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COMMENTARY

Educational Activity for the Radiation Emergency System in the Northern Part of Japan: Meeting Report on "The 3rd Educational Symposium on Radiation and Health (ESRAH) by Young Scientists in 2016"

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In the northern part of Japan, close cooperation is essential in preparing for any possible emergency response to radiation accidents because several facilities, such as the Low-Level Radioactive Waste Disposal Facility, the MOX Fuel Fabrication Plant and the Vitrified Waste Storage Center, exist in Rokkasho Village (Aomori Prefecture). After the accident at Fukushima Daiichi Nuclear Power Plant in 2011, special attention should be given to the relationship between radiation and human health, as well as establishing a system for managing with a radiation emergency. In the area of Hokkaido and Aomori prefectures in Japan, since 2008 an exchange meeting between Hokkaido University and Hirosaki University has been held every year to have opportunities to discuss radiation effects on human health and to collect the latest news on monitoring environmental radiation. This meeting was elevated to an international meeting in 2014 titled "Educational Symposium on Radiation and Health (ESRAH) by Young Scientists". The 3rd ESRAH meeting took place in 2016, with the theme "Investigating Radiation Impact on the Environmental and Health". Here we report the meeting findings on the continuing educational efforts after the Fukushima incident, what was accomplished in terms of building a community educational approaches, and future goals.

INTRODUCTION

Ionizing radiation has the potential to affect human tissues by energy deposition, causing mutation, cell death and cancer induction, via mainly DNA damage (*1*). By taking advantage of positive aspects of radiation (high permeability and energy convergence), not only image diagnosis but also radiotherapy have been achieved. However, damaging effects on normal tissues cannot be ignored from a radiation protection stand point. After the accident at Fukushima Daiichi Nuclear Power Plant (F1-NPP) following the earthquake and tsunami on March 11, 2011, large amounts of artificial radionuclides were released (*2*). This incident has focused close attention to human health after low-dose and low-dose-rate exposure (*3*). In the northern part of Japan, several facilities, such as the Low-Level Radioactive Waste Disposal Facility, the MOX Fuel Fabrication Plant and the Vitrified Waste Storage Center, exist in Rokkasho Village in Aomori Prefecture (*4, 5*). Close cooperation in this area is therefore crucial in preparation for any emergency radiation accidents. Young researchers and radiologists have the responsibility to ensure future human safety by investigating the relationship between ionizing radiation and human health.

For learning, precisely what effects radiation has on human health, it is important to provide the opportunity to share knowledge among specialists on radiation study. To provide this opportunity for young researchers, an idea exchange meeting between Hokkaido University and Hirosaki University has been held every year since 2008. After the accident at F1-NPP, in 2014 this meeting was elevated to an international meeting titled ''Educational Symposium on Radiation and Health (ESRAH) by Young Scientists'' (*6*). The topic of the meeting was ''radiation and human health'', and the 1st and the 2nd ESRAH were held

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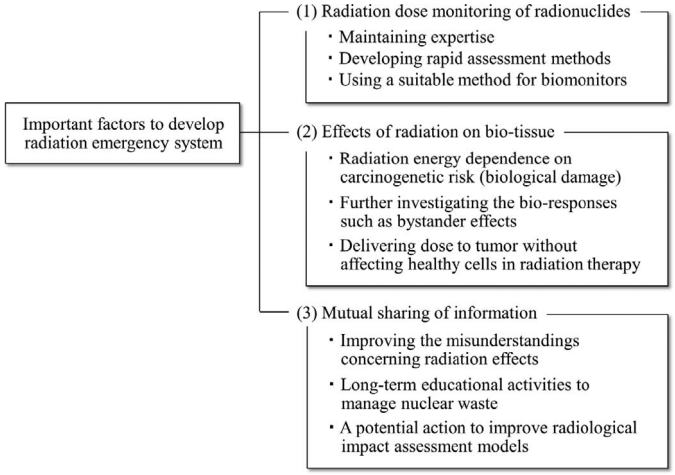

FIG. 1. Main three topics on radiation impact on human health: the information was obtained from the educational lectures and the invited talks from eight top-class researchers in this meeting.

in Hirosaki, Japan in 2014 and 2015 (*6, 7*). The meeting contributed to not only elevating the knowledge of radiation effects on human health but also establishing a network in the northern part of Japan, envisaging the construction of a radiation emergency system applicable to the whole world.

In 2016, the 3rd Educational Symposium on Radiation and Health by Young Scientists (ESRAH2016) was held on the theme of ''Investigating Radiation Impact on the Environment and Health''. At this meeting, three educational lectures and five invited top-class researchers gave talks, and more than 20 poster presentations by graduate students and young investigators were given. Here, we report on the achievement of the ESRAH2016 meeting. The activity through the meeting encouraged the participants to learn about the impact of radiation and to guide the direction of research in this field of study.

Educational Lectures and Invited Talks

Overview of Educational Lectures and Invited Talks. Current topics concerning the relationship between radiation and human health were discussed by eight top-class researchers from three main viewpoints (Fig. 1):

1. Radiation-dose monitoring of radionuclides.
2. Effects of radiation on bio-tissue.
3. Mutual sharing of information on radiation effects.

The titles of the lectures and talks are summarized in Table 1. The current state of the latest research on radiation was well presented in the lectures and talks.

Monitoring Radiation Dose in the Environment

Skills for monitoring radiation dose in the environment due to an accident at a nuclear power plant and of naturally occurring radioactive material (NORM) were introduced by Drs. K. Kelleher and T. Kovács. The focus of Dr. Kelleher's lecture was on the topic of ''radiation monitoring'' and ''lessons learned from nuclear accidents''. Kelleher showed the activity of radionuclides after three radiation accidents: the Windscale Fire (1957), the Chernobyl Accident (1986) and the Fukushima Accident (2011). Based on experiences from these accidents, Dr. Kelleher indicated that two actions are necessary in preparation for the nuclear accident: 1. Maintaining expertise and 2. Developing rapid assessment methods. Dr. Kovács proposed biomonitors (sensitive indicators) such as tobacco plant, which can realize the long-term controlling of the environmental and health effects of depositories (*8, 9*).

Biological Effects of Radiation on Tissue

Biological effects after exposure to radiation were discussed by Dr. J. Kildea, Dr. N. Autsavapromporn and Dr. T. Tippayamontri, with regards to radiobiology, dosimetry, Monte Carlo modeling and radiotherapy. Dr. Kildia talked about neutron-induced carcinogenic effects (NICE) featured by the energy spectrum (*10*). In this regard, Dr. Kildea proposed a method to quantify the carcinogenetic risk (biological damage) by a combination of energy spectra measurement and Monte Carlo modeling. Dr. Autsavapromporn presented findings on the mechanism to induce non-targeted effects (NTEs) by using microbeam experiments. Microbeam experiments show that NTEs may contribute to secondary cancer risks in cancer survivors (*11, 12*). From the view point of clinical practice, Dr. Tippayamontri talked about a method to treat cancer in consideration of the exposure of normal tissue to radiation in radiotherapy. To deliver the appropriate dose to cancer cells without affecting healthy cells, Dr. Thippayamontri showed an approach by using a targeted radionuclide therapy with a combination of ^{18}F-radioisotope (protective to healthy cells) and ^{5}FU (enhancing radiosensitivity in cancer cells) (*13–16*). The damage effect on normal tissue is also considered under the enhancement of cell killing in tumors.

Sharing Information on Radiation Effects

The importance of sharing correct information on radiation effects and the appropriate management of the nuclear waste was presented by Drs. M. Akashi, T. Kozaki and E. Fidanchevski. Dr. Akashi talked about ''Lack of Knowledge and Misunderstandings of Radiation Effects among Health Care Providers''. At the current time, there are a lot of misunderstandings concerning radiation exposure (*17*). Dr. Akashi strongly recommended that young scientists share the following information on radiation effects: 1. Exposure to radiation alone does not induce immediate death even when a very high dose is received (18); 2. Emergency workers can safely transport contaminated patients to hospital (*19*); and (3) Symptoms/signs usually do not appear in internal contamination (*20*). Dr. Kozaki showed us how to manage nuclear waste in Japan. It was also suggested that long-term educational

TABLE 1
List of Educational Lecture (EL) and Invited Talk (IT)

No.	Title	First author	Affiliation
EL1	The desired and undesired biological effects of ionizing radiation, with a focus on neutron-induced carcinogenic effects (NICE)	J. Kildea, Ph.D.	Medical Physics Unit, McGill University, Montreal, Quebec, Canada
EL2	Radiation monitoring in Ireland and the impact and lessons learned from nuclear accidents	K. Kelleher, Ph.D.	Environmental Protection Agency, Office of Radiological Protection, Ireland
EL3	Lack of knowledge and misunderstandings on radiation effects in health care providers	M. Akashi, M.D., Ph.D.	National Institutes for Quantum and Radiological Science and Technology, Japan
IT1	The non-targeted effects induced by microbeam irradiation	N. Autsavapromporn, Ph.D.	Chiang Mai University, Thailand
IT2	Nuclear waste management in Japan and its related capacity building activities at Hokkaido University	T. Kozaki, Ph.D.	Hokkaido University, Japan
IT3	Theranostic properties of intratumorally injected 18F-FLT and 5FU: concomitant tumor and metastases treatment	T. Tippayamontri, Ph.D.	Chulalongkorn University, Thailand
IT4-1	Biomonitoring of NORM contaminated sites	T. Kovács, Ph.D.	University of Pannonia, Hungary
IT4-2	NORM4BUILDING COST action: possibilities and challenges for young scientists	E. Fidanchevski, Ph.D.	Ss Cyril and Methodius University in Skopje, Macedonia

activities are essential to manage nuclear waste. To put it into practice, Dr. Kozaki proposed that the open course is a useful tool for nuclear waste management (*21, 22*). Dr. Fidanchevski introduced an activity called ''NORM4-BUILDING COST Action'', which has the potential to improve radiological impact assessment models for the reuse of NORM residues in building materials, which is being conducted in Europe.

Through these lectures, the participants will be able to recognize the lack of knowledge and misunderstandings of radiation effects on health care providers before making an attempt to establish a radiation emergency plan.

Poster Presentations by Young Scientists

Overview of the poster session. There were twenty posters presented, consisting of 11 posters on radiation biology, 3 on medical treatment, 2 on the Fukushima nuclear power plant accident and 4 on radiation measurement (Fig. 2). A one minute oral summarizing presentation was given by each young scientist. The details of the research subjects are summarized in Table 2. During the 90-min discussion period, enthusiastic arguments between the presenters and audience were made, encouraging various new findings. At the closing ceremony of the symposium, poster prizes were awarded to two poster presentations, which were judged by the educational lecturers, the invited speakers and seven teaching staff.

The poster session provided an exciting opportunity for young researchers and students. In the following sections, we outline the contents of the presentations and discussion.

Evaluation of Dose in the Environment and Animals after Nuclear Accidents

To monitor the activity concentration of radionuclides (such as ^{137}Cs, ^{134}Cs, ^{90}Sr or radon) and the dose in the environment or in a solid sample such as tissue, several approaches have been performed after nuclear accidents.

Methods for monitoring radiation of radon progeny, ^{90}Sr, ^{137}Cs and ^{134}Cs from samples such like soil or animal (human) tissue were developed. For example, a new method that is suitable for monitoring the radiostrontium activity concentration in a solid sample was presented by one group in Hungary, which may contribute to monitoring internal exposure after radiation accidents. In Japan, a group investigated the internal contamination of radioactive-cesium (^{137}Cs and ^{134}Cs) associated with the Fukushima Daiichi Nuclear Power Plant (F1-NPP) in the genital tissue of animal (*Felis silvestris catus*) which were protected by volunteers in Namie Town, Fukushima. However, there is no correlation between internal contamination level and air dose rate (or radioactive-cesium

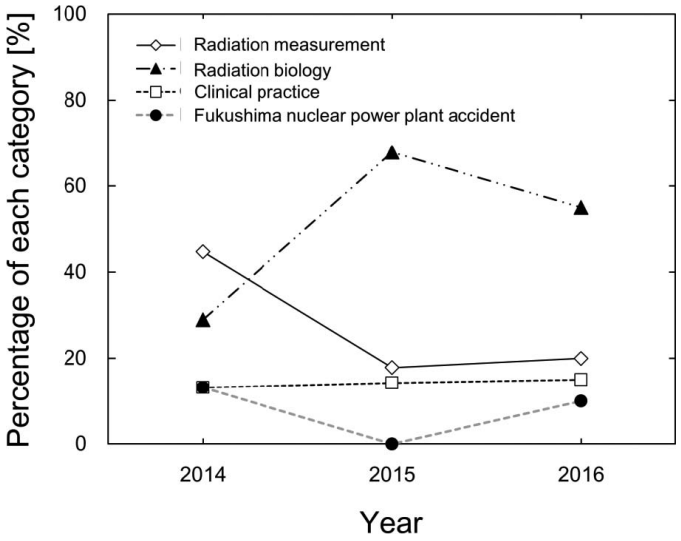

FIG. 2. Percentage of each category in the poster session by young scientists.

TABLE 2
List of Poster Presentation by Young Scientists

No.	Title of poster presentation	First author	Affiliation
1	Impacts of electron collision cross sections on electron track simulations in liquid water	T. Kimura	Hokkaido University, Japan
2	The mitigative effects of romiplostim, a recombinant c-mpl agonist on the survival of mice exposed to lethal ionizing radiation	M. Yamaguchi	Hirosaki University, Japan
3	Effect of the hyaluronan by X-ray irradiation to human prostate cancer cell line	K. Murata	Hirosaki University, Japan
4	Radiation dosimetry for the internal exposure of the feral cats in Namie Town, Fukushima	Y. Fujishima	Hirosaki University, Japan
5	A cell-killing model of targeted and non-targeted effects based on microdosimetry and biological processes	Y. Matsuya	Hokkaido University, Japan
6	X-ray irradiation to mouse neurons causes decrease in frequency of miniature excitatory synaptic currents	T. Tsujiguchi	Hirosaki University, Japan
7	Development of a portable continuous radon progeny monitor for the working environment	R. Yamada	Hirosaki University, Japan
8	Exposure dose estimation in abdominal dynamic computed tomographic examination using size-specific dose estimation	K. Yoshida	Hirosaki University, Japan
9	Ultraviolet B degrades oxytalan fibers in human nonpigmented ciliary epithelial cells in vitro	Y. Shiroto	Hirosaki University, Japan
10	New concept of dose distribution in rotational intensity-modulated radiation therapy (IMRT) planning by using filtered back-projection (FBP) theory	K. Nomura	Hirosaki University, Japan
11	Probability of radiation-induced DNA double-strand breaks in statistical considerations for radiation energy deposition and cell cycle	R. Mori	Hokkaido University, Japan
12	Uncertainty assessment of OER for reoxygenated tumor	R. Yamada	Hokkaido University, Japan
13	Radiostrontium monitoring in the region of Bakony Mountains	E. Tóth-Bodrogi	Pannonia University, Hungary
14	Radiation sensitizing effects of 4-methylumbelliferone targeting IL-6 signaling pathway	R. Saga	Hirosaki University, Japan
15	Allogeneic double-unit umbilical cord blood cell transplantation facilitates hematopoietic recovery in an irradiated host	K. Terui	Hirosaki University, Japan
16	Changes in stress level of the temporary housing evacuees after Fukushima nuclear accident	Y. Fukushi	Hirosaki University, Japan
17	Radon measurements and dose assessment of underground miners. Focus on new EU-BSS and Hungarian legislation	E. Kocsis	Pannonia University, Hungary
18	Estimated inhalation and external gamma doses in angolan adobe houses	J. P. Dembo	Eötvös University, Hungary
19	A fundamental study of the effect of radiation exposure on parasites that cause encephalitis: a treatment approach that has yet to be established	K. Yamanouchi	Hirosaki University, Japan
20	Evaluation of the size-specific dose estimates in 320 rows of area detector CT scanning with pelvis phantom	K. Mizonobe	Sapporo Medical University, Japan

concentration in soil). The problem is not solved at current status. Further, in Angola, the first investigation of dosimetry was performed, and the results reveal that the annual indoor radon activity concentrations in 14% of Angolan adobe houses are expected to have higher values than the WHO reference.

Looking toward biological evaluation, quantifying the pathological condition of tissue after exposure is essential in anticipation of accidental exposure to high-dose ionizing radiation (*23, 24*). Another group in Japan focused on microRNAs (miRNAs) that have recently emerged as biomarkers for predicting and diagnosing various pathological conditions by identifying the serum miRNA signature. It was suggested in this study that the serum miRNA may serve as a functional dosimeter and early-assessment biomarker of radiation-induced damage to monitor the dose in tissue after accidents.

Apparently, the interests of young investigators have been turned in radiation biology rather than the aftermath of F1-NPP accident as shown in Fig.2.

Approaches for Analyzing Biological Effects after Exposure

Effects of radiation were evaluated from many viewpoints, such as electron-track simulation, biological experiments, mathematical modeling and so on. The impact of radiation on bio-cells (i.e., a series of events to induce cell death) was discussed during the poster presentations.

DNA damage can be induced when the spatial distribution of energy deposition along the secondary electron track (*25*) is coincident with DNA location in the cell nucleus. A group presented an approach to evaluate the path length of an electron track in relation to the induction of DNA damage, i.e., DNA double-strand breaks (DNA-DSBs)

causing fatal DNA damage (*26–29*). The damage depending on the cell cycle was investigated by incorporating the experimental DNA concentration into a mathematical formula. The cell killing was also evaluated by using a mathematical model in consideration of both targeted effects (energy deposition to cell nucleus) mentioned above (*30*) and nontargeted effects (not only low-dose hyper-radiosensitivity but also medium transfer bystander effects).

The cellular mechanism after exposure is, however, still unclear from the view point of biological experiments. The behavior of hyaluronan (HA) and CD44 expression (radioresistance) in prostate cancer cell lines exposed to X rays was investigated by a group from Hirosaki University, Japan. An increase of HA in cancer cells after irradiation may be involved in clonogenic potencies. Intriguingly, the interleukin 6 (IL-6) signaling pathway is associated with an acquisition of radioresistance in cancer stem cell-like cells that express CD133. IL-6 is known as one of the signaling pathways of the bystander effect (nontargeted effects) (*31*). It is possible that the HA is linked to the bystander effect and signal-induced radioresistance (*32, 33*). On the provision of accidental high-dose exposure, a group tried to establish the transplantation of double-unit umbilical cord blood cells (dUCBCs) (*33*), which can be used to reconstitute the hematopoietic system. Especially, they focused on the use of an allogeneic UCBC source in dUCBC transplantation that does not require major histocompatibility complex compatibility for treatment in response to a radiation emergency. A project to establish a method to treat patients after accidental radiation exposure is underway.

It is likely that quantitative models can reproduce bio-responses such as DNA damage or cell-killing after irradiation. However, the cellular response including the signals after low-dose exposure still remains to be clarified. Further investigations will be necessary by the experimental approach and also by the construction of theoretical models to interpret the bio-response after irradiation.

Summary and Future Prospects

In 2016 the3rd ESRAH was held, this meeting suggested the direction of research interests mainly for the sake of young scientists and seemed to provide a valuable experience to the participants in a variety of radiation-related research fields, such as dosimetry, management of radiation, biological experiments, theoretical models, Monte Carlo simulations and so on. As a remarkable achievement, young scientists recognized their study phase, in which the knowledge or information about the effects of radiation on tissue (mainly cellular mechanisms) is still insufficient while the data related to biological response and the environmental dose are being gathered little by little after accidents such as F1-NPP. A comprehensive study including biological experiments and theoretical analyses will be effective to evaluate the impact of radiation on human health.

ESRAH is planned to take place every year, ESRAH2017, is scheduled to be held in Hirosaki city, under the direction of Prof. Yoichiro Hosokawa of Hirosaki University, Japan. We are expecting the participation of many radiation researchers. Finally, we express our gratitude to the eight scientists who accepted our offer to give the educational lectures and invited talks.

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