Simulation of microtube irradiation on the beam tubes of GA Siwabessy reactor for in-vitro boron neutron capture therapy

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Abstract. The BNCT in-vitro test using a microtube irradiated in the neutron beam of the RSG-GAS beam tubes has been simulated using PHITS code. The simulation was performed by modeling a microtube containing boron solution which was placed 5 cm in front of the beam tubes. Inside the beam tube was installed a beam shaping assembly (BSA) using 80 cm of MgF$_2$ as a filter to reduce fast neutron and gamma fluences. Microtube containing 1.5 mL of boron solution with boron enriched $^{10}$B of 90%. The microtube dose i.e alpha dose, $^7$Li dose, proton dose, and gamma dose were calculated for boron concentration of 1 ppm. The simulation of microtube containing 1 ppm boron solution showed that irradiated in the BSA-S5 neutron beam can produce 20 Gy dose in the shortest irradiation time of 2.5 hours.

1. Introduction

1.1 Boron Neutron Capture Therapy (BNCT)

The BNCT therapy is a type of radiotherapy based on thermal neutron irradiation of tissue enriched with $^{10}$B, which will produce alpha particles and $^7$Li ions with short-range interactions and high biological effectiveness [1]. Boron ($^{10}$B) has been widely used as a chemical agent where the technique is known as BNCT. The advantage is that the BNCT technique will only destroy tumor cells that contain a lot of boron, where boron is carried into tumor cells using an active compound called a carrier agent. This method can work well if the tumor cells are far from healthy cells. The principle of BNCT is based on the reaction of the $^{10}$B (n,α)$^7$Li boron neutron capture.

$$\frac{1}{2}n + ^{10}_2B \rightarrow ^4_2He + ^3_2Li + \gamma$$

(1)

The neutron capture reaction by $^{10}$B produces alpha-heavy particles ($^4_2He$) energy 1.47 MeV, lithium ($^3_2Li$) energy 0.84 MeV, and gamma rays with energy 0.48 MeV. Alpha and lithium particles have high linear energy transfer (LET). Both of these particles are able to store their energy in the tissue with a depth of 4.1 μm and 7.7 μm [2]. Alpha particles have 150 MeV/mm stopping powers, while 175 MeV/mm lithium. This large dose and short range makes the BNCT technique provide maximum radiation dose to target organs and minimum to healthy organs. The deposited energy depends on the ability of $^{10}$B core deposition and its concentration in the tumor [3,4].
1.2 BNCT In-Vitro Test

The development of neutron beam facilities for BNCT applications to humans (patients) has quite a long stage due to obtaining characteristics of beams according to IAEA recommendations [5]. Before applying to humans, a series of tests is needed. BNCT tests include pre-clinical and clinical trials. Pre-clinical trials consist of in vitro tests and in vivo tests. In vitro (in glass) is a treatment procedure given in a controlled environment outside a living organism. Many cellular biology experimental studies carry out treatments outside organisms or cells. The in vivo (in life) is an experiment using all living organisms. In vivo tries to avoid partial use of organisms or dead organisms.

In vitro tests for BNCT can use microtubes, while in vivo tests can be carried out using animals of mice, rabbits and makaka types. In vitro tests begin with microtube irradiation (micro-tubes) in which cells or tissues that have been mixed with compounds containing $^{10}$B are inserted as in which. shown in Figure 1. The test was carried out to obtain the maximum dose of variation in the concentration of $^{10}$B in the tissue. After the BNCT test on cells in a micro-tube is successful, it can be continued with in vivo, namely in test animals, such as mice (mice) and makaka. At this stage a $^{10}$B distribution test can be performed on the organs of test animals to determine the effectiveness of the carrier compound. After BNCT in animal testing is successful, clinical trials in humans can be carried out.

![Microtube for in-vitro BNCT test.](image)

1.3 Beam Tubes of G.A Siwabessy Reactor

The neutron source that can be utilized for BNCT is a nuclear reactor. The reactor produces neutrons from the $^{235}$U fission reaction with thermal neutrons on the reactor core. Fast neutrons (2 MeV) are produced from fission reactions partially moderated by cooling water to thermal and epithermal neutrons. The neutron beam from the reactor core exits through a file tube for irradiation application. Multi-purpose Reactor G. Siwabessy (RSG-GAS) in Indonesia operates with a power of 30 MW and has 6 tube tubes (S1, S2, S3, S4, SS4, and S6) with a length of 400 cm and a diameter of 30 cm as shown in Figure 2.

In this paper, the simulation results of microtube doses using neutron beam on the RSG-GAS beamtube will be presented. Simulations are carried out using the PHITS program in a PC Intel core i5-2.3 GHz processor, 4GB RAM. The interaction of boron in the microtube with the neutron beam of each beamtube was simulated with PHITS to obtain the dose distribution of alpha, 7Li, proton, and gamma in the microtube. The simulation results will show the beamtube and modified using beam shaping assembly (BSA) which produces the highest dose rate, so that it will provide the shortest irradiation time.
2. Methods

This simulation was carried out using a Monte Carlo based computer program namely Particle and Heavy Ion Transport System (PHITS). In this PHITS simulation there are three stages i.e. modeling of microtube geometry, modeling of radiation source, and calculation of alpha, $^7$Li, proton, and gamma dose in the microtube.

2.1 Microtube Irradiation Models

Geometry and material of microtube simulated in the form of 1.5 ml made from polyethylene with a thickness of 0.65 mm. In the tube filled with a solution of water or tissue material that has been mixed with boron compounds with a concentration of 1 ppm. The radiation source used is the result of a BSA output file simulation. The microtube dose function of the depth of each particle resulting from interaction in the solution is obtained using a tally deposit. The alpha dose, $^7$Li dose, proton dose, and photon (gamma) doses is simulated using PHITS.

The success of the test is determined by the percentage of the number of cells that die. The number of dead cells is directly proportional to the dose received by cell material. The greater the dose value received, the greater the number of cells that die. Parameters that can increase the dose of the microtube are neutron energy, neutron beam intensity, and the concentration of boron in the cell material. The geometry modeled in the microtube simulation is shown in Figure 3.
2.2 PHITS Simulation

The Particle and Heavy Ions Transport System (PHITS) is a multipurpose computer code based on 3D Monte Carlo for simulating the transport of particles and heavy ions with the order of energy of $10^5$ eV - 1 TeV [7]. The PHITS program is based on the Monte Carlo method, where the calculation results of particle flux values have statistical errors. Particles in the RSG-GAS beam tube output are neutrons and photons, while for BNCT test alpha particles, $^7$Li nuclei, and protons will be produced. Atomic and nuclear data used in the PHITS simulation for neutrons and photons using the Japan Evaluated Nuclear Data Library (JENDL) with version JENDL-4.0. For alpha particles and $^7$Li nuclei the evaporation (GEM) model and protons use the intra-nuclear cascade (INCL) model [7].

3. Results and Discussion

The PHITS input has been made for microtube irradiation at the RSG-GAS beam tubes. The PHITS output was obtained after the four inputs are run using a computer with an Intel core i5-2.3 GHz processor, 4GB RAM, and Windows 8.1 operating system. In this simulation the interaction of neutrons with materials was taken from JENDL-4.0 cross sections [7,8]. Large neutron flux will shorten the irradiation time so that in-vivo BNCT and BNCT clinics require large fluxes. As for in-vitro BNCT because it uses an abiotic media in the form of a microtube, the long irradiation time is not a problem. Therefore between neutron flux and irradiation time can adjust. The BSA output file was then simulated for microtube irradiation in the BNCT in-vitro test. From the simulation, a tissue dose rate will be generated. These results can then be used to estimate the dose and the length of time needed for irradiation until the tissue dies. The microtube tube has a thickness of 0.65 mm with material made of polyethylene (C$_2$H$_4$) n. The carbon and hydrogen elements in polyethylene have a cross section dominated by elastic scattering.

The results of simulation, the distribution pattern and main components of the microtube dose are strongly influenced by neutron and gamma energy. Thermal neutron flux contributes a microtube dose of $1.4\times10^{12}$ Gy of alpha dose and $6.6\times10^{13}$ Gy of $^7$Li dose, $2.5\times10^{10}$ gamma dose, proton dose $1.6\times10^{21}$ per cm$^2$ s$^{-1}$ neutron flux per ppm boron. Epithermal neutron flux contributes a microtube dose of $1.2\times10^{12}$ Gy alpha dose and $5.8\times10^{13}$ Gy $^7$Li dose, $2.1\times10^{17}$ gamma dose, proton dose $7.2\times10^{14}$ per cm$^2$ s$^{-1}$ neutron flux per ppm boron. Fast neutron flux contributes to a microtube dose of $1\times10^{10}$ proton dose per cm$^2$ s$^{-1}$ neutron flux. Gamma flux contributes microtube doses of $10^{15}$ Gy gamma per cm$^2$ s$^{-1}$ per gamma flux.

3.1 Microtube Irradiation on Beam Tubes

The characterization of neutron beam of the RSG-GAS beam tubes has been summarized by Rasito et al using MCNP [9]. The neutron beam which is then used to irradiate the microtube and calculate the dose in a simulation using the PHITS program. A microtube irradiation simulation using a neutron beam output directly on the radial type of beam tube S3 obtained the microtube dose distribution as shown in Figure 4 and Figure 5 for tangential type of beam tube S2. The BNCT in-vitro test was carried out by putting water in a 1.5 ml microtube. Boron compounds with a level of $^{10}$B 90% are dissolved in water homogeneously with a concentration of 1 ppm. A microtube containing boron solution is placed at a distance of 5 cm from the end of the beam tube to be irradiated. Thermal and epithermal neutron fluxes contribute to alpha and $^7$Li doses, fast neutron fluxes contribute to proton doses, gamma fluxes contribute to gamma doses. For this reason, the use of neutron beams directly from the beam tubes which are still dominated by fast neutrons and gamma will make a major contribution to the gamma dose. Radial tube type tubes will contribute much more than tangential type of beam tubes. In addition to the neutron flux factor, the concentration of boron and the level of boron enrichment greatly affect to dose resulted.
Figure 4. Simulation of microtube irradiation on the radial type of beam tubes (S3), (a) Neutron flux distribution, and (b) Dose distribution.

Figure 5. Simulation of microtube irradiation on the tangential type of beam tubes (S2), (a) Neutron flux distribution, and (b) Dose distribution in microtube.

3.2 Microtube Irradiation on BSA
A beam shaping assembly (BSA) has been designed using a 80 cm thick MgF$_2$ as a fast neutron filter that can reduce gamma doses to $10^4$ times, thermal and epithermal neutron fluxes $10^3$ times, fast neutron fluxes to $10^4$ times, so that the neutron flux ratio epithermal with fast neutrons is 10 times [10]. This BSA is placed in a beam tube and the microtube is placed at a distance of 5 cm in front of the BSA aperture.

Currently, MgF$_2$ has become a fairly effective neutron filter candidate [11,12] because it has small absorption capacity, small incoherent scattering and high coherent scattering cross section [13]. MgF$_2$ material is a potential alternative to produce epithermal neutrons besides the widely used AlF$_3$ material [14]. The accelerator-based BNCT facility at the University of Tsukuba has utilized MgF$_2$ material as the main component of the filter to generate epithermal neutrons [15]. It has been proven that compared to other materials, MgF$_2$ is able to produce optimum epithermal neutrons with the minimum thickness [16,17].
Figure 6. (a) BSA placed in the beam tubes, and (b) Microtube and BSA.

Placement of BSA which has a length of about 100 cm in the end of the beam tube, then the front end of the BSA is in the position of the distance of 350 cm of the beam tube. As shown in Figure 6, the neutron and gamma flux at that position is about 5 times greater than the flux at the outer end of the beam tube. The results of the simulation of neutron flux distribution and microtube dose distribution from BSA placement on the S2 tangential type of beam tube position 350 cm are shown in Figure 7. Placement of BSA on the beam tube that has fast neutron flux and low gamma which is the output of tangential type of beam tubes (S2 and S6) gives a ratio of alpha and $^7\text{Li}$ greater than the dose of proton and gamma. Therefore, as the results of the simulation, BSA placement at the end of the tangential type of beam tube is more effective than in other beam tubes because it produces a smaller dose of protons than the alpha and $^7\text{Li}$ doses.

Figure 7. (a) Neutron flux distribution on BSA-S2, and (b) Dose distribution in microtube.

In Figure 7b was shown the dose distribution of microtube that filled with 1 ppm boron solution with a level of $^{10}\text{B}$ 90% and irradiated in front of the BSA of S2 beam tube. In Table 1 was shown the dose distribution of microtube that irradiated in front of the BSA for all beam tubes. The microtube dose is generally still dominated by proton doses except for the irradiation results in BS- S6 beam tube. The
expected dose of microtube is dominated by alpha dose and $^7$Li dose. The dominance of alpha and $^7$Li doses can be increased by adding ppm concentrations of boron or using boron with $^{10}$B levels greater.

**Table 1.** The dose of microtube irradiated from each BSA beam tubes.

| BSA beam tube | Dose rate (Gy/s) | Irradiation time (hours) |
|---------------|------------------|--------------------------|
|               | Alpha            | $^7$Li                    | Proton | Gamma | Total | ~20 Gy |
| BSA-S1        | 3.34E-04         | 1.59E-04                  | 1.23E-03 | 1.31E-05 | 1.74E-03 | 3.2 |
| BSA-S2        | 1.06E-04         | 5.03E-05                  | 1.40E-04 | 9.76E-07 | 2.97E-04 | 18.7 |
| BSA-S3        | 2.59E-04         | 1.23E-04                  | 9.04E-04 | 1.22E-05 | 1.30E-03 | 4.3  |
| BSA-S4        | 2.48E-04         | 1.18E-04                  | 7.16E-04 | 1.08E-05 | 4.95E-04 | 11.2 |
| BSA-S5        | 3.71E-04         | 1.76E-04                  | 1.65E-03 | 1.69E-05 | 2.21E-03 | 2.5  |
| BSA-S6        | 7.20E-05         | 3.41E-05                  | 5.84E-05 | 7.31E-07 | 1.41E-04 | 39.4 |

The neutron beam generated from the RSG-GAS beam tube can be used for the BNCT in-vitro test by adding a BSA made from an MgF$_2$ filter. The ideal beam tube outputs are those that produce high doses of alpha and $^7$Li, low proton and gamma, doses and short irradiation times. The S5 beam tube provides the shortest irradiation time but the predominant radiation dose is given over the proton dose. Meanwhile, the S6 beam tube produced the longest irradiation time, but the dominant radiation dose was given from the alpha dose.

4. **Conclusion**

Microtube dose simulations resulting from neutron irradiation on the RSG-GAS neutron beam using PHITS code have been carried out well. By adding 80 cm MgF2 material as a filter in BSA which was placed at the end of the beam tube, a larger epithermal neutron ratio was obtained. The simulation results of microtube irradiation on the BSA-S5 tube tube showed that the total microtube dose was 20 Gy with the required irradiation time of only 2.5 hours.

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