., the skin, due to high linear energy transfer (LET) characteristic and are thus therapeutically not as useful. Though ^{10}B has the high (n,α) cross section for thermal neutron, it is not suitable for the treatment of deep-seated tumors. Therefore, for the treatment of deep-seated tumors, the incident neutron beam must have a somewhat higher energy than is thermal energy for the (n,α) reaction (i.e., an 'epithermal' energy). In this case, the body's abundance of ^{1}H serves as a neutron moderator, reducing the energy of the incident beam as it passes through the tissue. Consequently, an epithermal neutron beam has a thermal neutron flux peak at 2 ~ 3 cm depth in the tissue, delivers a much lower thermal neutron dose to the tissue at the surface, and can penetrate the tissue to give greater doses at depth. Previous works at Massachusetts Institute of Technology (MIT) [6] and Hanyang University [7] indicate the best neutron beam energy for BNCT ranges from 4 eV to 40 keV, which belongs to the epithermal energy region.

4.1. Dosimetric Properties Analysis

The mathematical model employed to represent the human brain and its surrounding structures is based on the geometry of a Monte Carlo model originally described by Snyder *et al* [8]. The model used in this work is the skin-skull-brain ellipsoidal brain phantom proposed by Deutsch and Murray [9] for Monte Carlo dosimetry calculations as shown in Figure 2. It is based on the geometry of three non-concentric ellipsoids representing skin, skull, and brain that contain homogeneous regions of skin-, bone-, or brain-equivalent materials. To estimate the contribution of individual dose components as a function of depth, the phantom model was divided into small cells. Various dose components were assessed in each cell.

In this study, the neutron and photon fluxes computed for each cell of the brain phantom were converted to dose rates by user-supplied kerma factors. The neutron and photon fluxes were modified by the flux-to-dose rate conversion factors of Caswell *et al.* [10] and Zamenhof *et al.* [11], respectively, to yield dose rate in cGy/min. To estimate the ^{10}B contribution to dose, the thermal neutron flux was modified by ^{10}B flux-to-dose rate conversion factors listed by Zamenhof *et al.* [11] and then multiplied by the ^{10}B concentration assumed to exist in either tumor or healthy tissue. In the tumor, a ^{10}B concentration of 40 ppm was assumed from the work of Coderre *et al.* [12], which has demonstrated a 4:1 ratio of ^{10}B in tumor to healthy tissue based on biodistribution studies in mice. This ratio has been adopted in the present work. RBE values of 4.0, 4.0, and 1.0 applied to the ^{10}B reaction products, neutrons, and photons, respectively, have also been used.

The dose components calculated in the brain phantom are used to define background dose, total tissue dose, and total tumor dose such as the followings.

- background dose = fast neutron dose + thermal neutron dose + induced photon dose,
- total tissue dose = background dose + 10 ppm boron dose,
- total tumor dose = background dose + 40 ppm boron dose.

The induced photon dose is defined as the dose by photons produced from the interactions of neutrons with structural materials and can be obtained from the MCNP neutron/photon coupling calculations.

4.2. Structuring Materials

The initial energy of the neutrons produced from the D-D reaction is about 2.45 MeV on the average. The energy of the neutrons must therefore be reduced to the epithermal energy through a moderator before the neutron interacts with the ^{10}B nuclei in the tumor cells. As an additional consequence of using moderator, gamma rays as well as neutrons of all other energies are present in the neutron beam, which themselves can give significant doses to the healthy tissue. These unwanted gamma rays or neutrons, especially, fast neutrons, must therefore be removed from the beam. That is to say, the neutron beam design for BNCT needs the procedure, which makes the neutron beam suitable for treatment of tumors from a neutron source, as well as the neutron source available. This is achieved by neutron beam assemblies using advantage of the nuclear characteristics of certain materials.

The neutron beam assemblies are configured in moderator, filter, reflector, and shield. A cylinder model is recommended because of the benefits of easy fabrication and modeling. This shape is chosen for the reflector, and the moderator and filter are designed as cylinders to fit inside the reflector. The requirements and selection of materials for each of the system components are as in the followings.

Because the purpose of the moderator is to reduce the energy of the neutrons emitted by the neutron source, it is most efficiently accomplished with low Z material. However, since the neutron beam to design in this work is the epithermal neutron beam, the moderator requires a material to moderate properly the neutron source of 2.45 MeV on the average. A variety of moderators were investigated using MCNP code and then the ^7LiF was finally determined. The light elements, e.g., ^1H and ^2H, thermalize neutrons very quickly and shift the neutron spectrum down to below epithermal energies. While the heavier element, ^7Li, does not shift the neutron spectrum down as fast as the light elements but is still very effective in slowing down neutrons in a short distance. The elastic scattering resonances of F extending down to about 27 keV can be beneficially to downscatter neutrons above this energy.

The neutrons moderated by the moderator have still fast neutrons, which contribute a substantially higher dose than any other dose component at the surface of brain, as well as thermal and epithermal neutrons, and therefore these neutrons must be filtered. In this study, the mixture of aluminum

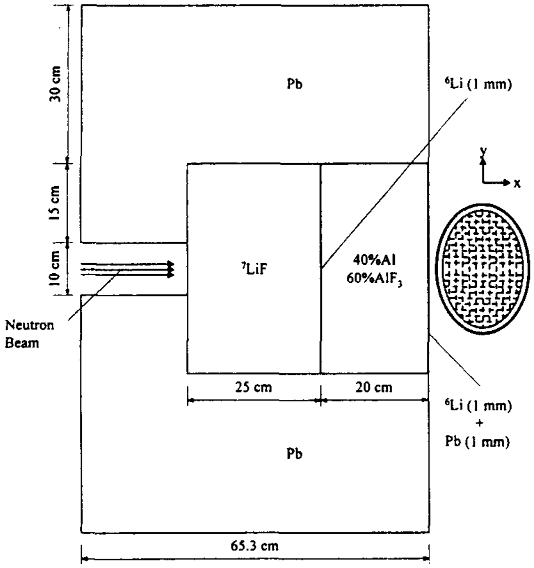

Fig. 3. Diagram of the Epithermal Neutron Beam System Using $^2H(d, n)^3He$ Reaction

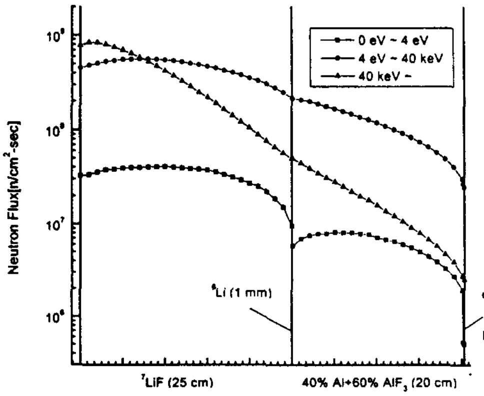

Fig. 4. Flux Distributions along Circular Surfaces of 20 cm in Radius within the Neutron Beam System

fluoride and aluminum (40%Al + 60%AlF^3) was determined as the filter material by analyzing neutronic characteristics of several candidate materials. The elastic scattering resonances of Al supplement the ones of F from 27 keV up to the high-energy tail. These resonances at high energies will preferentially reduce the number of neutrons above 27 keV.

The purpose of the reflector is to redirect neutrons back in the direction of the therapy beam and therefore it can be accomplished with high Z and dense materials. Especially, the reflector must have high absorption cross section as well as scattering cross section and effective potential in shielding of gammas. In this study, the lead was determined as the reflector material.

Shielding concerns for this system must include shielding of neutrons and photons for the patient and others in the surrounding area. The lead reflector will serve as the primarily photon shielding. Additional shielding can be added to the system by increasing the reflector thickness or by adding secondary shielding materials. However, shielding for the surrounding area is not treated in this design work because it is a secondary concern of this study.

4.3. Beam Design and Results

A neutron beam assembly suitable for the epithermal neutron beam was designed using the D-D neutron source, the structural materials, and the requirement of neutronic characteristics described above. The assembly is based on a cylindrical shape and the dimensions were determined by the repeated MCNP runs. A final diagram of the proposed D-D reaction based epithermal neutron beam system for BNCT is presented in Figure 3. This design shows that the moderator (^{7}LiF) is designed as the cylinder shape of 20 cm in diameter and 25 cm in thickness and the filter (40%Al + 60%AlF$_3$) of 20 cm in thickness is attached to the moderator. A small ^{6}Li filter of 1 mm between the moderator and filter is used to reduce the induced photons via (n,γ) reactions of Al within the filter. The reflector (Pb) thickness around the moderator and filter is 30 cm

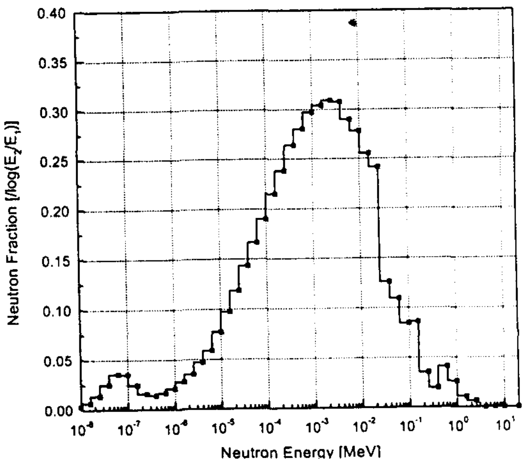

Fig. 5. Neutron Spectra of the Neutron Beam Designed at the Patient-End

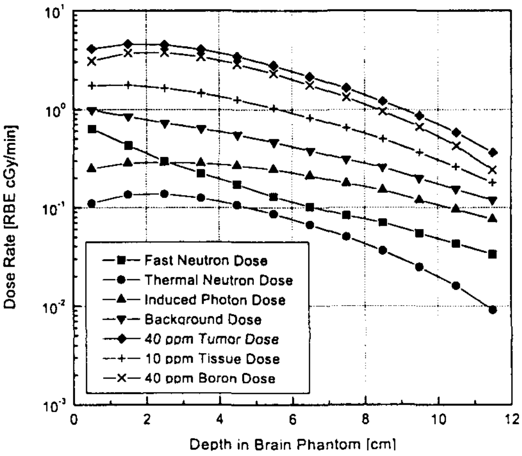

Fig. 6. Dose Components with Depth in the Brain Phantom

Table 1. Dosimetric Properties for the Epithermal Neutron Beam Designed

AD_{max} [cm]	AD_{mim} [cm]	AR	ADDR [RBE cGy/min]	Dose Rate at Brain Center [RBE cGy/min]
9.108	7.240	5.591	9.863	2.437

and one around the incident neutron sources is 45 cm. The ^6Li and Pb of 1 mm are also added after the filter to reduce the thermal neutrons and to shield the photons, respectively, at the patient-end.

Figure 4 and 5 show the flux distributions along circular surfaces within the neutron beam system and the neutron energy spectra of the neutron beam designed at the patient-end, respectively. The both figures indicates that about 82.5 % of neutrons are distributed in the epithermal energy region (4 eV ~ 40 keV).

Some of the dosimetric properties of the beam designed are listed in Table 1. Table 1 shows that the neutron beam designed in this study is predicted to be capable of providing a maximum AD of 9.108, a minimum AD of 7.240, an AR of 5.591, and a therapeutic RBE dose rate of 2.437 cGy/min at center of the brain phantom. Since typical tumors may take about 2000 RBE cGy to kill, the result indicates that a tumor can be treated over 27 times in about 30 minutes at one time. The total treatment time (~13.7 hours) is about 61 times less than the total treatment time (840 hours) provided by the neutron beam designed using the accelerator-based D-D reaction introduced by Verbeke *et al* [2].

A more complete breakdown of the dose components of the therapy beam is presented in Figure 6. This figure shows the dose components as a function of depth in a 2 cm diameter cylinder along the central axis of the ellipsoidal brain phantom. In Figure 6, the fast neutron dose falls off quickly due to rapid thermalization by the light elements such as hydrogen within the brain phantom while the thermal neutron dose shows the rise with depth. The curves representing the induced photon and boron doses are similar in shape to the thermal neutron dose since both are a direct result of the magnitude of thermal neutron flux at depth. However, the induced photon dose falls less rapidly at larger depths due to the larger path length of photons compared to either neutrons or the ^{10}B reaction products.

5. Conclusions

A conceptual design was performed to evaluate the feasibility of the epithermal neutron beam design for BNCT using neutrons produced from $^{2}H(d,n)^{3}He$ (D-D) reaction by MCNP simulations. The emphasis is on the D-D fusion reaction induced by plasma focus in the z-pinch in order to overcome the low probability of the accelerator-based D-D reactions. It was assumed that the flux of neutron source is 1.0×10^{11} neutrons/cm$^2 \cdot$ sec based on theoretical calculations and the neutrons are emitted monodirectionally across a 2 cm diameter flat circular surface with the Gaussian energy spectrum. The skin-skull-brain ellipsoidal phantom, which consists of homogeneous regions of skin-, bone-, or brain-equivalent material, was used in order to assess the dosimetric effect in brain. The repeated MCNP runs determined ^{7}LiF, 40%Al + 60%AlF_3, and Pb as a moderator, filter, and reflector of the epithermal neutron beam design for BNCT, in respective.

The dosimetric properties calculated within the phantom showed that the neutron beam designed in this work is effective in tumor therapy and the total treatment time needed for effective therapy will be reduced in the neutron beam designed through this study. If the neutron source flux is high enough, BNCT using the neutron source produced from the D-D reaction will be very feasible.

Acknowledgement

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