Atom Indonesia

Journal homepage: http://atomindonesia.brin.go.id

Investigation of Dose Effect of ICRP110 Male and Female Head Phantoms During BNCT and PBFT by Monte Carlo Simulations

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ARTICLE INFO

Article history:
Received 9 October 2024
Receivedinrevised form 3 December 2024
Accepted 6 January 2025

Keywords:

BNCT
PBFT
Brain
Geant4
Radiation dose
LET

ABSTRACT

Boron Neutron Capture Therapy (BNCT) and Proton Boron Fusion Therapy (PBFT) are of great interest in the field of radiation oncology. These treatment methods may offer different advantages and disadvantages depending on the type of tissue involved, as well as the location and size of the cancerous area. In this study, radiation dose effect of BNCT and PBFT on the brain, one of the most sensitive organs of the human body, was examined comparatively, based on the ICRP110 male and female head phantom models by using GEANT4 Monte Carlo simulations. Additionally, some necessary LET (Linear Energy Transfer) calculations are also presented in the article. Dose, LET and Energy deposition values of GEANT4 calculations were presented for BNCT and PBFT therapies in details for male and female phanthom comparatively.

INTRODUCTION

Cancer, affecting various tissues and organs, remains a major public health concern affecting populations across all regions of the world. Cancer, which is the second leading cause of death worldwide, can develop as either a benign or malignant tumor. Malignant tumors have the ability to spread throughout the body via the bloodstream and lymphatic system. Between 2018 and 2022, the cancer mortality rate was reported to be 146 per 100,000 males and females per year.

It is also observed that cancer mortality rate is higher in males than in females. Among males, the most common types of cancer are lung, prostate, colorectal, stomach, brain and liver. In females, the most common types include breast, colorectal, lung, cervical and thyroid cancer. The brain cancer mortality rate is approximately 4 per 100,000 for male and female. The United State, followed by China, has the highest cancer mortality rates globally. India is also among the top three countires in Asia in terms of cancer incidence and mortality. The survival rate of cancer patients varies widely, ranging from 4 % to 97 %, depending on the type of cancer and the economic condition of different countries. For brain cancer, it is estimated that only about 15 % to 17 % of patients survive for five years or more after diagnosis.

Nowadays, cancer treatment options include surgery, chemotherapy, radiation therapy, harmonal therapy, targeted therapy, stem cell treatment and immunotherapy. Among these, surgery is considered the most effective treatment when the cancer detected at an early stage, as it allows for the permanent removal of cancerous tissue or organs. Radiation therapy is also one of the most common and effective treatments, particuralry for controlling the growth of brain tumors, though it may not be suitable for every patient. In radiation therapy, high energy x-rays, gamma rays, electron, protron or neutron are used to damage the cancerous cells. Gamma rays arethe most commonly used type of radiation usedin various cancer treatment applications. Brachytherapy is a commonly used technique for treating cancers of the head, neck, breast, cervix, prostate, and eyes. Another form of radiation therapy, known as radioactive iodine (I-131) therapy, is specifically used to treat thyroid cancer.

Boron Neutron Capture Therapy (BNCT) is a long-established and unique technique that began in 1950s for treating cancer patients on a large scale

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DOI: https://doi.org/10.55981/aij.2025.1541

using compound containing ^{10}B. Japan is one of the leading country to approve the BNCT for clinical use in 2024. BNCT is used to treat highly radiosensitive organs, such as the spinal cords. The technique involves administering a stable boron-containing pharmaceutical that accumulates in cancer affected tissues or organs. Nuclear fission of boron is then triggered using thermal or epithermal neutrons directed at the cancer site. This process delivers a higher radiation dose to the tumor relative to adjacent normal tissues or offers better radiation protection compared to conventional external beam therapy.

Initially, research reactors served as the neutron source for BNCT; however, this has shifted towards accelerator-based system. currently, proton-neutron accelerators generating neutron flux are used for BNCT. In this therapy, the isotope ^{10}B absorbs low-energy (<0.5 eV) thermal neutrons and subsequently breaks up into an alpha particle (^{4}He) with energy of 2.31 MeV and a recoiled lithium nucleus (^{7}Li). These particles exhibit very high linear energy transfer (LET), ranging from 150 to 175 keV/μm. The ionization densities of alpha particles and recoiled lithium atoms are very high, which limits their energy transfer to a range of less than 10 μm length-sufficient to affect malingnant cancer cells that are typically up to 25 μm in size. Successful BNCT treatments for various cancer patients, including those of the head, nceck, lung and chest has been reported in the literature. However, because neutron beams can damage normal tissues before reaching the tumor, ongoing research aims to develop alternative method to reduce the dose to healthy tissue.

Recent developments in BNCT have been documented in a report by the International Atomic Energy Agency [1]. The fundamental principles of the method, along with its emerging clinical applications, are discussed in another study, which highlights the technique's potential despite its limited current use. The study emphasizes that BNCT could become a pivotal advancement in oncology treatment in the near future [2]. Another study that compiled the clinical applications of BNCT stated that this method represents a targeted therapy with promising results and acceptable toxicity in early clinical studies. It was also stated that further research is needed to define the role of BNCT in clinical practice [3]. The use of non-toxic material, nanostructured boron carbon nitride (BCN) in BNCT applications was recommended instead of BPA [4]. A study conducted to demonstrate the clinical applicability of reactor-based BNCT in treating malignant cells evaluated its use in head, neck, and brain tumors, while also discussing the method's limitations [5]. In another study involving animal experiments on spinal cord gliomas, BNCT was found to be feasible and effective in improving survival rates [6]. A notable example of BNCT's commercial application is a report by a private initiative, which focuses on the development of targeted drugs for treating refractory cancers using BNCT [7]. Technological and physical evaluations of BNCT in Finland were presented in a study covering various aspects such as neutron sources, beam dosimetry, treatment planning, boron imaging and quantification, as well as methods for assessing the effectiveness and outcomes of BNCT in patients [8]. In addition, a Monte Carlo modeling study aimed to enhance the accuracy of estimating tissue-absorbed doses by accounting for all radiation components involved in neutron capture therapy [9]. Another study explored reactor design improvements for BNCT by incorporating Teflon as a structural material [10]. Furthermore, dose calculations and preliminary treatment planning were carried out in a study investigating the clinical use of epithermal neutron beams from a fission converter, along with appropriate dosimetry methods [11].

Proton Boron Fusion Therapy (PBFT) has emerged as a promising technique, capable of deliver a similarly intense tumor dose distribution while exposing normal tissues to comparatively lower dose than BNCT.

The PBFT is an emerging cancer treatment technique that also utilizes alpha particles.In PBFT, the alpha particles are produced through a nuclear reaction between protons and boron ions $^{11}B(p, 3\alpha)$. Various have reported data on the physics, chemistry, biology and clinical aspects of PBFT. The PBFT was first introduced in late 1960s, involving the fusion reaction between a boron particle (^{11}B) and a proton (^{1}H), which emits three alpha particles. These alpha particles, with energies of approximately 3.74 MeV and 2.74 MeV, damage cancer cells in a manner similar to the alpha particles used in BNCT. It is important to note that the alpha particle emission rate in PBFT is three times higher than in BNCT. Therefore, the therapy efficacy per incident particle is considered three times lesser than of PBFT.

Monte Carlo simulation studies comparing Boron Neutron Capture Therapy (BNCT) and Proton Boron Fusion Therapy (PBFT) have evaluated both methods in terms of dose enhancement, with several findings highlighting the potential advantages and suitability of the PBFT approach [12-13]. In a study, a laser-driven, high-energy alpha source was designed and proposed for application in PBFT [14]. Another study provided a comprehensive evaluation of laser-driven PBFT systems, exploring their therapeutic potential [15]. Additionally, the feasibility of using alternative elementssuch as oxygen-16, carbon-12, and nitrogen-14instead of boron for alpha particle production was assessed in a separate investigation [16]. A distinct 719 keV prompt gamma-ray peak was detected as a result of the proton–boron fusion reaction, offering a possible avenue for treatment monitoring. The PBFT method was noted for several advantages, including the utilization of the Bragg peak for precision therapy, improved tumor targeting, enhanced therapeutic outcomes, and real-time monitoring of the treatment area. [17]. A study exploring the effects of target degeneracy emphasized the effectiveness of using 880 keV protons for PBFT, further supporting its suitability for clinical applications [18].

In the present investigation, only radiation interactions and associated physical parameters are discussed; the chemical and biological characteristics of boron compounds, as well as their biological effects, are not considered.

METHODOLOGY

BNCT and PBFT are common treatmants widely used in literature. Brief descriptions of both treatments in terms of nuclear medicine are given as follows. First of the two theraphy, BNCT is an effective method used especially in the treatment of brain tumors. A special liquid containing ^{10}B is injected into the body. Thus, ^{10}B only surrounds tumor cells. Thermal neutrons emitted from a source are sent to regions containing ^{10}B, causing a nuclear reaction. As a result of this reaction, alpha particles with 1.47 MeV energy and ^{7}Li nuclei with 0.84 MeV energy are formed. Since alpha particles cannot travel very far through matter, they act within a small distance and can only target and destroy cancerous cells without damaging the entire tissue. The treatment logic of PBFT, which is the second of these treatments, can be explained as follows. Firstly, a special liquid containing ^{11}B is injected into the patient. Thus, ^{11}B reaches the cancerous tissue through the bloodstream. After ^{11}B surrounds the cancerous cells, protons with the desired energy value are sent to the ^{11}B nuclei. The maximum cross-section occurs at about 600–700 keV (nearly 670 keV) proton energies and has been reported to be between 600–800 keV [27]. After this, nuclear fusion occurs, creating the unstable 12C nucleus, which emits alpha particles of 3.76 MeV. And after that, ^{12}C emits a pair of 2.46 MeV energetic alphas, forming the stable 8Be nucleus. Alpha particles released as a result of nuclear reactions destroy nearby cancer cells through direct and indirect effects due to their low peneatrability.

In this study, ICRP-110 female and male human head phantom models were used [19]. The volume and mass of the female brain model were 1,238.1 cm^3 and 1,300 g, respectively, while those of the male brain model were 1,381 cm^3 and 1,450 g. Differences between male and female phantoms are given in Table 1.

Table 1. Properties of full phantoms.

Property of Phantom	Adult male phantom	Adult fermale phantom
Height (m)	1.76	1.63
Mass (kg)	73.0	60.0
Slice thickness (mm)	8.0	4.84
Voxel in plane resolution (mm)	2.137	1.775
Voxels along x (columns)	254	299
Voxels along y (rows)	127	137
Number of Slices (along z)	222	348

The brain density was 1.050 g/cm^3 for both male and female. The geometric parameters and element composition of the brain model are presented in Table 2.

GEANT4 [20-22], used in this study, is a powerful and reliable Monte Carlo simulation package widely recognized in the fields of medical physics and nuclear medicine for modeling radiation interactions with living tissues. In the simulations, a 50 mg dose of Sodium Borocaptate (BSH) injection was was modeled as being administered for the BNCT method, corresponding to a concentration of 1. 3 mg/kg ^{10}B in brain tissue [23]. For the PBFT model, 65 mg/kg ^{11}B concentration was employed [16]. The appearances of the head phantom before and after irradiation (under the 100 particles test beam) are shown in Fig. 1.

Table 2. Geometric parameters and elemental composition of brain model.

Rectengular prism						Center of mass					
Column		Row		Slice		Voxels			Coordinates (cm)		
Min	Max	Min	Max	Min	Max	x	y	z	x	y	z
Adult Male											
95	158	23	105	204	220	126.00	66.44	212.00	26.93	14.20	169.60
Adult Female											
116	185	11	107	316	345	150.80	60.72	332.20	26.77	10.78	160.80
Elemental Composition (% Mass)											
			H	C	N	O	Na	P	S	Cl	K
Adult Male			10.7	14.3	2.3	71.3	0.2	0.4	0.2	0.3	0.3
Adult Female			10.7	14.4	2.2	71.3	0.2	0.4	0.2	0.3	0.3

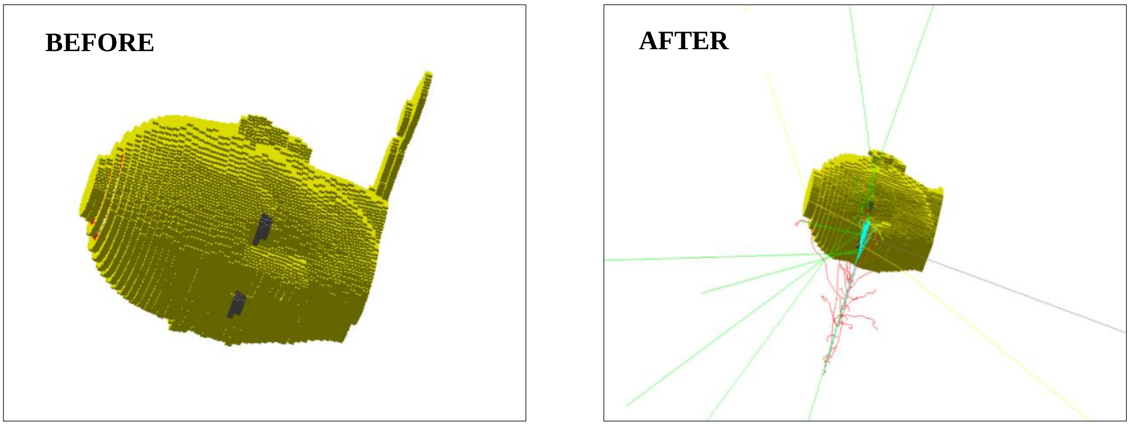

Fig. 1. Head phantom before and after irradiation.

More detailed information about the phantoms used in the study can be found in ICRP reports. In the report number 110 published by ICRP (International Commission on Radiological Protection), an adult human phantom was published and it was stated that these data could be used as a reference in dose calculations [24]. Basic anatomical and physiological data for use in radiological protection were given in report number 89 published by ICRP [25]. In ICRP publication number 103, the previous data were revised and presented [26]. Additionally, there are numerous studies in the literature referencing ICRP phantoms. One of these studies compared radiological risk data from thorium gas inhalation with ICRP data [27].

Upon defining the head phantom in the simulation setup, , irradiation was performed using 10^6 neutron particles with an energy of 0.025 eV for BNCT and 10^6 proton particles with 100 MeV energy for PBFT, to obtain dose and energy deposition outputs. To obtain LET values, brain tissue was irradiated with 1.47 MeV and 2.46 MeV alpha particles for BNCT and PBFT, respectively. In the simulations the QGSP_BIC_HP Physics List is adopted in this study. This modelemployes binarycascade, precompound and several de-excitation models for hadronicparticles. Additionally, itincludes a high-precision neutron model for energies below 20 MeV.

RESULTS AND DISCUSSION

In this simulation study, the application of BNCT and PBFT treatments, in which basic physical mechanisms were briefly described in methodology section, for targeting cancerous cells in the brain tissue was simulated using the GEANT4 Monte Carlo code. The results and corresponding evaluations are presented below. The male and female brains were models were constructed separately based on GEANT4 data, and the outcomes were analyzed accordingly.

Although modern cancer treatments primarily focus on effectively destroying cancerous cells, it is equally important to minimize damage to surrounding healty tissues. Therefore, key parameters such as dose (Gy), LET (MeV/cm), energy deposition (MeV) were calculated separately for both male and female models.

Radiation dose explains the amount of ionizing radiation energy absorbed by a substance extensively measured in Grays (Gy). Chiniforoush et al., (2021) conducted a Monte Carlo study (PBFT) for brain cancer by using Monte Carlo N Particle (MCNP) and reported the depth equivalent dose of PBFT. They also give in the paper equivalent dose (Sv) depending on 70–80 MeV and concentration for Proton Therapy (PT) and PBFT [16].

Linear energy transfer (LET) is known as the average energy deposited per unit path length along the track of an ionizing particle. The concept of LET is fundamentally based on the definition stopping power. Stopping power (***S***) consists of two main components, which are collision and radiative terms, expressed as (*dE/dx*). The radiative term accounts for energy loss due to Bremsstrahlung radiation, whilst it can be neglected for non-relativistic therapeutic proton beams.

$$S = \left(\frac{dE}{dx}\right)_{coll} + \left(\frac{dE}{dx}\right)_{rad} \tag{1}$$

The Eq. (1) also includes a third term for representing of stopping power, (*dE/dx*) nuclei based on nuclear interactions along the given range. As it is known, most of the time this term is neglected stemming from the negligible dose contribution.

Monte Carlo simulations typically present each energy deposition event associated with particles' energy loss (dE) and the length of the particle step (dx). All calculations are performed on a voxel by voxel basis, taking into account the density ρ of the each voxel to determine LET within a tissue of unit density, as shown in Eq. (2) [29]:

$$LET = \frac{1}{\rho}\frac{\sum_{events} dE.\left(\frac{dE}{dx}\right)}{\sum_{events} dE} \quad (2)$$

Dose, LET, and energy deposition of GEANT4 calculations for BNCT and PBFT methods for male and female phanthom are shown in Table 3 and Table 4, respectively.

Table 3. Dose, LET, and energy deposition values of GEANT4 calculations for BNCT.

Gender	Dose (Gy)	LET (MeV/cm)	Energy deposition (MeV)
Male	4.90 E-09	2118.06	7.10 E-09
Female	1.04 E-09	2118.02	1.35 E-09

Table 4. Dose, LET, and energy deposition values of GEANT4 calculations for PBFT.

Gender	Dose (Gy)	LET (MeV/cm)	Energy deposition (MeV)
Male	3.07 E-09	1532.92	4.46 E-09
Female	2.13 E-09	1531.01	2.77 E-09

BNCT and PBFT methods showed difference in male phantom models. One important point to consider when interpreting these values is the difference in the way the simulation were conducted for BNCT. In BNCT calculations, dose and energy deposition values were obtained by irradiating to the head phantom with thermal neutrons. However, LET results were derived by directly sending alpha particles, formed as a result of the reaction, into the brain tissue. The proportional differences observed in energy deposition and dose between male and female phantoms in BNCT can be attributed to the chemical composition differences between the male and female head phantoms.

For BNCT, the similarity in LET values between male and female phantoms can be attributed to the energy lost of alpha particles as they travel through brain tissue. This is likely because the brain tissue composition in both male and female phantomswas nearly identical, with only minor differences.

When the results are re-examined by comparing BNCT and PBFT treatments, several noteworthy points emerge. For the male phantom, the dose, LET and energy deposition values in PBFT were lower than BNCT. However, as shown in Table 4, this trend did not hold proportionally for the female phantom, where the dose, LET, and energy deposition values for BNCT and PBFT did not exhibit a consistent relationship. This discrepancy can be attributed to the fundamentally different nuclear reactions involved in BNCT and PBFT, which vary significantly in terms of electrical polarity, energy levels and energy distributions. Vermunt (2019), revealed there were correlations between the production of alpha particles, stored energy and cancer cell death [28]. Additionally, Kim et al., (2018), verified the effect of energy deposition induced by the alpha particles on the therapeutic effect of the PBFT treatment [29].

CONCLUSION

In this study, the LET, radiation dose, and absorbed energies values associated with BNCT and PBFT therapies, which both have well-established effectiveness in cancer treatments, were investigated using GEANT4 simulations for both male and female. The results, presented in Table 3 and Table 4 were found to be consistent with values reported in the literature. It was confirmed, in alignment with existing studies, that the types and structures of the incident particles (neutrons for BNTC and protons for PBFT), play a significant role in determining the effectiveness o=f these therapies. Consequently, the alpha particles produced in the nuclear reactions, with their characteristic energy levels, were observed to interact with male and female head phantoms and brain tissue as expected, based on their chemical composition.

ACKNOWLEDGMENT

We are deeply grateful to the Department of Nuclear Energy Engineering, Faculty of Engineering, Sinop University, Sinop, Türkiye, for their valuable support and resources.

AUTHOR CONTRIBUTION

H. Korkut, T. Korkut and V. P. Singh equally contributed as the main contributors of this paper. All authors read and approved the final version of the paper.

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