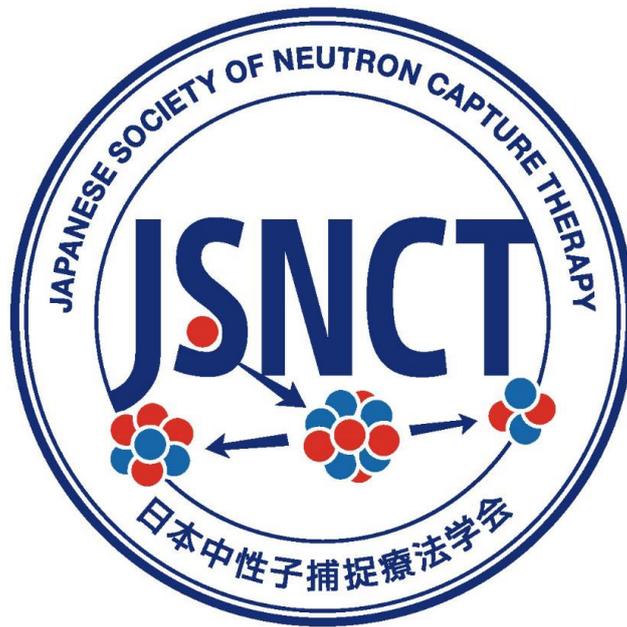


NCT letter Vol. 6
(English version)

May, 2020



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¹Laboratory for Chemistry and Life Science, Institute of Innovative Research, Tokyo Institute of Technology

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Director of Kansai BNCT Medical Center, Osaka Medical College

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Mitsunori Kirihata

Professor, Laboratory for Medicinal Chemistry for Boron Drug, Research Center
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Organization for Research Promotion, Osaka Prefecture University

- On receiving ***the Hatanaka Award***

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● *Introduction of the articles*

1. <Biology >

Title: Eosinophil depletion suppresses radiation-induced small intestinal fibrosis

Authors: Naoki Takemura, Yosuke Kurashima, et al.

The source: Science Translational Medicine, 2018 Feb 21; 10(429)

<https://stm.sciencemag.org/content/10/429/eaan0333/tab-pdf>

Presented by *Lichao Chen* (Department of Frontier Life Sciences, Nagasaki University Graduate School of Biomedical Sciences)

2. <Medicine >

Title: Boron neutron capture therapy for high-grade skull-base meningioma

Authors: Koji Takeuchi, Shinji Kawabata, *et al.*

The source: Physics in Medicine & Biology (2017) 62: 4421-4439

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6133692/>

Presented by *Yusuke Fukuo* (Department of Neurosurgery and neurovascular therapy, Osaka Medical College Hospital)

3. <Physics>

Title: Fast neutron dose evaluation in BNCT with Fricke gel layer detectors

Authors: G. Gambarini, G. Bartsaghi, *et al.*

Radiation Measurements 45 (2016) 1398-1401

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5100278/>

Presented by *Yuto Murakami, et al* (Graduate School of Engineering, Hiroshima University)

4. <Pharmacology>

Title: Design, synthesis, and evaluation of lipopeptide conjugates of mercapto-undecahydrododecaborate for boron neutron capture therapy

Authors: Aoi Isono, Mieko Tsuji, *et al.*

The sources: ChemMedChem (2019) 14 : 823-832

<https://chemistry-europe-onlinelibrary-wiley-com.remote.library.osaka->

u.ac.jp:8443/doi/full/10.1002/cmdc.201800793

Presented by *Kazuki Kawai* (Laboratory for Chemistry and Life Science Institute of Innovation Research, Tokyo Institute of Technology)

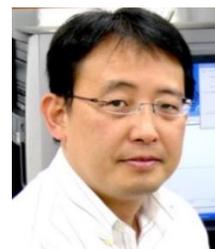
● *Editorial Postscript*

Itsuro Kato

Chief Editor of NCT letter

Department of Oral and Maxillofacial Surgery II, Graduate School of Dentistry, Osaka University

On the occasion of the publication of NCT letter issue No.6



Hiroyuki Nakamura

President, Japanese Society of Neutron Capture Therapy

Professor, Institute of Innovative Research, Tokyo Institute of Technology

Thanks to the efforts of the editor-in-chief Dr. Itsuro Kato and through cooperation with our colleagues, the sixth issue of NCT letter was successfully published. I take this opportunity to express my sincere gratitude to them.

In this issue, we asked three professors to write feature articles: Dr. Akira Maruhashi (Professor Emeritus, Kyoto University) who contributed greatly to the development of the world's first accelerator for BNCT, Dr. Jun Hatazawa (Professor Emeritus, Osaka University) who expressed his own research activity including ^{18}F -BPA PET imaging study, and Dr. Kazuyo Igawa (Associate Professor, Okayama University) who plays an active role as a pipe between the International Atomic Energy Agency (IAEA) and the International Society of Neutron Capture Therapy (ISNCT).

At the 18th International Congress on Neutron Capture Therapy (ICNCT18) held in Taipei last October, Prof. Koji Ono, the first president of the Japanese Society of Neutron Capture Therapy (JSNCT), received the Global Outstanding Achievement Award, and Prof. Mitsunori Kirihata, the second president of JSNCT, and Prof. Junichi Hiratsuka, the third president of JSNCT, received the Hatanaka Prize. In addition, Dr. Saki Shibata, Dr. Keita Okazaki, and Dr. Naonori Ko, received the Fairchild Award. These awards are very prestigious to JSNCT.

At the 15th Annual Meeting of the Japanese Society for Neutron Capture Therapy held in Hokkaido University in September last year, Dr. Kentaro Baba, Dr. Takahiro Nomoto, and Dr. Atsushi Tsuyuguchi received the Best Presentation Award. I wish to congratulate the award-winning members and wish them further progress and success in the future.

As you know, the Phase II clinical trial for the world's first accelerator neutron source for brain tumors and head and neck cancer that started in 2012 has been completed and is now under preparation for approval. In addition, the Phase II clinical trials for malignant meningiomas at Osaka Medical College and for malignant melanoma and angiosarcoma at National Cancer Center Hospital have commenced. Now, BNCT in Japan is facing a critical moment for the realization of "Treatment for Patients" ahead of the rest of the world. I hope that the members of JSNCT will work together so that many patients can

receive BNCT as soon as possible.

Thank you for your continued support and understanding.

Encounter with BNCT and wishes

Akira Maruhashi

Professor, Institute for Integrated Radiation and Nuclear Science, Kyoto University



1 Encounter with BNCT

In July 2002, I joined the Kyoto University Research Reactor Institute (renamed Kyoto University Institute for Integrated Radiation and Nuclear Science-KURNS in 2018) with the dream of building a proton therapy facility here. However, my feelings changed completely after witnessing the treatment of BNCT parotid gland cancer with epithermal neutrons, which was first attempted at KURNS in December 2001. I was truly shocked! I engaged in the endeavor of proving the clinical effectiveness of BNCT.

2 Kyoto Univ. Reactor Based Thermal- & Epithermal- Neutron BNCT

In March 2003, we started an annual plan review meeting mainly with doctors from the Department of Radiology at Kawasaki Medical School, Osaka University School of Dentistry, and Osaka Medical College Department of Neurosurgery, and a “clinical research implementation plan” was established, under the direction of Prof. Ono, to confirm the actual clinical evaluation of BNCT. A joint research system was organized mainly with the doctors mentioned above and the doctors from Osaka Prefectural University in the Research Department of BPA, in order to evaluate the effectiveness of BNCT. The main research subjects for about 3 years until 2005 were brain tumor, head and neck cancer, liver tumor, malignant melanoma, mesothelioma and lung cancer. During this period, the number of BNCT patients reached about 180. At that time, the situation was changing on the premise of the disposal of KUR. However, requests for continued use of KUR, including those from people involved with BNCT, were greatly approved. KUR-BNCT has been suspended for a while due to the Great East Japan Earthquake in March 2011, but is now operating smoothly.

3 Accelerator Based Epithermal Neutron BNCT

As mentioned above, when the possibility of reactor decommissioning was raised as a realistic issue, BNCT promoters were required to present and develop policies for future issues, taking into account the progress of research and the perspective of disseminating BNCT. A wide variety of accelerators has already been proposed mainly in Europe as neutron sources for NCT. In Japan, many of them were using a reaction between 2-3 MeV

protons and Li. This energy selection is presumed to be based on the understanding that NCT is based on thermal neutron irradiation (with a treatable depth of about 2.5 cm), assuming that there is a high probability of failure of fast neutrons. The main treatment targets for NCT were refractory Glioblastoma Multiforme (GBM) and malignant melanoma. In the case of GBM, which is a deep cancer, after surgery to remove the center of the lesion at the patient's main hospital, treatment was resumed at the reactor irradiation field operation site, and irradiation was performed with reduced depth. It seems that the accelerator's neutron generation system was devised along this flow. At the time of my previous job at the University of Tsukuba, I designed an irradiation system and shielding system for fast neutron radiation therapy using a neutron beam with an average energy of 70 MeV generated by 500 MeV protons, and worked to explore the possibility of its use for medical treatment. Based on experience including animal experiments using the Medical Science Institute's cyclotron neutrons, even in the FFAG accelerator utilization plan, it is relatively easy to operate the neutron generation system including the target. Therefore, I planned a proton beam and neutron generation target system of about 20 MeV, on the premise of maintaining homeostasis, important for medical treatment. In late 2005, I started negotiations with accelerator manufacturers based on this experience. In late 2006, a contract was signed with Stella Chemifa Corporation and Sumitomo Heavy Industries, Ltd. for a proton accelerator and neutron irradiation system (30MeV proton accelerator cyclotron) to be developed and installed in the medical building. Design production and joint research started in early 2007. This was made possible by Prof. Ono's efforts to provide the medical building with a budget for the development, production, and medical research of the BNCT accelerator neutron source and irradiation system. In May 2006, Mr. Hiroki Tanaka, currently associate professor, joined the research team and started to design and produce a neutron moderator and epithermal neutron irradiation facility. A facility approval certificate based on the Radiation Hazard Prevention Act was issued on February 28, 2008, and installation adjustment of the accelerator system to the medical building was started from the latter half of the year. On January 29, 2009, the beam trial operation started, and various rating measurements were carried out. A passing certificate was issued on March 31 of that year, and the Cyclotron Based Epithermal Neutron Source (C-BENS) operation started. From April, in order to verify the effects of irradiation, various tests were conducted, such as measurements in BNCT irradiation field, radiation fields inside and outside the facility, and animal irradiation experiments. In March 2014, a clinical trial of accelerator BNCT was started at this facility. In addition, a facility with BNCT accelerator irradiation equipment of the same standard as KURN's was constructed in Southern Tohoku Hospital in Koriyama City, Fukushima Prefecture,

in relation to reconstruction after the Great East Japan Earthquake. A clinical trial was conducted in collaboration with this facility, and in June last year, trials were completed for as many cases as needed to obtain national policy on brain tumors and head and neck cancer. In addition, a BNCT accelerator irradiation facility with the same standards as KURN's at Osaka Medical University, which had been under construction for two years, was completed in March. Preparatory work for clinical trial research has been carried out, and I am participating in basic research issues.

4 Wishes

My life at the Institute since 2002 has been completely immersed in BNCT. I am grateful for this wonderful environment. I believe that BNCT can be the ultimate weapon against multiple cancers.

Wishes concerning this BNCT:

- ① Current epithermal neutrons have a therapeutic depth of up to approximately 6 cm, and the whole body, especially the abdominal region such as the liver, is outside the portal (Evaluation of self-absorption is important for increasing the concentration of ^{10}B in cancer tissue). Let us break this limit! Deepening of the thermal neutron distribution (with an increase in the fast neutron component) is considered inevitable, and the introduction of gantry multidirectional irradiation is a prerequisite.
- ② Building an accelerator BNCT medical facility in Kumatori town, establishing a joint research system with the KURNS accelerator facility, creating a research and clinical mutual prosperity system, and leading the battle against cancer.

BNCT and PET

Jun Hatazawa

Professor, Research Center for Nuclear Physics, Osaka University



In March of this year (2019), I retired from professor at the Department of Integrated Radiation Medicine (Nuclear Medicine), Graduate School of Medicine, Osaka University. I gained a lot of experience and had a fulfilling time. Thanks to the warm guidance and support of the teachers at the faculty, I was able to complete successfully my 17-year term. I express my heartfelt gratitude. From April, I was assigned to the Research Center for Nuclear Physics, Osaka University where I continue my research toward new goals. I look forward to your continued guidance.

Nuclear medicine is a field that applies the power of atoms to medicine. Diagnostic imaging Image with γ -rays and positrons, and treatment with β -rays and α -rays are being carried out, and nuclear medicine practice is changing dramatically due to improved performance of imaging devices and the development of new radionuclide-labeled drugs. Among that, boron neutron capture therapy (BNCT) is considered to be a nuclear medicine treatment because the cell killing effect depends on the amount of radioisotopes produced in the tissue. The absorbed dose depends on the accumulation of ^{10}B administered intravenously, and the accumulated amount can be measured with PET. The PET micro-dose test method can be applied to develop a boron carrier with higher tumor accumulation.

After graduating from Tohoku University in 1979, I entered the doctoral program of Tohoku University Graduate School of Medicine and belonged to Department of Radiology, Research Institute for Tuberculosis and Cancer (Prof. Taiju Matsuzawa). My mentor was Dr. Hiroshi Fukuda, four years my senior (at that time, assistant Professor). Dr. Fukuda had been visiting Kansai several times a year for group meetings and experiments of the Mishima group. I remember that he was conducting irradiation experiments on cultured cells. At Matsuzawa Lab, he was working on the development of radiology using particle beams (such as proton radiography, PET, and PIXIE).

Prof. Tatsuo Ido, famous for the development of FDG, had a laboratory at the Cyclotron and Radioisotope Center, Tohoku University in Aobayama Campus, and in the mid 1980s,

Dr. Yoshio Imahori enrolled at Department of Neurosurgery, Kyoto Prefectural University of Medicine. At that time, I think I heard the term boron neutron capture therapy for the first time. Research on BPA labeled with ^{18}F began by Dr. Fukuda's idea. Dr. Kiichi Ishiwata succeeded painstakingly in ^{18}F -BPA synthesis. Since then, biodistribution has been experimented. Dr. Imahori (who returned to Kyoto Prefectural University of Medicine) and his research group conducted the clinical study of ^{18}F -BPA PET actively at Nishijin Hospital in Kyoto.

Around 2006, Prof. Hiroshi Fukuda of Tohoku University and Prof. Junichi Hiratsuka of Kawasaki Medical School visited the laboratory at Osaka University, and suggested the idea of starting a ^{18}F -BPA PET at Osaka University. Since I was assigned to Osaka University in 2002 and was working on the development of the laboratory, it took time to start. However, with Dr. Yasukazu Kanai (currently at Kansai BNCT Medical Center, Osaka Medical College), responsible for the radiolabeling synthesis, Dr. Kohei Hanaoka (currently at the Radiology Department, Kindai University Hospital), in charge of basic research, and Dr. Kayako Isohashi (currently at Kansai BNCT Medical Center, Osaka Medical College), in charge of the clinic, the ^{18}F -BPA PET started at Osaka University. Prof. Eku Shimosegawa (Dept. of Molecular Imaging in Medicine) evaluated the systemic distribution in healthy subjects and found that ^{18}F -BPA is rapidly excreted from normal organs and that accumulation is low (2016). We have also developed a method for estimating the BPA concentration in tissues when a therapeutic amount of BPA is administered based on ^{18}F -BPA PET. Dr. Hanaoka prepared a cell culture experimental environment and reported that the accumulation of tracer amount of ^{18}F -BPA and therapeutic amount of BPA are equivalent (2014). Dr. Isohashi measured changes over time in ^{18}F -BPA concentrations in tumor tissue and blood (2016). Dr. Tadashi Watabe (Nuclear Medicine) discovered that ^{18}F -BPA is specifically taken up by tumor cells via L-type amino acid transporter 1 (LAT1) (2017). Since LAT1 was known to appear in many human cancer cells, it was found that BNCT by BPA could be used to treat many major malignancies in Humans. At the same time, we understood through ^{18}F -BPA PET that, that itself could be a malignant tumor specific testing method. Dr. Roua'a Beshr, a PhD student from Yemen, reported that ^{18}F -BPA is highly accumulated in recurrent brain tumors and low in radiation necrosis (2018). Dr. Victor Romanov, a PhD student from Russia, analyzed the ^{18}F -BPA accumulation quantitatively with compartment model (2019).

What ^{18}F -BPA PET has to overcome is the yield of ^{18}F -BPA. With conventional methods, only two people's PET examination is possible with one radiolabel synthesis. Currently,

the research team of Prof. Mitsunori Kirihata at Osaka Prefectural University is actively working on the development of a new radiolabel synthesis method, and expectations are high.

In Kansai, many years of BNCT basic research and clinical research have been accumulated using a nuclear reactor as a neutron source (Prof. Koji Ono, Prof. Maruhashi, Prof. Minoru Suzuki). The Kyoto University Institute for Integrated Radiation and Nuclear Science (leading the world's BNCT medicine), the Osaka Prefectural University (conducting Boron carrier Research), and the Osaka University Mirai Medical Imaging Center are working closely together to promote research in this field. In 2018, the Osaka Medical University BNCT Center, the clinical center of accelerator BNCT, was opened (Director Koji Ono). The second phase of the world's first BNCT clinical trial has been completed at the Institute for Integrated Radiation and Nuclear Science, Kyoto University and the Southern Tohoku General Hospital, and preparations are now underway for the approval of the Pharmacopoeia Act. I heard that the National Cancer Center started a clinical trial. In the future, I hope that the PET method can contribute to the selection of BNCT adaptation examples, the evaluation of therapeutic effects, and the development of new boron carriers.

Boron Neutron Capture Therapy (BNCT) and International Atomic Energy Agency (IAEA) activity

Kazuyo Igawa

**Associate Professor, Neutron Therapy Research Center
Okayama University**



Outline of IAEA

In 1953, U.S. president Eisenhower proposed ‘Atom for Peace’ and the International Atomic Energy Agency (IAEA) was established as autonomous organization in 1957. In 2009, Yukiya Amano of Japan was elected as the Director General (DG) for the IAEA and have achieved the goal ‘Atoms for Peace and Development’ (Fig.1). After DG. Amano’s death in July 2019, Rafael Mariano Grossi of Argentina was appointed as DG in Oct. 28th 2019. The objective of IAEA is ‘...seek to accelerate and enlarge the contribution of atomic energy to peace, health and prosperity



Fig.1 Memory of 5th DG. Yukiya Amano

throughout the world’ and ‘...ensure, so far it is able, that assistance provided by it or at its request or under its supervision or control is not used in such a way as to further military purpose. [1] The three main mission of IAEA is Peaceful uses, Safeguards and Nuclear safety and the main function is General Conference, Board of Governors and Secretariat. IAEA consists of 6 departments such as Management (MT), Technical Cooperation (TC), Nuclear Energy (NE), Nuclear Safety and Security (NS), Nuclear Sciences and Applications (NA) and Safeguard (SG).

BNCT at IAEA

In 1959, Point 2 Article 1 of Agreement between the World Health Organization (WHO) and IAEA states that “...it is recognized by WHO that IAEA has the primary responsibility for encouraging, assisting co-ordinating research on, and development and practical application of, atomic energy for peaceful uses throughout the world without prejudice to the right of WHO to concern itself with promoting, developing, assisting and co-ordinating international health work, including research, in all its aspects [2]. This the reason why IAEA is fulfilling the mission on health consequences of radioactivity,

including Boron Neutron Capture Therapy (BNCT). BNCT is related with department of Nuclear Sciences and Applications (NA), that is consist of three divisions and two laboratories (Fig. 2). Especially two sections at NA, Physics and Chemical sciences (NAPC) and Human health (NAHU) assume important roles for BNCT.

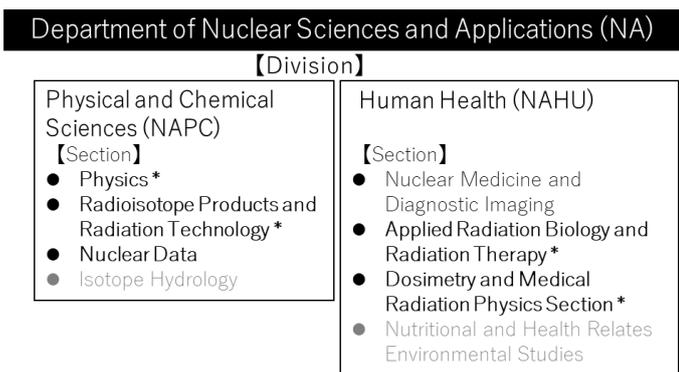


Fig. 2 Relevant sections to BNCT

A key objective of NAHU is to support member state’s fight against cancer, cardiovascular diseases and malnutrition and other diseases using nuclear and nuclear-related techniques, this is accomplished thorough support of cancer radiotherapy treatment and diagnostic imaging projects as well as support of nutrition centers and human resource development. NAPC assists member states with capacity-building, research and development in the nuclear sciences and supports them in using nuclear methods for a variety of practical industrial applications.

In 1999, Technical Meeting on Neutron Capture Therapy was held and IAEA-TECDOC-1223

Table 1 Meeting on BNCT at IAEA

Date	Meeting	Title	Scientific Secretary	
			Division	Section
1999	Technical Meeting	Current status of neutron capture therapy	NAHU	Applied Radiation Biology and Radiotherapy
			NAHU	Dosimetry and Medical Radiation Physics
			NAPC	Physics
2013, July	Technical Meeting	Research Reactor Users’ networks (RRUNs): Advances in neutron Therapy	NAPC	Physics
2017, Sep	Consultants Meeting	“New Compounds for Use in Boron Neutron Capture Therapy (BNCT)”	NAPC	Radioisotope Products and Radiation Technology

“Current status of neutron capture therapy” was published [3]. With the development of accelerator based BNCT from reactor based BNCT, the side event of 60th General Conference was held as “Recent Advances in Boron Neutron Capture Therapy Using Research Reactors and Accelerators” in 2016 (Table 1). After Najat Mokhtar was appointed Deputy Director General and head of NA on January 2019, the collaboration framework between NAPC and NAHU have set up. On October 2019, Consultancy Meeting on BNCT ‘current status and new developments’ was held at IAEA by NAHU and NAPC and the technical meeting on BNCT will be planned in 2020.

I would like to thank Dr. Kato for this opportunity.

Ref.

[1] <https://www.iaea.org>

[2] <http://www.crms-jpn.org/doc/IAEA-WHO1959.pdf>

[3] <https://www.iaea.org/publications/6168/current-status-of-neutron-capture-therapy>

Report on the 15th Japanese Congress on Neutron Capture Therapy



President Masayori Ishikawa
Professor, Graduate School of Health Sciences, Hokkaido University

“The 15th Congress on Neutron Capture Therapy” was held at the Hokkaido University Conference Hall on September 1st (Sat) and 2nd (Sun) 2019. The 6th BNCT Workshop (hosted by the Human Resource Development Committee of the Japanese Society of Neutron Capture Therapy and supported by this Congress) was held on the day before the Congress of August 31st.

It was very fortunate to be welcome participants in the refreshing climate unique to Hokkaido. In addition, a typhoon hit directly on September 4 immediately after the congress, and an earthquake of seismic intensity 7 occurred in Hokkaido before dawn on the 5th, and the entire Hokkaido was blacked out by the earthquake. Since the days of natural disasters continued, it would be impossible to held the congress if it had been scheduled one week after.

At the congress, 163 participants (79 regular members, 58 non-members, 26 students) joined the congress to present latest research results and make hot discussions in the fields of clinical medicine, pharmacy & chemistry, biology, and physics. I am full of gratitude



General presentation and poster session

for all the participants with their passion to BNCT.

Boron Neutron Capture Therapy (BNCT) is now on transition stage from irradiation based on research reactor to irradiation using accelerator-based neutron source and that may enable much more facilities to provide BNCT. The quality of the therapy has been secured by choosing the best therapy through trial and error for each case, however, to enable equivalent therapy to be provided by the facilities which are assumed to increase in the future, it is essential to share the consensus on the base technology and to establish the process of quality management/quality assurance of BNCT. For that purpose, the 15th Congress was held

with the theme “Towards Establishment of Base Technologies to Improve Therapy Quality”. BNCT is generally categorized into three fields; medicine & biology, physics & engineering and chemistry & pharmacology. The established technologies and technologies that still need to be discussed are mixed in each field. In the field of medicine & biology, careful discussion is necessary on prescribed dose and normal tissue tolerance dose in association with expanding the applicable diseases and devising the irradiation methods. In the field of physics & engineering, the appearance of irradiation facilities using accelerator-based neutron source raises the need to establish technologies for measuring and controlling precise neutron exposure. In the field of chemistry & pharmacology, establishment of methods for quantitative assessment of drug accumulation in tumors are the critical issue, as well as the new drug development.

The numbers of the presentations were 66 in total, consisting of 1 educational lecture, 1 luncheon seminar lecture, 6 symposium lectures, 40 general presentations and 18 poster sessions. Questions and answers were vigorously exchanged at the end of each presentation, the discussions were based on a view point of clinical necessity of each field. Meanwhile, those discussions were in line with each presentation which was among many other themes requiring a lot further discussions.

The educational lecture with the theme of “Development of synthetic diamond radiation detectors as well as semiconductor device and GPS scintillator” was delivered by the invited speaker of associate professor Junichi Kaneko (Graduate School/Faculty of Engineering of Hokkaido University), who has a lot of experience in developing neutron detecting element.

“Challenges for the establishment of base technologies” was the theme of the symposium and six speakers offered presentations of 1: Current status and challenges of BNCT as a part of multidisciplinary approach, 2: Current status and challenges with regard to development of next generation boron agents for BNCT, 3: Base technologies of medical physics and engineering necessary to predict biological effect, 4: Current status and challenges of treatment planning software for BNCT, 5: Establishment of irradiation facilities/ irradiation technique for diversification of BNCT, and 6: Quality control/quality assurance of BNCT as radiotherapy. Throughout the session, current conditions and challenges in the field of clinical medicine, drug development and physical engineering were reported while guidelines for establishment of the base technology were presented.

More than 100 participants attended congress dinner held at the Faculty House Trillium “Restaurant Elm” located in Hokkaido University. Attendees of the dinner party



String quartet entertained attendees of the congress dinner.

were entertained by the string quartet of Hokkaido University Symphony Orchestra that performed works by Dvorak and Mozart.

Finally, I would like to express my appreciation to Prof. Hiroyuki Nakamura, the President of the Japanese Society of Neutron Capture Therapy, Prof. Takai Yoshihiro, the chairman of the previous congress, Prof. Hironobu Yanagie, the chairman of the 13th congress and the members of the Society for their various fruitful advice, and to the staff of the management secretariat for their valuable efforts made for the management and practical

business for this congress, secretariat of Convention Linkage, Inc., and students of my laboratory. Let me also express sincere appreciation toward 17 companies which supported the management of this congress in the form of placement of advertisements, setting up of booths and sponsorship.

For further details of this congress, please refer to the “Information on Nuclear Technology in Medicine” Vol. 19 issued by the Association for Nuclear Technology in Medicine.

Participation to ICNCT18 (Taipei)

Associate professor Hiroaki Kumada
University of Tsukuba Faculty of Medicine, Proton
Medical Research Center



The 18th International Congress on Neutron Capture Therapy (ICNCT18) was held in Taipei from October to November 2, 2018. Since I participated in this international academic convention, I will introduce my impressions from my perspective of this convention.

First, this international convention has been held in rotation between Japan, Europe and America (including South America.), this time it was Japan's turn but, for the first time was held in a place other than Japan (In principal, the rotation rules for this venue have disappeared.) Taiwan, with its Tsinghua University Nuclear reactor: currently conducting clinical research using THOR, is one of the world's highest BNCT activity regions. It can be said that it was natural for this convention to be held in Taiwan. Also, based on recent Asian BNCT activities, places to hold this convention will continue to be selected from "Asia" instead of "Japan". Starting with Convention President Professor Fong-In Chou (picture 1), the support and program structure of the society secretariat, this was a convention where we could feel the enthusiasm "let's make this convention a success!" Personally, through participating in this convention I was able to enjoy this place called Taiwan, its people and atmosphere.

Looking at the convention's program, first off, "Educational sessions" and multiple "Invitation sessions" were quite distinctive. At previous conventions, on the first day from the "Welcome Reception" it was fine to simply participate at our ease, but at this convention before the "Welcome Reception" a 150 minute "Training Course" was set up with educational lectures by 4 instructors of different fields. I was also impressed by the fact that many of the participants in this session were not only students and young researchers but also experienced researchers. Regardless, many participated from start to finish, listening enthusiastically. This "Training Course" session was a good project that I hope will be continued in the next conventions onward.

In addition, the "Invited Lecture" sessions, which were held four times from the second day with each session having lectures given by 3 to 5 researchers from different fields, was an interesting program structure.

In the general program configuration, Plenary
Lecture session : 5, Parallel Session : 6,

Poster Session : 2, as well as Luncheon Seminar :
2 were set.

My impression was that the total number of
presentations was larger than at the previous 17th
convention (University of Missouri, US) and it
seemed as though the convention secretariat had

set more oral presentations (At the last
convention, Plenary Session : 9, Parallel Session :

4, Poster Session : 3) .

This is probably because many researchers from Japan were able to participate because the venue was held in Taipei, and many new researchers from China and South Korea also participated. Also, it is probably because of the high level of interest in BNCT in Taiwan. Looking at the number of presentations in each field, as could be expected, I felt that many presentations were about physical engineering and were very active. This is not only because I mainly participated in physical engineering sessions, but also looking back at the program for the entire convention many such programs were set. The number of sessions for both Plenary and Parallel was “Clinical”: 3, “Chemistry & Pharmacology”:4, “Boron Detection & Imaging”: 3, “Radiobiology “:3, “other”: 2, “Physical Engineering” was 8 sessions. Although this trend has been seen for quite a while, this is probably because research and development of the “accelerator-based neutron source device” has been actively carried out worldwide, and new research institutes and companies have started to enter this field of research. I especially feel that, as mentioned above, research institutes and companies in new regions such as China and South Korea have entered the BNCT field. Quickly counting, there were 16 presentations from China and South Korea. It was also introduced that 2 venture companies in the US, where BNCT activity has been limited so far, have entered the development of commercial accelerator-based treatment devices, and will also be implemented in Finland, China and Italy. Japan has been the world leader in this field so far, but it has become so that we have no time to waste. On the other hand, “clinical” related presentations are undeniably decreasing since there are



Professor Fong-In Chou declared the start
of the congress at the opening ceremony

only 4 nuclear reactor facilities in the world where research can be conducted. However, this tendency is likely to be realized in the near future when accelerator-based treatment devices are put into practical use, if treatment with the devices start, the number of presentations will increase, we can expect this to become the main session of the conventions again. At the earliest, at the next convention (Grenada) or perhaps the one after (Poland), there may be presentations related to treatment with accelerator-based treatment devices and clinical research. Personally, including hopeful observations, I hope the first presentation will be by a Japanese group.

Finally, I will introduce the changes in the structure of the International Society on Neutron Capture Therapy (ISNCT), which is the basis of this academic conference. Until now, the president of the ISNCT was also the chairman of the next academic convention, which changed every two years. However, in order to operate this international society stably and continuously, and to develop BNCT research internationally, starting from this convention, as with regular conferences, apart from the convention president, a “President”, “Vice President” and “Secretary” were established, and Professor Porras (Spain), Professor Matsumura (Japan) and Professor Bortolussi (Italy) were appointed respectively. With the evolution of this society and the BNCT “heat” felt in Taiwan, I hope that BNCT research will accelerate further and that it will be established and developed worldwide as an effective cancer treatment.

Report of BNCT session at AACR (American Association of Cancer Research), 2019

Akira Matsumura

Professor, Department of Neurosurgery, University of Tsukuba Hospital



From 29th March to 3rd April, 2019, a major symposium of BNCT was held at AACR, 2019 (Georgia World Congress Center, Atlanta, Georgia, USA).

The BNCT session was held on 31st March from 13 to 14:45 in a relatively big room. At the same time, about 20 parallel sessions were going on so that there were not so strikingly many participants, but there were active questions and discussions from the audience.



At AACR (from left; Matsumura, Koivunoro, Kankaanranta, Barth)

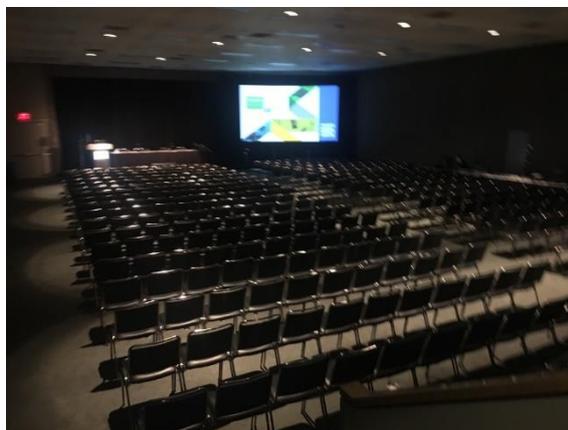
The chairman of the BNCT session was Dr. Leena Kankaanranta from Helsinki University. The first speaker was Dr. Rolf

Barth from Ohio State University presenting the results of their own experimental using F98 brain tumor model and the reviewed the clinical results of head and neck cancers and melanomas. He also mentioned the usefulness of BNCT in combination with chemotherapy and immunotherapy as a part of **multidisciplinary treatment**. He also referred the paper by Prof. Hiratsuka in urogenital melanoma and stressed the importance of preserving normal structure of sensitive part of the body. The second speaker was Dr. Hanna Koivunoro from Helsinki University and told about the principles and issues and medical physics issue of BNCT. She also introduced the BNCT accelerator system, patient setting system and treatment planning system installed in Helsinki University. As unpublished data, she presented that the clinical results are different among patient received below and above 18Gy-Eq. Next speaker was Dr. Leena Kankaanranta from the same institution presenting the clinical results of BNCT treatment in head and neck cancer and stressed that BNCT is extremely effective in recurrent cases

compared to other radiation therapy. Finally, Dr. Akira Matsumura from University of Tsukuba presented the principles of BNCT, characteristic of BSH and BPA, development of ^{18}F -BPA PET and its benefit for selection of indicated cases for BNCT and boron dose estimation using ^{18}F -BPA PET images. The development of Epithermal neutron beam with usage of treatment planning system was also introduced. The Japanese status of accelerator based BNCT was also demonstrated.

In general discussions, many questions about clinical trial were raised reflecting the interest towards BNCT as clinically available treatment modality. Especially, new boronated drugs were also of big interest of the audience because after accelerator has been established, new boronated drugs would become big research target in the pharmaceutical field.

Presenting BNCT at a big major conference like AACR was a big opportunity for BNCT and spreading the interest of BNCT to researchers who have not been familiar to BNCT would be also an important step to expand the BNCT in the future.



The room for BNCT session (A302) with a capacity for over 100 participants

The 10th Young BNCT Meeting 2019

Ignacio Porras
President of ISNCT
Departamento de Física Atómica, Molecular
y Nuclear Facultad de Ciencias
Universidad de Granada



The biannual meeting of the young researchers working in BNCT is an event that takes place since many years and it is consolidating as a fruitful moment to exchange ideas, train the newcomers in this research field and establish close networks across Countries. Young researchers can present their results, chair sessions, and give rise to discussion in a friendly and less official atmosphere. As we are all fostering BNCT as a future therapy to fight cancer, it is important to motivate and generate enthusiasm in the new generations of BNCT scientist. Welcome to the next edition of YBNCT in Finland!

Hanna Koivunoro
Medical Physicist at Neutron Therapeutics Inc
Finland



Dear Colleagues and Friends,

The 10th Young Member's Boron Neutron Capture Therapy (YBNCT) meeting will be held in **Helsinki Finland, September 26-29, 2019**. This year is remarkable in the history of BNCT. Finally, clinical accelerator based neutron sources are becoming a reality for BNCT. This year, the BNCT society is eagerly awaiting the results of the first clinical trials of head and neck, and brain cancer performed at the accelerator based BNCT facilities in Kyoto Research Reactor Institute and Southern Tohoku General Hospital, Japan. University of Tsukuba and Tokyo National Cancer Center are about to start the clinical trials using two different types of accelerator based neutron sources. At the same time, after some quiet years for clinical BNCT in Europe, the first Western accelerator based BNCT facility is under commissioning at Helsinki University Hospital in Finland.

The year 2019 is the year of the Pig, the last of the zodiac animals. According to a story, the Pig was late because he overslept. Another story says that a wolf destroyed his house. He had to rebuild his home before he could set off. When he arrived, he was the last one and could only take twelfth place. The Pigs are considered successful later in life, and associated with the wealth and fortune.

BNCT and the Pig share their spirit; ever since the emergent idea of G. L. Locher in 1936 and the first clinical trials by W. H. Sweet at Massachusetts General Hospital in 1951, BNCT has been slowly, but patiently built to become a promising radiotherapy modality. I trust BNCT will also be successful soon, later in its life. Thanks to the bright and enthusiastic BNCT researchers worldwide with the common aim, to make BNCT one additional therapy modality for cancer patients in need.

This year, we also celebrate the 10th anniversary of the biennial YBNCT meetings. The YBNCT meetings have been a great success ever since the first meeting in Petten, Netherlands, in 1999.

On behalf of the organizing committee, I proudly invite you to Helsinki during the foliage season to hear the latest BNCT news, listen to talks of BNCT researchers, and to enjoy the discussions with our cheerful young at heart society members.

Notice on the 16th Congress on Neutron Capture Therapy

President Minoru Suzuki
Professor, Institute for Integrated Radiation and Nuclear Science, Kyoto University



I am Minoru Suzuki from the Institute for Integrated Radiation and Nuclear Science, Kyoto University and I was appointed Chairman of the 16th Congress on Neutron Capture Therapy.

The Congress will be held on September 7th (Sat) and September 8th (Sun) 2019 at Uji Obaku Plaza in Uji Campus, Kyoto University, located in Uji City, Kyoto Prefecture.

For details, please refer to: (<http://jsnct16.umin.jp>) and we would appreciate it if many

of those concerned could participate. The theme of the 16th Congress is “Thinking about the Diversity in Neutron Capture Radiation (NCR) Research.” The aim of the theme is shown on the Congress website in the message from myself as the Congress Chairman. Hereby I would like to add a little bit more about the aim of the Congress.

The Japanese Society of Neutron Capture Therapy is an academic society which consists of researchers from diverse areas such as medicine, engineering, pharmacology, etc. “Neutron capture therapy” is a name of the treatment method and researchers with diverse backgrounds are working on their research with their own approach to advance the medical treatment called neutron capture therapy. As neutron irradiation is necessary for such research, many members of our society are jointly using the Kyoto University Research Reactor (KUR) at the Institute for Integrated Radiation and Nuclear Science, Kyoto University (hereinafter called ‘the Institute’) every year. About one third of the research topics adopted by the Institute in the year 2019 is related to neutron capture therapy.

As I mentioned on the Congress website, 6 years later KUR is scheduled to be shut down and decommissioned. Although utmost effort will be made to enable the provision of neutron irradiation field by accelerators after the KUR shut-down, I expect it would be difficult to have the same level of availability as the neutron irradiation field provided by KUR. In order to arrange a new neutron irradiation field at the Institute as well as arranging the neutron irradiation fields for the basic research in several locations in Japan, it is important to expand the range of neutron research. To that end, in this Congress, we hope that not only the above-mentioned research goal will contribute to the neutron

capture therapy which is a radiation therapy for cancer patients but also the research achievements or preliminary research achievements will be presented to give some inspiration to the research themes contributing to the entirely different disciplines.

With such expectation, the theme of this Congress was set forth as “Thinking about the Diversity in Neutron Capture Radiation (NCR) Research.” Boron Neutron Capture Therapy (BNCT) can play a role as a very unique radiation therapy, which destroys cancer cells selectively by NCR. If boron compound could be delivered to the arbitrary cell fraction in the body, such cell fraction could be exclusively destroyed. Basic research on selective irradiation of vascular endothelial cell and selective irradiation of macrophage is already reported as a B(NCR) research paper. Perhaps Auger electron by GdNCR could also produce some unique research achievements? As you can see, the research tool NCR could be applied to research in the disciplines such as radiobiology, botany, pharmacology, etc., which are unthinkable for a medical doctor like myself.

In this Congress, I do not expect that there will be so many research presentations which will take into account the diversity of NCR research. However, I hope that as many young researchers as possible will engage in unique research using neutron by applying NCR as one of their research tools, and in the future such research will involve other researchers around them. As a professor at the Institute, for many years I have been supporting the research of many researchers who jointly used KUR. From this experience, I strongly feel the significance of having to arrange the irradiation field for neutron capture therapy research.

Every year KUR is jointly used by many of those who are involved in neutron capture therapy. Many researchers including graduate students and young assistant professors are using KUR. When I see young researchers presenting their papers on their research achievements made by jointly using KUR, I feel happy as if they are my own research achievements. I truly hope that more and more young researchers will engage in basic research on neutron capture therapy or NCR basic research.

Some of you may find it difficult to get a sense of the theme of this Congress, “Thinking about the Diversity in Neutron Capture Radiation (NCR) Research.” I would be glad if you could understand from my message here that the theme implies our academic society’s determination that we are seriously going to work on expanding the range of NCR research towards the arrangement of the irradiation field for neutron capture radiation therapy research in the future. Finally, we hope that many of you will participate and register your presentation subject so that this academic congress will be a “hot” event, which is even hotter than the temperature in Kyoto on September 7th and 8th when the lingering summer heat is expected.



**We are happy to announce to you the definitive dates for next
year ICNCT meeting.**

Javier Praena

Congress Chair of ICNCT-19

Ignacio Porras

President of ISNCT



The Best Presentation Award of the 15th Annual Meeting of Japan Society for Neutron Capture Therapy

Development of the cylindrical neutron spectrometer for accelerator-based BNCT irradiation field.



Kentaro Baba
Graduate School of Biomedical Science and Engineering,
Hokkaido University

In recent year, accelerator-based neutron sources for BNCT have been developed. For estimation of the neutron energy spectrum, the Bonner sphere spectrometer combining neutron moderator with different sizes and neutron detector has been widely used. However, time and effort are required because it is necessary to change the moderator and make many measurements. Therefore, we focused on the Scintillator with Optical Fiber (SOF) detector, an ultra-small real-time thermal neutron detector. Most of the materials that make up the SOF detector are made of plastic, the effect of the SOF detectors on the neutron transport of the moderator is not greater compared to the case where the insertion holes are filled with moderator materials. Therefore, we considered that there is a possibility that neutron energy fluence can be estimated by one measurement by incorporating a plurality of SOF detectors in a row from the moderator surface and changing the depth. This is because even when the SOF detector is incorporated inside the moderator, it can be treated as a uniform moderator.

The cylindrical spectrometer was composed by combining an acrylic cylinder (material: PMMA, density: 1.18 g/cm^3 , diameter: 100 mm, length: 300 mm) and twenty-one SOF detectors. The SOF detector was placed from the position of 1.5 mm from the cylindrical surface along the central axis of the cylindrical moderator to the range of 201.5 mm from the cylindrical surface in 10 mm steps. The response function was calculated considering the angular distribution.

Measurements were performed using neutron beams in the Neutron Accelerator System for Biological Effect Experiments (NASBEE) at the National Institute of Radiological Sciences (NIRS), and neutron energy spectrum was evaluated by the unfolding method. Compared with the simulation result by the particle transportation Monte Carlo calculation code Geant4 ver.10.03.p03, the relative error of fast neutron fluence agreed with less than 1%, and the relative error of thermal and epithermal neutron fluence agreed with less than 10%. The proposed cylindrical neutron spectrometer was able to easily

obtain many measurements of different energy response characteristics by changing the depth at which the SOF detector was placed. Moreover, since there is a possibility that the neutron energy spectrum can be estimated by a single measurement, the system combining the SOF detector and the cylindrical moderator is considered to be a highly practical neutron spectrometer.

Finally, I would like to thank Prof. Masayori Ishikawa, the president of the 15th Neutron Capture Therapy Academic Conference, who selected this presentation as the best presentation award. I am grateful to Prof. Itsuro Kato for giving me the opportunity to write with the NCT Letter.

【reference】

1. M. Ishikawa, et al., Development of a wide-range paired scintillator with optical fiber neutron monitor for BNCT irradiation field study. *Nucl. Instrum. Meth. A* 551 (2005) 448-457.

The Best Presentation Award of the 15th Annual Meeting of Japan Society for Neutron Capture Therapy

Enhancing therapeutic potential of boronophenylalanine by controlling its metabolism using biocompatible polymers



Takahiro Nomoto¹, Yukiya Inoue¹, Ying Yao¹, Minoru Suzuki², Kaito Kanamori¹, Hiroyasu Takemoto¹, Makoto Matsui¹, Keishiro Tomoda¹, Nobuhiro Nishiyama¹

¹Laboratory for Chemistry and Life Science, Institute of Innovative Research, Tokyo Institute of Technology,

²Research Reactor Institute, Kyoto University

Boronophenylalanine (BPA) is taken up into a cell via the amino acid transporter LAT1, which is overexpressed in many tumor cells, and thus can selectively accumulate in tumors. In addition, a BPA derivative (¹⁸F-BPA) modified with fluorine (¹⁸F) permits companion diagnosis by positron emission tomography (PET), and BPA is an extremely useful drug in clinical practice. However, intravenously injected BPA does not always show long tumor retention. To maintain the intratumoral boron concentration necessary for obtaining a therapeutic effect, BPA needs to be additionally administered during thermal neutron irradiation. In clinical situations, BPA is additionally administered by infusion. However, this technique may complicate the procedures, resulting in increase of the treatment time spent on a patient. This raises the concern that usage time of neutron source cannot be efficiently utilized.

One possible explanation for the short retention time of BPA in tumors is the exchange transport mechanism of LAT1. When LAT1 takes an extracellular substrate such as phenylalanine into the cell, it exports the intracellular substrate such as glutamine. The reverse phenomenon may also occur. For example, when the extracellular BPA concentration decreases, extracellular amino acids are expected to be exchanged with intracellular BPA. A previous study about metabolic pathways of BPA indeed reported that intracellular boron concentration could be maintained at a high level in the absence of extracellular LAT1 substrates [*Radiat. Res.* **153**, 173-180 (2000)].

Hence, to avoid the unfavorable efflux of intracellular BPA, we conjugated multiple BPA molecules to a biocompatible polymer, polyvinyl alcohol (PVA) through

boronate esters. In this structure, the boronic acid moiety of BPA contributes to the conjugation, preserving the amino acid structure that has affinity for LAT1; thus, the PVA-BPA complex is expected to be recognized by LAT1 and internalized through endocytosis. Confocal laser scanning microscopy indeed illustrated that PVA-BPA was localized in endo/lysosomes whereas the fructose-BPA complex was transferred to the cytoplasm. In cellular uptake evaluation, a system L inhibitor significantly reduced the uptake of PVA-BPA. This evaluation also indicated that PVA-BPA retained in the cell for a longer time compared to fructose-BPA. These results suggest that PVA-BPA was taken up into cells through LAT1-mediated endocytosis, thereby suppressing the unfavorable efflux of BPA.

To investigate whether similar effects can be obtained in *in vivo*, we evaluated the accumulation of fructose-BPA and PVA-BPA in subcutaneous tumor models. Fructose-BPA showed extremely high tumor accumulation 1 h after intravenous injection, but significantly decreased the intratumoral boron concentration after 3 and 6 h. On the other hand, PVA-BPA could maintain the high concentration even after 6 h, reaching the tumor accumulation level equivalent to or higher than that of fructose-BPA 1 h after administration. In general, macromolecular drugs remain in the blood or accumulate in the liver, but the molecular weight of PVA used in this study was about 10,000, permitting efficient renal excretion and eventual quick clearance from the blood and normal tissues. To examine the effect of the intratumoral retention of BPA on the antitumor effect, BNCT was performed on subcutaneous tumors at the Kyoto University Research Reactor. PVA-BPA exhibited significantly higher antitumor activity than fructose-BPA. These results strongly indicate that PVA has the potential as an additive for improving the therapeutic potential of BPA. In this study, we used PVA as the platform because of its excellent safety. Since the dose of BPA is 500 mg/kg, the amount of the administered polymer is inevitably high. In this regard, PVA has an extremely simple structure and has been studied as a biocompatible material for many years; PVA has been used as a pharmaceutical additive. Furthermore, because PVA-BPA can be easily prepared by mixing PVA and BPA in water, ^{18}F -BPA with a short half-life is also expected to be easily incorporated into this system. To translate this research to practical application, we are currently optimizing the structure for a nonclinical study.

Finally, I would like to thank Prof. Masayori Ishikawa, Prof. Hiroyuki Nakamura, and Dr. Itsuro Kato for giving me the opportunity to introduce this study. I would also like to express my deep appreciation to Dr. Yoshinori Sakurai, Hiroki Tanaka, and Takushi Takata for their kind support in neutron irradiation.

The Best Presentation Award of the 15 th Annual Meeting of Japan Society for Neutron Capture Therapy

Development of neutron capture therapy using boron-binding adenovirus vector

Sayuru Tsuyuguchi, MD

Department of Neurosurgery, Graduated School of Biomedical and Health Sciences, Hiroshima University



The problem with boron neutron capture therapy (BNCT) for malignant glioma is their low permeability through the blood-brain barrier (BBB). Therefore, we have been addressing the research on development of novel boron drug delivery system (DDS) through the infection of the adenovirus vector conjugated with boron compound.

Human malignant glioma cell line, (U251MG) and replication-defective adenoviral vector expressing LacZ gene were used in this study. Evaluation of adenovirus gene expression was examined by β -gal staining. The boron compounds bound on the adenovirus surface were BODIPY, a fluorescent boron compound (CellTracker™ Green BODIPY®), and a colloidal gold compound (NANOGOLD), which binds to the SH-group on the virus surface via a maleimide group. Inductively coupled plasma atomic emission spectroscopy (ICP-AES) was used for intra-cellular boron determination. An electron microscope was used for determination the adenovirus vectors bound the NANOGOLD.

U251MG cells infected with BODIPY-conjugated adenovirus vector were yielded fluorescence, while the intracellular boron concentration was extremely small, and insufficient for BNCT. An electron microscope was shown that adenovirus vectors conjugated with NANOGOLD were detected in both cytoplasm and nucleus of the U251MG cells after infection of NANOGOLD-conjugated adenovirus vector. In addition, the expression of the LacZ gene was detected by β -Gal staining in the U251MG cells after infection of NANOGOLD-conjugated adenovirus vector.

The transfection efficiency could be maintained even when the NANOGOLD compound was bound on the adenovirus surface via a maleimide group in our study condition. In addition, adenoviruses are also accumulated in the nucleus, and we believe that BNCT can be expected to have a higher cell killing effect. Further studies with neutron irradiation has now been considered in order to apply boron compound-modified adenovirus for novel BNCT treatment as verifying the therapeutic effect and elucidating DDS.

As the next step, we are accumulating data on neutron irradiation experiments for boron compound-modified adenovirus, and we aim to apply it to future BNCT treatment by verifying the therapeutic effect and elucidating DDS.

In receiving the Special Award, Global Outstanding Achievement Award (18th ICNCT)

Koji Ono

Director

Kansai BNCT Medical Center, Osaka Medical College



It was my honor to receive the above award at the 18th International Congress on Neutron Capture Therapy held in Taipei from October 28th to November 2nd, 2018. The Congress bestows Hatanaka Award granted to researchers for their competent contributions and Fairchild Award granted to young researchers. Hatanaka Award is granted for contributions to research activities in individual area such as clinically specific cancer, chemistry, physics or biology, whereas, the Global Outstanding Achievement Award, as the name shows, has a different focus. This award honors comprehensive achievements in studies of BNCT. I assume that the staff concerned in the Congress in Taipei dared to give me the award to express their gratitude for my support for the Taiwan BNCT. I would first like to mention about this point. I first met Taiwan's BNCT researchers in October 2008 when the JASTRO Congress was held in Sapporo, through the mediation of Prof. Yasushi Nagata of the Department of Radiation Oncology, Hiroshima University (he is 9 years younger than me at Kyoto University). Another member of JASTRO, Prof. Junichi Hiratsuka of Kawasaki Medical School also joined the meeting. To my surprise, research on BNCT and preparation for starting clinical studies had already been in progress considerably in Taiwan. I was ashamed of myself for not knowing the fact. We then cooperated in the 1st case using the Tsing Hua Open Pool Reactor (THOR) at National Tsing Hua University and the 2nd case of BNCT for recurrent head cancer. I taught the Taiwanese researchers in detail about the two-step rate administration method of BPA, which was my idea, together with its background perspective, and also about the dose assessment method, perspectives on tumor dose and normal tissue dose, and CBE factor. The radiation facility of THOR, having been built after KUR and JRR4, has an excellent design presenting high neutron flux as well as optimum beam port height and collimator. It goes without saying that the success in the first 2 cases led to the continuing implementation of clinical studies. I also assisted in accepting Dr. Yi-Wei Chen and other doctors and medical physicists to Kyoto University Research Reactor Institute for training, and held some research meetings with the Taiwan group. For these purposes, my visit to Taiwan exceeded 10 times and, beyond this award, I had the honor of having my name mentioned twice with deep appreciation by Mr. Lee Teng-hui, the former President of

Taiwan, when he made a congratulatory speech at the international academic conference. Taiwan has become the second advanced country in the field of BNCT research after Japan in Asia. I look forward to the further development in Taiwan and would like to offer any support I can do.

BNCT is a therapy which is much more interdisciplinary compared with other radiation therapies. It relates with various areas of clinical radiology such as radiation oncology, nuclear medicine, and diagnostic radiology, as well as other related clinical areas and other basic areas such as physics, chemistry, pharmaceutical sciences and biology. Therefore, a headquarter to coordinate studies in these areas and successfully lead the whole research on BNCT is essential. A group with functions like the military staff headquarters is required. In 1991, I was transferred from Faculty of Medicine, Kyoto University to Kyoto University Research Reactor Institute (KURRI) in Kumatori. It was fortunate for me that the institute had Radiation Oncology and Medical Physics divisions that specify in BNCT research, and the cooperative division of Radiation Biology, which is why the KURRI has led BNCT research not only in Japan but also in the world from the 90s onward. Considering the role that KURRI should play, my group gave priority to basic research and technology development. Starting the research with Prof. Masunaga on the elucidation of the difference in radiation effects between BPS and BSH and working out how to overcome their respective weaknesses caused by the difference. Other researches include two-step rate administration method of BPA, BPA administration via intra-arterial tube, use of epi-thermal neutrons in place of thermal neutron, complete pre-setting of the patient's position and posture at the preparation room and automating transport to the irradiation room, joint basic research with Prof. Suzuki on application of BNCT to liver cancer, with medical physics group on central shield of irradiation field for improving depth distribution of neutrons, non-invasive injection of air into the dead space left after tumor resection, development of γ -telescope for liver cancer BNCT, joint research with Prof. Kinashi on the influence of whole-body exposure. I also led clinical studies, however, I left the initiated clinical studies to the doctors of the related departments as far as possible since the KURRI has no clinical hospital. I believe this expanded the network among researchers and cultivated their abilities. Based on the results of these studies, we were able to achieve the goal of developing the world's first BNCT dedicated neutron irradiation system in collaboration with Prof. Maruhashi's medical physics group and Sumitomo Heavy Industries, Ltd.

Irradiation in clinical trials has already been completed. I hope we can obtain the approval of BNCT from the Ministry of Health, Labour & Welfare in 2020 and start clinical BNCT using cyclotron neutrons.

More than 30 years have passed since I started studying BNCT, however, there are many points yet to be solved from the viewpoint of radiation oncology. I myself want to continue to tackle unsolved problems.

Hatanaka Award (18th ICNCT)

“On receiving the Hatanaka Award”

Mitsunori Kirihata

**Professor of the Laboratory for Medicinal Chemistry
for Boron Drug, Research Center for BNCT,
Organization for Research Promotion, Osaka Prefecture University**



Preface

I had an honor to receive Hatanaka Award at the 18th ICNCT held in Taipei on October 29th, 2018. My earning such distinction is fully attributed to the staff of the former Chemistry of Biological Control Laboratory and Laboratory for Medicinal Chemistry for Boron Drug, graduates and research students, and also to those who gave me direct and indirect assistance and cooperation through joint researches and obtaining competitive research funding. I would once again like to express my gratitude to everyone concerned.

① **“Memoir”**

I remember that I became involved with BNCT in 1987 or 88, a few years after I returned back from studying abroad. In those days, we considered natural non-protein amino acids (unusual amino acids) as the seeds for medicines and agricultural chemicals and used some of unusual amino acids having significant biological activity, including organophosphorus amino acid, as lead compounds to develop asymmetric synthesis method of such amino acids and to clarify the mechanism of the onset of activity and structure-activity correlation, employing techniques of organic chemistry. At that time, Dr. Yoshinori Kitaoka of KUR introduced us the cancer therapy using BNCT and the synthesis of D,L-BPA developed by Snyder. This became the springboard for me to get into this field. Since then, I added boron agent research as one of the themes of the graduation/master's theses, and in the 1990s, I conducted high-volume synthesis of D,L-BPA and its derivative with ethyl isocyanoacetate as the synthesizing element, asymmetric synthesis of L-BPA with bis-lactim ether as chiral auxiliary molecule, synthesis and biological evaluation of BPA derivative containing o-carborane, in order to clarify activity correlation between indispensable structure of BPA and tumor accumulation.

The ^{10}BPA BNCT initiated by Prof. Mishima in 1987 served as the basis for today's progress in BNCT. In those days, L- ^{10}BPA imported from the United States was expensive and had problems such as long delivery time and unstable supply. Clinical studies of ^{10}BPA BNCT showed progress in the 1990s and the demand for ^{10}BPA BNCT increased

accordingly, therefore, domestic production became necessary for stable supply in the late 1990s. I received requests for domestic production of L-¹⁰BPA from many doctors and professors and then I used to respond saying that domestic supply of ¹⁰B-boron (ingredient of L-¹⁰BPA) was the bottleneck.

The turning point was in 1999 when we came to know that a manufacturing plant of highly-condensed ¹⁰B-boron (Stella Chemifa Corporation) was located in the neighboring Izumiotsu City, just 15km away from our campus. Until then, I had assumed that all synthesis materials of ¹⁰B-boron had to depend on import from the US, therefore, knowing this was like a thunderclap to me. I was filled with surprise and gladness, and felt disappointed with myself at the same time for not knowing the local circumstances. Later, I visited the plant to confirm the manufacturing method of ¹⁰B-boron, its purity of condensation, quality and annual production. The condensed ¹⁰B-boron manufactured in the plant was useful not only for L-¹⁰BPA but also as a starting ingredient widely applicable to ¹⁰B-boron agents for BNCT, and thus was suitable for the domestic production of L-¹⁰BPA, solving the pending issues of ingredients.

In 2000, the demand for domestic production of L-¹⁰BPA and ¹⁰BSH increased further according to the increase in the number of cases. We considered that the overriding priority should be given to strong industry-academia-government collaboration to establish manufacturing methods of high-quality L-¹⁰BPA and ¹⁰BSH using domestic technology and domestically-produced ¹⁰B-boron, with the purpose of developing new drugs. Upon this view, a research consortium in which universities, industries and research facilities participate was constructed in 2002. Moreover, a laboratory base was organized in 2005 in the Innovation Plaza Osaka (later closed down) of the Japan Science and Technology Agency (JST) established in Izumi City. We got two competitive research funds (for ‘practical realization test’ and ‘development research for commercialization’) from JST. By that, we established high-volume production of L-¹⁰BPA and ¹⁰BHS, and obtained and accumulated numerous data for the production. Our experience of the industry-academia-government collaboration and joint research in the Plaza Osaka served as a base for making the highly reliable research proposal thereafter. In 2014, it also became a driving force for constructing a laboratory base for boron agent development aiming at medical realization of BNCT, and with the support of the Ministry of Economy, Trade and Industry, the BNCT Research Center was established in Nakamozu Campus, and the research activities continue to this day.

② “Message”

It is said that BNCT has almost reached its medical realization, however, some issues are yet to be solved. In the chemical and pharmaceutical area, development of a new boron agent more effective than L-¹⁰BPA or ¹⁰BSH is the most important issue. Boron agents for BNCT differ from ordinary pharmaceutical agents in quality and behavior. The traditional way of drug discovery, seeking new drugs from a number of boron compounds, prevails at present, however, boronated molecular-targeted drugs and middle-molecular drugs, and effective DDS are expected to be developed in the future. I yearn for young researchers of the next generation to proceed with the research on boron agents from a new perspective based on a steady basic research.



**BNCT Research Center,
Osaka Prefecture University**

Hatanaka Award (18th ICNCT)

“On receiving the Hatanaka Award”

Junichi Hiratsuka

**Professor of the Department of Radiation Oncology,
Kawasaki Medical School**



I was honored with the Hatanaka Award with the recommendation of the JSNCT members in the 18th ICNCT. I would like to express my sincere gratitude. I believe that the basic research and clinical studies I have done to the extent I can do have led to this award, and am now recalling the past with deep emotion.

In 1983, the late Prof. Yutaka Mishima of the Department of Dermatology, Kobe University invited me to the “Research on development of nuclear reactor therapy by metabolic activity of malignant melanoma” group of the Education Ministry’s Special Research I. I was expected to conduct radiobiological study in relation to BNCT. It was three years after graduation when I joined the group, and I was obliged to attend the group meeting (2 ~ 3 times per year). The discussions were difficult for me to understand thoroughly, but I remember I was drawn into the atmosphere of the seriousness and academic discussions of the professors and doctors. At the first group meeting I attended (1984), discussion was made on the existence of BPA toxicity, existence of the selectivity of melanoma cells and systemic pharmacokinetics. ‘¹⁰B-chlorpromazine’ had been used before BPA. Each time I see BPA being commonly administered at present, I recall the group meeting of those days. Among the members of those days were Professors Hidetake Kakihana, Kazuo Yoshino, Keiji Kanda, Toru Kobayashi and Hiroshi Fukuda. As a member of the group, I started research on radiation biology. Since Prof. Fukuda had been working on cell experiments, I focused on animal experiments using pigs, hamsters and mice (Fig. 1). Under such circumstances, I was very surprised to see the reaction where a huge naturally expressed melanoma in a pig disappeared by BNCT, and at the same time, I decided to keep on involved in BNCT research/clinical practice into the future (Fig. 2). In 1987, the world’s first BNCT using BPA was conducted in a case of melanoma occurred in occipital subcutaneous layer (NCT-1) (nuclear reactor, Musashi Institute of Technology). It was very lucky for me to join the medical team then. Medical irradiation has been continued thereafter and now the case number of the latest patient file in the bookshelf in my room is NCT-118 (treatment about 4 cases/year). Being involved in BNCT made me learn a lot firsthand: ①clinical practice is built upon the downright base

of basic medicine; ②importance of teamwork; ③necessity of exchanging opinions with doctors and professors of other areas; and ④importance of continuing research. BNCT has a high potential. I look forward to continuing working together with the BNCT staff. Especially I hope young researchers keep “importance of continuing research” in mind. Finally, I would like to give my heartfelt thanks to everyone for supporting my research activity. Thank you very much. I hope to continue working with you all.

The Fairchild Award of the 18th International Congress on Neutron Capture Therapy

Collimator Design of T/N-SPECT for BNCT

Saki Shibata

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1. Introduction

One of the most important issues we should solve for BNCT is realization of visualization of the treatment effect (local dose) in real-time. The author's group has been developing a SPECT system to monitor the three-dimensional treatment effect during BNCT, named BNCT-SPECT. The BNCT-SPECT can measure prompt gamma-rays of 478 keV emitted from residual excited ${}^7\text{Li}$ nucleus via ${}^{10}\text{B}(n, \alpha){}^7\text{Li}$ reaction, in order to know the treatment effect. In the present study, we develop a SPECT system to estimate T/N ratio (${}^{10}\text{B}$ concentration ratio of tumor to normal tissue) by measuring 2.22 MeV gamma-rays emitted via ${}^1\text{H}(n, \gamma)$ reaction being normally a background signal, in addition to measuring 478 keV gamma-rays. This system is called T/N-SPECT. The present report describes design study results of the detection element and collimator of the T/N-SPECT to be used in a very severe neutron background environment.

2. Calculation condition

Figure 1 shows the calculation model taking into account all the items existing in a real irradiation room. We set the statistical accuracy as the estimation index considering (1) thickness of the detection element, (2) collimator length and (3) collimator radius. And the image updating period was assumed to be less than 10 min. The T/N-SPECT was designed to meet the statistical accuracy to be less than 5%. In the calculation, we employed MCNP5 as a Monte Carlo transport code and estimated flux by F4 tally, flux and reaction rate by F5 tally and gamma-ray pulse height spectrum by F8 tally. Other conditions are as follows: The tumor size is 3cm in diameter, the head diameter is 20cm, and the source is a 10 keV broad parallel beam of 15 cm in diameter. As the detection element, a GAGG(Ce) scintillator was selected since it had a suitable energy resolution and detection efficiency for T/N-SPECT.

3. Calculation results

3.1 Thickness of detection element (GAGG)

With a typical calculation model like Fig. 1, the statistical accuracy of the number of counts was examined for the thickness of GAGG from 2 cm to 10 cm. As a result, for over 6 cm the statistical accuracy did not change largely. This is because the detection efficiency was saturated. From this, the thickness of the detection element was fixed to be 6 cm.

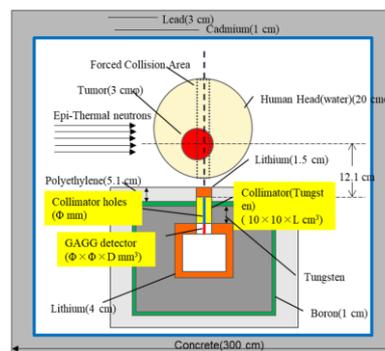


Figure 1 Calculation model.

3.2 Collimator length

If changing the collimator length and/or collimator radius, the spatial resolution can accordingly change. However, the spatial resolution is a crucial physical value, because it should be required to meet the medical doctor's query, i.e., less than 0.5 cm. In the present examination, we carried out calculations with variables of collimator length and spatial resolution. Besides, we set goals of the image updating period of less than 5 min. and the statistical accuracy of less than 5 %.

Calculations were performed for collimator length from 25 cm to 65 cm and spatial resolution from 3.5 mm to 6.5 mm. As a result, the best statistical accuracy was obtained for collimator length of 55 cm. Hence, the collimator length of T/N-SPECT was fixed to be 55 cm.

3.3 Collimator radius

Figure 2 shows the statistical accuracies for the spatial resolution change as a function of image updating period from 3 min. to 10 min. for the collimator length of 55 cm. Designs to meet the statistical accuracy goal of 5 % were realized as in the following table.

Table 1 Final design results.

<u>Spatial resolution (Collimator radius / length)</u>	<u>Image updating period</u>
5.5 mm (4.57 mm / 55 cm)	9 min.
6.0 mm (4.97 mm / 55 cm)	6 min.
6.5 mm (5.37 mm / 55 cm)	4 min.

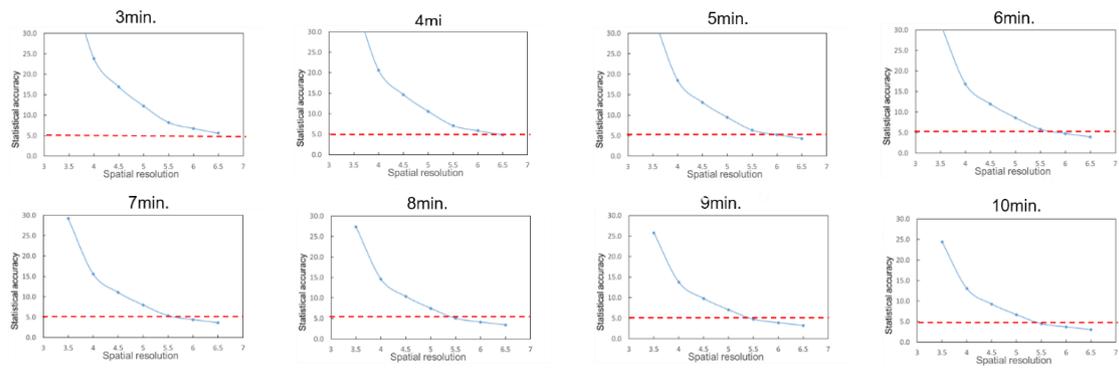


Figure 2 Relation of spatial resolution and statistical accuracy as a function of image updating period for collimator length of 55 cm.

4. Summary

In the present study, we were finally not able to realize the design meeting all the requirements, i.e., statistical accuracy of less than 5 %, spatial resolution of less than 5 mm and image updating period of less than 5 min. However, the obtained designs mostly reached the requirements, which could still be available depending on the medical doctor’s query. In the next step, we will try to develop a prototype detector and examine the performance by experiments.

Acknowledgement

Finally, the author would like to express her sincere gratitude to Prof. Isao Murata for his encouragement of preparation of the presentation for the Conference, and to Prof. Itsuro Kato for his having given a chance to me to submit a report to NCT 1

The Fairchild Award of the 18th International Congress on Neutron Capture Therapy

Development of a prompt gamma ray imaging detector using LaBr₃(Ce) scintillator and arrayed MPPC for boron neutron capture therapy



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Introduction

To evaluate the prescribed dose of BNCT, it is necessary to obtain ¹⁰B concentration in blood, normal and tumor tissues. In general, the information on ¹⁰B concentration in blood has been acquired by ICP methods or a high purity germanium detector at KUR before the treatment. However, these procedures cannot measure ¹⁰B concentration in real time. It is required that the information on ¹⁰B concentration is obtained in real time to evaluate the prescribed dose during the treatment. Thus, we have been developing a prompt gamma-ray imaging detector that consisted of a slab of LaBr₃(Ce) scintillator and an 8 x 8 array multi-pixel photon counter (MPPC). In this paper, we report the characteristics of our detector system.

Materials and methods

Our detector system was composed of a slab of LaBr₃(Ce) scintillator which was 50 mm x 50 mm x 10 mm, an 8 x 8 array MPPC, an amplifier unit, a shaper, and an ADC. An MPPC can detect the scintillation light from this scintillator, and amplified signals send to a PC. Lastly, we can get 64 channels' gamma-ray spectra on a PC. During experiments, we set up operating voltages to adjust each gain of an MPPC. First of all, the energy resolution for the 511 keV gamma-ray peak was evaluated with a source of ²²Na. In addition, we obtained 64 gamma-ray spectra when thermal neutrons irradiated samples loaded with boric acid whose concentration was 50 and 5000 ppm. The thermal neutron flux was 1.0 x 10⁵ n/cm²/s at 1 MW.

Results

The energy resolution for the 511 keV peak was 5.7 % on average. This energy resolution was sufficient to discriminate between 478 and 511 keV gamma-ray peaks. The 478 keV peak overlapped the 511keV peak, but we discriminated between the two gamma-ray peaks by defining two Gaussian distributions for each gamma-ray. After the elimination of the effect from 511 keV peak where the peak overlapped the 478 keV peak, we got the two-dimensional distribution of 478 keV gamma rays.

The impression of this conference

I learned lots of research that were performed in other countries through this conference, and I discussed my research topic with other researchers. This meeting was extremely wonderful. This meeting had a get-together where we could have a traditional dinner. This is my incentive to continue my research; thus, I will attend international conferences proactively.

I would like to appreciate Prof. Fong-In Chou giving me the Fairchild ward. Also, I appreciate Dr. Kato giving me this opportunity to write this article.



The ceremony



Members of my laboratory at banquet

Recipient of the Fairchild award at the 18th International Congress on Neutron Capture Therapy

Neutron beam quality measurement of an accelerator-based neutron source using microdosimetric technique

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Introduction

An accelerator-based neutron source is gaining interest due to its ability to perform treatments, such as BNCT in a hospital environment. Currently, many facilities are trialling accelerator based BNCT. The accelerator-based neutron source at Aomori prefecture Quantum Science Center (QSC) is primarily used for cell and small animal studies. In a typical BNCT field, there exists many different types of radiation with each having a different biological effect. To maximise the treatment efficiency, it is important to understand the beam quality of the neutron source. Microdosimetry is a technique used to measure radiation in a mixed field. Using this technique, it is possible to derive the relative contributions of each radiation component. A tissue equivalent proportional counter (TEPC) measures energy deposition in a simulated micrometer scale volume comparable to that of a living cell. The TEPC uses material and gases that are essentially equivalent to human tissue in chemical composition. This study aims to measure the microdosimetric quantities of an accelerator-based neutron source utilised for BNCT research using a tissue equivalent proportional counter (TEPC). The experimental data obtained with the TEPC was also compared against Monte Carlo simulation.

Material and method

The accelerator-based neutron source at QSC consists of a 20 MeV proton beam and a beryllium target. A moderator system was designed to slow down the fast neutron component to increase the thermal neutron flux. The microdosimetric spectrum was measured using the Far West Technology Inc. LET 0.5 inch TEPC. The counter was filled with a methane-based tissue equivalent gas at a pressure of 74.5 hPa to simulate a 1 μm diameter sphere. The neutron beam was measured at the centre of the field using the TEPC during approximately one hour in a free-air condition

Results

The absorbed dose from events exceeding $20 \text{ keV}/\mu\text{m}$ measured free in air for a one-hour irradiation was calculated as $1.31 \pm 0.02 \text{ Gy}$. The simulated results were $1.41 \pm 0.07 \text{ Gy}$. The measured and calculated values exhibit good agreement. The relative biological effectiveness (RBE) that was evaluated from the measured microdosimetric spectrum was calculated as 3.7 ± 0.02 , similar to the simulated value of 3.8 ± 0.1 .

Conclusion

The microdosimetric spectrum of the QSC accelerator-based neutron source was successfully measured. The results showed the PHITS Monte Carlo simulation can simulate both micro and macrodosimetric quantities accurately.

My experience at the 18th ICNCT in Taiwan

This was my first time presenting at the ICNCT. I had the opportunity to meet many researchers and exchange valuable ideas. The scientific sessions were interesting and extremely educational, and I am very grateful to my supervisors for supporting me.

Finally, we would like to thank the president of the 18th ICNCT, Prof. Fong-In Chou and the selection committee members for selecting myself as one of the recipients of the Fairchild award. In addition, we would like to thank Dr. Itsuro Kato for offering us the opportunity to publish our work in this letter.



Figure 1. Members of the research lab at the Institute for Integrated Radiation and Nuclear Science. (Author: Far right)



Figure 2. Strange dancing doll

that appeared at the banquet.

Article-introduction of the topic

1. <Biology >

Title: Eosinophil depletion suppresses radiation-induced small intestinal fibrosis

Authors: Naoki Takemura, Yosuke Kurashima, Yuki Mori, Kazuki Okada, Takayuki Ogino, Hideki Osawa, Hirosih Matsuno, Lamichhane Aayam, Satoshi Kaneto, Eun Jeong Park, Shintaro Sato, Kouta Matsunaga, Yusuke Tamura, Yasuo Ouchi, Yutaro Kumagai, Daichi Kobayashi, Yutaka Suzuki, Yoshichika Yoshioka, Junichi Nishimura, Masaki Mori, Ken J. Ishii, Mark E. Rothenberg, Hiroshi Kiyono, Shizuo Akira, Satoshi Uematsu

The source: Science Translational Medicine, 2018 Feb 21; 10(429)

<https://stm.sciencemag.org/content/10/429/eaan0333/tab-pdf>

Presented by **Lichao Chen** (Department of Frontier Life Sciences, Nagasaki University Graduate School of Biomedical Sciences)



2. <Medicine >

Title: Boron neutron capture therapy for high-grade skull-base meningioma

Authors: Koji Takeuchi, Shinji Kawabata, Ryo Hiramatsu, Yoko Matsushita, Hiroki Tanaka Yoshinori Sakurai, Minoru Suzuki, Koji Ono, Shin-Ichi Miyatake, Toshihiko Kuroiwa

The source: Physics in Medicine & Biology (2017) 62: 4421- 4439

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6133692/>

Presented by **Yusuke Fukuo** (Department of Neurosurgery and neurovascular therapy, Osaka Medical College Hospital)



3. <Physics>

Title: Fast neutron dose evaluation in BNCT with Fricke gel layer

detectors

Authors: G. Gambarini, G. Bartesaghi, J. Burian, M. Carrara, M. Marek, A. Negri, L. Pirola, L. Viererbl

The sources: Radiation Measurements 45 (2016) 1398-1401

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5100278/>

Presented by *Yuto Murakami, et al* (Graduate School of Engineering, Hiroshima University)

4. <Pharmacology>

Title: Design, synthesis, and evaluation of lipopeptide conjugates of mercaptoundecahydrododecaborate for boron neutron capture therapy

Authors: Aoi Isono, Mieko Tsuji, Yu Sanada, Akari Matsushita, Shinichiro Masunaga, Tasuku Hirayama, and Hideko Nagasawa

The sources: ChemMedChem (2019) 14 : 823-832

<https://chemistry-europe-onlinelibrary-wiley-com.remote.library.osaka-u.ac.jp:8443/doi/full/10.1002/cmdc.201800793>



Presented by *Kazuki Kawai* (Laboratory for Chemistry and Life Science Institute of Innovation Research, Tokyo Institute of Technology)

Editor's Postscript

On the Publication of NCT letter Vol. 6

Chief Editor of NCT letter

Itsuro Kato

The 2nd Department of Maxillofacial Surgery, Graduate School of Dentistry, Osaka University



I would like to take this opportunity to wish every success to all of the members of the Japanese Society of Neutron Capture Therapy (JSNCT). We could publish the NCT letter No. 6 supported by the all of contributors. The members I worked with for the NCT letter were Prof. Mitsuko Masutani of the department of Frontier Life Sciences, Nagasaki University Graduate School of Biomedical Sciences and Dr. Teruyoshi Kageji of the department of Neurosurgery, Tokushima Prefectural Kaifu Hospital as editors and Prof. Hideki Matsui of the department of Physiology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences as an advisor. This time also we sought advices from Prof. Hiroyuki Nakamura, the president of this Society.

The number of pages of NCT letter No. 6 was increased compared with that of No.5, because both manuscripts of awardees of BNCT related conferences and those whose reports BNCT related topic in the conference which is unrelated to BNCT were increased.

It means that the activities of JSNCT members were evaluated at domestic and foreign societies. Prof. Matsumura reported that BNCT session had been picked up as a major symposium at American Association of Cancer Research (AACR) 2019 at US as written in P 22. And Dr. Hirose, K. in Southern Tohoku BNCT center had presented "Safety and antitumor activity of accelerator-based BNCT in patients with inoperable recurrent and locally advanced head and neck cancer. -A phase II study" at poster session in American Society of Clinical Oncology (ASCO) in 2019, 5/31-6/4 at Chicago, whose report was not written in this letter.

I expect and wish every success to all of the members of JSNCT.

I will try to send an activity of all member to foreign countries as much as possible at real time, through linking HP of International Society of Neutron Capture Therapy (ISNCT) to that of JSNCT.

I want to take up the media news, the transfer of the member, a new plan, an article about BNCT including the contribution to this letter desired widely. I am happy if I can give frank opinion, information of members to me. Thank you for your cooperation.