Development of JCDS, a computational dosimetry system at JAEA for boron neutron capture therapy

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Abstract. Clinical trials of boron neutron capture therapy (BNCT) are being carried out using several research reactors throughout the world. In Japan, many medical groups perform clinical trials of BNCT using Japan Research Reactor No.4 (JRR-4) in Japan Atomic Energy Agency (JAEA). JAEA has developed a treatment planning system, JCDS, in order to evaluate radiation dose given to a patient in the BNCT.

JCDS employs a voxel calculation method to compute the radiation dose given to a patient. An initial version of JCDS created a voxel model, dividing a space into 1x1x1cm³ voxel cells. JCDS was improved to create a detailed voxel model consisting of minute voxel cells such as 2x2x2mm³ voxel cells. Verification of accuracy of calculations with the detailed voxel mode demonstrated that the detailed voxel model enables JCDS to evaluate more accurately the radiation doses to a patient undergoing BNCT.

Furthermore, the calculation code of JCDS is being incorporated into the PHITS system as a Monte-Carlo transport code. By employing the PHITS system in the dose evaluation, total doses given to a patient by combined modality therapy such as BNCT and X-ray therapy can be estimated accurately.

Here, an outline and the performances of the latest version of JCDS are presented, and a future system integrated with JCDS is introduced.

1. Introduction

Clinical trials of boron neutron capture therapy (BNCT) are being carried out using several research reactors [1]. BNCT was invented in 1936, and its medical application to malignant brain tumors has been demonstrated [2]. The physical principle of BNCT is a two-component or binary system, the nuclear reaction that occurs when the stable isotope $^{10}$B is irradiated with low energy or thermal neutrons to yield highly energetic helium-4 ($^4$He) nuclei (i.e., alpha particles) and recoiling lithium-7 ($^7$Li) ions. The ranges of the alpha-particle and the $^7$Li nucleus movement in tissue are comparable to the size of a typical tumor cell. Thus, the damage is limited to those cells that accumulate boron. Thereby, invasive tumor cells infiltrating normal tissue can in theory be destroyed without any significant damage to normal organs. In the last decade, the clinical trials of BNCT with an epithermal neutron beam (-10keV) have been performed at several research reactors in the world. By using the epithermal neutron beam, delivery is possible to deeper regions in the brain than a conventional thermal neutron beam (-1eV). In the recent BNCT studies, two boron compounds, BPA ($p$-boronophenylalanine) and BSH (sodium borocaptate, $\text{Na}_2^{10}\text{B}_{12}\text{H}_{11}\text{SH}$) were applied.

The clinical trials for brain tumor in Japan were performed using a thermal neutron beam from Japan Research Reactor No.2 (JRR-2), the Musashi Institute of Technology Reactor (MiITR), and the Kyoto University Research Reactor (KUR)[3]. To deliver thermal neutrons to deeper regions in the brain, the BNCT
procedure has included craniotomy with skin flap opening and bone removal. Intra-operative BNCT at JRR-4 also has been carried out, since 1999[4][5]. In recent years, BNCT studies with an epithermal neutron beam, which has potential for increased therapeutic effect, have been carried out at KUR and JRR-4 since October 2003[6].

To carry out the clinical trials based on accurate dosimetry, the JAEA Computational Dosimetry System (JCDS), a treatment planning system for BNCT, was developed by JAEA[7]. JCDS employs a voxel calculation method to compute the radiation dose given to a patient. JCDS was released for public use, after which BNCT clinical trials, including trials of treatment planning using JCDS, for malignant brain tumor were begun at JRR-4 in October 2003[8]. Clinical trials for head-&-neck cancer also have been performed at JRR-4 since 2005[9].

In the procedure for the head-&-neck cancer, calculation geometry for dose evaluation is very complex due to oral and nasal cavities and lung being in the geometry. Therefore, it is necessary to define a precise voxel model for the calculation in order to determine an optimum treatment plan. Also, in recent procedures for brain tumor in Japan, to enhance therapeutic efficacy, two boron compounds, BPA and BSH are administered together to a patient in an infusion, and then neutron irradiation is carried out[10].

In procedures using BPA, measurement of Tumor/Normal tissue ratio is performed using PET (positron emission computerized-tomography) in order to estimate accurately the boron concentration of BPA in the tumor region of each patient[11]. By these means, JCDS is being improved to make the dose evaluations for these recent procedures.

2. Material and method
2.1. Computational dosimetry system in JAEA

JCDS is a treatment planning system for BNCT. Fig. 1 shows the scheme of the dosimetry process of BNCT using JCDS. To simulate a neutron irradiation in a BNCT trial, first, JCDS creates a three-dimensional model including the affected region of a patient based on CT and MRI data. By using CT image data, compositions of the head such as bone, soft tissues and air are automatically differentiated based on CT values. MRI image data are used for definition of the “Region Of Interest (ROI)” such as tumor and critical organs. By superimposing particular points such as nasion, ears and vertex in the MRI images onto the corresponding points in the CT images, the detailed three-dimensional head model that includes both composition data and ROI definitions is created. To effectively compute behavior of neutrons and photons in the model, the detailed model is converted to a voxel model. Material data for individual voxel cells are defined based on the proportion of bone, soft tissue, tumor, skin and air present, rounded off to the nearest 10% fraction by volume. Several dose components given to a patient can be determined by calculating with MCNP-4C code, a general Monte Carlo n-particle transport code developed by Los Alamos National Laboratory[12]. For the public use of the system, the initial version of JCDS has been released by the Research Organization for Information Science and Technology.

![Figure 1 Process of treatment planning using JCDS](image-url)
2.2. Minute voxel calculations with mesh tally in MCNP5

To estimate radiation dose, JCDS in its initial version employed a voxel calculation method dividing a space into 10x10x10 mm voxel cells. The second version of JCDS was updated to be able to create a multi-voxel model combined with 5x5x5 mm voxel cells [13]. The dose in each voxel cell was determined by calculation applying the “Cell tally” function in MCNP. The calculation accuracy of JCDS was verified by comparison with measurements obtained from cylindrical water phantom experiments [14]. The verification results proved that JCDS performs well enough for dose evaluation, except for the evaluations near the phantom's surface. However, the results also indicated that JCDS creates discrepancies at the boundary region between air and soft tissues. In the treatment planning for head-&-neck cancer therapy by BNCT, skin, oral mucosa and nasal mucosa are regarded as the important regions which must be paid attention in determining limitation of the dose given to the patient. For this reason, doses of those regions shall be evaluated with higher accuracy.

The calculation accuracy will be improved by scaling down the voxel cell size. However, the smaller voxel cell size makes calculation time longer. Thus, employing a voxel model with minute voxel cells had not been practical for treatment planning so far. MCNP5 has a useful function named “mesh tally”, which enables calculation of dose distribution. JCDS was modified so that the mesh tally function can be applied to treatment planning. JCDS was also improved to be able to create a detailed voxel model consisting of 1x1x1mm voxel cells or 2x2x2mm voxel cells (2mm voxel). Fig.2 shows a 2mm voxel model for a brain tumor patient.

![Figure 2 2mm Voxel calculation model for malignant brain tumor](image)

2.3. Verification of the minute voxel calculations

In this section, verification of calculation performance of the new JCDS which applies a detailed voxel model using mesh tally is described. Fig.3-(a) shows a phantom’s voxel model consisted of 10mm voxel cells, and Fig. 3-(b) shows the voxel model with 2mm voxel cells. In the verification, the radiation beam selected for the phantom was the epithermal neutron beam which is applied to BNCT clinical trials. The beam outlet shape was applied a circular shape of 10cm diameter. Distributions of thermal neutron flux in the phantom were determined separately with the mesh tally and the cell tally, and then the calculation results were compared with the experimental values.

To confirm the usefulness of the calculation with the minute voxel model, the computing time for each voxel model were also estimated. In the calculations with the 10mm voxel model, three-dimensional distributions in the phantom were determined separately using the cell tally and the mesh tally. In determining the benchmarks for the 2mm voxel model, mesh tally calculation only was performed. The
benchmark tests were done by one standard PC. Pentium 4 CPU speed was 3.2 GHz. The number of particle histories for each condition was 800 million.

(a) 10mm voxel phantom model

(b) 2mm voxel phantom model

Figure 3 Voxel models for cylindrical water phantom

3. Results and discussion

3.1. Calculation accuracy of 2mm voxel model with mesh tally

First, the calculation accuracy of the mesh tally was confirmed by comparing the mesh tally calculations and the cell tally calculations. The cell tally values and the mesh tally values at each corresponding point were in good agreement, with error of less than 3%. The discrepancy is within statistical uncertainty of the MCNP calculations. Its results demonstrated that calculation with MCNP allows switching from cell tally to mesh tally.

The influence of the segmentalization of the voxel model was verified continuously. Experimental data and calculation values using the 10mm voxel model and the 2mm voxel model of the thermal neutron flux profiles along the beam's central axis in the phantom are shown in Fig.4. Both calculations were done by mesh tally. For both calculation profiles, the detailed distributions along the axis were determined by interpolating the calculated values of each voxel cell using a JCDS function. The two calculations for positions in the phantom deeper than 1 cm were similar to the experimental values, with error of less than 5%. The value of the 2mm voxel model on the phantom's surface also matched the experimental value within probable error, though the 10mm voxel model's value was overestimated by approximately 40%. These results demonstrated that accuracy of the dose evaluation can be improved by employing a detailed voxel model consisting of 2mm voxel cells.

3.2. Verification of practical use for BNCT

The time of cell tally calculation for the 10mm voxel model was approximately 550 hours. On the other hand, the time with mesh tally was 22 hours. The time for the 2mm voxel model using mesh tally was approximately 58 hours. Based on the benchmark test for the 2mm voxel model, if cell tally was applied, the time required in order to obtain reasonable results was estimated to be over a half year. The results
demonstrated that a detailed voxel model with 2mm voxel cells can be employed in treatment planning in actual BNCT trials by using mesh tally.

Figure 4 Thermal neutron flux profiles on beam’s central axis in the phantom

3.3. Dosimetry of clinical trials for head and neck cancer

The results of the verification show that calculation methodology adopting the 2mm voxel model is practical and efficient for dosimetry. Based on the results, treatment planning in the BNCT procedure for malignant brain tumor at JRR-4 has utilized calculation using a 2mm voxel model with mesh tally. “PC Cluster,” a parallel computing system constructed with 16 PCs, was also utilized in the dosimetry calculation.

By using a dosimetry total system including the new version of JCDS, clinical trials for melanoma and head-&-neck cancer have been performed at JRR-4 recently. Fig. 5 (a) and (b) show a 2mm voxel model for a clinical trial for oral cancer. A sagittal view of the voxel model is shown in Fig.5-(a), and Fig 5-(b) shows an axial view of the model. Voxel models for larynx cancer are shown in Fig. 6-(a) and 6-(b). By employing a 2mm voxel, the surface layer of skin, the oral and nasal cavity, and lung shape could be precisely represented. The calculation using the PC Cluster was done in a few hours. The statistical uncertainties around the target region were below 3%.

Figure 5 2mm Voxel models for a patient of oral cancer
4. Future Direction

4.1. Convert from MCNP to PHITS

JCDS is being improved so as to enable its application to dosimetry also employing PHITS (Particle and Heavy Ion Transport code System) as well as dosimetry by MCNP. PHITS can perform transport calculations for not only neutrons and photons but also protons and heavy particles [15]. By employing PHITS in the dose calculation, JCDS becomes to be able to perform dosimetry for proton therapy and heavy ion therapy as well as BNCT. Therefore, total doses given to a patient by combined modality therapy such as BNCT and conventional X-ray therapy or proton therapy can be evaluated accurately. Also, for BNCT using an accelerator, design of the neutron source and transport system as well as treatment planning can be done with PHITS.

4.2. Combination with PET data

In recent BNCT procedure with BPA in Japan, concentration distribution of BPA in a tumor region is determined by PET measurement. JCDS is being improved to be able to utilize PET data in treatment planning in combination with CT and MRI data. In this way it is hoped that JCDS will become able to pick out tumor regions more precisely using the PET value. Furthermore, radiation dose and its distribution can be determined according to concentration distribution of boron in the tumor region.

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