**Introduction**

In Japan, postal dose audits have been performed on radiation therapy units using radiophotoluminescent glass dosimeters (RGDs), since 2007 [1]. NIRS developed this auditing system and has supported its technical aspects continuously. For instance, the application of RGDs to a non-reference condition beam such as field size change or wedged field were studied by NIRS and successfully introduced in the routine dose audit in 2010 [2] [3].

The IAEA / WHO have performed postal dose audits worldwide since 1969 using thermoluminescent dosimeters (TLDs). Recently, they have considered the replacement of TLDs by RGDs. RGDs are made in Japan and offer some superior features: RGDs are almost completely free from the fading effect and can be read repeatedly. NIRS and IAEA have done an annual dosimetric intercomparison between RGDs and TLDs since 2008 (Fig.1). The outputs of both dosimeters agreed within ±1% (Table1). In 2013, IAEA installed a new RGD reader from Japan and started commissioning of the RGD system. IAEA asked NIRS to support this work and I stayed at the IAEA Dosimetry Laboratory for 1 year from August 2013 as a consultant on the RGD system commissioning.

**Table1** Results of dose intercomparison with RGD (NIRS) and TLD (IAEA). Values were in good agreement within the uncertainty. (Data in 2011 and 2012 are missing in part, due to the Fukushima disaster.)

<table>
<thead>
<tr>
<th>Year</th>
<th>Measured dose/Calculated dose</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RGD read at NIRS (irradiated at IAEA)</td>
<td>TLD read at IAEA (irradiated at NIRS)</td>
</tr>
<tr>
<td>2008</td>
<td>0.995</td>
<td>1.00</td>
</tr>
<tr>
<td>2009</td>
<td>0.998</td>
<td>0.99</td>
</tr>
<tr>
<td>2010</td>
<td>0.995</td>
<td>1.02</td>
</tr>
<tr>
<td>2011</td>
<td>0.991</td>
<td>-</td>
</tr>
<tr>
<td>2012</td>
<td>-</td>
<td>1.00</td>
</tr>
<tr>
<td>2013</td>
<td>0.997</td>
<td>1.01</td>
</tr>
</tbody>
</table>

**Fig.1** TLD irradiation at NIRS (upper photo) and RGD irradiation at IAEA (lower photo) for the dose intercomparison program.
IAEA Dosimetry Laboratory

The IAEA Dosimetry Laboratory is part of the Dosimetry and Medical Radiation Physics Section, Division of Human Health (Fig. 2). Its mission is (i) to develop, implement and maintain standards for dosimetry measurements in radiotherapy, diagnostic radiology and radiation protection, (ii) to provide dosimetry calibration services for Secondary Standards Dosimetry Laboratories (SSDLs) and to reference hospitals in countries where no SSDLs exist, and (iii) to provide dosimetry audit and verification services for applications in radiotherapy and radiation protection for SSDLs, hospitals and radiation protection services in Member states.

In implementing its third mission, a small plastic tube containing thermoluminescent powder is irradiated to a specified dose by a medical physicist in the hospital, following the same procedure as prescribed for patient treatment. The TLDs are returned to the IAEA Dosimetry Laboratory for readout and analysis. The dose received by the TLD is compared with the intended dose stated by the hospital staff. For hospitals with inconsistent results, the IAEA establishes a follow-up program for quality improvement, including on-site visits by local or international experts. It also provides support and training in medical physics to the hospital staff.

Technical Consultation at the Dosimetry Laboratory

When a RGD exposed to radiation is subjected to a UV-laser pulse in a RGD reader, it generates luminescence in orange pulses (radio photoluminescence: RPL). The amplitude of RPL generated from the RGD is in proportion to the exposure dose of the RGD. Therefore, in order to ensure accurate dosimetry, it is necessary to read the RPL with high precision. For example, a tiny offset of the RGD element on a reading tray, such as ±0.1 mm, would vary the reading output. Technical advice is mainly given for these kinds of careful readout procedures. In addition, to minimizing the fluctuation of each element’s response, an individual correction factor should be used. During my stay in the IAEA, the correction factors of 1000 elements were determined.

Research contribution on small field dosimetry

In the last half of the stay, I engaged in research work also. The topic was small field dosimetry using three solid state dosimeters for advanced dose audit in radiotherapy. This study aims at identifying suitable dosimeters for the postal dosimetry audit of small beams used for more advanced radiation treatments such as stereotactic radiation therapy (SRT) and intensity-modulated radiotherapy (IMRT). The dosimeters, RGDs, TLDs and optically stimulated luminescent dosimeters, are of interest for audits of small radiotherapy beams provided the appropriate corrections are applied. The results were presented at the ESTRO 33 meeting held at Vienna on 2014. Fig.3 is a photo showing measurements being done in a hospital in Vienna.

Summary

Working at an international organization is a valuable experience and an important part of the long term goals of NIRS. My chance to work at the IAEA was not only a cooperation between NIRS and IAEA, but also was a chance for me to improve my own research and technical skills.

References

Objectives
• To perform clinical research for clarifying usefulness of carbon ion therapy in order to establish new treatment for radioresistant tumors and to standardize the treatment for common cancers.
• To perform clinical research on utilization of the advanced technique of high-speed spot scanning irradiation of a carbon ion beam in the routine treatment for head & neck or pelvic tumors.
• To investigate the benefit of improving accuracy of imaging modalities, such as PET, MRI, and CT scan for carbon ion therapy.
• To investigate the possibility of prediction or evaluation of effectiveness of carbon ion therapy using novel information from imaging modalities.
• To develop and regulate the comprehensive database on radiotherapy, mainly carbon ion therapy in consideration of achieving evidence-based medicine. Additionally, to propose national database available for multi-institutional research on particle therapy of domestic and foreign institutions.

Progress of Research
The Program of Research on the Standardization and Clarification of Charged Particle Therapy consists of the Clinical Trial Research Team, Applied PET Research Team, Applied MRI Research Team, and Clinical Database Research Team. All the teams are performing research and development on charged particle therapy. Progress of research in each team is summarized below.

1) Clinical Trial Research Team
As of March 2015, a total of 9,021 patients had been treated with carbon ion beam therapy at NIRS (Fig.1). Carbon ion radiotherapy of these patients was carried out as more than 60 different phase I/II or phase II clinical trials or advanced medicine (HAMT; highly advanced medical technology).

Seven hundred and ninety-four patients were treated as new patients from April 2013 to March 2014. This number is about a 10% decrease compared to last year which was the largest number yet at NIRS. The main reason for the decrease was the drop in the number of radiation oncologists working at NIRS and that will be solved next year.

Fig.2 lists the numbers of patients for each tumor site. Prostate, bone and soft tissue, head and neck (1, 2), lung, and liver are the leading five tumors sites. Recently the numbers of cases of pancreatic tumor and recurrent rectal cancer have increased definitely.

Clinical trials for pancreas, esophagus, uterus (3) and kidney cancer are being conducted and patient enrollment has progressed. As an advancement of hypofraction of carbon ion therapy, the single session treatment for lung cancer and 12-fraction
treatment for prostate cancer could be established and they have started to be applied as advanced medicine (4).

The scanning irradiation became available for the routine treatment of less mobile targets in the head & neck or pelvic region. Actually more than 500 patients could be safely and efficiently treated with scanning at the New Treatment Research Facility. In addition, the clinical trial aiming to verify safety and steadiness of the respiratory-gated scanning system has been started. This system can perform high-speed re-painting (8 times) irradiation during the expiratory phase of the patient’s respiration and can provide a more conformal dose distribution than broad-beam irradiation of the carbon ion beam. The trial will be carried out for about 12 patients with a mobile tumor in the chest or abdomen and it is expected to be continue until the end of this year.

The new working group, named J-CROS Japanese Carbon-ion Radiation Oncology Study Group, for the multi-institutional clinical trial of carbon ion therapy was established last year (Fig.3). It consists of four carbon ion therapy facilities operating in Japan: the NIRS, the HIBMC in Hyogo, the GHMC in Gunma, and the HIMAT in Saga. In addition, other four institutes in Kanagawa, Osaka, Yamagata, and Okinawa will start carbon ion therapy in the near future and therefore the working group includes some members from these newest facilities. The group has started to prepare the data collection from the four operating institutes for retrospective analysis and to plan a protocol for prospective clinical studies for major tumor sites.

2) Applied PET Research Team

In the last year, we made some phantom experiments for confirming performance of the new respiratory gating system of PET and we could confirm that the images obtained using this new system were better than those obtained using the conventional system.

An additional experiment with a phantom has been carried out this year. Both the respiratory-gated images of PET and CT for carbon ion radiotherapy were obtained separately and image-fusion was done. Consequently, the positions of the target on both images were well matched and therefore this system can be used for target delineation in actual treatment planning for carbon ion therapy.

3) Applied MRI Research Team

To provide quantitative diagnostic information for heavy charged particle therapy, several MRI methods have been applied to clinical diagnosis. We developed a new algorithm to calculate indexes from signal change in the dynamic study of MRI. It can be expressed as a map on one image and the lesion with both early enhancement and rapid washout can be clearly demonstrated. It is practically useful in evaluation of treatment effect of carbon ion therapy and also in detection of any existing recurrent lesions.

4) Clinical Database Research Team

It is essential to prepare the dedicated database system to perform the multi-institutional trials of J-CROS and to have a leading role in the future trials. Thus, we developed a database system that can store the integrated information of the patients treated at all the institutions of this study group. The data include pretreatment information, treatment data, and outcome information. In addition, a conversion tool was developed, which is available for the different types of medical information of the participating institutions. The tool has been set up at each institute this year.

References

Although the 2nd term International Open Laboratory (IOL) was completed in March 2014, some ripple effects continue to come from this fine structure. Scientific publications appeared throughout the fiscal year 2014, and some other exciting things keep happening. In this article a few highlights for this fiscal year are described.

The Space Radiation Research Unit continues to accept international researchers who used to be supported by IOL in their own labs. They are engaging in active experimental research just as they were doing under the IOL setting. Some of the publications from these collaborations are listed at the end (See publication list #1, #2). The Particle Beam Quality Research Unit is working on collaborative publications with scientists from GSI (a German research institute), and manuscripts have been submitted to peer-reviewed respectable international journals.

The Particle Therapy Molecular Target Unit continues its collaboration with Colorado State University (CSU). Professor Jac Nickoloff at CSU, Distinguished Scientist for this unit, introduced some unit researchers to Professor Engleward’s lab at Massachusetts Institute of Technology (MIT). Through this connection, the researchers were able to receive transgenic RaDR (Rosa26 GFP direct repeat) mice from MIT (Fig.1) that are being used for radiation related research. With these mice, genomic events called homologous recombination (HR) at Rosa26 loci can be observed in vivo by green fluorescence signals. An advantage of RaDR mice is their application to study the fate of mutated cells in various tissues over their life time. The aim of this project is to know how an excessive dose of ionizing radiation can cause genome instability that accelerates those eventual mutations over the whole genome.

A JSPS KAKENHI grant (#24249067) that originated from the 2nd term IOL is continuing in 2014-2015. With this grant money, a post-doctoral researcher from South Korea has been recently hired and basic biological research related to heavy ion radiotherapy is being actively conducted (Fig.2). There also is a plan to submit a collaborative research grant to the National Institutes of Health (NIH), USA with CSU in 2015.

A substantial number of research papers bearing the name “International Open Laboratory” have been published after the completion of the 2nd term, and a partial list is provided at the end of this article. Many researchers keep mentioning the IOL activities in scientific meetings months after the completion. The effects of IOL at NIRS still continue and it is encouraging to hear the contributions IOL made.

Fig.1 RaDR mouse originally developed at MIT, USA
Partial list of IOL-related publications within fiscal year 2014:


The Ministry of Education, Science and Technology (MEXT) has been promoting the “Project for Creation of Research Platforms and Sharing of Advanced Research Infrastructure” for many years. This project encourages and promotes: (i) the use of advanced and high-tech research facilities and equipment in universities and Japanese Government corporate entities by researchers at Japanese industrial laboratories; and (ii) the formation of a supporting network for the use. By these activities, the project fulfills three major purposes: (i) to achieve important breakthroughs in the innovative science and technology arena of Japan (ii) to enhance and reinforce industrial competitiveness of Japanese industrial enterprises and (iii) to further improve R&D investment effects. The unique radiation irradiation facilities at NIRS, which are underpinned by long-term handling and operating expertise, were selected as advanced research infrastructure in the autumn of 2013. There were 34 facilities associated with the MEXT Project in 2014.

The research program pursued at NIRS is “Business use of various radiation fields related to humans”. In 2013, as a start-up, resources were dedicated for the program and the Office of Sharing of Advanced Research Infrastructure was organized. The Office then took initiatives to develop processes, procedures and formats to handle requests of upcoming applications and to develop promotional tools such as flyers, home pages, signs, etc. Promotions were made at academic conferences, exhibitions and business fairs. In fiscal 2014, as a result of the activities, 10 applications from companies, a local government-based research institute and universities were secured. Besides the completed applications, many other inquiries were received from horticultural, life science, and space science fields. In this article, the facilities available at NIRS under the MEXT Project and some of their relevant activities are explained to gain further attention from researchers who may want to participate in the future.

Sharing of Advanced Research Infrastructure Facilities in NIRS
1. PASTA (PIXE Analysis System and Tandem Accelerator). An electrostatic accelerator-based proton beam generator for PIXE analysis

PASTA uses the HVEE (High Voltage Engineering Europa Model 4117HC) coaxial Tandetron™ accelerator (maximum terminal voltage: 1.7MV) to produce 3 to 3.4MeV protons which are best fit for PIXE analysis, a simultaneous, multi-element analytical technique using particle-induced X-ray emission (Fig.1). PIXE analysis is a mainstay of many nuclear microprobe analysis studies as it provides 1-2 μm spatial resolution with ppm level sensitivities. The NIRS microbeam scanning PIXE can also output 2D images of elemental distributions as well as provide PIXE spectra. In 2014, two applications were received from the fields of extended environmental analysis (Fig.2, Fig.3) and dental material analysis.
2. SPICE (Single Particle Irradiation System to Cells), A microbeam irradiation system to cells

The SPICE beam line, diverged vertically from the micro-PXIE beam line, can automatically and precisely target the nucleus and/or cytoplasm of cells and hit them at a high speed rate of 400 cells per minute (Fig.4). The 3.4 MeV proton beam converged to 2 μm in diameter is routinely available, and it is the state-of-the-art proton microbeam line optimal for cellular biology research such as on the low dose rate effects of radiation cancer therapy and associated technology development. In 2014, though no applications were completed, several inquiries were received.

Fig.4 SPICE (Single Particle Irradiation System to Cells)

3. NASBEE (Neutron exposure Accelerator System for Biological Effect Experiment), An electrostatic accelerator based neutron generator

NASBEE uses the HVEE (High Voltage Engineering Europa Model 4120HC) coaxial Tandetron\textsuperscript{12} accelerator (the maximum terminal voltage of 2MV) with multi-cusp ion source to produce 4 MeV deuterons at maximum beam currents of 500μA. High intensity and dose rate and high speed neutrons are generated by a Be(d,xn) or Be(p,n) reaction. NASBEE, with a maximum dose rate of 7.5Gy/h and a fast neutron source, can be used for both biological and physics research purposes. In 2014, four applications received from the fields of horticultural applications, peripheral equipment development, and study of biological effects of cosmic rays.

4. Conventional radiation sources

X-ray radiation generators and gamma-ray radioisotope sources in NIRS are also available under the program. In order to ensure the quality of radiation fields, such as dose, dose rate and uniformity, ion chambers directly calibrated with the national primary standard in AIST every year, have been equipped with those conventional radiation sources. In 2014, four applications were received in the fields of equipment testing of radiation detectors and radiation resistance testing of electronic devices.

X-rays: 200kVp (1.1Gy/min 19cm at 50cm)
(0.206Gy/min to 3.0Gy/min at 120cm to 30cm)

Gamma-rays
\textsuperscript{137}Cs: 27μGy/h or 600mGy/h at 100cm
\textsuperscript{137}Cs: 1.3mGy/h to 120mGy/h at variable distances

Promotional activities

In fiscal 2014, the second full year of the program, many promotional activities were carried out to inform potential users of the facility availabilities. In addition to making facility introduction flyers, the Office updated the home pages, produced a promotional video and uploaded it to the internet, and gave presentations 14 times at various academic conferences and exhibitions such as JASIS. Many people who dropped by the program booth knew NIRS by its front-line HIMAC cancer therapy, but they did not know that NIRS also offered diversified radiation irradiation fields that were available for industrial uses, not just medical purposes, and that NIRS accepted diversified applications from various fields—agricultural to chemical, environmental and space, from engineers and researchers with companies and industry-government-academia entities.

In the future Anticipated users of the open facilities may not be fully aware of radiological sciences, or may not have experience in the operation of irradiation equipment. Or they may worry about the cost. In order to accommodate possible needs from non-professional users, the Office of Sharing of Advanced Research Infrastructure has a dedicated technical advisor and also have supporting members concurrently working with other NIRS divisions. The Office also has developed and implemented a free-of-charge program (for a maximum of one year) to encourage the use from commercial enterprises and industry-government-academia entities. With the aforementioned unique radiation irradiation facilities, the robust supporting team and easy-to-use programs, the Office will continue its efforts to further secure as many new applications as possible, to ensure the industrial competitiveness of Japan.
The general public often fear radiation irrationally. They receive most of their information about nuclear accidents or radiation through the media, such as TV programs or magazine articles. Balanced presentations in the media are important. Additionally, it is indispensable to ensure that broadcasters and publishers have correct information and understanding of radiation and its effects.

The Center for Human Resources Development, Radiation Safety Section, and REMAT conducted the “NIRS radiation course for German media”, on 10 September 2014 at NIRS. This was our first opportunity to give lectures to foreign media members in Japan in a course, or series of lectures and exercises. The participants were all working at ARD (Arbeitsgemeinschaft der öffentlich-rechtlichen Rundfunkanstalten der Bundesrepublik Deutschland) which is a public television company that operates the TV station called “Erstes Deutsches Fernsehen”. The course was organized at the request of ARD.

The participants were four German staff members and four Japanese staff members. The participants planned to go to Fukushima Prefecture, including the area near the TEPCO Fukushima Daiichi Nuclear Power Plant. They wanted to learn about radiation and practical skills for radiation protection before entering the area, and these were their direct motivations to attend this course.

The course curriculum is shown in Table1. After a brief opening and some guidance, the course started with a lecture on basics of radiation. Because the participants were neither radiation specialists nor scientists, the lecture covered very basic subjects. Nature and characteristics of radiation were taught. Main radiation quantities and units, such as effective dose and Sievert (Sv), were also explained. The next lecture covered radiation effects to humans. The concept of the stochastic effect was underscored and the principle of radiation protection was also explained.

The course included a large portion of hands-on exercises. In the first, participants used radiation measurement equipment such as Geiger-Mueller (G-M) survey meters by themselves (Fig.1). For many of them, it was their first experience to touch real radiation measuring instruments. The penetrating capacity of ra-
Radiation was shown to them as a demonstration. In the second exercise, they learned how to wear a protection suit (Fig.2, 3). Then, they practiced screening of surface contamination on each other by using G-M survey meters (Fig.4, 5). During this screening, weak radiation sources were inside the protection suit and the screener did not know its location. In this way, they practiced "searching" for contamination. After the screening, they also learned how to take off the protection suit without spreading the contamination. The last exercise "Monitoring" was conducted in a radiation controlled area. They learned how to measure ambient dose equivalent in the presence of a real source located at various distances (Fig.6).

In the discussion session, which was placed at the end of the course, they asked for an interpretation of the thyroid cancer screening results of Fukushima residents among other questions (Fig.7). They also acknowledged the usefulness of the course.

The participants had high motivations to get accurate and true information about the nuclear accident, human effects, and radiation protection. We thought that it is very important to provide suitable knowledge to media members, which could become a basis for future broadcasts. Thus, this kind of efforts contributes to transmission of correct understanding of radiation effects to the general public. We will be happy to provide such courses on request from other media groups.