V. 4. Design and Benchmark Experiment for Cyclotron-based Neutron Source for BNCT

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Introduction

Boron Neutron Capture Therapy (BNCT) is a promising treatment for brain tumors such as Glioblastoma Multiforme, which are at present considered to be inoperable. BNCT relies on two components, $^{10}$B-doped pharmaceuticals and neutrons for irradiation. The $^{10}$B component, which is delivered preferentially to the tumor cells, is administered to the patient, who is subsequently irradiated with an external neutron beam. The $^{10}$B ($n,\alpha$) $^7$Li reaction, on which BNCT is based, has a large cross section of 3837 barns for thermal neutrons and this interaction produces two particles, $\alpha$ and $^7$Li, with high Linear Energy Transfer (LET) and Relative Biological Effectiveness (RBE). The mean free path is about 10 $\mu$m and 5 $\mu$m for $\alpha$ particles and for $^7$Li, respectively. Considering that the mean cellular diameter is of the order of 10 $\mu$m, it is possible that BNCT may act selectively in killing cells.

The neutron field should exhibit an energy spectrum that delivers a therapeutic dose to tumor tissues in conjunction with a tolerable dose to normal tissues. Because of the large kerma coefficient of the $^1$H(n,n$'$)$^1$H reaction, it is not possible to kill a cell selectively with high neutron energy. On the other hand, Glioblastoma Multiforme often locates near the center of the brain surrounding healthy tissues, and can not be killed with thermal neutrons, which have feeble penetration and stop in the skins or in other healthy tissues.

To meet the above requirements, the use of epithermal neutrons in BNCT has recently met increasing interest, taking into account that incident neutrons are moderated in the human body. For example, Yanch et al\textsuperscript{1)} showed that epithermal neutrons in the energy range from 4 eV to 40 keV are most effective in the treatment of a brain tumor at a depth of
Many groups have investigated epithermal neutrons for BNCT with reactor- and accelerator-based neutron sources. Reactions such as $^7\text{Li}(p,n)$ ($E_p=1.95 \text{ MeV}$), $2.4\text{MeV}$ and $2.5 \text{ MeV}$, $^2\text{H}(d,n)^3\text{He}$ and $^3\text{H}(d,n)^4\text{He}$ ($E_d=100-400 \text{ keV}$) are currently being investigated as accelerator-based neutron sources. However they have not been realized yet in applications, mainly because they require a very high beam current from an accelerator which introduces difficulty in target cooling.

At the Cyclotron and Radioisotope Center (CYRIC), a cyclotron accelerator has been upgraded. This upgrade allows the use of the negative ion acceleration mode, where the maximum beam intensity of the cyclotron is $300 \mu\text{A}$ for $50 \text{ MeV}$ protons and $150 \mu\text{A}$ for $25 \text{ MeV}$ deuterons. Such a high particle energy may not be suitable for BNCT, because it results in the emission of high energy neutrons, which increase the skin dose due to $\text{H}(n,n')$ reactions. However, the neutron production yield of the $(p,n)$ reaction of heavy elements ($E_p=50 \text{ MeV}$) is about thousand times higher than that of the $^7\text{Li}(p,n)$ ($E_p=\sim2.5 \text{ MeV}$) reaction, as can be seen from Refs.6 and 7. The beam power is $15 \text{ kW}$ at the maximum heat load for incident $50 \text{ MeV}$ protons of $300 \mu\text{A}$ which allows an advantage in target cooling, compared with the beam power of $48 \text{ kW}$ for the $^7\text{Li}(p,n)$ ($E_p=2.4 \text{ MeV}$) reaction at $20 \text{ mA}$ beam intensity in Ref. 3.

Thus it appears possible to realize epithermal neutron yields sufficient for BNCT by using protons of $50 \text{ MeV}$, if the neutrons produced can be effectively moderated to epithermal energy with a low contamination of high energy neutrons.

In the previous study$^8$, we found the feasibility of a cyclotron-based BNCT by simulations using the MCNPX code$^9$. In the paper, we selected neutrons emitted at 90 degree from a thick (stopping-length) Ta target bombarded by $50 \text{ MeV}$ protons, as the neutron source, based on the measurement of angular distributions for neutron energy spectra$^{10}$. We also selected the assembly composed of iron, $\text{AlF}_3/\text{Al}_6\text{LiF}$ and lead as the moderator by simulations of neutron energy spectra passing through the moderator and the dose distribution in a cylindrical phantom.

**Experiment**

In order to realize the cyclotron-based BNCT, we should validate the simulations. At the first step, we had a plan to measure the epithermal neutron energy spectra passing through the moderator. The measurement of epithermal neutron spectrum to be used for the treatment planning is very important for accelerator-based BNCT. However the
spectrometry of neutrons in epithermal energy region, a few eV to several tens of keV, is very difficult and the measuring technique is not well established. Therefore we developed a new multi-moderator spectrometer for epithermal neutrons\textsuperscript{11}, and we applied evaluate the epithermal neutron field designed at CYRIC.

The measurements of the epithermal neutron energy spectra were performed at TOF room in CYRIC. The experimental arrangement is shown in Fig. 1. This arrangement is a little different from that in the simulations. For example, the figure of the moderator assembly was changed to rectangular due to a space limitation, while that used in the simulations was spherical. The moderators of AlF\textsubscript{3} and LiF were also thicker than that in simulations in order to make same the number of atoms between experiment and calculation, because AlF\textsubscript{3} and LiF were of powder and natural lithium was used for LiF in this experiment. Therefore the shape of the neutron energy spectrum passing through the moderator may be slightly different from simulations. However, its difference is not very serious for the aim to validate a simulation.

Result and Discussion

Figure 2 shows the comparison of measured and calculated detector counts. The calculations agree with the measurements without the Cd absorber within ~20 %. Scattered thermal neutrons, generated by the table, wall, floor and ceiling, may give the large uncertainly to the results, especially to those obtained with the detectors which were sensitive to thermal neutrons. Therefore we also performed measurements using detectors covered with a Cd absorber in order to decrease the effect of the thermal neutrons for four detectors. As shown in Fig. 2, the calculations agree with the measurements with the Cd absorber within ~10 %.

Figure 3 shows the comparison of measured and calculated neutron energy spectra passing through the moderator. The result was obtained by unfolding the measured counts with calculated response functions. These spectra are in agreement within ~10 %.

These results indicate that we can validate the accuracy of the calculation on the neutron energy spectra passing through the moderator. At the next step to realize the BNCT at CYRIC, we have a plan to measure the thermal neutron distribution and the absorbed dose distribution in a phantom.
References

5) Verbeke J.M., Vujic J. and Leung K.N., “Investigation of $^3$H(d,n)$^3$He and $^3$H(d,n)$^4$He Fusion Reactions as Alternative Sources for BNCT”, The 8th Int. Symp. on NCT for Cancer, 13-18 September 1998, Jolla CA.

Fig. 1. Illustration of the experimental arrangement.
Fig. 2. Comparison of measured and calculated detector count.

Fig. 3. Comparison of measured and calculated neutron energy spectra passing through the moderator.