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SIMULATION OF BORON DOSE AND IRRADIATION TIME IN LUNG CANCER TREATMENT WITH BORON NEUTRON CAPTURE THERAPY (BNCT) USING MCNP-6

Nita Handayani*[1], Kevin Kautsar Soelistiyono[1], and Fajar Arianto[2]
[1]Department of Physics, Faculty of Science and Technology, State Islamic University of Sunan Kalijaga, Yogyakarta, Indonesia
[2]Department of Physics, Faculty of Science and Mathematics Diponegoro University, Semarang, Indonesia
*nita.handayanii@uin-suka.ac.id

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ABSTRACT

Boron Neutron Capture Therapy (BNCT) is a cancer radiation treatment. This approach employs a boron carrier agent in the form of a chemical that is injected into the body and then travels to the cancer cells. In a lung cancer case study, BNCT treatment simulation was carried out using Monte Carlo N Particle (MCNP) software version 6.2. The goal of this study was to determine the most effective boron concentration and irradiation duration in lung cancer therapy utilizing the BNCT method. The geometry based on a phantom model created by Oak Ridge National Laboratory (ORNL). The simulated cancer geometry, which is placed in the right lung's middle lobe. The skin, ribs, and right lung are among the organs at risk. The skin, ribs, and right lung are among the organs at risk. The neutron source for the simulation is the collimator output from the Kartini Nuclear Reactor's thermal column. In this simulation, the variations in boron concentrations were 40 μg/g, 45 μg/g, 50 μg/g, 55 μg/g, and 60 μg/g of cancer tissue. The researchers discovered a link between boron injection concentration and irradiation time, with higher boron injection concentrations resulting in shorter irradiation times. The volume of boron injected determines the effective dose absorbed by healthy tissue surrounding cancer cells. The effective boron concentration for lung cancer therapy is 60 μg/g, with deterministic cell killing in the rib marrow and right lung. When utilizing a boron concentration of 60 μg/g, the irradiation time is 20.4 minutes. Boron concentrations of 60 μg/g are projected to create an effective irradiation time for BNCT-based lung cancer therapy based on the ALARA principle due to their shorter duration when compared to other concentration variations.

Keywords: Boron dose; BNCT; lung cancer; Monte Carlo.

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INTRODUCTION

Cancer is one of the most common non-communicable diseases in the world. The appearance of cancer is characterized by the presence of abnormal cells that develop uncontrollably and have the ability to attack and move between cells and body tissues. Lung cancer is a cancer that occurs in the lung organ. Cancer cells that grow uncontrollably in the lung organ cause fluid to form in the pleural cavity (the cavity located between the membrane lining the lungs and the chest cavity), causing patients to have difficulty breathing. In addition, the patient also experiences a decrease in endurance, which worsens his physical condition. In the case of

cancer, the highest number of deaths occurs in lung cancer, according to data released by the IARC [1]. Along with the development of science and technology, there are several methods or ways of treating cancer that have been found and used, such as radiotherapy, surgery, and chemotherapy. Lung cancer specialists perform treatment and therapy actions based on

observations of symptoms that appear, clinical examination results, and the condition of the patient's immune system. Several actions can be given to lung cancer patients by doctors, such as surgery, radiotherapy, chemotherapy, targeted therapy, or combination therapy (radiation and chemotherapy) [2].

At present, radiotherapy treatment methods have been widely used in curing various cancers. This method has advantages such as no need for surgery to remove cancer because it uses ionizing radiation to destroy cancer cells. One radiotherapy technique that is quite popular is BNCT (Boron Neutron Capture Therapy). BNCT has several advantages, including the fact that the dose will be concentrated in cancer cells after being injected into the body and does not damage surrounding healthy cells. BNCT uses the reaction of Boron-10 isotopes irradiated with thermal or epithermal neutrons to produce alpha particles and Lithium-7 nuclei. The method of treatment of BNCT is based on the reaction of element $^{10}B(n, \alpha)^{7}Li$. The result of this reaction is a high linear energy transfer (the α particle is in the range of 150 keVμm^{-1}, the nuclide ^{7}Li in the range of 175 keV μm^{-1}). The two particles are at a distance between 4.5 μm and 10 μm and thus obtain a limited residual energy result that measures up to the size of a single cell. The size of these particles can selectively radiate the tumor cells that have captured several ^{10}B particles and, at the same time, isolate the normal cells.

BNCT is a type of radiotherapy that uses non-radioactive nuclides, namely boron, which has a high tendency to capture low-energy neutrons (thermal neutrons) [3]. The reaction in BNCT, which results in a high linear energy transfer value, causes damage to the cancer DNA called double-strand break (DSB). The effect of this DSB is the inability of the DNA to continue the process of dividing and growing. Due to the inhibition of these processes, cancer cells will die slowly over a while [4].

The BNCT method requires boron carrier agents to be injected into the body, namely sodium borocaptate, or BSH, and boronophenylalanine, or BPA [5]. In the BNCT method, boron is first injected into the bloodstream, which will then be centered on cancer cells. The next step is to irradiate the boron centered in the cancer cells using low-energy neutrons (thermal neutrons). The source of these neutrons comes from the extraction of the fission reaction of the element uranium-235 in a nuclear reactor. During irradiation, the neutrons produced will cause fission reactions on Boron-10 atoms in the cancer cells, resulting in Helium-4 and Lithium-7 elements. The fission reaction also produces alpha particles, which are used to kill cancer cells [6].

BNCT therapy planning determines the success rate of cancer therapy. Before BNCT therapy takes place, experts with specialist doctors who treat patients will first coordinate, analyze, and calculate the BNCT dose to be used. In addition, planning is also carried out for the use of radiotherapy equipment. If the dose given is not follow the required dose limit, it will be fatal to the patient's body, such as the appearance of radiation effects on the body stochastically, non-stochastically, or effects that directly affect genetic cells [7]. In connection with BNCT therapy, a simulation of BNCT therapy can be carried out using the Monte Carlo N-Particle, or MCNP program. This program is transportation code modeling software or radiation activity made with the aim of tracking and modeling various types of particle activity. In practice, MCNP simulation uses a stochastic method called Monte Carlo. The Monte Carlo method uses probability sampling of the occurrence of successive individual events (in this case particles)

and follows each particle's life cycle, starting from the production stage to the particle destruction stage.

METHOD

This research uses MCNP-6 simulation based on the Monte Carlo method. The organs simulated are the lung organ, cancerous tissue, and healthy tissue around the lung organ. The Cristy and Eckerman (1987) phantom model at Oak Ridge National Laboratory (ORNL) served as the basis for simulating the body geometry. The shape of the cancer geometry is spherical, consisting of 3 parts: the Gross Tumour Volume (GTV), which is the main cancer tissue with a diameter of 3 cm; the Clinical Target Volume (CTV), which is the tissue surrounding the main cancer tissue with a diameter of 3.6 cm; and the Planning Target Volume (PTV), which is the tissue surrounding the CTV with a diameter of 4 cm. The CTV and GTV have the same constituent material characteristics. PTV tissue has the same characteristics as healthy tissue because it is located in the outermost layer of cancer tissue and is in direct contact with healthy tissue. This network design was simulated based on lung cancer simulation measurements from previous researchers using the PHITS program [8].

This study used a variation of boron doses of 40 μg/g, 45 μg/g, 50 μg/g, 55 μg/g, and 60 μg/g of cancer tissue at 5 μg/g intervals. This dose variation is based on previous research, where boron concentrations of more than 50 μg/g of cancer are still within safe limits for lung organs. Therefore, the dose range used is the closest range below and above 50 μg/g [8].

In this study, the neutron source used for simulation comes from the output of the collimator in the Kartini Nuclear Reactor thermal column. This collimator design was made by Fauziah (2013) and was inputted in this study using MCNP version 6.2 [9]. In BNCT applications, the neutron source used produces neutron flux in the form of thermal neutron flux or epithermal neutron flux. This study modifies the size of the collimator wall design by adding the same diameter as the diameter of the irradiation chamber. The design of the collimator adjusts the location of the cancer in the body so that the location of the radiation chamber is also centered on the cancer. The collimator in this study has a moderator thickness of 60 cm, a filter thickness of 15 cm, a gamma radiation barrier thickness of 3 cm, and a neutron radiation barrier with a thickness of 3.5 cm. The moderator wall has a thickness of 39 cm which adjusts to the diameter of the radiation chamber of 100 cm. In this study, the neutron source used for simulation comes from the output of the collimator in the Kartini Nuclear Reactor thermal column.

All the data that has been obtained is then entered into the MCNP-6 input code. This code generation contains information on the shape of the body, the shape of the lung organs, the shape of the cancer cells, and the materials that make up the model. After the process of making the input code, the data is then simulated. This simulation process is the MCNP-6 running process, and then the MCNP-6 output results are automatically saved in one folder with the input code file. After the running process is complete, the data is then visualized to display the geometry design. If the whole process has been completed, the next step is to process the data that has been taken from the MCNP-6 running output.

Calculation

In this study, the calculation and processing of data begin with the calculation of the boron mass concentration in BNCT for each tissue. Then, the calculation continues with the determination of the boron dose by finding the total dose rate. Data calculations in this study include the calculation of the total dose rate, irradiation time, and absorbed dose.

1. Boron Mass Fraction

The boron concentration variation is then calculated for each boron mass in the cancer tissue. After the mass of Boron in each tissue is calculated, the results are then used for calculations

in finding the value of the mass fraction of Boron in each body tissue for each variation of Boron concentration. The calculation of the Boron mass fraction is determined from the equation below:

$$Boron\ Mass\ Fraction = \frac{Boron\ Mass\ (g)}{Boron\ Mass\ (g)+Tissue\ Mass(g)} \quad (1)$$

2. Boron Dose Rate Calculation

The determined mass of boron is used to calculate the boron dose. In determining the boron dose, the calculation begins with finding the total dose rate. The calculation of the total dose rate includes the alpha dose rate, proton dose rate, and gamma dose rate.

a. Alpha Dose Rate

Alpha dose is the dose that shows the result of the interaction of Boron and thermal neutrons. The alpha dose rate is determined from the equation below [10]:

$$\dot{D}_{alpha} = \frac{\Phi.N_{B10-tissue}.\sigma_{a,B10}.Q\left(1{,}6\ X\ 10^{-13}\right)J/MeV}{1\,\frac{J/kg}{Gy}} \quad (2)$$

Where $\dot{D}_{alpha}$ is Alpha dose rate (Gy/s), Φ is Thermal Neutron Flux, $N_{B10\text{-}tissue}$ is the number of Boron atoms per kg of tissue (atom/kg tissues), $\sigma_{a,B10}$ is Boron absorption microscopic cross section (barn), Q is particle energy (MeV).

b. Proton Dose Rate

The proton dose is the dose that shows the result of the thermal neutron capture interaction with 14N. The proton dose rate is determined from the equation below [10]:

$$\dot{D}_{proton} = \frac{\Phi.N_{N-tissue}.\sigma_{a,N}.Q\left(1{,}6\ X\ 10^{-13}\right)J/MeV}{1\,\frac{J/kg}{Gy}} \quad (3)$$

Where $\dot{D}_{proton}$ is proton dose rate (Gy/s), $N_{N\text{-}tissue}$ is the number of Nitrogen atoms per kg of tissue (atom/kg tissues), and $\sigma_{a,N}$ is the Nitrogen Absorption microscopic cross section (barn).

c. Gamma Dose Rate

Gamma energy is produced from the reaction between hydrogen-1 in body tissues and epithermal neutrons. Gamma energy is obtained from the equation below [10]:

$$\dot{D}_{\gamma} = \ddot{R}\,.\,\Delta\,.\,\phi \quad (4)$$

With $\ddot{R}$ results obtained from:

$$\ddot{R} = \Phi\,.\,N_{H-tissue}\,.\,\sigma_{H} \quad (5)$$

Where $\dot{D}_{\gamma}$ are gamma dose rate (Gy/s), $N_{H\text{-}tissue}$ is Number of Hydrogen atoms per kg of tissue (atoms/kg tissue), $\sigma_{a,H}$ is Hydrogen absorption microscopic cross section (barn), Δ is absorbed dose rate's coefficient Gy.kg/Bq.s), Φ is gamma absorbed dose fraction, dan $\ddot{R}$ is Hydrogen-2 formation rate (foton/kg.s=Bq/kg).

d.Total Dose Rate

The total dose rate is obtained based on the accumulation of calculations which include the calculation of the alpha dose rate, proton dose rate, and gamma dose rate. To obtain the dose rate value, is obtained from the equation below [10]:

$$\dot{D}_{total} = (W_{alfa}\ X\ \dot{D}_{alfa}) + (W_{proton}\ X\ \dot{D}_{proton}) + (W_{neutron}\ X\ \dot{D}_{neutron}) + (W_{\gamma}\ X\ \dot{D}_{\gamma}) \quad (6)$$

The radiation quality factor (W) value is derived from several factors that affect biological effects. These biological effects can be in the form of radiosensitive, radioresistant, or radioresponsive effects. The radiation quality factor in is shown in Table 1 [4]:

Table 1. List of radiation quality factors in each tissue

Radiation Source	Radiation Quality Factor
Alpha	3,8 in tumor
	1,3 in soft tissues
Proton	3,2
Neutron Beam	3,2
Gamma	1

3. Irradiation Time

The next step is to calculate the irradiation time. The calculation is done after calculating the entire total dose rate. The irradiation time is obtained from the calculation using the equation below:

$$Iradiation\ Time\ (s) = \frac{minimum\ dose\ of\ cancer\ cell\ destroyer\ (Gy)}{total\ dose\ rate\ (\frac{Gy}{s})} \quad (7)$$

The irradiation time is obtained from the quotient between the minimum or standard dose to destroy cancer cells and the total dose rate obtained from equation (5). In the case of lung cancer, the minimum dose required for irradiation is 50 Gy to destroy cancer cells [8].

4. Absorption Dose

The absorbed dose is defined as how much tissue absorbs the amount of energy in BNCT therapy. The absorbed dose is obtained from the multiplication between the results of the irradiation time calculation and the calculated dose rate. The amount of absorbed dose is written in the equation below:

$$Absorbed\ Dose\ (Gy) = Iradiation\ time(s)\ X\ Total\ Dose\ Rate\ (\frac{Gy}{s}) \quad (8)$$

RESULTS AND DISCUSSION

1. Geometry

The program visualized in MCNP 6.2 consists of BNCT collimator design, cancer design, and human body or phantom design. The three geometries are shown in the figure 1.

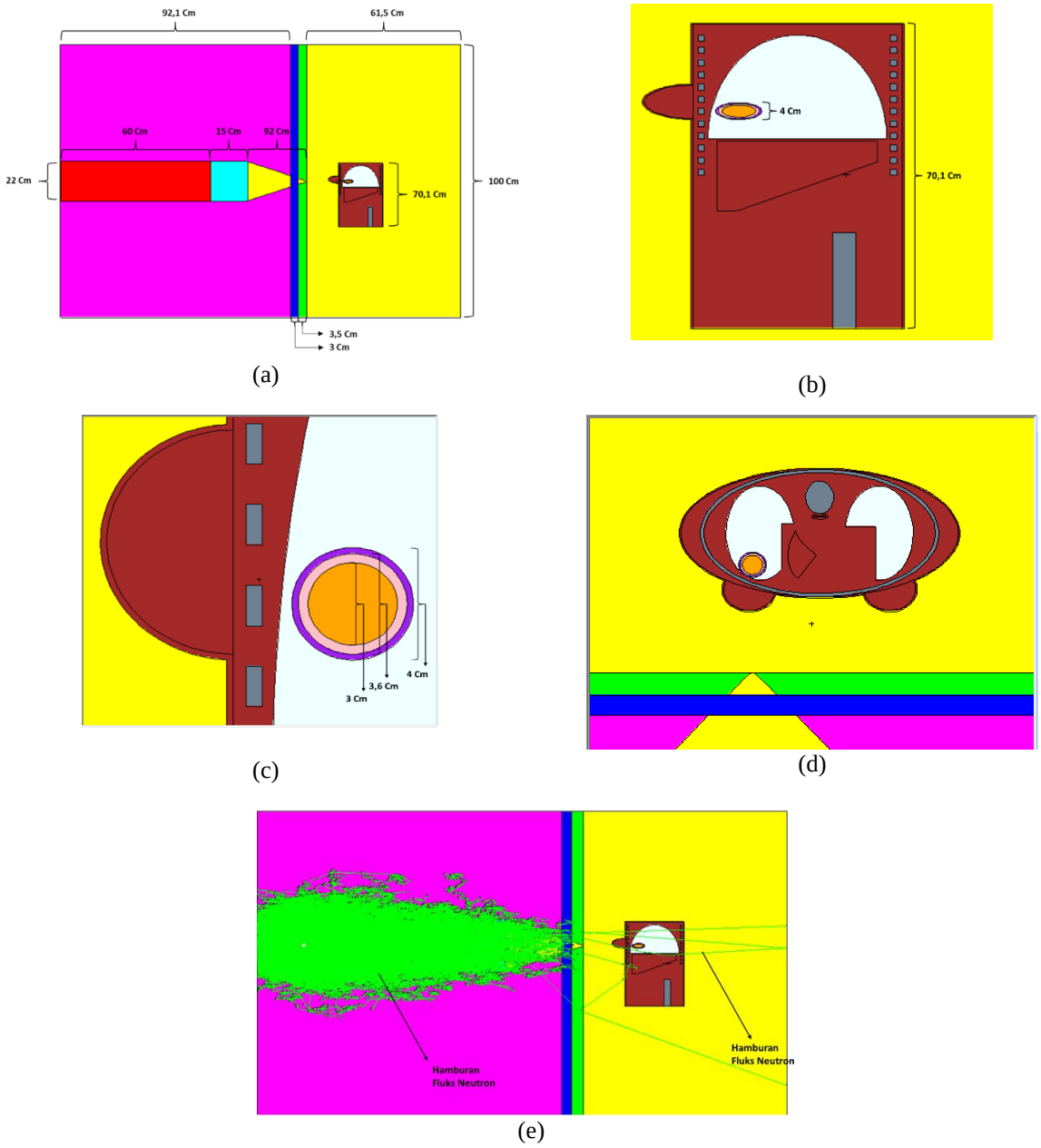


Figure 1. Visualization of MCNP 6.2 programs: (a) Colimator design; (b)Body phantom from side view; (c) NSCLC tissues in lung; (d) Body phantom from upper view; (e) Flux neutron beam particle's distribution

The phantom geometry design was obtained from a reference program created by Oak Ridge National Laboratory-Medical International Radiation Dosimetry (ORNL-MIRD). This study only uses part of the body geometry to be simulated, specifically the middle part of the body. Partial emptying of this organ is intended so that neutron scattering will focus on cancer cells and organs at risk (OAR) and be maximally absorbed. The simulated organs include the right lung and left lung, spine, ribs, and skin tissue only.

The dark gray color is the soft tissue part, the white color is the bone tissue part, and the light brown color shows the lung organ. Figure 1(c) shows the organ geometry of non-small-cell lung cancer (NSCLC). The shape of the cancer geometry is spherical, which consists of 3 parts: GTV, which is the main cancer tissue with a diameter of 3 cm; CTV, which is the tissue surrounding the main cancer tissue with a diameter of 3.6 cm; and PTV, which is the tissue

surrounding CTV with a diameter of 4 cm. The CTV and GTV have the same constituent material characteristics. PTV tissue has the same characteristics as healthy tissue because it is located in the outermost layer of cancer tissue and is in direct contact with healthy tissue.

2. Neutron Flux

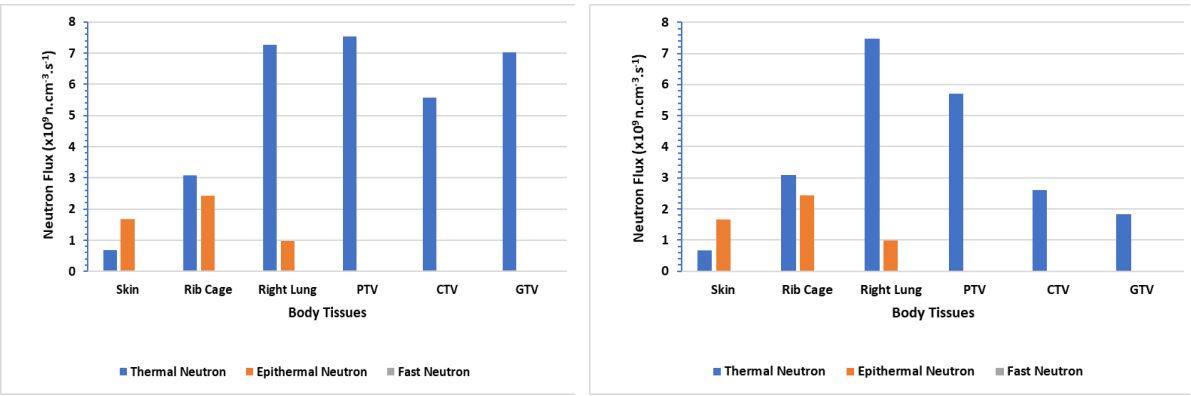
In this study, the neutron flux output from the collimator was obtained along with the neutron flux that hit each organ at each boron concentration variation. The neutron flux output from the collimator can be seen in the table 2.

Table 2. Result of IAEA standard in neutron flux output

Neutron Flux Parameter	IAEA Standard	Result	Value
Epithermal Neutron Flux ($Ø_{epithermal}$)	> 1,0 x 10^{9}	1,27894 x 10^{8}	$n.cm^{-2}.s^{-1}$
Fast Neutron Dose Rate per Epithermal Neutron Flux Ratio ($\dot{D}_f/Ø_{epithermal}$)	< 2,0 x 10^{-13}	4,57974 x 10^{-14}	$Gy.cm^2.n^{-1}$
Gamma Dose Rate per Epithermal Neutron Flux Ratio ($\dot{D}_\gamma/Ø_{epithermal}$)	< 2,0 x 10^{-13}	1,03893 x 10^{-13}	$Gy.cm^2.n^{-1}$
Thermal Neutron Flux and Epithermal Neutron Flux Ratio ($Ø_{thermal}/Ø_{epithermal}$)	<0,05	0,19	

Neutron flux output results from running MCNP 6.2 compared to a neutron source that complies with the recommendations issued by the IAEA. The standard that is considered according to the IAEA is that the epithermal neutron flux value must be greater than 1.0 x 10^{9} n.cm^{-2}.s^{-1}. Then the ratio between the fast neutron dose rate and the epithermal neutron flux and the ratio between the gamma dose rate and the epithermal neutron flux must be less than 2 x 10^{-13} Gy.cm^{2}.n^{-1} [11].

Based on table 2, the values of the ratio of the fast neutron dose rate per epithermal neutron flux and the value of the gamma dose rate per epithermal neutron flux have met the standards set by the IAEA. While the epithermal neutron flux value and the ratio between thermal and epithermal neutron fluxes have not met the standards recommended by the IAEA. Therefore, further research is needed so that the neutron flux value in this study can be improved and become a reference for use in BNCT therapy. Furthermore, the data obtained from this neutron flux output are thermal, epithermal, and fast neutron fluxes from each Boron concentration variation. The amount of neutron flux that passes through the tissue in the body is shown in Figure 2.



(a) (b)

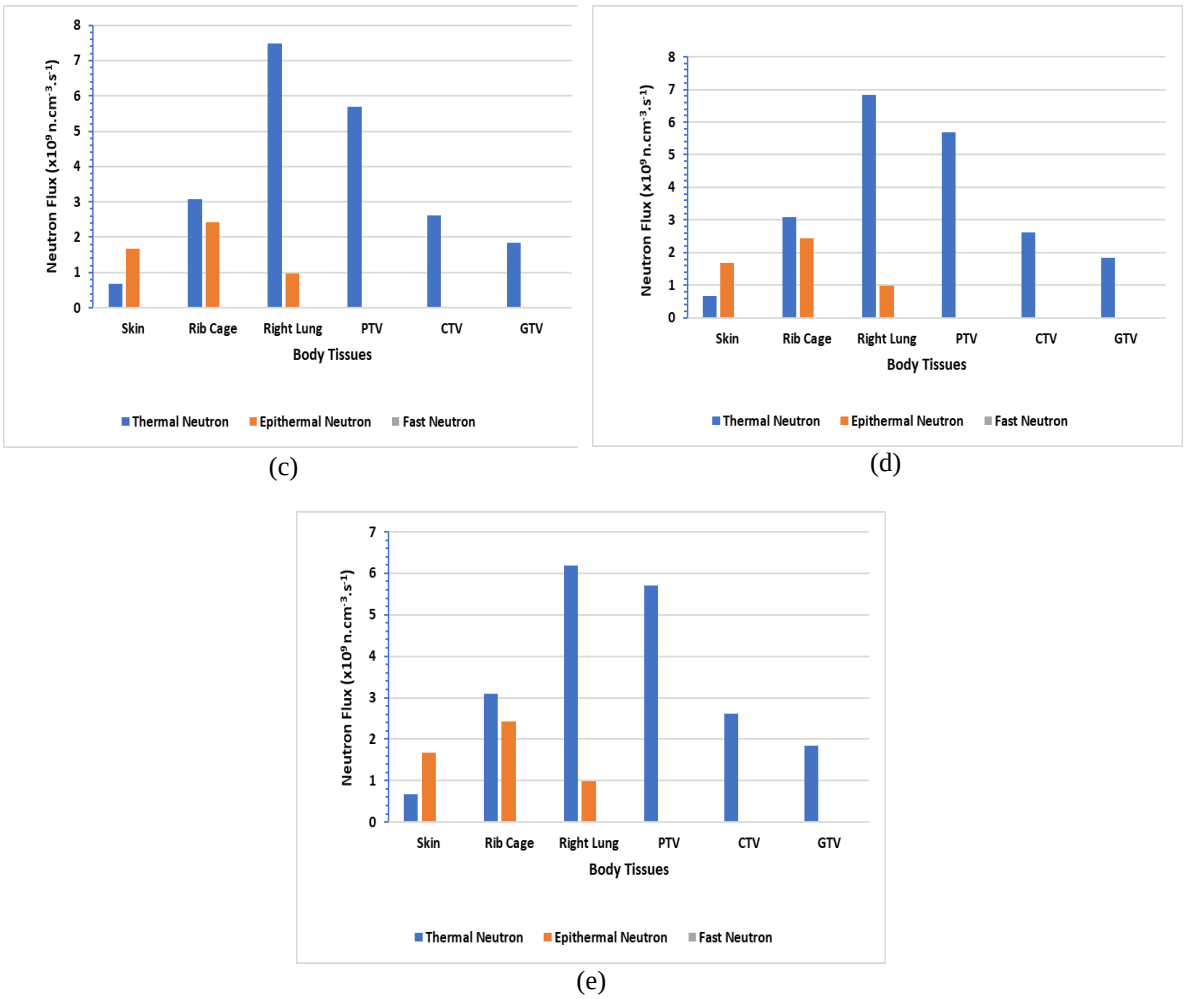


Figure 2. Graph of Neutron Flux Distribution in Body Tissues: (a) Boron Concentration 40 µg/g; (b) Boron Concentration 45 µg/g; (c) Boron Concentration 50 µg/g; (d) Boron Concentration 55 µg/g; (e) Boron Concentration 60 µg/g

The results showed that the thermal neutron flux value passing through the skin is smaller than in other body tissues. The simulated neutron source has an energy of 5 x 10^{-7} MeV (thermal neutrons), 0.01 MeV (epithermal neutrons), and 20 MeV (fast neutrons). In Figure 2, the relationship between thermal neutron flux and epithermal neutron flux is shown with the sequence of tissue trajectories and the organs it passes through. When the neutron flux exits the tip of the collimator, the epithermal neutron flux value is greater than the thermal neutron flux. Based on the graph at each concentration variation, the neutron flux passing through the skin has a small value, which then increases in value along with the entry of neutrons into the body, while the epithermal neutron flux decreases after passing through the ribs and is then zero after passing through the PTV tissue. This is because the human body contains hydrogen, which can moderate epithermal neutrons. This moderation process causes the epithermal neutron energy to also decrease until it approaches the thermal neutron energy level.

The highest peak of thermal neutron flux in the body occurred in the right lung tissue at concentration variations of 45 µg/g, 50 µg/g, 55 µg/g, and 60 µg/g, with respective values of 7.475880 x 10^9 n.cm^{-2}.s^{-1}, 7.47577 x 10^9 n.cm^{-2}.s^{-1}, 6.83773 x 10^9 n.cm^{-2}.s^{-1}, and 6.18301 x 10^9 n.cm^{-2}.s^{-1}. Then, at a concentration of 40 µg/g, the highest peak was in the PTV tissue at 7.53449 x 10^9 n.cm^{-2}.s^{-1}. At concentrations of 45 µg/g to 60 µg/g, the neutron flux value slowly decreases until it hits the cancer tissue, while at a concentration of 40 µg/g the neutron flux value increases when it hits the cancer tissue after decreasing in the CTV tissue.

3. Dose Rate

In this study, the boron concentration variations used were 40 µg/g, 45 µg/g, 50 µg/g, 55 µg/g, and 60 µg/g. Each boron concentration was then calculated through a ratio of 1:5:10, namely 10% for healthy tissue (including body tissue, bone tissue, lung tissue, and PTV), 50% for CTV tissue, and 100% for GTV tissue [8]. This concentration division is intended so that the radiotherapy process takes place selectively and is concentrated on cancer tissue. This percentage is entered into the MCNP program in the material data section according to the tissue by first converting it into a mass fraction using equation (1). After running and producing output, it is then entered into the calculation using equations (2) and (8). The results of the dose rate calculation will later be used in finding the irradiation time of each boron concentration against cancer, the absorbed dose received by the body, and analyzing them to obtain an effective dose. The results of the total dose rate calculation are shown in Figure 3.

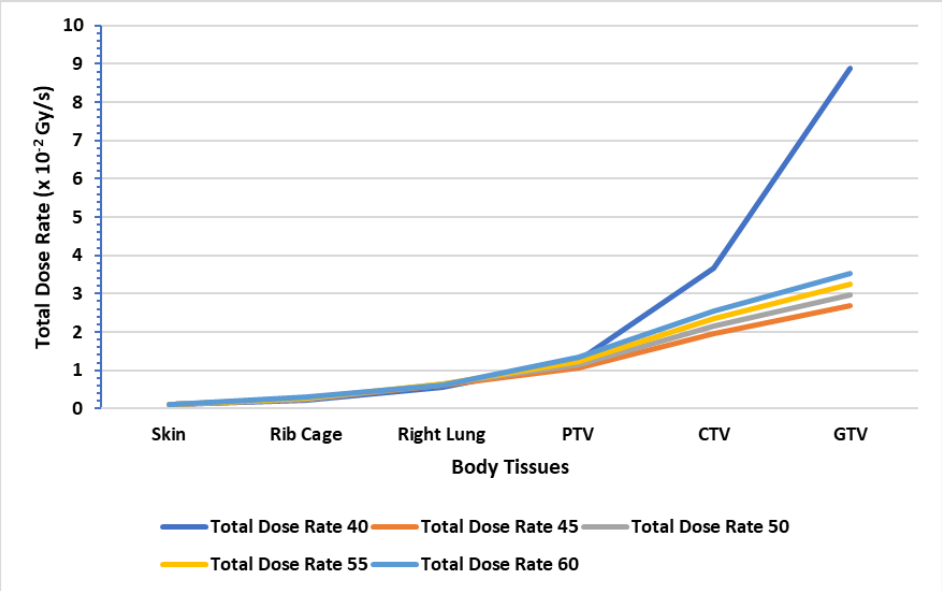


Figure 3. Graph of dose rate in each body tissue

From the calculation, the total boron dose rate increases as the boron concentration also increases in each tissue at boron concentrations of 40 µg/g to 60 µg/g. In Figure number 3, it is shown that the dose rate of GTV and CTV tissues has the highest value. In this tissue, the dose rate that has a high value is the alpha dose rate, because in BNCT therapy, the boron source has the largest number of particles among all body tissues. Therefore, there is an interaction between boron and thermal neutrons that produce alpha and lithium particles, and these particles will irradiate cancer cells that have captured several boron particles selectively and set aside normal cells. While the primary gamma dose rate decreases as it approaches the PTV, it then increases until it approaches the GTV network based on the output of the MCNP run. At the same time, other doses decreased in value when entering cancer tissue, such as the proton dose, secondary gamma dose, and neutron scattering dose at concentrations of 45 µg/g to 60 µg/g. This is because the effect of neutron flux on cancer tissue is smaller than the value of neutron flux on CTV tissue. In addition, the mass concentration of hydrogen and nitrogen has the same value in each tissue despite variations in the concentration of boron injected. Whereas at a concentration of 40 µg/g, both the proton dose rate and neutron scattering dose rate increase when approaching the right lung, then decrease until approaching the cancer tissue. At the secondary gamma dose rate, the concentration of 40 µg/g decreased in the right

lung tissue, then increased in the PTV tissue, until it decreased again near the GTV tissue. However, at a concentration of 40 µg/g boron, the dose rate in the CTV and GTV increased significantly. This occurs due to the influence of the neutron flux output as a result of MCNP-6 running, which is included in this dose rate calculation.

Furthermore, in healthy tissues, the right lung tissue has the highest dose rate value among other healthy tissues. This high value is inseparable from the large neutron flux hitting the lung tissue as well as the right lung tissue where the cancer is located before entering the cancer tissue. Because this lung tissue receives the highest exposure to neutron flux, it needs to be analyzed based on its absorbed dose in the discussion chapter related to irradiation time.

4. Irradiation Time

The results of the calculation of the dose rate in cancer tissue are then used to calculate the irradiation time. This calculation uses the minimum cancer-damaging dose in lung cancer of 50 Gy divided by the total dose rate of each concentration. Figure 4 presents a graph of the relationship between the amount of boron concentration and the length of irradiation time on cancer tissue.

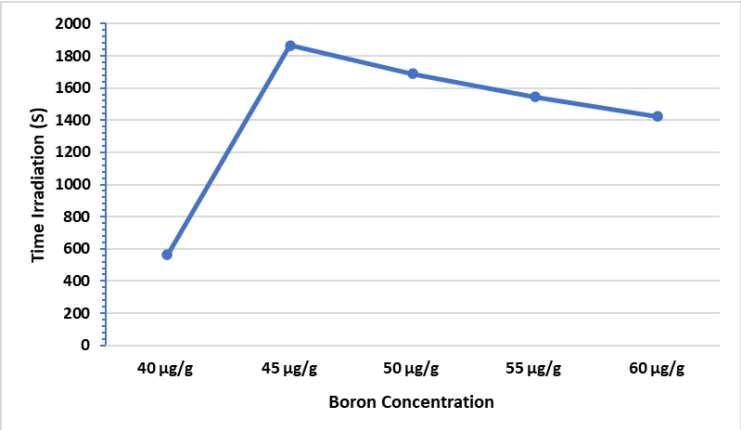


Figure 4. Graph of each boron concentration variation to irradiation time

From Figure 4, the least time to irradiate using 40 µg/g boron concentration with a duration of 562.1074606 seconds, or 9 minutes and 22 seconds, and the longest time using 45 µg/g boron concentration with a duration of 1866.179767 seconds, or 31 minutes and 6 seconds Furthermore, cancer irradiation time is used to obtain the value of the absorbed dose in each organ at risk (OAR).

This time calculation was then compared with a clinical trial of BNCT through a reactor source fired from the Kyoto University Reactor [12]. In the test, it took between 30 and 60 minutes for the irradiation to take place. In this study, the boron concentration variation of 45 to 60 µg/g is within the time range, while for the concentration variation of 40 µg/g the irradiation time is not close to the time range of the BNCT test results because the time duration is too short. Based on the ALARA principle, a boron concentration of 60 µg/g is considered an effective time to perform BNCT therapy because its duration is shorter than the other concentration variations [13].

5. Absorbed Dose

In the case of lung cancer, healthy organs were used in order between the collimator tip and the cancer, namely skin, breast, right lung, PTV tissue, and CTV tissue. The product of irradiation time and dose rate for each organ at risk is shown in the graph in Figure 5.

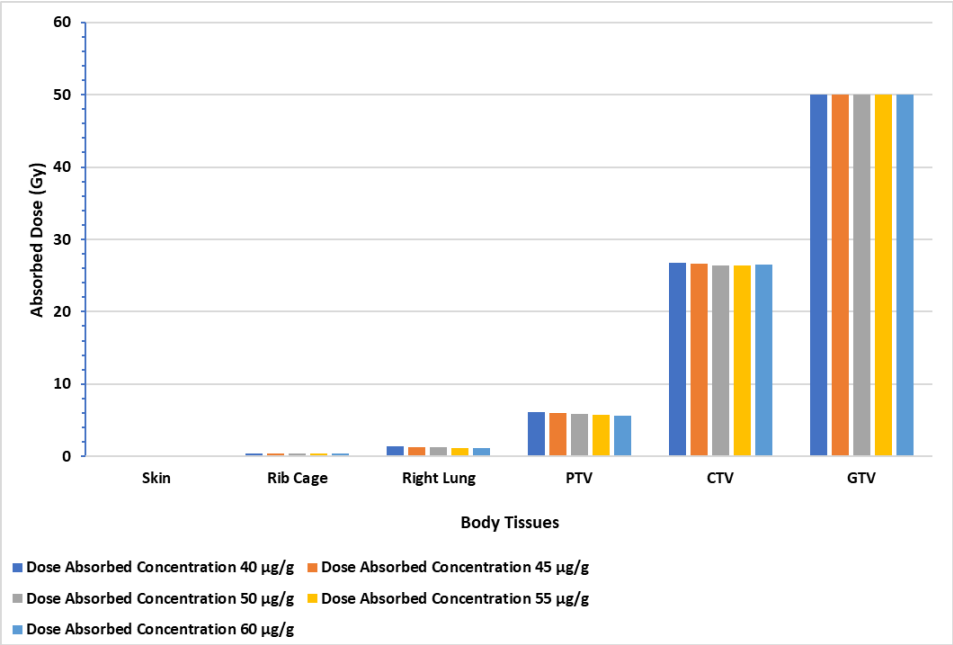


Figure 5. Graph of absorbed dose for each body tissue

Based on Figure 5, it is evident that among other at-risk organs, the right lung tissue receives the highest absorbed dose. However, as we go deeper, the dose absorbed by the body will increase. The increase in the amount of absorbed dose occurs significantly when approaching the CTV and GTV tissues. This is related to the distribution of boron concentration in a ratio of 1:5:10 between healthy tissues (including PTV), CTV, and GTV so that BNCT irradiation takes place selectively and effectively in cancerous tissues.

In analyzing the optimal irradiation time, it is necessary to consider the effects of radiation on organs at risk due to the absorbed dose received from irradiation therapy at each boron concentration. In this study, lung tissue is the part of the organ that is exposed to the highest radiation effect among other healthy tissues. Therefore, the radiation effects received by the body that are very likely to occur in this BNCT therapy are deterministic. Organs affected by deterministic effects are related to the receipt of absorbed doses, where the absorbed dose value exceeds the dose threshold in the organ. Therefore, the determination is also carried out based on the ALARA principle and applicable guidelines for determining the threshold dose.

The deterministic effect is one of the potential side effects of radiation exposure, as previously explained. This effect is the impact that occurs when the body tissue absorbs a dose greater than the predetermined threshold. In this study, the deterministic effect occurs in body tissues that are passed by neutron flux that leads to cancer cells, such as skin, ribs, and the right lung. Referring to the data released by the IAEA (1998), the dose threshold values in tissues affected by deterministic effects are shown in Table 3 [14].

Table 3. List of dose threshold values in tissues affected by deterministic effects

Organ At Risk	Side Effects	Absorbed Dose Threshold (Gy)
Bone Marrow	Cell Death	1,5
	Haematopoiesis	0,5
Lung	Cell Death	6
	Pneumonitis	3-5
Skin	Erythema	3
	Dry Desquamation	5
	Wet Desquamation	15
	Necrosis	50

Based on the data in Table 3, in bone marrow tissue, side effects will occur in the form of early cell death, hemopoiesis trauma, or disruption of blood cell formation. In the lung tissue, side effects such as early cell death and pneumonitis will occur. While in the skin, there will be side effects in the form of erythema, or reddish skin; dry desquamation, or scars that dry out; wet desquamation, or festering scars; and necrosis, or death of skin tissue. Table 4 shows the analysis that occurs in tissues affected by deterministic effects.

Table 4. Deterministic effects of organs at risk in each of Boron concentration

Boron Concentration (µg/g)	Organ at Risk	Total Dose Rate (Gy)	Absorbed Dose Rate (Gy)	Deterministic Effects
40	Skin	0,564	50	-
	Rib	1,281	1,5	-
	Lung	3,151	3 - 5	Pneumonitis
45	Skin	1,941	3	-
	Rib	4,553	1,5	Cell Death
	Lung	11,465	3 - 5	Cell Death
50	Skin	1,817	3	-
	Rib	4,396	1,5	Cell Death
	Lung	11,042	6	Cell Death
55	Skin	1,715	3	-
	Rib	4,257	1,5	Cell Death
	Lung	9,826	6	Cell Death
60	Skin	1,629	3	-
	Rib	4,154	1,5	Cell Death
	Lung	8,686	6	Cell Death

From the results of the analysis of the relationship between the amount of absorbed dose and the deterministic effects received, skin and lung tissue experienced side effects in the form of cell death at concentrations of 45 µg/g to 60 µg/g as described in Table 4, while at a concentration of 40 g/g, they experienced deterministic effects in the form of pneumonitis in the lungs. However, when referring to the results of BNCT clinical trials through reactor sources fired from the Kyoto University Reactor and the ALARA principle, the same concentration with an irradiation time of 1223.679 seconds, or 20.4 minutes, is the optimal irradiation time because it is the shortest time according to these two parameters.

CONCLUSION

Based on the results of the research and discussion that have been presented, the cancer therapy simulation in this study uses a lung cancer geometry design that is divided into 3 parts, namely PTV, CTV, and GTV, with a cancer diameter size of 3 cm. The cancer design display is located in the middle lobe of the right lung. Then the human body geometry design simulated in this study uses a phantom made by ORNL-MIRD. Meanwhile, the effective boron concentration value in this study is 60 µg/g with the risk of causing deterministic effects on lung tissue and rib tissue, which requires time for cancer to absorb neutron flux for 1223.679 seconds, or 20.4 minutes. For the next research, it is necessary to pay attention to the neutron flux output to comply with the standards issued by the IAEA. In addition, future research is expected to make variations in boron concentrations that exceed 60 µg/g after the results of this study showed this concentration to be an effective concentration for treating lung cancer cells.

REFERENCES

1 GLOBOCAN. 2020. *Estimated Number of Cancer Incidence, Mortality, and Prevalence Worldwide in 2020*. International Agency of Research for Cancer.

2 Kementerian Kesehatan Republik Indonesia. 2017. *Pedoman Nasional Pelayanan Kedokteran (PNPK) Untuk Kanker Paru*. Online: https://www.kemkes.go.id/id/media/subfolder/pedoman/pedoman-nasional-pelayanan-kedokteran-pnpk.

3 Sauerwein, W., Wittig, A., Moss, R., & Nakagawa Y. 2012. *Neutron Capture Therapy - Principles and Applications*. Springer-Verlag Berlin Heidelberg. Berlin Heidelberg Jerman. JRC77319.

4 Ardana, I.M., Noerwasana, A.D., & Sardjono, Y. 2018. Kajian Teknologi Boron Neutron Capture Therapy (BNCT) dan Aspek Regulasinya. *Prosiding Seminar Keselamatan Nuklir*. 95-101.

5 Sauerwein, W.A.G., Pierre M. B., & Wittig, A. 2012. Drugs for BNCT: BSH and BPA. *Jurnal Neutron Capture Therapy*: 117-140.

6 Ting, G., Chang, C. H., Wang, H. E., & Lee, T. W. 2010. Nanotargeted radionuclides for cancer nuclear imaging and internal radiotherapy. *Journal of biomedicine & biotechnology*, *2010*, 953537.

7 Hidayatullah, R., 2017. Dampak tingkat radiasi pada tubuh manusia. *Jurnal Mutiara Elektromedik, 1*(1).

8 Harish, A.F., Dwijohartoko, W., & Sardjono, Y. 2018. Dose analysis of boron neutron capture therapy (BNCT) treatment for lung cancer based on particle and heavy ion transport code system (PHITS). *ASEAN Journal On Science & Technology for Development*, *35*(3), 187-194.

9 Fauziah, N., Widiharto A., & Sardjono, Y. 2013. A Conceptual design of neutron collimator in the thermal column of Kartini research reactor for in vitro and in vivo test of boron neutron capture therapy. *Jurnal Teknologi Reaktor Nuklir*. *15*(2), 112-119.

10 Tesalonika, A., Widiharto, A., Sardjono, Y., & Triatmoko, I. M. 2016. Dosimetry of in vitro and in vivo trials in thermal column Kartini reactor for boron neutron capture therapy (BNCT) facility by using MCNPX Simulator Code. *Indonesian Journal of Physics and Nuclear Applications*, *1*(2), 63-72.

11 IAEA. 2001. *Current status of neutron capture therapy*. IAEA-TECDOC-1223. Vienna, Austria.

12 Suzuki, M., Suzuki, O., Sakurai, Y., Tanaka, H., Kondo, N., Kinashi, Y. Masunaga, Maruhashi, A. & Ono, K. 2012. Reirradiation for locally recurrent lung cancer in the chest wall with boron neutron capture therapy (BNCT). *International Cancer Conference Journal*, *1*, 235-238.

13 Yeung, A.W.K. 2019. The “As Low As Reasonably Achievable” (ALARA) principle: a brief historical overview and a bibliometric analysis of the most cited publications. *Radioprotection*, 54(2), 103-109.

14 International Atomic Energy Agency. 1998. *Health Surveillance of Persons Occupationally Exposed to Ionizing Radiation: Guidance for Occupational Physicians*, Safety Reports Series 5, Vienna, Austria.