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Design and Construction of Experimental System for Validation of a New Image Reconstruction Technique with Limited-view-angle Projection Data for BNCT-SPECT

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Abstract. Boron Neutron Capture Therapy (BNCT) is expected to be a promising radiation therapy for cancer, and research on various issues associated with it is still in progress. One of the unsolved issues is the construction of a system for observing the effect of the treatment (local boron dose) in real time under high-background circumstances. Thus, we set out to establish a method for measuring gamma-rays emitted promptly from the body following the boron neutron capture reaction and reconstructing images in a SPECT-like manner. We call this method BNCT-SPECT. We have been developing a new image reconstruction method based on Bayesian estimation for the BNCT-SPECT method. In the present study, the aims were to design and construct an experimental system capable of validating BNCT-SPECT and its image reconstruction method and to confirm BNCT-SPECT's performance. The crucial takeaway from this study is that we should consider the use of extremely high background radiation during BNCT. For the validation of BNCT-SPECT, we attempted to reproduce these conditions, despite this being quite challenging. We first constructed an experimental system capable of reproducing such conditions. Theoretical investigation was carried out to facilitate the design of the system using the Monte Carlo transport calculation code MCNP. Finally, we performed experiments with some standard gamma-ray sources to complete the system.

Keywords: BNCT-SPECT, image reconstruction, mock-up system, limited-view-angle projection.

1. Introduction

In Japan, malignant neoplasms (cancers) were the cause of 394,988 fatalities in 2021, accounting for 27.4% of all deaths. Since 1981, malignant neoplasms have been the primary cause of death among humans, according to the annual trends in death rates [1]. Oncological mortality and morbidity are expected to continue to rise. Therefore, Japan continues to conduct research on effective cancer treatment methods. The three primary cancer treatments are "surgery," "chemotherapy," and "radiation

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therapy." [2] Boron Neutron Capture Therapy (BNCT) [3, 4] is one of the novel radiation therapies that have been devised in the wake of advances in physical and biological technology.

BNCT uses ^{10}B and neutrons [5]. In the boron neutron capture reaction, depicted in equation (1), alpha-rays and a lithium nucleus are produced:

$$\begin{aligned} {}^{10}\mathrm{B} + \mathrm{n} \quad &\rightarrow {}^{7}\mathrm{Li} + \alpha + 2.79\ \mathrm{MeV}\ (6\%) \\ &\rightarrow {}^{7}\mathrm{Li}^{*} + \alpha + 2.31\ \mathrm{MeV}\ (94\%) \\ &\rightarrow {}^{7}\mathrm{Li}^{*} \rightarrow {}^{7}\mathrm{Li} + \gamma(478\ \mathrm{keV}) \end{aligned} \tag{1}$$

These products can effectively destroy cancer cells. Overall, 94% of the ^{7}Li produced by the $^{10}B(n,\alpha)^{7}Li$ reaction is in an excited state ($^{7}Li^{*}$), and consequently, the reaction emits a 478keV prompt gamma-ray via the transition to the ground state. The number of 478keV gamma-rays is directly proportional to the number of $^{10}B(n,\alpha)^{7}Li$ reactions, serving as a direct indicator of the therapeutic effect. BNCT exhibits a notably weaker impact on normal cells in contrast to other radiation therapies utilizing electromagnetic waves or charged particles [6, 7]. Moreover, BNCT uniquely permits repeated treatments in the same area, a substantial advantage in comparison to other treatment modalities [8].

In order to continuously monitor the therapeutic effects (local tumor dose) exerted under a severe radiation background, a new methodology for the reconstruction of images for BNCT has been proposed, Single-Photon Emission Computed Tomography (SPECT), leading to a specific joint methodology named BNCT-SPECT [9]. However, in the development of the BNCT-SPECT system, several challenging issues have been posed, and these issues need solving. Our research group is focusing on two issues, projection angle and background. Firstly, in a conventional SPECT system, the detector group typically covers a projection angle range of up to 360 degrees. Nevertheless, in BNCT-SPECT, we confront the constraint of positioning the patient's body on the surface of the neutron exit wall, as well as other medical limitations. Therefore, the available projection angle needs to be restricted to 180 degrees or less [10, 11].

In this study, we focus on addressing the issue of excessive background. Background radiation is generated by gamma-rays emitted by other reactions in the experimental system, except for the immediate onset 478 keV gamma-ray, which, as stated, derives from the $^{10}B(n,\alpha)^{7}Li$ reaction, representing the therapeutic effect; $^{1}H(n,\gamma)^{2}H$, $^{155}Gd(n,\gamma)$, $^{157}Gd(n,\gamma)$, and $^{nat}Gd(n,\gamma)$ gamma-rays are produced by neutrons in GAGG ($Gd_3Al_2Ga_3O_{12}$: Ce) [12] and water. These gamma-rays are all derived from the neutron reactions. Hence, in accordance with responses observed in practical therapeutic settings, our target signal-to-noise (S/N) ratio was set at 0.2 with the statistical accuracy of less than 5% [13]. We have formulated a novel image reconstruction method using Bayesian estimation. The primary objective of this study was to investigate this new image reconstruction method's validity, particularly under the rigorous conditions inherent to BNCT-SPECT. Leveraging the existing BNCT system as a foundation, we employed multiple gamma-ray sources instead of neutrons to reproduce the statistical accuracy and S/N ratio encountered in authentic therapeutic scenarios. This undertaking serves as a validation of the feasibility of the proposed method. Ultimately, we can substantiate this method's effectiveness by demonstrating its application in BNCT-SPECT.

2. Materials and Methods

2.1. SPECT system for BNCT

Figure 1 illustrates the fundamental principle of BNCT-SPECT. The patient is administered a drug containing ^{10}B, which accumulates in the cancer cells. Subsequently, the patient undergoes irradiation with either thermal neutrons or epithermal neutrons from external sources [14]. The boron neutron reaction is depicted in equation (1).

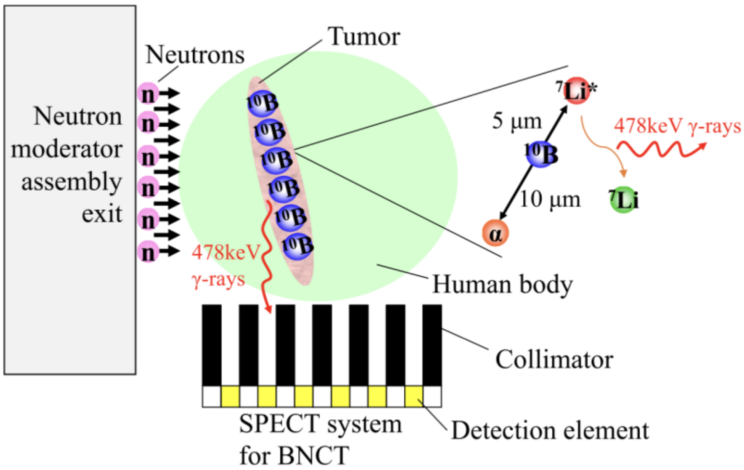

Figure 1. Conceptual figure of BNCT-SPECT [15]

Single-Photon Emission Computed Tomography (SPECT) is a nuclear medicine tomographic imaging technique that uses gamma-rays. SPECT imaging is carried out by employing a gamma-ray detector to capture multiple 2D images, commonly referred to as projections, acquired from various angles. Subsequently, a computer utilizes a tomographic reconstruction algorithm to process the ensemble of projections, culminating in the generation of a comprehensive 3D dataset. This dataset may subsequently be manipulated to display thin slices along any chosen axis of the body. The SPECT system quantifies the intensity distribution of the 478 keV gamma-ray emitted by the $^{10}B(n,\alpha)^{7}Li$ reaction according to equation (1). The number of 478 keV gamma-rays is directly proportional to the number of $^{10}B(n,\alpha)^{7}Li$ reactions, indicating the therapeutic effect. The attenuation coefficient of the target gamma-rays in tissue is minimal (0.1 cm^{-1}), allowing for most of the gamma-rays to exit the body [16]. A collimator fabricated from tungsten or lead capable of shielding gamma-ray radiation is positioned in front of the detector to collimate the direction of the 478 keV gamma-ray. Multiple gamma-ray detectors measure the objective gamma-rays that traverse through the collimator's apertures aligned before them, and the measured radiation is used to ascertain the $^{10}B(n,\alpha)$ reaction rate distribution within the tumor and construct a 3D image. In summary, BNCT-SPECT is indispensable for realizing a real-time assessment of BNCT's treatment effect [17]. Currently, scientists around the world are conducting related research to realize BNCT-SPECT. [18-21]

2.2. Bayesian estimation method

In this study, we employ the Bayesian estimation method, recognized as an engineering estimation technique, to ascertain the gamma-ray source distribution within the body [22]. To obtain the distribution of gamma-ray sources in a plane described by x and y axes, the entire head is partitioned into numerous small squares' regions. Specifically, a 3D brain is divided into n 2D slices, each slice of which is further divided horizontally (x and y axis) into n sections, resulting in a total of n^2 regions. Subsequently, n detectors and collimators are positioned orthogonal to the x-axis of the cell, with the center of the head serving as the origin. This system, comprising the detector and collimator, shall be henceforth referred to as the "detector system."

The intensity of the gamma-ray source within the j-th region (where j = 1, 2, ..., n^2) is represented by Nj [photons/sec], while the detector obtains the peak count rate [CPS] value at 478 keV, denoted by Ai at the i-th (where i = 1, 2, ..., n) measurement position. The initial configuration of the experimental system for a case where n = 5 is presented in figure 2.

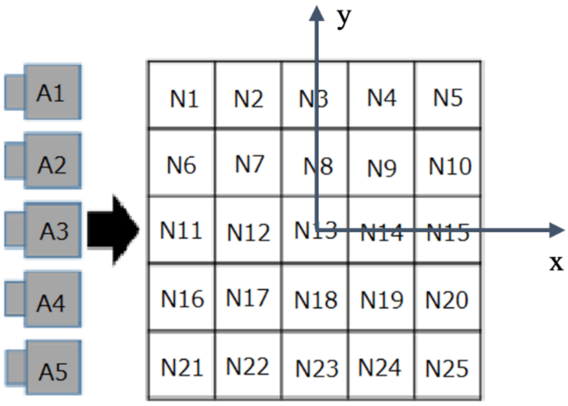

Figure 2. Image of the system (for n=5)

Following the initial measurement at the designated position, the detector system is rotated in a clockwise direction around the center of origin via a specific angle, and the measurement is performed once more. As illustrated in figure 3, this iterative process continues, adjusting the rotation angle to execute n measurements in total until the rotation angle relative to the initial state reaches 90 degrees. By doing this, cumulatively, the total of n^2 measurements from A_1 to A_{n^2} can be obtained.

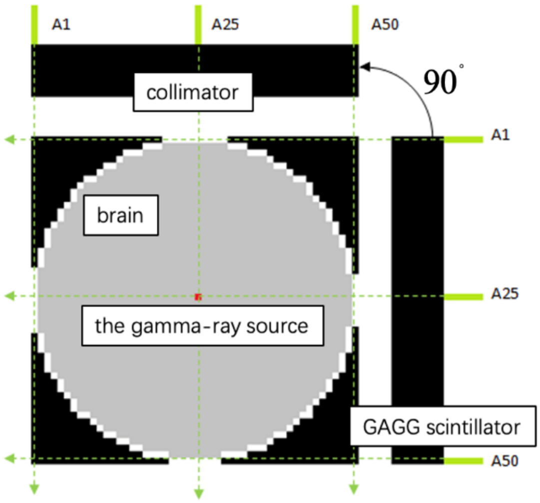

Figure 3. A simple schematic view of the detection process for experiments with moving angle θ=90 degrees and n=50. [23]

By detecting emitted gamma-rays in this way, we can treat Nj and Ai, defined earlier into vectors $\vec{N}$ and $\vec{A}$. Then, we define the probability that a gamma-ray emitted from the j-th region is deposited by a detector placed at the i-th position, causing a 478 keV photopeak, as $R_{i,j}$. This is the response matrix **R**. As a result, the relationships can be expressed in terms of the following matrix (equation (2)):

$$\vec{A} = \mathbf{R} \cdot \vec{N} \tag{2}$$

In BNCT-SPECT, $\vec{A}$ represents a known value, whereas $\vec{N}$ stands for an unknown quantity, necessitating the solution of the aforementioned matrix equation as an inversion problem. If the matrix **R** is a square, there exists a viable solution that can be obtained computationally [24]. Nevertheless, due to the fact that $\vec{A}$ constitutes a measured value and contains statistical errors, the mathematically solved values may not be representative of the true solution. Consequently, this research employs Bayesian estimation to acquire a meaningful solution from an engineering standpoint.

2.3. Monte Carlo N-Particle (MCNP)

MCNP is an abbreviation for A General Monte Carlo N-Particle Transport Code, a radiation transport calculation code [25]. MCNP5, the fifth version, was used for the simulation calculations described in this study. We devised and assembled a mock-up system and conducted experiments with it. The design of this system was informed by a theoretical examination conducted through the application of MCNP. Subsequently, the system was physically realized.

Ultimately, experimental trials were conducted utilizing standard gamma-ray sources to validate and finalize the functionality of the devised system.

2.4. The mock-up system

The construction of a mock-up system was performed so that the experimental specifications of the actual BNCT-SPECT system could be reproduced. We employed a ^{137}Cs source as a means of simulating the gamma-ray emitted from ^{10}B generated during an actual treatment and ^{60}Co to create the background in the designed BNCT. Figure 4 and table 1 show whole simplified mock-up system of BNCT-SPECT and the equipment.

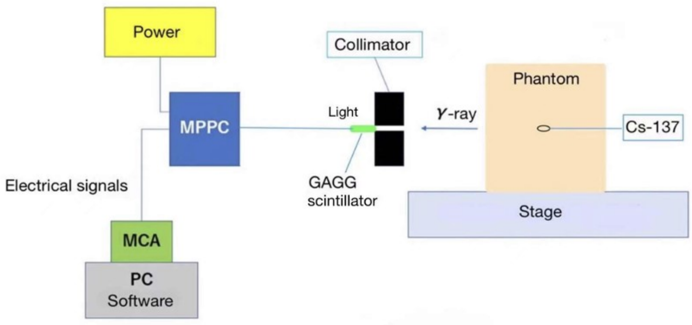

Figure 4. Simplified experimental system.

Table 1. Simulation condition.

Equipment	Product model
Motorized stage (rotation)	SIGMAKOKI OSMS-120YAW
Motorized stage (translation)	SIGMAKOKI OSMS26-200
Stage controller	SIGMAKOKI SHOT-702
MPPC [26]	HAMAMATSU MPPC C14047-9955
MCA	AMTEK MCA8000D

Figure 5 shows the front and top views of the actual developed mock-up system.

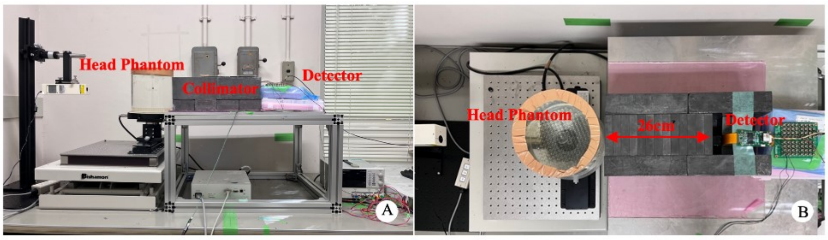

Figure 5. Mock-up system: front view (A) and top view (B).

A ^{137}Cs source is placed at the center of the head phantom made of acryl and water [27], and a ^{60}Co source is placed at various distances d from and just over the detector to examine the statistical accuracy and S/N ratio. Given its application in cancer treatment, the BNCT-SPECT system is designed to possess a spatial resolution of 0.5 cm or finer. As established in prior investigations, the ideal length of the collimator has been determined to be fixed at 26 cm. [28] A comprehensive summary of the designed mock-up system's specifications, as well as a comparison with those of the designed BNCT-SPECT system, is presented in table 2.

Table 2. Specifications of the experimental system compared to the designed BNCT-SPECT system.

Design item		Present mock-up system	Designed BNCT-SPECT
Scintillator	Material	→	GAGG(Ce)
	Dimensions	→	0.35 cm × 0.35 cm × 3 cm [28]
Collimator	Material	Pb	W
	Thickness	→	26cm
	Hole size	0.3 cm × 0.3 cm×64	Ø 0.35 cm×64
Phantom	Material	Acryl and water	-
	Dimensions	Ø20 cm × 20 cm	-
Statistical accuracy		4.39%	4.39%
(S/N)		0.21	0.21 [8]

3. Results

The BNCT-SPECT measurement system was validated using the mock-up system. The mock-up system was unable to replicate the precise accuracy of the designed BNCT-SPECT system. This limitation arises from the fact that the nature background in the mock-up experiment is notably weaker than that of the actual BNCT-SPECT system. Consequently, it became necessary to establish an experimental system capable of attaining a statistical accuracy and S/N ratio equivalent to those observed in the designed BNCT-SPECT system. To achieve this objective, we adjusted the positions of the ^{60}Co and carried out corresponding detection tasks.

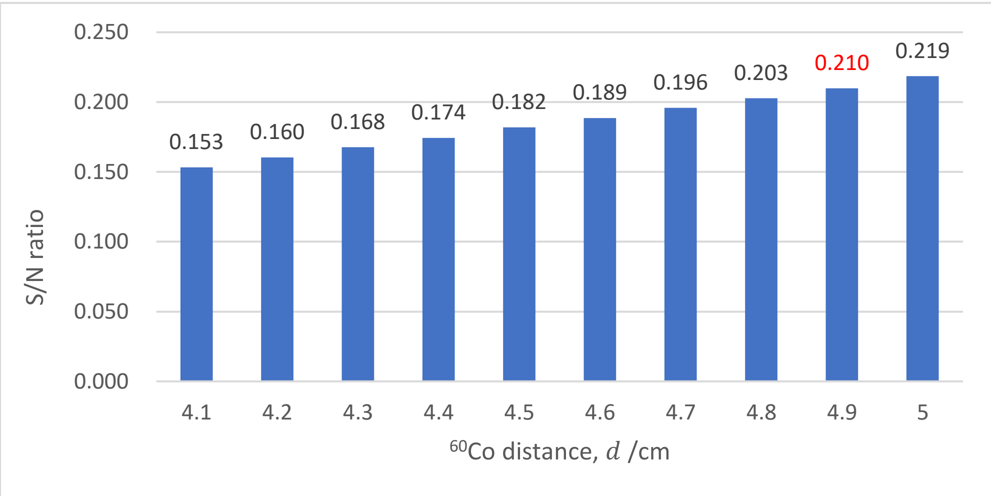

Figure 6. S/N ratio for the ^{60}Co distance.

Figure 6 shows the changes in the S/N ratio for the ^{60}Co distance. The most fitting S/N ratio was 0.21, observed at a ^{60}Co distance of 4.9 cm.

Subsequently, we conducted experiments utilizing the designed system as aforementioned. Additionally, we employed MCNP to establish a system identical to the designed mock-up system for comprehensive calculations.

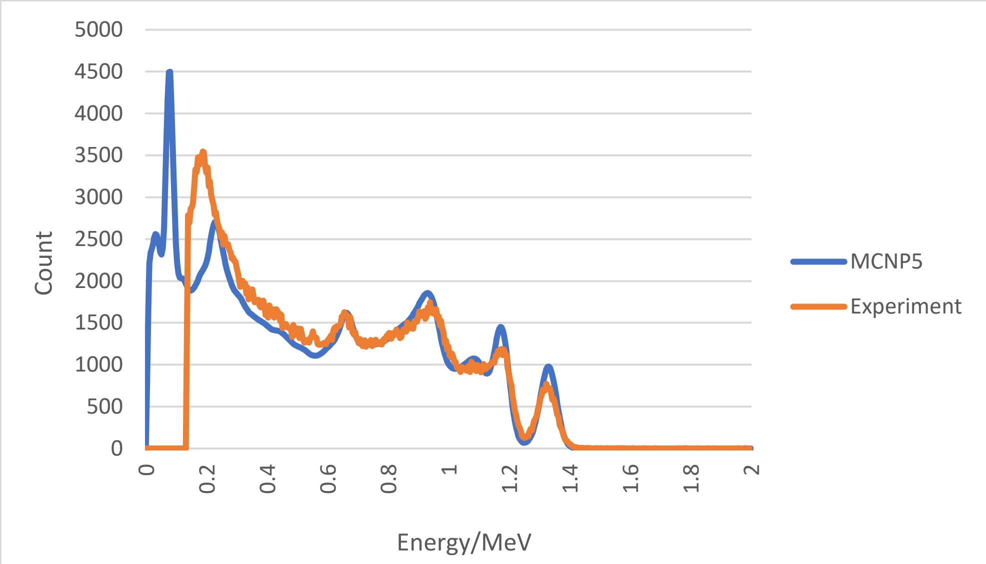

Figure 7. Comparison between experimental result and MCNP5 result.

Figure 7 compares the pulse height spectra obtained from the mock-up experiments and MCNP5 calculation, which demonstrate excellent agreement, and distinct ^{60}Co and ^{137}Cs peaks can be observed.

These peaks function as a background to replicate the designed BNCT-SPECT conditions. Table 3 shows the intensity of the ^{137}Cs and ^{60}Co gamma-ray sources. As in figure 2, the ^{137}Cs with an activity of 1×10^7 Bq is positioned at the center of the phantom, while the ^{60}Co source is placed 4.9 cm up to the detector, exhibiting an intensity of 1.06×10^6 Bq.

Table 3. Simulation condition.

^{137}Cs intensity	1×10^7 Bq
^{60}Co intensity	1.06×10^5 Bq

Table 4. Simulation results for the present study's mock-up system.

NET count	5474
BG count	26024
Counting time	0.48 h
^{60}Co distance, d	4.9 cm
Statistical accuracy	0.0438
S/N ratio	0.21

The simulation results are summarized in table 4. Through this mock-up system configuration, a remarkable accuracy of 4.39% was achieved in a counting time of 0.48h, which is less than 1 hour, closely approaching the real design result of the BNCT-SPECT system. The count rate per hour of ^{137}Cs proves that the mock-up system can adequately be applied for practical measurements. Notably, the designed mock-up system yielded a favorable statistical accuracy of 4.4% and a S/N ratio of 0.21, meaning that this system closely matches the performance of the designed BNCT-SPECT system in terms of statistical accuracy.

4. Conclusion and Discussion

We have successfully designed and constructed a mock-up system for the validation of the BNCT-SPECT system. Through conducting comprehensive MCNP calculations and basic experiments prior to the mock-up experiments, we successfully replicated the precise accuracy of the designed BNCT-SPECT system.

In the next step, we will conduct further experiments utilizing this mock-up system. For instance, in medical treatment, the projection angle needs to be 180 degrees of less, and the detectors' moving angle step should be within 90 degrees. Thus, we will endeavor to explore smaller projection angles with an appropriate moving angle to enhance the quality of results. Subsequently, we will implement a filter to mitigate artifacts, ensuring improved agreement between the reconstructed images and the true image.

Ultimately, our goal is to attain comprehensive limited-view-angle projection data through experimental approaches, with which we will validate the proposed image reconstructing technique.

The current study has shown the feasibility of using the limited-view-angle projection data acquisition for the BNCT-SPECT system. However, there are several limitations that warrant further investigation. For example, while initial experiments have validated system accuracy, the influence of noise and the effect of angle reduction on image quality still need to be addressed. Future work will focus on these aspects to ensure the system's robustness in practical applications. The successful integration of these techniques into real-world medical treatment processes is crucial for the widespread adoption of the BNCT-SPECT system.

References

[1] Ministry of Health, Labour and Welfare of Japan, "Annual Health, Labour and Welfare Report 2021" ,2023, https://www.mhlw.go.jp/toukei/saikin/hw/jinkou/kakutei21/dl/11_h7.pdf

[2] U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Institute, 2020, https://www.cancer.gov/about-cancer/treatment/types

[3] Menéndez, P. R., Roth, B. M. C., Pereira, M. D., Casal, M. R., González, S. J., Feld, D. B.,Santa Cruz, G.A.,Kessler, J.,Longhino, J.,Blaumann, H.,et al. "BNCT for skin melanoma in extremities: updated Argentine clinical results. *Applied Radiation and Isotopes*", *67*(7-8),(2009): S50-S53.

[4] Kankaanranta, L., Seppälä, T., Koivunoro, H., Saarilahti, K., Atula, T., Collan, J., Salli, E., Kortesniemi, M., Uusi-Simola, J., Mäkitie, A., et al. "Boron neutron capture therapy in the treatment of locally recurred head and neck cancer." *International Journal of Radiation Oncology* Biology* Physics* 69.2 (2007): 475-482.

[5] Fairchild, R. G., and V. P. Bond. "Current status of 10B-neutron capture therapy: enhancement of tumor dose via beam filtration and dose rate, and the effects of these parameters on minimum boron content: a theoretical evaluation." *International Journal of Radiation Oncology* Biology* Physics* 11.4 (1985): 831-840.

[6] Verbakel, W. F., Sauerwein, W., Hideghety, K., & Stecher-Rasmussen, F. "Boron concentrations in brain during boron neutron capture therapy: in vivo measurements from the phase I trial EORTC 11961 using a gamma-ray telescope." *International Journal of Radiation Oncology* Biology* Physics* 55.3 (2003): 743-756.

[7] Fantidis, J. G., Saitioti, E., Bandekas, D. V., & Vordos, N. Optimised BNCT facility based on a compact DD neutron generator. *International Journal of Radiation Research*, *11*(4), (2013): 207.

[8] Sauerwein, W. A., Wittig, A., Moss, R., & Nakagawa, Y. (2012). *Neutron capture therapy: principles and applications*. Springer Science & Business Media.

[9] Manabe, M., Nakamura, S., Murata, I. "Study on measuring device arrangement of array-type CdTe detector for BNCT-SPECT". Reports of Practical Oncology & Radiotherapy, 2016, 21(2): 102-107.

[10] Lee, P. Y., Liu, Y. H., & Jiang, S. H. Dosimetric performance evaluation regarding proton beam incident angles of a lithium-based AB-BNCT design. *Radiation protection dosimetry*, *161*(1-4),(2014): 403-409.

[11] Haruka, I., Shuto, T., Fan, L., Yuri, M., Singo, T., Sachie, K., Fuminobu, S., Isao, M."A New Image Reconstruction Technique with Limited View-angle Projection Data for BNCT-

SPECT". In *2020 IEEE Nuclear Science Symposium and Medical Imaging Conference (NSS/MIC),* (2020): (pp. 1-4).

[12] C&A, 2012. Crystals and Applications. https://www.c-and-a.jp/company.html/, 1st, September 2020.

[13] Japanese Society of Neutron Capture Therapy (JSNCT), 2018. The 15th Congress on Neutron Capture Therapy. Hokkaido University, Japan. Sept. 1–2, 2018.

[14] Lemmel, H.D., McLaughlin, P.K., Pronyaev, V.G., 2001. ENDF/B-VI Release 8 (Last release of ENDF/B-VI) The U.S. Evaluated Nuclear Data Library for Neutron Reaction Data, IAEA-NDS-100, Rev. 11.

[15] Murata, I., Kusaka, S., Minami, K., Saraue, N., Tamaki, S., Kato, I., Sato, F. "Design of SPECT for BNCT to measure local boron dose with GAGG scintillator". Applied Radiation and Isotopes, 2022, 181: 110056.

[16] Jaszczak, R. J., Coleman, R. E., Lim, C. B. "SPECT: Single photon emission computed tomography[J]". IEEE Transactions on Nuclear Science, 1980, 27(3): 1137-1153.

[17] IAEA, 2020. Virtual Technical Meeting on Advances in Boron Neutron Capture Therapy.EVT1905174. https://nucleus.iaea.org/sites/accelerators/TMBNCT/SitePages/Home.aspx, 22nd September 2020.

[18] Hales, B., Katabuchi, T., Igashira, M., Terada, K., Hayashizaki, N., & Kobayashi, T. "Predicted performance of a PG-SPECT system using CZT primary detectors and secondary Compton-suppression anti-coincidence detectors under near-clinical settings for boron neutron capture therapy." *Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment* 875 (2017): 51-56.

[19] Ishikawa, M., Kobayashi, T., Sakurai, Y., & Kanda, K. "Optimization technique for a Prompt Gamma-ray SPECT collimator system." *Journal of radiation research* 42.4 (2001): 387-400.

[20] Kobayashi, T., Sakurai, Y., & Ishikawa, M.. "A noninvasive dose estimation system for clinical BNCT based on PG-SPECT—Conceptual study and fundamental experiments using HPGe and CdTe semiconductor detectors". *Medical physics*, *27*(9), (2000): 2124-2132.

[21] af Rosenschöld, P. M., Minarik, D., Östlund, C., Ljungberg, M., & Ceberg, C. "Prompt gamma tomography during BNCT—a feasibility study." *Journal of Instrumentation* 1.05 (2006): P05003.

[22] Iwasaki, S. "A new approach for unfolding problems based only on the Bayes' Theorem" Proceedings of the 9th International Symposium on Reactor Dosimetry (1997) pp.245-252.

[23] Minsky, D. M., Valda, A. A., Kreiner, A. J., Green, S., Wojnecki, C., & Ghani, Z.. First tomographic image of neutron capture rate in a BNCT facility. *Applied Radiation and Isotopes*, *69*(12), (2011): 1858-1861.

[24] Iwasaki, S. "Solving method of Radiation Inverse Problems Based on the Iterative Bayes 'Estimation: Image Reconstruction Problem in CTs", Journal Article, 02853604, 1996

[25] MCNP Team, 2005. MCNP5-1.40 RSICC Release Notes. LA-UR-05-8617.

[26] Photonics, Hamamatsu, 2017. Multi-Pixel Photon Counters (MPPCs/SiPMs). https://www.hamamatsu.com/jp/en/product/optical-sensors/mppc/mppc_mppc-array/index.html, 1st April 2017.

[27] Kanno, I., Nishimatsu, D., Funama, F. "Simulation study on the feasibility of current-mode SPECT for B-10 concentration estimation in boron neutron capture therapy." *Journal of Instrumentation* 14.02 (2019): C02002.

[28] Minami, K., Saraue1, N., Ohya, R., Sato, F., Murata, I., 2017. Design of a proto-type array detector using GAGG scintillator for BNCT-SPECT. Nov. 13-15, 2017. In: 9th Young Researchers' BNCT Meeting (YBNCT 9). Uji Obaku Plaza, Kyoto. P8-3.