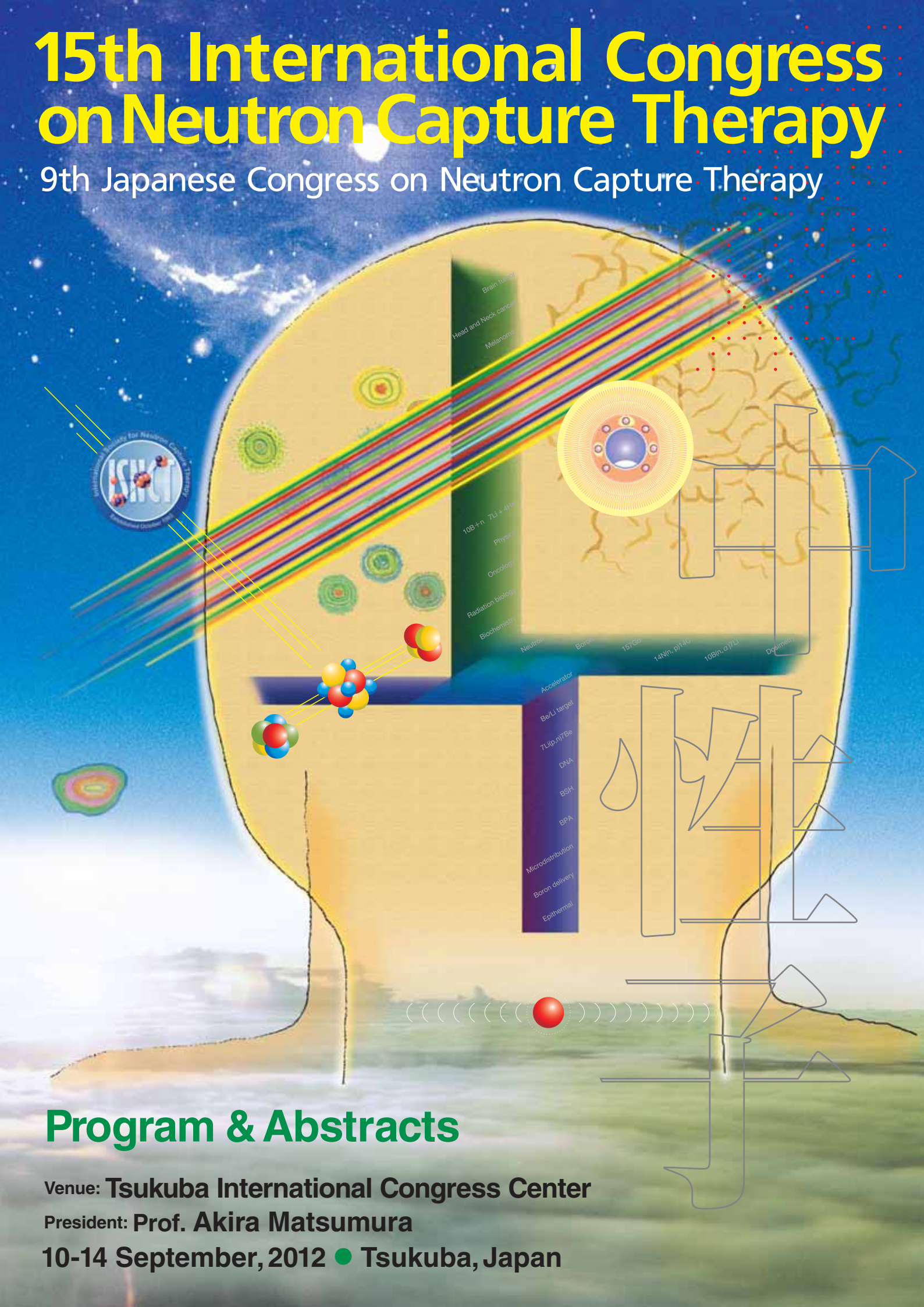
15th International Congress on Neutron Capture Therapy

9th Japanese Congress on Neutron Capture Therapy



Program & Abstracts

Venue: Tsukuba International Congress Center

President: Prof. Akira Matsumura

10-14 September, 2012 ● Tsukuba, Japan

15th International Congress on Neutron Capture Therapy

9th Japanese Congress on Neutron Capture Therapy

Program & Abstracts

Date
10-14 September, 2012

Venue
Tsukuba International Congress Center
Tsukuba, Japan

President
Prof. Akira Matsumura

Cosponsored by
Association for Nuclear Technology in Medicine

Cover illustration & design:
Co.,LTD designFF+I.Fukuzawa+M.Takada

CONTENTS

Dear Colleagues,

The 15th International Congress on Neutron Capture Therapy will take place in September 2012, marking the 30th anniversary of the biennial ICNCT.

Boron Neutron Capture Therapy is attracting increasing interest and demand as the "next-generation charged particle therapy" after proton or carbon ion therapy since it is the only radiation therapy that can focus on the cellular level.

The emerging interest in creating in-hospital accelerator-based BNCT is also increasing. This meeting will be a good opportunity to raise discussion about the realization of such an accelerator to make a paradigm shift in radiation therapy.

When accelerator-based BNCT becomes feasible, other research fields such as the fields of boron carriers and dosimetry will also be activated due to the broadening of therapeutic opportunity.

I invite all my colleagues to the 15th ICNCT and hope that it will be the occasion for fruitful discussion towards the development of neutron capture therapy as one of the standard therapies in radiation oncology in the near future.

With sincerest regards and hopes of meeting you in Tsukuba, Japan.

Akira Matsumura

University of Tsukuba.
President of the International Society for Neutron Capture Therapy & 15th ICNCT and 9th JCNCT

15th International Congress on Neutron Capture Therapy
Congress Committees

Local Organizing Committee

Akira Matsumura[1]
– President

Hideyuki Sakurai[2]
– Vice President

Tetsuya Yamamoto[1]
– Secretary General

Kei Nakai[1]

Masahide Matsuda[1]

Hiroaki Kumada[2]

Alexander Zaboronok[1]

Tomoya Takada[1]

Kyoji Tsuda[1]

Naoko Tanaka[1]

Yoshiko Saito[1]

1 *Department of Neurosurgery, Faculty of Medicine, University of Tsukuba*

2 *Proton Medical Research Center, University of Tsukuba*

Scientific Committee

Akira Matsumura,
Amanda Elena Schwint,
Andrea Wittig,
Andres J. Kreiner,
David Nigg,
Detlef Gabel,
Fong-In Chou,
Garth Cruickshank,
Grazia Gambarini,
Gustavo Santa Cruz,
Hanna Koivunoro,
Hideki Ichikawa,
Hiroki Tanaka,
Hiroyuki Nakamura,
Iiro Auterinen,
Javier Praena,
Junichi Hiratsuka,
Kei Nakai,
Kenichi Tanaka,
Kensuke Okuda,
Koji Ono,
Kumada Hiroaki,
Leena Kankaanranta,
Ling-Wei Wang,
Masaharu Hoshi,
Masakazu Yoshioka,
Masayori Ishikawa,
Milan Marek,
Ming-Hua Hsu,
Mitsunori Kirihata,
Mladen Mitev,
Paolo Colautti,
Raymond Moss,
Rolf Barth,
Sara Gonzalez,
Saverio Altieri,
Sergey Taskaev,
Shin-Ichi Miyatake,
Shin-Ichiro Masunaga,
Silva Bortolussi,
So Kamada,
Stead Kiger,
Stuart Green,
Teruyoshi Kageji,
Tetsuo Matsumoto,
Tetsuya Yamamoto,
Tooru Kobayashi,
Wolfgang Sauerwein,
Yhan-Hao Liu,
Yoshinobu Nakagawa,
Yoshinori Sakurai,
Yukio Nagasaki,
Yuko Kinashi

Award Recipients

Hatanaka Award:

Raymond Lloyd Moss

Fairchild Award: (alphabetical)

Fernanda Faião Flores

Maria S. Herrera

Marina Perona

Ming-Chen Hsiao

Ruben Oscar Farias

Ryohei Uchida

Tobias Schmitz

Yuki Hirota

The History of ICNCT

1st	Cambridge, USA	Brownell and Fairchild	1983 12-14 October
2nd	Tokyo, Japan	Hiroshi Hatanaka	1985 18-20 October
3rd	Bremen, Germany	Detlef Gabel	1988 31 May-3 June
4th	Sydney, Australia	Barry J. Allen	1990 4-7 December
5th	Columbus, USA	Albert J. Soloway	1992 14-17 September
6th	Kobe, Japan	Yutaka Mishima	1994 31 Octber-4 November
7th	Zurich, Switzerland	Borje Larsson	1996 4-7 September
8th	La Jolla, USA	Frederick Hawthorne	1998 13-18 September
9th	Osaka, Japan	Keiji Kanda	2000 2-6 October
10th	Essen, Germany	Wolfgang Sauerwein	2002 8-13 September
11th	Boston, USA	Robert Zamenhof	2004 11-15 October
12th	Takamatsu, Japan	Yoshinobu Nakagawa	2006 9-13 October
13th	Florence, Italy	Aris Zonta	2008 2-7 November
14th	Buenos Aires, Argentina	Sara J. Liberman	2010 25-29 October
15th	Tsukuba, Japan	Akira Matsumura	2012 10-14 September
16th	Helsinki, Finland	Leena Kankaanranta	2014

*ICNCT International Congress on Neutron Capture Therapy
（9th Japanese Congress on Neutron Capture Therapy）

Venue Location

JR Line + Bus

■ from Akihabara Station (Tsukuba Express)

45 minutes to **Tsukuba station** by rapid train ➡ 10 minutes walk from Tsukuba station A3 or A4 exit

■ from Ueno Station (JR Joban line)

- 43 minutes to **Tsuchiura station** by Limited express train ➡ Take the bus to "**Tsukuba center**" (25 minutes) ➡ Get off **Tsukuba center** ➡ 8 minutes on foot
- 60 minutes to **Hitachino-Ushiku station** by local train ➡ Take the bus to "Tsukuba center" (25 minutes) ➡ Get off **Tsukuba center** ➡ 8 minutes on foot

Highway bus

■ from Tokyo Station

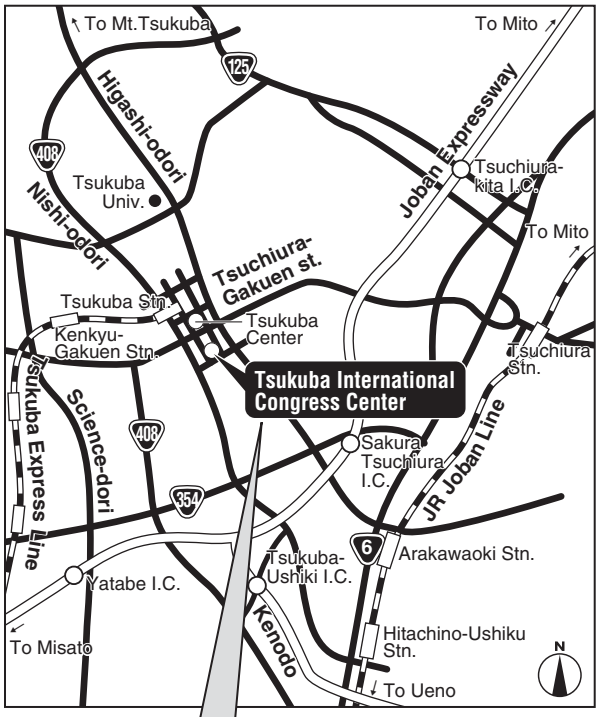
65 minutes by "**Tsukuba-Go**" from **Yaesu-South Exit** ➡ Get off **Tsukuba center** ➡ 8 minutes on foot

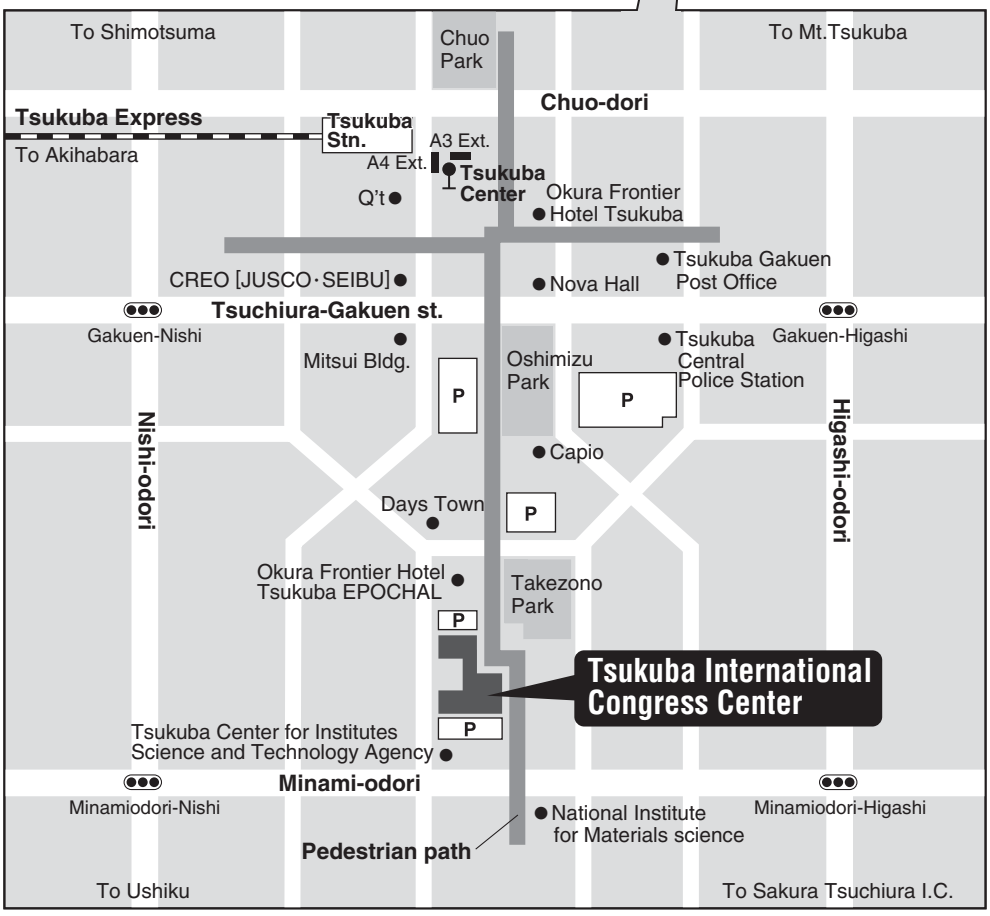
■ from Haneda Airport

80 minutes by bus ➡ Get off **Tsukuba center** ➡ 8 minutes on foot

■ from Narita Airport

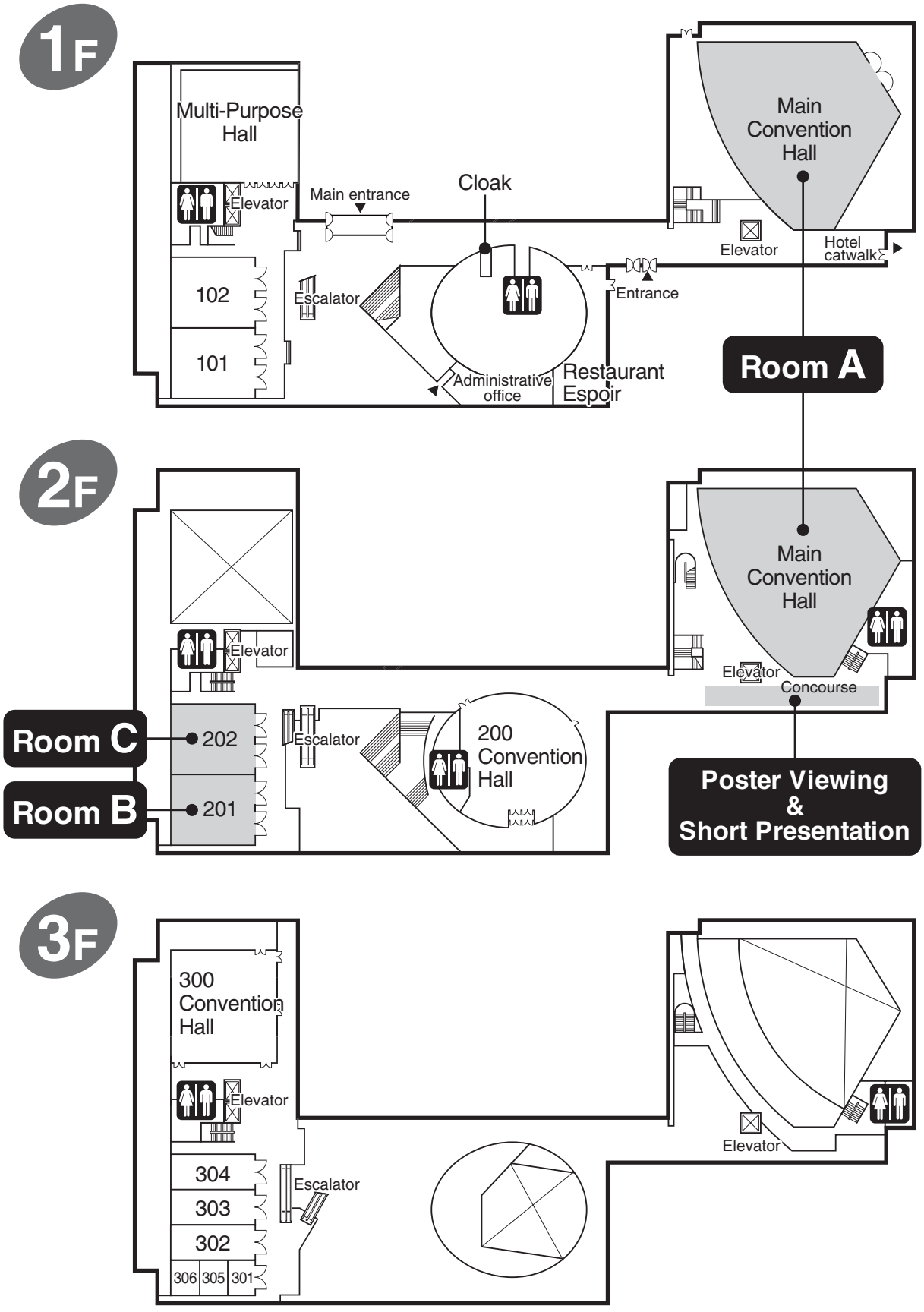
100 minutes by **Airport Liner (NATT'S)** ➡ Get off **Tsukuba center** ➡ 8 minutes on foot



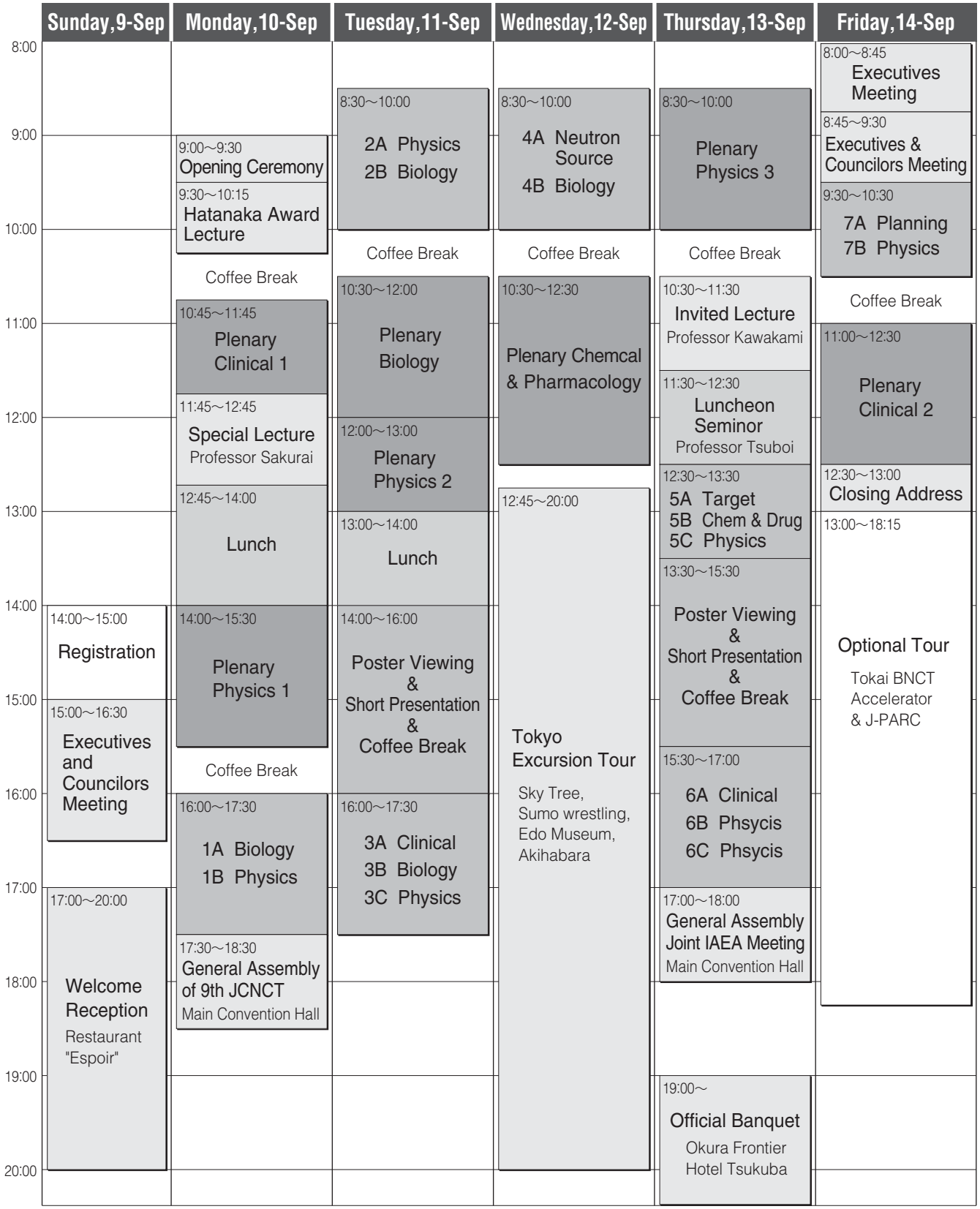


Floor Map

Tsukuba International Congress Center



Time Table


Sunday,9-Sep
Monday,10-Sep
Tuesday,11-Sep
Wednesday,12-Sep
Thursday,13-Sep
Friday,14-Sep
8:00
9:00
10:00
11:00
12:00
13:00
14:00
15:00
16:00
17:00
18:00
19:00
20:00
14:00～15:00 Registration
15:00～16:30 Executives and Councilors Meeting
17:00～20:00 Welcome Reception Restaurant "Espoir"
9:00～9:30 Opening Ceremony
9:30～10:15 Hatanaka Award Lecture
Coffee Break
10:45～11:45 Plenary Clinical 1
11:45～12:45 Special Lecture Professor Sakurai
12:45～14:00 Lunch
14:00～15:30 Plenary Physics 1
Coffee Break
16:00～17:30 1A Biology 1B Physics
17:30～18:30 General Assembly of 9th JCNCT Main Convention Hall
8:30～10:00 2A Physics 2B Biology
Coffee Break
10:30～12:00 Plenary Biology
12:00～13:00 Plenary Physics 2
13:00～14:00 Lunch
14:00～16:00 Poster Viewing & Short Presentation & Coffee Break
16:00～17:30 3A Clinical 3B Biology 3C Physics
8:30～10:00 4A Neutron Source 4B Biology
Coffee Break
10:30～12:30 Plenary Chemcal & Pharmacology
12:45～20:00 Tokyo Excursion Tour Sky Tree, Sumo wrestling, Edo Museum, Akihabara
8:30～10:00 Plenary Physics 3
Coffee Break
10:30～11:30 Invited Lecture Professor Kawakami
11:30～12:30 Luncheon Seminor Professor Tsuboi
12:30～13:30 5A Target 5B Chem & Drug 5C Physics
13:30～15:30 Poster Viewing & Short Presentation & Coffee Break
15:30～17:00 6A Clinical 6B Phsycis 6C Phsycis
17:00～18:00 General Assembly Joint IAEA Meeting Main Convention Hall
19:00～ Official Banquet Okura Frontier Hotel Tsukuba
8:00～8:45 Executives Meeting
8:45～9:30 Executives & Councilors Meeting
9:30～10:30 7A Planning 7B Physics
Coffee Break
11:00～12:30 Plenary Clinical 2
12:30～13:00 Closing Address
13:00～18:15 Optional Tour Tokai BNCT Accelerator & J-PARC

Congess Information

Congess Secretariat Information

Place: Room H103, 1st floor, Tsukuba International Congress Center

Office hours:

Sunday, 9-Sep: 14:00-17:00
Monday, 10-Sep: 8:00-17:00
Tuesday, 11-Sep: 8:00-17:00
Wednesday, 12-Sep: 8:00-12:00
Thursday, 13-Sep: 8:00-17:00
Friday, 14-Sep: 8:00-13:00

Phone: 029-861-0610 (Use "81" instead of the first "0" for international call)

Registration Desk

Place: Entrance of Main Convention Hall, 2nd floor

Opening hours:

Sunday, 9-Sep: 14:00-20:00 (17:00-20:00 at the Restaurant Espoir)
Monday, 10-Sep: 8:00-17:00
Tuesday, 11-Sep: 8:00-17:00
Wednesday, 12-Sep: 8:00-12:00
Thursday, 13-Sep: 8:00-17:00
Friday, 14-Sep: 8:00-13:00

Social Program

Sunday, 9-Sep

Welcome Reception

Venue: Restaurant Espoir, Tsukuba International Congress Center

Time: 17:00- 20:00

Thursday, 13-Sep

Social Dinner

Venue: Okura Frontier Hotel Tsukuba ANNEX
(NOT Hotel Okura Frontier EPOCHAL)

Time: 18:30 (welcome drink), 19:00 (start)

Takes 10 minutes from the Tsukuba International Congress Center to the venue pedestrian walkway, or you can go by taxi. A special shuttle bus will circulate on the route between The Congress Center (Hotel EPOCHAL) and The Hotel Okura Frontier Tsukuba from 18:00.

Internet Service

WiFi is available in the Tsukuba International Congress Center.
The information about WiFi is provided at the registration desk.

Official Language

English is the official language in this congress. A simultaneous translation service is not provided.

Sightseeing and Technical Tours

Tokyo downtown and Sumo Wrestling Tour

Tour time: 13:00-18:00, September 12th (Wednesday)

Visits place: Tokyo Sky Tree (drive through), Sumo Matches ~the September Tournament~ (venue: Kokugikan), Edo-Tokyo Museum (optional), Akihabara Electric Town

Meeting point: Meeting point: Main entrance hall of the congress center

Fee: 14,000 JPY

Tokai Accelerator Tour

Tour time: 13:00 – 18:00, September 14th (Friday)

Visits place: BNCT facility and J-PARC at Tokai

Meeting point: Main entrance hall of the congress center

Fee: Free of Charge

Instructions for Chairpersons and Speakers

For Oral Session Chairpersons

- On the session day, you are requested to visit the "chairperson and speaker's reception" in front of the conference hall up to 10 minutes before the beginning of the session you will chair.
- After the reception, please take a seat in the "next chairperson's seat" in the conference room up to 5 minutes before the session starts.
- Chairpersons will preside over the sessions. Please be sure not to exceed the scheduled time.

For Oral Session Speakers

- Presentation time table
  - ・Symposium (plenary session)

    The allocated time of the speech is 15 minutes, followed by 4-minute discussion.
  - ・Oral presentation (parallel session)

    The allocated time of the speech is 10 minutes, followed by 4-minute discussion.
- Please save your PowerPoint data with embedded font either in a CD-Rom or USB memory device and deliver it to the PC Center. Windows is the only operating system available for the presentations. If you have prepared the presentation data on a Macintosh, you are advised to bring your own PC that has display output interface with D-sub 15 pin. Please check if your PC has a D-sub 15 pin connector and if not please bring necessary equipment. For those wishing to show a movie, we recommend that you bring your own PC.
- Please submit your data to the PC Center, and check whether all the data are shown properly.
- If you do use your own PC, please check your presentation data at the PC center and bring your PC to the operation desk in the session room 30 minutes prior to the start of the session. Following the conclusion of your session, we will return your PC to you at the operation desk. Please come to the operation desk to take it.
- After data function conformation, please visit the "chairperson and speaker's reception" in front of the conference hall up to 10 minutes before the session starts; please, take a seat in the "next speaker's seat" in the conference room up to 5 minutes before the session.

For Poster Session Chairpersons

- The Poster Session Area is organized according to abstract categories. Poster sessions are divided into 3 according to poster numbers.
- Chairpersons are requested to visit the Poster Reception Desk up to 15 minutes before the beginning of the session they will chair and to be in front of the Poster Session Area no later than 5 minutes prior to the start of the session.
- The session schedule should be controlled and managed by the chairpersons.
- Please return the ribbon to the Poster Reception Desk when your session is finished.

For Poster Speakers

- Please check the Poster Session Area shown on the board at the Poster Reception Desk to find the location of your assigned poster board. Presenters are requested to mount their posters on the assigned board.
- Poster panels are 180 cm high × 116 cm wide. The upper part of the panel (13.5 cm high × 100 cm wide) will be used for labeling your poster title, affiliation, and authors' names, which should be prepared by presenters.
- Presentation time schedule: the allocated time of the speech is 4 minutes, followed by 2-minute discussion.
- Sticky tape for hanging the poster is attached to each panel.
- Presenters are requested to be in front of the poster panels no later than 5 minutes prior to the start of the session.

Program

10/Sep/Monday

Opening Ceremony (Main Convention Hall) **Room A**

Opening address Akira Matsumura (Chairman of 15th ICNCT, Professor & Chairman, Department of Neurosurgery, Faculty of Medicine, University of Tsukuba)

Welcoming address Masaru Hashimoto (Governor of Ibaraki Prefecture)
Nobuhiro Yamada (President of the University of Tsukuba)

Hatanaka Lecture 9:30 AM (Main Convention Hall) **Room A**

Session Chair: Akira Matsumura

BNCT – A Multi-Disciplinary Task

Raymond Lloyd Moss, M.Sc., Ph.D. Energy Systems Evaluation Unit, Institute for Energy/JRC Petten, European Commission, The Netherlands

Special Lecutre 11:45 AM (Main Convention Hall) **Room A**

Session Chair: Koji Ono

Proton beam therapy at University of Tsukuba –present & future–

Hideyuki Sakurai, M.D., Ph.D. Director, Proton Medical Research Center (PMRC)University of Tsukuba, Tsukuba City, Japan

13/Sep/Thursday

Invited Lecutre 10:30 AM (Main Convention Hall) **Room A**

Session Chair: Yoshinobu Nakagawa

Clinical trial, development, and regulatory environment of therapeutic medical device

Koji Kawakami, M.D., Ph.D. Professor and Chairman, School of Medicine and Public Health, Kyoto University, Kyoto, Japan
Deputy Vice President (Research), Kyoto University
Director (acting), Clinical Trial Management, Kyoto Univ. Hospital Translational Research Center
Adjunct Professor, Keio University Clinical Research Center

Lunchon Seminor 11:30 AM (Main Convention Hall) **Room A**

Session Chair: Akira Matsumura

Cell Inactivation Ability of High-Energy Proton Beams

Koji Tsuboi, M.D., Ph.D. Professor, Proton Medical Research Center, University of Tsukuba, Tsukuba City, Japan

Program

10/Sep/Monday

Plenary Clinical 1

(Main Convention Hall) **Room A**

Session Chairs: Teruyoshi Kageji, Ling Wei Wang

10:45 AM **01** **Pilot Clinical Study of Boron Neutron Capture Therapy for Recurrent Hepatic Cancer and Gastric Cancer**

Hironobu Yanagie (Japan)

The University of Tokyo, Department of Nuclear Engineering & Management, Cooperative Unit of Medicine & Engineering, The University of Tokyo Hospital

11:05 AM **02** **Boron Neutron Capture Therapy for Recurrent Head and Neck Malignancies**

Itsuro Kato (Japan)

Osaka University Department of Oral and Maxillofacial Surgery

11:25 AM **03** **Background and trial design of the Phase I, open label, dose escalation study for safety and tolerability of boron neutron capture therapy (BNCT) using boronophenylalanine (SPM-011) / accelerator BNCT system (BNCT30) for the patients with recurrent malignant glioma**

Shinji Kawabata (Japan)

Osaka Medical College, Department of Neurosurgery

Plenary Physics 1

(Main Convention Hall) **Room A**

Session Chairs: Hiroaki Kumada, Saverio Altieri

2:00 PM **01** **Feasibility Study on Pinhole Camera System for Online Dosimetry in Boron Neutron Capture Therapy**

Tatsuya Katabuchi (Japan)

Research Laboratory for Nuclear Reactors, Tokyo Institute of Technology

2:20 PM **02** **Alanine detector measurements in phantom and free in-air at the FiR 1 beam**

Iiro Auterinen (Finland)

VTT Technical Reserch Centre of Finland

2:40 PM **03** **Methods for dose measurements in small phantoms irradiated at NCT epithermal column**

Grazia Gambarini (Italy)

Physics Department, Università degli Studi di Milano, Milan, Italy

3:00 PM **04** **Study on detecting spatial distribution of neutrons and gamma rays using multi imaging plate system**

Kenichi Tanaka (Japan)

Sapporo Medical University, Center of Medical Education

Oral Session 1A biology

(Main Convention Hall) **Room A**

Session Chairs: Rolf Barth, Amand Elena Schwint

4:00 PM **01** **Combination therapy of BPA-BNCT and 5-ALA-PDT in Experimental Tumor Model**

Norio Miyoshi (Japan)

University of Fukui, Faculty of Medicine, Department of Tumor Pathology

4:15 PM **02** ***In vitro*** **and** ***In vivo*** **Studies on The Effects of L-Dopa Pre-Loading on the Uptake of Borononophenylalanine Using the F98 Glioma and B16 Melanoma Models**

Weilian Yang (United States)

Department of Pathology, The Ohio State University

4:30 PM **03** **Therapeutic efficacy and toxicity of single and double application BNCT protocols in an oral precancer model in hamster**

Amanda E. Schwint (Argentina)

National Atomic Energy Commission, Argentina

4:45 PM **04** **Preliminary *in vivo* tests on murine tumour models of MRI-guided NCT through a new Gd/B compound**

Nicoletta Protti (Italy)

University of Pavia, Department of Physics, Italy

5:00 PM **05** **Histological and biochemical analysis of DNA damage after BNCT rat tumor model**

Mitsuko Masutani (Japan)

Division of Genome Stability Research, National Cancer Center Research Institute

Oral Session 1B physics

(Main Convention Hall) **Room A**

Session Chairs: Tetsuo Matsumoto, Mladen Mitev

4:00 PM **01** **The impact of different source definition techniques on the simulated irradiation field of the TRIGA Mainz**

Matthias Blaickner (Austria)

AIT Austrian Institute of Technology, Vienna, Austria, Health & Environment Department

4:15 PM **02** **Microdosimetric Comparison for Irradiation Characteristics of Two BNCT Facilities in Kyoto University**

Tetsuya Mukawa (Japan)

Graduate School of Engineering, Kyoto University

4:30 PM **03** **The room scattering influence at THOR BNCT facility**

Ming-Chen Hsiao (Taiwan R.O.C.)

National Tsing Hua University, Institute of Nuclear Engineering and Science

4:45 PM **04** **Response evaluations of ionization chambers to develop Multi Ionization-Chamber System for Boron Neutron Capture Therapy**

Takaaki Fujii (Japan)

Kyoto University, Department of Nuclear Engineering

5:00 PM **05** **Investigation on F/M material aspects of IRT-Sofia NCT channel**

Mladen Mitev (Bulgaria)

Institute for Nuclear Research and Nuclear Energy of the Bulgarian Academy of Sciences

5:15 PM **06** **BNCT Hyperthermal beam B2 at RA-6 reactor: Configuration and performance of the new therapeutic facility**

Juan Manuel Longhino (Argentina)

Comisión Nacional de Energía Atomica.

33 **Are high energy proton beams ideal for AB-BNCT ? A brief discussion from the viewpoint of fast neutron contamination control and BSA shielding design**

Pei-Yi Lee (Taiwan)

National Tsing Hua University, Institute of Nuclear Engineering and Science

Poster Viewing 2F 2:30 PM 2F, Concourse

Session Chair: Paolo Colautti

34 **Beam shaping assembly optimization for $^{7}Li(p,n)^{7}Be$ reaction accelerator based BNCT**

Daniel Minsky (Argentina)

Gerencia de Investigación y Aplicaciones, Comisión Nacional de Energía Atómica

35 **Optimum design of moderator system based on dose calculation in the accelerator for Boron Neutron Capture Therapy**

Ryuichi Inoue (Japan)

Hokkaido University, Graduate School of Engineering

36 **Neutronic Design on a Small Accelerator-Based Be-9 (p, n) Neutron Source for Boron Neutron Capture Therapy**

Fujio Hiraga (Japan)

Hokkaido university, Quantum Science and Engineering, Faculty of Engineering

37 **Radiation fields of an accelerator neutron source**

Gennadiy Malyshkin (Russia)

Russian Federal Nuclear Center - Zababakhin All-Russian Scientific Research Institute of Technical Physics, Snezhinsk, Chelyabinsk Region, Russia

38 **Regimes of therapeutic beam forming for accelerator neutron source**

Elena Kashaeva (Russia)

Russian Federal Nuclear Center - Zababakhin All-Russian Scientific Research Institute of Technical Physics, Snezhinsk, Chelyabinsk Region, Russia

39 **An Improved Epithermal Neutron Source Design for BNCT Application**

A.X. Chena (USA)

Mechanical Engineering Dept., University of California, Berkeley, CA. 94720 USA

Oral Session 6A clinical (Main Convention Hall) Room A

Session Chairs: Shin-Ichi Miyatake, Garth Gruickshank

3:30 PM **01** **Bevacizumab for progressive radiation necrosis: Preliminary results and ongoing clinical trial**

Shin-Ichi Miyatake (Japan)

Osaka Medical College, Department of Neurosurgery

3:45 PM **02** **Case numbers for a randomized clinical trial of boron neutron napture therapy for Glioblastoma multiforme**

Detlef Gabel (Germany)

Jacobs University

4:00 PM **03** **BNCT in Argentina: An Interdisciplinary Approach**

Gustavo A. Santa Cruz (Argentina)
Department of BNCT, Division of Nuclear Chemistry and Health Sciences, National Atomic Energy Commission.

4:15 PM **04** **Introducing the BNCT option in a national health care system – the Finnish experience**

Iiro Auterinen (Finland)
VTT Technical Research Centre of Finland

Oral Session 6B physics

(201) **Room B**

Session Chairs: Sara Gonzalez, Masaharu Hoshi

3:30 PM **01** **Assessing an accelerator-based facility for Boron Neutron Capture Therapy in the treatment of different tumor targets**

María S. Herrera (Argentina)
Accelerator Technology and Applications, National Atomic Energy Commission (CNEA)

3:45 PM **02** **Application of a Bonner sphere spectrometer for the determination of the angular neutron energy spectrum of an accelerator-based BNCT facility**

Nafiseh Mirzajani (Italy)
University of Pisa,Department of Mechanical, Nuclear and Production Engineering

4:00 PM **03** **Reappraisal of the optimal neutron energy characteristic and spectrum for accelerator-based epithermal neutron source — PHITS analysis and trial production of the moderator —**

Masaru Nakamura (Japan)
Cancer Intelligence Care Systems, Inc., Department of R&D

4:15 PM **04** **Fusion-based neutron irradiation facility for explanted organ BNCT: dosimetry assessment**

Manuel Leonardo Sztejnberg (Argentina)
Instrumentation and Dosimetry Division, Instrumentacion and Control Department, CNEA

4:30 PM **05** **Collimator Design for Array-type CdTe Detector for BNCT-SPECT**

Masanobu Manabe (Japan)
Division of Electrical,Electronic of Information Engineering ,Osaka

5:45 PM **06** **Field improvements by changes in the irradiation compartment in the BNCT research facility at IEA-R1**

Paulo de Tarso Dalledone Siqueira (Brazil)
IPEN/CNEN-SP, Instituto de Pesquisas Energéticas e Nucleares, Comissão Nacional de Energia Nuclear

Oral Session 6C physics

(202) **Room C**

Session Chairs: Hanna Koivunoro, Grazia Gambarini

3:30 PM **01** **The effect of boron neutron capture therapy in melanoma cells using In-Hospital Neutron Irradiator**

Youxin Zhou (China)
Neurosurgery & Brain and Nerve Research Laboratory, The First Affiliated Hospital of Soochow University, Suzhou, Jiangsu, China

3:45 PM **02** **Analysis of the implementation of local background dose enhancers from beta radiation using aluminum pieces for use in treatment of cutaneous malignant melanoma in Boron Neutron Capture Therapy**

Esteban Fabián Boggio (Argentina)
Comisión Nacional de Energía Atómica, Gerencia de Área de Energía Nuclear, Departamento de Física de Reactores y Radiaciones

4:00 PM **03** **Microdosimetric features of LENA neutron irradiation vane**

Paolo Colautti (Italy)
INFN Legnaro National Laboratory

4:15 PM **04** **Track annealing studies of PADC track etch detector for the $^{10}B(n, \alpha)^{7}Li$ reaction rate measurement**

Barbara Smilgys (Brazil)
Department of Cosmic Rays and Chronology, Institute of Physics Gleb Wataghin, State University of Campinas

4:30 PM **05** **Pushing for Breakthrough in Boron Neutron Capture Therapy Technology Development**

K.J. Bradley (Hong Kong)
Neopanora Hong Kong Research & Development Centre Limited

4:45 PM **06** **The FiR 1 photon beam model adjustment according to in-air spectrum measurements with the Mg(Ar) ionization chamber**

Hanna Koivunoro (Finland)
HUS Medical Imaging Centre, Helsinki University Central Hospital

Oral Session 7A planning

(Main Convention Hall) **Room A**

Session Chairs: Raymond Moss, Hiroaki Kumada

9:30 AM **01** **Amaranthus - the new open source hadron therapy planning system**

Anastasia Makarova (Russia)

National Research Nuclear University "MEPhI", Department of Medical Physics

9:45 AM **02** **Physical neutron dosimetry for the university of pavia thermal neutron source for BNCT research**

Nicoletta Protti (Italy)

University of Pavia,Department of Physics

10:00 AM **03** **A general approach for calculating photon-isoeffective doses in clinical BNCT**

Sara J. Gonzalez (Argentina)

National Atomic Energy Commission (CNEA), Instrumentation and Control.

10:15 AM **04** **MultiCell model as an optimized strategyfor BNCT treatment planning**

Ruben Oscar Farias (Argentina)

Comision Nacional de Energia Atomica

Oral Session 7B physics

(201) **Room B**

Session Chairs: Yhao Hao Liu, Hiroki Tanaka

9:30 AM **01** **Dose measurements with primary and supplementary techniques in the Birmingham epithermal beam**

Zamir Ghani (United Kingdom)

School of Physics and Astronomy, University of Birmingham

9:45 AM **02** **Shielding Calculation for BNCT facility using the Neutron Shield Concrete**

Koichi Okuno (Japan)

HAZAMA corporation

10:00 AM **03** **New Materials for BNCT Neutron Beam Optimization**

Valeriy Korobeinikov (Russia)

State Scientific Center Institute of Physics and Power Engineering

10:15 AM **04** **Near-threshold ^{7}Li(p,n)^{7}Be Neutrons on the Practical Conditions using Thick Li-target and Gaussian Proton Energies for BNCT**

Tooru Kobayashi (Japan)

Kyoto University, Research Reactor Institute

Plenary Clinical 2

(Main Convention Hall) **Room A**

Session Chairs: Wolfgang Sauerwein, Hiratsuka Junichi

11:00 AM **01** **Fractionated BNCT for Locally Recurrent Head and Neck Cancer: Experience from a Phase I/II Clinical Trial at Tsing Hua Open-Pool Reactor**

Ling-Wei Wang (Taiwan, ROC)
Taipei Veterans General Hospital, Cancer Center

11:20 AM **02** **BNCT for Carotid lesion of Head and Neck Cancer**

Teruhito Aihara (Japan)
Kawasaki Medical School

11:40 AM **03** **Clinical use of PET amino acid imaging in boron neutron capture therapy for malignant brain tumor**

Tadashi Nariai (Japan)
Tokyo Medical and Dental University, Department of Neurosurgery

12:00 AM **04** **BNCT can significantly prolong the survival of recurrent malignant glioma cases**

Shin-Ichi Miyatake (Japan)
Osaka Medical College, Department of Neurosurgery

Abstracts

10/Sep/Monday

Hatanaka Lecture

BNCT – A Multi-Disciplinary Task

Raymond Lloyd Moss

Special Lecutre

Proton beam therapy at University of Tsukuba –present & future–

Hideyuki Sakurai

13/Sep/Thursday

Invited Lecutre

Clinical trial, development, and regulatory environment of therapeutic medical device

Koji Kawakami

Lunchon Seminor

Cell Inactivation Ability of High-Energy Proton Beams

Koji Tsuboi

9:30 AM

BNCT – A Multi-Disciplinary Task

Raymond Lloyd Moss, M.Sc., Ph.D.

Energy Systems Evaluation Unit, Institute for Energy/JRC Petten,
European Commission, The Netherlands

BNCT is a bi-modal form of radiotherapy that to be a success not only requires, from the functional point of view, the preferential uptake of boron-10 into each tumour cell and the delivery of a sufficient fluence of thermal neutrons to those cells, but also can only be carried out with an efficient multidisciplinary collaboration between medicine and biology, nuclear and medical physics, chemistry and pharmacology, mathematics and information technologies, etc. Moreover, each discipline cannot function alone and requires a multi-tasking nature such that, for example, a radiotherapist needs at times to think like a reactor physicist, a surgeon needs to understand radiation biology, a chemist needs to think on pharmacokinetics, etc. Furthermore, the whole symphony can only be created if there is a multidisciplinary, multi-tasking, multi-functioning conductor coordinating the whole orchestra. The conductor needs also to conduct quality assurance measures, administrative tasks and, at times, a diplomatic task to bring the different players together at the right time. This presentation will rely heavily on the experience gained while coordinating many of the above actions to realise BNCT at Petten. It will also give the opportunity to reflect on the perspectives for BNCT in the coming years and on some of the achievements attained during my time in BNCT.

EDUCATION:

University Degree was in Mathematics, followed by Ph.D. in Applied Mathematics from Nottingham University (UK) in 1975.

PROFFESSIONAL EXPERIENCE:

1. UK Atomic Energy Authority (UKAEA), 1975-1980 – reactor technology
2. Royal Dutch/SHELL Research, Amsterdam, 1980-83 – fracture mechanics
3. Joint Research Centre of the European Commission, Petten, The Netherlands, 1983 – today (almost 30 years service) – research reactor experiments, beam tube experiments, leading to BNCT
   Currently employed in Critical Metals/materials for the European energy market, with still some work in BNCT (prompt gamma measurements, writing publications, reviewer to BNCT papers), radiation protection officer for the Institute in Petten

ACTIVITIES in BNCT:

- Became involved in BNCT in 1987, when the HFR Petten was chosen as the test bed for BNCT in European Commission
- Led from the start the Petten activities, including coordinating the design and building of the different stages of the BNCT facilities
- Technical Coordinator of the Clinical Trials in Petten
- Involved in training of many young BNCT researchers (PhD students, post-docs)
- Organised (co-organised) numerous workshops, symposia, lectures in BNCT
- Secretary-General of the Tenth ICNCT, Essen 2002
- From 2000-2008, Secretary/Treasurer of the ISNCT
- Author/co-author of well over 100 publications/books in BNCT

Session Chair: Koji Ono

11:45 AM

Proton beam therapy at University of Tsukuba –present & future–

Hideyuki Sakurai, M.D., Ph.D.
Director, Proton Medical Research Center (PMRC)
University of Tsukuba, Tsukuba City, Japan

The University of Tsukuba started proton studies in 1983 using a synchrotron for physics studies at the High Energy Accelerator Research Organization (KEK). In 2000, a new in-house facility, called the Proton Medical Research Center (PMRC), was constructed adjacent to the University Hospital. The PMRC is equipped with a synchrotron and two rotating gantries. PMRC focuses mainly on cancers commonly found in Japanese people, such as liver cancer, lung cancer, prostate cancer, esophageal cancer and brain or skull base tumors. From September 1983 to March 2012, 2998 patients were treated in PMRC. Mont important work by PMRC has been an establishment of proton beam therapy (PBT) for hepatocellular carcinoma (HCC), which is a good model to demonstrate advantages of PBT. Most HCC develops in patients with cirrhosis of the liver, with its associated liver insufficiency, it is essential that therapy for HCC spares uninvolved liver tissue to minimize the risk of further impairment of the hepatic function. All tumors were irradiated using the respiratory gating method. The overall local control rate due to PBT is about 90 %, and approximately 50 % of patients survive over 5 years. PBT for HCC is now an appropriate option, especially for the elderly, or insufficient liver function, and for patients with portal vein tumor thrombosis.

At present, the PMRC is conducting 6 ongoing clinical trials for HCC, lung cancer, AVM, pediatric cancer and melanoma. PMRC would like to go into new clinical area using proton, such as “PBT with multimodality treatments” for advanced cancer, “hypofractionation” for photon resistant tumors, and “salvage therapy” for recurrent tumor. PMRC is also going to establish new machine for BNCT combined with PBT near future. Further efforts at PMRC Tsukuba are required for an establishment of new technique, better clinical protocols, and personnel training for professional.

EDUCATION and CERTIFICATIONS:

1988	M.D. (Medicine), Gunma University, Gunma, Japan
1992	Research fellow, MRC, Cambridge, UK
1996	PhD. (Medicine, Radiation Oncology), Gunma University, Gunma, Japan

PROFFESSIONAL EXPERIENCE:

1991	Instructor, Department of Radiation Oncology, Gunma University, Gunma, Japan
2001	Assistant Professor, Department of Radiation Oncology, Gunma University, Gunma, Japan
2006	Associate Professor, Department of Radiation Oncology, Gunma University, Gunma, Japan
2008.7.	Professor & Chairman, Department of Radiation Oncology, University of Tsukuba, Ibaraki, Japan
2008.10.	Director, Proton Medical Research Center (PMRC), University of Tsukuba, Ibaraki, Japan

ACADEMIC ACTIVITIES:

Japanese Society of therapeutic radiology and oncology (JASTRO)
European Society of therapeutic radiology and oncology (ESTRO)
American Society of therapeutic radiology and oncology (ASTRO)
Japan Radiological Society
The Japanese Cancer Association
Japan Society of Clinical Oncology
The Japanese Breast Cancer Society
The Japan Esophageal Society
The Japan of Lung Cancer
Japanese Society of Hyperthermia Oncology

AWARDS:

2000	Research Award in International Association of the Sensitization of Cancer Treatment
2001	Research Award in Kitakanto Medical Society
2001	Umegaki Memorial Award in JASTRO
2002	Best Paper Award in Japanese Society of Hyperthermia Oncology
2006	Memorial Award in International Association of the Sensitization of Cancer Treatment
2008	Abe Memorial Award in Japanese Society of Thermal Medicine

Session Chair: Yoshinobu Nakagawa

10:30 AM

Clinical trial, development, and regulatory environment of therapeutic medical device

Koji Kawakami, M.D., Ph.D.

Professor and Chairman, School of Medicine and Public Health,
Kyoto University, Kyoto, Japan
Deputy Vice President (Research), Kyoto University
Director (acting), Clinical Trial Management, Kyoto Univ. Hospital Translational Research Center
Adjunct Professor, Keio University Clinical Research Center

There is a variety of differences between drugs and medical devices in terms of clinical usage, regulatory pathway, and approval. Classification of medical devices contains 4 categories (class I to IV) and accordingly, required data to be submitted to regulatory agency is vary. In this lecture, regulatory and clinical environment of medical device development in Japan, USA, and EU will be discussed. Also, the current movement of clinical development of medical device in Japan will be delivered.

EDUCATION and CERTIFICATIONS:

MD	4/24/1997	Tsukuba University, Japan
PhD	3/31/2001	Yokohama City University, Japan

PROFFESSIONAL EXPERIENCE:

10/1/2011-present	Deputy Vice President (Research)	Kyoto University School of Medicine
3/1/2006-present	Professor and Chairman	Kyoto University, Japan
12/1/2004-2/28/2006	Associate Professor	University of Tokyo, Japan
5/1/2002-11/30/2004	IND reviewer (visiting associate)	Food and Drug Administration, USA

OFFICIAL ACTIVITIES:

2009-	Committee Member, Health Research Advisory Board Committee, Japan Cabinet
2007-	Project Member, Science and Technology Project, Life Science Policy Development, Japan Cabinet
2009-	Committee Member (R&D), Industrial Structure Advisory Committee, Ministry of Economy, Trade and Industry (METI)
2008-	Committee Member, Science and Technology Policy and Innovation, Ministry of Education, Culture, Sports and Technology (MEXT)
2007-	Committee Member, Health Science Advisory Committee (Technology), Ministry of Health, Labour and Welfare (MHLW)

AWARDS:

2004, 2003	Excellence in IND review, FDA-CBER
2003	Scientific Achievement award, FDA-CBER

INTERNTIONL MEETINGS:

2008-	Board Member (Regulatory Science), International Bio-EXPO
2009-	Development Committee, Fuculty in Regulatory Science, International Society for Biological Therapy of Cancer (iSBTc)

Session Chair: Akira Matsumura

11:30 AM

Cell Inactivation Ability of High-Energy Proton Beams

Koji Tsuboi, M.D., Ph.D.

Professor, Proton Medical Research Center, University of Tsukuba, Tsukuba City, Japan

The biological properties of high-energy protons were not fully understood. Here, I demonstrate *in situ* DNA double strand breaks (DSB), apoptosis, loss of clonogenicity as well as oxidative base-damage induced by high-energy protons with a comparison to X-rays.

Two human tumor cell lines ONS76 and MOLT4 were irradiated with10 MV X-rays or 200 MeV proton beams. *In situ* DDBS were evaluated by immunocytochemical analysis of γH2AX foci. Yield of apoptosis was measured by flowcytometry after Annexin-V and PI staining. Standard clonogenic survival assays were performed to obtain relative biological effectiveness (RBE) of protons to X-rays. For base-damage measurements, salmon testes DNA (ST-DNA) solution and MOLT-4 cells were irradiated with 200 kV X-rays or 155 MeV proton beams at plateau or near Bragg peak. 8-Hydroxydeoxyguanosine (8-OHdG) production was measured by high performance liquid chromatography. DSB in ST-DNA were evaluated by agarose gel electrophoresis.

Yields of γH2AX foci were always higher in proton than in X-ray irradiation with factors being 1.14 -1.44 in ONS76 and MOLT4. Proton beams induced apoptosis earlier than X-rays and the final yield of cell death was significantly greater in proton than X-ray irradiation. The ratios of apoptosis induced by proton beams and X-rays were 1.01-1.52 at 12 hours after irradiation in MOLT4. RBE of proton to X-ray at 10% survival and ratio of SF2 in clonogenic survival assay were 1.07 and 1.11, respectively in ONS76 cells. Furthermore, 8-OHdG yields in ST-DNA were significantly higher in X-ray than in proton irradiation. Also, DSB yields in ST-DNA were higher in protons than in X-rays. Although γH2AX foci formation in MOLT-4 cells after each irradiation was almost identical, the addition of the radical scavenger edaravone significantly suppressed foci formation only in X-ray irradiation.

Although the proton RBE values in the colony formation assay were within the range previously reported, the inductions of DSB and apoptosis were significantly higher in proton than in X-ray irradiation. In addition, the percentage of radical-induced indirect DNA damage was significantly lower in proton than in X-ray irradiation. Thereby, the underlying mechanisms in cell inactivation differ between these radiation qualities.

EDUCATION and CERTIFICATIONS:

1980 March	Graduated from School of Medicine, University of Tsukuba
1980 May	Medical License (M.D.)（No. 252820）
1982 May	E.C.F.M.G. certificate (No. 311-856-9)
1986 August	Japanese Board of Neurosurgery（No. 2026）
1986 December	Doctor of Medical Science (Ph.D.): University of Tsukuba (No. 384)

PROFFESSIONAL EXPERIENCE:

1980 April - 1986 March
Resident in Surgery, Emergency Medicine, Anesthesiology, Neurosurgery, University Hospital of Tsukuba

1986 April - 2004 March
Assistant Professor in Neurosurgery, University Hospital of Tsukuba

2004 April - 2006 February
Assistant Professor, Doctoral Programs in Functional and Regulatory Medical Sciences, Graduate School of Comprehensive Human Sciences, University of Tsukuba

2006 March -Present
Professor, Proton Medical Research Center, University of Tsukuba

1989 October - 1991 September
Visiting Scientist in Radiation Biology, Life Sciences Division, Los Alamos National Laboratory

1997 April – 1997 September
Visiting Scientist in Molecular Radiation Biology, Life Sciences Division, Los Alamos National Laborator

ACADEMIC ACTIVITIES:

The Japan Neurosurgical Society, Councilor

Radiation Research Society, USA (RRS), International member

Particle Therapy Cooperative Group (PTCOG), Steering committee member

Abstracts

Session Chairs: Teruyoshi Kageji, Ling Wei Wang

01 10:45 AM

Pilot Clinical Study of Boron Neutron Capture Therapy for Recurrent Hepatic Cancer and Gastric Cancer

Hironobu Yanagie[1)], Syushi Higashi[2)], Koji Seguchi[2)], Ichiro Ikushima[3)], Kazuyuki Oyama[4)], Yasumasa Nonaka[5)], Syoji Maruyama[6)], Ryo Hatae[6)], Takayuki Sairennji[6)], Shinji Takahashi[6)], Minoru Suzuki[7)], Shin-ichiro Masunaga[7)], Tomoko Kinashi[7)], Yoshinori Sakurai[7)], Hiroki Tanaka[7)], Akira Maruhashi[7)], Koji Ono[7)], Jun Nakajima[1,8)], Minoru Ono[1,8)], Hiroyuki Takahashi[1)], Masazumi Eriguchi[6)]

1) The University of Tokyo, Department of Nuclear Engineering & Management, Cooperative Unit of Medicine & Engineering, The University of Tokyo Hospital
2) Kojinkai Medical City East Hospital, Department of Surgery, Miyazaki, JAPAN
3) Miyakonojyo Metropolitan Hospital, Department of Radiology, Miyazaki, JAPAN
4) Japan Anti-Tuberculosis Association, Shin-Yamate Hospital, Department of Surgery, Tokyo, JAPAN
5) Kyoto University, Research Reactor Institute, Osaka, JAPAN
6) Japan Anti-Tuberculosis Association, Shin-Yamate Hospital, Department of Surgery, Tokyo, JAPAN
7) Kyoto University, Research Reactor Institute, Osaka, JAPAN
8) The University of Tokyo Hospital, Department of Cardiothoracic Surgery, Tokyo, JAPAN

Applications of boron neutron-capture therapy (BNCT) has been increased clinically in patients with a lot of cancers in hole body. The main two ^{10}Boron compounds(sodium mercaptoundecahydro- dodecaborate: ^{10}BSH, ^{10}B-*p* borono-phenylalanine (^{10}BPA) and its fructose complex) are used to clinical trials. Tumour cell destruction in BNCT is due to the nuclear reaction between ^{10}Boron and thermal neutrons. For effective BNCT therapy, it is necessary to accumulate ^{10}B atoms in the tumour cells without affecting adjacent healthy cells.

We started the pilot clinical studies of BNCT to recurrence breast cancer, hepatic cancer, and gastrointestinal cancers. In this paper, we present pilot clinical study in patients of hepatgic cancer and gastric cancer.

[Case 1] In accordance with the clinical results of Higashi and colleagues, water-in-oil-in-water (WOW) emulsion has been used as the carrier of anti-cancer agents on intra-arterial injections in clinical trials. We would like to apply BNCT for the treatment of HCC in order to increase the selection of therapies available for HCC patients. We developed a ^{10}BSH containing WOW emulsion using a double emulsification technique.

A 63-year-old man with multiple HCCs was enrolled as the first patient in a pilot study for treating BNCT with ^{10}BSH containing WOW emulsion. The patient had been performed right hepatectomy in 6 years ago. Hepatic arterial chemotherapies with epirubicin containing WOW emulsion were performed in the recurrence stages. The multiple tumours in the left liver lobe were treated with BNCT by selective intra-arterial infusion of ^{10}BSH containing WOW emulsion. The pre-BNCT dosimetry was performed using SERA(mean tumour fluence is 12Gy-Eq on 56 minutes BNCT (Maximum 19Gy-Eq on tumour), and maximum fluence of normal mucosa is 5.0 Gy-Eq). The tumour size was remained stable during 3 months after BNCT, and tumour marker (AFP and PIVKA-II) was shown20% decrease compared with pre-treated status. No adverse effect as a result of BNCT was observed during the treatment and follow-up period. The BNCT-treated tumours showed regrowth 3 months after BNCT, so the patient has continued the repeated hepatic arterial chemotherapy of epirubicin containing WOW emulsion. The present results showed that ^{10}B-containing WOW emulsion can be applied as a novel intra-arterial boron carrier for BNCT for HCC.

[Case 2] The 72-year-old man with recurrence gastric cancer was enrolled as the first patient in a pilot study for treating BNCT with ^{10}BPA. The patient had been performed total gastrectomy with lymph node (LN) dissection and cholecystectomy, and partial hepatic resection on 5 years ago. Two years later after operation, left cervical LN metastasis was occured, and the patients was administrated TS-1 and CDDP, and performed radiation therapy(total 70Gy). The metastatic tumour of left cervical LN had been partially reduced after therapies, but it regrowthed. The high accumulating images of metastased left cervical lymph node was acquired by ^{18}F labeled borono- phenylalanine(^{10}BPA)- positron emission tomograpy(PET). The tumour / blood ratio was 2.7. The pre-BNCT dosimetry was performed using SERA(more than 80% of tumour fluence is 20Gy-Eq on 48 minutes BNCT (Maximum 35Gy-Eq on tumour), and maximum fluence of normal mucosa is 5.6 Gy-Eq). The tumour growth suppression was recognized at 2 months after BNCT. Left carotid artery was re-entried after BNCT. Left cervical skin edema, oral erosion, throating pain, and throating discomfort were observed in the follow-up period after BNCT. In this study, we showed the possibility to apply BNCT to recurrenced gastrointestinal cancers.

02 11:05 AM

Boron Neutron Capture Therapy for Recurrent Head and Neck Malignancies

Itsuro Kato[1)], Naofumi Yamamoto[2)], Yusei Fujita[3)], Masatoshi Ohmae[4)], Yoshinori Sakurai[5)], Hiroaki Kumada[6)], Yoshio Imahori[7)], Isao Murata[8)], Tetsuro Sumi[1)], Souichi Iwai[1)], Mitsuhiro Nakazawa[1)], Koji Ono[5)]

1) Osaka University Department of Oral and Maxillofacial Surgery
2) Department of Oral and Maxillofacial Surgery, Saiseikai-Senri Hospital
3) Department of Oral and Maxillofacial Surgery, Higashiosaka City General Hospital
4) Department of Oral and Maxillofacial Surgery, Rinku General Medical Center
5) Research Reactor Institute, Kyoto University
6) Institute of Basic Medical Science, University of Tsukuba
7) CEO of Cancer Intelligence Care Systems, Inc.
8) Division of Electrical, Electronic and Information Engineering, Graduate School of Engineering, Osaka University

Introduction: Recurrent head and neck Malignancy (HNM) are often radio-/chemo-resistant and show extensive growth, necessitating a wide resection including surrounding tissues. To avoid severe impairment of oro-facial structures and functions, it is necessary to explore new treatments for HNM. Boron neutron capture therapy (BNCT) is tumor-cell targeted

radiotherapy that has significant superiority over conventional radiotherapies in principle.

Material and Methods: From December, 2001 to September, we had treated with 42 times of BNCT for 26 patients with a recurrent HNM treated after standard therapy. They were composed of 19 squamous cell carcinomas (SCC), 4 salivary gland carcinomas and 3 sarcomas All of them had received standard therapy and had developed recurrent tumors for which there were no other treatment options. All of the patients received in principle a combination of BSH: 5g and BPA: 250mg/kg or BPA: 500mg/kg alone administered intravenously. We report here that observations of clinical results and outcome of 26 patients with HNM, who have been treated with BNCT in the Kyoto University Research Reactor Institute (KUR) and at Japan Atomic Energy Agency (JAEA) Reactor.

Results: All cases are advanced such as 15 out of 26 patients (58%) had developed regional lymph node metastases. Distant metastases were developed in 6 cases during treatment. (1)10B concentration of tumor/normal tissue ratios (T/N ratio) of FBPA-PET studies were SCC: 1.8-5.7, sarcoma: 2.5-4.0, parotid tumor: 2.5-3.7. (1) Regression rates were CR: 12cases (46%), PR: 10cases (39%), PD: 3cases (12%), NE (not evaluated): 1case. Response rate was 85%. (2) Mean Survival time was 33.6 months. 2-year overall survival rate (OS) and 6-year OS were 37.0% and 31.7% , respectively. (3)BNCT improved QOL, PS and survival periods. (4)Survival periods after BNCT were 1-84 months. (5) Adverse events were brain necrosis, osteomyelitis and transient mucositis and alopecia and so on.

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03 11:25 AM

Background and trial design of the Phase I, open label, dose escalation study for safety and tolerability of boron neutron capture therapy (BNCT) using boronophenylalanine (SPM-011) / accelerator BNCT system (BNCT30) for the patients with recurrent malignant glioma

Shinji Kawabata[1)], Minoru Suzuki[2)], Shin-Ichi Miyatake[1)], Hiroki Tanaka[3)], Yoshiniri Sakurai[3)], Kouiki Uehara[4)], Toshimitsu Hayashi[4)], Toshinori Mitsumoto[5)], Yuji Kikuchi[5)], Koji Ono[2)]

1) Osaka Medical College, Department of Neurosurgery
2) Kyoto University Research Reactor Institute, Particle Radiation Oncology Research Center
3) Kyoto University Research Reactor Institute, Division of Radiation Life Science
4) Stella Pharma Corporation, Research & Development / Clinical Development Department
5) Sumitomo Heavy Industries, Ltd., Quantum Equipment Division, Design Department

The prognosis of recurrent malignant gliomas (MGs), especially glioblastoma is still poor. The standard treatment for recurrent MG has not yet been established. In most cases, a full course of radiotherapy has been applied after primary diagnosis; therefore, application of re-irradiation has to be applied with caution. We have applied a form of tumor-selective particle irradiation, boron neutron capture therapy (BNCT), for malignant gliomas (MGs) and malignant meningiomas including the patients progressed after full course of radiotherapy, as we discussed in the past ICNCT. Based on these favorable results and recent progress in development of the accelerator neutron source for clinical usage, we planned the Phase I clinical trial of accelerator-based BNCT. This study will become a first trial of BNCT using accelerator BNCT system.

The purpose of this trial is to determine the maximum tolerable dose (MTD) and dose-limiting toxicity (DLT) of GMP-grade boronophenylalanine (SPM-011, stella pharma, Japan) / accelerator BNCT system (BNCT30, Sumitomo heavy industries, ltd., Japan) for the patients with recurrent malignant glioma (MG). The trial should be also aimed for the approval to manufacture and market new drugs and new medical equipment under Japanese Pharmaceutical Affairs Law.

Recurrent MG patients (WHO grade III or IV), aged 20 to 75 years old with KPS ≥ 60 are eligible for this study. The recurrent tumor should be located supratentorial, single lesion without radiographical evidence of cerebro-spinal fluid dissemination or remote lesion. The history of radiation therapy is limited in this Phase I trial for the standard external beam X-ray irradiation with total given dose ranged 50 to 65Gy.

Accelerator BNCT system (BNCT30) with single boron containing drug, BPA (SPM-011), are planned to evaluate in this trial Blood boron concentration is kept during irradiation whereas a decline of the blood level was remarkable when we terminated BPA just before neutron irradiation. Any kinds of adverse events will be corrected base on CTCAE ver.4.0 during acute and chronic stage, dose escalation will be permitted after assessment of the tolerability / toxicity for acute phase on the lower dose level.

With recent technical advancement, radiation therapies have enabled to deliver high local doses as an effective salvage treatment with low rates of side effects. However, even if the radiographically remaining, progressed tumor could be targeted with higher irradiation doses, there is still remaining problem to be solved with the tumor with highly infiltrating / invasive nature or surrounding functional organ at risk for re-irradiation. BNCT might be overcome this problem with acceptable toxicity, and accelerator BNCT system should become popular for other location of cancers and called “should be given” treatment especially for the selected cases.

These proposals are current status at submission and any kind of the change will be possible in future.

Session Chairs: Raymond Moss, Hiroaki Kumada

01 9:30 AM

Amaranthus - the new open source hadron therapy planning system

Anastasia Makarova

National Research Nuclear University "MEPhI", Department of Medical Physics

Introduction: The new therapy planning system is announced based on object oriented programmimg language C++ and making use of Insight Segmentation and Registration Toolkit (ITK) and Visualization Toolkit (VTK) libraries, designed specifically for medical applications along with Geant4 toolkit for Monte Carlo dose calculations. First results for neutron dose calculations in a voxel model of patient are reported.

Matherials and Methods: Amaranthus is the open source system, that uses special medical image processing techniques, provided by ITK, allowing to segment stack of CT images in DICOM format and visualize them via three orthogonal planes and a 3D model. After segmentation is done (based on Honsefield units) the voxel model of patient is constructed for dose calculation. Geant4 toolkit based on C++ is integrated in the system, allowing to adjust the beam direction and the time of irradiation interactively.

Results: The first depth dose distributions and isodose curves are shown for epithermal neutron beam HEC-1 of MEPhI nuclear reactor. The processes of thermal and epithermal neutron interaction with matter, necessary to be taken into account for proper Geant4 calculation are discussed. Future improvements of the planning sistem are presented: implementation of semi-automatic segmentation techniques (active contours), optimization algorythms for beam direction and treatment duration, implementation of determenistic preliminary neutron dose calculations for faster optimization.

Conclusion: Amaranthus is flexible crossplatform system that allows insight in its code and able to make parallel calculations for multiprocessor computers. It is still at the stage of active development and testing.

02 9:45 AM

Physical neutron dosimetry for the university of pavia thermal neutron source for BNCT research

Nicoletta Protti[1,2], Silva Bortolussi[1,2], Michele Prata[2,3], Piero Bruschi[1], Saverio Altieri[1,2], David Nigg[4]

1) University of Pavia, Department of Physics
2) National Institute for Nuclear Physics (INFN), Section of Pavia, Italy
3) University of Pavia, Laboratory of Applied Nuclear Energy (LENA), Italy
4) Idaho National Laboratory, USA

Introduction: The University of Pavia and the Idaho National Laboratory are collaborating in the field of medical neutron dosimetry specific to Neutron Capture Therapy (NCT) applications. This effort resides within a larger framework for computational and experimental dosimetric intercomparison of the various different thermal neutron sources used for preclinical NCT radiobiology research worldwide. Recognizing the importance of accurate and reproducible physical beam dosimetry as an essential tool for combination of preclinical and clinical results from different facilities, we have conducted an experimental characterization of the neutronic performance of the thermal neutron source used for NCT at the University of Pavia TRIGA™ research reactor facility.

Materials and Methods: In accordance with international guidelines, the characterization methodology is based on neutron activation spectrometry coupled with rigorous least-squares-based spectral deconvolution and adjustment procedures to produce the desired information. Somewhat simplified versions of activation protocols adapted by the INL for NCT applications at a number of different facilities worldwide were employed. Bare gold and manganese foils, and cadmium-covered indium, gold, tungsten, manganese, and copper foils were used, along with a much heavier indium foil shielded within a hollow boron-10 sphere to emphasize a key inelastic scatter interaction required for the spectral measurement. Small flux wires composed of 1.55% gold by weight alloyed in natural copper were used for normalization of the three different irradiations that were conducted. The reactor power for the irradiations was 250 kW with irradiation times ranging from 10 minutes for the bare foils to several hours for the boron-shielded foil. Induced activities for all foils and wires were measured using a standard ORTEC HpGe gamma spectrometer system. The MCNP4c2 code with ENDF/B Version 6.0 cross section library data was used to compute the various *a-priori* neutron fluxes, reaction rates and effective shielded foil and wire cross sections needed for the spectral adjustment process. The *A-priori* flux covariance matrix for the spectral adjustment procedure was constructed in accordance with American Society for Materials Testing (ASTM) Standard E944-08.

Results and Conclusions: The measurements indicated that the Pavia neutron source is reasonably well thermalized, with a cadmium ratio for gold of about 75.0 and a thermal neutron flux in the range of 9 x 10^9 n/cm^{2}s at 250 kW. The overall spectrum is roughly comparable to that of the thermal neutron beam used for preclinical NCT radiobiological research at the University of Missouri.

03 10:00 AM

A general approach for calculating photon-isoeffective doses in clinical BNCT

Sara J. Gonzalez[1,2,3], Gustavo A. Santa Cruz[3]

1) National Atomic Energy Commission (CNEA), Instrumentation and Control.
2) CONICET
3) National Atomic Energy Commission (CNEA), Department of BNCT

Aiming at relating the effects observed in a clinical BNCT protocol to the corresponding outcomes in photon therapy, "RBE-weighted" doses are customarily derived by adding the different absorbed dose contributions, each one multiplied by a

fixed (dose and dose rate independent) RBE factor. These fixed RBE factors are traditionally accepted single numbers derived from different studies, biological systems and endpoints and, despite this diversity, they are assumed to be "representative" of the relative effectiveness of each radiation component. The most important objection that can be made to this standard practice is that, although these factors are taken as fixed numbers, it is well known that they are functionally dependent not only on dose (or survival level) but also on dose rate. As a result, constant RBE factors cannot describe sublethal damage repair and moreover, preclude the possibility of considering synergism between low and high LET radiations.

In this work, a general approach for calculating photon-isoeffective doses in BNCT is presented. The formalism, which is of sufficient simplicity to be included straightforwardly in all treatment planning systems, includes first-order repair of sublethal lesions and also considers synergistic interactions between different radiations. More importantly, it permits deriving photon-isoeffective doses without using a weighting procedure.

Different examples of interest in BNCT are depicted. First, the impact of applying fixed RBE factors for calculating RBE-weighted doses is analyzed, emphasizing the fact that the unrestricted use of fixed weighting numbers, despite having a formal inconsistency, will always lead to incorrect results. It is then demonstrated that the fixed RBE method usually derives unrealistically high tumor doses when compared to those delivered in single fraction radiotherapy to obtain a high tumor control (e.g., 90% control doses between 17 Gy and 25 Gy). For example, for a tumor that receives a mean total absorbed dose of 15 Gy, the resulting fixed RBE-weighted dose is 51 RBE-Gy, in contrast to photon-isoeffective doses of 28 Gy (IsoE) and 30 Gy (IsoE) (without and with synergism, respectively).

Finally, when the clinical outcome of the Argentine cutaneous melanoma treatments is assessed with regard to the doses derived from the standard weighting procedure, it follows that the fixed RBE approach is incapable of explaining the BNCT clinical outcomes in terms of the photon radiotherapy data. Even lowering the assumed 10-B concentration in tumor, the fixed RBE approach is still unsuitable to explain the observed outcomes (the model is always rejected with p-values almost zero). Conversely, the numbers of controlled tumors predicted by the proposed approach are statistically consistent with observed outcomes.

As a by-product of this work, a dose-response clinical reference for single-fraction melanoma treatments is also presented.

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04 10:15 AM

MultiCell model as an optimized strategyfor BNCT treatment planning

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2) CONICET
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Different treatment planning systems for BNCT have been developed in the last 20 years. Univels, regular lattice or multi lattice geometric descriptions are some of the implemented methods for optimizing treatment dosimetry. One of the main concerns in BNCT is the dose uncertainties at the boundary of the geometry. In this work we present an optimized strategy developed in the Computational Dosimetry and Treatment Planning group, CNEA. By means of an optimized geometrical reconstruction method we are capable to generate, based on patient CT images, an accurate volume description model. Our strategy exploits volumes homogeneity to build a combination of multiple sized parallelepiped bodies suitable for MCNP code. By this method we intend to obtain high reconstruction precision for different volumes of interest independently of their size, while reducing the total number of MCNP cells. As this method exploits MCNP multiple size cells we named it MultiCell method.

The reconstruction accuracy was tested by means of CT scans from regular phantoms and real patients. In each case, the complete volume was segmented in volumes of interest (VOI) using Hounsfield numbers-based thresholding and drawing tools. VOI of very different size (from 40 to 5000 cm^3) were reconstructed with the MultiCell method, and relative differences between reconstructed and segmented volumes were compared.

Dosimetry optimization was also studied. For this, dose components were calculated by MCNP F4 mesh tallies. Reference dosimetry was obtained using a 0.0156 cm^3 mesh grid, and these values were compared to 0.125 cm^3 and 1cm^3 mesh grids. Volumetric dosimetry differences for each dose component and the computational time required in each case were considered to determine the suitability of the analyzed grids.

MultiCell reconstruction method was finally used to reproduce three treatments plans performed with NCTPlan software within the context of the BNCT melanoma clinical trial in Argentina. MultiCell and NCTPlan derived dosimetries together with calculation times were compared.

The reconstruction accuracy achieved by MultiCell is higher than 98% in all the VOI considered, regardless of their sizes. The total number of cells required to completely describe a CT study (256x256 pixels and 128 slices) ranges from $2x10^3$ to $40x10^3$ depending on the volumes of interests segmented. In any case, these numbers are significantly lower than the one corresponding to the regular grid providing the same reconstruction accuracy, namely 10^6.

Differentmesh grid sizes were evaluated in order to determine dose accuracy and computational times required per beam.

Our results show that 0.125 cm^3 mesh grid gives dosimetry accuracy over 95% in all volumes of interest, with MCNP run times less than 12 hours (100 million nps @ 1 CPU) in all studied cases.

Finally, comparisons between our method and NCTPlan based on three representative melanoma treated patients show that the number of cells required to describe patient geometries with MultiCell barely doubles NCTPlan's (i.e., lower than 25 10^3 in all cases) while the geometric description provided by the proposed method drastically improves the NCTPlan's one. Regarding dosimetry, the MultiCell geometry combined with

a 1cm^3 tally mesh grid (that is, as the one used by NCTPlan) shows significant relative differences for thermal and boron dose components only in patient regions of very low dose. On the other hand, the detailed geometric reconstruction provided by MultiCell combined with the smaller mesh grid sizes has a major impact on dosimetry results.

Analytical methods are being studied in order to optimize dosimetry in the patient-air interface without increasing the required computational time. Currently, MultiCell method presents an accurate geometry description, deriving a suitable dosimetry for clinical and radiobiological applications. As a consequence, routine use of MultiCell in BNCT clinical practice is being evaluated.

Session Chairs: Yhao Hao Liu, Hiroki Tanaka

01 9:30 AM

Dose measurements with primary and supplementary techniques in the Birmingham epithermal beam

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Introduction: BNCT beam dosimetry is complex. Standard methods (foils and ionisation chambers) lead to assessment of photon and neutron dose components with large uncertainties. In such a situation it is essential to use supplementary techniques to validate the standard methods. Supplementary methods can include tissue equivalent proportional counters, TLD's, diodes and other techniques.
Materials & Methods: Central axis beam dosimetry in a Large Water Tank (LWT) has been performed. Dilute foils containing 1% by mass of gold and manganese in aluminium were used to derive Boron and Nitrogen dose components following the method of Freudenreich. Paired magnesium and A150 tissue equivalent ionisation chambers (Exradin M2 and T2) were used with Argon and Methane-based tissue equivalent gas respectively.
Supplementary methods were A150 tissue equivalent proportional counter (TEPC), for the thermal and fast neutron components and Lithium 7 fluoride TLD's for the photon dose component at large depths. In the case of the TEPC total neutron dose was measured and this was divided into thermal and fast components based on an MCNPX 2.6 calculated thermal/fast ratio. Foil measurements of nitrogen dose were converted to thermal dose with a conversion factor of 1/0.964.
Results of measurements with the standard techniques were fitted with shape preserving splines and interpolated to the depths of the supplementary measurements. Percentage deviation of the supplementary measurements from the fits were assessed.
All results were also compared with Monte Carlo simulations using MCNPX.
Results: Thermal neutron dose derived from the Freudenreich method was compared with that derived from the TEPC from depths of approximately 3cm to 8cm. The maximum difference measured was 15%, with an average difference of 7%.
Fast neutron dose derived from paired ionisation chambers was compared with TEPC measurements from depths of 3cm to 8cm. Percentage differences were large due in part to the very steep dose gradient.
Photon dose derived from paired ionisation chambers was compared with TLD measurements at depths of 14cm and 17cm. Differences were 7% and 8% respectively. Larger differences were apparent at depths of 10cm most likely due to the sensitivity of the TLD's to neutron interactions, which were not corrected in this experiment.
Conclusion: TEPC technique combined with MCNP is seen to be a valuable supplementary method for thermal and fast neutron dose components. Lithium-7 TLD's provide confirmation of photon dose component at depths of approximately 14cm and above in phantom.
Lithium-7 TLD's therefore can also provide a useful means of postal intercomparison of the photon dose component in BNCT beams.

02 9:45 AM

Shielding Calculation for BNCT facility using the Neutron Shield Concrete

Koichi Okuno

HAZAMA corporation

Mainly ordinary concrete is used for neutron shield. Although concrete is low price, it needed massive thickness for neutron shield. Therefore, recently, the novel neutron shield concrete using the colemanite, a natural rock containing boron as B_2O_3, and the peridotite a natural rock containing hydrogen as H_2O has been developed. The concrete has about 1.7 times better shielding ability than ordinary concrete for Cf-252 neutron source and has same material property for ordinary concrete.
Shield calculation for BNCT facility that using the neutron shield concrete was carried out by the PHITS (Particle and Heavy Ion Transport code System) code. Water phantom of 30 cm ϕ X 30 cm long was set in front of beam port. As a result of calculation, we have obtain reduction of shield thickness by a maximum of about 50%, compared to using the ordinary concrete. And also, amount of secondary gamma ray production in the treatment room is also reduced. Thereby, slim neutron shield wall and expansion of indoor space is realized by using the neutron shield concrete.

03 10:00 AM

New Materials for BNCT Neutron Beam Optimization

Valeriy Korobeinikov, Nikolai Soloviev, Artem Korobeynikov

State Scientific Center Institute of Physics and Power Engineering

The research aims the goals of evaluating the quality of different materials that can transform the energy spectra of initial sources to satisfy the needs BNCT procedure.
It was proved previously that the most suitable beam spectrum for BNCT contains the neutrons in 0,5 ev –30-40 kev range (epithermal region). While the real neutron sources do often have high number of the neutrons that are above this range (fast energy region). The moderators of different materials are usually applied to transform the energy structure of initial sources to the target ranges.
The research on materials selection which can be used as a moderator or filter for suitable spectra structure forming were preformed in a number of studies. However, as a rule, these works were oriented to adaptation of specific neutron source for BNCT. This paper is proposed to estimate the materials quality in more wide assumptions about a possible source

spectrum of a pure neutron source for BNCT purposes on the basis of importance functions modeling.
According to many authors the most suitable material for constructing such kind of moderators are those who contain fluorine, because of its large cross sections for high energy neutrons and small capture cross sections. Such widely used fluorides are: MgF_2 and AlF_3. The goal of the research was to discover some others.
Here is the extended list of materials, which were researched: D_2O, Al_4C_3, Al, AlF_3, BeF_2, CaF_2, CrF_2, CrF_3, CrF_4, S_2F_{10}, NaF, FeF_2, FeF_3, LiF, MgF_2, $Na_3[AlF_6]$, TiF_4, VF_3, ZrF_4, PbF_2, PbF_4, CF_2.
In most of our studies we originally supposed that neutrons of modeling sources were distributed on the fission spectrum. In computer experiments this source was surrounded by spherical enclosure of named materials with thicknesses 20, 30, 40 cm. For some calculation studies the design of special medical reactor was applied. The calculations were performed by Monte Carlo code MCNP.
It was discovered that PbF_4 and FeF_2 shows the best results that are close to MgF_2 and AlF_3 ones, while have even some other pros: PbF_4 may be useful for its ability of gamma-dose exclusion, and moderator made up of FeF_2 would not need any absorbing additions. It was also proved that the therapeutic ratio for 4 or 8 cm depth tumors is the best when the initial reactor-spectrum source is filtered with PbF_4 moderator.

04 10:15 AM

Near-threshold ^{7}Li(p,n)^{7}Be Neutrons on the Practical Conditions using Thick Li-target and Gaussian Proton Energies for BNCT

Tooru Kobayashi[1], Noriyosu Hayashizaki[2], Tatsuya Katabuchi[2], Kenichi Tanaka[3], Gerard Bengua[4], Noriaki Nakao[5], Kazuaki Kosako[5]

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Introduction: The near threshold ^{7}Li(p,n)^{7}Be neutrons by incident proton energy having Gaussian distribution with mean energies from 1.85 to 1.95MeV, were studied as a practical neutron source for BNCT wherein an RFQ type accelerator and a thick Li-target[1] are used. Additionally, the suitable thicknesses of both Lead layer to control the contaminant gamma rays in the neutron field and polyethylene layer as a boron dose enhancer (BDE) material, were surveyed by means of the concepts of PD(hcp), PD(gamma) and TPD[2, 3, 4].
Materials and Methods: The incident proton energy produced by a proton RFQ type were supposed to have a Gaussian distribution with the standard deviation energies of 0, 10, 20 and 40 keV for the mean proton energies from 1.85 to 1.95MeV are surveyed in 0.01MeV increments. A thick liquid Li-target is supposed 1 mm-thick with 50 mm width and 50 mm length which was established experimentally. The suitable incident proton energy and physical dimensions of Lead layer as gamma absorber and Polyethylene layer as a BDE were estimated using MCNP5 code.
Results and Discussions: The incident proton energy of 1.92MeV having a Gaussian distribution with the standard deviation energies of 20keV and a current of 10mA was selected from the viewpoint of practical conditions such as irradiation time and proton current. The suitable thicknesses of Lead layer as gamma absorber is estimated about 3 cm. The estimated thickness of the Polyethylene BDE were about 2.4 cm for an ideal proton current of 13 mA, and 1.8cm for a practical case where the proton current is about 10 mA. The optimum polyethylene BDE thickness and proton current are mutually dependent such that we need to estimate the condition of polyethylene BDE thickness and proton current for each patient condition.

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Session Chairs: Wolfgang Sauerwein, Hiratsuka Junichi

01 11:00 AM

Fractionated BNCT for Locally Recurrent Head and Neck Cancer: Experience from a Phase I/II Clinical Trial at Tsing Hua Open-Pool Reactor

Ling-Wei Wang[1,5], Yi.-Wei Chen[1,5], Shiang-Huei Jiang[2], Yen-Wan Hsueh Liu[2], Fong-In Chou[2,3], Yuan-Hao Liu[3], Hong-Ming Liu[3], Jinn-Jer Peir[3], Ching-Sheng Liu[1,5], Shyh-Jen Wang[4,5]

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Introduction: To report the dose, response, and toxicities of fractionated boron neutron capture therapy (BNCT) for treatment of recurrent Head & Neck cancer patients after conventional radiotherapy at Tsing Hua Open-Pool Reactor (THOR) in Taiwan.
Patients and methods: From 2010 to 2011, ten patients (M/F=8/2, median age 55.5 Y/O) were enrolled for this phase I/II clinical trial. Previous accumulated RT dose ranged from 63 to 136.4 Gy. BNCT was performed with Boronophenylalanine (BPA)-fructose (400 mg/kg) injected intraveneously in 2 phases. Two-fraction treatment at 30-day interval was scheduled for each patient. Before each fraction of treatment, BPA-PET scan was done to determine the Tumor/Normal tissue (T/N) ratios for each tumor. In-house designed THORplan was the treatment planning system. CT simulations were performed before each fraction and tumors were recontoured. Prescription dose (or V80) was intended to cover 80 % of Gross Tumor Volume (GTV) by dose volume histogram (DVH) while limiting mucosa volume receiving $>$ 10 Gy (Eq) as low as possible. Tumor responses were assessed using the RECIST (Response Evaluation Criteria in Solid Tumors) criteria v1.1 and adverse effects using the National Cancer Institute common toxicity grading v3.0.
Results: In a total 15 tumors were treated. Median T/N ratios was 3.4 (range 2.5 to 6.3) for the first fraction and 2.0 (range 1.8 to 2.8) for the second fraction. Median V80 dose was 19.6 (range 11.6 to 36.9) Gy (Eq) for the first fraction and 12.5 (range 3.8 to 21.1) Gy (Eq) for the second fraction. All except one case received 2 fractions of BNCT as planned. Median interval between 2 fractions was 28 (range 26 to 33) days. One patient was treated with collimator of smaller size at 2nd fraction due to dramatic tumor shrinkage after 1st treatment. After a median follow-up time of 11.3 (range 5.2 to 18.4) months, 3 patients had complete response, 3 had partial response, 2 had stable disease, 2 had progression of disease. Common acute toxicities included mucositis (3 with grade III and 6 with Gr I to II), alopecia (9 cases), and radiation dermatitis (9 cases). No Gr IV or worse toxicity observed.
Conclusion: Though our follow-up time is still short, fractionated BNCT at 30-day interval with adaptive planning according to changed T/N ratios and tumor volumes seems to be feasible, effective and safe for selected recurrent head & neck cancer in this trial.

02 11:20 AM

BNCT for Carotid lesion of Head and Neck Cancer

Teruhito Aihara[1], Norimasa Morita[1], Junichi Hiratsuka[2], Nobuhiko Kamitani[2], Koji Ono[3], Tamotsu Harada[1]

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Introduction: BNCT is a promising treatment for achieving local control of Head and Neck cancer. We examined the safety for the carotid lesion of head and neck cancer in BNCT.
Materials and Methods: Currently, clinical trials of BNCT for head and neck cancers are being conducted in some institutes to verify its usefulness. BNCT was performed in 19 patients with recurrent Head and Neck Cancer, 6 patients with newly diagnosed Head and Neck Cancer in our university. There were treated with with BNCT at KUR and JRR-4 between October 2003 and September 2007. The tumor/normal-tissue boron concentration ratio (T/N ratio) obtained from 18F-BPA-PET study was adopted to the dose estimation before neutron irradiation and dose evaluation after BNCT using SERA or JCDS. Neutron irradiation was performed using an epithermal beam at a reactor power of 5.0 MW (KUR) or 3.5 MW (JRR-4) after intravenous administration of BPA in fructose solution at a dose of 500 mg/kg body weight. The tumor dose at the deepest part and the dose of both normal skin and mucosa were planned more than 20 Gy-Eq and less than 15 Gy-Eq, respectively.
Results and Discussions: Eleven patients showed carotid lesion in the irradiation field. Two patients resulted in carotid hemorrhage after treatment. These cases were skin defect of the radiation field. No severe acute or chronic normal-tissue reactions were observed in other patients. BNCT is effective and safe in the patients with head and neck cancer.

03 11:40 AM

Clinical use of PET amino acid imaging in boron neutron capture therapy for malignant brain tumor

Tadashi Nariai[1], Motoki Inaji[1], Yoji Tanaka[1], Masaru Aoyagi[1], Tetsuya Yamamoto[2], Akira Matsumura[2], Shinichi MIyatake[3], Kiichi Ishiwata[4]

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Introduction: To plan the optimal boron neutron capture therapy (BNCT) for patients with malignant brain tumor, estimation of the ratio of boron concentration in tumor tissue against that in the surrounding normal brain is important. We reported that use of positron emission tomography (PET) using ^{18}F-borono-phenyl-alanine (FBPA) or ^{11}C-methionine (MET) enabled it in clinical situation. Use of PET amno acid

probe may be useful to monitor the effectiveness of BNCT. We presents our experience by now.
Methods: 27 patients with malignant brain tumor underwent PET imaging with FBPA or MET to determine the indication for BNCT. 8 of them (6 glioblastoma, 1 CNS melanoma, 1 atypical meningioma) underwent BNCT . Post treatment PET scan using MET was performed in 5 patients.
Result: PET tumor images obtained with FBPA and MET are almost identical. Based of our previous report, indication of BNCT for glioblastoma were deterimined by MET-PET in recent cases. Post teattment scan was useful to monitor the effective ness of BNCT. Marked reduction of MET uptake was noted only 2 weeks after the treatment of glioblastoma and malignant melanoma. PET was also useful to differenciate active tumor recurrence for radiation injury. In spite of such rapid treatment of early phase, some patients shower recurrence from remote cite.
Conclusion: Use of FBPA or MET PET was useful to select an appropriate candidate for BNCT. Post-treatment use of PET was also useful to precisely monitor the biological effect of treatment. Accumulation of such information with PET should be useful to accumulate the evidence to support the effectiveness (and also limitation) of BNCT against malignant brain tumor.

04 12:00 PM

BNCT can significantly prolong the survival of recurrent malignant glioma cases

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Boron neutron capture therapy (BNCT) is based upon the nuclear reaction that occur when non-radioactive boron-10 (^{10}B) is irradiated with low energy neutrons to produce high energy a particles (^{10}B[n,alpha] ^{7}Li). In order for BNCT to be successful, a sufficient amount of ^{10}B and neutrons must be delivered to the tumor. We have applied tumor selective particle radiation known as boron neutron capture therapy (BNCT) to malignant brain tumors. As there has been no standard treatment for recurrent gliomas so far, it has been difficult to evaluate the results of BNCT for recurrent malignant gliomas. Here we introduce the survival benefit of BNCT for recurrent malignant glioma patients, with special reference to new RPA classification recurrent malignant gliomas advocated by New Approaches to Brain Tumor Therapy CNS Consortium (NABTT, J Clin Oncol 2007).
Methods: Since 2002, we have treated 29 cases of recurrent malignant gliomas with BNCT. All cases had been treated by radiotherapy mainly by fractionated external beam X-ray irradiation prior to BNCT. Median age was 51 with M: F of 18: 11. KPS at relapse was ranged 50 to 100 (median; 80) and tumor volume was 34.9 (2.5 – 67.5) mL. After BNCT, patients were followed by MRI and F-BPA (amino acid) – positron emission tomography (PET). Also overall survival was evaluated with special reference to Recursive Partitioning Analysis (RPA) classes advocated by NABTT as above. Adverse events were assessed by CTCAEv3.0 during follow-up.
Results: The median survival time (MST) of BNCT-treated recurrent gliomas was 11.0 (95%CI: 7.8 – 11.7) months, while that of total NABTT cases (N=333) was 7.0 (6.2 – 8.0) months. MST of NABTT RPA classes were 25.7, 17.2, 3.8, 10.4, 5.6, 6.4 and 4.9 months for classes 1 to 7, respectively. The MST of our BNCT-treated cases were 32.6, 23.7, 9.6, 9.1, 10.3, 11.7 and 10.1, for classes 1 to 7, respectively. BNCT showed good survival benefit especially for the poorest prognostic group (RPA class 3+7) from 4.4 months (NABTT) to 9.6 months. Some of the prognostic factors of malignant glioma, such as age, KPS, initial histology, tumor volume are not independent factor each other. Patients with larger tumor (≥ 34.9mL of Gd(+) lesion on MRI) showed MST of 11.5 month, on the other hand, MST of smaller group was 10.1 month and there were no significant difference (p=0.58). Radiation necrosis required surgical resection was occurred in 3 cases but survive longer than median OS (12.4, 15.3, 11.4 months from BNCT). Main cause of death was cerebrospinal fluid dissemination (51.7%) with good local control.
Conclusion: Recently we showed our modified BNCT protocol prolonged survival of the patients with glioblastoma. BNCT is tumor cell selective particle irradiation therapy, but its selectivity depends on the accumulation of boron compounds. Therefore, we modified several points to improve distribution of boron compounds into the tumor cell.
In this retrospective, case controlled clinical study of re-irradiation using BNCT for recurrent malignant gliomas showed survival benefit with acceptable adverse events. Advantage of this tumor-selective irradiation, BNCT, compare with other radiotherapeutic modality is applicability for large target of the tumor and some poor prognostic factors would be overcome by using BNCT as we analyzed in this report. Further clinical study had been planned by accelerator based neutron capture therapy instead of the nuclear reactor as a neutron source in this year in Japan.

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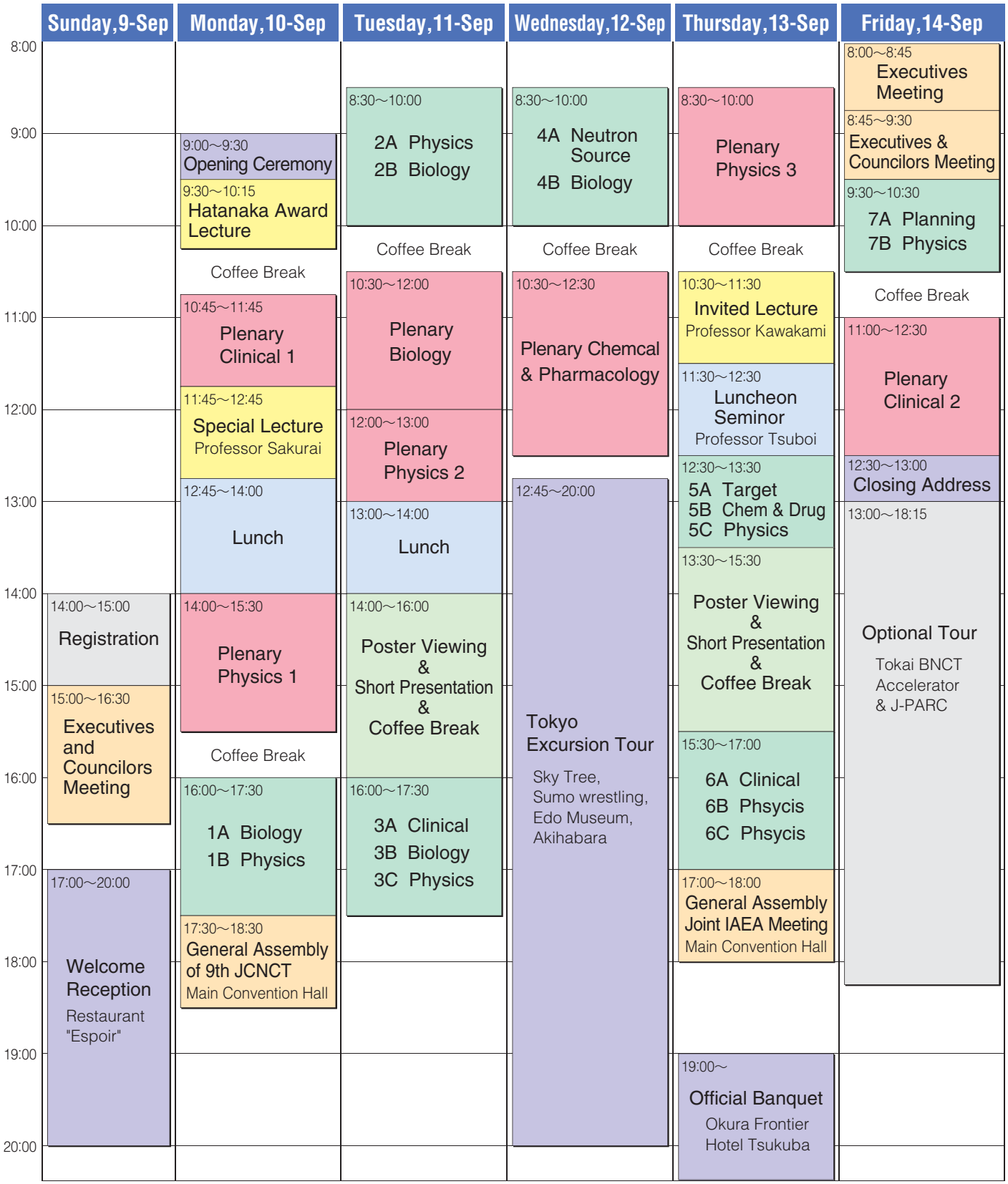

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