

## Estimation for 3D Distribution of Biological and Chemical Doses for BNCT

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**BACKGROUNDS AND PURPOSES:** For the further advancement of BNCT, it is important to improve the estimation for biological effect due to neutrons. At Heavy Water Neutron Irradiation Facility of Kyoto University Reactor (KUR-HWNIF), the fundamental studies for BNCT in the fields of medicine, biology, chemistry and pharmacology, etc., have been performed. Through these studies, the difficulty in the estimation for neutron biological effects is being acutely realized. In the BNCT irradiation field, it is difficult to monochromatically generate neutrons with a specific energy, and neutrons with the various energy ranges such as thermal, epi-thermal and fast neutrons, and also gamma rays are mixed. Furthermore, the neutron energies and the types and energies of secondary charged particles due to the nuclear reactions in living body are different. The biological effect estimation for BNCT are being studied by multiple groups in the world, but the consistent estimations have not been possible due to the difficulty of estimation for the biological effects, particularly regarding neutrons. The final goal of this project research is to develop a consistent estimation method of the biological effects for BNCT. In 2023, the estimation method for the 3D dose distribution, focused on the biological effects, and the chemical effects as precursors to the biological effects.

**RESEARCH SUBJECTS:** The collaboration and allotted research subjects (ARS) were organized as follows;

**ARS-1 (R5P8-1):** “Establishment of beam-quality estimation method in BNCT irradiation field using dual phantom technique (VII)”, Y. Sakurai, *et al.*

**ARS-2 (R5P8-2):** “Effect of co-culture of astrocytes and gliomas using spheroids on the efficacy of BNCT”, N. Kondo and Y. Sakurai.

**ARS-3 (R5P8-3):** “The effect of BNCT on cancer associated fibroblasts using 3D oral cancer model”, K. Igawa, *et al.*

**ARS-4 (R5P8-4):** “Verification of BNCT effect on hematological cancer cells and dosimetry for expansion of BNCT cases”, S. Yoshihashi, *et al.*

**ARS-5 (R5P8-5):** “Imaging measurements of 478 keV prompt gamma rays of the boron neutron capture reaction at the KUR-HWNIF and the E-3 Facility”, T. Mizumoto, *et al.*

**ARS-7 (R5P8-7):** “Development and evaluation of 3D gel dosimeter for the measurement of dose distribution in BNCT”, S. Hayashi, *et al.*

**ARS-8 (R5P8-8):** “Establishment of three-dimensional dose distribution estimation method for BNCT using radiochromic gel dosimeter”, Y. Sakurai, *et al.*

**ARS-9 (R5P8-9):** “Survey of luminescent material with varied wavelength-dependence for beam quality measurement in BNCT”, K. Tanaka, *et al.*

**ARS-10 (R5P8-10):** “The study for development and application of tissue equivalent dosimeter - feasibility of proton magnetic resonance analysis of Fricke dosimeter -”, M. Oita, *et al.*

**ARS-11 (R5P8-11):** “Comparison of measurement of contamination gamma-ray dose using thermo-luminescence dosimeter and glass dosimeter”, S. Nakamura, *et al.*

**ARS-12 (R5P8-12):** “Influence of tissue water content in dose calculation for BNCT”, T. Takata, *et al.*

ARS-6 (R5P8-6) could not be performed mainly because of the lack of budget.

## Establishment of Beam-quality Estimation Method in BNCT Irradiation Field using Dual Phantom Technique (VII)

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**INTRODUCTION:** Before the start of treatment with BNCT, the relative biological effectiveness (RBE) for the fast neutrons incident to the irradiation field must be estimated. Measurements of RBE are typically performed by biological experiments with a phantom. Although the dose deposition due to secondary gamma rays is dominant, the relative contributions of thermal and fast neutrons are virtually equivalent in a water and/or acrylic phantom. Uniform contributions to the dose deposited from thermal and fast neutrons are based in part on relatively inaccurate dose information for fast neutrons. The aim of this study is to establish the accurate beam-quality estimation method mainly for fast neutrons by using two phantoms made of different materials [1]. In 2023, verification experiments for the dual phantom technique were performed using Heavy Water Neutron Irradiation Facility installed in Kyoto University Reactor (KUR-HWNIF) as in the previous year [2].

**MATERIALS AND METHODS:** Figure 1 shows the experimental setup using the dual phantom technique. One of the dual solid phantoms was made of polyethylene with natural lithium fluoride for 30 weight percent (LiF-polyethylene phantom), and the other phantom was made of polyethylene with 95%-enriched lithium-6 fluoride for 30 weight percent ( $^6\text{LiF}$ -polyethylene phantom). Glioblastoma cells were divided in two groups. One was treated group using p-boronophenylalanine (BPA, containing B-10) for B-10 concentration of 25 ppm, and the other was non-treated group. The depth dose distributions for the thermal neutron, fast neutron and gamma-ray components were determined based on the simulation calculation results normalized referring to the measured values. The epi-thermal neutron irradiation mode was used for the phantom experiments.

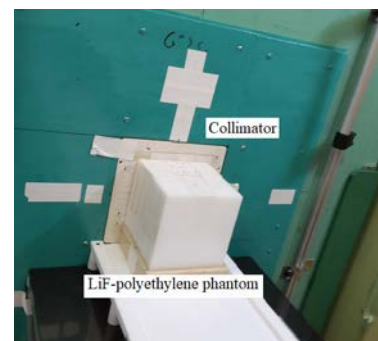


Fig. 1. Experimental setup for the dual phantom technique.

**RESULTS:** It was confirmed that the survival fraction became smaller as the thermal neutron flux became larger in the LiF-polyethylene phantom. The survival fraction for the non-treated cell was higher than that in BPA-treated cell. In the  $^6\text{LiF}$ -polyethylene phantom, the survival fraction showed no difference between non-treated and BPA-treated cells. The  $^6\text{LiF}$ -polyethylene phantom absorbs thermal neutrons although it has not significant effect in fast neutron dose. No difference in survival fractions between non-treated and BPA-treated cells with  $^6\text{LiF}$ -polyethylene phantom indicated fast neutrons might not effect cell survival. On the other hand, due to mixture of thermal neutron in LiF-polyethylene phantom, BPA-treated cells were killed effectively compared with non-treated cells through n-alpha reactions.

**ACKNOWLEDGMENT:** This work was supported by JSPS KAKENHI Grant Number JP 16H05237.

### REFERENCES:

- [1] Y. Sakurai, *et al.*, Med. Phys., **42** (2015) 6651-6657.
- [2] Y. Sakurai and T. Kobayashi, Nucl. Instr. Meth. A., **453** (2000) 569-596.

## Effect of co-culture of astrocytes and gliomas using spheroids on the efficacy of BNCT

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### INTRODUCTION:

Until now, BNCT evaluations for brain tumors have used two-dimensional cultures of only tumor cells when evaluating in vitro. Actual tissue contains many types of cells in addition to tumor cells, so it is not sufficient to evaluate biological effects. Furthermore, when evaluating in vivo, small animals (mice) have been used. However, because the size is significantly different from that of an actual human, there is a large gap in the spatial dose distribution. Therefore, we will use 3D co-culture of tumor cells and other cells to construct a more realistic irradiation system and evaluate its biological effects.

### EXPERIMENTS:

#### Cells:

We used astrocytes that were derived from fetal C57BL/6 mouse brain and GL261 mouse glioma cells. They were cultured in DMEM with 10% heat-inactivated fetal bovine serum in 5 % CO<sub>2</sub> incubator. They were cultured separately in ultra-low attachment T75 flasks. One day before thermal neutron irradiation, astrocytes and gliomas were counted and co-cultured in ultra-low attachment 6-wells at the ratio of 1:1 (co-culture group). The number of cells were  $2 \times 10^5$  respectively. The mono-culture group consisted of  $2 \times 10^5$  astrocytes or GL261 cells alone, respectively.

#### Boronophenylalanine (BPA) Treatment:

A stock solution of the p-<sup>10</sup>B-para-boronophenylalanine (BPA)- fructose complex was used. The <sup>10</sup>B concentrations was approximately  $1000 \pm 4.55$  ppm. The day before irradiation, BPA was dissolved in the cell culture medium at a concentration of 25 ppm.

#### Thermal Neutron Irradiation:

The collected spheroids in 1.5-ml plastic tubes were irradiated for 10 or 20 min at room temperature using a neutron beam at the Heavy Water Neutron Irradiation Facility installed in the Kyoto University Reactor (KUR-HWNIF). The operating power of the reactor was 1 MW. After irradiation, half of the spheroids were spread in each ultra-low attachment 6-well.

#### Cell count:

The spheroids were collected after centrifugation and rinsed with PBS. They were trypsinized and the cells were counted 9-11 days after irradiation.

### RESULTS:

Compared with the non-irradiated control group, the cell numbers of the BNCT-treated groups tended to smaller in all the GL261 alone, astrocytes alone and the co-culture groups. However, that of co-culture group tended to be larger than GL261 alone or astrocytes alone group.

## The effect of BNCT on cancer associated fibroblasts using 3D oral cancer model

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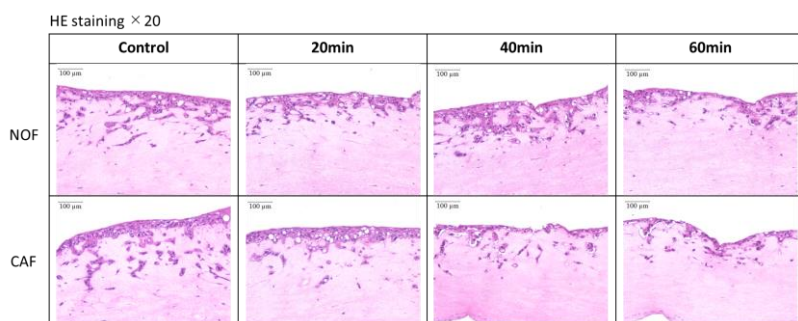
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**INTRODUCTION:** It has been reported that cancer associated fibroblasts (CAFs), one of the important cells that form the tumor microenvironment, govern local invasion and metastasis of cancer and are involved in cancer cell proliferation and resistance to cancer therapy, and that the prognosis is poor when CAFs are abundant in the stroma, and that the tumor microenvironment has a significant impact on the grade and progression of oral cancer. Therefore, focusing on CAFs, we will apply the evaluation of cancer therapy [1] to an oral cancer model consisting of normal oral fibroblasts (NOFs) and human squamous cancer cells (HSCs), and examine the prognosis of BNCT by seeding CAFs in cancer stroma.

**EXPERIMENTS:** At first the 3 D cancer models using oral CAFs and HSC-4 (JCRB0624) were fabricated as a control used oral NOFs. CAFs and NOFs were provided by Niigata University. Collagen matrix solutions containing either NOFs or CAFs ( $2.0 \times 10^5$  cells/mL) in a 12-well tissue culture insert were incubated for 7 days. After 7 days, HSC-4 cells ( $2.0 \times 10^5$  cells/well) were seeded on the top surface of the collagen matrix in which NOFs and CAFs are embedded. Then the 3D cancer models were cultured at the air–liquid interface from day 14. On day 15, 10 % BPA of medium was added for 24 hours and neutron beam was irradiated at Heavy Water Neutron Irradiation Facility of KUR on day 16. On day 21, the 3D oral cancer models were fixed and the sections were stained with HE staining for histological evaluation.

**RESULTS:** The 3D oral cancer model was irradiated with .neutron beams for 0, 20, 40, and 60 mins in the direction from the cancer cell layer to the cancer stromal layer. As shown in the Figure1, a decrease in the cancer cell layer was observed in both the NOF and CAF groups as the neutron irradiation dose increased. In the cancer stromal layer, the number of NOFs were not decreased with increasing irradiation dose, but the number of CAFs were decreased.



**Fig. 1. HE staining of 3D oral cancer model.**

## REFERENCES:

[1] Igawa, K., K. Izumi, and Y. Sakurai, *BioTech.*, **12**(2) (2023) 35.

## Verification of BNCT Effect on Hematological Cancer Cells and Dosimetry for Expansion of BNCT Cases

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**INTRODUCTION:** The number of newly diagnosed patients with major hematologic cancers (malignant lymphoma, multiple myeloma, and leukemia) in Japan was 58,547 in 2019 [1], and 5,853 hematopoietic stem cell transplants were performed in FY2022 as the last treatment option for these refractory hematologic cancer patients [2]. While autologous transplantation is a desirable medical technique for patients because it does not require long-term administration of immunosuppressive drugs and prevents immune reactions (GVHD) caused by HLA incompatibility, the grafts contain tumor cells, which must be removed and treated with chemotherapy and radiotherapy, which are pre-treatment procedures. We are now conducting basic research to remove tumor cells in grafts by Ex Vivo BNCT. The target will initially be acute promyelocytic leukemia (APL) patients who have developed resistance to anticancer drugs, but allogeneic transplant recipients waiting for an HLA-matched donor and patients with poor post-transplant performance will also be treated.

**EXPERIMENTS:** In this study, to verify the applicability of Ex Vivo BNCT, we first evaluate boron uptake in a cell line of multiple myeloma (MM) and a hematopoietic stem cell model. We use a new boron agent OKD-001 which was discovered by Okayama University. Then, we evaluate the applicability of Ex Vivo BNCT to blood cancers by measuring the cell survival rate of cells with and without boron drug exposure and irradiating them with thermal neutrons. The neutron distribution in the moderator is measured using a gold foil, and the boron dose in the cell back-up will be evaluated together with the boron uptake evaluation results. Next, by neutron irradiation we evaluate the feasibility of Ex Vivo BNCT for blood cancer cells by evaluating the cell viability of the boron-induced cells for MM model and stem cell model. The neutron distribution in the moderator is measured using a gold foil, and the boron dose in the cell bag is evaluated together with the results of the boron uptake.

**RESULTS:** When the cells of multiple myeloma (MM) cell line are exposed to the boron agent OKD-001 and then irradiated with neutrons, tumor cells tend to die, as shown in Figure 1, while cells do not tend to die without the boron agent. On the other hand, we have confirmed that hematopoietic stem cells are not killed by neutron irradiation after exposure to OKD-001. We are currently testing the efficacy of Ex Vivo BNCT on various tumor cell lines and developing a test method to determine its effectiveness.

### REFERENCES:

- [1] National Cancer Center (Japan), Current Cancer Statistics, [https://ganjoho.jp/reg\\_stat/statistics/stat/summary.html](https://ganjoho.jp/reg_stat/statistics/stat/summary.html) (2024.02.19).
- [2] Japan Hematopoietic Cell Transplantation Center (JDCHCT): Hematopoietic Cell Transplantation in Japan Annual Report of Nationwide Survey 2022, [http://www.jdchct.or.jp/data/report/2022/\(2024.02.19\)](http://www.jdchct.or.jp/data/report/2022/(2024.02.19)).

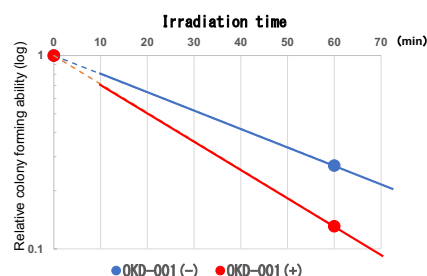


Fig. 1. Cell survival rates by neutron irradiation for MM cells with and without OKD-001.



## Imaging Measurement of 478 keV Prompt Gamma Rays of the Boron Neutron Capture Reaction at the KUR-HWNIF

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**INTRODUCTION:** We have been developing electron-tracking Compton cameras (ETCCs) for application to the monitoring of prompt 478 keV gamma rays from boron neutron capture reaction in BNCT by imaging. In this report, we present the results of experiments at the Heavy Water Neutron Irradiation Facility (HWNIF) with an ETCC based on previous studies [1].

**EXPERIMENTS:** To demonstrate the effectiveness of the ETCC in a real BNCT environment, we performed 478 keV prompt gamma-ray image monitoring of boron solution phantoms installed in the irradiation room of the HWNIF during neutron irradiation in epithermal mode under 5 MW operation. The phantom consisted of a 10 cm cubic acrylic container filled with a boric acid solution with a  $^{10}\text{B}$  concentration of 100 ppm and 230 ppm. The 478 keV prompt gamma rays emitted from the phantom passed through a cylindrical hole in the ceiling and were measured by the ETCC placed directly above the hole, facing downward. A schematic view of the experimental setup is shown in Fig. 1.

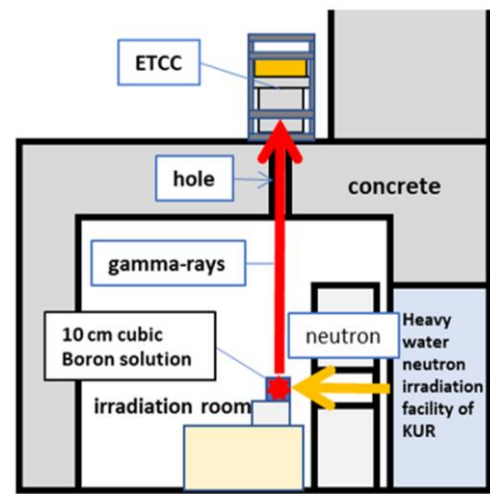


Fig.1. Schematic of the measurement setup.

**RESULTS:** We have successfully measured images of 478keV gamma rays from a boron solution phantom with a  $^{10}\text{B}$  concentration of 230 ppm, irradiated for the first time with neutrons under the conditions of the 5 MW epithermal mode using ETCC as shown in Fig. 2. Even with a short exposure time of 10 minutes, the location of the phantom appears bright enough in the image. On the other hand, the clear image was not obtained from the phantom with a  $^{10}\text{B}$  concentration of 100 ppm. There is a possibility that clearer images could be obtained by shielding the front of the ETCC with thin lead sheet to suppress the incidence of low-energy gamma rays. In addition, quantitative evaluation remains a future task.

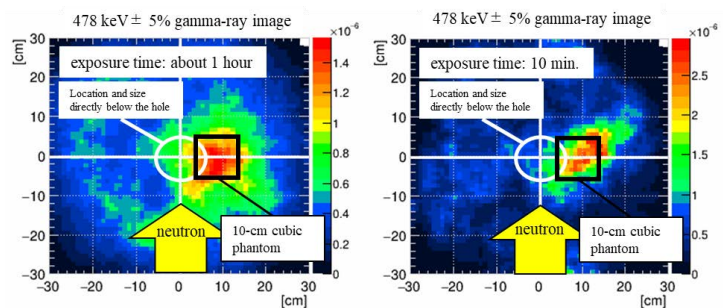


Fig.2. Measured 478 keV gamma-ray images of a boron solution phantom with a  $^{10}\text{B}$  concentration of 230 ppm irradiated neutrons under 5 MW epithermal mode operation. The exposure times of left and right images are approximately 1 hour and 10 minutes, respectively.

### REFERENCES:

[1] S. Komura *et al.*, KURNS Progress Re-port 2022.

## Imaging Measurement of 478 keV Prompt Gamma Rays of the Boron Neutron Capture Reaction at the E-3 Facility

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**INTRODUCTION:** In BNCT, quantitative imaging measurements of 478keV prompt gamma rays are effective for determining the distribution of boron concentration in the body and the boron dose during neutron irradiation. To achieve quantitative imaging in the neutron environment, we have been developing electron-tracking Compton cameras (ETCCs). In this report, we present the results of experiments at the E-3 irradiation port facility with ETCCs based on previous studies [1].

**EXPERIMENTS:** In the E-3 beamline, two phantoms with <sup>10</sup>B concentrations of 500 ppm and 1000 ppm were placed on the neutron beam to demonstrate the measurement of 478 keV prompt gamma rays. The phantoms were exposed to thermal neutron beams under 1 MW operation.

We also performed a test of stereo imaging measurement of 478 keV prompt gamma rays from neutron irradiated BPA-dosed cancer bearing mice using two ETCCs (ETCC1 and ETCC2) installed orthogonally to each other at E-3. Nude mice bearing MeWo tumors of approximately 1 cm diameter on the shoulder received BPA by subcutaneous injection at a rate of 400 mg/kg/h for two hours. Each mouse was anesthetized, fixed in an acrylic container, placed just above one of the ETCCs (ETCC1), and exposed to thermal neutron beams at the tumor site for 3 hours at E-3 under 5 MW operation.

**RESULTS:** Fig.1 shows the images of ETCC1 measurements when the two phantoms were irradiated simultaneously. This is the first time that the multiple-phantom separated 478 keV gamma-ray image has been successfully obtained with an ETCC.

As shown in Fig.2, both ETCCs successfully generated back-projection images of the mice viewed from two different directions. The bright areas in both images corresponded well to the areas of the mice irradiated with neutrons. We also obtained measurement results from ETCC1 indicating that the detection rate of 478keV gamma rays remained generally constant during the first 3 hours after administration. While the validity of the results needs to be investigated, we demonstrate the potential for measuring dynamic changes in mice administered sustained doses.

## REFERENCES:

[1] S. Komura *et al.*, KURNS Progress Report 2022.

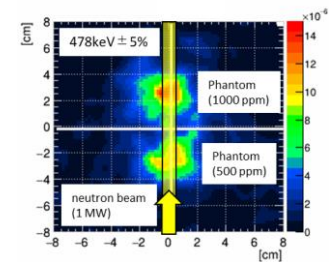


Fig.1: Measured 478 keV gamma-ray image of two phantoms.

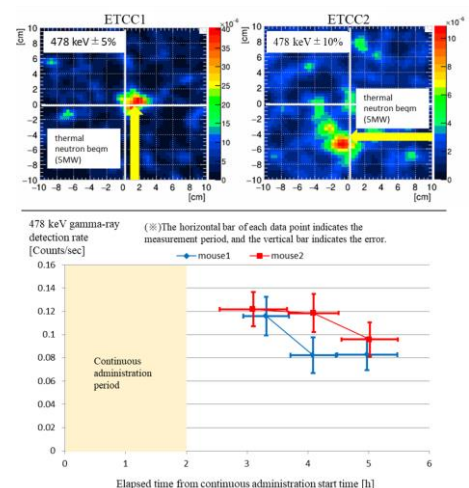


Fig.2: Measurement results of mice. (Top): 478 keV gamma-ray images taken by ETCC1 and ETCC2. (Bottom): Time variation of the detection rate of 478 keV gamma rays measured by ETCC1.

## Development and evaluation of 3D gel dosimeter for the measurement of dose distribution in BNCT

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**INTRODUCTION:** Three-dimensional (3D) gel dosimeters have been developed for the 3D dose measurement of the complex conformal dose distributions in radiation therapy [1]. These devices are composed of radio-sensitive substances and an aqueous gel matrix to preserve spatial information about the absorbed dose. The 3D absorbed dose distribution is deduced from the distribution of the reaction products measured by 3D imaging modalities such as MRI and Optical CT. In previous studies, we have developed a PVA-GTA-I radiochromic gel dosimeter that utilizes red color development due to the complex formation of polyvinyl alcohol (PVA) and iodide [2, 3].

In this work, as a preliminary experiment for evaluating the 3D dose distribution using optical CT, we evaluated the depth dose distribution in response to neutron beams from a nuclear reactor by combining small gel dosimeters with different compositions into blocks.

**EXPERIMENTS:** The PVA-GTA-I gel dosimeter is composed of partially saponified PVA, potassium iodide (KI), potassium nitrate (KNO<sub>3</sub>), glutaraldehyde, fructose, glucono- $\delta$ -lactone, and water. As a thermal neutron sensitizer, boric acid (B(OH)<sub>3</sub>) naturally containing <sup>10</sup>B of 20% was added into some gel dosimeters. The resulting solution was subdivided by pouring into PMMA cuvettes (4.5 mL, 1 cm path length). The neutron irradiations were performed using the HWNIF of KURR (1 MW). The samples were irradiated in the air at room temperature. The three different modes (thermal neutron-rich, fast neutron-rich, and mixed modes) of neutron beams made by heavy water spectrum shifter and cadmium thermal-neutron filters were applied to the samples.

**RESULTS:** Fig. 1. shows the result in mixed mode as an example. The beam was delivered from the left side of the pictures. In the pictures, asterisks (\*) indicate gel dosimeters containing boron. As a result, the color development attenuates from the surface (left) to the deeper parts (right) in all sets and the coloring becomes locally deeper in samples containing boron. Therefore, it is shown

that the PVA-GTA-I gel dosimeter is effective for depth dose measurement and can measure sensitization due to boron against neutron irradiation. Similar results were confirmed in other modes. The results demonstrate the potential of the PVA-GTA-I gel dosimeter for future 3D dosimetry using optical CT. The comparison with Monte-Carlo simulations will be also performed as a next step.

### REFERENCES:

- [1] Y. De Deene, Gels., **8** (2022) 599.
- [2] S. Hayashi *et al.*, Radiat. Meas., **131** (2020) 106226.
- [3] S. Hayashi *et al.*, J. Phys.; Conf. Ser., **2167** (2022) 012014.

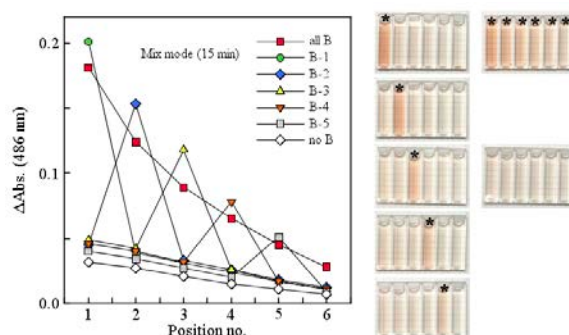


Fig. 1. The change of absorbances in depth (corresponding to relative depth dose distribution) in mixed mode, and the irradiated PVA-GTA-I radiochromic gel dosimeters. The asterisks (\*) in the pictures indicate the samples with boron.



## Establishment of Three-dimensional Dose Distribution Estimation Method for BNCT using Radiochromic Gel Dosimeter

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**INTRODUCTION:** Development in accelerator-based irradiation systems for BNCT is underway. BNCT using newly developed accelerator systems is being implemented at multiple facilities around the world. However, there are still issues that need to be improved for further advancement of BNCT. The advancement of dose estimation is one of these, and the estimation of biological dose is particularly important. As part of the advancement of biological dose estimation for BNCT, we focus on chemical effects, which are the precursor to biological effects. We are studying on the estimation method using chemical dosimeters, especially gel dosimeters [1]. Gel dosimeters are made of materials similar to living tissue and can be formed into any shape. Using a phantom made from gel dosimeter that models human body, three-dimensional dose distribution estimation becomes possible. Among the various types of gel dosimeters, we are especially focusing on “radiochromic gel dosimeters” that can be read out using optical CT, etc.. The purpose of this study is to establish three-dimensional dose distribution estimation method for BNCT using multiple types of radiochromic gel dosimeters. In 2023, the characteristic estimation for micellar gel dosimeters containing leuco crystal violet (LCV) was performed [2].

**MATERIALS AND METHODS:** The compositions of the LCV micellar gel dosimeters were determined based on the simulation calculation. The experiments for the characterization were mainly performed using Heavy Water Neutron Irradiation Facility of Kyoto University Reactor (KUR-HWNIF) [3] and Cobalt-60 Gamma-ray Irradiation Facility in KURNS. Three irradiation modes were used in the experiments using KUR-HWNIF: standard mixed neutron irradiation mode, standard epi-thermal neutron irradiation mode, and standard thermal neutron irradiation mode. The absorbance of the gel dosimeters after the irradiation was measured at the peak wavelength of 600 nm using a spectrophotometer. Figure 1 shows the experimental setup using Cobalt-60 Gamma-ray Irradiation Facility. Figure 2 shows the micellar gel dosimeters after the gamma-ray irradiation.

**RESULTS:** The experimental results confirmed that boric acid is particularly effective as a neutron sensitizer. Those also confirmed that the dose response of each gel dosimeter depended on the linear energy transfers (LETs) of the particles produced in each dosimeter. The experimental data analysis is currently underway to evaluate parameters for each gel dosimeter and each radiation component.

### REFERENCES:

- [1] R. Narita and Y. Sakurai, J. Phys: Conf. Ser., **2630** (2023) 012016.
- [2] S. Babic, *et al.*, Phys. Med. Biol., **54** (2009) 6791-6808.
- [3] Y. Sakurai and T. Kobayashi, Nucl. Instr. Meth. A, **453** (2000) 569-596.



Fig. 1. Experimental setup using Cobalt-60 Gamma-ray Irradiation Facility.

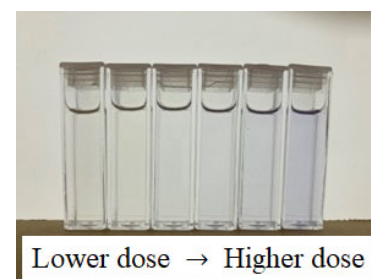


Fig. 2. Micellar gel dosimeters after the gamma-ray irradiation.

## Survey of luminescent material with varied wavelength-dependence for beam quality measurement in BNCT

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**INTRODUCTION:** Measurement of beam fluence spatial distribution is required for quality assurance in the irradiation field, in boron neutron capture therapy. The imaging plate has been tested for usage in this purpose[1]. In imaging plate, the light for excitation and luminescence are investigated with respect to a single constant range of wavelength. However, BaFBr:Eu, *i.e.*, the luminescence material for imaging plate, has multiple peaks in its excitation spectrum[2]. Each peak corresponds to a excited state of electron and ion BaFBr:Eu. The efficacy in excitation to each level is expected to depend on the beam quality of the irradiated radiation, which deposits energy on the luminescence material. In this case, the dependence of the quantity of the luminescence on the wavelength of the excitation light, or possibly luminescence, will specify the beam quality. Also, one can predict the absorbed dose by using the quantity of the luminescence. Thus, this study investigated the use of the luminescence for measurement of both quantity and quality of the radiation. The preliminary survey for the suitable luminescence material is reported.

**EXPERIMENTS:** As an initial candidate, the imaging plate (Fujifilm Corporation, BAS-TR) is used for this study. In this imaging plate, BaFBr:Eu is embed in blue-colored film. In this study, BaFBr:Eu was also fabricated and utilized as a sample, in case the blue film distort the influence of the beam quality of the dependence of the luminescence quantity of wavelength. The samples were irradiated with gamma rays from <sup>60</sup>Co, and neutrons and gamma rays at the standard mixed neutron irradiation mode of Kyoto University Reactor Heavy Water Neutron Irradiation Facility at 1 MW of the power. In the latter, the samples were driven with Irradiation Rail Device. The fluorescence spectrofluorometer (Hitachi corporation, F-2700) was used to measure the dependence of the fluorescence quantity on the wavelength.

**RESULTS:** An example of the excitation spectrum is shown in Fig. 1 for BAS-TR. The ratio of the luminescence quantity by excitation at 630 nm to that at 650 nm is 7% lower for KUR than that for Co, where the uncertainty of the measured ratio is about 5%. These aspects suggest that the dependence of the quantity of the luminescence on the wavelength is a promising indicator of the beam quality. The attempt to measure the beam quantity by using the luminescence dependence on wavelength is undergoing for usage of BAS-TR and fabricated BaFBr:Eu.

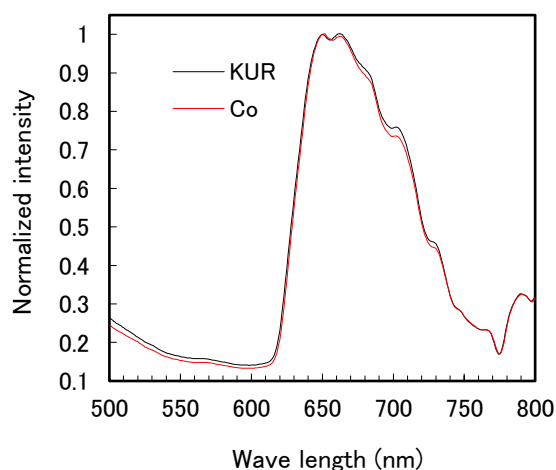


Fig. 1. Excitation spectrum of BAS-TR

### REFERENCES:

- [1] K. Tanaka *et al.*, Appl. Rad. Isot., **115** (2016) 212-220.
- [2] K. Abe, Rad., **25** (1999) 31-49. (in Japanese)

## The Study for Development and Application of Tissue Equivalent Dosimeter - Feasibility of Proton Magnetic Resonance Analysis of Fricke Dosimeter -

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**INTRODUCTION:** In recent years, the clinical application of Accelerator-Based Boron Neutron Capture Therapy (AB-BNCT) has been introduced to make significant contributions to the treatment of intractable cancer such as glioblastoma multiforme, superficial head and neck cancer, and melanoma in Japan. In clinical situations, a radiochromic film (RCF) is one of the most helpful dosimetry tools in the advantages of high spatial resolution and tissue equivalence<sup>1,2</sup>. However, there are some limitations for mapping 3D dose distribution, so there has been increasing interest in gel or liquid dosimeters recently. Although the Fricke dosimeter<sup>3</sup> is rare among these findings, the authors have recently developed a new approach expected to lead to new developments.

**EXPERIMENTS:** A ferrous sulfate solution using a <sup>60</sup>Co gamma source was evaluated. To make a total of 500 ml of sulfuric acid solution, 197 ml of 1N dilute sulfuric acid and 303 ml of distilled water were mixed. To this solution, 30 mg sodium chloride and 200 mg ferrous ammonium sulfate hexahydrate were added to prepare an aqueous solution of the average concentration of ferrous ammonium sulfate. Each cylindrical polyethylene bottle contained 25 ml of this solution. For irradiation, polypropylene boxes containing a set of three bottles were placed 20 to 70 cm from the <sup>60</sup>Co source. Then, all of the boxes, ranging from 0 to 873 Gy, were irradiated in the KUR <sup>60</sup>Co gamma-ray irradiation facility. After irradiation, all bottles were subjected to proton magnetic resonance (1.5T clinical MRI system, AvantoFit, Siemens Inc.).

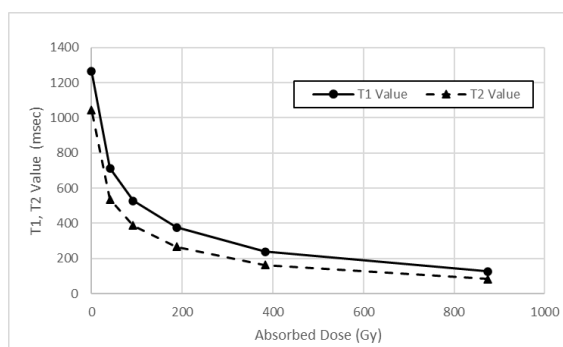


Fig. 1. Change of T1 and T2 values irradiated by the KUR <sup>60</sup>Co gamma-ray source. The variation of T1 and T2 value is higher at low-dose region.

**RESULTS:** Fig.1 shows the T1 and T2 values change irradiated by the KUR <sup>60</sup>Co gamma-ray. The average change in T1 and T2 values per Gy ranged from 0-40 Gy were approximately 13.5 and 12.4 msec, respectively. The dose resolution was relatively higher than that of the conventional analysis method. Further approaches could be feasible for using low-dose regions, neutron components, and contributions of gamma rays using Monte Carlo simulation and additional experiments with a cadmium filter.

### REFERENCES:

- [1] Niroomand-Rad, Azam *et al.*, Medical physics **25** (1998) 2093-2115.
- [2] B. V. Casanova *et al.*, J. Appl. Clin. Med. Phys., **14**(2) (2013) 4111.
- [3] Fricke H, Hart EJ: Chemical dosimetry. In: Attix FH, Roesch WC, Tochilin E eds. Radiation dosimetry: Instrumentation., (1966) 167-239, Academic Press, New York.

## Comparison of Measurement of Contamination Gamma-ray Dose using Thermoluminescence Dosimeter and Glass Dosimeter

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**INTRODUCTION:** Several types of accelerator-based neutron source can achieve the sufficient neutron flux for performing boron neutron capture therapy (BNCT). Thus, it is expected that BNCT will be widely used at hospitals because those sources can be implemented easier than the research reactor. Neutron beam from those sources has contamination gamma-rays as well as that from the research reactor. However, evaluations of contamination gamma-rays has been conventionally performed with a specially designed thermoluminescence dosimeter (TLD) of beryllium oxide (BeO) powder enclosed in a quartz glass tube [1], and it may be one of the problems limiting the wide-spread. Therefore, this study aims to discuss the evaluations of contamination gamma-rays in the neutron beam emitted from the research reactor using the commercial radiophotoluminescence glass dosimeter (RPLD), which was generally utilized in conventional radiotherapies [2], through comparing those using the TLDs.

**EXPERIMENTS:** The commercial RPLD (GD-302M, AGC Techno Glass Co., Ltd. Tokyo, Japan) was utilized in this study, and the custom-made TLD consisted of BeO powder and quartz glass was utilized for the comparison. To eliminate the effect of thermal neutrons to reading value on RPLD, RPLD was encapsulated with <sup>6</sup>LiF capsule of which thickness was 2 mm and actual density was 85% of the ideal density for LiF (2.24 g/cc). Relationship between the reading value and the delivered dose in the RPLD had been acquired using 6 MV-X ray emitted from the medical linear accelerator (TrueBeam, Varian, Palo Alto, CA). To compare the dose of contamination gamma-ray evaluated by the TLD and RPLD, we carried out the measurements at the edge of irradiation port without a phantom at the Heavy Water Neutron Irradiation Facility of Kyoto University Research Reactor. The thermal irradiation mode was applied in this study, and the irradiation time was 0, 5, 10, and 15 min.

**RESULTS:** As shown in Fig. 1, the dose evaluations of contamination gamma-ray using the TLD and the RPLD were comparable, and the linearity between the irradiation time and the dose was observed in both the TLD and the RPLD. Discrepancies of the dose evaluations between the TLD and the RPLD were within 7.3%, and decreased with increasing the irradiation time. At the irradiation time of 15 min, the discrepancy was 1.2%. Therefore, this study indicated the feasibility of the dose evaluation for the contamination gamma-ray using RPLD.

### REFERENCES:

[1] N. Hu *et al.*, *Radiat. Oncol.*, **16** (2021) 243.

[2] JSMP, Guideline for radiophotoluminescence glass dosimeter. (2022).

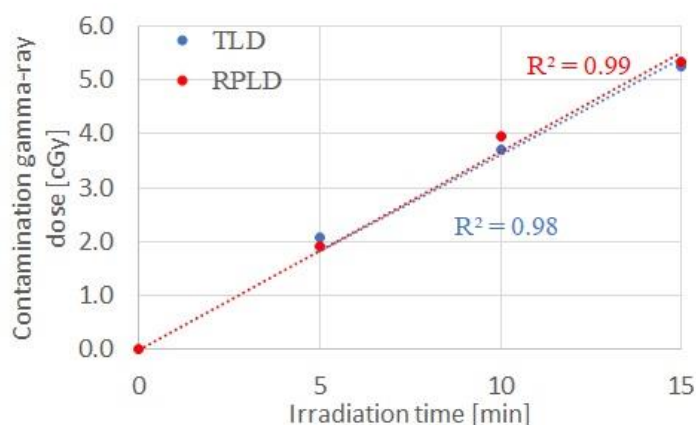


Fig. 1: Comparison of gamma-ray dose evaluations using TLD and RPLD.

## Influence of Tissue Water Content in Dose Calculation for BNCT

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**INTRODUCTION:** A Monte Carlo method is commonly employed in dose calculations for BNCT, where radiation transport calculations are performed by specifying material information corresponding to each tissue in the body, such as density and elemental composition. Conventionally, typical values described in literature such as ICRU Report 46 are assigned as fixed values [1]. However, this method cannot reflect the details of material information, such as differences among patients or a detailed water content distribution in tissue. In this study, we aim to establish a method for quantitative evaluation of material density and water content by using data acquired by multi-energy X-ray CT, and to reflect the material information in the dose calculation. To confirm the importance of this method, the effect of tissue water content on dose calculations was examined.

**MATERIALS AND METHODS:** The dose calculations were performed to simulate irradiation for brain tumors. A voxel phantom was constructed from the CT images of the head phantom, and brain tissue, skull, and soft tissue were specified as the material of each voxel. For skull and soft tissue, elemental compositions and densities described in the ICRU report were assigned [1]. For brain tissue, the composition was based on the ICRU report, whereas the water content was varied in a range of  $\pm 2\%$  from the reference value of 78.5% [2]. A negative correlation between water content and specific gravity of brain tissue, reported in studies of vasogenic cerebral edema, was assumed to derive the density from the water content [3]. The thermal neutron flux and gamma-ray dose rate were derived by using PHITS code [4], where the epi-thermal neutron irradiation of the phantom from the parietal region was simulated assuming the neutron source of the Heavy Water Neutron Irradiation Facility at KUR [5].

**RESULTS:** The depth profiles of the thermal neutron flux and gamma-ray dose rates relative to the reference water content are shown in Fig. 1. For a water content of 80.5% (+2% of the reference value), the thermal neutron flux and the gamma-ray dose rates increased up to about 4-cm and 6-cm depths, respectively. At the greater depths, decreases in both values were observed. The opposite trend was observed for a water content of 76.5% (-2% of the reference value) as for 80.5%. These reflect changes in the moderating and thermalizing ability of the epi-thermal neutrons and the absorption/capture reaction rate of the thermalized neutrons due to the increase or decrease in hydrogen density.

### REFERENCES:

- [1] ICRU Report 46 (ICRU, Bethesda, MD, 1992).
- [2] E. M. Widdowson *et al.*, *Biochem J.*, **77** (1960) 30-43.
- [3] H. W. Bothe *et al.*, *Acta Neuropathol.*, **64** (1984) 37-42.
- [4] T. Sato *et al.*, *J. Nucl. Sci. Technol.*, **55** (2018) 684-690.
- [5] Y. Sakurai, T. Kobayashi, *Med. Phys.*, **29** (2002) 2328-2337.

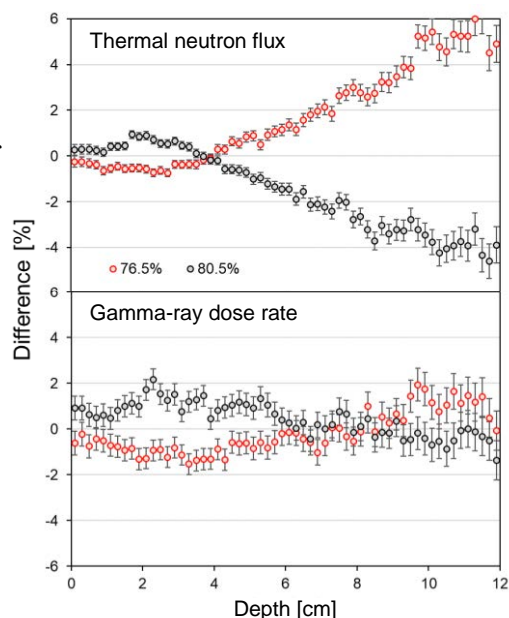


Fig. 1. Depth profiles of thermal neutron flux and gamma-ray dose rates relative to reference water content.