INVESTIGATION OF PHOTON DOSES REACHING HEALTHY TISSUES IN THE USE OF DIFFERENT NEUTRON ENERGIES IN BORON NEUTRON CAPTURE THERAPY

by

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Technical paper
https://doi.org/10.2298/NTRP2204334T

Boron neutron capture therapy is a unique treatment method that aims to kill the tumor cells with the help of heavy particles. Particles resulting from the interaction of the tumor region containing ^{10}B atoms with thermal or epithermal neutrons have the most important role in this treatment method. In this study, gamma radiation reaching healthy tissues, which is the result of $^{10}B(n,)^{7}Li$ reaction, was investigated. A simulation suitable for boron neutron capture therapy treatment, including the human head model, was created by the Monte Carlo N-Particle (MCNP) program. By using five different neutron energies, the gamma radiations resulting from the $^{10}B(n,)^{7}Li$ reaction in the determined regions, close to the tumor tissue, were investigated. It was observed that the healthy tissue between the tumor area and the surface is exposed to the highest gamma flux and the highest gamma radiation absorption. It was also observed that these values increase as neutron energy decreases. It was found that the gamma doses received by some regions outside the neutron irradiation area could be significant. It has been understood that the change in neutron energy may cause significant changes in gamma radiation values reaching healthy tissues, especially in regions close to the surface. In boron neutron capture therapy treatments, the neutrons sent to the tumor should be selected depending on the location of the tumor and the size of the tumor area. This study contains significant data about photon doses in healthy tissues around the brain region treated using different neutron energies with the boron neutron capture therapy technique.

Key words: boron neutron capture therapy, MCNP program, neutron energy

INTRODUCTION

The boron neutron capture therapy (BNCT) is a type of radiotherapy, based on nuclear reaction. It is mostly applied for head and neck cancer, skin cancer and glioblastoma multiforme treatment [1-6]. It is based on the absorption of the ^{4}He particle formed by the interaction of non-radioactive ^{10}B atoms with low energy neutrons (thermal or epithermal neutron) by the tumor tissue. At the end of this interaction, ^{10}B atom turns into ^{7}Li atom. The ^{4}He particles release high energy along their short path. The path crossed by the ^{4}He particle is roughly the size of a cell. Therefore, the reaction takes place in a single cell [6].

The success of BNCT treatment is directly dependent on the accumulation of ^{10}B agents in tumor cells. The most commonly used boron agents in clinical studies and research are borocaptatesadium (BSH) and boronophenylalanine (BPA) [6, 7]. The trouble that may be a problem in BNCT treatment is the accumulation of boron atoms in healthy tissues after intravenous injection of BSH or BPA into the body and the possibility of these tissues being exposed to neutron radiation [8]. The studies performed a BPA-administered rats showed that the rate of boron concentration, collected in the tumor and healthy tissue, was safe and suitable for treatment [9-11].

Since the tumor needs amino acids in case such as protein synthesis and the tumor has a higher metabolic activity than healthy tissue, the compounds with ^{10}B agent applied intravenously to the patient are collected 3-4 times more in the tumor cell compared to the healthy tissue [1, 12].

The ^{10}B atoms accumulate under specified conditions in malignant cells coexisting with healthy cells. After sending thermal neutrons to the area to be treated, the resulting ^{7}Li and ^{4}He heavy particles destroy malignant cells [6, 13].

As a result of the $^{10}B(n,)^{7}Li$ reaction, 2.79 MeV energy is released. In 94 % of nuclear reactions, gamma ray with energy of 0.48 MeV occurs. The remaining 2.3 MeV particle energy is transferred to the

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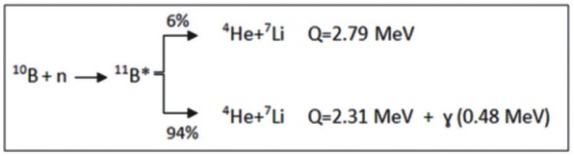

Figure 1. Energies arising in the reaction $^{10}B(n,)^{7}Li$

tissue. In 6 % of the reaction, the ^{10}B atom directly undergoes basic decay [1, 13]. The energies and probabilities occurring in the reaction are shown in fig. 1.

The reason for using boron is that nuclear reaction can be done with low neutron energies and has a high capture cross section [8].

An important handicap of BNCT treatment is that thermal neutrons (neutrons of energies less than 1 eV) cannot move far through the body. This causes the desired dose not to be given to deep tumors. For this reason, epithermal neutron (1 eV < En < 10 keV) beams with higher energy than thermal neutron beams have been utilized in BNCT clinical trials [6].

When an epithermal neutron beam enters the tissue, it creates the maximum flux at a depth of 2-3 cm and the flux begins to decrease as the depth increases. Thermal neutron beam almost creates maximum flux at the surface and it flux decreases as it goes deeper. This means that it is better to use a thermal neutron beam for tumors close to the surface, and an epithermal neutron beam for the treatment of deeper located tumors [6, 14-16].

Since the energy transfer resulting from the nuclear reaction is limited to the cells in which neutrons are captured, dose transfer occurs at the cellular level. With this feature, BNCT, becomes a good option for the treatment of tumors that cannot be reached surgically, tumors that cannot be treated with methods such as photon treatment and stereotactic body radiation therapy.

This study aims to investigate the gamma radiation dose received by the healthy tissues around the tumor tissue containing ^{10}B atom in BNCT treatments, using different neutron energies. In order to achieve this purpose, a simulation suitable for BNCT treatment was created in the MCNP program, and the gamma radiation absorption resulting from the nuclear reaction, in different regions around the tumor tissue, was calculated using the Monte Carlo method.

MATERIALS AND METHODS

The MCNP program

In this study, MCNP v.2.6.0 radiation transport code [17] was used to calculate the doses that could occur in the environment and to make modeling. The MCNP is an advanced code system that works with the Monte Carlo method. The MCNP technique follows all particles that may occur in environment from birth to death and takes into account all interactions (absorption, collision *etc*.) they make in the environment. Particle transport is calculated using random numbers. We need to input the results we want to obtain, with the help of some commands. In this input sequence, the desired results in a volume are obtained by the commands called *tally*. We used F4 and F6 tallies in our study. The DE/DF command system was used both to calculate the kerma for each identified material and to calculate the rate of nuclear reactions. Equivalent doses in the desired volume were obtained in millisievert (mSv) by using flux-to-dose conversion factors with the help of F4 and DE/DF cards in MCNP. In addition, the absorbed dose in the desired volume was calculated in $MeVg^{-1}$ with the help of the F6 card [18]. Since gamma radiation will be examined, the letter *p* symbolizing gamma radiation has been added to the sides of the *tally* cards. The 1 10^{8} histories were run for simulation in the software. For detailed information, the MCNP manual booklet can be studied [19, 20].

For the dosimetric comparison, the neutron energies generated in the MCNP were chosen in the thermal and epithermal neutron energy range, and these values were 250 eV, 25 eV, 2.5 eV, 0.25 eV, and 0.025 eV. The field to be irradiated was modeled similar to the human head, including skull bone. The neutron source used in modeling was defined 5 cm above the head surface, similar to previous studies [1, 21]. In addition, the neutron source was formed in a circular structure. A 20 cm thick lead shield was formed around the neutron source. The diameter of the neutron source used in our study is 10 cm, since the 10 cm diameter beam field is used most frequently in BNCT treatments [1,15].

The human head model was simulated in MCNP. The part to a depth of 0.8 cm from the surface was defined as the skull. A tumor structure with a diameter of 4 cm was placed at a depth of 2 cm from the surface. The skull density was defined as 1.4 gcm^{-3} and the inside of the head as soft tissue. The part defined as the tumor was created with ^{10}B material. Five voxels with a volume of 0.5 cm^{3} were created in regions close to the tumor tissue. The 3-D version of the simulation created in MCNP is shown in fig. 2. In fig. 2, the thick big hoop structure, small sphere and boxes represent the lead shield, the tumor structure and the volumes of interest, respectively. As shown in the fig. 2, each voxel has been assigned a number so that the studied volume can be easily understood. The distances of 1-5 cells to the surface of the tumor region are 10 mm, 10 mm, 3 mm, 3 mm, and 35 mm, respectively.

Boron neutron capture therapy

The BNCT is a type of radiotherapy based on the destruction of the tumor cell by heavy particles formed due to neutron irradiation of this region, after the accumulation of a boron atom in tumor cells. To deposit the ^{10}B atom into cancer cells, agents containing protein

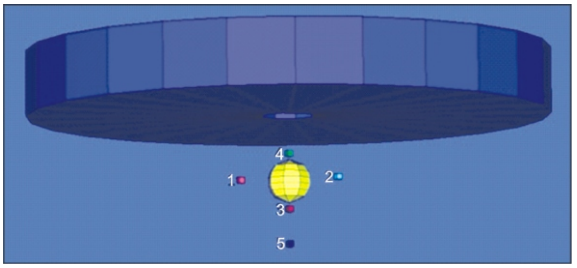

Figure 2. The 3-D version of the simulation (excluding skull and head model)

compounds are often used. When ^{10}B captures thermal or epithermal neutron, ^{4}He and ^{7}Li particles are formed in the environment and their ranges are 9 μm and 5 μm, respectively [1].

After the boron atom accumulates in tumor cells, the tumor area is irradiated with thermal or epithermal neutrons. Nuclear reactions occur when neutrons are captured by ^{10}B atoms. The energy generated during the reaction is absorbed by the tumor tissue, thus treating the tumor area. Since the distance that the particles created during the reaction can travel is very small, healthy tissues are protected. The effect of the treatment is directly related to the sufficient amount of ^{10}B atoms in tumor region and sufficient neutrons to be sent to the fields [1]. When considering the penetration of thermal neutrons or epithermal neutrons, the energy of the sent neutron should be chosen depending on the depth of the tumor.

When ionizing radiation is given, the biological response to occur in the environment depends on the type of radiation and this biological response is expressed by relative biological effectiveness (RBE). In the $^{10}B(n,)^{7}Li$ nuclear reaction, due to the inhomogeneous distribution of the boron compound in the tumor tissue and the short distances of the particles formed, the absorbed dose definition cannot be defined for this nuclear reaction. The RBE cannot be identified in BNCT treatments and the biological factor cannot be also determined, as the RBE is valid when the absorbed dose is known. However, as defined IAEA-TECDOC-1223, these data can be defined separately with experimental data. The sum of additives from different doses, including biological factors, helps us achieve the total dose in BNCT treatment [1]. The weighted total dose D_{WTD} is expressed as the sum of the different components, taking into account the different biological efficiency of each component and it can be expressed as following [13, 22]

$$D_{WTD} \quad D_y W_y \quad D_P W_P \quad D_B W_B \quad D_N W_N \quad (1)$$

where W_y, W_P, W_B, and W_N are the RBE factors of gamma, proton, boron components and neutron, respectively. In addition, the D_y, D_P, D_B, and D_N are the gamma dose, proton dose, boron dose and neutron dose, respectively.

RESULTS

The 2-D version of the simulation is shown in fig. 3, where, the two-rectangle structures, small circle and thin shell structure represent the lead shield, the tumor structure and the skull, respectively.

When the ^{4}He particles that may occur in the surrounding tissue as a result of the simulation created in MCNP are examined, the result in fig. 3(b) is obtained. The formation of ^{4}He particles in the region containing the ^{10}B atom also indicates that the simulation was modeled correctly.

In the simulation performed with MCNP software, the gamma radiation in the regions to be examined was reviewed with three different units as $cm^{-2}s^{-1}$ (particle flux), $MeVg^{-1}$ (absorbed dose) and mSv (equivalent dose).

The gamma radiation flux obtained by the simulation after the reactions is shown in the tab. 1.

DISCUSSION

When the Cells remaining 3 mm below (Cell 3) and 3 mm above (Cell 4) from the tumor region containing ^{10}B atoms along the neutron radiation axis are examined, it is seen that the gamma flux in the Cell 4 is

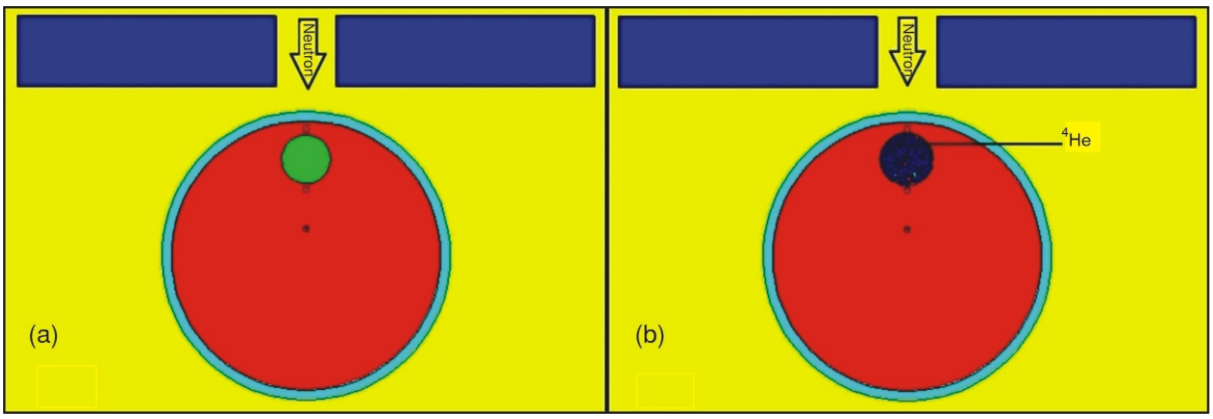

Figure 3. The 2-D version of the simulation on X-Z axis (a) and ^{4}He particles formed in the environment as a result of neutron irradiation (for 2.5 eV neutron energy (b)

Table 1. The flux values obtained at different neutron energies

Particle flux [$cm^{-2}s^{-1}$]					
Cell	250 eV neutron energy	25 eV neutron energy	2.5 eV neutron energy	0.25 eV neutron energy	0.025 eV neutron energy
1	$3.4721 \cdot 10^{-3}$	$3.4266 \cdot 10^{-3}$	$3.4329 \cdot 10^{-3}$	$3.3891 \cdot 10^{-3}$	$3.8958 \cdot 10^{-3}$
2	$3.5235 \cdot 10^{-3}$	$3.4523 \cdot 10^{-3}$	$3.4684 \cdot 10^{-3}$	$3.4103 \cdot 10^{-3}$	$3.9883 \cdot 10^{-3}$
3	$3.8639 \cdot 10^{-3}$	$3.6859 \cdot 10^{-3}$	$3.6210 \cdot 10^{-3}$	$3.5213 \cdot 10^{-3}$	$4.2953 \cdot 10^{-3}$
4	$1.3645 \cdot 10^{-3}$	$1.6322 \cdot 10^{-3}$	$1.7737 \cdot 10^{-3}$	$1.8290 \cdot 10^{-3}$	$2.8673 \cdot 10^{-3}$
5	$1.5409 \cdot 10^{-3}$	$1.5061 \cdot 10^{-3}$	$1.4666 \cdot 10^{-3}$	$1.3939 \cdot 10^{-3}$	$1.6106 \cdot 10^{-3}$

Table 2. The absorbed dose values of gamma radiation in the environment

Absorbed dose [$MeVg^{-1}$]					
Cell	250 eV neutron energy	25 eV neutron energy	2.5 eV neutron energy	0.25 eV neutron energy	0.025 eV neutron energy
1	$6.1788 \cdot 10^{-5}$	$6.1538 \cdot 10^{-5}$	$6.1065 \cdot 10^{-5}$	$6.0302 \cdot 10^{-5}$	$5.1596 \cdot 10^{-5}$
2	$6.3493 \cdot 10^{-5}$	$6.2577 \cdot 10^{-5}$	$6.3153 \cdot 10^{-5}$	$6.2307 \cdot 10^{-5}$	$5.3045 \cdot 10^{-5}$
3	$5.6107 \cdot 10^{-5}$	$5.4145 \cdot 10^{-5}$	$5.3905 \cdot 10^{-5}$	$5.1318 \cdot 10^{-5}$	$5.1552 \cdot 10^{-5}$
4	$3.5572 \cdot 10^{-3}$	$3.9664 \cdot 10^{-3}$	$4.1983 \cdot 10^{-3}$	$4.2883 \cdot 10^{-3}$	$6.2828 \cdot 10^{-3}$
5	$2.3156 \cdot 10^{-5}$	$2.2277 \cdot 10^{-5}$	$2.2042 \cdot 10^{-5}$	$1.9941 \cdot 10^{-5}$	$1.7058 \cdot 10^{-5}$

Table 3. The equivalent dose values obtained at different neutron energies

Equivalent dose [mSv]					
Cell	250 eV neutron energy	25 eV neutron energy	2.5 eV neutron energy	0.25 eV neutron energy	0.025 eV neutron energy
1	$2.5828 \cdot 10^{-7}$	$2.5640 \cdot 10^{-7}$	$2.5543 \cdot 10^{-7}$	$2.5219 \cdot 10^{-7}$	$2.5981 \cdot 10^{-7}$
2	$2.6302 \cdot 10^{-7}$	$2.5968 \cdot 10^{-7}$	$2.6315 \cdot 10^{-7}$	$2.5961 \cdot 10^{-7}$	$2.6732 \cdot 10^{-7}$
3	$2.6263 \cdot 10^{-7}$	$2.5048 \cdot 10^{-7}$	$2.4678 \cdot 10^{-7}$	$2.3763 \cdot 10^{-7}$	$2.7199 \cdot 10^{-7}$
4	$1.3355 \cdot 10^{-5}$	$1.5667 \cdot 10^{-5}$	$1.6910 \cdot 10^{-5}$	$1.7398 \cdot 10^{-5}$	$2.6772 \cdot 10^{-5}$
5	$9.8621 \cdot 10^{-8}$	$9.5028 \cdot 10^{-8}$	$9.3111 \cdot 10^{-8}$	$8.6498 \cdot 10^{-8}$	$9.0123 \cdot 10^{-8}$

much higher than in the Cell 3 and other Cells. The reason for this is the gamma radiation that occurs as a result of the interaction of neutrons with the hydrogen (H) atoms in the soft tissue in the Cell 3 [9]. As stated in the work of Pereira *et al*., [1] the energy of gamma rays resulting from the $^{1}H(n,)^{2}H$ reaction can be 2.2 MeV. As neutron energy decreases, the penetration of neutrons decreases and neutrons are located closer to the surface. Therefore, as the neutron energy decreases, the amount of neutrons in the Cell 3 will increase, so the resulting gamma radiation flux becomes larger.

In other Cells, gamma radiation flux decreases as neutron energy decreases. Since the amount of neutrons reaching the tumor region containing ^{10}B atom will decrease, the amount of nuclear reaction that can occur will also decrease. This is directly related to the gamma radiation that may occur. It is seen that the flux decreases as the neutron energy decreases in the 250 eV and 0.25 eV energy range (except Cell 3). However, at 0.025 neutron energy, the flux increases again. This can be attributed to the amount of gamma radiation that occurs as a result of the increase in the amount of neutrons in the region containing the H atom. Due to the small amount of neutrons in the deep region along the neutron radiation axis, the gamma radiation formed in the Cell 5 is the least. This is also an expected result. Cell 1 and Cell 2 are outside the neutron irradiation field. The flux formed in these regions is due to the gamma radiations that emerge in the nuclear reaction that occurs as a result of the interaction of ^{10}B atom and neutrons. The Cell 3 is in the neutron irradiation field. The flux formed in this region is caused by gamma radiation resulting from the $^{10}B(n,)^{7}Li$ reaction and the interaction of neutrons with the H atoms. Although Cell 3 is within the neutron irradiation field, the amount of flux produced in this Cell is close to the amount of flux formed in Cell 1 and Cell 2.

When the gamma radiation absorbed in the Cells is examined in air around the head, as seen in tab. 2, the gamma absorption in the Cell 1, Cell 2, Cell 3, and Cell 5 decreases as the neutron energy decreases. On the other hand, gamma absorption in Cell 4 increases as neutron energy decreases. This increase is due to the increasing of the neutron-hydrogen interaction in this region as the amount of neutrons accumulated in the Cell 4 will increase as the neutron energy decreases. In Cell 4, the absorbed dose value ($MeVg^{-1}$) obtained at 0.025 eV neutron energy is approximately fifty percent greater than the values obtained at other energies. Unlike the flux values, the absorbed dose values obtained in Cell 1 and Cell 2 are greater than the value obtained in Cell 3.

When tab. 3 is examined, the millisievert values of the equivalent dose in the Cells to be examined show similar characteristics with the $MeVg^{-1}$ values of the absorbed dose. The lowest millisievert values were obtained in Cell 5. Except for Cell 5, the highest value in other Cells was obtained as a result of irradia-

tion with 0.025 eV neutron energy. With this result, millisievert values are also similar to flux values. As seen in the results, significant differences can occur in the dose values obtained at different locations. By choosing the energy values appropriately, the decrease in the doses occurring at certain points or the overdose of the healthy tissues can be prevented.

CONCLUSION

The amount of ^{10}B atoms accumulated in the tumor tissue and the number of neutrons reaching this area greatly affect the quality of BNCT treatment. In BNCT treatments, the neutrons sent to the tumor should be selected depending on the location of the tumor and the size of the tumor area. In the use of wrong neutron energy, either the desired amount of neutrons in the tumor cell will not be obtained and the effect of the treatment will decrease, or the amount of radiation to which the healthy tissues are exposed will increase because the neutron's penetration will increase. Although the radiations generated as a result of the nuclear reaction make a great contribution to the total dose, the contributions from the secondary radiations can create significant differences in healthy tissue and tumor tissue. Depending on the tumor location, the contribution of undesirable secondary doses can cause irreversible damage to healthy tissues, causing undesirable consequences. Previous studies report that these contributions can reach up to 67 % of the total dose. The results obtained in our study will contribute to obtaining the desired radiation dose in the tumor area by better protecting healthy tissues in BNCT applications. In addition, this study provides information about the doses that can occur in healthy tissues.

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Received on November 8, 2022
Accepted on March 31, 2023

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ИСТРАЖИВАЊЕ ДОЗА ФОТОНА КОЈИ ДОПИРУ ДО ЗДРАВИХ ТКИВА ПРИ КОРИШЋЕЊУ РАЗЛИЧИТИХ ЕНЕРГИЈА НЕУТРОНА У ТЕРАПИЈИ ЗАХВАТОМ НЕУТРОНА БОРОМ

Терапија захватом неутрона бором јединствена је метода лечења која има за циљ да убије туморске ћелије уз помоћ тешких честица. Честице настале интеракцијом туморског региона који садржи ^{10}B атоме са термичким или епитермичким неутронима имају најважнију улогу у овој методи лечења. У овом раду испитивано је гама зрачење које допире до здравих ткива, што је резултат реакције $^{10}B(n,\alpha)^{7}Li$. Симулација погодна за прорачун терапије захватом неутрона бором, укључујући модел људске главе, креирана је програм MCNP. Коришћењем пет различитих енергија неутрона, испитивана су гама зрачења која настају у реакцији $^{10}B(n,)^{7}Li$ у одређеним регионима у близини туморског ткива. Уочено је да је здраво ткиво између подручја тумора и површине изложено највећем гама флуксу и највећој апсорпцији гама зрачења. Такође је примећено да се ове вредности повећавају како се енергија неутрона смањује. Утврђено је да дозе гама зрачења које примају неки региони изван подручја неутронског зрачења могу бити значајне. Промена енергије неутрона може изазвати знатне промене у вредностима гама зрачења које доспева до здравих ткива, посебно у регионима близу површине. У третманима захватом неутрона бором, неутроне који се шаљу на тумор треба бирати у зависности од локације тумора и величине туморског подручја. Овај рад садржи корисне податке о дозама фотона у здравим ткивима око региона мозга третираних различитим енергијама неутрона у терапији захватом неутрона бором.

Кључне речи: терапија захватом неутрона бором, MCNP програм, енергија неутрона