Union of Compact Accelerator-Driven Neutron Sources (UCANS) I & II

A Project of Boron Neutron Capture Therapy System based on a Proton Linac Neutron Source

Yoshikai KIYANAGI\textsuperscript{a}, Kenji ASANO\textsuperscript{b}, Akihiro ARAKAWA\textsuperscript{a}, Shin FUKUCHI\textsuperscript{b}, Fujio HIRAGA\textsuperscript{a}, Kenju KIMURA\textsuperscript{b}, Hitoshi KOBAYASHI\textsuperscript{c}, Michio KUBOTA\textsuperscript{d}, Hiroaki KUMADA\textsuperscript{d}, Hiroshi MATSUMOTO\textsuperscript{c}, Akira MATSUMOTO\textsuperscript{d}, Takeji SAKAE\textsuperscript{d}, Kimiaki SAITO\textsuperscript{e}, Tokushi SHIBATA\textsuperscript{e}, Masakazu YOSHIOKA\textsuperscript{c}

\textsuperscript{a}Graduate School of Engineering, Hokkaido University
Kita-13 Nishi-8, Kita-ku, Sapporo, Hokkaido 060-8628, Japan
\textsuperscript{b}Ibaraki Prefecture, 978-6 Kasahara-chō, Mito, Ibaraki 310-8555, Japan
\textsuperscript{c}KEK, Oho 1-1, Tsukuba, Ibaraki 305-0801, Japan
\textsuperscript{d}Institute of Clinical Medicine, University of Tsukuba, 2-1-1 Amakubo, Tsukuba, Ibaraki 305-8576, Japan
\textsuperscript{e}Japan Atomic Energy Agency, Tokai, Ibaraki, 319-1195, Japan

Abstract

At present, the clinical trials of Boron Neutron Capture Therapy (BNCT) are being performed at research reactor facilities. However, an accelerator based BNCT has a merit that it can be built in a hospital. So, we just launched a development project for the BNCT based on an accelerator in order to establish and to spread the BNCT as an effective therapy in the near future. In the project, a compact proton linac installed in a hospital will be applied as a neutron source, and energy of the proton beam is planned to be less than about 10 MeV to reduce the radioactivity. The BNCT requires epithermal neutron beam with an intensity of around 1x10\textsuperscript{9} (n/cm\textsuperscript{2}/sec) to deliver the therapeutic dose to a deeper region in a body and to complete the irradiation within an hour. From this condition, the current of the proton beam required is estimated to be a few mA on average. Enormous heat deposition in the target is a big issue. We are aiming at total optimization of the accelerator based BNCT from the linac to the irradiation position. Here, the outline of the project is introduced and the moderator design is presented.

© 2012 Published by Elsevier B.V. Selection and/or peer-review under responsibility of UCANS

Open access under CC BY-NC-ND license.

Keywords: Accelerator based neutron source, Boron Neutron Capture Therapy, Moderator-reflector systemn; Proton linac

* Corresponding author. Tel.: +81-11-706-6650; fax: +81-11-706-7368.
E-mail address: kiyanagi@qe.eng.hokudai.ac.jp.
1. Introduction

Clinical trials of the boron neutron capture therapy (BNCT) are carried out in the world and have demonstrated benefit in treatment glioblastomas [1] and other cancers. BNCT as next-generation particle radiotherapy is expected to be the key method for the treatment of intractable cancer. At present, the clinical trials of BNCT are being performed at research reactor facilities. However, in Japan it is impossible to establish a reactor-based BNCT as a medical treatment due to the difficulty caused by related regulations. An accelerator based BNCT has a merit that it can be built in a hospital. Therefore, the BNCT based on the accelerator has been built using 30 MeV protons [2].

Now, epithermal neutron beam is applied to most clinical trial of BNCT in order to deliver therapeutic dose to deeper region in human body. Common definition for the epithermal energy range is used, namely 0.5eV to 10keV. And circular beam aperture of 10 to 14cm diameter is being usually applied to the present clinical trials.

To reduce burden on a patient and to keep high concentration of boron compound in tumor region, irradiation is required to complete within an hour. Therefore, to meet the requirement, a desirable epithermal neutron flux would be over 1x10^9 \( \text{(n/cm}^2\text{s)} \) at the beam aperture. If the neutron intensity is lower than that value, irradiation time will be prolonged. Boron concentration in tumor affects the requirements for beam intensity. In current BNCT, two boron compounds as BSH and BPA are used. If the boron concentration can be raised from the value of the conventional compounds, the beam intensity requirement will be reduced.

To reduce damage to skin and scalp and to deliver the therapeutic dose to deeper region, thermal neutrons in the incident beam should be minimized. According to recommendation by IAEA, a target number for the ratio of thermal neutron flux to epithermal neutron flux should be 0.05 [3].

In the energy range for fast neutrons is taken as >10keV. The fast neutron as invariably accompany the incident beam affect adversely to healthy organs around tumor region, because the fast neutron has undesirable characteristics such as the production of high LET proton with a resulting energy dependence of their induced biological effects. Thus in the neutron beam design, the fast neutron component in the beam must be reduced as much as possible. A target number should be 2x10^{-13} Gycm^2 per epithermal neutron.

The neutron beam generated from reactor source as well as that from the accelerator source involves gamma-ray component (primary gamma-ray). And the neutrons given to a patient also generates gamma-ray (secondary gamma-ray) by the reaction between neutron and several elements like hydrogen that form human body. The both gamma-ray components affect not only tumor but also a large volume of healthy tissue. Hence it is desirable to reduce as much gamma radiation from the beam as possible. IAEA recommends that the target number for the gamma-ray contamination should be 2x10^{-13} Gycm^2 per epithermal neutron.

Furthermore, the BNCT facility in a hospital may be required to be low radioactivity and easiness of maintenance and decommissioning. Therefore, we have planned to use lower energy protons, say less than 10 MeV. Here, we present the design consideration on the proton linac based BNCT system using protons lower than 10 MeV, and the result on the simulation calculation for the moderator system of the BNCT system.
2. Basic consideration on neutron generation

2.1. Neutron generation reaction

Two types of the neutron generation reaction have been considered. One is p-Li reaction and the other is p-Be reaction. The p-Li reaction gives larger number of neutrons than the p-Be reaction at low proton energy region around 2-3 MeV, and the neutron energy is much lower than that produced by the p-Be reaction at higher proton energy. Therefore, there exists the possibility to use directly the neutrons produced by the p-Li reaction. In the p-Be reaction the neutron energy is around MeV, and the situation is similar also in the p-Li reaction at the higher energy protons. Therefore, in such case we need the neutron moderator. Here, we consider the two types of systems. One is the direct use of the neutrons produced by the p-Li reaction around the threshold energy, 1.9 MeV. The other is the case using the moderator for 2.5 to 3.0 MeV p-Li reaction and for the p-Be reaction at 11MeV. Here, we assumed the 11 MeV protons since there were no data on the energy and the angular distributions at other energies less than 10 MeV. Information of the produced neutron numbers and their energies are summarized in Table 1. For these studies we used MCNPX [4] neutron transport code and LIYIELD[5] for the calculation of the generated neutron by the p-Li reaction. We used the experimental data on the neutron production of the p-Be reaction [6]. In the table the neutron number for 11 MeV proton is obtained by the experimental result of the differential measurement. The value is less than the value commonly used. Here, we assume that the neutron spectrum must fulfill the following conditions:

1. Thermal neutron flux<5.0x10^5 n/cm^2/sec
2. Epithermal neutron flux>1.0x10^9 n/cm^2/sec
3. Ratio of fast neutron<1.0x10^{-12}(Gycm^2),

Here, the thermal neutron is less than 0.5eV, epithermal from 0.5eV to 10keV, and fast neutron above 10keV. We chose the ratio of fast neutron as five times larger than the IAEA recommended value since this value is realistic values used in BNCT facilities.

Table 1: The numbers and the energy of neutrons produced by p-Li and p-Be reactions.

| Li(p,n) reaction | Neutron yield | Emerged neutron energy |
|------------------|--------------|------------------------|
| 1.9MeV           | 1.5 x 10^{10} (n/sec/mA) | Max 90 keV, Mean 38 keV |
| 2.5MeV           | 8.8 x 10^{11} (n/sec/mA) | Max 787 keV, Mean 326 keV |
| Be(p,n) reaction | 11MeV        | 2.15 x 10^{13} (n/sec/mA) | Max 8.55 MeV, Mean 2.37 MeV |

2.2. Direct use of p-Li neutrons produced by 1.9 MeV protons

Figures 1 shows the calculation setup for the direct use system. There is a reflector around the target to increase the neutrons toward the irradiation area. We obtained the neutron intensity at various angles as shown in the figure since the high energy neutrons are emitted in the forward direction, and this increase the ratio of fast neutron. The results are indicated in Table 2. The ratio of
fast neutron decreases with increasing the angle, but the value is larger than the required value 1.0x10^-12Gy·cm². However, if we can expand the upper energy of the epithermal neutron to 40 keV, the condition is fulfilled. For this system the most serious problem is the Li target since the material is very active and difficult to handle. Since the direct use system may cause difficulty in the use at a hospital, we then studied the moderator system using higher energy proton energy.

### Table 2: Calculated values of the thermal neutron flux, the epithermal neutron flux and the ratio of fast neutrons at various angles for the case of the direct use of the generated neutrons using p-Li.

| Irradiation angle (Degree) | Thermal neutron flux (n/sec/cm²/mA) | Epithermal neutron flux (n/sec/cm²/mA) | Ratio of fast neutron (Gy·cm²) |
|---------------------------|-------------------------------------|---------------------------------------|-------------------------------|
| 0                         | 2.11 x 10³                         | 1.29 x 10⁸                            | 3.63 x 10⁻¹²                 |
| 15                        | 2.05 x 10³                         | 1.17 x 10⁸                            | 3.40 x 10⁻¹²                 |
| 30                        | 1.67 x 10³                         | 9.39 x 10⁷                            | 2.59 x 10⁻¹²                 |
| 45                        | 6.82 x 10²                         | 3.70 x 10⁷                            | 1.33 x 10⁻¹²                 |

2.3. Moderated neutron use by the higher energy protons for p-Li and p-Be reactions

In the case of the higher proton energies the produced neutron intensity is much higher than that of the p-Li reaction around the threshold energy. Therefore, we next consider the neutron generation using the proton energy 2.5-3.0 MeV for the p-Li reaction and 11 MeV for the p-Be. Figure 2 shows the calculation model for the slab geometry in which the target was placed at opposite side of the beam extraction surface. We also studied a wing geometry in which the target is placed at side surface of the moderator. However, the results were not better than the slab geometry system. Therefore, we did not mention this system here.

We calculated the neutron intensities from many moderator materials including fluorine, F. From these results we decided the moderator materials; MgF₂ for the p-Li reaction and LiF for the p-Be reaction. We also studied the reflector materials. The results indicated that a Pb reflector was best for the slab geometry. Figure 3 shows the energy spectra (lethargy) from the slab geometry moderators. The spectrum from the p-Be gives more flat distribution than the p-Li cases. Table 3 shows the optimal size of the moderator and the three values required for the BNCT system. In the case of the p-Li reaction, we can get the epithermal neutron intensity around 3.2x10⁷ n/sec/cm²/mA and in the case of the p-Be reaction the intensity is 1.63 x10⁸ n/sec/cm²/mA. Therefore, the required beam current is much larger in the p-Li reaction than the p-Be reaction and the beam power is greater as well.

![Figure 2 Calculation model of the slab geometry moderator system](image)

Figure 2 Calculation model of the slab geometry moderator system
Furthermore, we studied the neutron intensity other than the beam extraction area to reduce the neutron dose at that area. We calculated the neutron intensity at 35 cm from the center of the beam extraction area. The criteria are 1/20 of the intensity of the center and the dose less than 1 Sv/hr. To attain the criteria we placed a layer of 13 cm boric-acid water-solution just behind the surface. From this change of geometry the beam extraction position moved outwards at the same size. Therefore, the viewed area on
the moderator increased. This causes the increase of epithermal neutron intensity up to 2.79x10^8 n/cm^2/sec/mA. The required power under this condition is about 40 kW.

3. Accelerator and target system

3.1. Technology choice

The technology chosen for the accelerator should be based on a feasibility study of the target system. Several combinations of accelerator and target system have been proposed to realize an accelerator-based BNCT. Typical combinations can be classified into two groups:

(a) Low energy (<3 MeV), high current linac with a lithium (Li) target, and
(b) A 30 MeV cyclotron with a beryllium (Be) target.

For case (a), direct production of epithermal neutrons at the target is possible and the moderator can be eliminated as discussed before. But the management and handling of a Li target presents problems which have not been solved in a way practical for use outside of research facilities. On the other hand, for the case (b) approach, it should be noted that a group at Kyoto University has constructed a facility with the collaboration with Sumitomo Heavy Industries Ltd. and the STELLA PHARMA Corporation [6]. They will soon begin carrying out clinical investigations on patients. Our technology choice differs from these two approaches. A schematic drawing of our proposal is shown in Fig. 4. The accelerator consists of a 324 MHz RFQ and a DTL (Drift Tube Linac). The operational beam energy and power are chosen to be 8 MeV and 80 kW from consideration of the following desiderata:

(a) To produce a high flux of epithermal neutrons, of more than 10^9 n/s/cm^2,
(b) To keep radiation and activation of components as low as possible,
(c) To lower the production rate of fast neutrons to reduce needed shielding materials,
(d) To be able to use a thin Be-plate for the target material.

These factors are essential that the facility could be built in a hospital.

![Figure 4: Schematic drawing of the system. Two parameter sets are shown, either set achieves a beam power of 80 kW: Peak beam current: 50 or 100 mA, Repetition rate: 200 or 100 Hz. The beam pulse width is 1 ms for both cases. The output energy from the RFQ is 3 MeV and the further energy gain from the DTL is 5 MeV.](image)

3.2. Target system

In this BNCT proposal, the most difficult part from the technical point of view is the target system. The key technological problems to be overcome in developing a practical target system are summarized as follows:

(a) How to dissipate or remove the high-density heat load from the Be-plate, and
(b) Impact of a high-power proton beam on the target causes a hydrogen problem.
These cause problems such as how to develop a long lived target and/or how to develop a remote handling and maintenance system.

If the diameter of the target disk is 15 cm, then the energy density on the target is 453 W/cm². We need to choose an optimal thickness for the Be-plate so as to not cause an excess heat load and fatal damage to the Be-plate. We are studying thicknesses between 0.1 to 0.5 mm. The target system which produces neutrons should also double as a vacuum window at the end of the beam line. In order to provide enough mechanical strength to withstand the forces from atmospheric pressure, the Be-plate could be backed with a carbon block, which could be water-cooled and so also help with the heat diffusion from the Be-plate[8].

3.3. Accelerator

The current front-end linac of the J-PARC consists of a 50 keV negative hydrogen ion source (H⁻), a 3 MeV RFQ and a 181 MeV DTLs as shown in Fig. 2. The accelerator system in the present proposal is based on these J-PARC technologies [8].

(RFQ)

The detailed RF and mechanical design and fabrication method for the RFQ are described in [9]. The main parameters for the J-PARC injector are: RF frequency: 324 MHz, peak current: 30 mA, pulse width: 0.6 ms, repetition rate: 50 Hz, and the maximum surface gradient in the structure is 33~35 MV/m. The differences between the J-PARC injector and the proposed BNCT application are as follows:

(a) The beam is positive hydrogen (H⁺) instead of H⁻,

(b) Since the most important requirement for the BNCT application is just the beam power, and beam structure is immaterial, no bunching system is necessary.

(c) A certain level of beam loss in the RFQ is allowable.

Figure 5 RFQ 3D drawing (upper left), photograph of an RFQ fabrication step in a precision machining procedure (left, below), and a picture of a DTL (upper right).

The lengths of the RFQ and DTL are 3 m and 2.5 m, respectively.

In order to increase the peak current from 30 mA H⁻ beam to 100 mA H⁺ beam, a slight modification of the RF design is necessary. The most important technical change between the J-PARC and the BNCT application is in the water-cooling system. The duty factor for the J-PARC case is only 3 % but for BNCT application this would be increased up to 10 to 20 %. The necessary design work is currently in progress.
The RF design is common for the J-PARC and BNCT application. The main difference is in the focusing magnets. Electro-magnets are used by J-PARC, but permanent magnets will be used for the BNCT application to reduce power consumption and to simplify the system.

The parameters of the present klystron are: RF frequency: 324 MHz, peak power: 3 MW, pulse width: 0.6 ms, repetition rate: 50Hz. We will have to modify the klystron for operation at a higher duty-cycle, but since the required peak power is only 1 MW (33% of J-PARC), only a slight modification is required.

4. Conclusions
We have launched the project for constructing the BNCT facility based on a proton accelerator. The proton energy we are considering is much lower than the existing one to reduce the radiation from the target and the surrounding materials as low as possible. This may make it easier to install the BNCT facility near the hospitals. However, there are many things to be developed and optimized concerning to the accelerator, the moderator system including a target, the collimator system, the shield, the activity and so on. We have started detailed and comprehensive research to build the compact BNCT system near the hospitals.

References

[1] T. Yamamoto, K. Nakai, T. Kageji, H. Kumada, K. Endo, M. Matsuda, Y. Shibata, A. Matsumura, “Boron neutron capture therapy for newly diagnosed glioblastoma. Radiother Oncol.” 2009 A91(1): 80-4.
[2] H. Tanaka, et. al., Nuclear Instruments and Methods in Physics Research B 267 (2009) 1970–1977
[3] International Atomic Energy Agency, “Current status of neutron capture therapy”, IAEA-TECDOC-1223, 2001
[4] J. F. Briesmeister (ed.), MCNP_A General Monte Carlo N-Particle Transport Code, Version4A, LA-12625, (1993).
[5] C.L. Lee, X.-L. Zhou, Nucl. Instr. Meth. B 152, 1 (1999)
[6] S. Kamada, et al., Preprints 2006 Spring Meeting of At. Energy Soc. Jpn., K42, (2006). [in Japanese]
[7] K. Ono, http://www.s-tokku.kuhp.kyoto-u.ac.jp/modules/tokku2/pdf/4.pdf
[8] Patent pending 2010-264724 (Japan)
[9] K. Hasegawa, T. Kobayashi, Y. Kondo, T. Morishita, H. Oguri, Y. Hori, C. Kubota, H. Matsumoto, F. Naito and M. Yoshioka, “Status of the J-PARC RFQ”, Proceedings of IPAC’10, Kyoto, Japan, May 24-28, 2010 (MOPEC067)