PR8 Translational Research on BNCT for Clinical Application

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Background and Objective

Using Kyoto University Research Reactor (KUR), patients with malignant tumors greater than 500 have been treated with boron neutron capture therapy (BNCT). Malignant brain tumors and head and neck cancers have been main malignancies treated with BNCT. Our laboratory (Division of Particle Radiation Oncology) has investigated the possibilities for new applications for BNCT. According to promising results in pre-clinical study, we have already treated some patients with liver cancers with BNCT and carried out clinical study on phase I study on BNCT for malignant pleural mesothelioma (MPM).

Promising clinical results of BNCT using the research reactor encouraged us to go to further stage of BCNT using an accelerator-based (AB) BNCT system. Co-operation of Kyoto University Research Reactor Institute and Sumitomo Heavy Industry have developed AB BNCT system with compact cyclotron as an accelerator. In 2012 and 2014, clinical studies on BNCT for recurrent malignant brain tumors and head and neck tumors to get an approval as a medical device from the Pharmaceuticals and Medical Devices Agency (PMDA), a Japanese regulatory agency. In a transition period from reactor-based (RB) BNCT into AB-based BNCT, many research issues should be dissolved from impending and long-term viewpoints.

Main objectives of our project is to dissolve many impending clinical issues to perform BNCT safely in AB-BNCT system and to investigate many research projects for many patients with cancer to be treated with AB-BNCT system.

Research Subjects

To advance RB-BNCT into AB-BNCT, a lot of researchers in various research fields such as clinical radiation oncology, medical physics, pharmacology, boron chemistry, and accelerator engineering are needed to be involved in our research projects. In this viewpoint, this research project consists of three research subjects (RS) as follows,

RS1. Clinical studies on BNCT

RS2. Pre-clinical studies on physiological and pharmacological aspects of BNCT

RS3. Medical physics studies on BNCT.

Main Results

Unfortunately, KUR has been unavailable since May in 2014. Only 7 reports could be submitted.

RS1. Clinical studies on BNCT

Although no BNCT using KUR was performed, Fujimoto et al. reported a case report on BNCT for axillary lymph node metastasis of breast cancer which was carried out in 2013. In this report, BNCT successfully reduced the size of the lymph node metastases and alleviate the radiating pain in the arm. Case reports are very meaningful to consider the possibility of new applications of BNCT.

RS2. Pre-clinical studies on physiological and pharmacological aspects of BNCT

Yanagie et al. reported two pre-clinical studies. One was a preclinical BNCT study for VX-2 rabbit liver tumor model using borocaptate sodium (BSH) entrapped water-in-oil-in-water (WOW) consist with surfactant HCO40 or PGCR. Another one was a treatment planning study on BNCT for breast cancer

RS3. Medical physics studies on BNCT

Hayashi et al. investigated the influence of various lithium compounds of the dose response and the stability of polymer gel dosimeters.

Tanaka K et al. reported the imaging plate system to measure the beam components such as thermal, epithermal, fast neutrons and gamma rays separately.

Sakurai et al. studied the QA/QC in BNCT using ionization chamber and Bonner sphere in BNCT irradiation field.

PR8-1

Evaluation of Neutron Dosimetry for Boron Neutron Capture Therapy using Images of Breast Cancer

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INTRODUCTION: The JAERI Computational Dosimetry System (JCDS), which can estimate distributions of radiation doses in a patient's head by simulating in order to support the treatment planning for epithermal neutron beam BNCT, was developed. Kumada et al had reported that JCDS is a software that creates a 3-dimensional head model of a patient by using CT scan and MRI images, and that generates a input data file automatically calculation of neutron flux and gamma-ray dose distributions in the brain with the Monte Carlo code MCNP, and that displays these dose distributions on the head model for dosimetry by using the MCNP calculation results.

We evaluatied the dosimetry of thermal neutron using JCDS in the condition of Single field irradiation or Bilateral irradiation to tumour constructed with MRI imagings of a breast cancer patient.

EXPERIMENTS: Neutron dosimetry with JCDS for a breast cancer patient: BNCT was simulated in a patient with a 7cm tumour in the lower half of the R breast. LiF collimation was used to selectively irradiate the tumor while sparing the adjacent normal organs (lung, heart). The Neutron Beam Facility at JRR4 enables to carry out boron neutron capture therapy with epithermal neutron beam.

RESULTS:

Simulation 1: Epithermal Neutron mode
Beam colimation : φ7 c m, BPA : 24ppm, T/N=3.5,
Restriction : Skin RBE dose as 10Gy-Eq

The blood concentration of BPA by drip infusion just before NCT was estimated as 24ppm, and T/N ratio was also estimated as 3.5 according to 18F-BPA-PET.

Simulation 1: Beam collimation was performed in 7cm field and epithermal neutron beam was irradiated with the tangenital direction (33min.) in restricted maximum skin RBE dose as 10Gy-Eq. The maximum tumor RBE dose was 87.5 Gy-Eq, the mean tumor RBE dose was 48.3 Gy-Eq, and the minimum tumor RBE dose was 11.5 Gy-Eq. The actual maximum skin RBE dose was 11.1 Gy-Eq (RBE=1.35).

Simulation 2: Epithermal Neutron mode
Beam colimation : φ8 c m, BPA : 24ppm, T/N=3.5,
Restriction : Skin RBE dose as 10Gy-Eq

Simulation 2: The beam direction was changed to oblique direction. The maximum tumor RBE dose was 86.6 Gy-Eq, the mean tumor RBE dose was 46.1 Gy-Eq, and the minimum tumor RBE dose was 19.3 Gy-Eq. The minimum tumor RBE dose was increased to 19.3 Gy-Eq from 11.5 Gy-Eq with the epithermal neutron in this oblique direction(70% up).

Simulation 3: Tangenital direction irradiation was performed in Simulation1, and Oblique direction irradiation was performed in Simulation 2. Combined two directional Irradiation was performed in Simulation 3 (70% of Simulation 1 (Irradiation time 23.9 min） + 79％ of Simulation 2(Irradiation time : 23.9min)) in restricted maximum skin RBE dose as 10Gy-Eq.

The maximum tumor RBE dose was 107.3 Gy-Eq, the mean tumor RBE dose was 70.3 Gy-Eq, and the minimum tumor RBE dose was 28.0 Gy-Eq. This date shown that BNCT with two directional epithermal neutron irradiation can increase the RBE tumor dose to 2.4 times of Simulation 1 and 1.5 times of Simulation 2.

We hope to start BNCT clinical studies for recurrenced & advanced breast cancer patients. The irradiational directions will be decided using the JCDS or SERA simulation with the restriction of normal tissue tolerant RBE Dose.
We applied the JCDS to dosimetry of epithermal neutron, direction of neutron beam, and patient's positioning on BNCT. High resolution whole body dosimetry system, as JCDS and SERA will be very useful to evaluate the thermal/epithermal neutron dosimetry and the application of BNCT to recurring or advanced breast cancer.
Multi directional irradiations are hope to be available to increase the tumour RBE dose in the based on the tolerant dose of normal skin in BNCT field.

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PR8-2 Anti-tumor Effect of Boron Neutron Capture Therapy (BNCT) on Axillary Lymph NodeMetastasis of Breast Cancer

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INTRODUCTION: Breast cancer is the most morbid malignancy in women, and in Japan about 60,000 new cases are encountered every year. Although hormone therapy, chemotherapy and molecularly targeted therapy have improved its prognosis, 30% of such patients die from distant metastases. When systematic pharmacotherapy is not effective in metastatic cases, the disease is difficult to control. In this study, BNCT was assessed for lymph node metastasis of breast cancer (luminal type A). Additionally, the uptake of BPA was analyzed with the use of hormone-sensitive breast cancer cell lines.

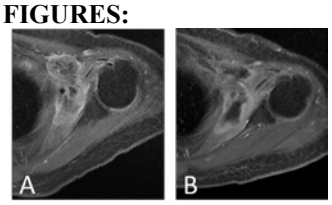
PATIENT AND METHODS: (1) Patient: A 65-year-old woman diagnosed with left breast cancer (luminal A) and axillary lymph node metastasis underwent axillary lymph node dissection, mastectomy and radiation therapy for the area of the left axillary lymph nodes. Although subsequent lymph node and lung metastasis recurred, all tumors disappeared after both chemotherapy and hormone therapy. Nonetheless, local recurrence of tumors in the left lymph nodes was detected, for which chemotherapy was ineffective; therefore, intra-arterial chemo-embolization was carried out at a nearby clinic. The tumor was, however, not controlled; furthermore, palsy of the left axillary nerve was detected, and the patient complained of severe pain all over the upper left limb. Examination by Gd-enhanced MRI confirmed regrowth of the tumor; therefore, BNCT was administered.

(2) Boron concentration in tumor cell lines: Hormone-sensitive breast cancer cell lines (T47D, MCF-7), clear cell sarcoma (CCS) cell line (MP-CCS-SY) and melanoma cell line (G-361) were cultured and exposed to BPA (10, 20, 30 ^{10}B μg/ml) in the medium. Subsequently, the cells were washed, detached and collected; the concentration of ^{10}B in the cells was then determined by ICP-AES.

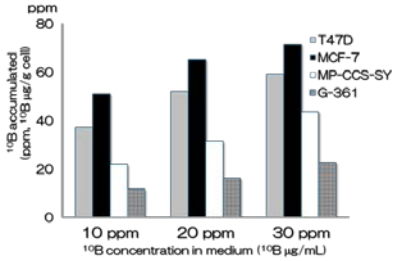
RESULTS: An ^{18}F-BPA-PET study conducted before BNCT showed accumulation of BPA in the tumor, with a tumor to blood (T/B) ratio of 2.2. Since the tumor was located deep in the body, BNCT was administered by two-gate irradiation to the area of the left axilla, with the patient in a sitting position: ventrally, 5MW for 47min and dorsally, 5MW for 27min. The mean value of boron concentration in blood during BNCT was 29 ppm ventrally and 28.5 ppm dorsally, and neutron fluence on the surface of the body was 3.34×10^{8} $cm^{-2}s^{-1}$ ventrally and 4.89×10^{8} $cm^{-2}s^{-1}$ dorsally. The calculated average dose to the target and the left axillary nerve was 25 Gy-Eq and 4.3 Gy-Eq, respectively. Gd-enhanced MRI revealed that the recurrent tumor mass in the left axilla shrank two months after BNCT [Fig.1]. Moreover, the patient was free from the severe pain in the left arm, and the progress of paralysis ceased. Also, the two breast cancer cell lines demonstrated higher uptake of boron than did the CCS and melanoma cell lines that have already shown good outcome of BNCT [Fig. 2].

CONCLUSION: BNCT was effective in the treatment of metastatic breast cancer that had been resistant to all other methods of treatment. Additionally, in vitro studies demonstrated high uptake of BNCT by hormone-sensitive breast cancer cell lines. These data suggest the applicability of this new method of treatment to metastatic breast cancer.

FIGURES:



[Fig.1] Axial Gd-enhanced T1 MRI shows a reduction in the tumor mass in the area of the left axillary lymph nodes post-BNCT (B) compared with pre-BNCT (A).



[Fig.2] Two hormone-sensitive breast cancer cell lines (T47D, MCF-7), CCS cell line (MP-CCS-SY) and melanoma cell line (G-361) were tested for their uptake of boron. Each cell line took up the boron in a concentration-dependent manner. The uptake of ^{10}B by breast cancer cells was higher than that by the CCS and melanoma cells.

PR8-3 Evaluation of Boron Concentrations in Liver by Intra-arterial Delivery of WOW Emulsion to VX-2 Hepatic Tumor Model for Neutron Capture Therapy to Hepatocellular Carcinoma

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INTRODUCTION: Water-in-oil-in-water(WOW) emulsion has been used as the carrier of anti-cancer agents by modifying of IPSO on intra-arterial injections in clinical. Higashi et al prepared a long term inseparable WOW for use in arterial injection therapy to treat patients with hepatocellular carcinoma(HCC) by the double emulcificating technique[1]. We performed preclinical BNCT study for VX-2 rabbit tumour model using ^{10}BSH entrapped WOW [2, 3]. We also proceeded clinical BNCT study for HCC using this system[4].

In this study, we prepared ^{10}BSH entrapped WOW in verifying the component of surfactant, and evaluated the boron delivery activity to measure the ^{10}B concentrations of organs in VX-2 hepatic tumour model on time course after intra-arterial injection using ICP-Mas.

EXPERIMENTS: ^{10}BSH entrapped WOW were administrated with intra-arterial injections via proper hepatic artery (^{10}BSH : 20 mg/kg rabbit) on VX-2 rabbit hepatic tumour models. One and three days after arterial injections, the boron concentrations of the tumor nodules and normal liver tissues were determinated by ICP- Mass Spectroscopy of Jyuntendo University.

RESULTS: VX-2-bearing rabbits (n = 3) were given intra-arterial injection with 2 ml of ^{10}BSH WOW emulsion consist with surfactant HCO40, or PGCR. The mean ^{10}B concentration prepared in ^{10}BSH-WOW was 10000 ppm in this experiment. The size of WOW was controlled to 70 μm.

The ^{10}B concentration in VX-2 tumour was 170.8 ppm, 58.3 ppm by WOW with HCO40 after day1, day3 inta-arterial injection, respectively. The ^{10}B concentration of tumour was 186.0ppm, 40.4ppm by WOW with PGCR after day1, day3 same injection, respectively. ^{10}B concentration in normal liver tissue / blood were 8.0 / 0.3 ppm in HCO40 group, and 15.1 / 0.1 ppm in PGCR group at day 3, respectively in the same procedures of WOW.

We can deliver ^{10}BSH to tumor site by intra-arterial injection with WOW emulsion. The effective ^{10}B concentration (higher than 30ppm) was achieved in day1 and day3. It has be able to change the deliverable ^{10}B atoms according to the sizes of WOW, and the type of surfactants. We hope to perform toxicity examinations of WOW emulsion to develop the more suitable WOW emulsion for intra-arterial born delivery system.

Table1. ^{10}B concentration (ppm) of VX-2 hepatic tumor bearing rabbit model after intrarterial injection of ^{10}B-WOW emulsion.

WOW	Tumour	Normal liver		Blood
		Near Tumour	Another Lobe	
HCO40				
Day1	**170.8±27.3**	**31.9±4.3**	**33.9±30.9**	**0.73±0.4**
Day3	**58.3±23.1**	**24.7± 17.1**	**8.02±1.7**	**0.33± 0.1**
Day7	**12.9 ±7.5**	**2.9 ±0.6**	**1.7±0.4**	**0.12±0.0**
PGCR				
Day1	**186.0±115.2**	**72.79±2.5**	**69.1±42.1**	**1.27±0.5**
Day3	**40.47**	**56.7**	**15.1**	**0.14**
Day7	**40.66**	**37.3**	**13.8**	**0.14**

The ^{10}B conc. were determined by ICP-Mas. at Jyuntendo University.

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PR8-4 Establishment of QA/QC Using Ionization Chamber and Bonner Sphere in BNCT Field (II)

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INTRODUCTION: After the restart of the operation of Kyoto University Reactor (KUR) in May 2010, 235 clinical studies of boron neutron capture therapy (BNCT) have already been carried out as of May 2016 [1]. Also, the BNCT clinical trial using Cyclotron-based BNCT Epi-thermal Neutron Source (C-BENS) started in November 2012 [2]. In the while, the research and development into several types of accelerator-based irradiation systems are underway by several research groups in the world at present time. With this situation in mind, it is important that the physical and biological estimations for dose quantity and quality are performed consistently among several irradiation fields, and that the equivalency of BNCT is guaranteed, even across BNCT systems. The aim of this research is the establishment of quality assurance and quality control (QA/QC) in BNCT irradiation field. As part of the QA/QC system, we are developing estimation method for neutron energy spectrum using Bonner sphere.

METHODS: For our spectrometer using Bonner sphere, liquid such as pure water and/or boric acid solution is used as the moderator [3]. As shown in Fig. 1, a multi-layer concentric-sphere case with several sphere shells is prepared. The moderator and its diameter are changeable without entering the irradiation room, by the remote supply and drainage of liquid moderator in the several layers. For the detector, activation foils are remotely changed, or online measurement is performed using SOF (scintillator with optical fiber) detector containing boron, etc.. On the assumption of the application in a typical BNCT irradiation field, the combination of the moderators for boron-10 (B-10) concentration and diameter was optimized by our originally-developed method, "High Independence Selection (HIS)" [4]. For the B-10 concentration, the selection was performed among ten values such as 0, 0.01, 0.016, 0.028, 0.048, 0.082, 0.14, 0.24, 0.41 and 0.7 weight percent (wt%). For the diameter, the selection was performed among ten values from 11 to 20 cm in 1 cm increment. Manganin foil was assumed to be used as the detector, which has high response mainly to thermal neutrons. The optimized combination was decided among one hundred and one combinations; the combinations of ten B-10 concentrations and ten diameters, additionally the case of manganin foil only without the moderator.

RESULTS: The optimized combination was selected by HIS as follows: manganin foil only, 0.7-wt% boron acid solution of 13 cm in diameter, 0.7-wt% boron acid solution of 18 cm in diameter, 0-wt% boron acid solution (namely pure water) of 18 cm in diameter, and 0.028-wt% boron acid solution of 20 cm in diameter. Then, the optimized structure of the spectrometer was decided as follows: three sphere shells such as 13, 18 and 20 cm in diameter, and three liquid moderators such as pure water, 0.028-wt% boron acid solution and 0.7-wt% boron acid solution. It is not thought that this structure is necessary to be changed when the detector is changed from manganin foil to boron-containing SOF detector.

CONCLUSION: We have a plan to make the Bonner-sphere spectrometer, based on the optimization result. Additionally, we have a plan to perform the spectrometry experiments at Kyoto University Reactor (KUR), etc., in order to confirm the efficacy of this spectrometer.

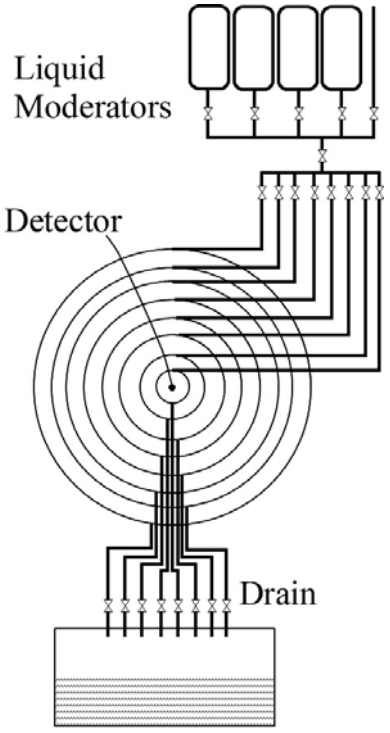

Fig. 1. Concept design of the Bonner-sphere spectrometer for QA/QC in BNCT.

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PR8-5 A Consideration of the Influence by the Radiation Type on the Measurement of the Spatial Distributions of the Beam Components in BNCT Using the Imaging Plate

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INTRODUCTION: For boron neutron capture therapy (BNCT), measurement of the spatial distributions of neutrons and gamma rays is one of the potential options for the quality assurance and quality control. It is desirable to measure the beam components such as thermal, epithermal, fast neutrons and gamma rays, separately. This study investigates the usage of the imaging plate (IP) for this purpose. The influence by the radiation type which deposits the energy in the IP on the resultant beam component distribution is discussed here.

METHODS: Two IPs set in a converter were irradiated[1] at the collimator aperture of the standard epithermal neutron irradiation mode at the Kyoto University Reactor Heavy Water Neutron Irradiation Facility (KUR-HWNIF). The converters were the epoxy resin doped with boron which is attempted to enhance epithermal neutrons via secondary particles from the $^{10}B(n,\alpha)^{7}Li$ reaction, and carbon which is not expected to enhance neutrons due to its low neutron interaction. The fluence ϕ_j was determined using the following model;

$$PSL = \begin{pmatrix} PSL_1 \\ PSL_2 \end{pmatrix} = \begin{pmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{pmatrix} \begin{pmatrix} \phi_1 \\ \phi_2 \end{pmatrix} = A \cdot \phi \quad (1),$$

$$\phi = A^{-1} \cdot PSL \quad (2),$$

where PSL_i denotes the signal intensity of the ith IP, a_{ij} the sensitivity of the ith IP for the component j. For j, 1 denotes gamma rays, and 2 epithermal neutrons. In this analysis, the energy deposition calculated by the PHITS code was used as a_{ij}. The problem is that the dependence of the radiation type on the efficiency that the energy deposition is converted to the IP signal is not included. In the present report, the dependence of the IP signal on the radiation type is investigated from the previous studies. Then, its influence on the experimental result of the component distributions is discussed.

RESULTS and DISCUSSION: The dependence of the IP signal intensity on the radiation type that deposits the energy in the sensitive region of the IP, or its LET, has been investigated during past years. However, the mechanism or its quantitative influence has not been concluded consistently among the publications. However, there are several proposals on it.

One of the earliest and most comprehensive studies was conducted by Thoms in 1996[2]. They categorized the processes potential to be influenced into two, i.e., readout of the IP signal, and fading of the signal.

As to the readout, the influential process is considered to be the attenuation of the readout light emitted from the sensitive region, the efficiency of converting the energy deposition into the IP signal will be higher for the alpha particles than that for the gamma rays. Bennet [3] reported that the readout light is attenuated to 1/e (37%) by the IP sensitive region with the thickness of 113-211 μm the IP by Fujifilm Co. Ltd used in the experiment[1]. The sensitive region has the thickness of 50 μm and it is supposed to attenuate the readout light by 21-36 %. In addition, the readout light spreads and results in decrease of the IP signal intensity. The decrease was reported to be by 13 % for the thickness of 50 μm by Thoms[2]. Alpha particles and ^{7}Li nuclei deposits its energy within a few micro meters from the IP surface, while the recoil protons and secondary electrons from the converters deposit the energy in whole the thickness of 50 μm. The efficiency of the energy deposition to be the IP signal will be higher for the former, by possibly a few tens percents. Accordingly, the contribution of the epithermal neutron components to the IP signal is expected to be slightly higher than the calculated sensitivities for the equation (1).

On the other hand, the time dependence of the fading of the IP signal has been reported to be independent from the radiation type[2,4]. However, the results of investigation by Nakamura[5] showed that the IP signal produced by alpha particles reduces more rapidly than those by X-rays. At 30 minutes or more after the irradiation, which corresponds to the experiment[1], the difference was reported to be about 30 to 40%.

These factors, i.e., the readout light attenuation and IP signal fading, have opposite influences, i.e., the former increases the sensitivity to the alpha particles, and the latter decreases. In total, the type of radiation could double the IP signal, while it could be an overestimation. To include its influence, the sensitivity a_{ij} should be adjusted. For example, if the sensitivity for the secondary particles of $^{10}B(n,\alpha)^{7}Li$ reaction that enhances the epithermal neutron component is β times, a_{i2} for all the IPs should be replaced with βa_{i2}. Consequently, the solution will be $\phi_{epi}' = \phi_{epi}/\beta$. This means that including the influence by the radiation type does not change the relative distribution of the resultant fluences, which is what this study aimed to assure. The analysis without considering the dependence of IP signal on radiation type will be enough to assure the temporal change in the spatial distribution of the irradiation field.

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PR8-6 Development and Evaluation of 3D Polymer Gel Dosimeter for the Measurement of dose Distribution in BNCT

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INTRODUCTION: Polymer gel dosimeters have been investigated for the three-dimensional (3D) dose measurement of the complex conformal dose distributions in the clinical applications [1]. These devices utilize radiation-induced polymerization reaction of vinyl monomer in the aqueous gel matrix to preserve information about the radiation dose. The 3D absorbed dose distribution is deduced from the created polymer distribution measured by imaging modalities such as MRI and Optical CT.

Polymer gel dosimeter is also regarded as tissue equivalent to neutron beam because the components are mainly water and a small amount of other chemicals consisting of carbon, nitrogen and oxygen. A further advantage of polymer gel dosimeters is that the interaction with neutron could be controlled by addition of some compounds with neutron-capture-nuclei such as ^{6}Li and ^{10}B. It means that each dose component might be distinguished from complex dose due to various primary and secondary radiations by the variety of elemental composition.

In the previous work, we have investigated that the dose response of polymer gel dosimeter irradiated by thermal neutron beam was enhanced by addition of a very small amount of ^{10}B (50 ppm) [2]. In this work, the influence of various lithium compounds on the dose response and the stability of polymer gel dosimeters was investigated by high-energy photon beam before the future experiments using neutron beam.

EXPERIMENTS: In this work, MAGAT-type (methacrylic-acid-based) polymer gel dosimeter was employed because of the high sensitivity. Various lithium salts (LiCl, $LiNO_3$, LiOH, Li_2SO_4 and Li_3-citrate, which have comparatively high solubility in water) containing ^{6}Li in the natural ratio were mixed into the polymer gel in the concentration of 100 and 200 ppm of ^{6}Li, respectively. The resulting gels were subdivided by pouring into test tubes.

The irradiations were performed using 6 MV X-ray from a medical linear accelerator (Novaris-TX, Varian/BrainLAB) and gamma ray from ^{60}Co source. The doses upto 5 Gy were delivered to each sample.

The read-out from the samples was performed using a 1.5 T MRI scanner (SIGNA HDxt 1.5T, GE Healthcare) with a head coil the day after irradiation. A multiple spin-echo sequence was applied and the transverse relaxation rate R_2 ($=1/T_2$) was obtained as the function of absorbed dose.

RESULTS: In the results, the dose-R_2 responses (sensitivities) of the polymer gel dosimeters containing $LiNO_3$, LiOH and Li_3-citrate decreased significantly (40-70% lower at 5 Gy) comparing with that of the basic gel dosimeter without lithium salts. Also, Li_3-citrate did not dissolve enough in the gel solution and the gel was translucent. On the other hand, the gel dosimeters containing LiCl and Li_2SO_4 showed the comparable sensitivity to the basic gel dosimeter and the rather sensitivity enhancement was also observed.

From these results, it was suggested that LiCl or Li_2SO_4 was a suitable additive to introduce lithium to the polymer gel dosimeter. When lithium salts containing the enriched ^{6}Li could be used, the clearer enhancement due to ^{6}Li would be expected even in a smaller amount of additive.

(These results would be presented at 17th International Congress on Neutron Capture Therapy, ICNCT-17 in Missouri, USA.)

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PR8-7 Patient-Position-Error Measuring System for BNCT Irradiation

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INTRODUCTION: In boron neutron capture therapy (BNCT) irradiations carried out at Kyoto University Research Reactor, sitting position has been applied in many cases, considering a flexibility of patient positioning and structural restriction of an irradiation facility. In those cases, the patient position is sometimes unstable, resulting in a displacement from an initial set-up position determined by a treatment planning process. The displacement and motion during an irradiation period cause uncertainty in estimation of delivered dose.

Aiming to improve the dose estimation accuracy, we have prepared a patient-position-error measuring system using a motion sensor. An outline of the measuring system and initial test operation are described.

MATERIALS AND METHODS: An outline of the measuring system is shown in Fig. 1. A MEMS motion sensor module (IMU-Z 2, ZMP Inc., Tokyo) including tri-axial accelerometer, gyroscope and magnetometer was used to track a position and a rotation angle during an irradiation period. The sensor module (36×52×11 mm) and a battery box (36×62×15 mm) are sufficiently small. In addition, the module has a wireless data transmission function. These features enable us to fix the sensor on patient surface without interference in patient setup and irradiation process.

A displacement can be calculated by integrating accelerometer data twice with respect to time. Also, a rotation angle can be calculated by integrating gyroscope data with respect to time in motion phase and by direction of gravitational acceleration and geomagnetic field at resting phase. The estimated displacement and rotation angle are displayed and saved as a log data over an irradiation period. The log data can be utilized for post-irradiation dose evaluation.

This system is considered to be useful for head cases, where the measuring object is regarded as a rigid body. For those cases such as brain tumor or head and neck tumor, the sensor module and battery box are fixed on top of head so that the sensor coordinate system is aligned to anterior-to-posterior, left-to-right and inferior-to-superior directions of the patient. The position and rotation angle of the head is measured in the reference coordinate system defined on the irradiation room.

RESULTS: An initial test operation of the motion sensor was conducted. Time fluctuations were observed in the accelerometer output as well as the gyroscope and magnetometer. High frequency component of the accelerometer output, related to a sensor noise, was observed in the amplitude range of about 0.3% with respect to the gravitational acceleration. This component can be removed by using an appropriate high-pass filter. Low frequency component, related to a sensor bias, showed time-dependent behavior, which resulted in abnormal divergence of velocity obtained from integration of raw accelerometer output. This phenomenon is well known as velocity drift in general applications of motion sensor. The velocity drift can be corrected at a resting state, at which velocity is adjusted to zero. The resting state need to be detected based on the sensor outputs using appropriate threshold values. These filtration and correction are under examination and need to be optimized to clinical situation of BNCT irradiation.

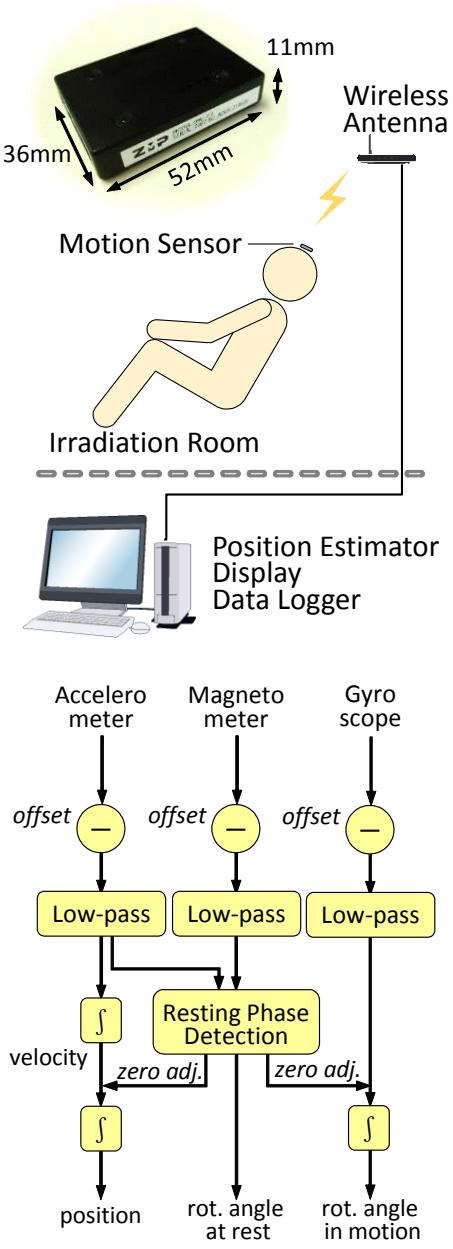

Fig. 1. An outline of patient-position-error measuring system.