Multimodal Monte Carlo treatment system capable of microdosimetry with PHITS

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Abstract. Boron neutron capture therapy (BNCT) is a radiation therapy that combines neutrons and boron drugs. An industry-academia-government collaboration team is currently developing the linac-based treatment device and several peripheral devices to establish this therapy. In the project, a demonstration device, "iBNCT001", for a linac-based neutron source applicable to BNCT treatment is being developed. We are developing Tsukuba Plan, a multimodal Monte Carlo-based treatment planning system, in addition to the linac-based neutron source device. Tsukuba-Plan has adopted a Particle and Heavy Ion Transport code System (PHITS) as the Monte Carlo-based dose calculation engine. PHITS has a microdosimetric function that can compute a lineal energy distribution and determine relative biological effectiveness through combination with the stochastic microdosimetric kinetic model parameters. By utilising these functions, Tsukuba-Plan is expected to estimate the weighted doses administered to the tumour region and normal tissues in the irradiation field more accurately.

1. Introduction
Boron neutron capture therapy (BNCT) [1] has attracted attention as a radiation therapy for intractable cancers for which effective therapy has not yet been established. BNCT combines neutrons and boron-10 compounds. Clinical studies of BNCT against cancers, such as malignant brain tumour, malignant melanoma, and head-and-neck cancer, have been conducted using research reactors because the treatment requires high-intensity neutrons. The results of the clinical studies have proven the effectiveness of BNCT for intractable cancer. However, the radiotherapy has not been established yet. Meanwhile, the recent progress of accelerator-based neutron source technologies has enabled us to generate neutrons required to BNCT by using a compact accelerator installable in a hospital. Based on this situation in the physics field of BNCT, many development projects for accelerator-based neutron sources for BNCT are ongoing in the world. In Japan, especially, some commercial-based treatment devices have been produced and installed in hospitals, some of which have already succeeded in conducting clinical studies for several cancers. Based on the background, an industry-academia-government collaboration team, headed by the University of Tsukuba, is promoting a project named “iBNCT project” for developing an accelerator-based neutron source for boron neutron capture.
therapy (BNCT) [2]. The project team consists of the University of Tsukuba, High Energy Accelerator Research Organization, Ibaraki prefecture, and several manufactures. The purpose of the iBNCT project is to develop an accelerator-based neutron source applicable to BNCT treatment and to conduct clinical trials using the device. We already completed constructing the demonstration device and succeeded in generating neutrons by the device in 2016. In the project, not only the accelerator-based treatment device but also several peripheral devices required performing BNCT treatment are being developed. As part of the development of peripheral devices, a treatment planning system for BNCT is being developed. Details of the developments in the iBNCT project are explained in the next sections.

2. iBNT001, a linac-based neutron source for BNCT
To carry out BNCT using an accelerator-based neutron source, high-intensity neutrons that are comparable to a nuclear reactor must be generated by the device. Concretely, to complete irradiation against a patient within 1 hour using an epithermal neutron (0.5 eV < Energy < 10 keV) beam, the flux of the epithermal neutron at a beam port is required to be \( \geq 10^8 \text{n/cm}^2/\text{s} \). Moreover, the contaminations for the high-energy neutrons (10 keV > Energy), thermal neutrons (0.5 eV < Energy), and gamma-ray are also required to be as low as possible. Furthermore, we thought that the treatment device needs to avoid radiation activation and irradiation time should be shortened as much as possible. Thus, the development of a device generating higher-intensity and lower-energy neutrons was required. Based on the essential conditions, in the project, a demonstration device of the accelerator-based neutron source named “iBNCT001” has been designed and produced [3].

In the conceptual design of the device, first, we adopted beryllium as the material of the neutron target. Next, the energy of a proton beam irradiating on the beryllium target was specified as 8 MeV based on the various evaluations and analyses in the design stage. Finally, the average proton current of our accelerator was set at 5 mA or more to generate sufficient intensity of neutrons based on the neutron yield from the reaction between beryllium and 8 MeV proton. Regarding the type of proton accelerator of iBNCT001, to achieve the specifications required for the accelerator as proton current and energy, a linac consisted of a Radio-Frequency Quadrupole Linac (RFQ) and a Drift Tube Linac (DTL) type linac, has been adopted. The basic specifications of the linac of J-PARC [4] have been applied to the linac tubes of iBNCT001. Meanwhile, for the peripheral devices of the accelerator such as ion source and cooling system, dedicated devices for iBNCT001 have been developed and then combined with the J-PARC-based linac tubes. A photograph of both linac tubes is shown in figure 1.

![Figure 1. Linac tubes of iBNT001](image_url)

3. Outline of Tsukuba Plan
In the iBNCT Project, various types of peripheral equipment, such as a treatment planning system, a patient positioning system, and radiation monitors, are being developed in addition to the accelerator-based neutron source for BNCT; these devices are required to implement the BNCT treatment. The
A treatment planning system (TPS) is an indispensable software in radiation therapy that determines an optimal irradiation condition for individual patients. In the conventional external radiation therapy as X-ray therapy and particle therapy, many commercial-based TPSs are already spread and practically used for the actual treatment. However, in BNCT field, there are few commercial-based TPSs. The behaviours for several particles relating to doses in BNCT are complicated; therefore, in the BNCT treatment planning, the full-Monte Carlo transport calculation method has been used for a long time to calculate the dose. Based on this background, we are developing a multi-modal Monte Carlo based treatment planning system applicable to BNCT (developing code name: Tsukuba Plan) [5]. For the Monte Carlo calculation engine of Tsukuba Plan, Particle and Heavy Ion Transport code System (PHITS) as a multi-purpose Monte Carlo transport code developed in Japan has been adopted [6]. Furthermore, for the cross-section library as essential data of the Monte Carlo transport calculation, the Japanese Nuclear Data Library, JENDL-4.0, has been combined with PHITS [7].

Figure 2 shows a schematic of the dose estimation procedure using the Tsukuba Plan. To determine an irradiation condition, first, Tsukuba Plan creates a three-dimensional (3D) model of a patient based on computed tomography (CT) images of a patient. The 3D model is converted into a voxel calculation model described by the PHITS’s input format. PHITS computes several physical doses (absorbed doses) generated by the reaction with neutron and various atoms around the irradiation field by loading the input file of the voxel calculation model. Then, the total weighted doses administered to a tumour region and normal tissues are determined. By repeating this dose estimation procedure, the Tsukuba plan leads to optimum irradiation conditions for the patient.

4. Improvement of dose estimation by combination with a microdosimetry method

To sophisticate the performance for the dose estimation of the Tsukuba Plan, we are making various new approaches. As a part of the improvement, to raise the accuracy of dose estimation, we intend to apply a microdosimetric technology to the dose estimation method of Tsukuba Plan. A microdosimetry function, which is applicable to BNCT dosimetry based on the stochastic microdosimetric kinetic (SMK) model, is already installed in PHITS [8]. Therefore, PHITS can compute a lineal energy distribution and determine relative biological effectiveness (RBE) through combination with the SMK model. In a conventional dose estimation in BNCT, the weighted dose is determined by multiplying an absorbed dose by fixed values for each RBE obtained from biological experiments [9]. However, since the neutron spectrum changes with depth in a body, the RBE value also changes with depth. Meanwhile, in the dose estimation with the SKM model, PHITS can compute the RBE that varies, depending on the neutron’s spectrum. Eventually, the weighted dose is determined based on each RBE value at that position. Figure 3 shows a comparison between weighted doses estimated by fixed RBEs and the flexible RBEs, respectively. The orange line indicates the fixed RBE for neutrons as "2.5". Moreover, RBE for gamma-ray dose is "1.0", as indicated by the brown line. The distribution for the weighted dose determined by multiplying the fixed RBEs is plotted by the blue line. On the other hand, the green line indicates the flexible neutron's RBE computed with the SMK model of PHITS. The

![Image](image_url)
change in RBE depending on the depth is demonstrated. Therefore, the distribution for weighted dose determined by multiplying the flexible RBEs plotted by the red line differed slightly with the distribution (blue line) for the weighed dose determined via the conventional method.

Figure 3. Comparison between conventional weighted dose distribution (blue line) with fixed RBEs (orange, brown) and the microdosimetry-based weighted dose distribution (red line) determined by multiplying the flexible RBE (green line)

5. Conclusion
iBNCT project is developing Tsukuba Plan as the Monte Carlo-based multi-modal treatment planning system in addition to the development of the linac-based BNCT device. Tsukuba-Plan has adopted PHITS as the Monte Carlo calculation engine. Since the dose calculation with the SMK model can compute the RBE that changes with the change of neutron’s spectrum, Tsukuba Plan, combined with PHITS, has the potential for realising treatment planning based on the microdosimetric technology. Moreover, it is expected to improve the accuracy of the dose estimation for radiation therapy.

6. Acknowledgments
This work was supported by MEXT/JSPS KAKENHI (Grant number JP18K19899). This research was supported in part by Multidisciplinary Cooperative Research Program in CCS, University of Tsukuba.

7. References
[1] Sweet W H 1997 J. Neutro-Oncol. 33 19–26
[2] Kumada H et al 2014 Appl. Radiat. Isot. 88 211-15
[3] Kumada H et al 2019 AIP Conference Proceedings 20160 (050013) 10
[4] Ikegami M 2012 Prog. Theor. Exp. Phys. 02B002 1-17
[5] Kumada H et al 2017 Radiat. Prot. Desim. 180 286-90
[6] Iwase H et al 2002 J. Nucl. Sci. Technol. 39 1142-51
[7] Shibata K et al 2012 J. Nucl. Sci. Technol. 48 1-30
[8] Sato T et al 2018 Sci. Rep. 8-988 1-14
[9] Kumada H and Takada K 2018 Ther. Radiol. Oncol. 2 1-11