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STATUS OF THE iBNCT ACCELERATOR

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Abstract

Accelerator-based boron neutron capture therapy (BNCT) has been studied worldwide. The iBNCT (Ibaraki BNCT) project began in collaboration with KEK, the University of Tsukuba, Ibaraki Prefecture, and related private companies in Japan in 2010. The iBNCT project aims to realize linac-based BNCT by irradiating a beryllium target with protons accelerated to 8 MeV. The accelerator configuration comprises an ECR ion source, a 3-MeV radio-frequency quadrupole linac, and an 8-MeV Alvarez-type drift tube linac, which is based on the Japan Proton Accelerator Research Complex linac techniques. The iBNCT project has achieved stable operation with an average proton beam current of 2 mA with a repetition of 75 Hz and a beam width of 0.92 ms. After the completion of the non-clinical studies in the fiscal year 2022, we finished preparing to start a clinical study in the year 2023 for both the medical and accelerator sides. The iBNCT project began as a Phase-I Investigator-initiated clinical trial in January 2024. In this paper, the current status of the iBNCT accelerator and its prospects are discussed.

INTRODUCTION

Accelerator-based boron neutron capture therapy (BNCT) has been extensively studied in recent years as a novel cancer therapy. It has a long history of clinical research on nuclear reactors; however, medical treatments in nuclear reactors cannot be a general treatment owing to constraints on its operation and management. Therefore, an accelerator-based BNCT has gained popularity. The iBNCT project was launched in 2010 in collaboration with the University of Tsukuba, High Energy Accelerator Research Organization (KEK), related private companies, and Ibaraki Prefecture in Japan [1]. The iBNCT project aims to realize accelerator-based BNCT with the accelerator configuration of 3-MeV radio-frequency quadrupole (RFQ) linac and 8-MeV Alvarez-type drift tube linac (DTL), whose feasibility has already been proven in the Japan Proton Accelerator Research Complex (J-PARC). Figure 1 shows a schematic of the iBNCT accelerator. The apparatus was installed at the Ibaraki Neutron Medical Research Center in Tokai, Ibaraki Prefecture, Japan. A bird's-eye view of the iBNCT accelerator can also be found in Ref. [2]. Assuming that all the accelerator configurations are installed in a hospital, the size of the entire system should be as small as possible. As shown in Fig. 1, the proton beam passes from left to right. The primary proton beam was generated using an ECR ion source (ECR-IS) and accelerated to 50 keV under an electro-static field of 50 kV. The ECR-IS is driven by a 2.45-GHz magnetron with a maximum RF power of 3 kW. After the low-energy beam-transport line (LEBT), a 3-MeV RFQ is placed. The RFQ design was based on the J-PARC RFQ-II [3]. A 324 MHz klystron provides RF for both the RFQ and DTL simultaneously [4]. The typical rated power is 340 kW for the RFQ and 320 kW for the DTL. The medium-energy beam-transport line (MEBT) between the RFQ and the DTL contains three permanent quadrupole magnets and a beam-position monitor. After the MEBT, the DTL is placed. The design of the DTL is also based on the J-PARC DTL; however, it differs from the J-PARC DTL in its length and quadrupole magnets in the drift tubes. In the iBNCT accelerator, the output energy is optimized to be 8 MeV; thus, the length of the DTL is only 3.1 m. Another point is the application of permanent magnets for the quadrupole in each drift tube to save on electricity costs. A beam transport line (BT) of approximately 15 m in length was located after the DTL. In the straight line immediately before the neutron-generation beryllium target, a beam expander, which comprises two quadrupole and two octupole magnets, is installed alternative to expand the beam lateral size and reduce the beam intensity per unit area on the target. The beryllium target has a three-layer structure comprising 0.5-mm thick beryllium, 0.5-mm thick palladium, and 10-mm thick copper. A detailed description is provided in Ref. [5, 6]. The neutron moderator and collimator were located after the beryllium target. This apparatus not only decreases neutron energy generated by ^{9}Be(p, n) reaction from a few MeV to the epi-thermal neutron region below 10 keV but also suppresses unwanted γ-rays and high-energy neutrons for BNCT. Guidelines have been established by the IAEA for the desired neutron flux for BNCT, which requires an intensity of more than 1×10^9 n/cm^2/s [7]. Therefore, high proton beam intensity is required. Thus, the iBNCT accelerator must be designed with a higher proton beam intensity than that of the J-PARC accelerator, which forms the basis for the design.

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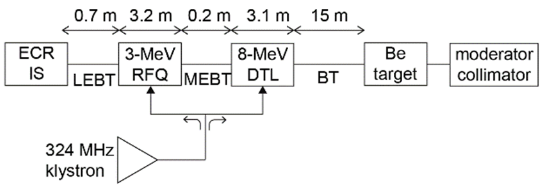

Figure 1: Schematic of the iBNCT accelerator. Proton beam is accelerated from left to right. Abbreviations in the figure are explained in the manuscript.

BEAM COMMISSIONING STATUS

The present and designed operational parameters of the iBNCT accelerator are summarized in Table 1. The present intensity did not reach to the designed values; however, it was sufficient for initiating clinical studies. The details are described later.

Table 1: Operational Parameter of the iBNCT Accelerator

	Present	Design
Particle	proton	
Energy [MeV]	8	
Peak current [mA]	30	50
Beam width [ms]	0.92	1
Repetition [Hz]	75	200
Average current [mA]	2	10

Present Beam Current

Figure 2 shows typical waveforms of the beam current measured by the ACCTs placed after the ion source and 2 m upstream of the beryllium target. The peak current before the target, indicated by the green line in Fig. 2, was approximately 30 mA with a beam width of 0.92 ms. Under a repetition of 75 Hz, which is currently achieved for stable operation, the resulting average current was 2 mA. One of the reasons why the present peak current is lower than the design value is that we are currently using the plasma electrode of the ion source with a small diameter of 6 mm to focus on RFQ stability. If we replace it with a larger one, for example an 8 mm diameter one, we consider that the peak current can be increased, and this is one of the important studies that will be conducted after the completion of the clinical study started this year.

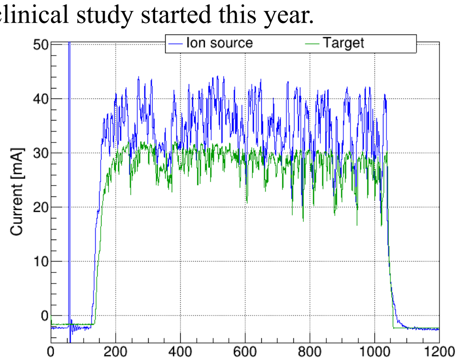

Figure 2: Typical pulse of the beam current by ACCTs placed at the ion source (blue) and 2 m upstream of the target (green), respectively.

Stability

BNCT treatments must be completed within a limited irradiation time owing to the concentration of boron in cancers. Thus, the stability of accelerator operation is extremely important for BNCT. In the iBNCT accelerator, irradiation is interrupted by the discharges of the ion source and the RFQ. In the ion source case, discharges do not occur frequently; if they do occur, they are not a serious problem because irradiation can be resumed within 30 seconds. In the discharges of the RFQ case, a quick recovery function developed at J-PARC [8], which restarts the RF operation within a short time (referred to as quick recovery hereinafter), was implemented. Once a quick recovery fails, the RF must be restarted from a low amplitude, which requires a certain amount of time to resume beam irradiation. Therefore, the discharge rate of the RFQ and the success rate of quick recovery are important issues for the iBNCT accelerator. Figure 3 shows trends in recent years. In Fig. 3, the red line indicates the number of RFQ discharges per hour of operation, and the blue line shows the success rate of the quick recovery. The RFQ discharge rate was once per hour and the quick recovery success rate was approximately 90%. From these results, if the BNCT treatment lasted 30 min, quick recovery roughly failed after 20 rounds of BNCT treatment. Because it was difficult to completely reduce the RFQ discharge, we attempted to shorten the RF restart time by increasing the water flow through the RFQ. This will be described later in this paper.

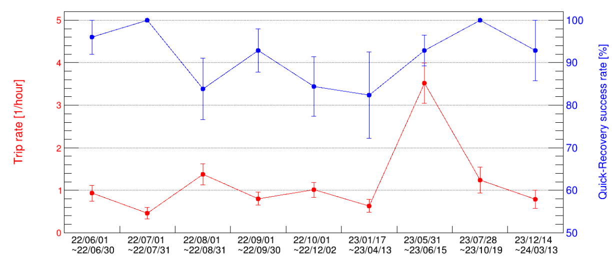

Figure 3: Trend of RFQ discharge rate (red) and success rate of quick recovery (blue) in recent years.

Operation Statistics

As reported in Ref. [9], the beryllium target in the iBNCT accelerator was replaced in May 2020. Figure 4 shows the history of the integrated charges of the ion source and target measured by ACCT, shown in Fig. 2. In Fig.4, the origin of the X-axis represents the installation time of the second beryllium target. As of July 2024, the integrated charge was greater than 4700 Coulomb, whereas the neutron yield was sufficient for BNCT treatment. Even after January 2024, the iBNCT accelerator was operated for the beam commissioning, and the amount of integrated charge after January 2024 does not represent the charge for clinical studies alone.

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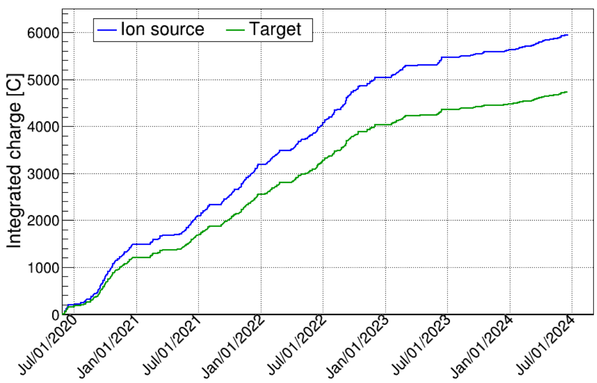

Figure 4: History of amount of integrated charge after the installation of the second beryllium target. Blue and green lines shown in Fig. 2 represent ACCT data as described in the manuscript. Total amount of the charge on the target is approximately 4800 C as of July 2024.

ACCELERATOR UPGRADE

Cooling Water System Upgrade

Because the iBNCT project aims to ensure the entire system is installed in a hospital, the initial cooling water system was designed to be minimal. Therefore, the accelerator cooling water system was also compact, and the flow rates were limited to 90 and 100 L/min for the RFQ and DTL, respectively. In this concept, the maximum temperature difference between inlet and outlet temperature is accepted for 10 °C at an operation of 200 Hz repetition. The average of the inlet and outlet temperatures is maintained constant while raising the cavity RF power to the rated level because the resonance frequency of the RFQ must be controlled by its temperature. However, when a discharge occurs inside the RFQ, the large temperature difference causes a large temperature deviation owing to the missing heat load caused by RF shutdown. As explained, when quick recovery fails, if the temperature must be changed significantly during the restart of the RF operation, it takes a certain amount of time to wait for a change in the temperature. Therefore, minimizing the temperature change in the cavity is important. In the original design, the recovery time was 30 min, which was not acceptable because of the limited treatment time for BNCT. Therefore, one of the important tasks of the iBNCT accelerator is to enhance the cooling water system to stabilize the RFQ. The upgrades performed thus far are described as follows.

- Enhancement of the cooling water circulation pump: A circulation pump for the cooling water with 5-kW output power was initially installed to suit the overall cooling water design flow rate. To increase the amount of cooling water flow, the pump was replaced with an 11-kW output pump in 2018, resulting in an increase in the total flow rate from 330 to 600 L/min.
- Modification of the cooling water path inside the RFQ:
  The main body of the RFQ comprises of three units. The cooling water path was designed to be supplied from the center of the RFQ, turned back at the upstream and downstream ends, and returned to the center again. This configuration increases the pressure loss inside the RFQ. Although the number of pipes increased, the flow path shortened for each unit. This helps to reduce the pressure loss inside the RFQ. Furthermore, the original pipes were made of copper with a 90° elbow joint, however, to reduce the pressure loss, larger-diameter plastic tubes were used with a curvature.
- Replacement of the cooling water piping of the RFQ: The piping had a diameter of 2.5” near the RFQ; however, it was squeezed down to 1” immediately before the inlet and after the outlet of to match the design flow rate. These points became bottlenecks for improving the RFQ flow rate. Therefore, all the 1” pipes had been replaced with 2.5” pipes.
- Reinforcement of the cooling water circulation pump: In March 2022, the circulation pump was replaced from 11 to 22 kW to further increase of the flow rate. Simultaneously, the diameter of a pipe between a 400-L buffer tank and the circulation pump was increased from 2.5” to 4”.
- Changing the balance of the water flow rate:
  Because the DTL has a movable tuner to adjust the resonance frequency and the discharge rate is much lower than that of the RFQ, the RFQ requires a much higher temperature stability. Most of the increased flow rate was assigned to the RFQ by maintaining DTL similar to its original value.

With the improvements described above, the total and RFQ flow rates increased from 1070 and 770 L/min, respectively. Figure 5 shows the trends in the inlet and outlet temperatures during the recently studied beam restart trial. Assuming an RFQ discharge and failure of quick recovery, RF was manually stopped and restarted at approximately 11:58. In this study, the RF recovery time was only 2 min, and the beam could be restarted only 4 min after the RF was stopped. Therefore, the RF recovery time at the failure of quick recovery was significantly shortened by the upgrade of the cooling water system.

Vacuum System Upgrade

In the first half of 2017, the instability of the RFQ was a serious problem in achieving sufficient irradiation time for BNCT, even with a low repetition rate. Several improvements were made as described in Ref. [10]. In the upgrade, a manifold at the RFQ fixed-tuner port to enforce pumping is shown in the upper part of Fig. 6. The manifold was connected to the 2-stage turbo molecular pumps that effectively evacuated the hydrogen gas.

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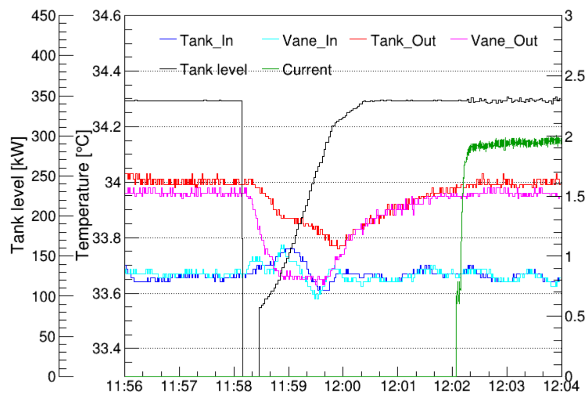

Figure 5: Trend of the inlet and outlet cooling water temperature, RFQ tank level, and beam current at an RF restart trial. A beam operation can be started after an RF stop within 4 min.

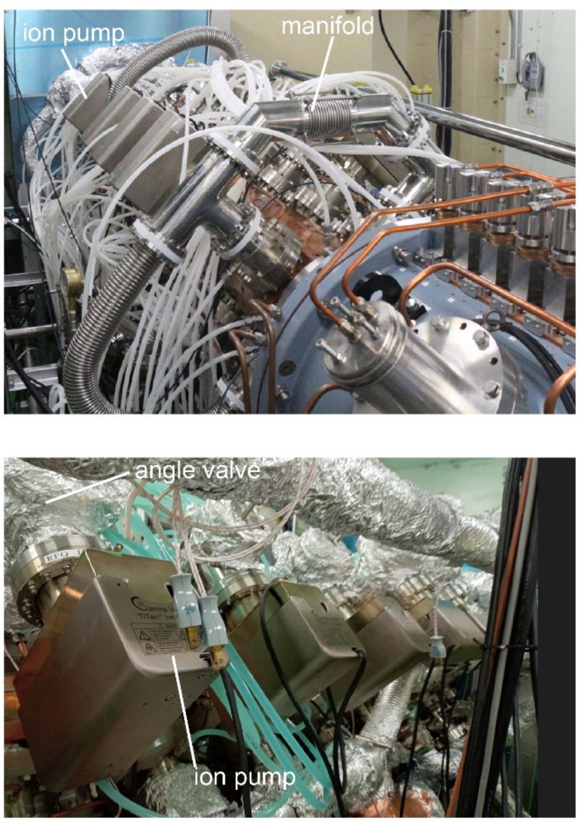

Figure 6: Photographs of the vacuum system upgrade. Upper figure shows the work in 2017 to install the manifold to reinforce the evacuation of the hydrogen. At that stage, the ion pumps were directly connected to the fixed-tuner port of the RFQ. Lower figure shows the upgrade of the relocation of the ion pumps of the RFQ performed in 2023.

Furthermore, unexpected small particles were found at the flange inside the RFQ from the most upstream fixed tuner port. Because a non-evaporating getter pump (NEG) was attached to the same port and the partial pressure of hydrogen was higher than 10^{-5} Pa during beam irradiation owing to the gas flow from the ion source, it was considered that the observed particles were generated by hydrogen embrittlement of the zirconium element of NEG. We consider this to be one of the causes of RFQ instability. This was because the NEG was mounted downward on the fixed tuner port, and the observed particles were also found in the oblique fixed-tuner port, where the shortest path to the port was through the vane of the RFQ. Subsequently, we dismounted the NEG. However, the RFQ still equips eight ion pumps directly connected downward to the other fixed-tuner ports. A similar situation may be expected with the titanium electrodes of ion pumps. Because purging the RFQ was necessary to change the configuration of these ion pumps, performing replacement work during continuously requested beam time during non-clinical studies and neutron characteristic measurements was not possible. After the completion of the beam time, the configuration of the ion pumps changed in April 2023. First, three out of eight ion pumps with increased ion currents were removed. Furthermore, angle valves were installed between the fixed-tuner port and ion pumps, as shown in the lower part of Fig. 6. This is because of following two reasons: The first one is to prevent the titanium in the ion pump from falling into the RFQ when hydrogen embrittlement occurs at the titanium electrode. The second one is to enable dismounting without pursuing the vacuum of the RFQ. From the experience of the operation of the iBNCT accelerator, it took at least one month for RF conditioning to resume stable operation after purging the RFQ vacuum; thus, this replacement work was performed before starting the clinical study.

TROUBLES

Failure of the Klystron High-Voltage Power Supply

In recent accelerator operations, two failures in the high-voltage power supply of the klystron occurred in October 2022 and October 2023. Both cases occurred in a droop compensator (DRC), which compensates for the flatness of the high-voltage pulses to the klystron. In October 2022, a protection circuit comprising four-series of diodes and varistors was broken. The diode used in the circuit was already discontinued, but we have spares, and by replacing the broken parts, the beam operation could be resumed within a week. However, the reason why the protection circuit was broken is not yet understood, and modification of the protection circuit should be considered for spare parts. In October 2023, a different part of the DRC was broken. The DRC comprises a series of 48 chopper boards to compensate a 3-kV droop of the during the high-voltage pulse with a length of 1 ms. At that time, two boards were found to be broken in investigations by the manufacturing company. One board provides 65 V compensation, but the current operation does not require the operation of all boards; broken boards are removed, and hardware connection and software in the DRC are rearranged to maintain the operation. In that case, it took approximately 1.5 months to resume the operation.

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DEVELOPMENT FOR CLINICAL STUDY

After the completion of the non-clinical study in 2022, the iBNCT project began preparing for clinical studies. In 2023, in parallel with medical procedures, the accelerator side must develop a system that combines existing accelerator systems with a medical system developed by the University of Tsukuba. The medical system must operate in a network that is independent of the accelerator control system. Furthermore, the accelerator information, such as average beam current and integrated charge, must be provided during BNCT treatments. To achieve this, a programable logic controller (PLC) sub-system with a multi-CPU configuration was installed. The sub-system contains two PLC CPU modules; a Linux CPU and sequence CPU modules. The Linux CPU and sequence CPU modules are connected to the accelerator and medical networks, respectively. In this sub-system, accelerator information is provided to the medical side with shared memory between two CPU modules during BNCT treatment at any time. Furthermore, because accelerator controls such as starting beam irradiations are regarded as medical treatments, they must be performed by medical doctors instead of accelerator operators. A doctor-operated control panel was newly developed for medical doctors unfamiliar with accelerator operations. Figure 7 shows a photograph of the developed control panel. It is equipped with a touch panel for control via the PLC sub-system and an emergency switch directly connected to the magnetron of the ion source and hard-wired to stop beam irradiation. Using this system, the iBNCT project began a Phase-I Investigator-initiated clinical trial in January 2024.

Figure 7: Photograph of developed doctor-operated control panel.

SUMMARY

The iBNCT project aims to realize accelerator-based BNCT with a configuration of 3-MeV RFQ and 8-MeV DTL with a beryllium neutron generation target. The current accelerator-operation parameters were a repetition of 75 Hz, a beam width of 0.92 ms, and a peak beam current of 30 mA. The resulting average current before the target was approximately 2 mA. This value is sufficient fort us to proceed with the clinical study. After the completion of the non-clinical study in the fiscal year 2022, we started the clinical study in January 2024, which is an important milestone in the iBNCT project. The clinical study will continue at the end of the fiscal year 2025, and subsequently we will attempt to increase the beam current by increasing the repetition rate. The increase in the beam current directly shortens the treatment time of BNCT and expands the applicable cancer type; therefore, it is of great significance for the iBNCT project in the future.

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