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Preparation of Dosimetry of Boron Neutron Capture Therapy (BNCT) for In vivo Test Planning system Using Monte Carlo N-Particle Extended (MCNP-X) Software

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Abstract-Cancer is a disease with second largest patients in the world. In Indonesia, the number of radiotherapy facility in Indonesia is less than 30 units and every patients needs more than single exposure, so that it result a long waiting list of treatment up to one year. Now, a new treatment of cancer is developed. It is Boron Neutron Capture Therapy that using capture reaction of neutron by Boron-10. Before this method is applied to patient, it requires some testing which is one of them is in vivo test. This research has been conducting to prepare the in vivo test, especially in dosimetry. Preparation of dosimetry includes collimator design and mouse phantom model. The optimum specification of the collimator is consist of Nickel collimator wall with 2 cm of thickness, Aluminum moderator with 10 cm of thickness and lead gamma shield with 3.5 of thickness. This design result in 1.18 x 10^8 n/cm^{2}s of epithermal and thermal neutron flux, 2,24 x 10^{-11} Gy cm^2/s of fast neutron component dose, 1.35 x 10^{-12} Gy cm^2/s of gamma dose component, and 7.18 x 10^{-1} of neutron current and flux ratio. Mouse phantom model is built by two basic kind of geometry, they are Ellipsoid and Elliptical Tory. Both of basic geometry can be used to make all important organs of mouse phantom for dosimetry purpose.

Keywords : dosimetry, MCNPx, BNCT, In vivo

INTRODUCTION

The prevalence of cancer over five years (2007-2012) has been shown that there were 6.3 million breast cancer patients from the 32.5 million people with cancer. Followed by 3.9 million prostate cancer case, 3.5 million colorectal cancer case and 1.9 million lung cancer case (Bray et al. 2012). Indonesian Association of Radiation Oncology noted that the number of radiotherapy facility in Indonesia is less than 30 units. Moreover, one patient may require multiple therapies. The unbalanced number between patients and radiotherapy facility caused long waiting list, up to one year. During that period, the stage of the cancer has been increasing, so the cancer cases which are able to be handled are only about 60%. Because of this problem, more efficient methods of cancer therapeutic is needed.

The reason for repeated treatments such as radiotherapy (LINAC, Tele-cobalt, etc.) and chemotherapy is due both healthy cells and cancer cells are equally damaged. By taking the principle of "As Low As Reasonably Achievable (ALARA)", these therapies generally are applied gradually with a certain faction that focuses on cancer cells. This is due to the limited ability of healthy cells for regenerating (Alotiby 2012). Therefore, it has developed several methods of other cancer therapies based on neutron radiation, it is Boron Neutron Capture Therapy (BNCT). The therapy is a binary form (a combination of chemotherapy and radiotherapy) that are expected to cover the disadvantages of some of the above methods.

BNCT uses epithermal and thermal neutrons with energies below 2 MeV. Neutrons

can be produced from a variety of sources. That are thermal reactor (~ 2 MeV), ^{252}Cf or by reaction of ^{9}Be (p, d) ^{8}Be then ^{3}H (d, n) ^{4}He (A. Anonim 2014). BNCT is using a secondary radiation that will only appear if the thermal neutrons interact with ^{10}B, and generating radiation beam α and ^{7}Li. The range of these radiations are from 4.5 to 10 μm in water (phantom) or tissue. Thus, the energy deposited in the medium is limited to a single cell diameter (<10 m) (Saurwein et al. 2012). The advantage of BNCT therapy compared to conventional therapy is its ability to damage tumor cells with a small radius of destruction, so the side effects on surrounding healthy tissue is low. This is because in this therapy involves radiation that has high Linear Energy Transfer (LET).

^{10}B is one of BNCT is non-toxic and non-radioactive therapeutic agent, hence the side effects when injected into the body is much smaller than chemotherapy (Saurwein et al. 2012). In order to get successful therapy, the therapeutic agent should be a compound that fulfill following conditions: selectively accumulates in tumor cells, have a minimum ratio of ^{10}B concentration between tumor and blood which is 3: 1, and reach therapeutic concentrations in the cell (20 μg ^{10}B / g tumor). ^{10}B carrier compound must also fulfill some general requirements, such as have low toxicity and quickly removed from the body. Due to this problem, currently its being developed ^{10}B compounds carrier curcumin analog (derivative) based. These compounds will recognize a HER2 specific receptor in breast cancer. Hence it will only be deposited in the tissues (Meiyanto, et al., 2014).

Before the analog curcumin ^{10}B carrier compound was applied clinically to humans, preclinical trials need to be done before in vivo test. It is a test of the sample organisms that have similar biological properties to human beings, so that the pharmacologic effects and radiation effects can be seen directly. The sample organisms are mice that had been injected with tumor types T47D. This tumors will grow specifically only in the mammary gland.

For in vivo testing preparation, there must be designed the Experimental Setup related to radiation which includes radiation dosimetry. Dosimetry for BNCT treatment of breast cancer has been taken computationally by Novianti (2013) with a thermal neutron source from column Reactor through simulation using Monte Carlo N Particle version 5 (MCNP5). In this version, the available features are limited to the radiation beam of photons, neutrons and electrons (B. Anonim 2003). In fact, the interaction of particles in BNCT involve secondary radiation such as heavy ions (α particles and ^{7}Li recoil._Whereas, dosimetry of heavy ions couldn't be solved by numerical computation method of MCNP5 but was approached by analysis of dose calculations which only refers to the flux of neutrons and photons, so the accuracy was low (Novianti 2013)._

The next version of MCNP5 is MCNP-eXtended (MCNPX). This version can analyze particle track and its interaction more comprehensive due to simulating 35 kinds of radiation beams, including heavy ions. By this software, more accurate dosimetry for in vivo test planning, can be calculated. Because of that background, this topic is chosen as subject of research to solve the breast cancer problem.

MATERIALS AND METHODS

Material

The chosen method of this research is through numerical computational simulations using a set of Personal Computer with supporting software, such as the Monte Carlo N-Particle eXtended (MCNPX), Microsoft Excel 2013, Notepad ++ v6.6.7, Visual Editor Version 26e.

Procedure

Before modeling, modifications of collimated neutron source reference will be carried out. The collimated neutron source is a neutron radiation beam that comes out from the radial piercing beam port of Kartini nuclear Reactor 100 kW through a collimator with specifications as shown in Figure 1.(a), thus it satisfy some of the IAEA requirements. This modification is conducted to prepare the in vivo tests due to inefficient of previous collimator. It because of the aperture hole is too small and only irradiate a sample. Thus, this modification purpose is to expand the area of irradiation so that the experiment process becomes faster. Estimated results of these modifications are shown in Figure 1.(b).

Modifications will start with eliminating the aperture part, consisting of a truncated hollow cone, thermal neutron filter (Boral) and a gamma shield (Pb). Then the new geometry is simulated by MCNPX to be evaluated. If it meets the requirement, the output of the radiation beam can be used for irradiation. But if it does not meet that, collimator wall and / or moderators thickness will be changed

Parameter of IAEA Recommendation	Modified parameter of Radiation Beam on In vivo test	Specification
f_{th} (n / cm^{2}s)	($f_{epi}+f_{th}$) (n / cm^{2}s)	>1.0× 10^9
$\dot{D}_f / f_{epi}$ (Gy cm^2 / n)	$\dot{D}_f / (f_{epi}+f_{th})$ (Gy cm^2 / n)	< 2.0× 10^{-13}
$\dot{D}_g / f_{epi}$ (Gy cm^2 / n)	$\dot{D}_g / (f_{epi}+f_{th})$ (Gy cm^2 / n)	< 2.0× 10^{-13}
f_{th} / f_{epi}	Not specified	< 0.05
J / f_{epi}	$J / (f_{epi}+f_{th})$	>0.7

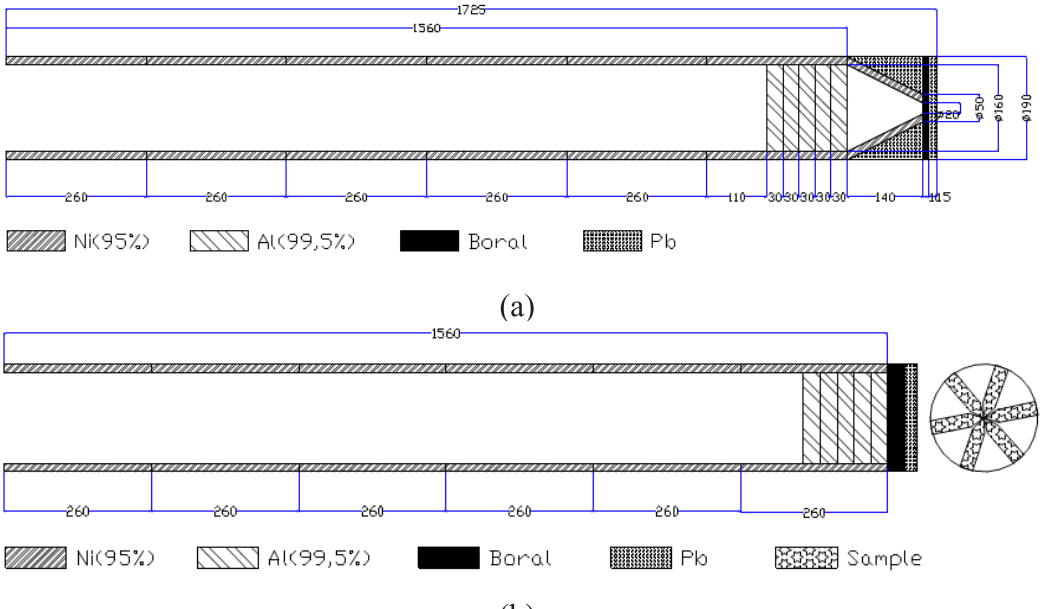

Figure 1. (a). Neutron Collimator on Radial Piercing Beam Port Kartini Nuclear Reactor (Arrozaqi 2013) (b). Estimated modification of collimator without aperture part

in accordance with the unmet requirement parameter. If needed, it also will be added the thermal neutron filter and / or radiation shield with a variety of thicknesses using the same materials with reference collimator. Each variation of the thickness of each component, refers to the mean free path interaction of the material components. This simulation is conducted continuously to obtain a required radiation beam or optimum specification of the radiation beam. Although in clinical therapy refers to the IAEA recommendation, radiation beams specification in the in vivo test is modified depend on the organisms, in this case are mice.

As a preparation of simulation, it is important to choose the parameters that would be the basis of optimization. In the case of modification collimator, the parameters may include epithermal neutron flux, the thermal neutron flux, the flux neutron total, fast neutron dose rate, the gamma dose rate and neutron current. Besides, in terms of dosimetry, it is needed to calculate alpha dose rate, protons and recoil ^{7}Li as a primary dose. In the calculation of these parameters are used tally mode in accordance with the purpose of calculation. Calculation of neutron flux and fast neutron dose rate using tally type F4: N, photon dose rate calculations using tally F4: P and neutron current calculation using F1: N. For a primer dose, using F6: a for alpha, F6: h for proton and F6: # 7003 for 7Li recoil.

Generally, application of tally F4 is for calculating the average flux passing through a volume geometry, while calculating the flux passing through a surface used tally F2. However, in practical use, F4 is more flexible to use because it can define different sections that are restricted to the same surface. As mentions in the previous paragraph, F4 is used in three different calculation purposes. But in MCNP was not allowed use the same kind of tally in all calculations. Therefore, it is necessary to add an index to distinguish each of these calculations. The index is placed between the F letter and n (number of tally). In this study, F4: N is used for the calculation of neutron flux, F14: N for fast neutron dose rate calculations, and F24: P for the calculation of the gamma dose rate.

When executed, MCNP simulates the particles track and iterates several times in order to obtain a value of flux with a small relative error. This value is presented a percentage or fraction of the probability of the particles in the measured point. Therefore, it needs multiplier factor, which represents a source strength to obtain the real flux. The multiplier factor is a result of a power conversion rate from fission rate, as follows:

$$\left(10^{5}\,\mathrm{W}\right)\left(\frac{1\ \mathrm{J/s}}{\mathrm{W}}\right)\left(\frac{1\ \mathrm{MeV}}{1,602\times10^{-13}\,\mathrm{J}}\right)\left(\frac{1\ \mathrm{fisi}}{200\,\mathrm{MeV}}\right)=$$

$$3,121\times10^{15}\,\frac{\mathrm{fisi}}{\mathrm{s}}$$

To generate 100 kW thermal power, its required $3,121\times10^{15}$ fisi/s. By that fission rate data, the multiplier for each tally can be determined refer to radiation beam. Multiplier factor for neutrons is as follows

$$\left(3,121\times10^{15}\,\frac{\mathrm{fisi}}{\mathrm{s}}\right)\left(\frac{2,42\ \mathrm{n}}{\mathrm{fisi}}\right)=7,553\times10^{15}\ \mathrm{n/s}$$

This value will be used in the calculation of neutron flux (F4: N) and the calculation of neutron dose rate (F14: N), while the multiplier for gamma photons are as follows

$$\left(3,121\times10^{15}\,\frac{\mathrm{fisi}}{\mathrm{s}}\right)\left(\frac{1}{\mathrm{fisi}}\right)=3,121\times10^{15}\ \mathrm{n/s}$$

This value will be used in the calculation of gamma dose rate (F24: P). In the calculation of the neutron current (F1: N), it needed to be divided by the area of neutron output at the

collimator. In this study has been set aperture collimator diameter of 19 cm, thus the multiplier factor is

$$\frac{7{,}553\times10^{15}\,\mathrm{n/s}}{\delta\,(8{,}5\ \mathrm{cm})^2}=3{,}328\times10^{12}\,\frac{\mathrm{n}}{\mathrm{cm^2 s}}$$

These factors will be used to convert tallies input files in a special card (fm card).

Fm card for F6 is a conversion of MeV / g units into J / kg which is equivalent to 1 Gy. The value of fm6 is $1{,}602\times10^{-10}$.

After the supporting factor is defined, the procedures will follow several steps below

Step 1.

The first step is choosing candidate material according the properties in interacting with neutron. The Collimator wall material must have a high elastic cross section interaction, the moderator material must have a high inelastic cross section and gamma shielding must have a high density. Three of those kind of material should have a low absorbing cross section to prevent reducing neutron flux.

Step 2.

All of attached material is simulated by MCNPX and all of the radiation parameter is measured at the end of beam port. The simulations is conducted for several thickness of materials until the specified recommended value is obtained. If that value can be reached, the optimum value will be considered. The simulation will follows a sequences which start with simulation of collimator wall, moderator then gamma shield. The final optimum result of radiation specification will be used for in vivo test.

Step 3.

The phantom geometry of mouse will be modeled and evaluated by Visual Editor. This phantom will be placed in front of the collimated radial piercing beam port so that can be exposed with radiation that came from the core of Kartini Nuclear Reactor. The prepared model is ready for dosimetry purpose.

RESULTS AND DISCUSSION

Modification of Collimator

The candidate of collimator walls are copper, nickel, iron, Aluminum, Carbon, Bismuth, Lead and Titanium. All of those material can be found easily in industrial material and they have a low absorption cross section and high elastic cross section. Because its function is to keep neutron flux stay high, the

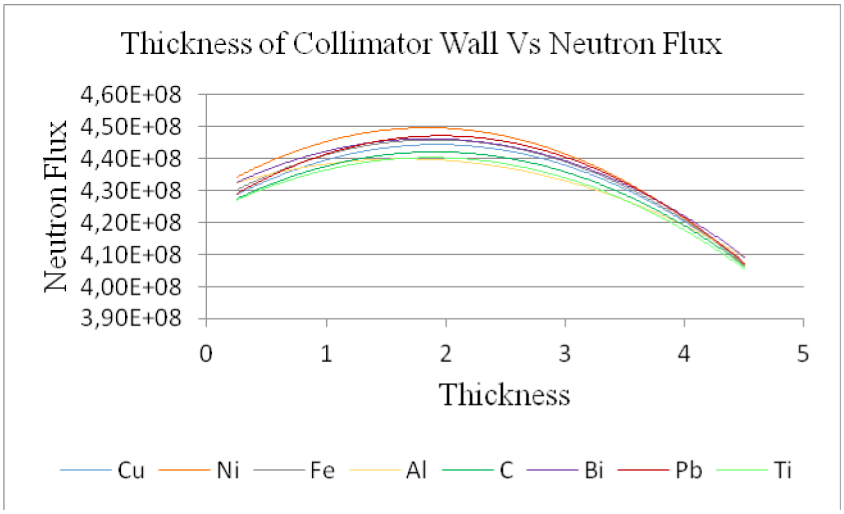

Figure 2. Total Neutron Flux over beam port Vs Variation of Thickness after collimator wall was attached

parameter analyzed is total neutron flux through the end of beam port. The simulation data are represented in Figure 2. below.

The data show that all of materials cannot keep total neutron flux high enough to meet the requirement. Thus, the optimum condition for each material is taken as shown in the Figure 3.

Base on that chart, nickel with 2 cm of thickness has been chosen as collimator wall material of beam port.

The next section is moderator. This section serves to decrease the energy of fast neutrons become epithermal neutron or thermal neutron that is needed in BNCT. To make a decision for choosing a proper material, the ratio of fast neutron dose per epithermal and thermal flux is analyzed. Then this parameter is called Fast neutron dose component.

We can see that Aluminum and sulphure has good ability to decrease fast neutron dose component. To make a decision between aluminum and Sulphur, it is needed to present more accurate data. The additional data is shown in Figure 5.

Aluminum is more powerfull to decrease fast neutron component dose than sulphure, but it reduce the neutron flux faster, whereas we need a high neutron flux. Because of that reason we choose sulphure moderator with 10 cm of thickness.

The next simulation is to evaluate gamma shield that provide by Lead, Bismuth and Tungsten. Those material have high density, so that they are suitable as gamma shield. In the section, we need a lowest gamma dose, but we are not lost a large number of neutron flux. Thus we have done an optimization beetween

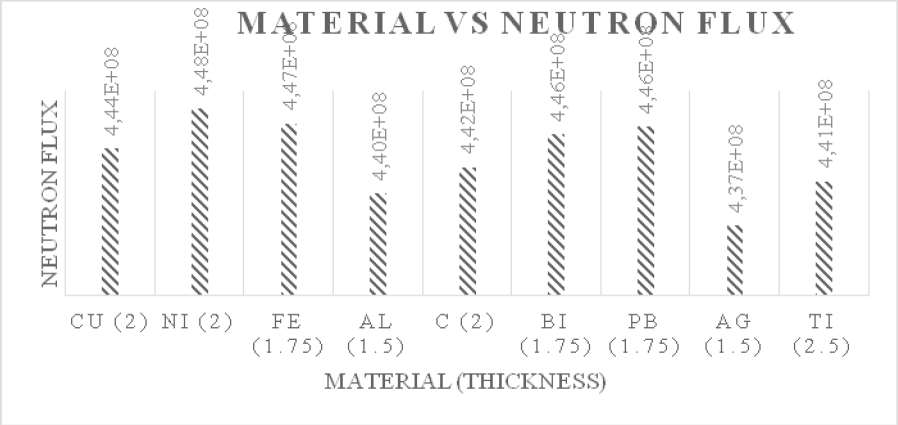

Figure 3. Maximum Total Neutron flux through beamport for each material (thickness)

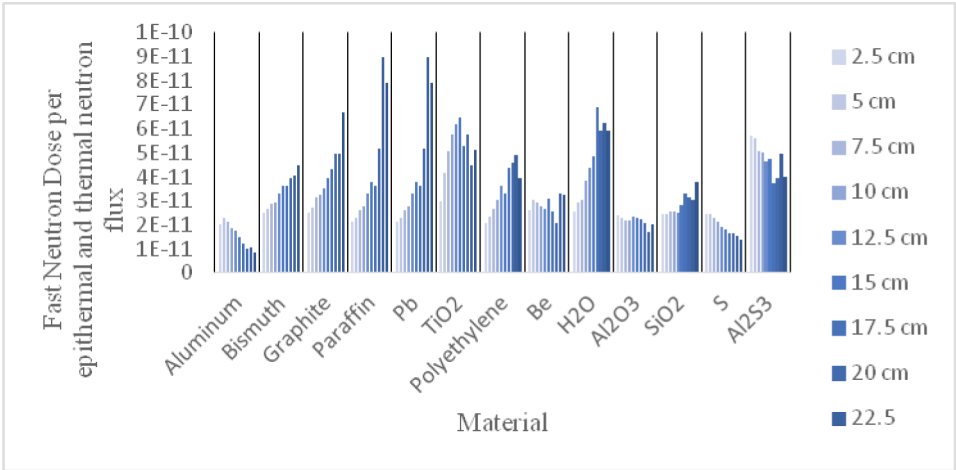

Figure 4. Fast neutron dose component after moderator of each material attached

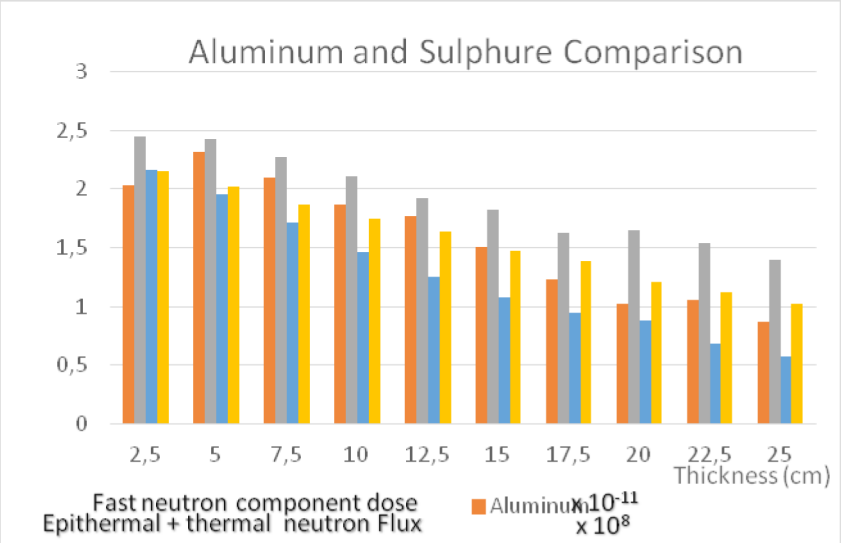

Figure 5. Aluminum and shulphur comparison related neutron flux and fast neutron dose component

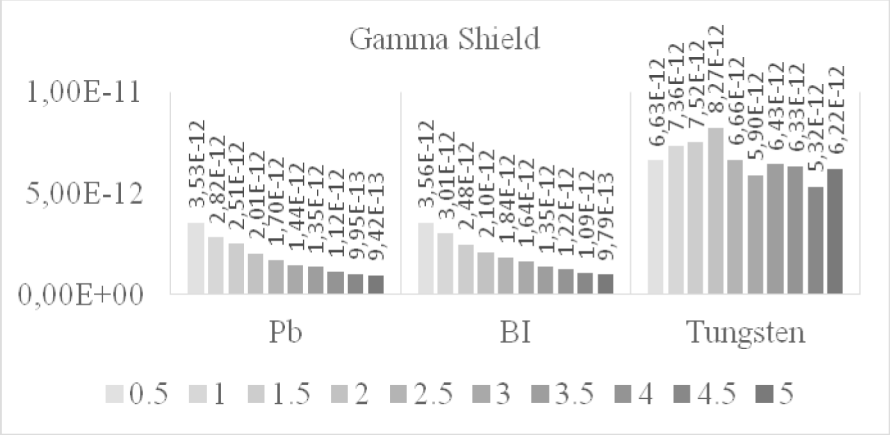

Figure 6. Gamma dose component for each tickness of material candidates

both of those paramater. The data are shown at Figure 6. To make it easier for analyzing, we define a ratio between gamma dose rate per epithermal and thermal neutron flux as gamma dose component.

That figure shows, Lead and bismuth have a good properties to be gamma shield. Lead is little bit faster to decrease gamma dose component than bismuth. Hence, we choose lead for this part of collimator component. To get an optimum result, we have to consider the decreasing epithermal and thermal neutron flux too.

We can see that after 3.5 cm of thickness, there is no significant decreasing of gamma dose component. Thus, we don't need more lead that cause reducing neutron flux instead. Hence, we choose lead with 3.5 cm of thickness as optimum gamma shield. The final optimization design is resulting radiation beam specification that presented in Table 2.

Table 2. Radiation specification after collimated

Modified parameter	Specification
$(f_{epi} + f_{th})\ (n / cm^2 s)$	1.18 x 10^{8}
$\dot{D}_f / (f_{epi} + f_{th})\ (Gy\,cm^2 / n)$	2,24 x 10^{-11}
$\dot{D}_g / (f_{epi} + f_{th})\ (Gy\,cm^2 / n)$	1.35 x 10^{-12}
$J / (f_{epi} + f_{th})$	7.18 x 10^{-1}

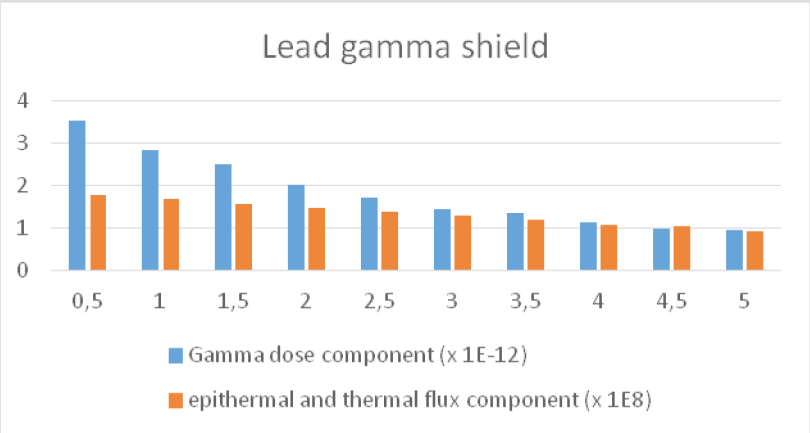

Figure 7. Gamma dose component and flux of epithermal and thermal neutron

Table 3. Mathematic Definitions and Parameters Used for Stylized mouse phantom Model (Konijnenberg et al. 2004).

Ellipsoids	$\left(\frac{x-x_0}{a}\right)^2+\left(\frac{y-y_0}{b}\right)^2+\left(\frac{z-z_0}{c}\right)^2=1$						Angle with z-axis
Organ	a (cm)	b (cm)	c (cm)	x_0 (cm)	y_0 (cm)	z_0 (cm)	θ
Liver	1.8	2.35	1.15	0	1	0.5	0°
Spleen	0.3	1.6	0.375	0.5	1.25	−1	−13°
Kidney	0.5	0.7	1.1	±1	0	−1.5	0°
Surface	0.4	0.6	1.0	±1	0	−1.5	0°
Cortex	0.3	0.45	0.725	±1	0	−1.5	0°
Lungs	0.475	1.6	1.9	±0.75	1	3.5	±10°
Heart	0.6	0.7	1.0	0	0	4	0°
Stomach	0.75	1.1	1.75	0	−2	−0.5	0°
Small bowel	1.9	0.5	2.5	0	−1	−2	0°
Large bowel	0.63	2.31	2.36	0	0	−5	0°
Thyroid	0.29	0.074	0.66	0	2	5	0°
Pancreas	1.8	0.5	0.26	0	0	−0.5	0°
Bladder wall	0.2	0.5	0.625	0	−0.25	−10	0°
Contents	0.15	0.45	0.575	0	−0.25	−10	0°
Testis	0.47	0.94	0.94	±0.47	1.0	−10	0°
Skull	0.85	1.6	4.0	0	0	10.5	0°
Brain	0.75	1.5	1.5	0	0	10.5	0°
Body contour	1.65	13.3	12.9	0	0	0	0°
Cylinders	$(x-x_0)^2+(y-y_0)^2=r^2$ with $\lvert z-z_0\rvert \le A$						Angle
Organ	r (cm)	A (cm)		x_0 (cm)	y_0 (cm)	z_0 (cm)	θ
Femur	0.2	5.55		±0.79	−1	−9	±4.5°
Marrow	0.1	2.3		±0.79	−1	−9	±4.5°
Elliptical tori	$\left(\frac{x}{b}\right)^2+\left(\frac{\sqrt{(y-\bar{y})^2+z^2}-a}{c}\right)^2=1$, with $\lvert x\rvert \le 9$ and $y<0$						
	a (cm)	b (cm)	c (cm)	$\bar{y}$ (cm)			
Spine	42.5	0.25	0.2	39.25			
Spinal core	42.5	0.1	0.1	39.25			

Mouse phantom modeling

Model of mouse phantom is refer to this dimmension as shown in Tabel 3.

From those data, geometry of mouse can be built by MCNPX and Vised as shown in Figur 8.

CONCLUSION AND REMARKS

Preparation of dosimetry of BNCT for in vivo test includes collimator design and mouse phantom model. For this purpose, the optimum design of collimator has been obtained. The specification of the collimator is consist of Nickel collimator wall with 2 cm

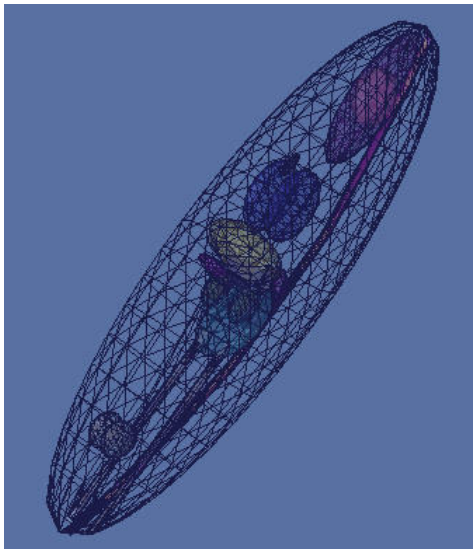

Figure 8. Mouse phantom model (built by MCNPX and Vised)

of thickness, Aluminum moderator with 10 cm of thickness and lead gamma shield with 3.5 of thickness. This design result in 1.18 x 10^8 n/cm^{2}s of epithermal and thermal neutron flux, 2,24 x 10^{-11} Gy cm^2/s of fast neutron component dose, 1.35 x 10^{-12} Gy cm^2/s of gamma dose component, and 7.18 x 10^{-1} of neutron current and flux ratio. Mouse phantom model is built by two basic kind of geometry, they are Ellipsoid and Elliptical Tory according Table 3. Both of basic geometry can be used to make all important organ of mouse phantom for dosimetry purpose.

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