The Proceedings of the 4th International Symposium on Radiation Emergency Medicine at Hirosaki University

The 2012 Hirosaki University International Symposium

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The 4th International Symposium on Radiation Emergency Medicine at Hirosaki University

Organized by
Hirosaki University Graduate School of Health Sciences

Sponsored by
Hirosaki University Institute of Radiation Emergency Medicine
Hirosaki University Education Program for Professionals in Radiation Emergency Medicine
The Radiological Nursing Society of Japan

Supported by
National Institute of Radiological Sciences (NIRS)

PREFACE

Over the past 5 years, Hirosaki University Graduate School of Health Sciences has worked to create an advanced professional education program for radiation emergency medicine. During this period, the curricula for both postgraduate education and entry-level undergraduate education in the School of Health Sciences, which have been in place since April 2010, were modified based on the established educational philosophy and objectives. The mission of the present project is both to improve the quality of education and to promote research based on the development of human resources for medical professionals in this field.

In line with these initiatives, the International Symposium on Radiation Emergency Medicine, which has a theme of "Radiation Sciences and Radiation Emergency Medicine", has been held annually since 2009 with the aim of sharing information on the future development of human resources for radiation emergency medicine. During these symposia, participants have had useful discussions on the current status of the radiation medicine-related research being conducted around the world. The executive committee made the preparations to host the 4th International Symposium at Hirosaki University on 30 September 2012. The focus of the 4th International Symposium was the future of the development of human resources for radiation emergency medicine. Major topics, in addition to human resources development, included the establishment of a training program for nurses who want to specialize in radiation medicine. The 4th International Symposium placed a particularly strong emphasis on interdisciplinary studies and the future direction of this field.

The Symposium consisted of talks by invited speakers and both oral and poster presentations. It was our privilege to host the following two distinguished speakers: Zhanat A. Carr from the World Health Organization (WHO) in Switzerland and Christophe Dody from Service de Protection Radiologique des Armées (SPRA) in France. Four sessions of presentations comprised 27 speakers who gave lectures on topics related to their current research. Participants were deeply impressed by the special guest speakers, and the symposium successfully promoted the exchange of recent developments in this field. This report summarizes the presentations and discussions held at the symposium. We would like to acknowledge everyone who contributed to this symposium, including the members of the governing board and, above all, the authors and participants.

Hitoshi Tsushima
Chief Chair, The 4th International Symposium on Radiation Emergency Medicine in Hirosaki University
Dean of the Graduate School of Health Sciences, Hirosaki University

Symposium

Opening by Professor Hitoshi Tsushima, Dean of Hirosaki University Graduate School of Health Sciences, Project Leader, The 1st presenter

Guest Professor　Mikinori Kuwabara,
Hirosaki University Chair of Symposium Ⅰ

Lecture Toshiko Tomisawa,
Hirosaki University The 2nd presenter

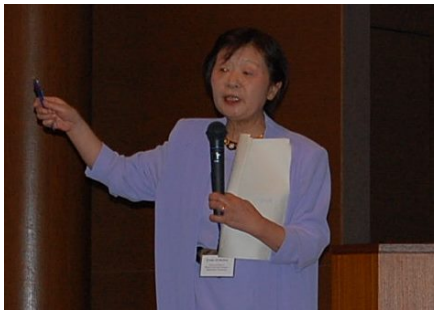
Professor Ruriko Kidachi,
Hirosaki University The 3rd presenter

Associate Professor Takao Osanai,
Hirosaki University The 4th presenter

Professor Koichi Ito,
Hirosaki University The 5th presenter

Professor　Ikuo Kashiwakura,
Hirosaki University
Chair of Special Lecture

Dr Zhanat Carr,
WHO,　The 6th presenter



Dr Emiko Konishi, R.N., President,
The Radiological Nursing Society of Japan,
Kagoshima University　The 7th presenter

Professor Mitsuaki Yoshida,
Professor Yuka Noto,
Hirosaki University Chair of SymposiumⅢ

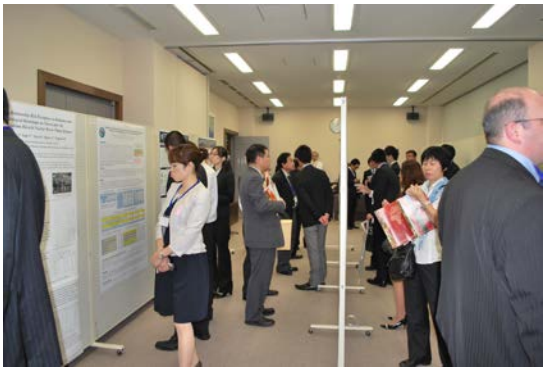
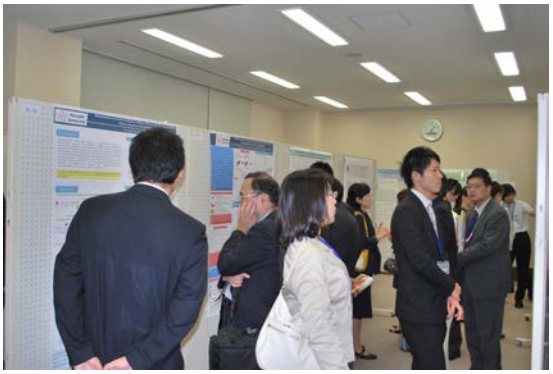
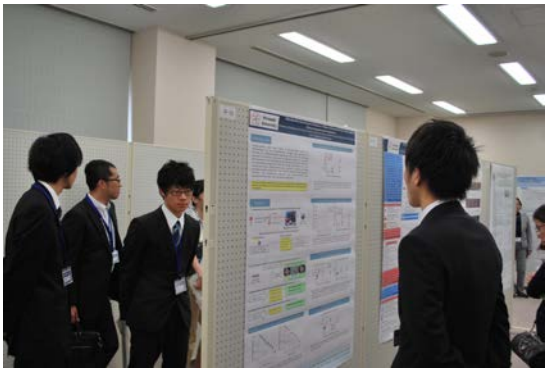
Lt. Christophe Dody,
Service de protection radiologique des armées
(SPRA)　The 8th presenter

Dr Takako Tominaga, National Institute of
Radiological Sciences　The 9th presenter

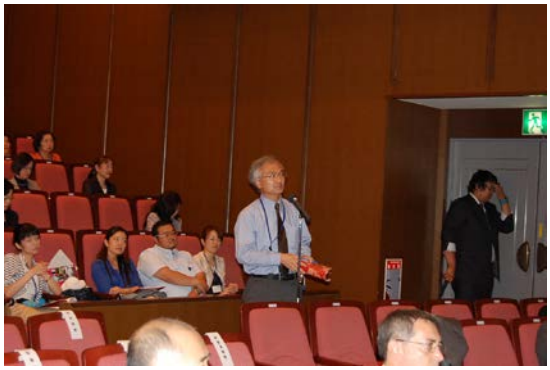
Professor Yoshiko Nishizawa,
Hirosaki University　The final presenter

Hirosaki University,
50th Anniversary Auditorium

Symposium Ⅱ　Poster presentation

Closing by Professor Kazuyuki Kida,
Deputy Head of Hirosaki University
Graduate School of Health Sciences



The 4th International Symposium
on Radiation Emergency Medicine
in Hirosaki University
Hirosaki University
50th Anniversary Auditorium, Hirosaki Japan
September 30, 2012

第4回 緊急被ばく医療国際シンポジウム
弘前大学大学院保健学研究科

Joint Reception

合同懇親会
Joint Reception

合同懇親会
Joint Reception

Contents

iii Preface

iv Photographs in the Symposium

viii Photographs in the Joint Reception

Symposium I

1 Developing human health resources for radiation emergency medicine at Hirosaki University: a panoptic report on the 5-year project effort
Hitoshi Tsushima, Project Leader
Department of Development and Aging, Division of Health Sciences,
Dean of Hirosaki University Graduate School of Health Sciences

5 Practice and Evaluation of the Radiation Emergency Medicine Education Program at Hirosaki University
Toshiko Tomisawa, Chieko Itaki, Manabu Nakano, Shuhei Koeda, Saichi Wakayama, Tomoko Ichinohe, Yoshimitsu Otomo and Toshiya Nakamura, Education Group
Hirosaki University Graduate School of Health Sciences

9 Results of staff education and training in radiation emergency medicine: Summary from the Planning Department
Ruriko Kidachi[1], Yoshiko Nishizawa[2], Hideaki Yamabe[2], Shoji Chiba[3], Yuka Noto[4], Chiaki Kitamiya[2], Takashi Ishikawa[5], Koshi Sumigawa[2,] Hirokazu Narita[1] and Minoru Osanai[6]
1 Department of Development and Aging, Division of Health Sciences,
2 Department of Health Promotion, Division of Health Sciences,
3 Department of Biomedical Sciences, Division of Medical Life Sciences,
4 Department of Disability and Health, Division of Health Sciences,
5 Department of Pathologic Analysis, Division of Medical Life Sciences,
6 Department of Radiological life Sciences, Division of Medical Life Sciences,
Hirosaki University Graduate School of Health Sciences

13 Activities of the Social Coordination Group in Radiation Emergency Medicine, 2009-2011
Takao Osanai[1], Yoko Saito[2], Terumi Kogawa[3], Hiroyuki Nozaka[4], Kiyotada Washiya[5], Kumiko Saito[6], Tomoko Ichinohe[3], and Kazuyuki Kida[3]
1 Department of Disability and Health, Division of Health Sciences,
2 Department of Radiological Life Sciences, Division of Medical Life Sciences,
3 Department of Health Promotion, Division of Health Sciences,
4 Department of Biomedical Sciences, Division of Medical Life Sciences,
5 Department of Pathologic Analysis, Division of Medical Life Sciences,
6 Department of Development and Aging, Division of Health Sciences,
Hirosaki University Graduate School of Health Sciences

17 **Reserch activities of co-medical education program in radiation emergency medicine**
Koichi Ito, Research Group
Department of Biomedical Sciences, Division of Medical Life Sciences,
Hirosaki University Graduate School of Health Sciences

Special Lecture

21 **Radiological Nursing of Japan: Values and Responsibilities**
Emiko Konishi,
President, The Radiological Nursing Society of Japan
Kagoshima University Graduate School of Medical and Dental Sciences

Symposium Ⅱ

Poster Session

25 **Acute Radiation Syndrome and Quality of Life in Head and Neck Cancer Patients Undergoing Radiation Therapy**
Yuka Noto[1], Harumi Shikanai[2], Yoshiko Nishizawa[1], Noriko Ogura[1], Eriko Kudo[2], Hideaki Yamabe[1], Yoichiro Hosokawa[1] and Masahiko Aoki[2]
1 Hirosaki University Graduate School of Health Sciences,
2 Hirosaki University School of Medicine and Hospital

31 **Analysis of Japanese newspaper articles with keywords “radiation,” “nuclear energy,” and “disaster”**
Reiko Narita[1] and Ruriko Kidachi[2]
1 Division of Nursing, Hirosaki University
Graduate School of Health Sciences
2 Department of Development and Aging, Division of Health Sciences,
Hirosaki University Graduate School of Health Sciences

35 **Development of the Attitude Scale on Radiation Emergency Medicine for Japanese Nurses and Evaluation of its Reliability and Validity**
Yuka Noto, Noriko Ogura, Mayumi Urushizaka, Maiko Kitajima,
Yoshiko Nishizawa, Tomoko Ichinohe and Hideaki Yamabe
Hirosaki University Graduate School of Health Sciences

43 **Responses of public nurses to the consultations they provided to residents following a nuclear disaster**
Chiaki Kitamiya[1] and Ruriko Kidachi [2]
1 Department of Health Promotion, Division of Health Sciences,
2 Department of Development and Aging, Division of Health Sciences,
Hirosaki University Graduate School of Health Sciences

47 **Effects of rehabilitation for skin and muscle damage caused by high-dose radiation**
-Developing an animal model of local radiation damage to the hind limbs-
Hirokazu Narita[1], Shuhei Koeda[1], Koichi Ito[2], Kyoko Ito[2] and Hitoshi Tsushima[1]
1 Department of Development and Aging, Division of Health Sciences,
Hirosaki University Graduate School of Health Sciences
2 Department of Biomedical Sciences, Division of Medical Life Sciences,
Hirosaki University Graduate School of Health Sciences

51 **The relationship of risk perception of radiation and radiologic knowledge of nurses after the Fukushima Dai-ichi Nuclear Power Plant disaster**
Toshiko Tomisawa[1], Chieko Itaki[1], Keiko Aizu [1], Ayako Ohgino[1] and Kyoko Tagami [2]
1 Hirosaki University Graduate School of Health Sciences,
2 Department of Education,Hirosaki University

57 **Educational effect and assessment before and after radiation emergency medicine personnel training**
Assessment and effects of undergraduate education−Trends over three years
Saichi Wakayama
Department of Development and Aging, Division of Health Sciences,
Hirosaki University Graduate School of Health Sciences

61 **Recipient-transferred allogeneic umbilical cord blood cells reconstitute the hematopoietic system and immunological functions in a murine model**
Hideaki Sato[1,2], Ayumi Wakayama[1,3], Kyoko Ito[1], and Koichi Ito[1]
1 Department of Biomedical Sciences, Division of Medical Life Sciences,
Hirosaki University Graduate School of Health Sciences
2 Cell Technology Center, Stem Cell Institute Inc.
3 Transfusion and Cell Therapy Center, Hakodate Municipal Hospital

65 **Double unit umbilical cord blood transplantation induces MHC-matched single unit dominance with development of immunocompetent lymphocytes in recipients**
Akira Nakano[1], Hideaki Sato[2], Kyoko Ito[1], and Koichi Ito[1]
1 Department of Biomedical Sciences, Division of Medical Life Sciences,
Hirosaki University Graduate School of Health Sciences
2 Cell Technology Center, Stem Cell Institute Inc.

71 **Mitochondrial Involvement in Response of Human Hematopoietic Stem Cells to Radiation**
Masaru Yamaguchi and Ikuo Kashiwakura
Department of Radiological Life Sciences, Division of Medical Life Sciences, Hirosaki University Graduate School of Health Sciences

75 **Combined pharmaceutical drugs approved in Japan protect mice against lethal ionizing radiation**
Tokuhisa Hirouchi[1], Koichi Ito[2], Manabu Nakano[2], Satoru Monzen[3], Hironori Yoshino[3], Mitsuru Chiba[2], Masaharu Hazawa[3], Akira Nakano[2], Junya Ishikawa[3], Masaru Yamaguchi[3], Kimio Tanaka[1], and Ikuo Kashiwakura[3]
1 Department of Radiology, Institute for Environmental Sciences
2 Department of Biomedical Sciences, Division of Medical Life Sciences,
3 Department of Radiological Life Sciences, Division of Medical Life Sciences, Hirosaki University Graduate School of Health Sciences

81 **Morphological study of the digestive, nervous and sensory organs, bone marrow, and lymph node in X-irradiation mice**
Shoji Chiba[1], Yuhei Higuchi[2], Tomoya Nakai[3], Ibuki Higashidate[4], Hitomi Sato[5], Syuji Fukushima[6], Yuhei Nakamura[6], Koichi Itoh[7], Kyoko Itoh[7], Manabu Nakano[7], Haruhiko Yoshioka[1]
1 Department of Pathologic Analysis, Division of Medical Life Sciences, Hirosaki University Graduate School of Health Sciences
2 Yamagata University Hospital, 3 Nakamura Memorial Hospital (Sapporo)
4 Iwate Prefectural Central Hospital, 5 Obihiro-Kosei General Hospital
6 Students in Department of Radiological Technology, Hirosaki University School of Health Sciences
7 Department of Biomedical Sciences, Division of Medical Life Sciences, Hirosaki University Graduate School of Health Sciences

89 **Alteration of extracellular matrix components by X-ray irradiation in rat bone**
Komei Tanaka[1], Yurie Kudo[2], Takashi Ishikawa[1], Kyoko Nakano[1], Mitsuru Chiba[1], Naoki Nanashima[1], Manabu Nakano[1], Koichi Ito[1], and Toshiya Nakamura[1]
1 Department of Biomedical Sciences, Division of Medical Life Sciences, Hirosaki University Graduate School of Health Sciences,
2 Department of Medical Technology, Hirosaki University School of Health Sciences

95 **Effect of ascorbic acid and X-irradiation on human leukemia HL-60 cells and the role played by reactive oxygen species in this effect**
Shingo Terashima[1], Yoichiro Hosakawa[1], Satoru Monzen[1], Ikuo Kashiwakura[1] and Toshiya Nakamura[2]
1 Department of Radiological Life Sciences, Division of Medical Life Sciences,
2 Department of Biomedical Sciences, Division of Medical Life Sciences, Hirosaki University Graduate School of Health Sciences

99 **Radioactive aerosol measurement after the Fukushima nuclear disaster**
Masahiro Hosoda[1], Shinji Tokonami[2], Atsuyuki Sorimachi[2], Hirofumi Tazoe[3], Masatoshi Yamada[3], Satoru Monzen[1], Minoru Osanai[1], Hironori Yoshino[1] and Ikuo Kashiwakura[1]
1 Department of Radiological Life Sciences, Division of Medical Life Sciences, Hirosaki University, Graduate School of Health Sciences
2 Department of Radiation Physics, Hirosaki University, Institute of Radiation Emergency Medicine
3 Department of Radiation Chemistry, Hirosaki University, Institute of Radiation Emergency Medicine

103 **A novel parameter, cell-cycle progression index, for biological dose estimation in premature chromosome condensation assay**
Tomisato Miura[1], Kanako Kikuchi[1], Ami Makino[1], Akifumi Nakata[2], Kosuke Kasai[1], Eiki Tsushima[3], Natalia I. Ossetrova[4], Mitsuaki A. Yoshida[2], and William F. Blakely[4]
1 Department of Pathologic Analysis, Division of Medical Life Sciences, Hirosaki University Graduate School of Health Sciences
2 Department of Radiation Biology, Institute of Radiation Emergency Medicine, Hirosaki University (IREM/HU)
3 Department of Development and Aging, Division of Health Sciences, Hirosaki University Graduate School of Health Sciences
4 Armed Forces Radiobiology Research Institute (AFRRI), Bethesda, MD, USA

107 **Development of rescue support system for complex disaster with radiation medicine**
Hiroyuki Nozaka
Department of Biomedical Sciences, Division of Medical Life Sciences, Hirosaki University Graduate School of Health Sciences

Symposium Ⅲ

111 **Education of nurses or paramedics in the framework of the management of radio-contaminated or irradiated patients: a very important challenge for the French defence radiation protection service (SPRA)**
C Dody[1], X Michel[1], G Weber-Donat[2], F Entine[1], M Gauthier[3], JC Amabile[1] and P Laroche[1]
1 French defence radiation protection service (SPRA), Clamart, France
2 Radiology department, Military Hospital Percy, Clamart, France
3 Military health service Headquarters (DCSSA), Vincennes, Francel

117 The human resource development and training courses on radiation emergency medicine at NIRS

Takako Tominaga[1], Misao Hachiya[2], Hideo Tatsuzaki[1] and Makoto Akashi[3]

1 Department of Radiation Emergency Medicine, Research Center for Radiation Emergency Medicine, National Institution of Radiological Sciences, Chiba, Japan

2 Planning and Promotion Unit, Research Center for Radiation Emergency Medicine, National Institution of Radiological Sciences, Chiba, Japan

3 National Institution of Radiological Sciences, Chiba, Japan

123 The plan of educational program for Certified Nurse Specialist in radiological nursing at Hirosaki University

Yoshiko Nishizawa[1], Yuka Noto[2], Chieko Itaki[2], Toshiko Tomisawa[1], Ruriko Kidachi[3], Tomoko Ichinohe[1], Seiko Kudo[2] and Hideaki Yamabe[1]

1 Department of Health Promotion, Division of Health Sciences

2 Department of Disability and Health, Division of Health Sciences

3 Department of Development and Aging, Division of Health Sciences

Hirosaki University Graduate School of Health Sciences

Developing human health resources for radiation emergency medicine at Hirosaki University: a panoptic report on the 5-year project effort

Hitoshi Tsushima[1]

[1] *Department of Development and Aging, Division of Health Sciences, Graduate School of Health Sciences, Hirosaki, Japan*

Abstract. In 2008, a project to develop human health resources for radiation emergency medicine started at Hirosaki University Graduate School of Health Sciences. The social impetus to this project was the presence of many atomic energy–related institutions in Aomori Prefecture, Japan; Hirosaki University was therefore called on to establish a system for radiation emergency medicine in northern Japan. The goal of the project was to initiate an education program focused on radiation emergency medicine and to have the program on track within 5 years. An additional goal was to promote research in this field from a health sciences perspective. Over the last 5 years we have promoted education aimed at cultivating human resources in specialized radiation emergency medicine. During this period, the curricula for both postgraduate education and entry-level undergraduate education at the School of Health Sciences have been modified on the basis of the established educational philosophy and objectives. These curricula have been in place since April 2010. In addition, recurrent education for incumbent staff at a neighboring core hospital has been started, and the program has been modified every year. By a collective effort, our faculty members provided support for the response to the accident that occurred at the Fukushima I nuclear power plant at the time of the Great East Japan Earthquake, on 11 March 2011. A total of 22 staff members took turns in participating in these missions over a 67-day period, and their efforts were very successful. In this article, a progress report on the current project and an outline of future plans are presented.

Key Words: development of human resources, health professionals, radiation emergency medicine

Background

Although careful attention is paid to the safe use of radiation and substantial radiation protection measures are taken, the probability of accidental exposure to radiation remains. Therefore, as a precautionary measure against such an occurrence, a system must be in place that ensures both the provision of radiation emergency medicine and the prevention of similar incidents. In Japan, nuclear facilities are located in or near 19 prefectures, which are separated into either the eastern or western division. The radiation emergency system in Japan is centered on the National Institute of Radiological Sciences and Hiroshima University, both of which are designated as local tertiary radiation emergency hospitals for the eastern and western divisions, respectively. Consolidating advanced medical technologies is indispensable for radiation emergency medicine. In addition, specific countermeasures, such as nursing care for patients exposed to radiation, measures for contamination control, decontamination, radiation dosimetry, and specific clinical assays, are required. However, present radiation-related education is part of the general medical curriculum in Japan. Therefore, a

[1] Corresponding to: Hitoshi Tsushima, Professor, Hirosaki University, 66-1, Hon-cho, Hirosaki, 036-8564, Japan.
E-mail: pttusima@cc.hirosaki-u.ac.jp

special educational program that focuses on radiation emergency medicine is required.
Numerous nuclear energy-related institutions are located in Aomori Prefecture, and the prefectural government has designated Hirosaki University Hospital as the local tertiary radiation emergency hospital. The mission of Hirosaki University in radiation emergency medicine is to create a system for the effective treatment of heavily exposed patients and to develop human resources in the field of radiation emergency medicine. Against such a background, Hirosaki University Graduate School of Health Sciences has been developing human resources for radiation emergency medicine since 2008.

In this article, a progress report on the current project and an outline of future plans are presented.

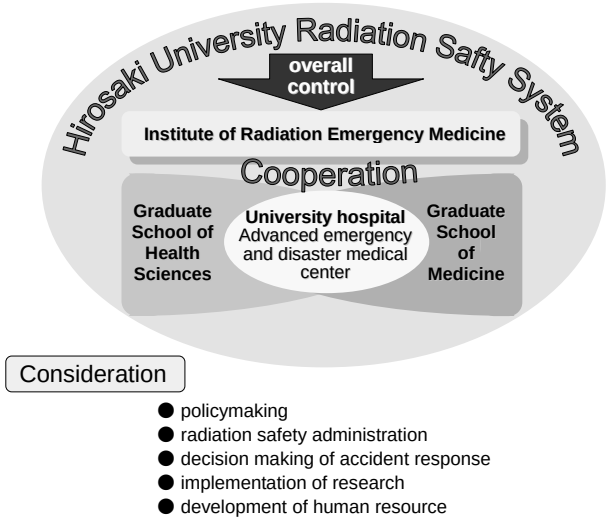


Figure 1 Cooperation framework within the university

Step 1: Goal setting and organization building

At the start of the project, project goals were clarified and activities were organized and developed. Hirosaki University established a radiation safety system to provide the framework for radiation safety-related cooperation within the university. Decisions were made regarding the five points of consideration indicated in figure 1. In addition, an executive committee for the project was set up in the school of health sciences that consists of the four sectors, each with their own role. Because the school did not have a specialist, the entire faculty had to learn about the basics of radiation emergency medicine at the start of the project. Consequently, nearly every staff member participated in a 3-day training session at the National Institute of Radiological Sciences. Finally, we were able to accumulate knowledge, information, and skills through repetitive learning, training and visits to relevant domestic and overseas organizations.

Step 2: Development of basic philosophy and curriculum design

In the second step, we established the foundation for new education in radiation emergency medicine for health professionals. A plan for the development of human resources was designed and the curriculum was systematized. This

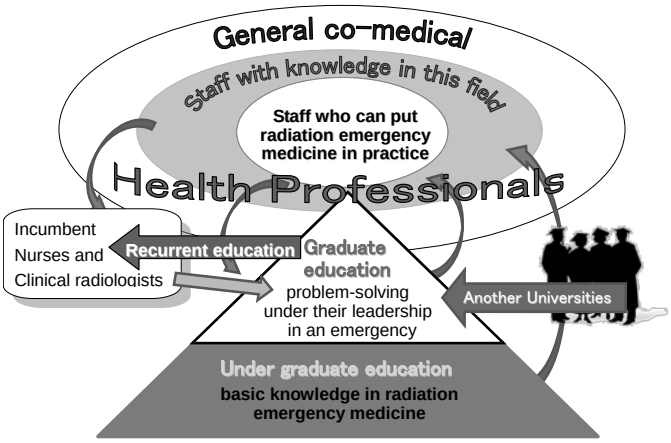


Figure 2 Basic educational philosophy for human resources cultivation

is a conceptual diagram of the basic educational philosophy for human resources cultivation (figure 2).
The education program consisted of three domains: undergraduate, postgraduate, and continuing education. In undergraduate education, the goal is to be able to have basic knowledge in radiation emergency medicine as well as specialized knowledge in each field. The goal of graduate education is to provide students with expertise in radiation emergency medicine and to enable them to solve problems and play a leadership role in emergencies such as radiation disasters. An additional goal is for health professionals to be able to promote education and research in radiation emergency medicine. In continuing education, the goal is to prepare medical professionals to respond

to radiation emergencies with appropriate knowledge and skill.

Step 3: Start-up of the education and research

In the next step, education programs in each domain were started and academic research on radiation emergency medicine was begun in the field of health sciences. Two radiation-related subjects related were allocated to liberal arts curriculum for undergraduates. Radiation coursework and 15 new subjects related to radiation emergency medicine were added for graduate education. In addition, a program certified by Hirosaki University for specialists was established. For those in continuing education, a 2.5-day course for nursing staff and a 2-day course for radiological technologists were conducted. The objectives for students are to acquire essential radiation emergency medicine knowledge and to undergo training that enables the performance of appropriate responses and safety management in radiation emergencies. Additionally, research activities were systematically started in the field of health sciences. As a result, over 54 studies have been conducted in the areas of medical life sciences and health care sciences in the past 4 years (figure 3).

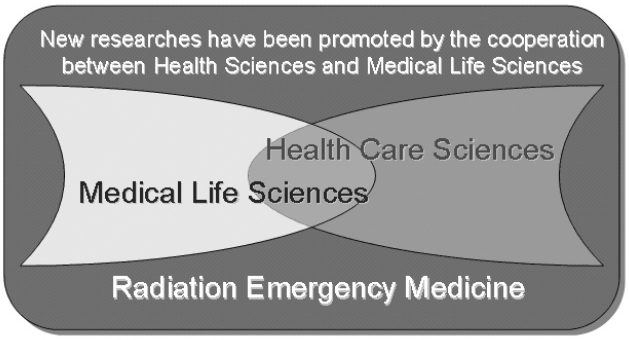


Figure 3 Promotion of the research on Radiation Emergency Medicine

Step 4: Support for the response to the Fukushima Nuclear Power Plant accident

Just as the project was progressing smoothly and consciousness was heightening, the Great East Japan Earthquake occurred, which led to the nuclear disaster at Fukushima Dai-ichi Nuclear Power Plant. Response support was organized at Hirosaki University, and on the basis of decisions made by the university radiation safety organization, 582 faculty members, including nursing staff and radiological technologists in the school of health sciences, were sent to Fukushima to survey the disaster evacuees for radiation. This took place from the time of the accident until the end of July 2011.

Figure 4 Feature of the support activity of Hirosaki University in Fukushima

- The staff sent from our school were able to demonstrate the results cultivated in the project of developing human resources to the support activities.
- They were involved in the radiation survey and medical checkup at temporary homecoming for the victims.
- Especially the nursing staff developed the aggressive activity to relieve anxiety of victims and children.

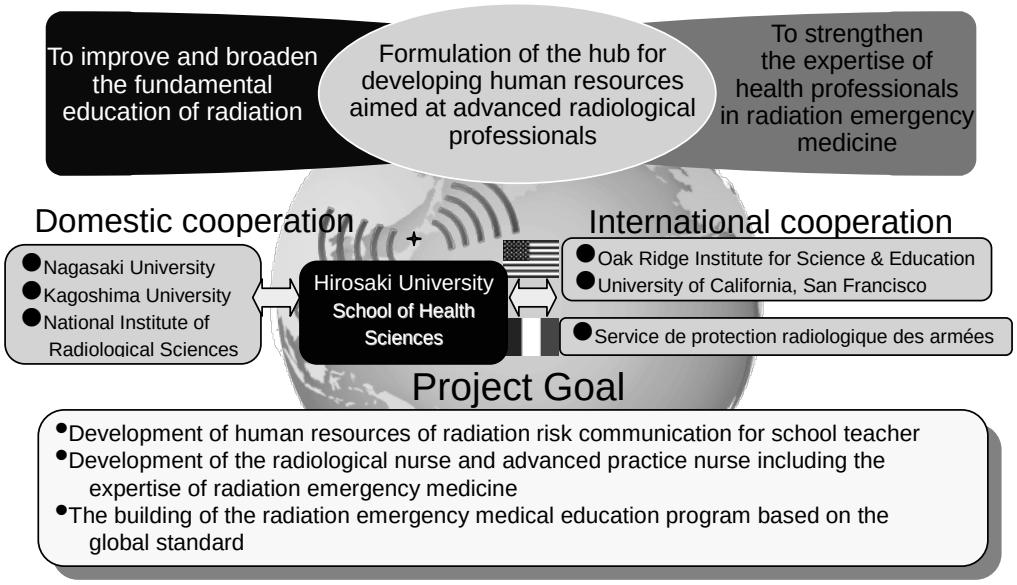


Figure 5 the conceptual plan towards the following

At the end of May 2011, Hirosaki University was asked to support medical check-ups in a temporary homecoming project for evacuees. Three nurses and three radiological technologists from our school were sent to perform this task over a period of 16 days. They were able to clearly demonstrate the results of the human resources development project for support activities. In particular, the nursing staff proactively strived to relieve the anxiety of the evacuees and their children. These points seem to be important features of the support activity of Hirosaki University (figure 4).

Step 5: Generalization of the project toward subsequent steps

The goal in the last phase of the project was to promote cooperation and collaboration with radiation emergency medicine-related organizations both within and without the university in relation to education and research. Based on the 5-year results from the program, measures were discussed for ongoing human resources development programs and strategies for further program development were devised. These discussions led to the drafting of basic concepts for the next project. The budget request for the project was subsequently submitted to the Ministry of Education, Culture, Sports, Science and Technology. The mission of the new project is both to cultivate health professionals who can be leaders in the practice of radiation emergency medicine and to develop effective human resources for the purpose of radiation risk communication (figure 5).

The Radiological Nursing Society of Japan was established on September 20, 2012 in cooperation with Nagasaki University and Kagoshima University, which both have special graduate school courses in radiation nursing. This society will continue its work to build on our academic foundation by remaining active in its pursuits to establish a radiation nursing program able to certify nursing specialists.

Conclusion

The objectives of this 5-year project seem to have been achieved. However, while continuing to increase the development of human resources for radiation emergency medicine, it is still necessary to verify and reexamination its effects in areas including skill improvement for both teachers and students. It is also critical to transmit positive information to Asian nations, where concern about radiation contamination has been increasing.

Practice and Evaluation of the Radiation Emergency Medicine Education Program at Hirosaki University

Toshiko Tomisawa[1*], Chieko Itaki [1]
Manabu Nakano[1], Shuhei Koeda[1], Saichi Wakayama[1]
Tomoko Ichinohe[1], Yoshimitsu Otomo [1]and Toshiya Nakamura[1]

[1] Hirosaki University, Hirosaki, Japan
Hirosaki University Graduate School of Health Sciences
E-mail: tmtott@cc.hirosaki-u.ac.jp

Abstract. It is necessary to provide complementary radiation education to both students and working professionals to prepare for rare and unexpected nuclear disasters. This paper introduces the current radiation education program at Hirosaki University introduced 5 years ago and suggests future enhancements for inclusion in the program. The current program consists of a curriculum for undergraduates, postgraduates, and working professionals. Education aimed at undergraduate students is designed to provide them with information about radiation emergency medicine and risk management of nuclear disasters. Education for postgraduates is designed to develop human resources with Radiation Emergency Medicine (REM)-related advanced specialized knowledge and skills, human resources with the ability to exercise leadership and problem-solving in the event of emergencies, and human resources with the ability to advance REM-related education and research. Unexpectedly, due to the accident at the Fukushima Daiichi Nuclear Power Plant, our students participated as J village medical treatment group members. Education for working professionals is designed for nurses and radiological technologists who are currently working in medical facilities. We will start a new education project, including a Certified Nurse Specialist of Radiological Nursing Course, next year.

Key Words: radiation emergency medicine, radiological education

Introduction

The impact of the Fukushima Nuclear Power Plant Disaster is still ongoing, although 1.5 years have passed since the disaster occurred. Many Japanese people came to fear nuclear power and radiation after the Japan Nuclear Fuel Conversion Co. accident in Tokai-mura, Japan [1)], and the perception of radiation risk among Japanese people seems to have increased after this accident. Medical staff also expresses anxiety about radiation exposure[2)].

In a radiological emergency, medical stabilization and treatment of patients take priority over decontamination efforts[4)]. Emergency Department (ED) staff and non-ED staff who can treat patients in a radiological emergency should be identified and trained in advance. However, specialists in radiology and radiation protection have reported that the curriculums of health science students in Japan do not contain radiological training-related issues needed for medical staff other than radiological technologists, although systematic

[*] Corresponding to: Toshiko Tomisawa, Hirosaki University Graduate School of Health Sciences, 66-1 Bunkyo-cho, Hirosaki, 036-8564, Japan.
E-mail: tmtott@cc.hirosaki-u.ac.jp

radiological education is important for all medical caregivers[5-7].

It is almost 5 years since the Radiation Emergency Medicine Education (subsequently referred to as REM) program was started in Hirosaki University. This education program consists of three levels of training, including that for undergraduates, postgraduates, and working professionals.

This report describes the REM Education Program for all three groups as well as the training received by our staff and changes to the' curriculum after the Fukushima Daiichi Nuclear Power Plant Disaster. Additionally, it describes an evaluation of the REM program at Hirosaki University and proposes activities for the future.

2. REM Education Program in Hirosaki University

1) Undergraduate students

The educational objectives are that undergraduate students will understand three subjects, including basic radiological knowledge and radiation protection, risk management for medical treatment, and the outline of the REM program. Our program provides two subjects, including "Introduction to Basic Radiation" and "Medical Risk Management." "Introduction to Basic Radiation" is part of the liberal arts curriculum and is a required subject for health sciences students**.** This subject is taken by first-year students of health sciences except for those majoring in Radiological Technology. The unit consists of seven 90- minute lectures and a 90-minute test. The contents of this subject cover various topics in radiology. "Medical Risk Management" is medical professional and a required subject for third-year health science students. The objective of this second class is for students to understand crisis-management involving cooperation among medical personnel. This subject includes two lectures that cover risk management methods in medical situations, guidelines for the prevention of medical radiological accidents, risk communication for telling patients about short- and long-term effects of radiation exposure, types of radiation accidents, acute radiation syndromes, and the priorities and processes of the REM program. Both classes were result in an increased understanding of basic radiological knowledge and medical care contents as well as an improved risk perception regarding radiation.

2) Postgraduate students

We developed the REM course to be part of the Master's degree program. The education objectives are that students will have advanced expertise and skills related to REM and be able to manage a situation and provide treatment in emergency conditions. Additionally, we expect students to promote education about the REM and undertake a research study.

The curriculum of the postgraduate REM course is shown in Table 1. Common subjects need to account for eight or more credits and research subjects need to account for 14 credits. An additional eight credits are required in optional subjects, which include four different classes worth four credits each. When students meet the requirements and finish the REM course, they will be able to get a Radiological Health Scientist License from the Department by passing the curriculum alone. Unexpectedly, due to the accident at the Fukushima Daiichi Nuclear Power Plants, our students participated as J village medical treatment group members. They played an important role in the start-up of temporary housing as part of the primary radiation emergency medicine organization where set up by Japanese government.

Table 1. Postgraduate curriculum for the REM course

Category	Total Credit	Subject	Number of subjects	Credit
Common Subjects	8	related to REM	3	6
		related to Health Science	1	2
Research subjects	14	Seminar		2
		Advanced Seminar		2
		Thesis		10
Optional subjects	8	related to REM	2	4
		related to Health Science	2	4

3) Working Professionals

Education for working professionals is available to nurses and radiological technologists who are currently working in medical facilities. We had provided for students of undergraduates a lecture about radiological medicine and Radiation

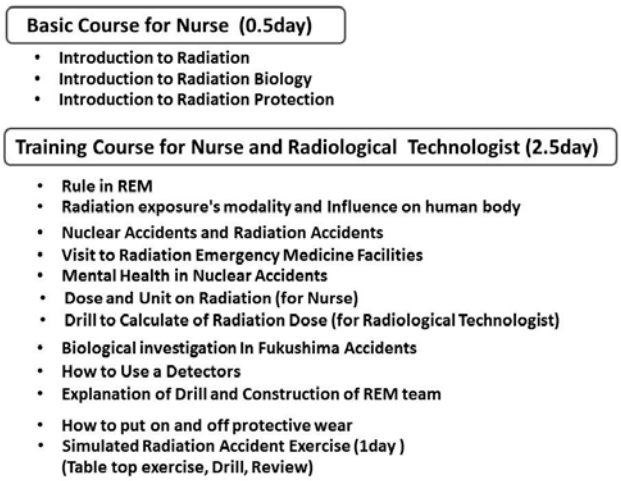


Figure1. Program for working professionals

Emergency Medicine before 2010. However, almost staffs were not specialist on radiology and radiation emergency medicine. Therefore, we made a lot of preparation for university staff to be trained and tried to develop the program from 2008 to 2010. The actual education program started in 2010. Furthermore, we revised this program after the disaster in 2010. It was strengthened to include content about the knowledge needed and skills necessary for Radiation Emergency Medicine, the appropriate correspondence and cooperation needed with other caregivers and patients during an emergency, and information about the disaster in Fukushima (Fig. 1).

The educational objectives are that nurses and radiological technologists will have the knowledge and management skills necessary for REM and will be able to engage in appropriate correspondence and cooperation with each other during an emergency. We have held this training three times already from 2010 to 2012, and 59 nurses and radiological technologists have participated. However, we also have to provide for students and working healthcare providers the complementary simulation training contained more complex cases, although nuclear disasters are rare. We will be discussing our practices over the next 3 years and planning future advancements for the REM program in Hirosaki University starting in 2013.

3. Staff and student practicum after the Fukushima Daiichi Nuclear Power Plant Disaster

We developed the REM program and started to educate people in each subject. To our regret, actual knowledge and experience were applied to develop these programs, although our project was started to ensure people's safety and to provide relief in preparation for an emergency accident. We undertook three practices at the request of the Japanese Government after the disaster.

3.1. Dispatch of Radiation Exposure Research Team

The mission of this team was to perform screening tests of evacuated people and residents in temporary refuges or established survey places in the Fukushima Prefecture and to detect environmental radiation doses around refuges. We dispatched 363 staff members for this task.

3.2. Support to "Temporary Home Visit Project" in the hazard area

A "Temporary Home Visit project" was developed to help to go back home in a hazard area for evacuated residents. The mission of this team was to provide health management to temporary visitors from hazard areas and give advice to residents. A total of 202 staff members cooperated with other specialists for this task.

3.3. Support to establish the REM medical facility in J village

This mission of this team was to establish an REM medical facility at J village, which was 18-20 km from Fukushima Dai-ichi Nuclear Power Plant. J village is a front-line for accident handling. Emergency department doctors and nurses were dispatched. Nurses were graduates students who were attending the REM course.

4. Evaluation of REM program and Activities for the Future

Our projects include holding an REM training drill for ourselves; several nonprofessional staff members in radiology joined in the seminars and workshops (Fig. 2). Almost staff in department could join in this educational project for 4 years. Our projects have resulted in a lot of staff members becoming more familiar with radiology.

There have been many activity included in open lectures, research workshops, and international conferences. We think that we have learned many

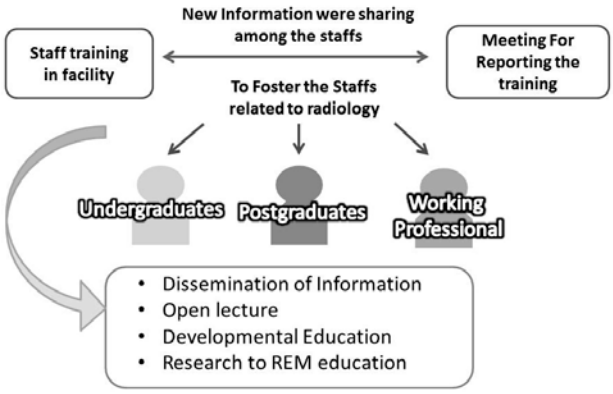


Figure 2. Outcomes of Hirosaki University Radiation Emergency Medicine Projects

things as our project has advanced. First, it is not enough to provide radiological knowledge for healthcare workers as is done in the current continuing education system in our country. Additional training is needed. Second, it is difficult to provide actual practice and manage REM training at the same time. Therefore, it is necessary to provide training repeatedly and to cooperate with the public disaster prevention system. Third, there are few professional staff members available for risk communication on radiation in Japan. We had some experience with the refuges through the dispatch of staff to Fukushima. However, it is necessary to reinforce the education program how to communicate to people regarding the risks of radiation. We plan to start a new education project next year (Table 2). First, we will develop a Certified Nurse Specialist curriculum in our radiological nursing course. Second, we will develop an education program for school teachers to promote risk communication skills. Finally, we will modify the working professional program to allow for practice during actual accidents.

Table 2. Future projects in Hirosaki University

1. Specialist of Radiological Nursing Development for Certified Nurse Specialist of Radiological Nursing Course
2. Personnel involving in Risk Communication Development of teachers for school as to promote Risk Communication
3. To do practice adequately In the disaster Modifying REM course and Collaboration of Local Disaster Prevention System and REM course

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Results of staff education and training in radiation emergency medicine: Summary from the Planning Department

Ruriko Kidachi[1*], Yoshiko Nishizawa[2], Hideaki Yamabe[2], Shoji Chiba[3], Yuka Noto[4], Chiaki Kitamiya[2], Takashi Ishikawa[5], Koshi Sumigawa[2], Hirokazu Narita[1] and Minoru Osanai[6]

[1] Department of Development and Aging, Division of Health Sciences,
[2] Department of Health Promotion, Division of Health Sciences,
[3] Department of Biomedical Sciences, Division of Medical Life Sciences,
[4] Department of Disability and Health, Division of Health Sciences,
[5] Department of Pathologic Analysis, Division of Medical Life Sciences,
[6]Department of Radiological life Sciences, Division of Medical Life Sciences,
Hirosaki University Graduate School of Health Sciences

Abstract. The purpose of the Planning Department is to plan, implement, and evaluate staff education and training in radiation emergency medicine. We report our results from 2008-2012. 74 staff members attended the training course on radiation emergency medicine offered by the National Institute of Radiological Sciences, 27 staff members participated in nuclear power emergency drills sponsored by the Radiation Emergency Medicine Information Network, and 28 staff members participated in the training course on disaster prevention sponsored by the Nuclear Safety Technology Center. All staff members participated voluntarily in order to advance their knowledge in this field. Outside of Japan, several staff members participated in annual training at the Radiation Emergency Association Center/Training Site of the Oak Ridge Institute for Science and Education. In 2010, six staff members visited the Defense Radiation Protection Service. All training reports were collated and their content on the cultivation and utilization of human resources is summarized. A meeting to report on the above lectures and training sessions was held to promote the sharing of staff knowledge 3-5 times annually. Specialists and persons with experience in radiation emergency medicine were invited to give lectures and conduct seminars three times annually. Ninety-three staff members inspected the atomic energy institution and 22 staff members participated in a disaster prevention drill supported by Aomori Prefecture. After the nuclear accident at the Fukushima Daiichi Nuclear Power Plant, many staff members went to Fukushima Prefecture and offered aid to the residents. Several staff members also presented lectures at various meetings. The information provided by these staff members was essential for determining the ongoing activities of the Planning Department.

Key Words: radiation emergency medicine, staff education, staff training

Introduction

The purpose of the Planning Department is to plan, implement, and evaluate the education and training of staff members in radiation emergency medicine. Herein, we report our results from 2008–2012. Based on the status, the planning group decided to educate the staff about radiation and radiation exposure and to implement staff training in radiation emergency medicine. The following action plans were structured to achieve this goal within five years.

*Corresponding to: Ruriko KIdachi, Professor, Hirosaki University, 66-1, Hon-cho, Hirosaki, 036-8564, Japan
E-Mail: kidachi@cc.hiroski-u.ac.jp

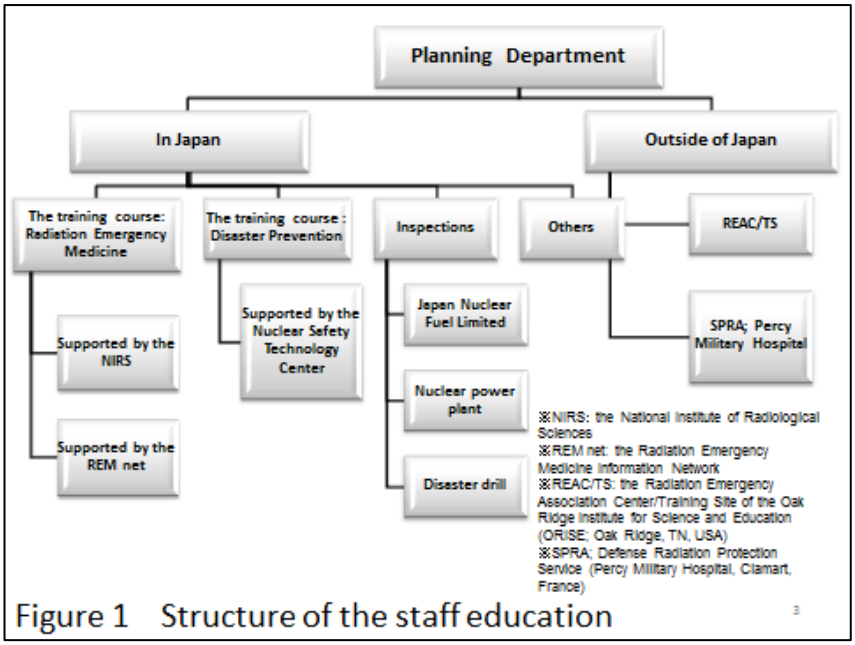

Figure 1 Structure of the staff education

Structure of the staff education

Figure 1 shows the structure of the staff education. The staff education is comprised of training courses both in and outside of Japan. In Japan, the course includes education in radiation emergency medicine, disaster prevention, and inspections, as well as other areas. All staff members participated voluntarily in order to advance their knowledge in these fields.

All training reports were analysed and their content on the cultivation and utilization of human resources were summarized. Furthermore, a meeting to report on the above lectures and training sessions were held to promote the sharing of staff knowledge 3–5 times annually.

On the other hand, specialists and individuals with experience in radiation emergency medicine were invited to give lectures and conduct seminars three times annually. These events were open to the public.

Training in Japan

The training course on radiation emergency medicine was mainly offered by the National Institute of Radiological Sciences (NIRS) or the Radiation Emergency Medicine Information Network (REM net).

Table 1 shows the results of the training course on radiation emergency medicine offered by NIRS. Eighty-four staff members attended the training course on radiation emergency medicine, which was held at the National Center for Radiation Emergency Medical Preparedness in Japan.

Table 1 Results of training on radiation emergency medicine offered by NIRS, 2008–2011

Training course	Date	Number of Attendees
The 1st-NIRS/Hirosaki University radiation emergency medicine	March 5–7, 2008	20
The 2nd-NIRS/Hirosaki University radiation emergency medicine	March 4–6, 2009	23
The 3rd-NIRS/Hirosaki University radiation emergency medicine	August 31 to September 2, 2009	20
The 4th-NIRS/Hirosaki University radiation emergency medicine	March 7–10, 2011	18
The 2nd-NIRS radiation emergency medicine, 2010	September 27–29, 2010	1
2011 NIRS-IAEA-REAC/TS Training Course: International Medical Management of Radiation Incidents	August 23–26, 2011	2

NIRS: the National Institute of Radiological Sciences
IAEA: International Atomic Energy Agency
REAC/TS: the Radiation Emergency Association Center/Training Site

Table 2 Results of the nuclear power emergency drills training sponsored by REM net, 2008–2011

Training course	Date and Place	Number of Attendees
The Forum in Aomori	September 20, 2008	2
Basic course: Radiation Emergency Medicine	October 24, 2009 at Towada-shi, November 28, 2009 at Noheji-machi	5
	June 10, 2011 at Hirosaki-shi, November 15, 2011 at Aomori-shi	9
Advanced course: Radiation Emergency Medicine II; Medical staff course	February 2–3, 2010	5
	May 13–14, 2011 at Sapporo-shi	3
	June 15–6, 2011 at Tachikawa-shi	1
	December 17–8, 2011 at Sapporo-shi	3

REM net: Radiation Emergency Medicine Information Network

Table 3 Results of the training course on disaster prevention sponsored by the Nuclear Safety Technology Center, 2009–2011

Training course	Date and Place	Number of Attendees
Basic course	July 1–2, 2009 at Aomori-shi, August 26–28, 2009 at Rokkasyo-mura	2
	July 7–8, 2010 at Aomori-shi, August 25–26, 2010 at Rokkasyo-mura	7
Administrative course	July 21–23, 2010 at Tokyo, January 18–20, 2011 at Tokyo	2
	January 17–19, 2012 at Tokyo	1
Monitoring course	September 13–15, 2011 at Tokyo	1
First-aid station course	May 29–30, 2008 at Noheji-machi	2
	Jury 21–22, 2009 at Sapporo-shi, August 26–27, 2009 at Mito-shi	3
	July 13–14, 2010 at Aomori-shi, September 7–8, 2010 at Yokosuka-shi	4
	July 6–7, 2011 at Aomori-shi, November 1–2, 2011 at Sendai-shi, December 5–6, 2011 at Yokosuka-shi	5

Table 4 Results of inspections 2009–2010

Drill or institution	Date and Place	Number of Attendees
The disaster prevention drill supported by Aomori Prefecture	August 20–21, 2009 at Rokkasyo-mura	10
	November 4–5, 2010 at Higashidori-mura	6
Civil protection drill	January 29–30, 2011 at Mito-shi	7
Japan Nuclear Fuel Limited; JNFL	March 17, 2008	18
Higashidori Nuclear Power Plant and Japan Nuclear Fuel Limited	September 29–30, 2008	19
	September 7–8, 2009	22
	September 27–28, 2010	12

Table 2 shows the results of nuclear power emergency drills sponsored by the REM net. Twenty-eight staff members participated in the nuclear power emergency drills step by step.

Table 3 shows the results of the training course on disaster prevention sponsored by the Nuclear Safety Technology Center. Twenty-seven staff members participated in the training course on disaster prevention, e.g., the basic course, the first-aid station course, the administrative course, and the monitoring course. Several of these staff members actually participated in multiple training courses.

Table4 shows the results of the inspections. Seventy-one staff members inspected an atomic energy institution and 23 staff members inspected the disaster prevention drills supported by Aomori or Miyagi Prefecture.

Table 5 Results of training outside of Japan, 2008–2011

Course	Date	Number of Attendees
Radiation Emergency Medicine (REAC/TS)	October 21–24, 2008	4
Health Physics in Radiation Emergency (REAC/TS)	February 8–15, 2009	3
Radiation Emergency Medicine (REAC/TS)	August 18–21, 2009	3
Health Physics in Radiation Emergency (REAC/TS)	February 8–15, 2010	2
Percy Military Hospital (SPRA)	March 22–28, 2010	5
Radiation Emergency Medicine (REAC/TS)	September 14–17, 2010	3
Radiation Emergency Medicine (REAC/TS)	November 1–4, 2011	5

*REAC/TS: the Radiation Emergency Association Center/Training Site of the Oak Ridge Institute for Science and Education (ORISE; Oak Ridge, TN, USA)
*SPRA: Defense Radiation Protection Service (Percy Military Hospital, Clamart, France)

Table 6 Domestic and international lectures or information provided after the nuclear accident in Japan

	Date
UCSF; The University of California, San Francisco, CA	November 3, 2011
Oncology Nursing Society 12th Annual Meeting Institutes of Learning, Salt Lake City, UT	November 5, 2011
Aomori University of Health and Welfare	July 21, 2011 at Aomori-shi
The National Institute of Radiological Sciences: NIRS	September 8–9, 2011
Exchange Meeting on the 31st Academic Conference of the Japan Academy of Nursing Science	December 2–3, 2011 at Kochi-shi
FM apple Wave	December 21, 2011
Nursing School of the Hirosaki Medical Association	February 1, 2012
Exchange Meeting on the International Hiroshima Conference on Caring and Peace	March 23–25, 2012 at Hatsukaichi-shi
Teacher certification renewal system at Hirosaki University	August 22, 2012
Seminar of the Aomori Nursing Association	October 12, 2012 at Aomori-shi

Training outside of Japan

Outside of Japan, several staff members participated in annual training at the Radiation Emergency Association Center/Training Site: REAC/TS of the Oak Ridge Institute for Science and Education (ORISE; Oak Ridge, TN, USA). In 2010, five staff members visited the Defense Radiation Protection Service (SPRA; Percy Military Hospital, Clamart, France) (Table 5).

After the nuclear accident

After the nuclear accident at the Fukushima

Daiichi Nuclear Power Plant, many staff members went to Fukushima Prefecture and offered aid to the residents. Several staff members also presented lectures at various meetings. The information provided by these staff members was essential for determining the ongoing activities of the Planning Department (Table 6).

Conclusions: Vision for the future

We looked back at the Planning Department activity during the last 5 years. With the cooperation of all of the staff members who participated in the education, the knowledge and practicable abilities certainly improved. We thank all the people and institutions that provided educational opportunities, and thank all of the staff members who participated. Finally, we suggest the following vision for the future to share our experiences with the world.

1. Continuous education of staff within the department of Hirosaki University
2. Continuous sharing of information about our radiation medicine experiences both domestically and internationally
3. Promotion of activities to raise the scientific foundation of radiation care
4. Development of the Certified Nurse Specialist in Radiological Nursing as part of graduate school education

Activities of the Social Coordination Group in Radiation Emergency Medicine, 2009-2011

Takao Osanai[1*], Yoko Saito[2], Terumi Kogawa[3], Hiroyuki Nozaka[4], Kiyotada Washiya[5], Kumiko Saito[6], Tomoko Ichinohe[3], and Kazuyuki Kida[3]

[1] Department of Disability and Health, Division of Health Sciences, Graduate School of Health Sciences, Hirosaki, Japan
[2] Department of Radiological Life Sciences, Division of Medical Life Sciences, Graduate School of Health Sciences, Hirosaki, Japan
[3] Department of Health Promotion, Division of Health Sciences, Graduate School of Health Sciences, Hirosaki, Japan
[4] Department of Biomedical Sciences, Division of Medical Life Sciences, Graduate School of Health Sciences, Hirosaki, Japan
[5] Department of Pathologic Analysis, Division of Medical Life Sciences, Graduate School of Health Sciences, Hirosaki, Japan
[6] Department of Development and Aging, Division of Health Sciences, Graduate School of Health Sciences, Hirosaki, Japan

Abstract. The Social Coordination Group in Radiation Emergency Medicine was created to collect information associated with the urgent medical care of patients with radiation exposure, build a database system in cooperation with non-member organizations, and publicize the summary, plan, progress, and results of our project on a website. In this time, we conducted survey about attitudes toward this Project in Aomori prefecture, survey about the employment situation in the institutions concerning with radiation for graduate students completing the course of Radiation Emergency Medicine in Hirosaki University and hearing of the needs for training professionals in the prefectures with nuclear power plants. 86% of hospitals in Aomori prefecture knew the project. 90% of hospitals expected the chance concerning radiation emergency medicine 0% or few%. 72% of hospitals had no plan to employ the expert. In the employment situation concerning with radiation for graduate students, 16% of institutions had intention to employ the expert who could cope with radiation emergency medicine, but 82% of institutions had no intention to employ the expert. In the recognition about the Project in Japan, 90% of institutions did not know. These results suggested it is necessary to make an effort so that our project makes it known to everyone.

Key Words: social coordination, recognition of radiation emergency medicine

Introduction

The Social Coordination Group in Radiation Emergency Medicine was created to collect information associated with the urgent medical care of patients with radiation exposure, build a database system in cooperation with non-member organizations, and publicize the summary, plan, progress, and results of our project on a website.

Along the purpose mentioned above, we visited many associations of medical professions concerning with the urgent medical care of patients

[*] Corresponding to: Takao Osanai, Associate Professor, Graduate School of Health Sciences, 66-1, Hon-cho, Hirosaki, 036-8564, Japan.
E-mail: osanai@cc.hirosaki-u.ac.jp

with radiation exposure public relations. We visited local government with nuclear power plant to collect information about job situation of expert for radiation emergency medicine. And we conducted survey about attitudes toward Radiation Emergency Medicine Human Resources Development Project in Aomori prefecture, survey about The employment situation in the institutions concerning with radiation for graduate students completing the course of Radiation Emergency Medicine in Hirosaki University and hearing of the needs for training professionals in the prefectures with nuclear power plants.

In this paper, we described survey about Attitudes toward Radiation Emergency Medicine Human Resources Development Project in the Aomori Prefecture, survey about The employment situation in the institutions concerning with radiation for graduate students completing the course of Radiation Emergency Medicine in Hirosaki University and hearing from local government with nuclear power plant.

Attitudes toward Radiation Emergency Medicine Human Resources Development Project in the Aomori Prefecture.

The Radiation Emergency Medicine Human Recourses Development Project needs cooperation of many hospitals to let this project succeed. Therefore, we surveyed attitudes of hospitals in the Aomori prefecture toward the Radiation Emergency Medicine Human Resources Development Project in Hirosaki University. The first survey was conducted in January 2011. Subjects were 49 hospitals for emergency care in Aomori prefecture. The questions were recognition about the Radiation Emergency Medicine Human Resources Development Project in Hirosaki University, their expectation of the possibilities for concerning the Radiation Emergency Medicine and job situation for expert for the Radiation Emergency Medicine in the hospital.

We received answers from 31 hospitals (rate of answers was 63%). The number of the hospitals recognizing the Radiation Emergency Medicine Human Resources Development Project in the Hirosaki University was 23(75%). In the expectation for the chance concerning radiation emergency medicine, 25(80%) hospitals expected the chance were 0% or few%. In the job situation, 6(20%) hospitals had already employed expert for radiation emergency medicine or had a plan to employ them, but 25(80%) hospitals had no plan to employ them.

The second survey was conducted in August 2011.

Subjects were 48 hospitals for emergency care in Aomori prefecture. The questions were the same as question of first survey.

We received answers from 29 hospitals (rate of answers was 60%). The number of the hospitals recognizing the Radiation Emergency Medicine Human Resources Development Project in the Hirosaki University was 25(86%). In the expectation for the chance concerning radiation emergency medicine, 26(90%) hospitals expected the chance were 0% or few%. In the job situation, 8 (28%) hospitals had already employed expert for radiation emergency medicine or had a plan to employ them, but 21(72%) hospitals had no plan to employ them.

The first survey was carried out before Fukushima Nuclear Power Plant accident in March, 2011. And the second survey was carried out after the accident. In the second survey, the number of hospitals recognized of the Radiation Emergency Medicine Human Resources Development Project in Hirosaki University was increase. However, in the expectation of the possibilities for concerning the Radiation Emergency Medicine, 26 hospitals expected they had no chance concerning with radiation emergency medicine. In job situation for expert for the Radiation Emergency Medicine, 21 hospitals had no plan to employ the expert.

The employment situation in the institutions concerning with radiation for graduate students completing the course of Radiation Emergency Medicine in Hirosaki University.

We conducted a survey about the employment situation in the institutions concerning radiation for graduate students completing the course of Radiation Emergency Medicine in Hirosaki University. The purpose of this survey was to know the acceptance situation of the professional completed the course of Radiation Emergency Medicine.

Subjects were 2615 institutions using radiation located in the East Japan and in prefectures with nuclear power plant. The questionnaires were sent via mail. The contents of the questionnaires were kind of institution, Presence of the expert for

radiation emergency medicine, need for the expert, training situation of the expert, intention of employment for the professional completed the course of Radiation Emergency Medicine and recognition of the Radiation Emergency Medicine Human Resources Development Project in Hirosaki University. 142 questionnaires were sent back in address ignorance. Finally, questionnaires were sent to 2473 institutions. We received answers from 615 institutions (rate of answers was 24.8%) at March 2012.

The number of institutions replying the answer to questionnaire were hospitals or medical facilities was 149(24%), university or educational facilities was 92(15%), a research institute was 77(13%), a private enterprise was 224(36%), other institution was 59(10%) and institution with no answer was 14(2%). The number of institutions which employed the expert who could cope with radiation emergency medicine was 102(16%). The number of institutions which did not employ the expert was 502(82%) and 14(2%) institutions did not answer. In the need for the expert who could cope with radiation emergency medicine, 203(33%) institutions answered they needed the expert, 396(64%) institutions answered they did not need the expert and 16(3%) institutions did not answer. In the situation of training the expert who could cope with radiation emergency medicine, 16(3%) institutions had already trained the expert enough, 85(14%) institutions had already trained the expert, but were insufficient, 381(61%) institutions had no plan to train the expert and 18 institutions did not answer. In the intention of institutions for employment the expert who completed the course of Radiation Emergency Medicine in Hirosaki University, 2(0.3%) institutions had intention to employ the expert voluntarily, 48(8%) institutions considered employment of the expert, 320(52%) institutions had no intention to employ the expert, 234(38%) institutions could not decide employment or unemployment for the expert and 12(2%) institutions did not answer. In the recognition about Radiation Emergency Medicine Human Resources Development Project in the Hirosaki University, 14(2%) institutions knew the project very well, 20(7%) institutions had heard the project, but they did not know, 552(90%) institutions had not heard and they did not know.

The level of recognition about the course of Radiation Emergency Medicine in Graduate School of Health Sciences, Hirosaki University had been low in Japan yet. Then it is necessary to make an effort so that our project makes it known to everyone.

Needs of local government in possession of nuclear power plants for training professionals

We visited the local government with nuclear power plant in Fukui, Niigata, Ibaraki and Hokkaido. We heard the present situations of the nuclear power plant of the local government and their opinions for the training or the needs of the expert for radiation emergency medicine.

The safety measures of the nuclear power plant were to make the manual of radiation emergency medicine, to hold a class of radiation emergency medicine, to build a network with association of medical profession and enforcement of the disaster prevention drill for radiation accidents. The local governments with nuclear power plant recognized the need for experts in radiation emergency medicine, however, the training expert needed much costs. Then, they had no intention of training the experts by themselves.

Conclusion

We surveyed about attitude of hospitals toward The Radiation Emergency Medicine Human Recourses Development Project in Aomori prefecture, an intention to employ the expert completed the course of Radiation Emergency Medicine in Hirosaki University in institutions using radiation located in East Japan and a situation of local government in prefectures with nuclear power plant. Many hospitals in Aomori prefecture recognized the project. But many hospitals thought they were not concerned with radiation emergency medicine. And many hospitals had no plan to employ the expert. Many institutions using radiation did not have the plan to employ the expert who completed the course of Radiation Emergency Medicine. And many institutions did not know the project of Radiation Emergency Medicine in Hirosaki University. On the other hand, many local governments with nuclear power plant thought they needed an expert of radiation emergency medicine. These result suggested that we had to make more effort to publicize about the project.

Research Activities of Co-medical Education Program in Radiation Emergency Medicine

Koichi Ito*, Research Group

Department of Biomedical Sciences,
Division of Medical Life Sciences,
Hirosaki University Graduate School of Health Sciences,
Hirosaki, Japan

Abstract. Since 2008, we have been gathering insights in the field of radiation emergency medicine through research performed in two areas, the Division of Health Sciences and the Division of Medical Life Sciences. With respect to the accident at the Tokyo Electric Power Fukushima Daiichi nuclear power plant, the content of many of these studies has had direct practical applications. The results of these studies have not only been published in peer-reviewed academic journals and presented at international academic conferences but have also been made widely available to the general public through open public lectures. During the project period, two members of our research group also studied at nuclear-related teaching and research institutions in France and the United States, to gain specialist knowledge of the biological effect of radiation. We have also been performing long-term radiation monitoring in the town of Namie, Fukushima Prefecture, which was affected by the nuclear accident, and have developed a research framework to obtain scientific data that can be passed down to future generations. All our results are reviewed by external specialists every year, with the aim of improving the level of research.

Key Words: radiation emergency medicine, research, health science, medical life science

Introduction

The objective of our research group's activities is the systematic development of research related to radiation emergency medicine in the field of public health, through enhanced collaboration between the Division of Health Sciences and the Division of Medical Life Sciences. The results of studies in these two areas with respect to the radiation medicine-specific physical and mental nursing of people exposed to radiation, radiation decontamination and dose measurement, and the biological effect on people exposed to radiation and their treatment must be collated and made available for use in future radiation medicine. The Fukushima nuclear accident occurred while the project was underway, meaning that these research topics became matters of practical relevance.

Research Themes

In the Division of Health Sciences, studies on seven topics are currently underway. They cover areas including medical treatment for radiation exposure, as well as psychological

* Corresponding to: Koich Ito, Professor, Hirosaki University Graduate School of Health Sciences, 66-1 Hon-Cho, Hirosaki, 036-8564, Japan.
E-mail:kohito@cc.hirosaki-u.ac.jp

nursing, image analysis, rehabilitation, and education. In the Division of Medical Life Sciences, studies on ten topics are underway. They include research on medical treatment for radiation exposure, its biological effect, dose measurement, and the development of an emergency communication system. Rather than engaging in joint studies of single topics, our two divisions are each working on various research themes, in the hope that this will lead to more comprehensive solutions to radiation medicine issues in the field of health sciences.

Publication of Papers

Table 1 shows the numbers of papers published from 2008 to 2011. Five papers were published in 2008, six in 2009, five in 2010, and 24 in 2011 (a total of 40 publications to date). Almost all were published in English-language peer-reviewed journals, and the number of publications increased markedly in 2011.
This showed that work on most of the research topics was approaching completion. One paper that made an impact was “The time variation of dose rate artificially increased by the Fukushima nuclear crisis” by Hosoda et al., which was published in Scientific Reports in 2011. This concerned the accident at the Fukushima nuclear power plant and described radiation doses detected in the atmosphere between Fukushima City and Hirosaki City. This was an important report, as its results showed how atmospheric contamination with radioactive substances was spreading.

Conference Presentations

Table 2 shows the number of conference presentations from 2008 to 2011. Thirty presentations were given in Japan and overseas in 2008, 18 in 2009, 27 in 2010, and 73 in 2011. Presentations by the Division of Health Sciences were added in 2010, greatly increasing the number.

Table 1. Number of Original Research Articles

	English	Japanese
2008	5	0
2009	6	0
2010	5	0
2011	21	3

Table 2. Conferences

	International	Domestic
2008	9	21
2009	6	12
2010	22	5
2011	46	27

Overseas Study

Our members studied overseas while the project was underway. During their time abroad, one member studied radiation-induced skin damage at HIA Percy in France, and the other studied new methods of biodosimetry at AFRRI in the United States. This experience of research in advanced nuclear nations will prove extremely valuable in the responses to any future nuclear accidents.

Social Contributions by Our Research Group

We are contributing to the society in two main ways. First, by holding a number of public lectures in addition to publishing our results in the professional arena, we are endeavoring to enable people to acquire correct basic knowledge about radioactivity. These lectures have included wide-ranging content, covering the properties of radiation, its effect on health, and nursing activities during radiation disasters. The other is evidenced in the content of the partnership agreement signed on September 29, 2011, by Hirosaki University and the town of Namie, Fukushima Prefecture, from which almost all the residents were forced to evacuate as a result of the accident at the Tokyo Electric Power Fukushima Daiichi nuclear plant. Our research group is carrying out long-term radiation dose monitoring of the soil, plants, and other aspects of agricultural land in order to gather scientific data for future generations and assisting with recovery by implementing environmental improvements, including decontamination of the town, health checkups, and other activities.

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Conclusions

Our research group has so far been engaged in research on dealing with radiation exposure, and in the future, it will be necessary to put the results achieved from these activities to more practical use.

Radiological Nursing of Japan: Values and Responsibilities

Emiko Konishi, RN, PhD

President, The Radiological Nursing Society of Japan
Kagoshima University Graduate School of Medical and Dental Sciences

Abstract. This paper discusses values and responsibilities in radiological nursing by learning from cases in the following historical events that Japan experienced:
1. Atomic bombing in Hiroshima and Nagasaki, 1945
2. Fukushima Nuclear Power Plant accident, 2011
3. Nuclear fuel facility accident,1999
In emergency situations like these, nurses are challenged by a dilemma between: A) good for this particular patient, and B) good for many other people. The nurse's code of ethics states that the nurse's fundamental professional responsibility is to those who require nursing care. The three nuclear emergency cases challenge nurses to discern their most important values and responsibilities from many other demands. The paper then looks at Japan's current situation after the tragic Fukushima accident. It is now necessary for radiological nursing to transform from the traditional model to a wider new model where nurses care for not only patients receiving radiation treatment but also for people living in accident prone communities, patients suffering radiation injuries, and radiation industry workers in daily as well as in emergency situations. With academic and clinical nurses working together, we must increase knowledge and improve radiological nursing care across hospitals, clinics and communities.

Key Words: radiological nursing, Japan, Values and Responsibilities

Introduction

We announced the establishment of the Radiological Nursing Society of Japan on September 29, 2012. Radiological nursing has developed over the years mainly in hospitals and clinics. Recent practice of radiation oncology nurse specialists symbolizes this development. Yet, future direction of Japan's radiological nursing is not limited to practice in hospitals and clinics. The recent urgent need for widening the scope of radiological nursing practice has led to the establishment of advanced practice course for radiological nursing in the graduate schools of Hirosaki, Nagasaki, and Kagoshima Universities. These developments tell us that radiological nursing of Japan has a promising future.

And when thinking about the future, it is important to learn from the past. Therefore, today, I want to discuss values and responsibilities in radiological nursing by learning from cases in the following historical events that Japan experienced:

1.Atomic bombing in Hiroshima and Nagasaki, 1945
2.Fukushima Nuclear Power Plant accident, 2011
3. Nuclear fuel facility accident,1999

In emergency situations like these, nurses are challenged by a dilemma between:
A: good for this particular person
B: good for many other people

1. Nurses in Hiroshima and Nagasaki, 1945

The atomic bomb was dropped on Hiroshima and Nagasaki in August 1945. In this extremely devastated and confused environment, nurses placed themselves at risk, working tirelessly to care for the wounded and thereby saved lives. Their extensive nursing care was not known until quite recently when a nursing research group led by our colleague Yuko Matsunari detailed those nurses' experiences. These researchers interviewed with nine nurse survivors who were in their early 20s at

the time of the bombing and now are in their 80s or 90s.

The nurse's narrative testimonies (Courtesy, Y Matsunari)

Nurse A: When I was alone working in the nurses' station, I heard a high-pitched noise and suddenly everything went dark. I had no idea what was going on. But I remembered that the patients had all been put in the basement, so I rushed off. Downstairs, everyone was fine. I told them to gargle and to wipe their bodies. A medicine cabinet had fallen on me and broken my ribs, and I was bleeding. At the time, I didn't even notice the broken ribs.

Nurse B: People wanted water, but there was none. They clutched at the hem of my uniform. I had no choice but to tell them "Please wait," otherwise they wouldn't let me go. Later I regretted this because they were suffering so much.

Nurse C: On the 3rd day after the bombing, when I was doing rescue work, I became sick. I vomited several times and could not work. So I went home. A month later when I came back to work I knew that so many colleagues and patients had died. I was so deeply sorry for not having worked during such an important time. Still now, I am apologizing to them.

What shapes these nurses' testimonies is their great concern for those suffering and feelings of guilt. The nurses themselves were victims, yet, throughout their lives, they have never been free from guilt feelings for not giving water to burnt people, not giving nursing care to dying people in order to save people with a better chance of survival, or not being able to work because of their own radiation sicknesses.

The Matsunari group's research emphasizes the need to teach disaster nursing so that nurses will not feel guilty after their relief activities. I totally agree with their point. We need to teach nurses how to organize their work in disasters and how to cope with their reactions. We must reassure them that they did the right thing in very difficult situations. In extreme emergency situations like Hiroshima-Nagasaki, the long-held nursing values and responsibilities for 'the good of this particular patient' is shifted to a framework where nurses are responsible for the greatest good for the greatest number of individuals. This is triage ethics. Nurses should not feel they must sacrifice themselves trying to save all patients when this is not possible. Nurses are an invaluable resource to society.

2. A nurse administrator and the Fukushima Nuclear Power Plant accident, 2011

As we all know, the major earthquake and Tsunami on March 11th,2011, triggered the Fukushima Nuclear Power Plant accident. The mandatory evacuation order allowed no exception, therefore the hospitals and clinics near the power plant had to move all the patients to distant facilities. In this evacuation process, numbers of frail patients died.

Later there was a television interview with a nurse administrator of one such hospital. This nurse said to the helicopter rescuers: 'This person is not breathing but is living'. 'I understand', the rescuer replied and put that person in the helicopter.

At first, I was deeply moved by this nurse's comment. Her respect for and devotion to the patient greatly touched my heart. But soon afterwards, a question arose in my mind. 'What about other patients who were living and breathing at that time?' Those patients may have missed the chance of being rescued because of that patient who was already dead. I know how difficult it was for this nurse to abandon her patient who was not breathing. However, that was an extreme emergency situation. While this nurse's wholehearted caring was what she had been taught, she did not see the larger context and therefore failed to execute her more important professional responsibility required in that situation.

I want to re-state that in extreme emergency situations, professional nurses must overcome the difficulty in refocusing from the long-held values and responsibilities in one-to-one usual patient care situations to those in a one-to-many care framework where nurses are responsible for the greatest good for the greatest number of individuals. And I think this difficulty can be overcome by nurses who are taught to be aware of individuals. It is only as we have awareness of individuals that we can create the larger picture, as you will see in the next case.

3. Two values in transporting the nuclear accident patient, 1999

In 1999, a criticality accident occurred at a nuclear fuel facility where two workers died several months later from fatal doses of radiation. When the most severely exposed worker, Mr O, was brought to the local first aid hospital, he already had fever, vomiting, difficulty breathing and other acute radiation syndromes. Also, primary radiological surveys detected gamma -rays from his body surface, which led to the suspicion that his body surface was radioactively contaminated. Because of these data, the patient was transferred to the designated central hospital responsible for radiation emergencies. In this transport process, this nuclear accident patient was wrapped in a plastic sheet which is normally used for transporting radioactive materials.

Later, I was surprised to read about this treatment in a medical report detailing this accident. In my paper titled "Two values: thoughts on transporting the nuclear accident patient", I raised a question: In this situation which is the first priority?

A. To safe-guard the dignity, comfort and life of this patient, or
B. To protect the environment and people from a possible spread of radioactive contamination

In this case, what the professionals did was to take B as the first priority. However, I, as a nurse, would take A. The most important thing in this situation was to provide care for the dignity, comfort and life of the patient who was suffering life threatening injuries. To wrap the patient in a plastic sheet is very dangerous because it produces more fever, sweat and dehydration, and seriously damages body fluid balance.

For the transport of such a seriously injured person nurses takes the following procedure: dress the patient in a clean and soft gown, prepare the stretcher with a clean, soft cloth covering, place the patient on it, and then lay clean, soft sheets over the patient. A gargle basin and other nursing goods will be provided when necessary. This nursing care comforts the patient and preserves the patient's dignity, but at the same time prevents the spread of possible radioactive contamination, because the patient is confined in a layer of clean gown and cloths. .
This case is an example that It is only as we have awareness of individuals that we can create the larger picture.

The nurses' code of ethics states that the nurse's fundamental professional responsibility is to those who require nursing care. The three nuclear emergency cases I just presented challenge nurses to discern their most important values and responsibilities from many other demands.

After the Fukushima accident

Before closing, I want to look at Japan's current situation after the tragic Fukushima accident. More than a year after the tragedy, the accident stricken reactors are under control, however, long-term contaminated areas remain. Although efforts continue to reduce the radiation level of the environment, concerns and anxieties are spreading nationwide, irrespective of the distance from the power plant. The problems include:

- Still today, many people do not want to buy any food from Fukushima prefecture although the food is now confirmed safe.
- Children relocated from Fukushima are often bullied and discriminated by class mates who say "You are dirty and contaminated and we don't want to get infected from you".
- A number of young mothers who lived in Fukushima aborted the pregnancy

Nurses in the hospitals, clinics and the community face questions from people including:

- I hear that children are most vulnerable to radiation. Does that mean that our child develops cancer sometime?
- Is it safe to swim in the pool of this town?

People's need for radiation related information is obvious. Henderson, Orem and other nurse theorists state that health information is a basic human need that requires nursing care and teaching.

The International Commission on Radiological Protection (ICRP), in its recommendations for the protection of people living in long-term contaminated areas after a nuclear accident states:
-The complexity of post-accident situations cannot be managed without addressing all the affected domains of daily life, including environmental, health, economic, social, cultural, and ethical.
-Dissemination of a practical radiological protection culture within all segments of the population, and especially within professionals in charge of the public health and education is key to the success of protection strategies in the long term.

These statements of the ICRP and our nurse theorists guide the direction of radiological nursing of Japan. It is now necessary for radiological nursing to transform from the traditional model to a wider new model where nurses care for not only patients receiving radiation treatment but also for people living in accident prone communities, patients suffering radiation injuries, and radiation industry workers in daily as well as in emergency situations. With academic and clinical nurses working together, we must increase knowledge and improve radiological nursing care across hospitals, clinics and communities.

Acute Radiation Syndrome and Quality of Life in Head and Neck Cancer Patients Undergoing Radiation Therapy

Yuka Noto[1*], Harumi Shikanai[2], Yoshiko Nishizawa[1], Noriko Ogura[1], Eriko Kudo[2], Hideaki Yamabe[1], Yoichiro Hosokawa[1] and Masahiko Aoki[2]

[1]Hirosaki University Graduate School of Health Sciences, Hirosaki, Japan
[2]Hirosaki University School of Medicine and Hospital, Hirosaki, Japan

Abstract. This study aimed to measure the severity of acute radiation syndrome and its resulting effect on the quality of life (QOL) in patients being treated for head and neck cancer. The subjects were 16 patients with head and neck cancer undergoing radiation therapy at Hirosaki University School of Medicine and Hospital, Japan. They were asked to record their symptoms in a diary from the day before the start of radiation therapy until its completion. The recorded symptoms were classified from Grade 1 to Grade 5 according to the Common Terminology Criteria for Adverse Events v3.0, Japanese translation JCOG/JSCO. The standard version of the 8-item short form health survey (SF-8^{TM}) was used to assess patient QOL on three occasions: before irradiation, immediately after completing irradiation, and 4 to 6 weeks after irradiation. All patients had two or more symptoms within the radiation therapy period. Fatigue, anorexia, nausea, and decrease of body weight loss were recognized as general symptoms. Stomatitis, dysphagia, dry mouth, dermatitis, itching, pain, cough, and voice changes were reported as local symptoms. Many patients exhibited Grade 2 or 3 anorexia, stomatitis, dysphagia, pain, and voice changes. Many of the acute radiation side effects remained until the completion of irradiation. Most patients had oral cavity symptoms from early in the irradiation period (within 1 week), and a couple developed symptoms after 2 weeks. More than half of these patients were classified as having Grade 2 or 3 symptoms. Dermatitis appeared early in a few patients at a radiation dose of 6 Gy, and it appeared in half of the patients at a dose of 10 Gy. It was classified as Grade 2 or 3 in several patients. In many cases, fatigue appeared early in the irradiation period, and it was classified as Grade 2 or 3 in several patients. In some patients, it started immediately after radiation therapy. At the three measurement intervals, the eight domain scores and two summary scores of the SF-8^{TM} were lower than the Japanese standard values in all cases. The physical functioning (PF) and the physical component summary (PCS) scores were significantly lower after radiation therapy than before radiation therapy ($p < 0.05$). It became clear that symptoms appeared from early in the irradiation period, and that local symptoms were severe. QOL scores decreased as a result of radiation therapy. Thus, nursing intervention from soon after the start of radiation therapy is necessary to ease these symptoms and improve QOL.

Key Words: radiation therapy, head and neck cancer, acute radiation syndrome, QOL

Introduction

The head and neck are irreplaceable. Among other things, they are important for breathing, food intake and speaking. The face is the focal point for human communication and is also a significant part of our persona. Therefore, the disorder and sequela which arise from head and neck cancer treatment pose serious problems. Operative therapy sometimes changes the appearance of the patient,

* Corresponding to: Yuka Noto, Hirosaki University Graduate School of Health Sciences, 66-1, Hon-cho, Hirosaki 036-8564, Japan
E-mail: noto@cc.hirosaki-u.ac.jp

which can have a serious impact on psychological health and result in a significant decline in QOL. However, a lot of head and neck cancer is squamous cell carcinoma, and the susceptibility of this type of cancer to radiation therapy or chemotherapy is comparatively high. Recently, the modality combining these treatments is often opted for in many cases. These treatments can preserve form and function, and they can reduce the decline in QOL. Radiation therapy is a cure led treatment using the difference in the susceptibility to radiation between the tumor and normal tissue. Therefore, some adverse reactions of normal tissue to radiation are unavoidable. In particular, it is known that radiation therapy for head and neck cancer has a high appearance ratio of adverse reactions. While concurrent chemo-radiotherapy, which uses chemotherapy together with radiation therapy, has a curative effect, it does have a high appearance ratio of adverse reactions [1]–[3].

This study aimed to measure the severity of acute radiation syndrome and its resulting effect on the quality of life (QOL) in patients being treated for head and neck cancer.

Method

Subjects

The subjects were 16 patients with head and neck cancer undergoing radiation therapy at Hirosaki University School of Medicine and Hospital, Japan.

Sampling

A three-part survey was used to collect the data, and included a demographic questionnaire, the standard version of the 8-item short form health survey (SF-8^{TM}), and a symptom diary. The demographic questionnaire obtained information on age, gender, and smoking status (i.e., smoker or non-smoker). The diagnosis, stage of cancer, radiation therapy (irradiation regions, fraction, and dose) operative therapy, and chemotherapy methods were obtained from the patients' medical records. Fractionation is the division of the total dose of radiation into smaller doses (fractions). The conventional or standard fractionation is one fraction of 2 Gy given daily, 5 days per week.

Instruments

1. Symptoms diary

The patients were asked to record their symptoms in a symptom diary from the day before the start of radiation therapy until its completion. The recorded symptoms were classified into Grade 1 to Grade 5 according to the Common Terminology Criteria for Adverse Events v3.0, Japanese translation JCOG/JSCO.

2. SF-8 ^{TM}

The SF-8^{TM} was used to determine patient QOL on three occasions: before irradiation, immediately after completing irradiation, and 4 to 6 weeks after irradiation.

The SF-8 ^{TM} measures eight concepts commonly represented in widely used surveys: physical functioning (PF), role limitations due to physical health problems (role physical, RP), body pain (BP), general health (GH), energy/fatigue (vitality, VT), social functioning (SF), role limitations due to emotional problems (role emotional, RE), and psychological distress and well-being (mental health, MH). Two summary measures are produced, the physical component summary (PCS) and mental component summary (MCS). Different versions of SF-8 ^{TM} have been developed and validated for three recall periods: standard (4-week), acute (1-week), and acute (24-hour).

Ethical considerations

This study was approved by the Ethics Committee of Hirosaki University Graduate School of Medicine. The intent of the study was explained to the patients, and the study was conducted after obtaining informed consent.

Data collection period

Data was collected from November 2010 until June 2012.

Results

Patient characteristics

The mean age of the patients was 59.8±11.4 (range 25–76) years and 14 (87.5%) patients were male. The irradiation fraction was 17 to 40, and the total radiation dose was 36.6 to 69 Gy. Almost all patients had received irradiation in two or more parts. Seven patients underwent operative therapy before radiation therapy, and 14 patients underwent concurrent chemo-radiotherapy. The patients' characteristics are shown in Table 1.

Table 1 Patients characteristics n=16

Age(years)	
Median±SD	59.8±11.4
Range	25-76
Sex	
Male	14
Female	2
Diagnosis	
pharyngeal cancer	5
laryngeal cancer	3
malignant lymphoma	2
lingual cancer	2
maxillary cancer	2
other	2
Treatment	
Mode of treatment	
RT, RT+S	3
CRT, CRT+S	13
5-Fu	9
Radiation dose	36.6-69Gy

SD: standard deviation, RT: radiotherapy, S: surgery, CRT: chemo-radiotherapy

Acute radiation damage during irradiation

All patients had two or more symptoms within the radiation therapy period. Fatigue (12 patients), anorexia (11 patients), nausea (10 patients), and decrease of body weight (9 patients) were recognized as general symptoms. Stomatitis (15 patients), dysphagia (15 patients), dry mouth (15 patients), dermatitis (12 patients), itching (10 patients), pain (15 patients), cough (9 patients), and voice changes (8 patients) were reported as local symptoms. Many patients exhibited Grade 2 or 3 anorexia, stomatitis, dysphagia, pain, and voice changes. Many of the acute radiation side effects remained until the completion of irradiation.

Symptoms occurring during irradiation

1. Problems of oral nutrition intake

1) Oral cavity symptoms

Most patients had oral cavity symptoms from early in the irradiation period (within 1 week), and a couple developed symptoms after 2 weeks. More than half of these patients were classified as having Grade 2 or 3 symptoms. The patients with oral cancer had shown dysphagia before radiation therapy. The dysphagia which appeared after radiation therapy started at the same time or a little later than the problems in the oral cavity.

2) Appetite problems

Anorexia and nausea appeared in the early stages (less than 1 week) in many patients, and continued during irradiation.

2. Skin problems

Dermatitis appeared early in a few patients at a radiation dose of 6 Gy, and it appeared in half of the patients at a dose of 10 Gy. It was classified as Grade 2 or 3 in several patients. Dermatitis appeared usually 1 or 2 weeks after irradiation and was often accompanied by itching.

3. Other symptoms

In many cases, fatigue appeared early in the irradiation period, and it was classified as Grade 2 or 3 in several patients. In some patients, it started immediately after radiation therapy. Many patients suffered from pain. While the direct cause of the pain could not be specifically identified, it was likely caused by stomatitis and dermatitis.

Change in QOL

At the three measurement intervals, the eight domain scores and two summary scores of the SF-8™ were lower than the Japanese standard values in all cases. The PF and the PCS scores were significantly lower after radiation therapy than before radiation therapy ($p < 0.05$) (Figure 1).

Discussion

Adverse events during the radiation therapy period

Two or more adverse events appeared in every patient, and they continued until the end of radiation therapy. Stomatitis emerges during radiation therapy in the second to third (20 to 30 Gy) week of the irradiation. However, in the patients in this study, it appeared at an earlier stage rather than during the second to third week. A serious case of stomatitis will occur when fluorouracil (5-Fu) is used as an antineoplastic drug [4][5]. 5-Fu was used for the patients who participated in this study. Therefore, it is considered that the appearance of early stomatitis is because of a combination of chemotherapy and radiation therapy. There was also a high frequency of dry mouth and dysphagia. As for the problems of the oral cavity, not only pain but the amount of oral nutrition intake decreased. Moreover, the loss of appetite and nausea appeared at an early stage, and it continued during the radiation therapy in many cases. Therefore, it was surmised that these

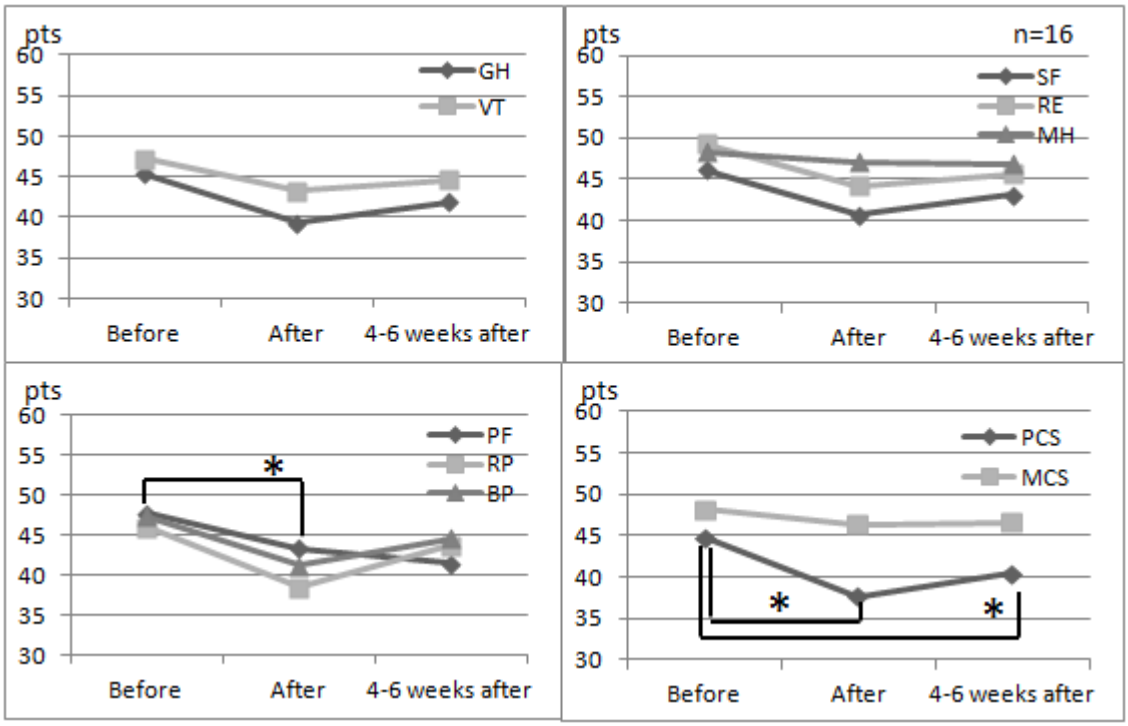

Figure 1 Changes in QOL n=16, Wilcoxon signed rank test *:p<.05

symptoms were due to rather than an effect of radiation therapy. In the patients who received concurrent chemo-radiotherapy compared with single radiation therapy, the problems of oral nutrition intake appeared at an early stage, and it continued until the end of treatment. Therefore, pain control and nutrition management beginning early in the irradiation period is needed. It is known that dermatitis will appear from the second to the third week (20 to 30 Gy) after the start of radiation therapy. Half of the participants' symptoms in this study appeared at 20 Gy. Since dermatitis was often accompanied by itching, we think it is important to provide suitable care to prevent stimulus to the skin.

Change in QOL

At the time radiation therapy started, the participants' QOL was already low, and their QOL decreased further during the course of treatment. QOL did not recover for 4 to 6 weeks after the treatment was completed. Stomatitis peaks 1 to 2 weeks after the end of radiation therapy and then gradually improves. Similarly, dermatitis peaks 2 to 3 weeks after the end of medical treatment, and then gradually improves. These adverse events are in the middle of being improved and therefore may not have an actual feeling of the QOL improvement, at 4 to 6 weeks after treatment.

Conclusion

It became clear that symptoms associated with radiation syndrome in patients with head and neck cancer undergoing radiation therapy appeared from early in the irradiation period and that local symptoms were severe. QOL scores decreased as a result of radiation therapy. Thus, nursing intervention from soon after the start of radiation therapy is necessary to ease these symptoms and improve QOL.

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Analysis of Japanese newspaper articles with keywords “radiation,” “nuclear energy,” and “disaster”

Reiko Narita[1*] and Ruriko Kidachi[2]

[1]*Master course in Division of Nursing, Hirosaki University Graduate School of Health Sciences*
[2]*Department of Development and Aging, Division of Health Sciences, Hirosaki University Graduate School of Health Sciences, Hirosaki, Japan*

Abstract. This study analyzed statements concerning "radiation," "nuclear energy," and “disaster” in Japanese newspaper articles. We analyzed newspaper articles with keywords “radiation,” “nuclear energy,” and “disaster,” found in the Japanese newspaper databases “Yomidasu: Yomiuri Newspaper, 1995-2011” and “Visual Kikuzo II: Asahi Newspaper, 1984-2012.” The number of articles with keywords increased from 2 before to 11 after the Chernobyl nuclear plant accident in 1986. The number of articles increased from 11 before to 74 after a nuclear radiation accident in Tokai-mura in 1999. The number of articles increased from 7 before to 442 after the nuclear accident at the TEPCO Fukushima Daiichi nuclear power plant in 2011. The appearance rates of the words " safety " and " exposure" increased after the Chernobyl nuclear plant accident in 1986 and the Tokai-mura nuclear radiation accident in 1999, and that of “disaster prevention" increased after the Tokai-mura nuclear radiation accident in 1999. The appearance rate of "damage caused by rumor" increased after the nuclear accident at the TEPCO Fukushima Daiichi nuclear power plant in 2011.

Key Words: radiation, nuclear energy, disaster

Introduction

There are few previous studies on nuclear disasters. Therefore, this study analyzed statements using the keywords "radiation," "nuclear energy," and “disaster” in Japanese newspaper articles.

Methods

We analyzed newspaper articles using the keywords “radiation,” “nuclear energy,” and “disaster,” found in the Japanese newspaper databases “Yomidasu: Yomiuri Newspaper, 1995-2011” and “Visual Kikuzo II: Asahi Newspaper, 1984-2012.” From the 1,048 articles found, we analyzed the annual number of these articles, the number before and after nuclear accidents, the appearance frequency of the words "safety," "radiation exposure," "disaster prevention," and "damage caused by rumor,” and the differences in appearance frequency between prefectures with and without nuclear facilities.

Results

The number of articles with keywords increased from 2 before to 11 after the Chernobyl nuclear plant accident in 1986. The number of articles increased from 11 before to 74 after a nuclear radiation accident in Tokai-mura in 1999. The number of articles increased from 7 before to 442 after the nuclear accident at the TEPCO Fukushima Daiichi Nuclear Power Plant in 2011. (Figure 1, Table 1)

* Corresponding to:Reiko Narita ,Master course, Hirosaki University ,66-1,Hon-cho,Hirosaki,036-8560,Japan.
e-mail: h12gg105@stu.hirosaki-u.ac.jp

Table 1 Overview of the main radiation accidents in the world since 1984

Accident	Occurrence time and overview accident	International nuclear event scale	Exposure,injuries and deaths
Chernobyl power plant accident	April 26,1986 Workers experimented with the safety device off. Many mistakes because of insufficient cooling water. Steam explosion occurred.	Level 7	33 people died. About 160,000 people emigrated.
Nuclear radiation Accident in Tokai-mura	September 30,1999 Uranium solution had reached the critical state in the nuclear fuel fabrication. Criticality incident lasted about 20 hours.	Level 4	Two workers died. One worker was seriously injured. 667 people were exposed to radiation.
Nuclear accident at The TEPCO Fukushima daiichi Nuclear power plant	March 11,2011 Power was lost because of natural disasters. Cooling function was impaired. Nuclear reactor core became molten.	Level 7	30 employees and 88 citizens possibly exposed.

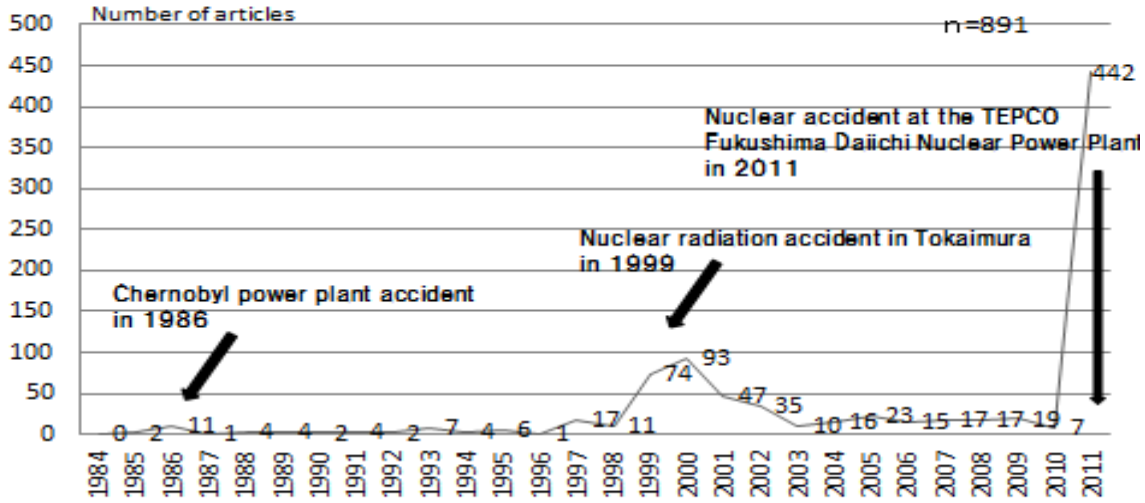

Figure 1 Trends in the annual number of articles were searched for the keywords “radiation,” “nuclear energy” and “disaster” (Visual Kikuzo Ⅱ : Asahi Newspaper)

The appearance rate of the word "safety" was 63.6% in 1986, 74.3% in 1999, and 47.0% in 2011. The appearance rate of "exposure" was 81.8% in 1986, 55.4% in 1999, and 6.5% in 2011. The appearance rate of "disaster prevention" was 18.1% in 1986, 72.9% in 1999, and 27.6% in 2011. The appearance rate of “damage caused by rumor" was 0% in 1986, 5.4% in 1999, and 11.9% in 2011. (Figure 2)

In addition, 141 (64.6%) of all 218 articles in “Yomidasu” in 2011 were from prefectures where nuclear facilities were located. (Figure 3)

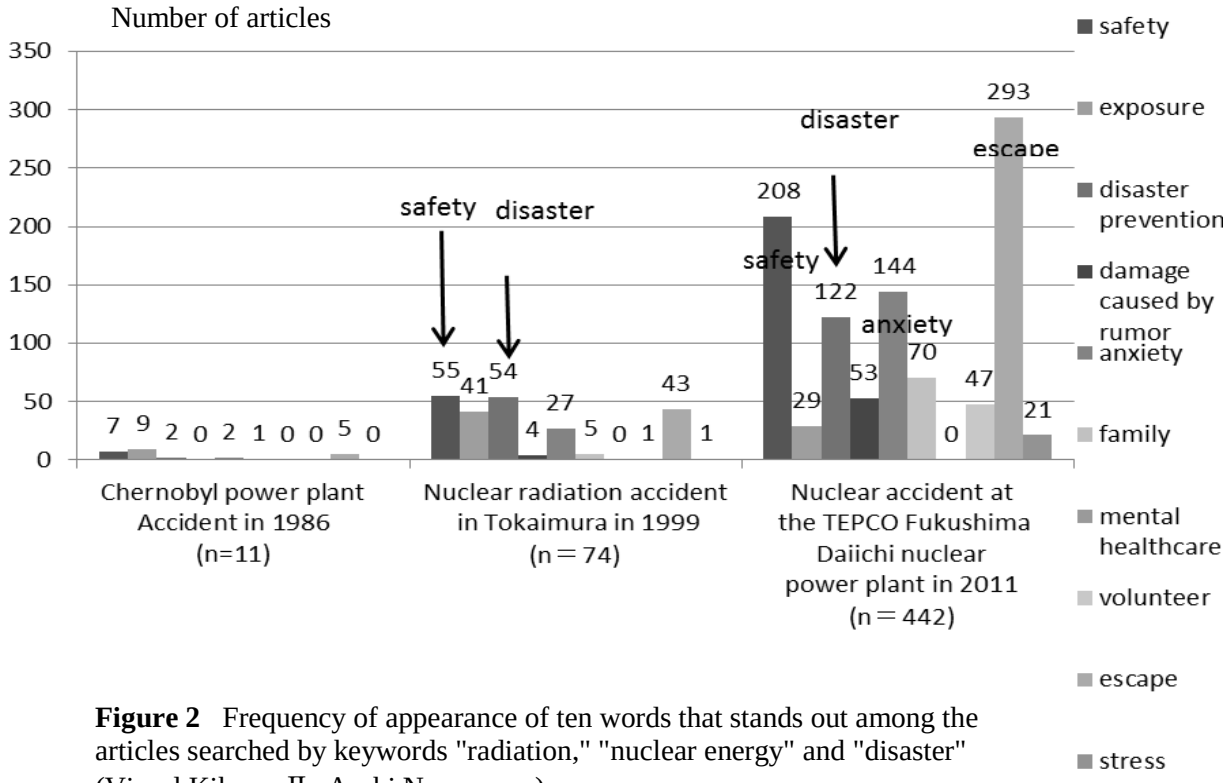

Figure 2 Frequency of appearance of ten words that stands out among the articles searched by keywords "radiation," "nuclear energy" and "disaster" (Visual Kikuzo Ⅱ: Asahi Newspaper)

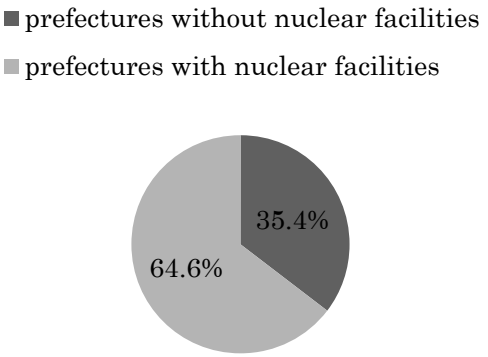

Figure 3 Comparison of the appearance rate of newspaper articles from prefectures that had or did not have nuclear facilities in 2011 (Yomidasu: Yomiuri Newspaper)

Conclusions

The appearance rates of the words "safety" and "exposure" increased after the Chernobyl nuclear plant accident in 1986 and the Tokai-mura nuclear radiation accident in 1999, and that of “disaster prevention" increased after the Tokai-mura nuclear radiation accident in 1999. The appearance rate of "damage caused by rumor" increased after the nuclear accident at the TEPCO Fukushima Daiichi nuclear power plant in 2011.

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Development of the Attitude Scale on Radiation Emergency Medicine for Japanese Nurses and Evaluation of its Reliability and Validity

Yuka Noto[1*], Noriko Ogura, Mayumi Urushizaka, Maiko Kitajima, Yoshiko Nishizawa, Tomoko Ichinohe and Hideaki Yamabe

[1]Hirosaki University Graduate School of Health Sciences, Hirosaki, Japan

Abstract. This study aimed to develop an Attitude Scale on Radiation Emergency Medicine (ASREM) for Japanese nurses and to evaluate its reliability and validity. The original ASREM was developed based on interview data and a comprehensive review of the literature. A revised 35-item version was developed by examining the content validity of the original scale. Subsequently, we investigated the reliability and validity of the scale in 798 nurses employed at 31 primary, secondary, and tertiary medical institutions providing radiation treatment in Japan. Valid responses were received from 376 nurses aged 38.1 ± 9.0 years (mean ± SD). After selecting items based on response bias, we conducted exploratory factor analysis using principal factor analysis with promax rotation. The following four factors comprising 25 items were finally extracted: 14 items for the first factor, "confidence in knowledge and skills"; six items for the second factor, "psychological resistance"; three items for the third factor, "responsibility as a medical professional"; and two items for the fourth factor, "interest in radiation emergency medicine". The reliability of the scale was confirmed by a Cronbach's alpha internal consistency reliability coefficient of 0.93 (0.69–0.72 for subscales; the correlation coefficient for the fourth factor was 0.52). Criterion-related validity was confirmed by intervention using the resistance score related to nurses' fears of contamination from patients with radiation exposure. Construct validity was confirmed using consent to participate in the radiation exposure medical care team. Average scores for the ASREM factors were 1.46 □ 0.85 for "confidence in knowledge and skills", 2.37 □ 0.82 for "psychological resistance", 2.45 □ 0.83 for "responsibility as a medical professional", and 1.99 □ 1.02 for "interest in radiation emergency medicine". Thus, the participants in the present study demonstrated responsibility as medical professionals and experienced little psychological resistance to radiation emergency medicine, although they lacked confidence in their knowledge and skills. We also found that age, employment position, and participation in radiation emergency medicine training influenced the attitudes of participants toward radiation emergency medicine. The present ASREM was determined to be appropriate for Japanese nurses and to have satisfactory reliability and validity.

Key Words: attitude, scale, Radiation Emergency Medicine

Introduction

The improvement of the radiation emergency medicine system is an urgent social need in Japan. Nurses are concerned with the mid- and long-term care of victims after a radiation accident, and assume an important role. The population of Japan, as the only country ever to have been subjected to a nuclear attack, is very sensitive to the issue of radiation, and the nation has strong negative emotions toward radiation. Logical thinking about radiation is enabled by acquiring knowledge, and the awareness for the risk is reduced; however, a sensible fear persists

* Corresponding to: Yuka Noto, Hirosaki University Graduate School of Health Sciences, 66-1, Hon-cho, Hirosaki 036-8564, Japan
E-mail: noto@cc.hirosaki-u.ac.jp

Aim

This study aimed to develop an Attitude Scale on Radiation Emergency Medicine (ASREM) for Japanese nurses and to evaluate its reliability and validity.

Method

Preparation of the item pool

First, seven nurses who were familiar with radiation emergency medicine were interviewed in semistructured formal interviews. We asked them their "thoughts about acceptance and the nursing of patients with radiation exposure and contamination from a radiation accident" to collect the items which constituted the attitude of nurses toward radiation emergency medicine. The interviewer used an interview guide and tape-recorded the interviews. Data analysis was conducted by using a qualitative descriptive method. Transcriptions of the tape-recorded interviews were coded. These sorted codes were used to form categories. We also extracted an item from previous studies [1]–[8] about behavior and the recognition of nurses to engage in radiation nursing and radiation exposure medical care. Based on these, we developed an original 35-item scale for assessing the attitude of nurses toward radiation emergency medicine.

The items were assessed by using a five-point Likert scale: 0 ("Disagree"), 1 ("Moderately disagree"), 2 ("Neither agree nor disagree"), 3 ("Moderately agree") and 4 ("Agree"). For the items on negative attitude, the scoring weights were reversed (reversed items). The weighted scores of responses marked 0, 1, 2, 3, and 4 for the reversed items were 4, 3, 2, 1, and 0, respectively. High scores indicated a more positive attitude toward radiation emergency medicine. We then sought opinions about the validity, clarity of expression, and ease of answering each item from radiation emergency medicine specialists and nursing faculty members. We revised the expressions of the question items and developed the Attitude Scale on Radiation Emergency Medicine (ASREM).

Participants

The participants were nurses who were employed by primary, secondary, and tertiary radiation emergency medical institutions in Japan, and who might provide radiation emergency medicine. A request for cooperation with this survey was sent to 78 institutions, and 798 nurses of 31 institutions agreed to participate in the study.

Survey procedures

The manager of the nursing department distributed a paper questionnaire, and subjects returned the questionnaire by mail after completing it. The distributed questionnaire covered the following:

· Characteristics (age, sex, employment position, and participation in radiation emergency medicine training)

· A feeling of resistance for assisting patients with radiation exposure and contamination

· Whether you would accept a request to participate as a member of a radiation emergency medicine care team.

· An Attitude Scale on Radiation Emergency Medicine (ASREM)

Statistical analysis

The statistical analyses were conducted using SPSS 20.0J (SPSS Japan, Tokyo, Japan). The construct validity of the ASREM was examined by an exploratory factor analysis. The Cronbach's alpha coefficient was used to test the internal consistency of each factor and that of the entire scale. The factor score of the ASREM and the characteristics of participants were compared by using the t-test and one-way ANOVA. All of the statistical tests were two-sided and the significance was defined as $p < .05$.

Ethical considerations

This study was approved by the Ethics Committee of Hirosaki University Graduate School of Medicine. The intent of the study was explained to the participants, and the study was conducted after obtaining informed consent.

Results

Participants' characteristics

Of the 798 questionnaires sent to 31 institutions, 403 replies were received (50.5%). The number of valid responses was 376 (response rate = 47.1%). The age of the participants was 38.1 ± 9.0 years (mean ± SD). There were 354 female and 22 male respondents. The employment positions consisted of 277 staff nurses and 97 chief nurses or nurse

manager, with 2 respondents failing to provide an answer. The number of responders who had attended radiation emergency medicine training was 188 and the number of those who had not attended any training was 188 (Table 1).

Reliability and validity of the Attitude Scale on Radiation Emergency Medicine (ASREM)

A ceiling effect or a floor effect was shown for four of 35 items. We performed factor analysis (principal components analysis, Promax rotation) using 31, excluding those four items. An eigenvalue of > 1 was set as the criterion for factor extraction and items of low factor loading (< .04) were excluded. A scale consisting of four factors with 25 items that could measure the attitude of nurses toward radiation emergency medicine was subsequently obtained. The results of this factor analysis are shown in Table 2.

The following four factors comprising 25 items were finally extracted: 14 items for the first factor, "confidence in knowledge and skills"; six items for the second factor, "psychological resistance"; three items for the third factor, "responsibility as a medical professional"; and two items for the fourth factor, "interest in radiation emergency medicine".

The reliability of the scale was confirmed by a Cronbach's alpha internal consistency reliability coefficient of 0.93 (0.69–0.72 for subscales; the correlation coefficient for the fourth factor was 0.52). Criterion-related validity was confirmed by intervention using the resistance score related to nurses' fears of contamination from patients with radiation exposure and contamination. Construct validity was confirmed using consent to participate in the radiation emergency medicine team.

Table 1 Characteristics of the participants (n = 376)

Characteristics	
Mean age	38.0 ± 9.0 (21–60)
Gender	
Female	354 (94.1)
Male	22 (5.9)
Employment position	
Staff nurse	277 (73.7)
Chief nurse or nurse manager	97 (25.8)
No response	2 (0.5)
Attended radiation emergency medicine training	
Yes	188 (50.0)
No	188 (50.0)
The resistance related to nurses' fears of contamination from patients with radiation exposure and contamination	
Feel	84 (22.3)
Feel some	157 (41.8)
Do not know	56 (14.9)
Do not feel much	63 (16.8)
Do not feel any	16 (4.3)
Consent to participate as a member of the radiation emergency medicine team	
Accept	224 (59.6)
Decline or neither	152 (40.4)

Data are N (%) or mean ± SD (range).

Table 2 Factor loadings in the Attitude Scale on Radiation Emergency Medicine (n = 376)

Items	Factor loading				Communality
	Factor 1	Factor 2	Factor 3	Factor 4	
Factor 1: Confidence in knowledge and skills (α = 0.94)					
When I take care of patients with radiation exposure and contamination, I think that I cannot give appropriate instructions to a team member. *	0.843	0.117	−0.223	−0.039	0.684
I include knowledge and skills necessary to take care of patients with radiation exposure and contamination.	0.816	−0.002	0.068	−0.025	0.683
I can image the care of patients with radiation exposure and contamination concretely.	0.788	−0.184	0.131	0.068	0.650
I think that procedures necessary to prevent radiation exposure and the spread of contamination to medical personnel can be provided.	0.773	0.002	0.116	−0.095	0.594
I am sure to act based on the principles of treating patients with radiation exposure and contamination.	0.767	−0.059	0.090	0.003	0.604
I do not have confidence in planning the necessary care depending on the situation of patients with radiation exposure and contamination. *	0.765	0.003	−0.101	−0.015	0.537
I do no think that I act without instructions on how to care for patients with radiation exposure and contamination. *	0.737	0.184	−0.015	−0.160	0.566
I have no confidence to act in consideration for minimizing my radiation exposure during the care of patients with radiation exposure and contamination. *	0.725	0.175	−0.002	−0.237	0.511
When a radiation emergency medicine team is formed, I can suggest a better method for providing care.	0.702	−0.156	−0.021	0.287	0.661
When a radiation emergency medicine team is formed, I can point out mistakes in assessments and care methods to a team member.	0.684	−0.101	0.009	0.175	0.561
I am sure to cope with an unexpected situation that are not covered in training of patients with radiation exposure and contamination appropriately.	0.662	−0.073	−0.011	0.165	0.524
I do not think that I can confidently reply to questions from patients with radiation exposure and contamination and their family. *	0.653	0.141	−0.213	−0.003	0.449
When I take care of patients with radiation exposure and contamination, I think that I can play my role as a member of a team.	0.555	0.029	0.059	0.279	0.608
I think that I can apply my principles depending on the situation after having understood the principles of treating patients with radiation exposure and contamination.	0.414	−0.086	0.218	0.028	0.253
Factor 2: Psychological resistance (α = 0.81)					
When a place of employment determines the acceptancof patients with radiation exposure and contamination, I do not want to be engaged in care. *	−0.022	0.693	0.017	0.246	0.682
After having removed contamination, I feel resistance to caring. *	−0.007	0.668	−0.023	0.027	0.443
I am against a place of employment accepting patients with radiation exposure and contamination. *	−0.158	0.644	0.028	0.106	0.424
When my family objects, they have a negative attitude toward my caring for patients with radiation exposure and contamination. *	0.052	0.530	0.057	0.138	0.437
It is not acceptable that I am exposed to radiation while I care for patients with radiation exposure and contamination that I. *	0.052	0.518	0.154	0.086	0.465
When I take care of patients with radiation exposure and contamination, I think that the change from the feelings associated with normal duties is difficult. *	0.162	0.429	0.097	−0.227	0.239
Factor 3: Responsibility as a medical professional (α = 0.69)					
In the case of an emergency, I think that it is necessary to undertake responsibilities in addition to those I have as a nurse.	−0.053	0.036	0.663	−0.018	0.431
When there is not a method to completely avoid radiation exposure, I provide the necessary care.	0.024	0.137	0.631	−0.047	0.479
If it is a very small amount of radiation exposure, I provide the necessary care.	−0.030	0.134	0.501	0.047	0.353
Factor 4: Interest in radiation emergency medicine (r = 0.52)					
If there is an opportunity to experience radiation emergency medicine, I want to provide care positively.	0.054	0.230	−0.076	0.637	0.566
I am interested in radiation accidents and radiation emergency medicine.	0.061	0.086	0.077	0.497	0.385
Correlation of factors					
Factor 2	0.425				
Factor 3	0.323	0.493			
Factor 4	0.508	0.421	0.522		

*: Reversed

Table 3 Correlates of ASREM (n = 376)

	Factor 1		Factor 2		Factor 3		Factor 4		Total score	
Age (n)										
20–29 (72)	1.09 ± 0.77		2.26 ± 0.83		2.49 ± 0.82		1.90 ± 1.09		1.60 ± 0.65	
30–39 (142)	1.48 ± 085	*	2.33 ± 0.76	n.s.	2.37 ± 0.88	n.s.	2.00 ± 1.05	n.s.	1.83 ± 0.69	n.s.
40–49 (109)	1.56 ± 0.81	***	2.43 ± 0.81	n.s.	2.48 ± 0.74	n.s.	2.03 ± 0.92	n.s.	1.93 ± 0.65	*
50–60 (52)	1.66 ± 0.89	**	2.56 ± 0.88	n.s.	2.59 ± 0.80	n.s.	2.02 ± 1.09	n.s.	2.02 ± 0.71	**
Employment position										
Staff nurse (277)	1.35 ± 0.83		2.27 ± 0.80		2.36 ± 0.86		1.90 ± 1.05		1.73 ± 0.68	
Chief nurse or nurse manager (97)	1.77 ± 0.83	***	2.66 ± 0.78	***	2.70 ± 0.70	***	2.24 ± 0.89	**	2.14 ± 0.61	***
Radiation emergency medicine training										
Participation (188)	1.80 ± 0.89		2.52 ± 0.85		2.53 ± 0.81		2.29 ± 1.01		2.10 ± 0.73	
No participation (188)	1.12 ± 0.65	***	2.22 ± 0.75	***	2.37 ± 0.84	n.s.	1.71 ± 0.95	***	1.58 ± 0.52	***

Factor 1: Confidence in knowledge and skills, Factor 2: Psychological resistance, Factor 3: Responsibility as a medical professional, Factor 4: Interest in radiation emergency medicine

The values are the item mean ± SD. *p < 0.05, **p < 0.01, ***p < 0.001, n.s.: not significant

Factors for age were compared using an ANOVA; a significant difference was found between those 20–29 years old and those in the older age groups. Differences in "Employment position" and "Radiation emergency medicine training" were compared using a non-paired t-test.

Comparison of the participants' characteristics

Mean scores for the ASREM factors were 1.46 □ 0.85 for "confidence in knowledge and skills", 2.37 □ 0.82 for "psychological resistance", 2.45 □ 0.83 for "responsibility as a medical professional", and 1.99 □ 1.02 for "interest in radiation emergency medicine".

From the comparison of participants characteristics, the first factor "confidence in knowledge and skills" had a significantly higher score for individuals 30 years of age or over compared to individuals 30 years of age or younger. From the comparison of the employment position, all factors had a significantly higher score for the chief nurses or nurse manager compared to those for a staff nurse. Furthermore, all factors except "responsibility as a medical professional" had a significantly higher score for individuals who had attended in the radiation emergency medicine training compared to the individuals who had not attended the training (Table 3).

Discussion

Factor structure and characteristics of the ASREM

The four factors constituting the ASREM are "confidence in knowledge and skills", "psychological resistance", "responsibility as a medical professional", and "interest in radiation emergency medicine".

"Confidence in knowledge and skills" includes items asking about the degree of confidence in being able to perform the following activities:

- nursing intervention of patients with radiation exposure and contamination
- act based on a principle
- demonstrate practical ability for unexpected situations
- minimize the radiation exposure of medical personnel
- conduct measures for extended contamination prevention
- take on an active role as a member of a radiation emergency medicine team
- collaborate with team members
- support and advise team members

Because the medical care for radiation exposure is different than ordinary medical care, there are few persons who have accumulated sufficient experimental knowledge by practice. Therefore, we believe influencing attitudes toward this type of care is related to how realistically medical care personnel can image the situation. In other words, that they can imagine providing appropriate care for

patients with radiation exposure or contamination. Furthermore, so that they have a realistic image, it is essential for them to have confidence in dealing with radiation and radiation protection, and have basic knowledge and skills about radiation emergency medicine.

"Psychological resistance" includes the following:

- having a feeling of psychological resistance toward care of patients with radiation exposure and contamination, and toward oneself being exposed to radiation by care
- thinking the care of patients with radiation exposure and contamination is different from normal care

The psychological resistance to a phenomenon increases when the phenomenon is unknown and associated with fear. Thus, the vague anxiety about radiation and radiation exposure will decrease if knowledge about radiation and radiation protection, and basic knowledge and skills about radiation emergency medicine are acquired. By thinking logically through obtaining knowledge, the recognition of the crisis is reduced. However, a sensible fear persists. We think that these anxieties and fears become the basis of the resistance for the care of patients with radiation exposure and contamination.

"Responsibility as a medical professional" includes the following:

- when the radiation exposure of oneself is inevitable, care even if it is a very small amount
- during an emergency, perform activities beyond those of nursing

During a crisis, nurses give top priority to medical treatment for patients only if they can be convinced that secondary radiation exposure to themselves will not damage their health. We think that this behavior is equivalent to the social accountability demanded of healthcare professionals.

“Interest in radiation emergency medicine” includes the following:

- degree of interest in radiation emergency medicine

We think that an individual who is made aware of radiation emergency medicine as part of the nursing specialty is more likely to have a positive attitude toward this type of medical care.

Reliability and validity of ASREM

In this study, the Cronbach's alpha coefficient for the entire scale was 0.93, while it was 0.69–0.94 for the subscales, the correlation coefficient for the fourth factor was 0.52. Factors 3 and 4 were comprised of three and two items, respectively, which was considered to be a little number of items. Therefore, we think the reliability is good.

We think that the content validity is confirmed for the following reasons; 1) the ASREM was developed by an item from an original scale from a previous study and from the results of interviews with nurses who were familiar with radiation emergency medicine, and 2) a positive opinion was obtained regarding the ASREM from a radiation emergency medicine expert and nursing faculty members.

Furthermore, there are no other scales that can measure a positive and a negative attitude to direct behavior regarding radiation emergency medicine. Therefore, we investigated the degree of the resistance to care for patients with radiation exposure and contamination. Because this score and ASREM revealed a significant correlation, we think that the criterion-related validity was confirmed.

Moreover, attitudes and behavior influence each other and are thought to be directly related to positive outcomes in given situations. However, we cannot observe real behavior because radiation emergency medicine is not a daily phenomenon. Participants were asked if they would participate in a radiation emergency medical team and could respond "participate", "decline", or "neither".

As a result of dividing this into an aggressive group and the non-aggressive group for radiation emergency medicine, the ASREM score was significantly higher in the aggressive group. Thus, it can be concluded that the construct validity was confirmed.

Attitude toward radiation emergency medicine for nurses

The average scores for “psychological resistance” and “responsibility as a medical professional” of ASREM exceeded an intermediate value (two points). Therefore, when the care of patients with radiation exposure and contamination is requested, it was found that respondents could overcome their “psychological resistance” and provide care, under “responsibility as a medical professional”. On the other hand, there was no

“confidence in knowledge and skills” for care and the team-based care for patients with radiation exposure and contamination, and “interest in radiation emergency medicine” care was low. The chief nurses or nurse manager had significantly higher scores for all factors and a significantly higher total score than those who participated in the radiation emergency medicine training and those who participated had significantly higher scores than those who did not participate.
Furthermore, because older individuals had a significantly higher score for “confidence in knowledge and skills”, compared to younger individuals, it was inferred that age, the employment position, and participation in radiation emergency medicine training influenced the formation of a positive attitude toward radiation emergency medicine. Usually confidence in correspondence develops from familiarity and experience. However, experience with radiation emergency medicine is not something that can be obtained routinely. For nurses is in situations that they have not experienced previously, they can rely on their years of clinical experience and have the confidence that they can cope.

Leaders and those in management, compared with staff nurses, feel a commitment to their institution and responsibility not only as an employee but also as a medical professional, which affects their behavior. Participation in training also has a large effect on behavior.

We did not ask about the contents of the training in this study; however, the contents seemed to be basic knowledge and skills about radiation, radiation protection and the radiation emergency medicine, and simulation of the hospitalization of patients with radiation exposure and contamination. By participating in the training event at least once, participants can better image radiation emergency medicine and form a more positive attitude toward radiation emergency medicine.

Conclusion

We developed a scale to measure personal attitude toward radiation emergency medicine and examined its reliability and validity. The four factors comprising 25 items for the ASREM were “confidence in knowledge and skills”, “psychological resistance”, “responsibility as a medical professional”, and “interest in radiation emergency medicine”. The ASREM has good reliability and validity. The participants in the present study demonstrated responsibility as medical professionals and experienced little psychological resistance to radiation emergency medicine, although they lacked confidence in their knowledge and skills. We also found that age, employment position, and participation in radiation emergency medicine training influenced the attitude of participants toward radiation emergency medicine. The present ASREM was determined to be appropriate for Japanese nurses and to have satisfactory reliability and validity.

Acknowledgment

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Responses of public nurses to the consultations they provided to residents following a nuclear disaster

Chiaki Kitamiya[1*] and Ruriko Kidachi [2]

[1] Department of Health Promotion, Division of Health Sciences, Graduate School of Health Sciences, Hirosaki, Japan
[2] Department of Development and Aging, Division of Health Sciences, Graduate School of Health Sciences, Hirosaki, Japan

Abstract. The purpose of this study was to classify the support provided by public health nurses who consulted with residents following a nuclear disaster. Study participants were eight public health nurses working in health centers in X Prefecture. All nurses had prior experience with radiation disasters. Semi-structured interviews were conducted from February 10 to 15, 2012, and comprised the following three questions. (1) What actions did health care providers take following the disaster? (2) What kind of support was provided to the Fukushima evacuees living in shelters? (3) What had you learned from your prior experience with radiation disasters that was useful in this situation? Data were analyzed qualitatively. This study was approved by The Committee of Medical Ethics of Hirosaki University Graduate School of Medicine, Hirosaki, Japan. Interviews ranged in length from 70 to 100 minutes and lasted an average of 81 minutes. This study is a qualitative analysis of these interviews. As a result, three categories were extracted from seven subcategories. These three categories were: (1) transmitting, (2) understanding, and (3) giving advice. 'Transmitting' comprised simply providing information, 'understanding' was based on the public health nurses' understanding, and 'giving advice' was based on knowledge, understanding, and judgment.

Key Words: Radiation disaster, Public health nurse, Health Crisis management, Consultation

Introduction

On March 11, 2011, the Great East Japan Earthquake led to a massive tsunami and subsequent nuclear disaster. It is still fresh in our memories that many residents lost everything and were forced to evacuate to temporary shelters. Some of the affected areas have yet to be rebuilt, and thus, many residents continue to live in shelters.

Many of these residents have been concerned about the effects that the nuclear power plant accident will have on their health. Some of them have conveyed their fears to public health nurses through channels such as telephone consultation and other public health services.

Purpose

The purpose of this study was to classify the support provided by public health nurses who consulted with these residents.

Explanation of occupation

Public health nurses are civil servants who work for the public health center of the local government and the prefectural establishment. They are engaged in work to preserve residents' health following disasters. For instance, they provide health care in shelters and health counseling for the residents.

* Corresponding to: Chiaki Kitamiya, Associate Professor, Hirosaki University, 1-66, Hontyou,036-8564, Japan
E-mail:chiaki@cc.hirosaki-u.ac.jp

Method

Method of research

Study participants were eight public health nurses working in health centers in X Prefecture. All nurses had prior experience with radiation disasters.

Semi-structured interviews were conducted from February 10 to 15, 2012, and comprised the following three questions:

(1) What actions did health care providers take following the disaster?
(2) What kind of support was provided to the Fukushima evacuees living in shelters?
(3) What had you learned from your prior experience with radiation disasters that was useful in this situation?

Data were analyzed qualitatively from seven interviews; one group interview was conducted with two nurses and individual interviews were conducted for the other six nurses. Six participants were in their 50s and two were in their 40s at the time of the interview. We expected that knowledge from prior experience with radiation disasters would have a significant influence on the responses. Special attention was paid to specific verbs used in the interviews, including 'tells', 'says', and 'answers'.

Procedure

The study request was mailed to each local government and health-care center. The main points of the study, its purpose, and content were included in the document. The consent was obtained by mail. A candidate's recommendation was requested from the organization that expressed their intention to cooperate in the study.

The main points of the study, purpose, details of the study, and ethical considerations were specified in the document. We coordinated the time and place with the candidate for the interview.

Data from the interviews as well as additional data obtained at the time of the study, including how well the evacuees of each prefecture accepted their situation, were analyzed qualitatively.

This study was approved by the Committee of Medical Ethics of Hirosaki University Graduate School of Medicine in Hirosaki, Japan. Verbal and written explanations of the ethical considerations were provided to all participants at the time of their interviews and the study was started only after written informed consent was obtained.

Interviewee

- Public health nurses from cities, towns, and villages: 5 people
- Health center public health nurses: 3 people

Results

1. Outline of the interviews

Interviews ranged in length from 70 to 100 minutes and lasted an average of 81 minutes.

2. How did public health nurses deal with anxious residents?

Public health nurses provided consultations with a focus on mental care. They described their consultations using words and phrases such as "listening", "residents are understood", and "responses matched the condition of the resident". The public health nurses also offered information on radiation to the residents and the manner in which they shared this information was categorized. As a result, three categories were extracted from seven subcategories (Table 1).

These three categories were: (1) transmitting, (2) understanding, and (3) giving advice.

The first category identified was 'transmitting'. This comprised simply providing information. Public health nurses felt a sense of helplessness, expressed as "I could say nothing to help", when residents could not understand the situation yet wanted to know how much radiation they had received, and the questions had to be referred to a specialist.

The second category identified was 'understanding'. This was based on each public health nurse's understanding of the situation. They passed on information that was understood by the residents and that which was not understood was explained.

The last category identified was 'giving advice'. It was based on knowledge, understanding, and judgment. They knew that the residents were put at ease by the information, explanations of the situation, and additional information based on knowledge that the nurses provided. Narratives about this third category included "I have proposed to residents, 'Shall we do things like this?' Such suggestions come from training and/or experience. We are studying what public health nurses can do in natural disasters and learning about nuclear

Table 1. Response levels to the consultations

Category	Subcategory
Transmitting (Transmission of information)	· The inquiry is received without understanding. · Confusion while passing on information from a specialist. · A specialist must be consulted.
Understanding (Own understanding is deepened)	· Information is understood and the public health nurse imparts the information to the residents. · Lack of understanding is changed into understanding.
Giving advice (The residents' understanding is improved and the public health nurse advises)	· Information is clearly connected. · The public health nurse explains the situation using personal experience and knowledge and advises.

energy. Our activities and learning will probably be united."

The 'transmitting' part of the narratives produced the largest source of conflict among public health nurses because they told residents that their health would not be affected by the radiation even though they were not able to honestly make such a judgment. The public health nurses could not think of answers that could satisfy the residents' questions. "People were directly questioning the municipality. They were requesting the response of not doing the radiation exposure." However, they were not necessarily doing the radiation exposure with influence on health. "They wanted to be told that they were not exposed to dangerous levels of radiation, but did not believe it when they were told that the amount of radiation they had been exposed to was below levels that could influence health." Even though the nurses were worried themselves, they tried to listen patiently to the residents and attempted to correct any mistaken perceptions so that the residents could have a correct understanding of radiation. "The situation frazzled my nerves".

Discussion

The public health nurses in this study had prior experience with radiation disasters. The narrative part of the study corresponding to consultations varied according to the extent of the nurses' knowledge. Conflict existed among public health nurses concerning whether residents could understand and judge information on their own or if they had to be convinced. This conflict produced responses in which public health nurses either 'attempted to learn information (in order to provide better answers during consultations)' or 'desired to leave judgment to a specialist (defer consultations on radiation to a specialist)'. We found that public health nurses would request a specialist depending on their own response level when the request for consultation was received.

The activities of public health nurses concerning mental care are especially important following a disaster, when supportive mental care from public health nurses is needed. However, in this case, public health nurses had conflicting ideas concerning the 'transmission' of information at their consultations. To reduce these conflicts in the future, public health nurses should be required to have at least a minimal amount of knowledge and training concerning radiation-related disasters. Having this knowledge and training will address aspects of morale when it is not possible to consult a specialist promptly.

Acknowledgments

The cooperation of Mr. Hitoshi Araki of the Ibaraki Hitachinaka health center in this study is deeply appreciated. The authors wish to express their gratitude to public health nurses who provided interviews.

Effects of rehabilitation for skin and muscle damage caused by high-dose radiation -Developing an animal model of local radiation damage to the hind limbs-

Hirokazu Narita[1*], Shuhei Koeda[1], Koichi Ito[2], Kyoko Ito[2] and Hitoshi Tsushima[1]

[1] Department of Development and Aging, Division of Health Sciences, Hirosaki University Graduate School of Health Sciences, Hirosaki, Japan
[2] Department of Biomedical Sciences, Division of Medical Life Sciences, Hirosaki University Graduate School of Health Sciences, Hirosaki, Japan

Abstract. The purpose of this preliminary study was to develop an animal model of skin and muscle damage caused by high-dose radiation. Six male Wistar rats were randomly allocated into a control group, 15-Gy X-irradiation group (15Gy-G) and 30-Gy X-irradiation group (30Gy-G). Only the hind limbs of the rats were irradiated, with the rest of the body shielded by lead. The spontaneous activity, locomotor performance and weight of the rats were measured for 6 weeks after irradiation. At the final examination, the range of motion (ROM) for dorsiflexion of the ankle joint was also measured, and soleus muscles were extracted for measurement of wet weights. The 30Gy-G showed hair loss, blistering and bleeding of the hind limb. The spontaneous activity and body weight were decreased temporarily in 30Gy-G. The 15Gy-G showed only slight hair loss on the hind limb. The ROM and wet weight of the soleus muscle were lower in 30Gy-G than in the other groups. As irradiation at 15 Gy did not greatly affect the skin, spontaneous activity and ROM, irradiation > 30 Gy should be considered necessary for developing animal models of skin and muscle damaged by radiation exposure. In future studies, we will need to inspect the extracted soleus muscle histopathologically and examine the effect of radiation on skin and muscle in greater detail.

Key Words: Radiation damage, skin, muscle, animal model, rehabilitation

Introduction

We have reviewed the literature about rehabilitation for patients with large-dose radiation exposure, and considered the role of rehabilitation in radiation emergency medicine [1]. As a result, the importance of the rehabilitation focused on the radiation damage of the locomotor apparatus, such as skin and muscle, and respiratory management was highlighted. However, because there are very few fundamental studies and reports about rehabilitation offered to patients suffering from radiation exposure, the effect rehabilitation has on skin and muscle exposed to large doses of radiation remains uncertain.

The purpose of this preliminary study was to develop an animal model of radiation damage, with the goal of evaluating the effects of rehabilitation for skin and muscle damage caused by high-dose radiation. This progress report describes the development of the animal model, some preliminary findings and future tasks.

Materials and Methods

Six 4-week-old male Wistar rats (Clea, Tokyo, Japan) were used. All rats were given ad libitum access to standard laboratory diet and water under a 12-h light/dark cycle. Rats were randomly allocated

[*] Corresponding to: Hirokazu Narita, Assistant Professor, Hirosaki University Graduate School of Health Sciences, 66-1 Hon-cho, Hirosaki 036-8560, Japan. E-mail: narihiro@cc.hirosaki-u.ac.jp

into three groups, a control group (CON), 15-Gy X-irradiation group (15Gy-G) and 30-Gy X-irradiation group (30Gy-G); each group had two rats (A, B). We then acclimated the rats to the Running Wheel (Lafayette Instruments, Lafayette, USA) and Rotarod (Muromachi Kikai Co., Tokyo, Japan), which were used to measure spontaneous activity and locomotor performance, respectively, until rats reached 9 weeks of age.

At 9 weeks old, rats were anesthetized with an intraperitoneal injection of sodium pentobarbitone (40 mg/kg) and only their hind limbs were irradiated using a fixation device which was developed in our laboratory. The rest of the body was shielded with 4-mm-thick lead (Fig. 1). The X-irradiation was performed using an X-ray generator MBR-1520R (150 kV and 20 mA, Hitachi Medical Corporation, Tokyo, Japan). CON was subject to an operation similar to 15Gy-G and 30Gy-G, except there was no X-irradiation.

To assess the changes in the hind limbs of rats caused by X-irradiation over time, we measured their body weight and conducted a Rotarod test on the day before irradiation, and on 1 day, 3 days, 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks and 6 weeks after irradiation. Referring to a study by Ishida [2], the Rotarod test was performed as follows; the number of falls from the bar over a 60-s period while the bar was rotating at 3, 5, 10, and 15 rpm was recorded. If a rat fell from the bar ten times within 60 s, the test was stopped. We also photographed the state of the hind limbs with a digital camera on the same days. The spontaneous activity of each rat was measured once a week as the number of complete turns of the Running Wheel over a 24-hour period. At the final examination 6 weeks after irradiation, we measured the range of motion (ROM) for dorsiflexion of the ankle joint by reference to that in previous reports [3, 4]. Briefly, the anesthetized rat was laid on its side and its knee joint was flexed approximately 90 degrees. The ankle was passively dorsiflexed maximally. In this study, we defined the ROM for dorsiflexion as the angle obtained from a line connecting the lateral malleolus and the center of the knee joint and a line parallel to the bottom of the heel, and took measurements at five-degree intervals using an angle meter. At the end of the experimental period, all rats were killed and their soleus muscles were extracted for measurement of wet weights.

All procedures were carried out in accordance with Guidelines for Animal Experimentation of our institution

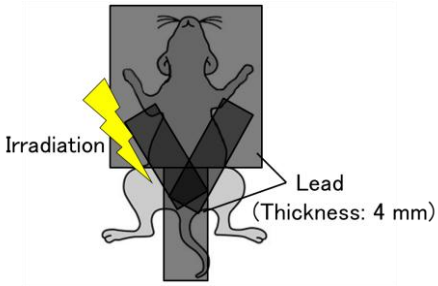

Fig. 1 Schema of X-irradiation to the rat

Results

The 30Gy-G showed hair loss, blistering and bleeding of the hind limb, especially at the bottom of the paw, approximately 2 weeks after irradiation (Fig. 2). Afterward, from 3 or 4 weeks after irradiation, the state of the bottom of the paw improved gradually (Fig. 3). The 15Gy-G showed slight hair loss on their hind limbs from approximately 5 weeks after irradiation (Fig. 4).

The spontaneous activity was maintained or increased in CON and 15Gy-G, but decreased temporarily in 30Gy-G from 2 weeks to 4 or 5weeks after irradiation (Fig. 5).

Body weight in CON and 15Gy-G increased gradually, but decreased in 30Gy-G from 2 weeks to 3 weeks after irradiation, then increased again (Fig. 6).

The ROM for dorsiflexion and wet weight of the soleus muscle were lower in 30Gy-G than in the other groups (Tables 1 and 2).

No specific tendencies were seen for locomotor performance with this Rotarod procedure referring to Ishida [2] because there was no apparent association between the number of falls and the radiation dose.

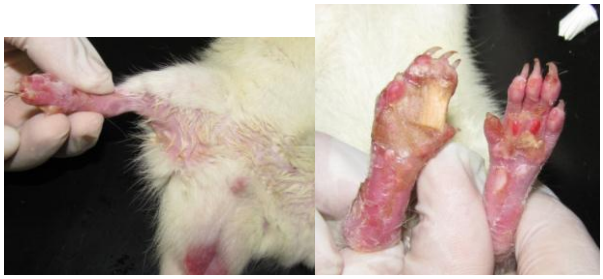

Fig. 2 Hind limb and bottom of paw in 30Gy-G at 2 weeks after X-irradiation

Fig. 3 Hind limb and bottom of paw in 30Gy-G at 4 weeks after X-irradiation

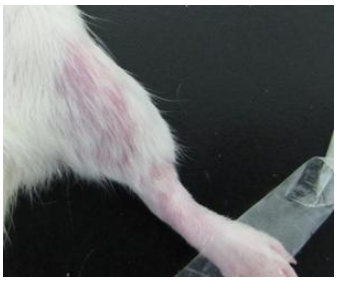

Fig. 4 Hind limb in 15Gy-G at 5 weeks after X-irradiation

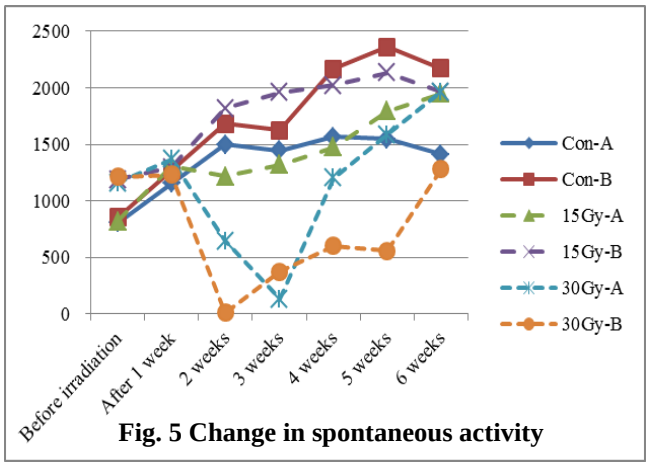

Fig. 5 Change in spontaneous activity

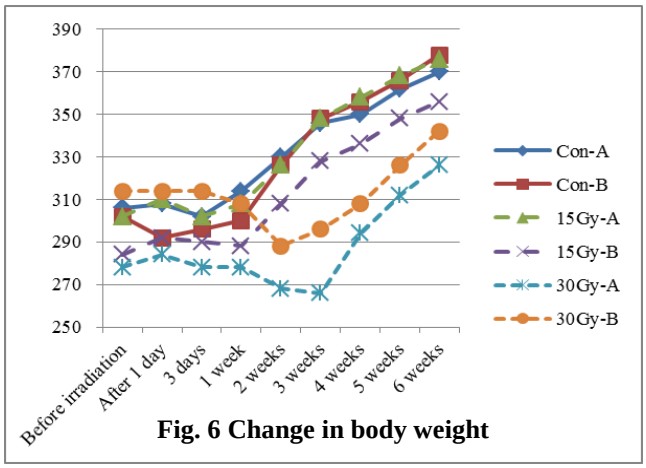

Fig. 6 Change in body weight

Table 1 ROM for dorsiflexion of the ankle joint (degrees)

		Right	Left
CON	A	60	60
	B	70	60
15Gy	A	50	50
	B	60	55
30Gy	A	60	40
	B	35	55

Table 2 Wet weight of the soleus muscle (g)

		Right	Left
CON	A	0.18	0.16
	B	0.19	0.19
15Gy	A	0.19	0.18
	B	0.16	0.16
30Gy	A	0.14	0.13
	B	0.13	0.16

Discussion

Because irradiation at 15 Gy did not greatly affect the spontaneous activity, ROM and state of the skin, 15 Gy of irradiation was thought to be insufficient for developing an animal model of local radiation damage to the hind limbs of rats.

It is reported that when skeletal muscle is damaged, the proliferation and differentiation of satellite cells play important roles in the recovery process [5]. However, Rosenblatt et al. [6] and Phelan et al. [7] reported that more than 25 Gy irradiation inhibited the activity of the satellite cells. In this case, it is easily conceivable that once skeletal muscle is damaged, it may not recover. Thus, because it is assumed that the activity of the satellite cells is inhibited in cases of high-dose radiation exposure, irradiation of a sufficient dose to inhibit the activity of the satellite cells is necessary to develop the animal model and examine the effects of rehabilitation. Moreover, according to the results of studies by Modular et al. [8] and Kaneko et al. [9], more than 30 Gy irradiation is likely necessary to cause apparent skin radiation damage. In our results, 30Gy-G showed lower ROM for dorsiflexion and spontaneous activity than the other groups, and also showed apparent skin damage from radiation. Therefore, more than 30 Gy irradiation is thought to be necessary to develop the animal model. However, the shielding method resulted in marked

damage to the bottom of the irradiated paw, potentially exerting substantial effects on spontaneous activity, ROM and weight reduction. Hereafter, it is necessary to shield the bottom of the paw, and examine the changes of spontaneous activity, ROM and weight after the irradiation of various doses greater than 30 Gy. In this study, although we irradiated only local parts such as the hind limbs, it was thought that the inflammatory response throughout the body might affect spontaneous activity and weight reduction. Therefore, to take blood samples and investigate the general condition of the rats is also necessary.

We did not find any tendency in the results of the Rotarod test. In other studies using the Rotarod test, the time until rats or mice fell from an accelerating rotating bar was measured [10, 11]. Reexamining locomotor performance using this latter method is necessary in future studies.

Furthermore, the extracted soleus muscle will need to be inspected histopathologically to examine the effect of radiation on muscle tissue in greater detail.

Conclusion

To develop an animal model of local radiation damage to the hind limbs, irradiation > 30 Gy and shielding the bottom of the paw are necessary. Additionally, the Rotarod approach needs to be reconsidered, and the extracted soleus muscle needs to be inspected histopathologically to examine the effect of radiation on muscle tissue in greater detail.

Hereafter, we need to solve the above-mentioned challenges, increase the number of animals and construct the animal model. We can then assess the effect of rehabilitation for skin and muscle damage caused by high-dose radiation, using the animal model.

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The relationship of risk perception of radiation and radiological knowledge of nurses after the Fukushima Dai-ichi Nuclear Power Plant disaster

Toshiko Tomisawa[1*], Chieko Itaki[1], Keiko Aizu [1]
Ayako Ohgino[1] and Kyoko Tagami [2]

[1]Hirosaki University Graduate School of Health Sciences,
[2]Department of Education,Hirosaki University
Hirosaki University Graduate School of Health Sciences, Aomori, Japan
E-mail: tmtott@cc.hirosaki-u.ac.jp

Abstract. This study aimed to clarify nurse's radiation risk perceptions after the disaster in Fukushima and to verify the relationship between risk perception of radiation and knowledge about radiation or experience with radiation nursing. Data collection and analysis were conducted from February to March 2012. Participants were nurses who were working at 430 hospitals with more than 300 hospital beds each in Japan. The selection of the hospitals was carried out using stratified random sampling to allow for a proportionate allocation of hospitals by region based on the number of hospitals in each region. Questionnaires were sent to 2628 nurses. Data collected included background data as well as information regarding nurses' image of risk (Fear image score and Unknown image score) and the severity of the Fukushima disaster. A total of 591 responses were received. Fear image score and unknown image score were significantly lower in participants with experience in radiology nursing compared with those who had only attended a study meeting about radiation ($p<0.05$). The mean risk perception score regarding the severity of the disaster was 8.1 ± 2.2 (range 0-10). Fear image scores in the high-severity group were significantly higher than in the low-severity group ($p<0.001$). Nurses living in a prefecture where nuclear power plants exist rated the nuclear plant accident as significantly more severe than other nurses ($p < 0.05$). These findings suggest that fear image scores and unknown image scores might be increased among nurses who do not have a career in radiation nursing or an opportunity to learn about radiation. An education system in which medical staff can learn radiological knowledge and skills is needed, as the medical use of radiation will continue in the future.

Key Words: radiation, risk perception, radiological knowledge, education

[*] Corresponding to: Toshiko Tomisawa, Hirosaki University Graduate School of Health Sciences, 66-1 Bunkyo-cho, Hirosaki, 036-8564, Japan.
E-mail: tmtott@cc.hirosaki-u.ac.jp

Introduction

The use of medical radiation has expounded the range of applications for radiotherapy and radiological examinations. Techniques have been improved and become more specialized every year. At the same time, medical exposure to radiation in Japan has become an international problem. Therefore, nurses who can do consultations and communicate effectively about the risks of radiation exposure on medical are needed. Educational contents regarding radiation range from liberal arts subjects to specialty subjects in basic nursing education programs in Japan, but few lecture courses on radiation alone are available (Inoue, 2011; Shingu, 2011; Ota, 2000. et al). Moreover, many residents who were living in Tohoku felt threatened after the Fukushima Dai-ichi nuclear power plant disaster. Communication regarding radiation risks was not handled as well as it could have been, and many people became uneasy due to the unsettling nature of the disaster, media reports, and lack of specialists on radiology and radiological protection. Therefore, the need has increased for accurate radiological information and additional specialists on radiation. Training of nurses with radiological knowledge needs to take place, because nurses play an important role in the physical and mental care of irradiated patients. Medical staff should have an appropriate level of risk perception of radiation and be able to easily communicate the risks to residents and patients to help ease their anxiety. The amount of radiological knowledge is one factor that influences risk perceptions of radiation（Jankowski,1995 ; Sticklin, 1994; Seldom, 1985). However, the risk perception of radiation among medical staff after the nuclear disaster in Fukushima has not been clarified, and the relation between the amount of knowledge and risk perception is unclear. This study aimed to clarify nurses' perceptions of radiation risk after the disaster in Fukushima and to verify the relationship between these risk perceptions and nurses' knowledge level regarding radiation or their experience providing nursing care related to radiation exposure.

2. Methods

2.1. Methods and Materials

Participants were nurses who were working at 430 hospitals in Japan that had more than 300 hospital beds each. Selection of hospitals was done using a stratified random sampling method based on the proportionate allocation of the number of hospitals in each region in Japan. The 430 selected hospitals included 100 radiation emergency hospitals, 150 cancer speciality hospitals and 150 non-cancer speciality hospitals. Then, half of 430 hospitals were in prefectures where nuclear power plants exist. After briefing the head of nursing divisions on the nature of the survey and securing their cooperation, a questionnaire survey was sent to 2628 nurses through the hospital. Data collection and analysis were conducted from February to March 2012.

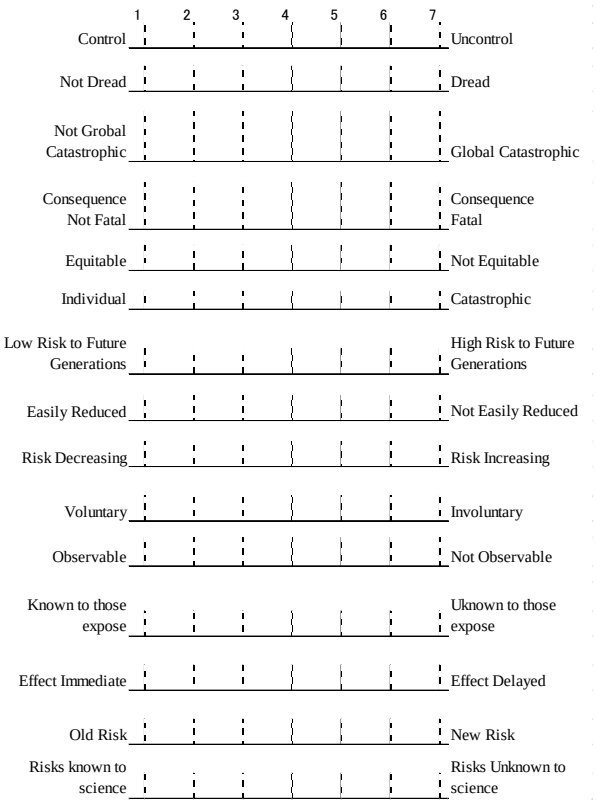

Figure 1. Questionnaire of risk images (Slovic, 1987)

2.2. Questionnaire

The questionnaire included background information on each nurses' career, academic background, career experience in radiological nursing, and perceptions of risk (Slovic, 1987) (Dread risk image score and Unknown risk image score by semantic differential scale methods),

experience in training about radiation emergency medicine, the prefecture where they live, how they rated the severity of the Fukushima accident on themselves (range 0-10) and resources they use to gain radiological knowledge.

2.3. Statistical analysis

Data were analysed using SPSS software (version 19.0) for Windows (SPSS Inc., Chicago, IL). Statistical significance was defined as $p<0.05$. Differences among answers in background data were determined by the chi-square test.

The analysis of the Dread risk image score and the Unknown risk image score was done using the unpaired t-test.

2.4. Ethical considerations

All study protocols were approved by the Committee for Medical Ethics of the Hirosaki University. Returning the questionnaire was regarded as providing informed consent.

3. Results

3.1. Backgroun d data of participants

A total of 591 responses were received (valid response rate, 14.2%). The rate of response for each region is shown in Table 1. The mean±SD number of career years in nursing was 18.2±9.8 years, indicating that a lot of senior nurses participated. Other background data included the following: 52% of nurses engaged in radiological nursing, 40.2%

Table 1. Rate of responses (n=591)

	Number of Response	%	Number of Send	Rate of Response
Hokkaido	62	10.5	198	31.3
Tohoku	98	16.6	228	43.9
Kanto	98	16.6	618	17.2
Chubu	158	26.7	492	33.4
Kinki	82	13.9	432	20.6
Shikoku/Chugoku	56	9.5	348	13.1
Kyushu	34	5.8	312	13.0
Unknown	3	0.5	-	-
Total	591	14.2	2628	

Table 2. Resources for radiological knowledge (multiple answers could be provided)

contents	N	%
Study meeting	340	57.5
Brochure	98	16.6
Standard protection by Facilitie	33	5.6
Guidance from senior	241	40.8
Specialists as the doctor and the radiology technician	362	61.3
Television , Radio	157	26.6
Newspaper	92	15.6
Magazine	69	11.7
Internet	96	16.2
Friend, Acquaintance	11	1.9
Nothing	21	3.6

Table 3. Comparisons of risk image scores by background data (n=591)

	n	Dread Risk Image	p	Unknown Risk Image	p
Eastern Japan	413	46.67	n.s.	21.07	n.s.
Western Japan	171	45.58		19.98	
Career of Radiation Nursing	308	43.67	***	20.08	***
No Career of Radiation Nursing	279	49.28		21.48	
Experience of Training of REM	138	44.08	*	19.76	*
NoExperience of Training of REM	443	47.04		21.02	
Experience of Study Meeting	336	44.58	***	20.26	*
No Career of Study Meeting	247	48.72		21.48	
Living in the prefecture where exists in nuclear power plants	238	47.42	n.s.	21.15	n.s.
Nothing the nuclear power plants	335	45.57		20.41	
High Severity（＞8）	394	47.81	***	20.92	n.s.
Low Severity （≦8）	193	43.32		20.38	

Numbers of risk images are mean values. Statistical analysis used the unpaired t-test.
***p<0.001 **p<0.01 *p<0.05 n.s. not significant

lived in a prefecture where nuclear power plants exist, 23.5% had experience in training for radiation emergency medicine, and 56.9% had participated in a study meeting about radiation.Resources for specialists included doctors and radiological technologists (61.3%), study meeting (57.5%), and guidance from senior nurses (40.8%) (Table 2).

3.2. Risk images of radiation

Dread risk image scores and unknown risk image scores were significantly different among nurses who had a career in radiation nursing and those who only participated in a study meeting ($p<0.05$). There were no significant differences in either score among nurses who lived in a prefecture that had a nuclear power plant and nurses with experience in training in radiation emergency medicine. The severity of the disaster was rated as 8.1 ± 2.2 (means $\pm$ SD). The high severity and low severity groups were separated by 8.1, the severity means scores of the disaster. The high severity group showed significantly higher ratings than the low severity group ($p<0.001$) (Table 2).

Severity scores did not differ significantly based on education about radiation or experience in training in radiation emergency medicine. Severity scores were significantly higher among nurses who lived in a prefecture with a nuclear power plant than nurses who did not live in these prefectures ($p<0.05$).

3.3. Worry and concern about the Fukushima Dai-ichi Nuclear Power Plant accident

Worries and concerns that subjects expressed after the Fukushima Dai-ichi nuclear power plant accident are shown in Table 3. The most common responses were “Influence of radiation on human body” (n=80, 13.5%), followed by “Influence of radiation on child/fetus” (n=51, 8.6%). Other concerns included “Safety of food in terms of radioactive contamination” (n=42, 7.1%), “Safety of nearby nuclear power plant” (n=35, 5.9%), and “Current state and future of residents affected by the disaster and Fukushima prefecture” (n=29, 4.9%).

Table 4. Worries and concerns after the Fukushima

Influence of radiation on human body	80
Influence of radiation on child/fetus	51
Safety of food about radioactive contamination	42
Necessity of correct information or radiological knowledge about radiation / accident	38
Safety of nearby nuclear power plant	35
Current state and in future on struck residents by disaster and Fukushima prefecture	29
Influence of radioactive contamination on environment	27
Influence on human body to nurse assisting the radiological examination	18
Current state and in future on Fukushima Dai-ichi nuclear power plant	18
Extent and expansion of radioactive contamination	14
Correspondence to Fukushima's accidents of Japanese government	14
Prospect of nuclear power plant	13
Radiation Emergency Medicine on individual and clinic	11
Decontamination	10
negative perception to radiation	9
Harmful rumors	8
Impact around Fukushima prefecture	7
Internal exposure	6
How to deal with radioactive waste	6
Overreact to radiation	5
Increasing the question about radiation from patient	4
Radiation protection	3
Mass communication on radiation accident	2
Our country in future	2
Other	8
No coment	131

4. Discussion

This study analysed nurses’ perceptions of radiation risk perception, and the relationship between these risk perceptions and nurses’ knowledge level regarding radiation or radiological nursing care. Our findings indicated that dread image scores and unknown image scores might be increased among nurses who do not have a career in radiation nursing or an opportunity to learn about radiation. That is, risk perception about radiation might be contribute to knowledge and experience of nursing care level regarding radiation. In addition, residents who live further away from the disaster area seemed to have less concerns about radiation that those who live closer to the disaster area. However, fear of radiation is probably affected by the level of radiological knowledge. There is no systematic radiological education in Japan. A previous study reported that fear of radiation can negatively affect patient care[8-11]. An education system in which medical nursing staff can learn

radiological knowledge and skills systematically and continuously is needed. In addition, knowledge about communicating about radiation risks is also needed. The highest rated concerns regarding radiation were those regarding how it would influence the human body.

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Educational effect and assessment before and after radiation emergency medicine personnel training Assessment and effects of undergraduate education —Trends over three years

Saichi Wakayama*

Department of Development and Aging,
Division of Health Sciences,
Hirosaki University Graduate School of Health Sciences

Abstract. The Radiation Emergency Medicine (REM) course "Introduction to Basic Radiation" started at Hirosaki University in April 2010 and was compulsory for all 160 first-year students of the School of Health Sciences who were not enrolled in the Radiation Technology course. In 2011, the class was unable to begin until May due to the Great East Japan Earthquake and nuclear disaster at Fukushima on March 11. The aim of the class is to provide paramedical personnel with both a basic knowledge of radiation protection and an outline of REM. In 2012, we started “Medical Risk Management”, a faculty education class aimed at providing a further understanding of REM and crisis-management involving cooperation among paramedical personnel. This study presents a three-year summary of the "Introduction to Basic Radiation" compulsory undergraduate course. We examined trends in the number of enrolled students and their overall performance during a 3-year period. Response Card for student were used to confirm student responses to questions concerning various aspects of basic radiation, ranging from their impressions of radiation and radioactivity to their knowledge of the nuclear-related facilities in Aomori Prefecture. Differences of opinions regarding these subjects on the final exam were also analysed. Enrolment in the course varied from 165 students in 2010 to 191 students in 2011 and 176 students in 2012. The average grades earned by students of School of Health Sciences were 81.6, 79.5, and 73.0 in 2010-2012, respectively. Responses from both the student clickers and the final exams are currently being analysed. In 2011, the disaster at the Fukushima nuclear power plant appeared to greatly influence student responses. For the past 2 years, survey results have indicated an increasing understanding of the subjects presented in the class, and feedback in relation to the course contents has been positive. However, students earned a lower average grade in 2012, and this finding requires further discussion.

Key Words: radiation emergency medicine, undergraduate education, Trends over three years

Background and purpose

As one part of the developing human resources for radiation emergency medicine started in the 2008 academic year, the School of Health Sciences added a class called “Basics of Radiation Protection” to the first semester, first year curriculum, and a class called “Medical Risk Management” was added to the first semester, third year curriculum (Table 1)[1)].

With the aim of providing students with an understanding of the basics of radiation and radiation protection, and a general outline of radiation emergency medicine, “Basics of Radiation

*Corresponding to: Saichi Wakayama, Professor, Hirosaki University Graduate School of Health Sciences, 66-1 Hon-cho, Hirosaki, 036-8564, Japan, E-mail: swaka@cc.hirosaki-u.ac.jp

Table 1 REM-related classes for undergraduate students

Subjects	Grade, Semester, Unit	Class Goals
< Liberal Arts Education > Introduction to Basic Radiation	1st Grade, Spring semester 1 Unit, 16 hours	Basic understanding of radiation protection and a general outline of REM
< Faculty Education > Medical Risk Management	3rd Grade, Spring semester 1 Unit, over 30 hours	Further understanding of REM and crisis-management involving cooperation among paramedical personnel

Protection," a 21st century education class, was started in 2010 in the first semester, first year liberal arts education for students of all four departments in the School of Health Sciences except for the Department of Radiological Technology. Three years have now passed. In 2012, the "Medical Risk Management" class was started as a third year requirement for all departments in the specialty curriculum.

We investigated the results of the 21st century education class "Basics of Radiation Protection" over the three years since it was started in April 2010 from the trends in the number of students and their results in the class, the clicker response during class, and free opinions of students given at the conclusion of the class. Based on this, we look at the current status of this class and undergraduate education, and future issues.

Methods

Subjects: Students who took "Basics of Radiation Protection" in the three years from 2010 to 2012
Methods: Aggregation and comparison of the following data for the three years from 2010 to 2012

(1) Number of students
(2) Results on final examination
(3) At the first class meeting of each year, questions on basic radiation were asked using a clicker and response card with Turning Point 2008, and the response results were tabulated with the response card. Some of the question content was prepared with reference to a public opinion survey on the dissemination of knowledge and awareness of the use of nuclear power (Japan Atomic Energy Relations Organization).[2)]
(4) At the final examination, students were asked to write their opinions of the class and wishes for the following year, and the results were classified and aggregated by content.

Results

1. Number of students and test results

The numbers of students who took the class from 2010 to 2012 are shown in Tables 2. The class was a designated class (handled the same as a requirement) for first-year students in the School of Health Sciences, but it was an elective for other students.

The score on the final examination was 81.6 points in 2010, 78.6 points in 2011, and 73.0 points in 2012 (Table 3). Because the test did not contain the exact same problems each year and the class had an omnibus format, in 2011 and 2012, the examination was separated into two different days with supplementary lectures and other materials.

Table 2 Number of Students

	2010	2011	2012
Nurse(N)	80	80	87
Medical Technology(T)	40	39	42
Physical Therapy(PT)	21	21	21
Occupational Therapy(OT)	20	20	20
Other faculty	4	27	6
Total	165	187	176

Table 3 Final Exam. Score

	2010	2011	2012
N	80.2	79.5	70.4
T	86.1	82.2	78.8
PT	80.5	76.7	74.6
OT	79.8	77.3	70.2
Other	78.8	73.2	72.7
All	81.6	78.6	73.0

2. Clicker response

Knowledge about the nuclear power-related facilities in Aomori Prefecture differed clearly between 2010 and 2011, 2012, with higher percentages of correct answers in 2011 and 2012 (Table 4).

In view of the Fukushima nuclear disaster, items for the students' impressions and awareness of radiation and radioactivity changed in 2011. In 2010, the Hiroshima and Nagasaki atomic bombs and nuclear power generation were highest in students' minds, in that order, but in 2011 and 2012, the order changed to the Fukushima nuclear disaster and the Chernobyl disaster (Table5-1, 5-2).

3. Free opinions

At the final examination, students were asked to write their opinions of the course and wishes for the next year.

Nearly all students wrote opinions and wishes. The trends over the three years showed an increase in positive opinions from 2011. The following summary is organized by content, with consideration of the percentage of opinions. There were repetitions of material in the class, which received both positive (A) and negative (B) opinions, with trends shown in Figure 1.

(1) Positive opinions on class content

• I am happy to have gained knowledge on subjects such as radiation, radiation protection, and radiation medicine.

• I felt the material in this class was necessary for health and medical workers, and found it interesting.

• The same things were repeated in the class, but I thought they were repeated because they are important. (A)

(2) Negative opinions and items for improvement in the class content

• There was duplication in the class material, and the same things were said repeatedly. I would have liked other material to be included. (B)

• I would like to have learned more about radiation medicine.

• I would like to have handled and tried using radiation measuring instruments.

(3) Positive opinions on class methods

• With the omnibus format, every class meeting was interesting.

• Classes using a clicker were fresh, and I could concentrate and enjoy them.

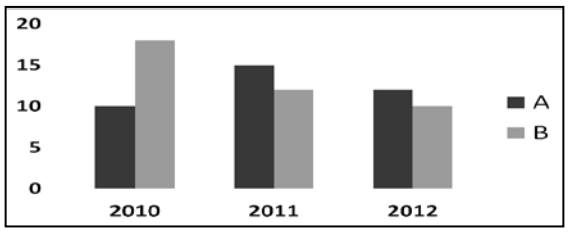

Figure 1 Trends in opinion on the course content duplication(%) A: positive, B:

Table 4 What nuclear-related facilities are located in Aomori Prefecture ?

	2010		2011		2012	
Nuclear power plant	9	5.8%	71	39.9%	34	23.9%
Reserves of low-level radioactive waste facility	59	37.8%	9	5.1%	19	13.4%
Reserves of high-level radioactive waste facility	55	35.3%	24	13.5%	17	12.0%
Nuclear fuel reprocessing plant	15	9.6%	60	33.7%	49	34.5%
Nuclear ship 'Mutsu'	18	11.5%	14	7.9%	23	16.2%
Total	**156**	**100%**	**178**	**100%**	**142**	**100%**

Table 5-1 Impression of radiation and radioactivity

	2010	
Scary	30	19.6%
Atomic bombs of Hiroshima and Nagasaki	64	41.8%
Nuclear power plant	50	32.7%
JCO Accident	3	2.0%
Nothing special	6	3.9%
Total	**153**	**100%**

Table 5-2 Impression of radiation and radioactivity

	2011		2012	
Nuclear disaster at Chernobyl in Russia	58	32.6%	50	31.3%
Atomic bombs of Hiroshima and Nagasaki	30	16.9%	25	15.6%
Nuclear power plant	13	7.3%	15	9.4%
JCO Accident	2	1.1%	5	3.1%
Nuclear disaster at Fukushima	75	42.1%	80	50.0%
Total	**178**	**100%**	**160**	**100%**

Discussion

The number of students who took “Basics of Radiation Protection” in the School of Health Sciences increased partly because of third-year students who transferred from other faculties. The number of students from other faculties reached double digits in 2011 and returned to single digits in 2012. This is often said to be because the Fukushima nuclear disaster is fading from people’s consciousness with time, and that may be part of the reason. With respect to the test results, the test problems change a little each year, and it may be that the test was purposely made more difficult in 2012 because it was too easy in 2010 and 2011. There was no attempt to set a target range for mean scores, and in 2012, a fairly large difference was seen between teachers. As a result, the overall score is thought to have decreased. To counter this, it may be necessary to adopt measures such as having the test on the same day and setting a uniform target range for the mean score (difficulty of problems).

The use of clickers rose from two teachers in 2010 to three teachers in 2011. The advantage of dynamic responses without breaking concentration was rated positively in the free opinions of each year[1,3]. Understanding of the facilities in Aomori Prefecture rose in 2011 and was generally maintained in 2012. The fading of nuclear concerns from consciousness may be affecting the number of students, but knowledge including impressions and awareness of radiation seems to be maintained.

Opinions on the class at the time of the final examination have not changed greatly over the three years, but a trend for an increase in positive opinions (Figure 1) is seen. Because this is an omnibus class, ongoing coordination among teachers may be necessary.

Continued investigation is necessary to determine the level of objectives the School of Health Sciences should aim to achieve as part of undergraduate education.

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Recipient-transferred allogeneic umbilical cord blood cells reconstitute the hematopoietic system and immunological functions in a murine model

Hideaki Sato[1,2], Ayumi Wakayama[1,3], Kyoko Ito[1], and Koichi Ito[1*]

[1] *Department of Biomedical Sciences, Division of Medical Life Sciences, Hirosaki University Graduate School of Health Sciences*
[2] *Cell Technology Center, Stem Cell Institute Inc.*
[3] *Transfusion and Cell Therapy Center, Hakodate Municipal Hospital*

Abstract. Murine allogeneic umbilical cord blood cells (UCBCs) were studied for their ability to reconstitute the hematopoietic system. UCBC prepared from C57BL/6 (H-2^b) mice were transferred into lethally irradiated BALB/c (H-2^d) lacking T- and B-lymphocytes (RAG2 knockout). In this UCBC transplantation model, the all surviving recipient mice were hematopoietic chimeras possessing all lineages. In this study, the *in vitro* responsiveness of reconstituted T cells in both chimeras was verified by allogeneic (specific) or mitogen (non-specific) stimulation. Although the T cells responded appropriately to both types of stimulation, their reactivity was relatively low as compared with that in normal control mice. This tendency was especially marked in the case of allogeneic stimulation. Furthermore, we have demonstrated for the first time that B-1a cells, which produce natural IgM antibodies against pathogens such as *Streptococcus Pneumoniae*, can be generated from UCBCs but not from BMCs.

Key Words: murine umbilical cord blood cell transplantation, hematopoiesis, immune reconstitution

Introduction

An increasing number of clinical trials have demonstrated the usefulness of cord blood as a source of hematopoietic stem cells (HSCs) for reconstitution of the hematopoietic system. Umbilical cord blood cell (UCBC) transplantation is an effective treatment for not only various hematological diseases [1-3] but also accidental high-dose total-body irradiation exposure [4]. Nevertheless, due to the lack of convenient animal models, information regarding the immunological competence of UCBC-derived lymphocytes is relatively limited [1-3]. Recently, we established a murine UCBC transplantation model that reconstituted the hematopoietic system in syngeneic recipients [5]. Here, considering that HSCs may often have to be transplanted into HLA-mismatched patients, the immunological competence of UCBC-derived lymphocytes matured in allogeneic recipients was studied. For comparison, allogeneic bone marrow cell (BMC) transplantation was also performed.

Materials and Methods

UCBC and BMC transplantation

RAG2$^{-/-}$BALB/c (H-2^d) recipient mice lacking T- and B-lymphocytes subjected to 8-Gy irradiation received a transplant of 1×10^6 UCBCs or BMCs, which had been depleted of mature T cells, obtained from green fluorescent protein-transgenic C57BL/6 (GFPTg-B6) (H-2^b) mice. At 16 weeks after transplantation, the ability of the UCBCs and BMCs to reconstitute the hematopoietic system was studied in both sets of recipients. The experimental procedure was approved by the Animal Research Committee of Hirosaki University, and performed in accordance with the Institutional Guidelines for Animal Experimentation.

* Corresponding to: Koich Ito, Professor, Hirosaki University Graduate School of Health Sciences, 66-1 Hon-Cho, Hirosaki, 036-8564, Japan.
E-mail:kohito@cc.hirosaki-u.ac.jp

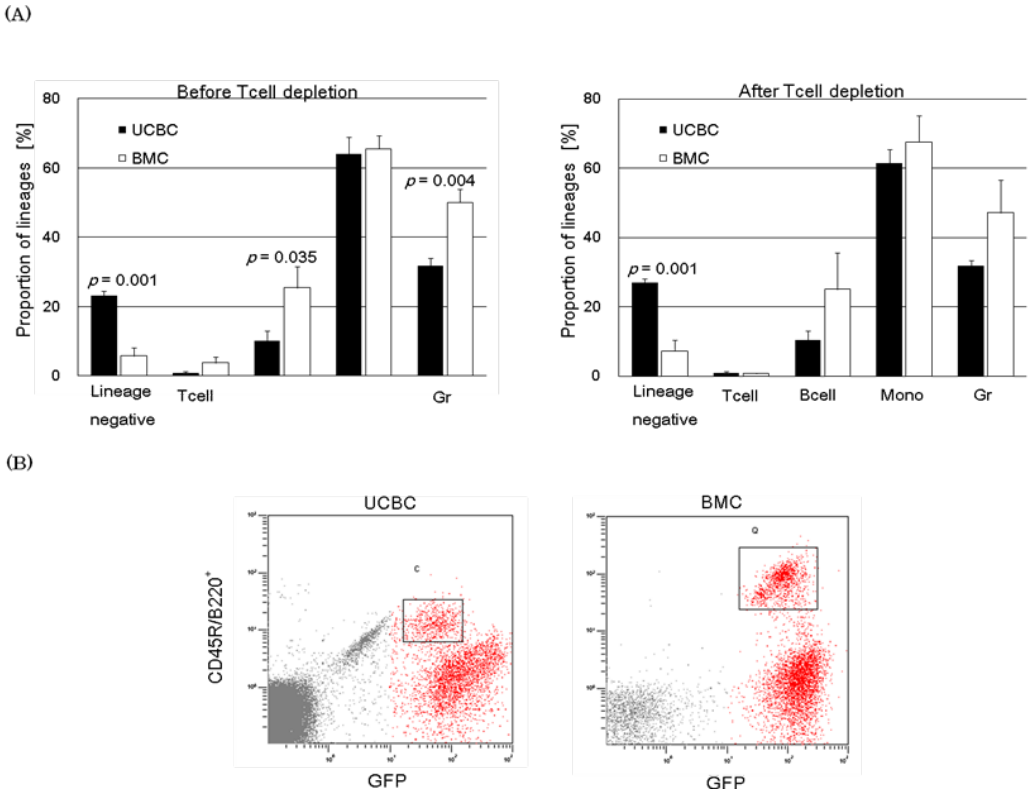

Figure 1. **Profile of donor cells used for transplantation**

Results and Discussion

Profile of donor cells used for transplantation

UBCBs and BMCs prepared from GFPTg-B6 mice were stained with antibodies against the lineage markers CD3e (T cells), CD45R/B220 (B cells), CD11b (monocytes) and Ly-6G (granulocytes). The percentage of cells of each lineage was determined by flow cytometry (Figure 1A). Essentially, UCBCs did not include mature T cells (before T-cell depletion: 0.9±0.4; after T-cell depletion: 0.8±0.4). The percentage of T cells among BMCs decreased to a level similar that of UCBCs after T-cell depletion (before T-cell depletion: 3.8 ± 1.7; after T-cell depletion: 0.8±0.2). In addition, relative to BMCs, UCBCs contained approximately 4 times as many lineage-negative cells after T-cell depletion with a mixture of lineage antibodies (UCBCs: 26.9±1.3; BMCs: 7.3 ± 3.0), indicating that hematopoietic progenitor cells were enriched in UCBCs. Another feature of the phenotypic profile of UCBCs, relative to BMCs, was the presence of many B cells (Figure 1B). The phenotype of these B cells was CD45R/B220^{low} in UCBCs and CD45R/B220^{high} in BMCs, indicating that the B cell population in UCBCs is less mature than that in BMCs.

Development of the hematopoietic system after allogeneic transplantation

Both UCBC- and BMC-recipients showed comparably high survival rates (more than 90%) (data not shown). At 16 weeks after transplantation, flow cytometric analysis revealed that the transferred cells had developed into T cells, B cells, monocytes and granulocytes in allogeneic UCBC- and BMC-transplanted mice (Figure 2A). The noteworthy point here is that the rate of B cell reconstitution was higher in the mice that received UCBCs than in mice that received BMCs. As shown in Figure 2, this result may be related to the difference in the maturity of the B cells used for transplantation. We previously found that although a slight delay was evident in comparison with normal control mice, both sets of recipients had a similar ability to reject third-party skin grafts and to produce antigen-specific antibodies (data not shown). In this study, the in vitro responsiveness of reconstituted T cells in both chimeras was verified by allogeneic (specific) or mitogen (non-specific) stimulation (Figure 2B). Although the T cells responded appropriately to both types of stimulation, their

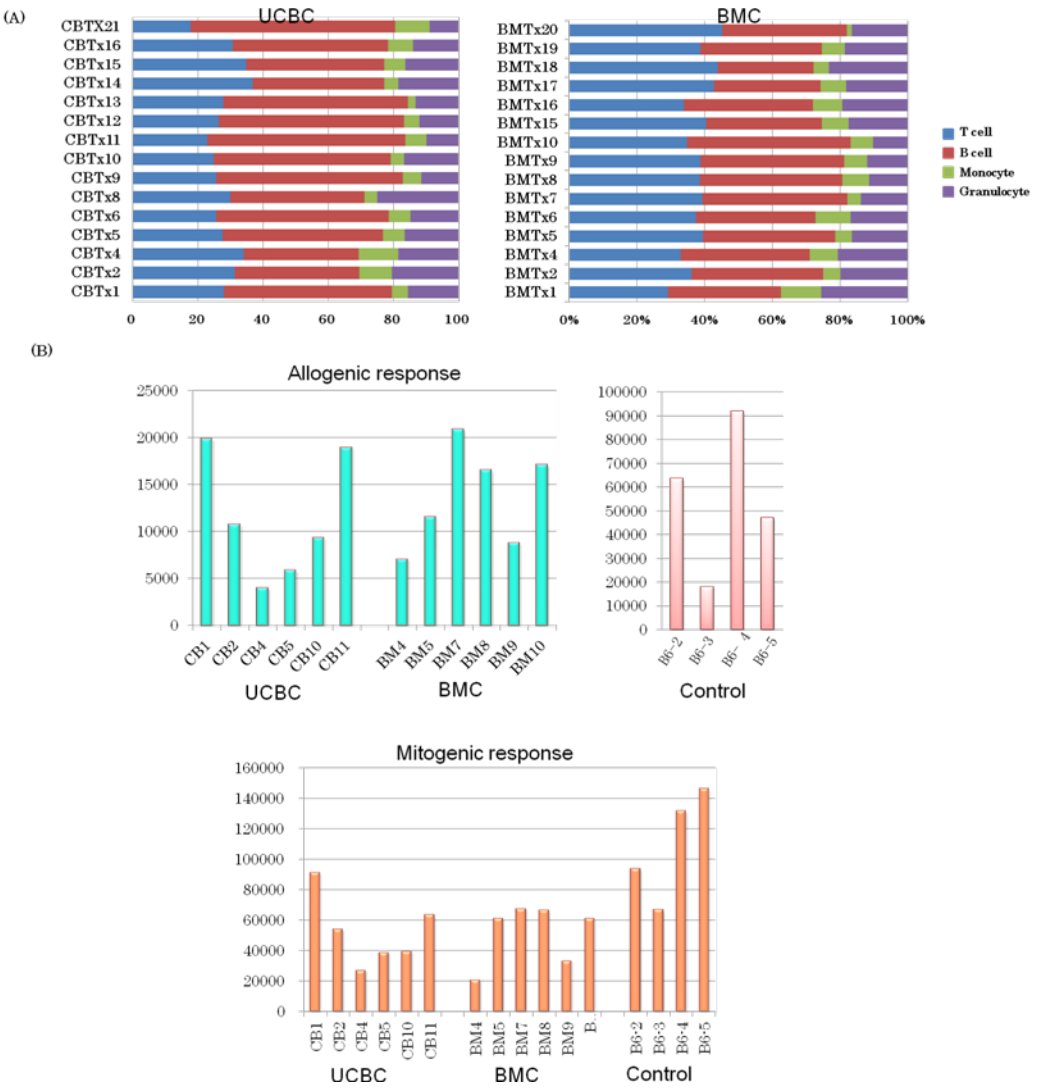

Figure 2. Development of the hematopoietic system after allogeneic transplantation

reactivity was relatively low as compared with that in normal control mice. This tendency was especially marked in the case of allogeneic stimulation. Collectively, these results suggest that UCBC-HSC and BMC-HSC have essentially the same ability to reconstitute the functional hematopoietic system, even in an allogeneic environment.

Reconstitution of peritoneal B-1 cells in recipients after UCBC or BMC transplantation

Our previous study had indicated that UCBCs have considerable promise for reconstituting bacterial polysaccharide-reactive natural IgM-producing B-1 cells in the peritoneal cavity. In this study, the reconstitution of B-1 cells in both chimeric recipients was confirmed in a peritoneal cell (PC) transfer experiment (Figure 3). RAG2(-/-) B6 or BALB/c mice were transferred into the peritoneal cavity with the indicated number of PCs from UCBC recipients, BMC recipients or normal B6 mice. At 8 weeks after cell transfer, the bacterial polysaccharide-reactive IgM was observed in the mice that had received PCs, which included a rich B-1 cell subset, from normal B6 and UCBC-recipient mice, and the amount of IgM was dependent on the number of PCs transferred. In contrast, PCs from BMC-recipient mice induced a marginal level of IgM in the transferred mice.

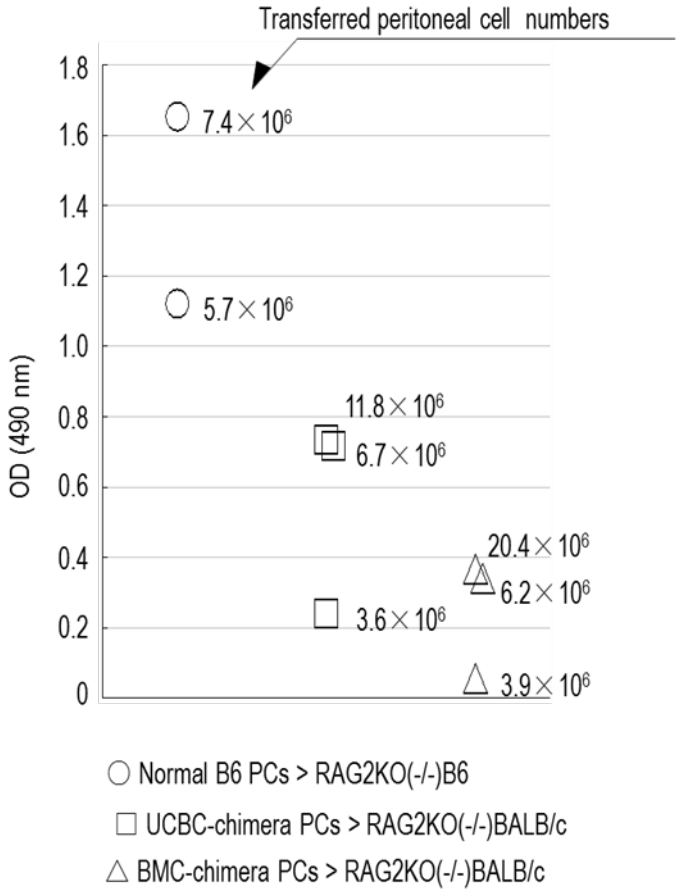

Figure 3. Reconstitution of peritoneal B-1 cells in recipients after UCBC or BMC transplantation

Conclusions

UCBCs and BMCs have essentially similar abilities for reconstitution of the functional immune system even in an allogeneic environment. Furthermore, this study demonstrated that UCBCs have considerable potential for reconstitution of B-1 cells, thereby replenishing bacterial polysaccharide-reactive IgM as a front-line defensive factor against invading pathogens. These findings are of clinical relevance for hematopoietic stem cell transplantation.

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Double unit umbilical cord blood transplantation induces MHC-matched single unit dominance with development of immunocompetent lymphocytes in recipients

Akira Nakano[1], Hideaki Sato[2], Kyoko Ito[1], and Koichi Ito[1*]

[1] Department of Biomedical Sciences, Division of Medical Life Sciences, Hirosaki University Graduate School of Health Sciences
[2] Cell Technology Center, Stem Cell Institute Inc.

Abstract. Umbilical cord blood cell (UCBC) transplantation is an effective treatment for lethal-dose total-body irradiation exposure. In the present study, we examined the ability of double unit UCBCs (dUCBCs) to reconstitute the immune system. At 16 weeks after transplantation, the MHC-matched single unit from dUCBCs acts as the sole source of long-term hematopoiesis. On the other hand, the hematopoiesis with allogeneic dUCBC transplantation is reconstituted by the recipients' own X-ray-resistant hematopoietic stem cells. In addition, all recipients received skin grafting to assess the functional maturity of the newly developed immune system. Our observations indicate that T and B lymphocytes derived from dUCBC transplants are immunologically fully competent with the ability to distinguish self from non-self using different MHC antigens.

Key Words: double unit umbilical cord blood cell transplantation, major histocompatibility complex, immune reconstitution

Introduction

Double unit umbilical cord blood cell (dUCBC) transplantation has emerged as an effective strategy for improving the engraftment of umbilical cord blood stem cells in the bone marrow of recipients. Due to a lack of convenient animal models, analyses of the differentiation capacity of dUCBCs in recipients have been limited to *in vivo* xenogeneic experiments [1-3] and clinical observations [4-6]. In the present study, we evaluated the characteristics of immune reconstitution induced by dUCBC transplantation in mice.

Materials and Methods

dUCBC transplantation

Natural killer cells were depleted from female C57BL/6 (B6) [H-2^b] recipient mice by intraperitoneal administration of rabbit anti-asialo GM1 polyclonal antibody 1 day before transplantation (Figure 1). On the following day, the 9-Gy X-ray-irradiated B6 recipients were given transplants of three different combinations of dUCBC {group (1) GFP-Tg B6 [H-2^b] and C3H [H-2^k]; group (2) GFP-Tg B6 [H-2^b] and BALB/c [H-2^d]; group (3) BALB/c [H-2^d] and C3H [H-2^k]}, each combination containing an equal number of cells. At 16 weeks after transplantation, the reconstitution and functional maturity of the newly developed immune system was assessed in the recipients. The experimental procedure was approved by the Animal Research Committee of Hirosaki University, and performed in accordance with the Institutional Guidelines for Animal Experimentation.

* Corresponding to: Koich Ito, Professor, Hirosaki University Graduate School of Health Sciences, 66-1 Hon-Cho, Hirosaki, 036-8564, Japan.
E-mail: kohito@cc.hirosaki-u.ac.jp

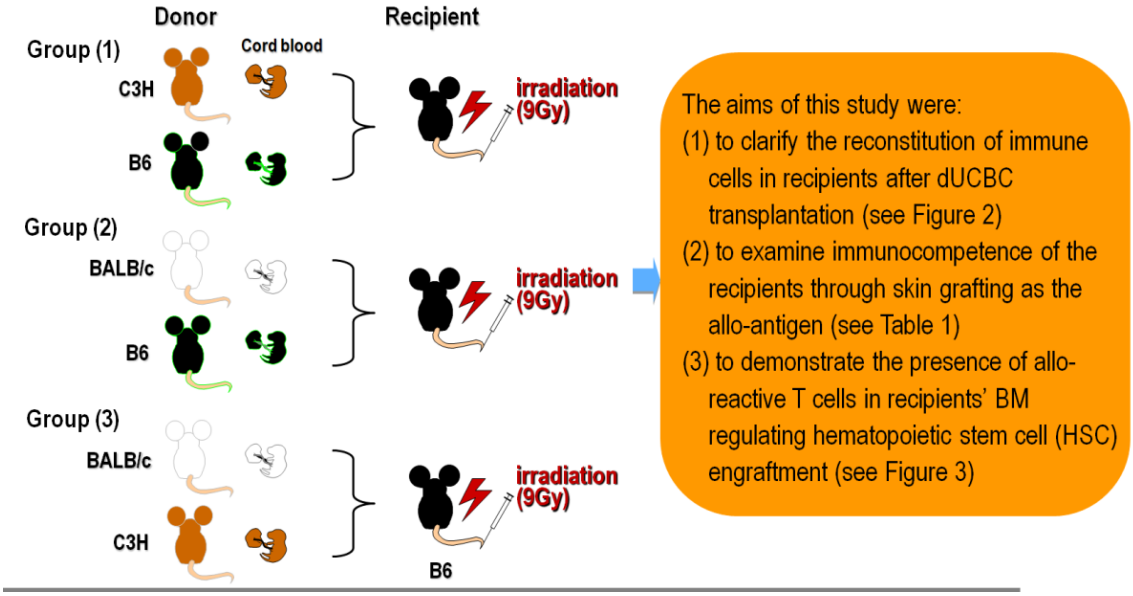

Figure 1. dUCBC transplantation

Results and Discussion

Reconstitution of the immune system by dUCBC transplantation

At 16 weeks after transplantation, reconstitution of immune cells was evaluated by flow cytometric analysis utilizing specific antibodies against the lineage markers CD3 (T cells), CD45R/B220 (B cells), CD11b (macrophages), and Ly-6G (granulocytes). The donor origin of each lineage population was determined by staining with anti-H-2K^{k} (for C3H) and /or H-2K^{d} (for BALB/c) antibody. GFP^{+} lineage cells were identified as being of B6 donor origin (Figure 2). The survival rate at 16 weeks after transplantation was 92% (12/13) for group (1), 73% (8/11) for group (2), and 50% (3/6) for group (3) (data not shown). Bar graphs show the percentage of cells of each reconstituted lineage in peripheral blood. The analysis revealed that the UCBCs had developed into T cells, B cells, monocytes, and granulocytes in all recipients. The pie chart displays individually the proportions of donor MHCs in each lineage population of the bar graph. In the great majority of groups (1) and (2), in which dUCBCs were administered as a stem cell source, the MHC-matched single unit from GFP-Tg B6 acted as the sole source of long-term hematopoiesis (100% (12/12) for group (1); 75% (6/8) for group (2)). CD3^{+} T cell peripheral blood chimerism from BALB/c was observed in two of the eight B6 survival recipient mice in group (1) at an early stage of hematopoiesis, predicting the long-term engrafting unit (data not shown). On the other hand, hematopoiesis in group (3) with fully allogenenic dUCBC transplantation was reconstituted by the B6 recipients' own HSCs.

Skin graft rejection

Skin grafting was performed in the recipients of group 1 to assess the functional maturity of the newly developed immune cells reconstituted as the B6 background by dUCBC transplantation (Table 1). These recipients were tolerant of skin grafted from B6, whereas they rejected skin from BALB/c and C3H within 20 days, indicating that both CD4^{+} helper and CD8^{+} killer T cells were functionally mature in the recipient mice. Correspondingly, only the alloantibody to BALB/c and C3H was produced in the recipients.

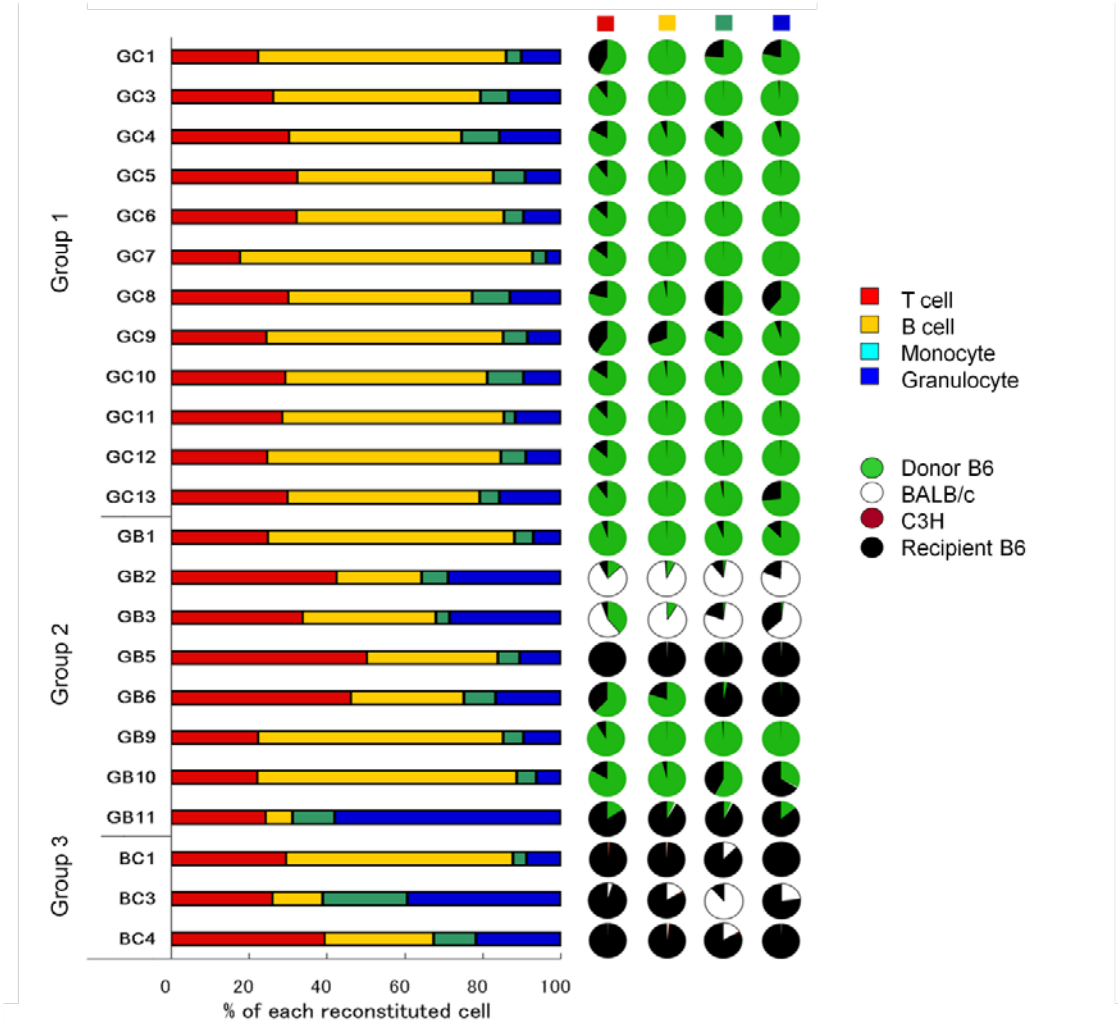

Figure 2. Reconstitution of the immune system by dUCBC transplantation

Memory T cells in bone marrow

Our results depicted in Figure 2 indicate that MHC-matched UCBC-HSC were predominantly engrafted in the recipient's BM after dUCBC transplantation. However, the nature of the selective mechanism involved remains largely unknown. Bone marrow is one HSC engraftment site. Therefore, it is thought that the selective mechanism involves allo-reactive $CD4^+$ helper and $CD8^+$ killer T cells existing in the recipient' s BM. To examine this possibility, we first analyzed BM cells from normal B6 mice using flow cytometry along with spleen cells. A representative result shown in Figure 3 suggests that the proportion of $CD44^{high+}$ cells indicating the memory type within $CD4^+$ or $CD8^+$ cells was higher in the BM (90% in $CD4^+$ and 46% in $CD8^+$) than in the spleen (65% in $CD4^+$ and 36% in $CD8^+$) or peripheral blood (28% in $CD4^+$ and 11% in $CD8^+$). These results indicate that the BM-resident T cell population is enriched with memory type cells and differs from splenic T cells or peripheral blood T cells. Currently, we are investigating the allo-reactivity of the accumulated memory $CD8^+$ T cells in the recipient' s BM.

Table 1. Skin graft rejection

Recipients	Rejection time (days)		
	B6	BALB	C3H
GC1	>30	20	10
GC3	>30	13	10
GC4	>30	16	11
GC5	>30	11	10
GC6	>30	13	10
GC7	>30	12	14
GC8	>30	13	12
GC9	>30	16	11
GC10	>30	14	15
GC11	>30	12	12
GC12	>30	12	12
GC13	>30	9	9
GB1	12	16	10
GB2	NT	NT	NT
GB3	11	8	8
GB5	>30	9	13
GB6	NT	NT	NT
GB9	>30	9	15
GB10	>30	11	11
GB11	13	16	15
BC1	10	9	10
BC3	NT	NT	NT
BC4	>30	11	11

Conclusions

dUCBC transplantation clearly rescued mice that had been subjected to lethal X-ray irradiation. Furthermore, our observations indicate that immune cells derived from dUCBC transplantation are immunologically fully competent with the ability to distinguish self from non-self MHC antigens. In dUCBC transplantation, the included allogeneic cells probably act as stimulators for promoting the differentiation and maturation of MHC-matched HSCs through activation of certain types of signal transduction (for example, through cytokine secretion).

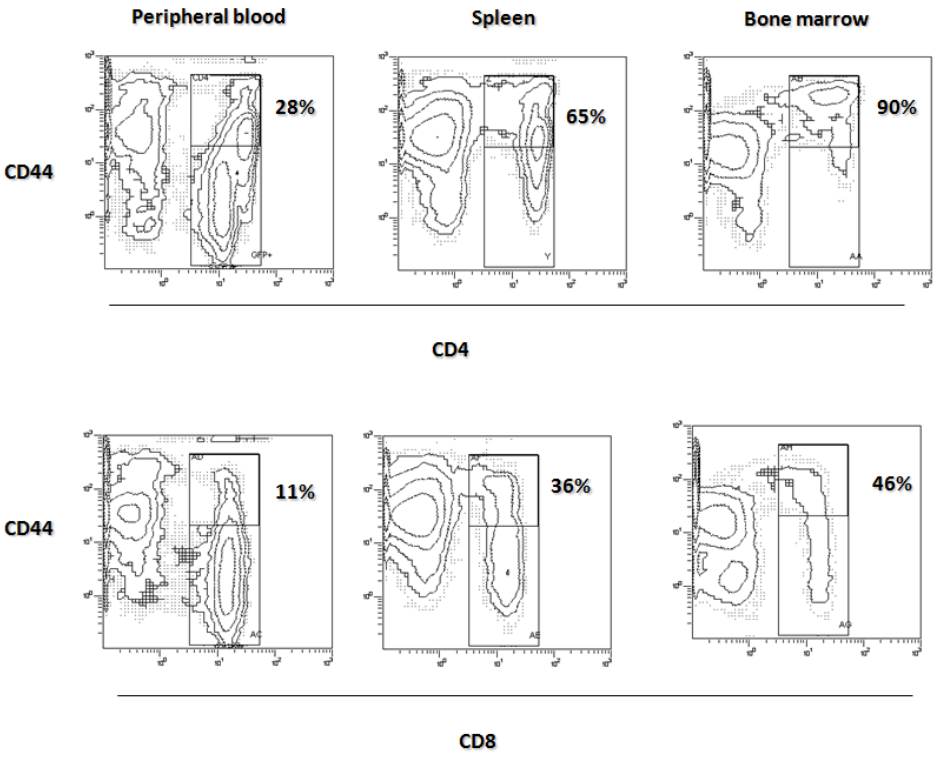

Figure 3. Memory T cells in bone marrow

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Mitochondrial Involvement in Response of Human Hematopoietic Stem Cells to Radiation

Masaru Yamaguchi and Ikuo Kashiwakura*

Department of Radiological Life Sciences, Division of Medical Life Sciences, Hirosaki University Graduate School of Health Sciences s, Hirosaki, Japan

Abstract. Hematopoietic stem cells (HSCs) are extremely sensitive to oxidative stress because of their high proliferative potential. HSC quiescence and stemness are maintained through the regulation of mitochondrial biogenesis and reactive oxygen species (ROS). However, the relationship between HSC radiosensitivity and mitochondrial function are not clear. We evaluate the ROS generation and mitochondrial function in the proliferation and differentiation of HSCs exposed to X-irradiation. $CD34^+$ HSCs were X-irradiated and incubated for 0 – 7 days with cytokines (G-CSF, GM-CSF, IL-3, SCF and EPO). Harvested cells were assayed for progenitors using methylcellulose culture stimulated with the same cytokines. Intracellular ROS, mitochondrial superoxide and mitochondrial contents were analyzed by flow cytometry. The growth and clonogenic potential of HSCs irradiated with 4 Gy X-rays were dramatically suppressed for 3 and 7 days. The mitochondrial contents similarly increased in the irradiated and non-irradiated cells. The intracellular ROS increased 4-fold on day 3 in X-irradiated cells, whereas the mitochondrial superoxide did not significantly differ. The present findings suggest that the increase in oxidative damage leads to the loss of clonogenic potential in HSCs. However, more precise approaches will be required to clarify the involvement of mitochondria in the proliferation and differentiation of HSCs exposed to X-irradiation.

Key Words: hematopoietic stem cells, mitochondria, reactive oxygen species

Introduction

Hematopoietic stem cells (HSCs) can self-renew to maintain own undifferentiated phenotype and differentiate into all functional mature hematopoietic cells. HSCs are usually present in a special microenvironment called a niche, which maintains the stemness of HSCs by control of reactive oxygen species (ROS) [1]. In these environments, physiological levels of intracellular ROS play an important role on endogenous growth signals, cell survival, proliferation and differentiation of HSCs [2-4]. But since HSCs are extremely sensitive to various oxidative stresses such as anti-cancer agents, radiation or accumulation of much higher level of ROS [5-7], ROS overproduced higher than a physiological level cause HSCs damages [8-10]. In addition, since HSCs are generally required very small energy because of G_0 state, therefore, HSCs have relatively lower intracellular mitochondrial contents rather than other functional mature cells [11, 12]. However, little information about the relationship between the radiosensitivity of HSCs and mitochondrial function has been reported. In this study, to clarify the involvement of mitochondrial state and intracellular ROS on the radiosensitivity of human HSCs, $CD34^+$ HSCs exposed to X-irradiation were cultured with appropriate cytokine stimulation and were analyzed for their characters.

Material and Methods

This study was approved by the Committee of Medical Ethics of Hirosaki University Graduate School of Medicine, and informed consent was obtained from the mothers following full-term deliveries by the description and vernal explanation.

* Corresponding to: Ikuo Kashiwakura, Professor, Hirosaki University, 66-1, Hon-cho, Hirosaki, 036-8564, Japan.
E-mail: ikashi@cc.hirosaki-u.ac.jp

The CD34 positive cells were purified from human placental/umbilical cord blood using a magnetic cell sorting kit and frozen at –150°C until the experiment. The thawed cells suspended in serum-free medium were exposed to X-irradiation. These cells were incubated at 37°C under 5% CO_2 for 0–7 days with cytokines (G-CSF, GM-CSF, IL-3, SCF, and EPO). Harvested cells were assayed for the progenitors by using methylcellulose culture stimulated with the same cytokines. Intracellular ROS, mitochondrial superoxide, and mitochondrial contents were analyzed using CM-H2DCFDA, MitoSOX Red, and MitoTracker, respectively, by flow cytometry.

Results and Discussion

In order to check the radiosensitivity of HSCs, we assayed for colony-forming cells (CFCs), including colony-forming unit-granulocyte macrophage (CFU-GM), burst-forming unit-erythroid (BFU-E), and colony-forming unit-granulocyte erythroid, macrophage, megakaryocyte (CFU-Mix) cells using methylcellulose cultures (figure 1), and table 1 summarizes the D_0 and n values. As a result of X-irradiation with doses from 0 to 7 Gy, each progenitor-derived colony formation was dose-dependent decrease.

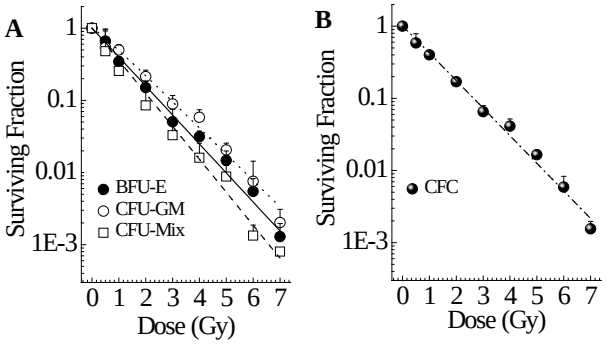

Figure 1. Radiation dose-response curves of each progenitor-derived colony.

Table 1. Radiosensitivity of hematopoietic myeloid progenitor cells

Survival curve parameter	D_0	n
CFU-GM	1.19 ± 0.11	1.20 ± 0.13
BFU-E	1.08 ± 0.08	1.01 ± 0.14
CFU-Mix	0.95 ± 0.08	1.03 ± 0.14
CFCs	1.14 ± 0.10	1.03 ± 0.10

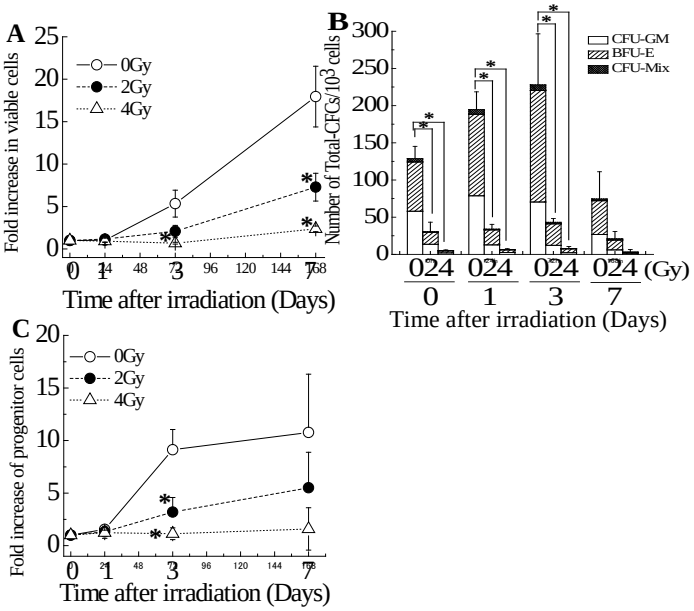

Figure 2. Effect of X-irradiation on the cell growth and clonogenic potential of $CD34^+$ HSCs. *P < .05

Next, we evaluated the effect of X-irradiation on the growth and clonogenic potential of the $CD34^+$ HSCs. Total number cells of control culture showed an approximately 18-fold increase from the initial input at Day 7 (figure 2A). In contrast, a significant decrease was observed in the cultures of 2 or 4 Gy X-irradiated HSCs compared with control at Day 3 and 7. The total number of each progenitor was evaluated to assess the colonogenic potential after each incubation time. In addition, the total number of CFCs and containing myeloid hematopoietic progenitor cells in the control cultures increased (figure 2B, C). Conversely, a significant decrease in the number of CFCs was observed in the culture of 2 or 4 Gy X-irradiated HSCs at Day 0, 1 and 3. However, the total number of CFCs in the control cultures decreased at Day 7 and there was no significant difference between the control and irradiated cells. Little change was observed in the total number of CFCs between the irradiated HSCs in each incubation time.

Furthermore, we evaluated the effect of X-irradiation on intracellular ROS, mitochondrial superoxide, and mitochondrial contents of the $CD34^+$ HSCs. Intracellular ROS in non-irradiated HSCs increased and reached a maximum level on Day 1 (figure 3A). In the case of 4 Gy irradiated HSCs, significant differences were observed compared with control cells at Day 1 and 3, and reaching a peak on Day 3 (approximately 4-fold increase from initial input). Mitochondrial

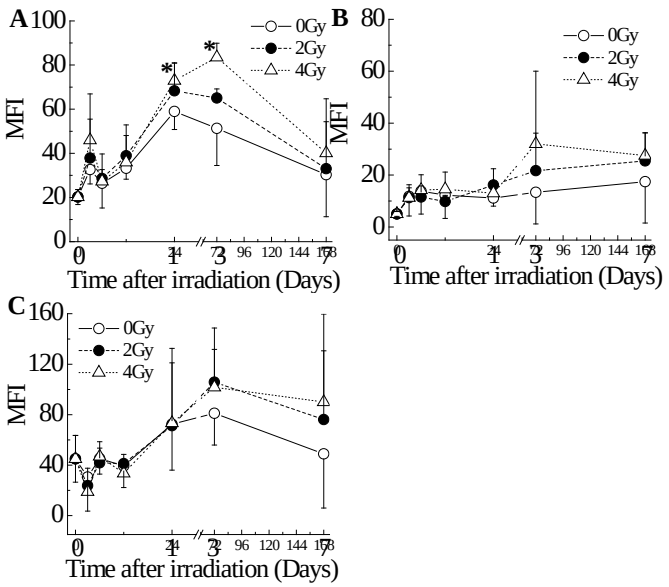

Figure 3. Effect of X-irradiation on intracellular ROS, mitochondrial superoxide, and mitochondrial contents of $CD34^+$ HSCs. *P < .05

superoxide levels in the non-irradiated HSCs were no significant difference from Day 0 to Day 7 (figure 3B). In the case of 4 Gy irradiation, it was reached a peak on Day 3 (approximately 7-fold increase from initial input) but no significant difference was observed compared with control HSCs. In addition, the mitochondrial contents in the control cultures reached a maximum level on Day 3 (figure 3C). In the case of X-irradiation, no significant difference was observed compared with control cells, reaching a peak on Day 3 (approximately 2.5-fold increase from initial input).

Generally, HSCs enter a predominantly quiescent state in the niche, which less susceptible to DNA damage caused by oxidative damage. HSC differentiation and proliferation are controlled by cytokines and ROS [2, 4, 13]. Hematopoietic cytokines induced intracellular ROS production, leading to activation of various signaling pathways as well as transactivation of cytokine receptors, and cell cycle progression [3, 14, 15]. It is known that a mild increase in intracellular ROS inhibits also the phosphatase activity of phosphatase and tensin homologue, and promotes cell survival and proliferation [2]. The present study confirmed that non-irradiated HSCs were promoted the cell proliferation (figure 2A) and the differentiation into myeloid progenitor cells (figure 2C), and induced late progressive increase in intracellular ROS (figure 3A). Conversely, we demonstrated that X-irradiated HSCs were inhibited the cell proliferation and dramatically reduced the clonogenic potential, and occurred intracellular ROS overproduction. Yahata et al. have reported that ROS levels within $CD34^+$ HSCs by treatment with a glutathione synthetics inhibitor BSO aggravated the extent of DNA damage, and then activated the expression of cell-cycle inhibitors, leading to the premature senescence among HSPCs, and ultimately to the loss of stem cell function [6].

Tuberous sclerosis complex-mammalian target of rapamycin, which is the downstream of PI3K/Akt signaling pathway, maintains quiescence and function of HSCs by repressing mitochondrial biogenesis and ROS production to reduce oxidative risk [8, 16]. That is to say, up-regulation of mitochondrial biogenesis in stem cells parallels loss of pluripotency [17]. Indeed, the mitochondrial contents in non-irradiated HSCs was gradually increasing (figure 3C) and then the clonogenic potential was decreased on Day 7 (figure 2B), suggesting the depletion or loss of functions of HSCs by mitochondrial biogenesis. However, neither the mitochondrial superoxide nor contents in X-irradiated HSCs were statistically significant higher (figure 3B, C). Yamamori et al. have recently reported that ionizing radiation to tumor cells induces mitochondrial ROS production accompanied by mitochondrial content [18]. In addition, Wang et al. have demonstrated that exposure of mice to total body irradiation induces persistent oxidative stress selectively in HSCs in part via up-regulation of NADPH oxidase 4 [19]. It is perhaps a difference between tumor cells and normal cells, and considered that radiation-induced increase in ROS in human HSCs may be attributed to ROS production from NOX family but not mitochondria.

In conclusion, we suggested that increase in intracellular ROS production by X-irradiation to HSCs aggravated the extent of secondary DNA oxidative damage, leading to the premature senescence and the loss of stem cell function, but involvement of mitochondria is still unknown. Since $CD34^+$ HSCs we used in this study are heterogeneous, it is necessary to analysis considering the relevance of its differentiation antigens, mitochondrial ROS and own genes in detail.

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Combined pharmaceutical drugs approved in Japan protect mice against lethal ionizing radiation.

Tokuhisa Hirouchi[1], Kouichi Ito[2], Manabu Nakano[2], Satoru Monzen[3], Hironori Yoshino[3], Mitsuru Chiba[2], Masaharu Hazawa[3], Akira Nakano[2], Junya Ishikawa[3], Masaru Yamaguchi[3], Kimio Tanaka[1], and Ikuo Kashiwakura[3*]

[1] Department of Radiology, Institute for Environmental Sciences, Kamikita-gun, Japan
[2] Department of Biomedical Sciences,
Hirosaki University Graduate School of Health Sciences, Hirosaki, Japan
[3] Department of Radiological Life Sciences,
Hirosaki University Graduate School of Health Sciences, Hirosaki, Japan

Abstract. One of the first priorities in managing exposure to lethal ionizing radiation is to reduce mortality and recover radiation damage to tissues that rapidly undergo renewal, such as the hematopoietic system. Medication is appropriate for mass casualties who require prompt treatment. However, almost drugs/growth factors that have proven useful in previously are not available in Japan for pharmaceutical applications. Prompt responses are required during emergencies and standby responses can be problematic; thus appropriate countermeasures based on pharmaceutical drugs that are approved in Japan are required. The aim of this study is to establish an appropriate therapeutic protocol for victims exposed to lethal radiation. Eight-week-old female C57BL/6J Jcl mice were exposed to 7 Gy of total body irradiation, and then recombinant human erythropoietin (EPO), granulocyte-colony stimulating factor (G-CSF), romiplostim and nandrolone decanoate (ND) were administered shortly thereafter. All irradiated mice without medication dead by 30 days. About 75% of those administered with combination 5 (ND for 2 days; G-CSF + EPO + romiplostim for 5 days) survived for 30 days. However, none of the measured parameters significantly differed among the surviving mice. These results indicated that an appropriate combination of drugs approved in Japan can rescue victims exposed to lethal radiation.

Key Words: hematopoietic system, combined pharmaceutical drugs approved in Japan, victims exposed to lethal radiation, acute radiation syndrome

Introduction

Treatment of nuclear and/or radiological accidents that cause mass-casualty scenarios have been increasing [1]. This type of accidents could result in the exposure of thousands of people, resulting in death and/or severe illness from acute radiation syndrome (ARS) [2]. One of the first priorities in managing exposure to lethal ionizing radiation is to reduce mortality and recover radiation damage to issues that rapidly undergo renewal, such as the hematopoietic system, intestinal mucosa and skin [3-5]. Medications can be applied as primary care because hematopoietic stem cell transplantation is not appropriate for mass casualties who require prompt treatment. Therefore, several therapeutic strategies in radiation casualties have been developed [2, 4-7]. However, almost all of the drugs/growth factors that have proven useful during radiation accidents are not available in Japan for pharmaceutical applications [8]. Prompt responses are required during emergencies and standby responses can be problematic; thus appropriate countermeasures based on

[*] Corresponding to: Ikuo Kashiwakura, Professor, Hirosaki University, 66-1 Hon-cho, Hirosaki, 036-8560, Japan.
E-mail: ikashi@cc.hirosaki-u.ac.jp

pharmaceutical drugs that are approved in Japan are required. The present study assesses the effects of approved drug combinations in a mouse model to establish an appropriate therapeutic protocol for victims exposed to lethal radiation.

Materials and Methods

Reagents, Animals and Radiation Exposure

Recombinant human granulocyte-colony stimulating factor (G-CSF) was purchased from Chugai Pharmaceutical Co., Ltd. (Tokyo, Japan). Recombinant human erythropoietin (EPO) and recombinant human romiplostim were purchased from Kyowa Hakko Kirin Co., Ltd. (Tokyo, Japan). Nandrolone decanoate (ND) was purchased from Fuji Chemicals Industrial Co., Ltd. (Tokyo, Japan). Each drug was administered to mice at a concentration of 100 μg/kg, 100 U/kg, 1 or 50μg/kg, and 50μg/kg, respectively.

Eight-week-old female C57BL/6J Jcl mice were exposed to 7 Gy of ^{137}Cs γ-rays at dose rate of 0.9 Gy/min and were housed in a specific pathogen-free animal room under 12 h light/dark cycles.

Treatments and Follow-up

After irradiation, each mice was immediately administered drug combination; (1) 1 day of ND, 3 days of G-CSF and EPO, (2) 2 days of ND, 5 days of G-CSF and EPO, (3) 5 days of G-CSF and EPO, (4) 2 days of ND, 5 days of G-CSF, EPO and 1μg/kg romiplostim, (5) 2 days of ND, 5 days of G-CSF, EPO and 50μg/kg romiplostim.

Mice were monitored daily for survival during 30 days. After 30 days, surviving mice were weighted, and were killed by cervical dislocation. Peripheral blood cells were analyzed by using Celltacα (NIHON KOHDEN, Tokyo, Japan). Femoral bone marrow was harvested and the total mononuclear cells were counted by using Burker-Türk solution (Nacalai tesque, Kyoto, Japan), and were analyzed several fractions by using FACSAria (Becton Dickinson, California, USA). Clonogenic potential of mononuclear cells was evaluated by using MethoCult M3434 (StemCell Technology, Tokyo, Japan).

Results and Discussion

Survival at day 30

Approximately 10% of irradiated control mice without medication survived for 21 days, and all mice were dead by 30 days. On the other hands, about 62.5% of mice that were administered with combination 3 (5 days of G-CSF + EPO) survived for 30 days (Figure 1A), and also 75% of mice that were administered with combination 5 (ND for 2 days; G-CSF + EPO + romiplostim for 5 days) survived for 30 days (Figure 1B). These results suggested possibility that administration of ND and/or romiplostim were important for survival of mice in this study. However, survival of mice that were administered drug combination 4 was only 28.6%. Consequently, concentration of romiplostim might be most effective for survival of mice.

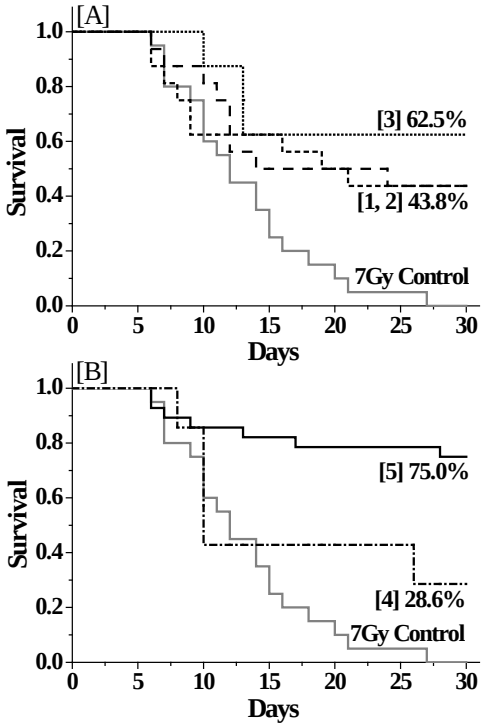


Figure 1: Survival at day 30.
Approximately 10% of irradiated control mice without medication survived for 21 days, and all mice were dead by 30 days. In contrast, the mice that were administered with drug combination 5, about 75% survived for 30 days.

Composition of Peripheral Blood Cells

Peripheral blood cells were dramatically decreased by exposure to lethal radiation, especially white blood cells, in survival mice at day 30. This result consists with previous radiation accident [8]. In which, there are no significant differences between each drug combination (Figure 2).

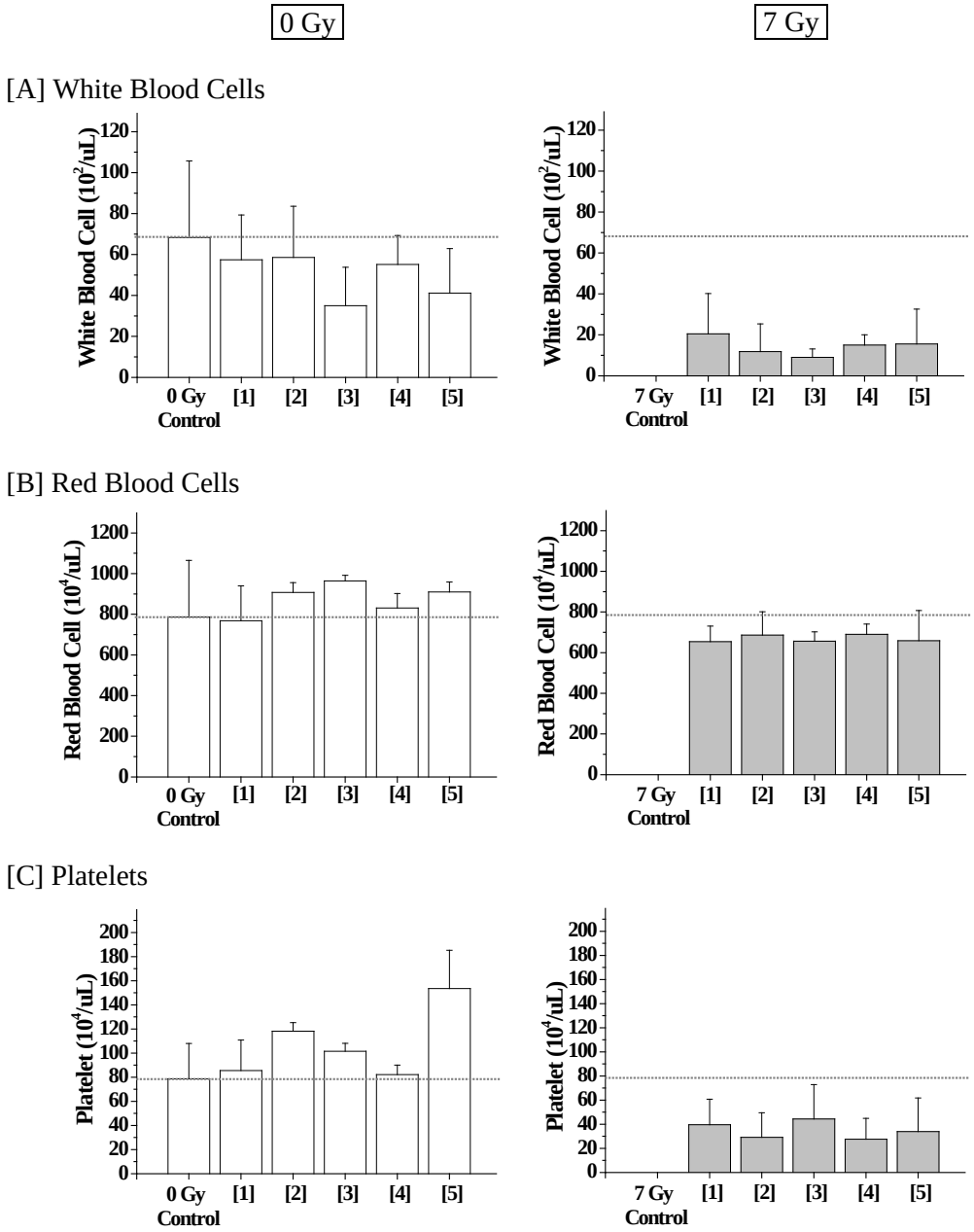


Figure 2 Composition of Peripheral Blood Cells

[A-C] Peripheral blood cells were sampled from fundus and were analyzed by using Celltacα. Peripheral blood cells were dramatically decreased by exposure to lethal radiation, especially white blood cells, in survival mice at day 30. In which, there are no significant differences between each drug combination.

These results suggested possibility that exposure to ionizing radiation induces decline of the immunity system caused by hematopoietic failure. Moreover, because infection that was caused by weakened immunity results in deadly damage, it's important object for treatment to reconstruction of the immunity system.

Composition of Bone Marrow Cells

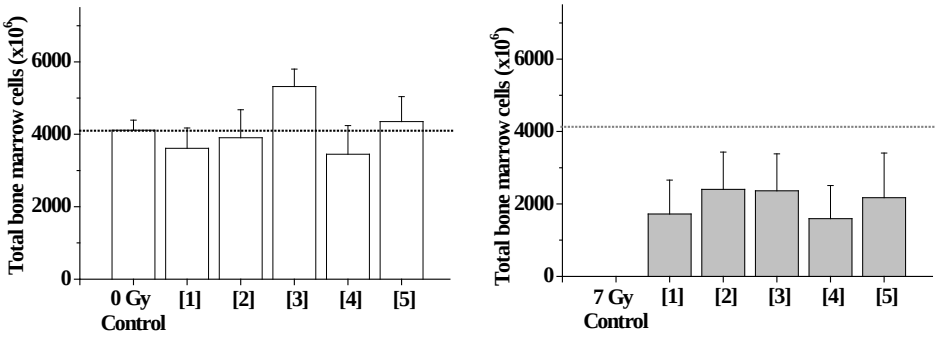
Ionizing radiation induced severe bone marrow suppression in survival mice at day 30 (Figure 3A). This severe bone marrow suppression might be result in dramatically decreasing of white blood cells exposed to lethal radiation.

Next, we investigated several immature cell fractions (i.e. $Kit^+Sca\text{-}1^+Lin^-$ cells suggest hematopoietic stem cells, $Kit^+Sca\text{-}1^+Lin^+$ cells suggest hematopoietic progenitor cells,

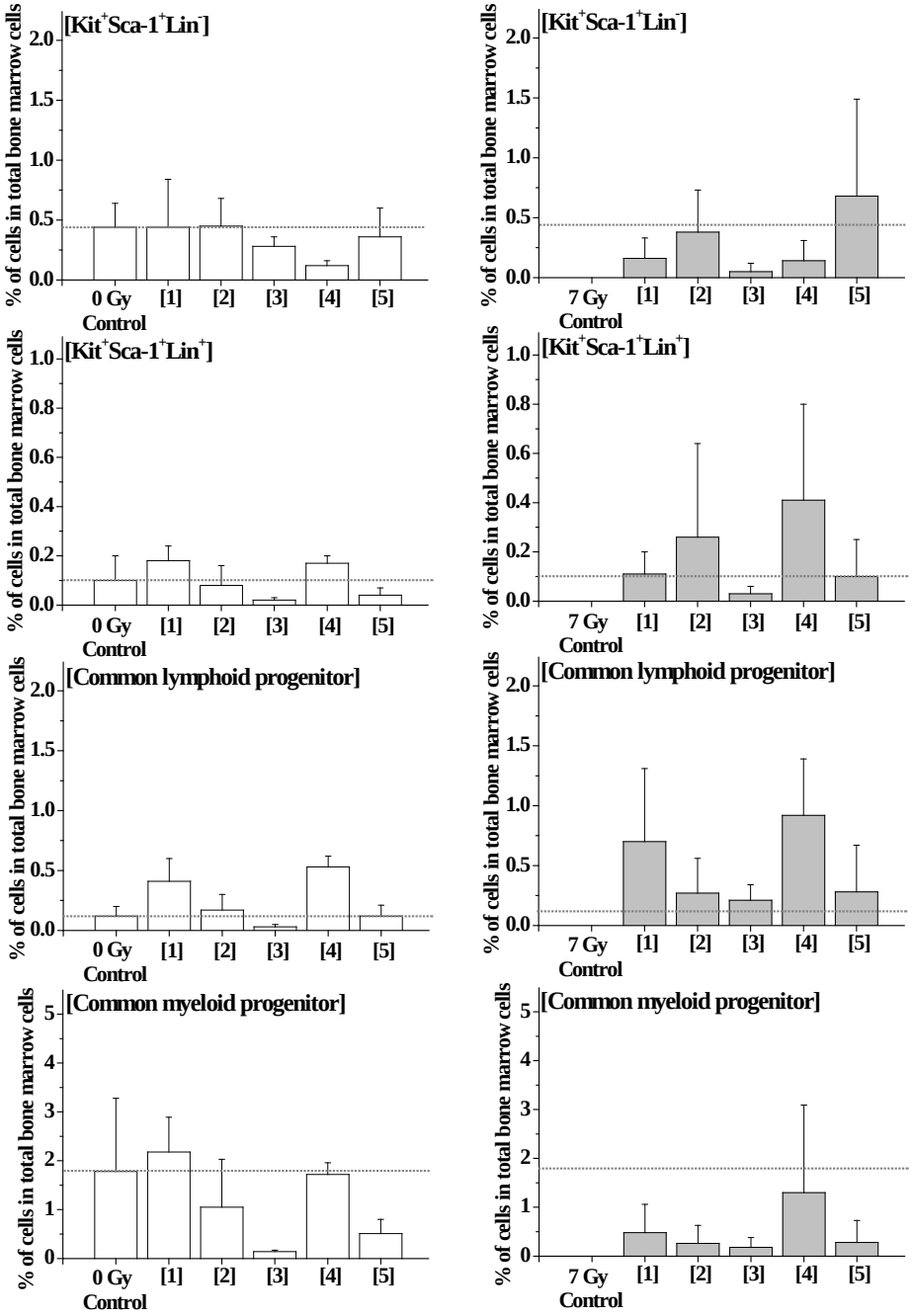
0 Gy

7 Gy

[A] Number of total bone marrow cells



[B] Fraction of bone marrow cells



[C] Colony forming cells

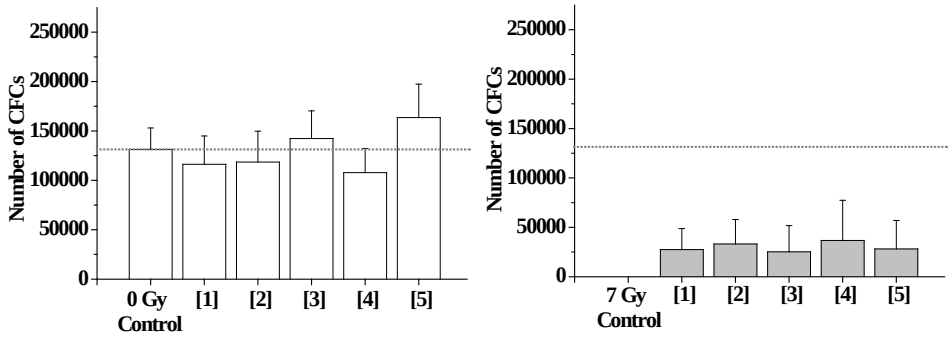


Figure 3 Composition of Bone Marrow Cells

[A] Mononuclear cells were sampled from femoral bone marrow and were counted using Burker-Turk solution. [B] Mononuclear cells were stained combination of several fluorescence labelled antibodies and were analyzed several fractions by using FACSAria. [C] Clonogenic potential of mononuclear cells was evaluated by using methylcellulose method. Ionizing radiation induced severe bone marrow suppression in survival mice at day 30. In which, there are no significant differences between each drug combination.

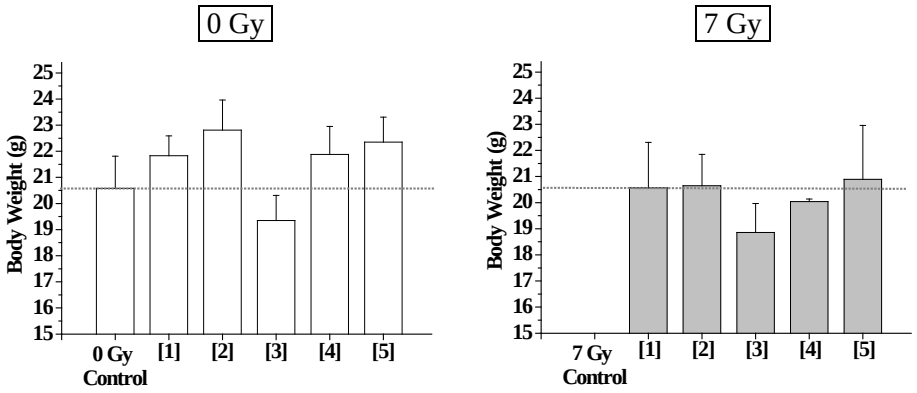


Figure 4 Body weight at day 30

Each mouse that survived at day 30 was measured body weight. However, there are no significant differences between each drug combination.

Common lymphoid progenitors, and Common myeloid progenitors) using fluorescence labelled specific antibody (Figure 3B). In which, there are no significant differences between each drug combination. Also, no significant differences were observed in number of colony-forming cells (CFC), including burst-forming unit-erythroids (BFU-E), colony-forming unit-granulocytes/macrophages (CFU-GM), and colony-forming unit-granulocytes/ erythroids/macrophages/megakaryocytes (CFU-Mix) (Figure 3C). These results suggested that exposure to ionizing radiation induced severe bone marrow suppression and decreasing clonogenic potential. This phenomenon resulted in decreasing of peripheral blood cells and caused declining of immunity system. However, these mice were survived at day 30, suggesting hematopoietic system might be plays a minimal role for survival. Thus, these damages to hematopoietic system by irradiation might not be critical for death of mice in this study.

Body Weight at day 30

To evaluate the effects of ionizing radiation on the growth of the irradiated mice, we measured each mouse of body weight (Figure 4). As shown in drug combination 1, 2, 4, and 5, administration of ND might be work to increase the body weight. However, there are no significant differences between each drug combinations.

Conclusion

Our results indicate that an appropriate combination of drugs that are approved in Japan can rescue victims exposed to lethal radiation.

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Morphological study of the digestive, nervous and sensory organs, bone marrow, and lymph node in X-irradiation mice

Shoji Chiba[1], Yuhei Higuchi[2], Tomoya Nakai[3], Ibuki Higashidate[4], Hitomi Sato[5], Syuji Fukushima[6], Yuhei Nakamura[6], Koichi Itoh[7], Kyoko Itoh[7], Manabu Nakano[7], Haruhiko Yoshioka[1]

1 Department of Pathologic Analysis, Division of Medical Life Sciences, Hirosaki University Graduate School of Health Sciences

2 Yamagata University Hospital , 3 Nakamura Memorial Hospital (Sapporo)

4 Iwate Prefectural Central Hospital , 5 Obihiro-Kosei General Hospital

6 Students in Department of Radiological Technology, Hirosaki University School of Health Sciences

7 Department of Biomedical Sciences, Division of Medical Life Sciences, Hirosaki University Graduate School of Health Sciences

Abstract. In order to morphologically confirm acute radiation damage and organ radiosensitivity in mice, we performed whole body X-ray irradiation at single doses of 0 (control), 2, 4, 8, and 10 Gy. We did not observe a constant change in the lengths of the intestinal and gastric glands and intestinal villi as well as in the features of Paneth cells and the various cells in the gastric gland. No differences were found in the morphological features of the various tissues of the nervous system and sensory organs, some organs in the neck, and abdominal aorta between non-exposed and exposed mice. However, X-irradiation caused an obvious decrease in lymphocyte number in the submandibular lymph node, in the number of progenitor cells for leukocytes and lymphocytes, and in the number of megakaryocytes in the bone marrow. Lymphocyte number in the lymph node decreased at 4 Gy. These decreases were obvious in the lymph node and bone marrow at 8 and 10 Gy.

Key Words: acute X-radiation damage, visceral organs, nervous system, sensory organs, lymph node, bone marrow, morphology, mouse

Introduction

Textbooks on radiation describe acute injuries to tissues and cells when organs are exposed to X-irradiation [1-3]. The present study was conducted to confirm previously documented morphological damage from X-irradiation of the digestive system (from the esophagus to the sigmoid colon), nervous system (brain, spinal cord, and sciatic nerve), sensory organs (eyeball and tongue), submandibular and thyroid glands, trachea, abdominal aorta, bone marrow, and submandibular lymph node.

Materials and Methods

The whole bodies of 7-week-old ICR mice (2 males and 2 females; 2 exposed to each dose in the A and C series) were exposed to 2, 4, 8, and 10 Gy of X-irradiation at a dose rate of

0.133 Gy/min using an X-ray generator (Hitachi MBR-1505R2).

Ten days after X-irradiation, the mice and their organs were stored in 10% formalin. In 2010, we prepared the digestive organs (except for the esophagus) and cut 5-μm HE sections [4]. The intestinal villi and the longitudinal axis of each length of both the intestinal and gastric glands were comparatively measured on photomicrographs using slide calibers. Statistically significant differences between the lengths exposed to both 0 and 10 Gy were determined with the two-sample *t*-test.

In 2011, we removed the nervous system organs, sensory organs, submandibular and thyroid glands, trachea, esophagus, and abdominal aorta from the mice and prepared 5-μm HE sections [5]. Recently, we prepared 5-μm HE sections of the submandibular lymph node and also prepared 10-μm HE sections of the thoracic vertebra with bone marrow following Plank and Rychlo's method of decalcification [6].

In the A and C series of this study, we obtained digital photographs of the organs to certify bleeding around the organs and examined HE sections under a light microscope to detect morphological changes in the tissues.

Results

During organ removal in 2011-2012, we observed bleeding in the brain due to dislocation of the cervical vertebrae we did not find bleeding around the organs as a result of the X-irradiation (Figs. 1a-d).

Although the lengths of the intestinal glands and villi exposed at 10 Gy often were longer or shorter compared to those exposed to 0 Gy, a statistically significant change in the lengths of intestinal glands and villi was not found. Paneth cells and their granules were similar in appearance in mice exposed to both 0 and 10 Gy. Regarding the components of the gastric gland, the mucous cells in the gastric pit decreased in number, the length of the pit was shorter, and the parietal cells swelled and broke as the cavity of the gastric gland enlarged.

Regarding the nervous system, cellular features of both the cerebellar cortex and hippocampus, which each consist of three layers, were similar between mice exposed to both 0 and 10 Gy (Figs. 2a-3b). The sciatic nerve is composed of many axons ensheathed by Schwann cells. The upper thoracic vertebral region of the spinal cord consists of anterior and posterior horns and their cells. The features of these structures were the same in mice exposed to both 0 and 10 Gy.

Regarding the eyeball, the conjunctival fornix consists of stratified squamous epithelium of 2-3 cells. The cornea consists of stratified squamous epithelium of 3-4 cells, the substantia propria, and a simple squamous epithelium. The features of these structures and the cellular distributions were similar in mice exposed to both 0 and 10 Gy (Figs. 4a-5b).

Regarding the tongue, the dorsum and inferior surface were enveloped with a keratinized stratified squamous epithelium of about 10 cells. Their histological features were similar in mice exposed to both 0 and 10 Gy (Figs. 6a-7b).

In the cervical region, the histological appearance of the submandibular gland was very different between male and female mice, with many intercalated ducts in males. However, features of the duct and acinus in each of the sexes were similar in mice exposed to both 0 and 10 Gy.

The thyroid gland consists of many follicles formed with a simple cuboidal epithelium, parafollicular cells, and colloid in the follicles. The trachea consists of pseudostratified columnar epithelium, the serous and mucous cells of the tracheal gland, and tracheal cartilage. The esophagus consists of keratinized stratified squamous epithelium of 5-10 cells and circular and longitudinal striated muscles. The histological features of the thyroid gland, trachea, and esophagus were similar in mice exposed to both 0 and 10 Gy (Figs. 8a-10b).

The abdominal aorta consists of the endothelium, elastic fibers, and smooth muscles, and these features were the same in

mice exposed to both 0 and 10 Gy (Figs. 11a, b).

In the submandibular lymph node, leukocytes first decreased with 4 Gy, and most had disappeared with both 8 and 10 Gy, while reticular cells were surviving. It was difficult to distinguish lymphatic nodules from the medulla in the node. Bleeding was seen in the marginal sinus and medulla with 4, 8, and 10 Gy (Figs. 12a-d).

In the bone marrow of the body of the middle thoracic vertebra, many progenitor cells for leukocytes and lymphocytes, as well as megakaryocytes, had completely disappeared in the medullary cavities following exposure to both 8 and 10 Gy. Only erythroblasts and their derivatives had survived along with the reticular cells. With 10 Gy, the erythroblasts and their derivatives decreased in number by half (Figs. 13a-d).

Discussion

Because we did not observe a constant change in the lengths of the intestinal and gastric glands and intestinal villi, we removed the constant sites of the intestinal canals for comparison. Regarding Paneth cells and the various cells in the gastric gland, we must improve our techniques for preparation for sectioning, HE staining, and others.

In general, no differences were found in the morphological features of the various tissues of the nervous system and sensory organs, and some tissues of the organs in the neck between non-exposed and exposed mice [1-3].

However, X-irradiation caused an obvious decrease in lymphocyte number in the submandibular lymph node, in the number of progenitor cells for leukocytes and lymphocytes, and in the number of megakaryocytes exclusive of erythroblasts, their derivatives, and reticular cells in the bone marrow.

Lymphocytes in lymph nodes and many progenitor cells in bone marrow were extremely sensitive to X-irradiation [1, 2], indicating the equivalent value of the radiosensitivity of the spleen, thymus, and lymphoid nodules in the intestines [4, 5].

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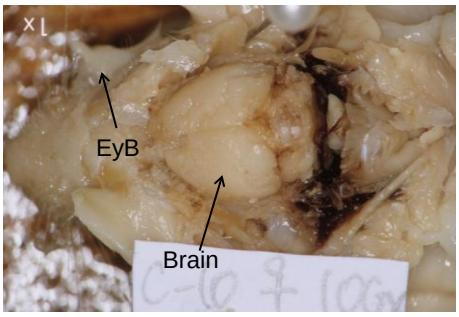
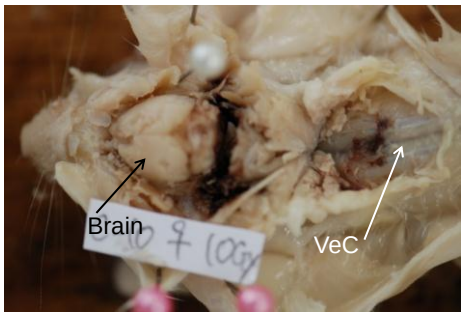
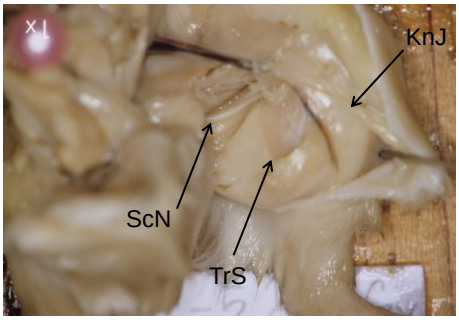


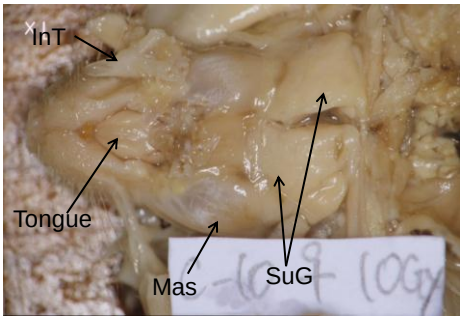
1a. Eyeball and brain in C (Female at 10Gy)



1b. Spinal cord in C (Female at 10Gy)

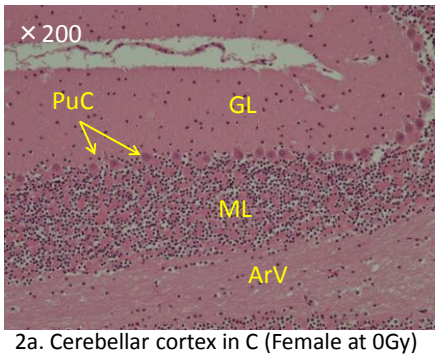


1c. Sciatic nerve in C (Male at 10Gy)

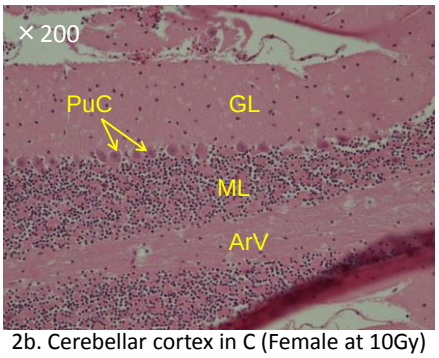


1d. Tongue and gland in C (Female at 10Gy)

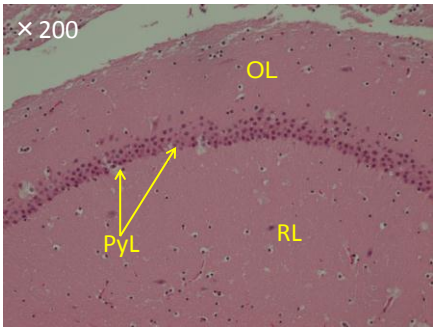
Figs. 1a-d. Dissection of the eyeball (EyB), brain, spinal cord, sciatic nerve (ScN), tongue, and submandibular gland (SuG) in mice after removing the skin, muscles, skull, incisor tooth (InT), and vertebral column (VeC). KnJ, knee joint; Mas, masseter; TrS, triceps surae



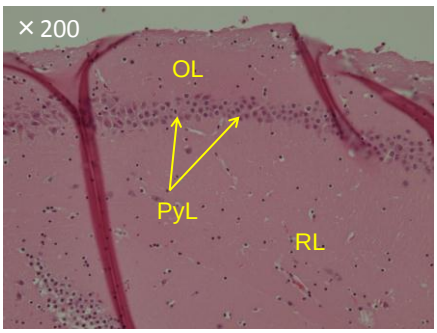
2a. Cerebellar cortex in C (Female at 0Gy)



2b. Cerebellar cortex in C (Female at 10Gy)

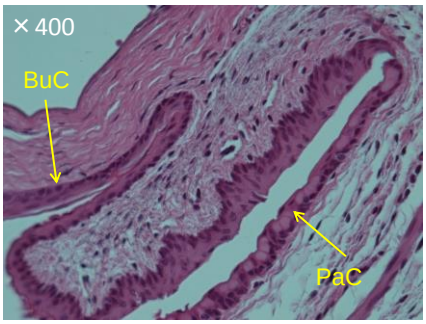


3a. Hippocampus in A (Male at 0Gy)

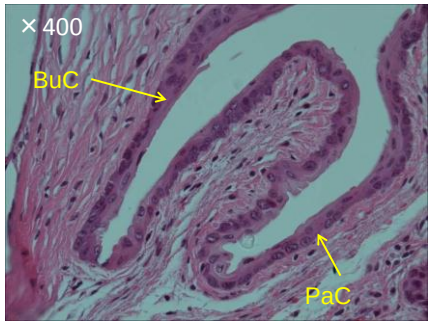


3b. Hippocampus in A (Male at 10Gy)

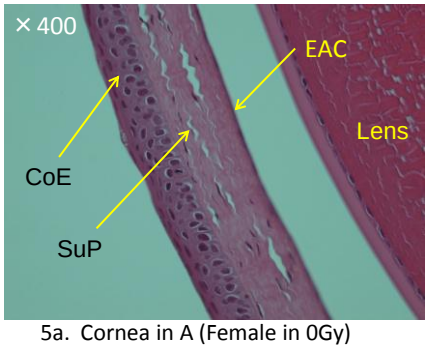
Figs. 2a-3b. Internal features of the cerebellar cortex and hippocampus. H&E staining. Magnification 200x. ArV, arbor vitae; GL, granular layer; ML, molecular layer; OL, oriens layer; PuC, Purkinje cell, PyL, pyramidal layer; RL, radiate layer



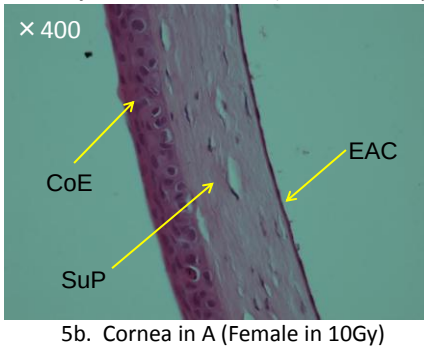
4a. Conjunctival fornix in A (Female in 0Gy)



4b. Conjunctival fornix in A (Female in 10Gy)

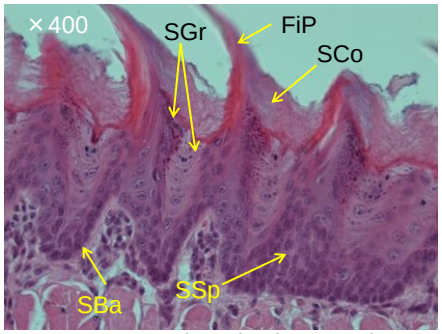


5a. Cornea in A (Female in 0Gy)

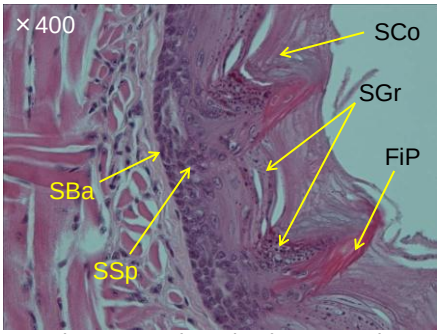


5b. Cornea in A (Female in 10Gy)

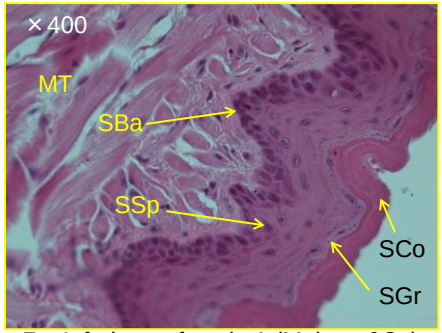
Figs. 4a-5b. Sections of the superior conjunctival fornix and cornea. H&E staining. Magnification 400x. BuC, bulbar conjunctiva; CoE, corneal epithelium; EAC, endothelium of anterior chamber; PaC, palpebral conjunctiva; SuP, substantia propria



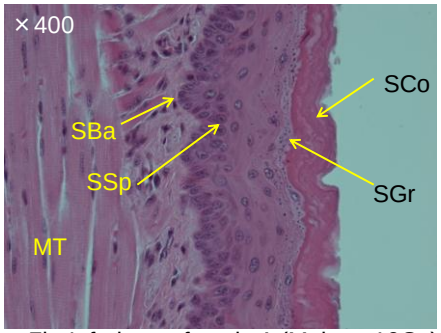
6a. Dorsum in C (Male at 0Gy)



6b. Dorsum in C (Male at 10Gy)

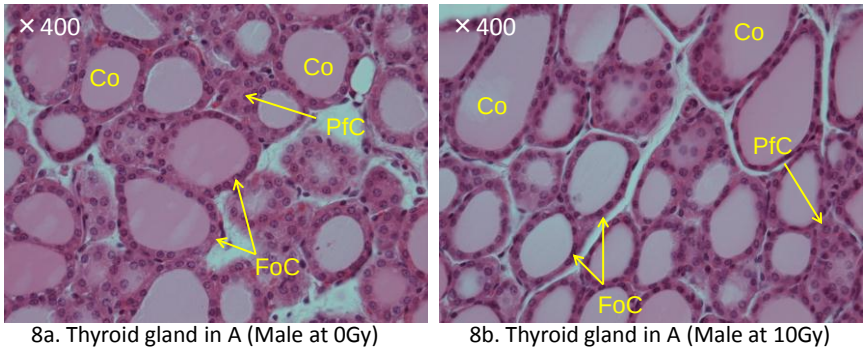


7a. Inferior surface in A (Male at 0Gy)

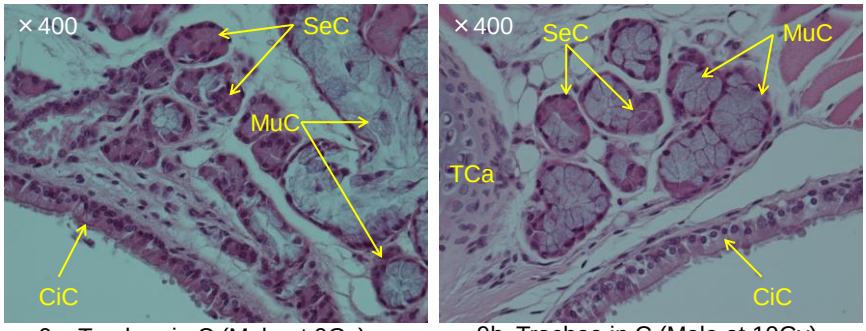


7b. Inferior surface in A (Male at 10Gy)

Figs. 6a-7b. Dorsum and inferior surface of the tongue. H&E staining. Magnification 400x. Fip, filiform papillae; MT, muscles of tongue; SBa, stratum basale; SCo, stratum corneum; SGr, stratum granulosum; SSp, stratum spinosum

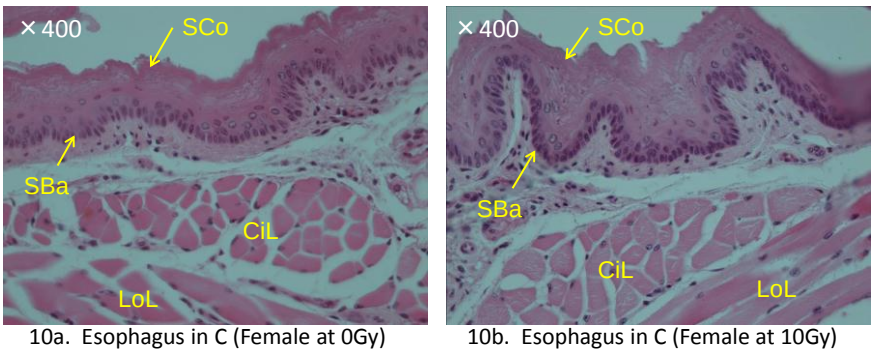


8a. Thyroid gland in A (Male at 0Gy) 8b. Thyroid gland in A (Male at 10Gy)

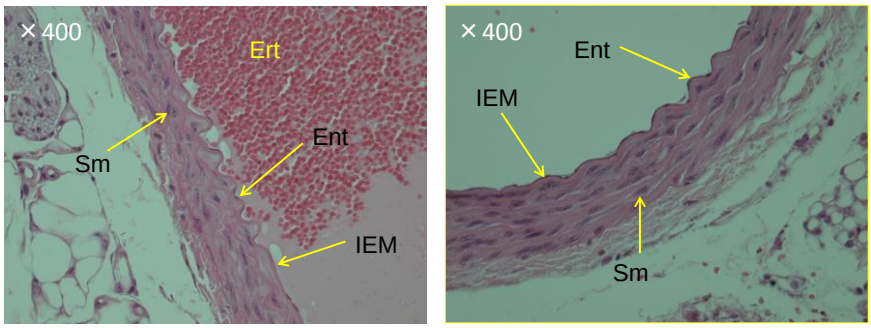


9a. Trachea in C (Male at 0Gy) 9b. Trachea in C (Male at 10Gy)

Figs. 8a-9b. Sections of the thyroid gland and trachea. H&E staining. Magnification 400x. CiC, ciliated cell; Co, colloid; FoC, follicular cell; MuC, mucous cell; PfC, parafollicular cell; SeC, serous cell; Tca, tracheal cartilage

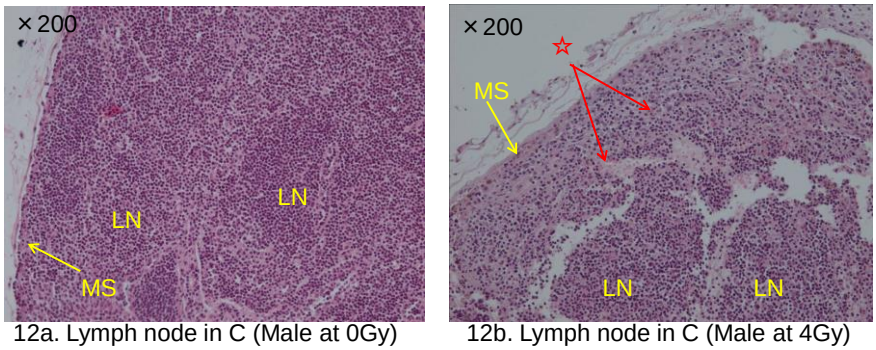


10a. Esophagus in C (Female at 0Gy) 10b. Esophagus in C (Female at 10Gy)



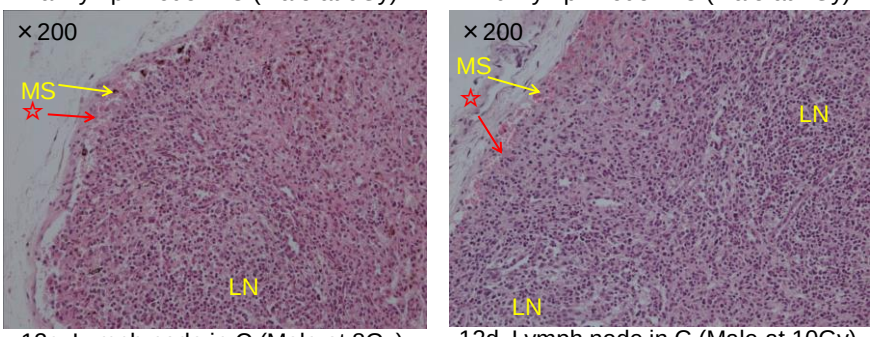
11a. Abdominal aorta in C (Male at 0Gy) 11b. Abdominal aorta in C (Male at 10Gy)

Figs. 10a-11b. Photomicrographs of the esophagus and abdominal aorta. H&E staining. Magnification 400x. CiL, circularly oriented layer; Ent, endothelium; Ert, erythrocyte; IEM, internal elastic membrane; LoL, longitudinally oriented layer; Sba, stratum basale; SCo, stratum corneum; Sm, smooth muscle



12a. Lymph node in C (Male at 0Gy)

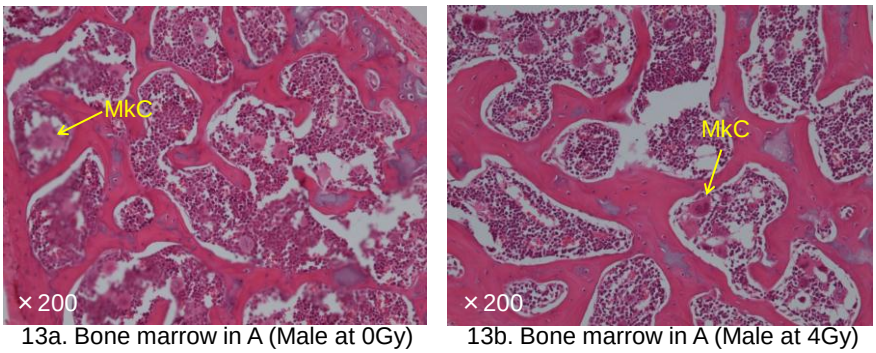
12b. Lymph node in C (Male at 4Gy)



12c. Lymph node in C (Male at 8Gy)

12d. Lymph node in C (Male at 10Gy)

Figs. 12a-d. Photomicrographs of the submandibular lymph nodes. H&E staining. Magnification 200x. LN, lymphatic nodule; MS, marginal sinus; ☆, bleeding



13a. Bone marrow in A (Male at 0Gy)

13b. Bone marrow in A (Male at 4Gy)

13c. Bone marrow in A (Male at 8Gy)

13d. Bone marrow in A (Male at 10Gy)

Figs. 13a-d. Photomicrographs of bone marrow at the middle level of the thoracic vertebra. H&E staining. Magnification 200x. ErB, erythroblast; MkC, megakaryocyte

Alteration of extracellular matrix components by X-ray irradiation in rat bone

Komei Tanaka[1], Yurie Kudo[2], Takashi Ishikawa[1], Kyoko Nakano[1], Mitsuru Chiba[1], Naoki Nanashima[1], Manabu Nakano[1], Koichi Ito[1], and Toshiya Nakamura[1]*

[1]Department of Biomedical Sciences, Division of Medical Life Sciences, Hirosaki University Graduate School of Health Sciences,
[2]Department of Medical Technology, Hirosaki University School of Health Sciences, 66-1 Hon-cho, Hirosaki 036-8564, Japan

Abstract. Cancer patients who receive radiotherapy are known to show an increased risk of osteoporosis as a side effect several months later. Elucidation of the mechanisms underlying this effect is thus important. The present study examined the effects of X-irradiation on extracellular matrix components in cultured fetal rat osteoblasts and rat femora. Cells cultured in serum-free medium were X-irradiated at 2 or 5 Gy. After 48-h cultivation, hyaluronan levels in the medium were determined by ELISA-like assay. Gene expressions of matrix metalloproteinase (MMP)-2, MMP-13, type-I collagen and decorin were analyzed by real-time polymerase chain reaction. The activity and gene expression of MMP-13 were increased, while gene expressions of type-I collagen and decorin were decreased. Synthesis of hyaluronan and gene expression of MMP-2 in cells were unaffected by X-irradiation. Sprague-Dawley rats were then X-irradiated at 2 or 5 Gy. After 1-3 months, the rats were sacrificed and the femora were extracted. Glycosaminoglycan fractions were purified from the femora and the uronic acid content determined. The fraction was examined by glycosaminoglycan chain size and unsaturated disaccharide unit analysis. Uronic acid content was seen to be decreased, but chain size was unaffected. The main unsaturated disaccharide unit of the glycosaminoglycan was ΔDi-4S, indicating chondroitin/dermatan sulfate as the main glycosaminoglycan in the bone, and no structural alteration of the glycosaminoglycan was apparent after X-irradiation. The core protein and dermatan sulfate chain of decorin have been reported to bind with type-I collagen and to type-IX collagen, which binds to type-I collagen, respectively. The present results thus suggest that a decrease in both decorin and type I-collagen levels after X-irradiation in bone may contribute to a loss of mechanical strength in bone tissue.

Key Words: Osteoblasts, femurs, X-ray irradiation, extracellular matrix, osteoporosis, decorin, glycosaminoglycan

Introduction

It is known that cancer patients who receive radiotherapy tend to suffer from osteoporosis as a side effect several months later[1, 2]. The improved survivorship of cancer patients who receive radiotherapy increases the importance of understanding the causal mechanisms and long-term effects of radiation-induced bone loss. The incidence of hip fractures is significantly increased following targeted radiotherapy for cancer. This decline in bone health can have a severe impact on the patient's functional capabilities. On the other hand, astronauts on the International Space Station have reported 0.8-1.5% bone loss per month in the vertebrae and femora [3, 4]. During exploratory missions, astronauts face not only microgravity but also radiation from cosmic and solar sources [5, 6]. Therefore,

* Corresponding to: Toshiya Nakamura, Ph.D. &Professor, Hirosaki University Graduate School of Health Sciences, 66-1 Hon-cho, Hirosaki 036-8564, Japan.
E-mail: toshiyan@cc.hirosaki-u.ac.jp

elucidation of the mechanism of radiation-induced osteoporosis is an important issue.

In this study, the effect of X-irradiation on extracellular matrix components was investigated using cultured rat fetal osteoblasts and rat femurs.

2. Materials and methods

2.1. X-irradiation of osteoblasts and rats

Osteoblasts were then X-irradiated at 2 or 5 Gy (150 kVp, 20 mA; 0.5-mm aluminum and 0.1-mm copper filters at a dose rate of approximately 1.0 Gy/min), and culture was continued. After 24 h or 48 h, the conditioned medium was recovered and the cells were collected by trypsin treatment.

Sprague-Dawley rats (SD rats, six weeks, male; CLEA Japan Inc.) were X-irradiated simultaneously under the same conditions, and after 1, 2, and 3 months postexposure were euthanatized. Their femurs were extracted and stripped of any surrounding connective tissues. The cartilages at both ends of the femur were removed and the bone marrow was washed out with phosphate-buffered saline. These femurs were then used for glycosaminoglycan extraction.

2.2. Real-time reverse transcription-polymerase chain reaction (RT-PCR)

Gene expression of matrix metalloproteinase (MMP)-13, MMP-2, type-I collagen, and decorin was measured by real-time PCR using TaqMan probes. PCRs were performed in a StepOnePlus Real-Time PCR system (Applied Biosystems) using 40 cycles of 95^{o}C for 10 min, 95^{o}C for 15 s, and 60^{o}C for 1 min.

2.3. Preparation of the glycosaminoglycan fraction from rat femurs

Rat femurs were crushed using a Micro Smash MS-100R and were decalcified in 0.5 M disodium ethylenediaminetetraacetate (EDTA-Na) for a week, replacing the solution with fresh 0.5 M EDTA-Na on the 3rd day. The decalcified samples were then delipidated in chloroform-methanol (2:1) solution for 24 h with shaking. Decalcified and delipidated samples were digested with actinase. To the supernatant of the digests were added 4 volumes of ethanol saturated with NaCl and centrifuged. The pellet was dissolved in 0.04 M NaCl and treated with 5% cetylpyridinium chloride. The solution was centrifuged and the resulting pellet was dissolved in 2 M $MgCl_2$. To the solution were added 4 volumes of ethanol saturated with NaCl. After centrifugation, the pellet was recovered, dried with absolute ethanol and ether, and used as the glycosaminoglycan fraction.

2.4. Cellulose acetate membrane electrophoresis

Glycosaminoglycan fractions were incubated with chondroitinase ABC (*Proteus vulgaris*), chondroitinase AC-II (*Arthrobacter aurescens*), hyaluronidase (*Streptomyces hyalurolyticus*), and heparitinase (*Flavobacterium heparinum*), respectively, according to the procedures described in the manufacturer's protocol (Seikagaku Biobusiness, Tokyo). The reaction products were electrophoresed on cellulose acetate membrane in 0.1 M formic acid-pyridine buffer (pH 3.0) at 1 mA/cm for 30 min. The glycosaminoglycans on the membrane were then visualized by alcian blue staining.

2.5. High-performance liquid chromatography (HPLC)

Reducing terminals of sugar chains in the glycosaminoglycan fractions were labeled with 2-amino-pyridine. HPLC connected to a fluorescence detector was used. The fluorescence-labeled glycosaminoglycans were analyzed on a Shodex OHpak SB-804 HQ gel-permeation column with 0.2 M NaCl at a flow rate of 1.0 ml/min at 30°C. For detection, the eluates were monitored at excitation and emission wavelengths of 320 and 400 nm, as described previously[10].

For unsaturated disaccharide analysis, the glycosaminoglycan fraction was digested with chondroitinase ABC. The resulting unsaturated disaccharide units were analyzed by HPLC using a YMC-pack Polyamine II column. The column was eluted with a combination of solution A (16 mM NaH_2PO_4) and solution B (1 M NaH_2PO_4) delivered as a linear gradient (0-60 min, solution A 100-53% and solution B 0-47%) at a flow rate of 1.0 ml/min. Unsaturated disaccharides were detected at 232 nm.

2.6. Analytical methods

Uronic acid was determined by the method of Bitter and Muir[11]. Hyaluronan was determined by an ELISA-like assay.

3. Results

3.1. Effect of X-irradiation on extracellular component of cultured rat osteoblasts

Rat osteoblasts were X-irradiated at 2 or 5 Gy. The cells were then cultured for 48 h and the amount of hyaluronan in the medium was determined. As shown in Fig. 1, the synthesis of hyaluronan in cultured osteoblasts was not affected by X- irradiation under the conditions employed (Fig. 1, A). The cells were then X-irradiated at 2 or 5 Gy, and cultured for 24 h. Total RNA were extracted from the cells and the expression of the MMP-13, MMP-2, type-I collagen and decorin genes was analyzed by real-time RT-PCR. It was found that the expression of MMP-13 was dose-dependently increased by X-irradiation (Fig. 1, B), whereas the expression of type-I collagen and decorin was decreased (Fig. 1, C & D).

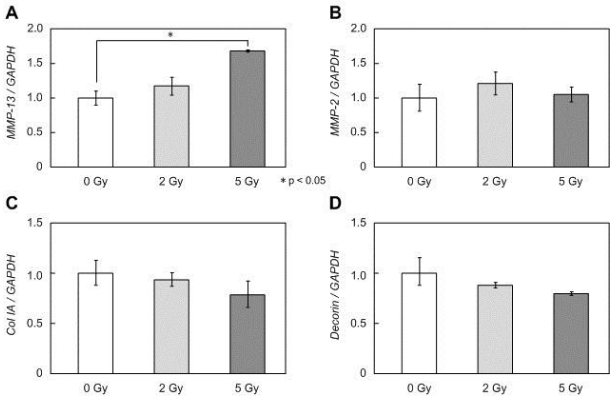


Fig. 1. Effect of X-irradiation on mRNA expression in cultured rat osteoblasts.
A, MMP-13; B, MMP-2; C, type-I collagen; D, decorin.

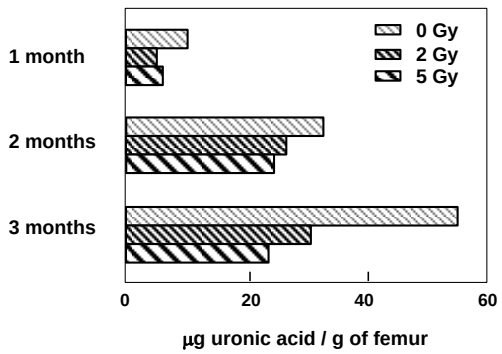


Fig. 2. Effect of X-irradiation on uronic acid content of rat femurs.

3.2. Effect of X-irradiation on glycosaminoglycan in rat femurs

Since expression of the decorin gene was shown to be decreased by X-irradiation in cultured osteoblasts, the effect of X-irradiation on glycosaminoglycans in rat femurs was examined. SD rats were X-irradiated at 2 or 5 Gy and then euthanatized at 1, 2 and 3 months after exposure. Glycosaminoglycan fractions were purified from the femurs, and the uronic acid content of each fraction was determined. As shown in Fig. 2, the uronic acid content per unit bone weight was dose-dependently decreased by X-irradiation. In order to identify the main glycosaminoglycan in the femur, glycosaminoglycan fractions obtained 3 months after exposure to 5 Gy were electrophoresed on cellulose-acetate membranes before and after incubation with mucopolysaccharidases. The results indicated that the main glycosaminoglycan in the femur was dermatan sulfate, irrespective of X-irradiation (data not shown).

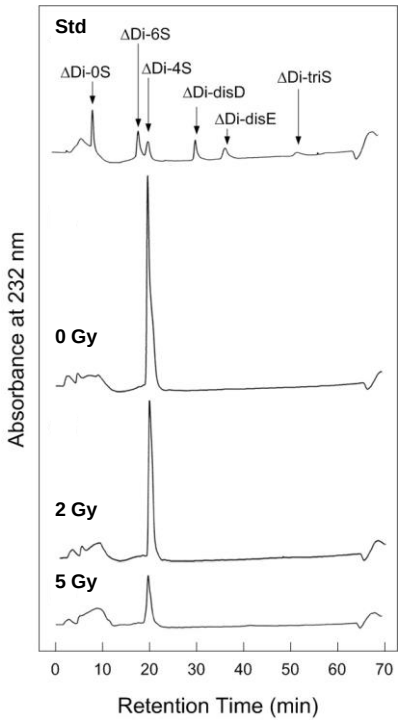


Fig. 3. Analysis of unsaturated disaccharide units by HPLC.

Glycosaminoglycan fractions were purified from femurs of 5 Gy X-irradiated rats at 3 months after exposure. The fractions were digested with chondroitinase ABC and the resulting unsaturated disaccharides were separated by HPLC using a YMC-pack Polyamine II column.

The reducing terminals of glycosaminoglycans obtained 3 months after exposure to 5 Gy were labeled with the fluorescent reagent, 2-amino-pyridine, and subjected to gel-permeation HPLC. As a result, pyridylaminated glycosaminoglycans were eluted at the same retention time, indicating that the glycosaminoglycan chain size was not altered by X-irradiation. Next, in order to investigate the effect of X-irradiation on the sulfation content and sulfation position of glycosaminoglycans, glycosaminoglycan fractions obtained 3 months after exposure to 5 Gy were digested with chondroitinase ABC, and unsaturated disaccharides in the reaction products were analyzed by HPLC. As shown in Fig 3, the main disaccharide unit of glycosaminoglycan in the femur was found to be ΔDi-4S, and this was not altered by X-irradiation (Fig. 3).

4. Discussion

Although radiation exposure is known to induce osteoporosis, details of the mechanism involved have not been clarified. This study analyzed the weakening of bone resulting from exposure to X-irradiation, and its effects on extracellular matrix components. The main extracellular matrix component in bone is type-I collagen, which is known to be synthesized by osteoblasts[12, 13]. Osteoblasts also produce MMP-13, the main collagenase in bone tissue[14, 15], which contributes to reconstruction of bone tissue.

It has been reported that expression of the MMP-13 gene in osteoblasts is increased by gamma-ray irradiation[16]. Our present study also demonstrated an increase in the expression of MMP-13 after X-irradiation (Fig. 1, B). The gene expression of MMP-2, the main gelatinase in bone tissue[17], and the synthesis of hyaluronan, were not significantly affected by X-irradiation, while expression of the type-I collagen and decorin genes was reduced (Fig. 1). These results suggested that X-irradiation affected the metabolism of extracellular components of cultured osteoblasts, thus reducing the strength of bone tissue.

Next, we focused on the glycosaminoglycan of decorin. Decorin is a proteoglycan comprising a single glycosaminoglycan chain bound to a core protein and is known to be one of the main proteoglycans in bone tissue[18]. The glycosaminoglycan chain has been identified as dermatan sulfate, which has a fundamental repeating disaccharide unit consisting of L-iduronic acid and *N*-acetyl-D-galactosamine-4-sulfate. Interestingly, it has been reported that the core protein and dermatan sulfate chain of decorin binds with type-I collagen and also to type-IX collagen, which binds to type-I collagen, respectively[19-21]. Therefore, interaction between the sugar chain of decorin and type-IX collagen seems to play a very important role in determining the strength of bone tissue. Then, we investigated the effect of X-irradiation on the length and structure of the decorin sugar chain. Hamilton et al.[22] reported that significant loss of the trabecular bone volume fraction in C57BL/6 mice occurred at 110 days after irradiation with 2-Gy doses of gamma radiation, or accelerated proton, carbon, or iron ions. In our present study, SD rats were X-irradiated at 2 or 5 Gy. After 1-3 months, the rats were sacrificed and their femurs were extracted. Glycosaminoglycan fractions were purified from the femurs, and their uronic acid content was determined. The fraction was also subjected to analysis of glycosaminoglycan chain size and unsaturated disaccharide units. It was found that the uronic acid content was decreased, but the chain size was unaffected. The main glycosaminoglycan in rat femurs was totally digested with chondroitinase ABC, and analysis of the unsaturated disaccharide units revealed that its sulfate content was unaffected. These results indicate that the main glycosaminoglycan in the rat femur is chondroitin/dermatan sulfate, and that no structural alteration of the glycosaminoglycan occurs after X-irradiation.

In this investigation, it was found that X-irradiation induced alteration of the extracellular matrix component of rat bone. Gene expression of type-I collagen was decreased, while that of MMP-13 was increased in cultured rat osteoblasts. Furthermore, the gene expression of decorin core protein and the uronic acid content of the femur were found to be decreased by X-irradiation. Although the structure of glycosaminoglycan chains in the femur appeared not to be significantly altered, the present results suggest that decreases in the levels of both decorin and type I-collagen in bone after X-irradiation may contribute to a loss of mechanical strength in bone tissue. The relationship between decorin and

bone strength should be investigated in a future study.

Acknowledgement

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Effect of ascorbic acid and X-irradiation on human leukemia HL-60 cells and the role played by reactive oxygen species in this effect

Shingo Terashima[1*], Yoichiro Hosakawa[1], Satoru Monzen[1], Ikuo Kashiwakura[1], and Toshiya Nakamura[2]

[1]Department of Radiological Life Sciences, Division of Medical Life Sciences, Hirosaki University Graduate School of Health Sciences
[2]Department of Biomedical Sciences, Division of Medical Life Sciences, Hirosaki University Graduate School of Health Sciences, Hirosaki, Japan

Abstract. Ascorbic acid (AsA) shows cytotoxic effects against tumor cells that exhibit less intracellular catalase neutralizing H_2O_2. Therefore, the generation of reactive oxygen species (ROS) derived from H_2O_2 is thought to be involved in the cytotoxicity. Of note, most cell death induced by X-irradiation depends on the production of intracellular ROS. In the present study, the action of AsA combined with X-irradiation and the role of ROS was studied using human promyelocytic leukemia HL-60 cells. Additive cytotoxic effects were observed when the cells were exposed to 2 Gy X-irradiation after 2.5 mM AsA treatment. When catalase was added to the culture with AsA alone, the cytotoxic effects of AsA disappeared. The intracellular ROS production was measured by a flow cytometer using the ROS-sensitive fluorescent probe 2′,7-dichlorofluorescin diacetate (H_2DCFDA) and MitoSOX Red mitochondrial superoxide indicator. The intracellular ROS production peaked at 12 h after X-irradiation alone, but AsA alone and in combination with X-irradiation decreased the levels of many kinds of ROS, including superoxide generated by mitochondria. These results suggest that there are different action pathways of the hydroxyl radical derived from H_2O_2 following the application of AsA and X-irradiation.

Key Words: X-irradiation, ascorbic acid, reactive oxygen species, cancer therapy

Introduction

Ascorbic acid (AsA), also known as vitamin C, therapy has been considered a therapeutic option for cancer therapy that has few side effects. This therapy can be used alone or in combination with chemotherapy. AsA is also known as a radical scavenger. Conflicting data shows that AsA inhibits cytotoxic effects in combination with antineoplastic drugs or X-irradiation [1,2].

AsA exhibits cytotoxic effects on tumor cells, which have a small amount of intracellular catalase that degrades H_2O_2 [3]. Therefore, the generation of reactive oxygen species (ROS) derived from H_2O_2 is thought to be involved in the cytotoxicity. Of note, most cell death induced by X-irradiation depends on the production of intracellular ROS, and mitochondria are well known as major intracellular sources of ROS. It has been reported that one of the mechanisms, in H_2O_2 derived from AsA damaged to mitochondria. In the present study, the action of AsA combined with X-irradiation and the role of ROS was studied using human promyelocytic leukemia cells.

[*] Corresponding to: Shingo Terashima, Research Associate , Hirosaki University, 66-1, hon-cho, Hirosaki, 036-8564, Japan. E-mail: s-tera@cc.hirosaki-u.ac.jp

Materials and Methods

Cell culture, X-irradiation and drug treatment

The human promyelocytic leukemia cell line HL-60 was used in these experiments. Cells were cultured in RPMI1640 supplemented with 10% fetal bovine serum and were maintained at 37°C with 95% air and 5% CO_2. X-irradiation was delivered using an X-ray machine MBR-1520R-3 (Hitachi) at 150 kV and 20 mA through a 0.5 mm Al and 0.3 mm Cu filter at a dose rate of 1.0 Gy/min. L(+)-ascorbic acid was purchased from Wako. The AsA was dissolved in RPMI-1640 medium and disacidified with sodium hydrate before treatment. Catalase was added to the culture for a final concentration of 1,300 U/mL.

Cell viability assay

A total of 4.0×10^5 cells/ml were cultured for 6 h. A final concentration of 0.01–10.0 mM AsA was then added to the culture and the number of viable cells was counted by trypan blue stain 24 hours later. For the next experiment, 4×10^5 cells/ml of HL-60 cells were cultured with or without catalase for 6 h. We then added 1.0 or 2.5 mM AsA to the cells in combination with exposure to 2 Gy X-irradiation. We counted the viable cells after 24 h.

Measurement of intracellular ROS

A total of 1.5×10^5 cells/ml cells were cultured with or without catalase for 6 hours. We then added 2.5 mM AsA to the cells in combination with exposure to 2 Gy X-irradiation. The intracellular ROS production was measured using a flow cytometer (Cytomics FC500, Beckman Coulter) using the ROS-sensitive probe 2′,7-dichlorofluorescin diacetate (H_2DCFDA) at the indicated times during exposure to X-irradiation. In brief, cells were washed with PBS (without Ca^{2+} and Mg^{2+}), incubated at 37°C with 5 μmol/L H_2DCFDA in PBS for 15 min, washed in PBS, and then resuspended in PBS containing 8 g/mL propidium iodide to exclude dead cells.

Measurement of mitochondrial superoxide

The cells were treated with AsA and/or X-irradiation as described above without catalase. The mitochondrial superoxide was measured using the flow cytometer with the mitochondrial superoxide indicator MitoSOX Red at indicated times after exposure to X-irradiation. In brief, cells were washed with PBS, incubated at 37°C with 5 μmol/L MitoSOX Red in HBSS (with Ca^{2+} and Mg^{2+}) for the 15 min, washed in PBS, and then resuspended in PBS.

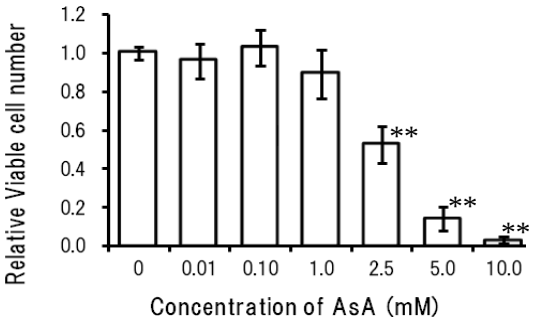

Figure 1. Relative viable cell number 24 h after AsA treatment. $^{**}p < 0.01$ vs. 0 mM.

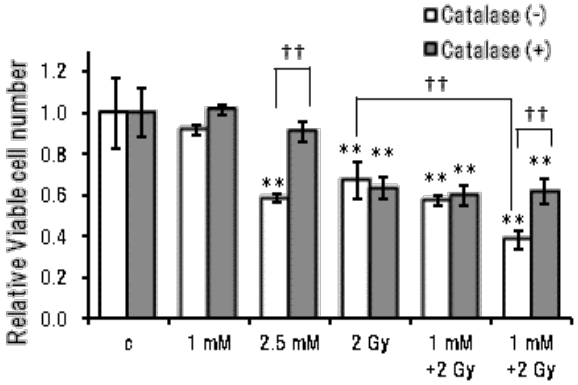

Figure 2. Relative viable cell number 24 h after AsA and X-irradiation and these combinations with/without catalase. $^{**}p < 0.01$ vs. 0 mM. †† indicate that p is < 0.01.

Statistical analysis

Statistical comparisons were performed using the Tukey-Kramer test. All results are presented as the mean±SD from the results of at least three independent experiments.

Results and discussion

AsA showed cytotoxic effects on the growth of HL-60 cells in a dose-dependent manner from about 1 mM (Figure 1). Additive cytotoxic effects were observed when the cells were exposed to X-irradiation after AsA treatment. When catalase was added to the culture with AsA alone, the cytotoxic effects of AsA disappeared. Moreover, the additive cytotoxic effects decreased to the same level obtained by X-irradiation alone (Figure 2).

Figure 3 shows the changes in intracellular ROS levels as analyzed by flow cytometer. The intracellular ROS levels peaked at 12 h after X-

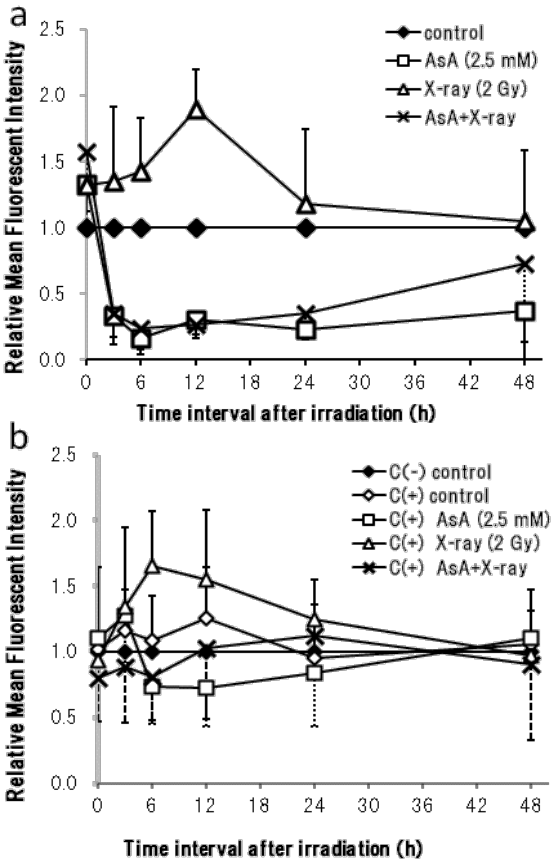

Figure 3. Intracellular ROS levels without catalase (a) and with catalase (b) after X-irradiation.

irradiation alone, but AsA alone and in combination with X-irradiation significantly decreased intracellular ROS levels. In the presence of catalase, the intracellular ROS levels of X-irradiated cells increased slightly and reached a peak after 6 h. ROS levels of cells treated with AsA alone and in combination with X-irradiation were not significantly altered in control cells. These changes in intracellular ROS levels indicated that AsA hardly scavenged intracellular ROS. Thus, H_2O_2 derived from AsA is thought to decrease intracellular ROS levels in the absence of catalase. The ROS levels of cells treated with the combination of AsA and X-irradiation were significantly higher than those of the control cells at 0 h after X-irradiation, and this difference was statistically significant ($p < 0.05$). For the precise evaluation of ROS production just after X-irradiation, we labeled the cells with H_2DCFDA before AsA and X-irradiation treatment. ROS of cells treated with AsA alone and in combination with X-irradiation significantly increased just after AsA and X-irradiation treatment (data not shown).

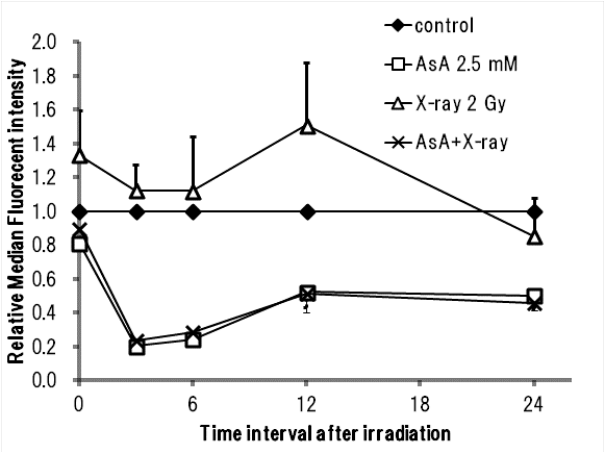

Figure 4. Mitochondrial superoxide after X-irradiation.

Figure 4 shows the changes in mitochondrial superoxide as analyzed by flow cytometry. These changes were similar to the changes in intracellular ROS. Therefore, it is considered that mitochondria were damaged earlier by AsA, which generated H_2O_2.

These results suggest that the action pathway of hydroxyl radicals derived from H_2O_2 is different between AsA and X-irradiation treatments. Moreover, delayed ROS production did not necessarily affect cell death by AsA treatment.

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Radioactive aerosol measurement after the Fukushima nuclear disaster

Masahiro Hosoda[1], Shinji Tokonami[2], Atsuyuki Sorimachi[2], Hirofumi Tazoe[3], Masatoshi Yamada[3], Satoru Monzen[1], Minoru Osanai[1], Hironori Yoshino[1], Ikuo Kashiwakura[1]

[1] Department of Radiological Life Sciences, Division of Medical Life Sciences, Hirosaki University Graduate School of Health Sciences, Hirosaki, Japan
[2] Department of Radiation Physics, Hirosaki University, Institute of Radiation Emergency Medicine, Hirosaki, Japan
[3] Department of Radiation Chemistry, Hirosaki University, Institute of Radiation Emergency Medicine, Hirosaki, Japan

Abstract. An air-borne radionuclide concentration provides important information for the estimation of internal dose due to inhalation after nuclear disasters. Therefore, a simple technique to measure air-borne radionuclide concentrations that does not require an AC power supply is needed. In this study, radioactive aerosol sampling using a glass fiber filter and a battery-powered pump was carried out at several locations in Fukushima Prefecture from March 17 to 19, 2011. The inhalation exposure by particulate I-131 was negligible during this period. The surface distribution of radioactive aerosols on the filter is also important due to the counting efficiency in the high-purity germanium (HPGe) detector measurement. Therefore, the surface distribution with the same system as *in-situ* sampling was evaluated using a radioactive aerosol chamber at the National Institute of Radiological Sciences, Chiba, Japan. The surface distribution of radioactive aerosols on the filter was visualized using an imaging plate technique, and the distribution of radioactive aerosols seemed to be homogeneous. Therefore, the simple filter sampling system used for this study is an effective technique for collecting airborne radionuclides in an emergency situation.

Key Words: glass fiber filter, battery-powered pump, radioactive aerosol, Fukushima, imaging plate

Introduction

On March 11, 2011, the power supply for the cooling system at the Fukushima Daiichi Nuclear Power Station (F1-NPS) failed due to the deluge of a tsunami generated by a 9.0 magnitude earthquake [1, 2]. This accident led to hydrogen explosions in the nuclear reactor buildings at F1-NPS, and artificial radionuclides such as radioiodine and radiocesium were released. On March 12, the Japanese Government ordered the evacuation of the residents who lived in an area within 20 km from F1-NPS. The screening survey of contamination by radionuclides for evacuees was carried out as a result of this evacuation. The first team from Hirosaki University carried out a screening survey from March 15 to 19, 2011 at safe shelters or public facilities in Fukushima Prefecture [3]. The members of this team carried out not only screening surveys for evacuees but also evaluations of ambient dose rates and air-borne aerosols sampling. One of the problems from the nuclear power station accident is the internal radiation exposure of the thyroid by inhalation of released I-131 and I-132. It should be noted that I-131 and I-132 have a half-life of 8 days and 2.3 h, respectively, and therefore it is necessary to take activity measurements of these air-borne radionuclides rapidly. An air-borne radionuclide concentration provides important information for the estimation of internal dose due to inhalation after nuclear disasters. Therefore, a simple technique to measure air-borne radionuclide concentration that does not require an AC power supply is needed.

In this study, radioactive aerosol sampling using a glass fiber filter and a battery-powered pump was carried out at several locations in Fukushima Prefecture.

Materials and Methods

Filter sampling site

Air-borne radionuclide sampling was carried out at four sites (#1–#4) in Fukushima Prefecture shown in Fig. 1. All filter sampling sites were being used as safe shelters or public facilities. The distance between F1-NPS and each filter sampling site was approximately 45–65 km. The weather at each site was fine during the period from March 17 to 19.

Measurement of air-borne radionuclide concentrations

Ambient radioactive aerosols were collected using a two-stage sampling technique with glass fiber filters (Whatman GF/F) and a battery-powered pump (MP-Σ300, Sibata Scientific Technology Ltd.). The sampling flow rate was set to 2.0 L min^{-1} at each sampling site. The filter samples were enclosed in a 48 mm × 55 mm cylindrical polypropylene container. Air-borne radionuclide concentrations on the filter were evaluated using a high-purity germanium (HPGe) detector (GEM-100210, ORTEC). Since I-131 has a short half-life of 8 days, the measurement time was set at 600 s. For evaluation of a long half-life nuclide, such as Cs-134 or Cs-137, the measurement time was set at more than 16,000 s. The concentrations of I-131, Cs-134 and Cs-137 were evaluated using photon peaks of 345 keV, 796 keV and 662 keV, respectively. The obtained radionuclide concentrations were corrected to the value of a sampling date for each physical half-life.

Evaluation of surface distribution of radioactive aerosols on the filter

The surface distribution of radioactive aerosols on the filter is also important due to the counting efficiency of the HPGe detector measurement. Therefore, the surface distribution on filters from the same in-situ sampling system was evaluated using a radioactive aerosol chamber (internal volume: approximately 25 m^3) at the National Institute of Radiological Sciences (NIRS), Chiba, Japan. This radioactive aerosol chamber is environmentally controlled for temperature and relative humidity. The temperature and relative humidity can be controlled in the range of 5 to 30°C with an error of 0.5°C, and 30 to 90% with an error of 3%, respectively [4]. In this study, radon concentration, temperature and relative humidity were set to 10,000 Bq m^{-3}, 20°C and 60%, respectively. Carnauba wax was used as the aerosol material and the particle size had the distribution which made approximately 100 nm maximum [5]. The two glass fiber filters with a battery-powered pump that were used for the in-situ sampling were used for the performance test. The sampling flow rate was set to 2 L min^{-1} and radon decay products were collected over 3.5 h. After the aerosols were collected, the gross alpha measurements were recorded over consecutive 1-min intervals during a total recording period of 60 min.

Distribution images of the radon decay products on the filter

An imaging plate technique (BAS-MS 2025, FUJIFILM Co.) was used to obtain the distribution images of the radon decay products on the glass fiber filter. All radionuclides other than H-3, which has low beta energy of 18.6 keV, can be detected by this technique. Information in the imaging plate was obtained after 3 days using a reading system (FLA-5100, FUJIFILM Co.). The gradation and resolution for the reading system was set to 16 bit and 25 μm, respectively.

Results and Discussion

I-131 was detected at three sites (#1–#3) excluding Kawamata Town, as shown in Table 3. The air-borne I-131 concentration at Iwaki City located south of F1-NPS was observed as the higher value of 10.0 ± 2.6 mBq m^{-3}. On the other hand, air-borne concentrations of Cs-134 and Cs-137 at Kawamata Town were observed as the higher values of 88.8 ± 22.8 and 66.3 ± 18.0 mBq m^{-3}, respectively. The concentrations of I-131, Cs-134 and Cs-137 at Koriyama City, observed as the highest ambient dose rates, were 2.3 ± 0.8, 5.6 ± 4.3 mBq m^{-3} and under the detection limit (*ND*), respectively. The maximum values of the thyroid equivalent dose for residents in Namie Town were estimated to be 33 mSv, according to the report by Tokonami *et al*. [6]. Moreover, the atmospheric I-131 concentration on March 15 was estimated to be

23 kBq m^{-3} [6]. This result suggested that the inhalation exposure by particulate I-131 was negligible during the period from March 17 to 19, 2011.

Radon decay products were collected more than 99% on the first stage as the result of a performance test of the filter sampling system in the NIRS radon chamber. Moreover, radionuclide distributions on the glass fiber filters obtained by Imaging Plate measurements seemed to be homogeneous, as shown in Fig. 2. Therefore, the simple filter sampling system used for this study was an effective technique for collecting airborne radionuclides in an emergency situation.

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Acknowledgments

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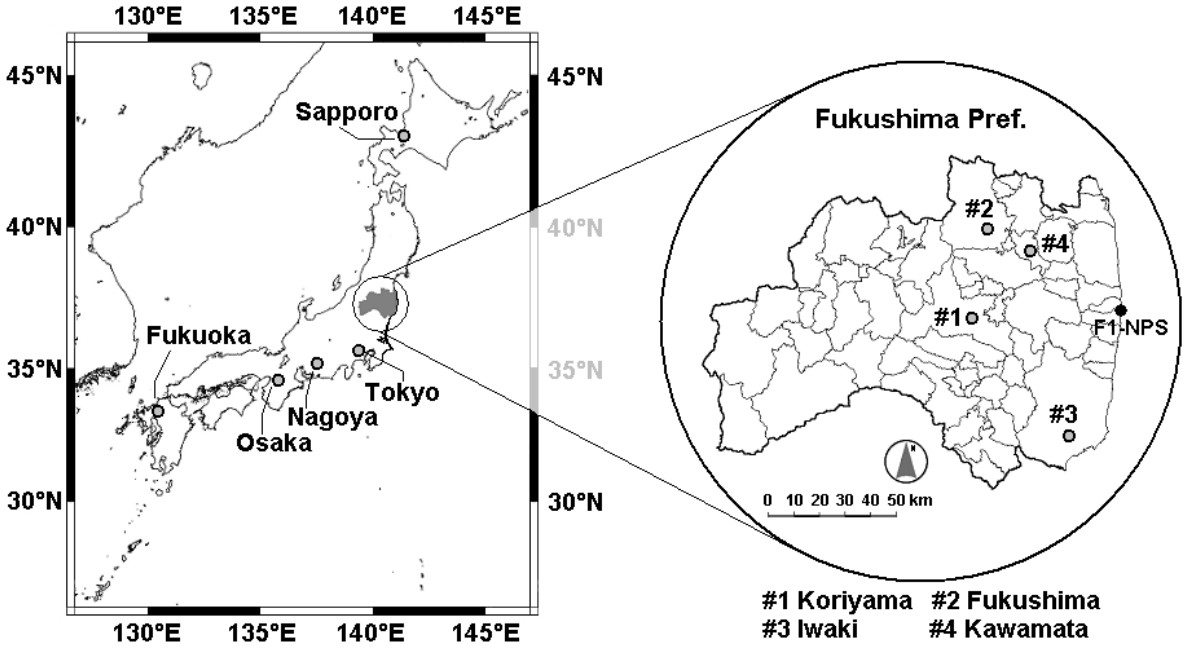

Figure 1 The location of the radioactive aerosol sampling sites.

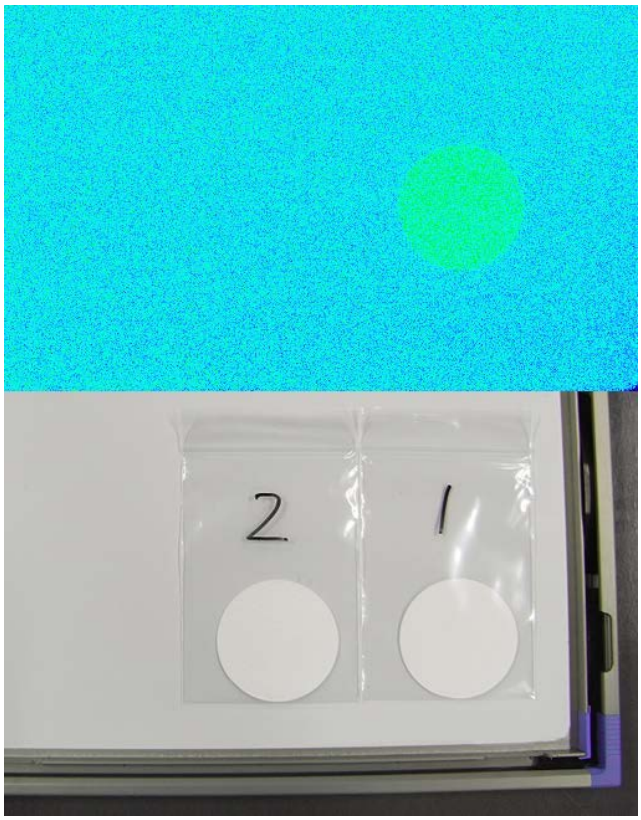

Figure 2 Radionuclide distributions on the glass fiber filter obtained by imaging plate.

A novel parameter, cell-cycle progression index, for biological dose estimation in premature chromosome condensation assay

Tomisato Miura[1*], Kanako Kikuchi[1], Ami Makino[1], Akifumi Nakata[2], Kosuke Kasai[1], Eiki Tsushima[3], Natalia I. Ossetrova[4], Mitsuaki A. Yoshida[2], and William F. Blakely[4]

[1] Department of Pathologic Analysis, Division of Medical Life Sciences, Hirosaki University Graduate School of Health Sciences, Japan
[2] Department of Radiation Biology, Institute of Radiation Emergency Medicine, Hirosaki University (IREM/HU), Japan
[3] Department of Development and Aging, Division of Health Sciences, Hirosaki University Graduate School of Health Sciences, Japan
[4] Armed Forces Radiobiology Research Institute (AFRRI), Bethesda, MD, USA

Abstract. The calyculin A-induced premature chromosome condensation (PCC) assay is a simple and useful method for assessing the cell cycle distribution in cells, since calyculin A induces chromosome condensation in various cell cycles. In this study, a novel parameter, named the cell cycle progression index (CPI), was validated as a novel biomarker for biodosimetry. Peripheral blood was drawn from healthy donors after informed consent had been obtained. CPI was investigated using a human peripheral blood lymphocyte (PBL) ex vivo irradiation (^{60}Co-γ rays: ~0.6 Gy/min, or X-ray: 1.0 Gy/min; 0 to 10 Gy) model. The calyculin A-induced PCC assay was performed for chromosome preparation. PCC cells were divided into following 5 categories according to cell cycle stage: non-PCC, G1-PCC, S-PCC, G2/M-PCC, and M/A-PCC cells. CPI was calculated as the ratio of G2/M-PCC cells to G1-PCC cells. The PCC-stage distribution varied markedly with irradiation doses. The G1-PCC cell fraction was significantly reduced, and the G2/M-PCC cell fraction increased, in 10-Gy-irradiated PBL after 48-h of culture. The CPI was significantly correlated with the irradiation dose ($p < 0.05$), and an exponential dose-response curve was obtained with X-ray irradiation [$Y = -0.3743 + 0.9744 \exp(0.3321D)$, $r^2 = 0.999$]. There were no significant individual ($p = 0.853$), age ($p = 0.415$), or gender effects ($p = 0.951$) on the CPI in the human peripheral blood ex vivo irradiation model. Furthermore, CPI has a predominance that it is calculable in a short time (<20 min/case). These results suggest that the CPI is a useful screening tool for doses ranging from 0 to 10 Gy in radiation emergency medicine.

Key Words: PCC assay, cell cycle, biological dosimetry, biomarker, irradiation, human PBL

[*] Corresponding to: Tomisato Miura, Ph. D. Hirosaki University Graduate School of Health Sciences, 66-1, Hon-cho, Hirosaki, 036-8564, Japan.
E-mail: tomisato@cc.hirosaki-u.ac.jp

1. Introduction

Biological dosimetry, based on the analysis of conventional Giemsa-stained dicentric chromosomes, has been used since the mid-1960s. The dicentric analysis has become a routine component of the radiological protection programs. In the investigation of radiation accidents it is important to estimate the dose to exposed persons. The metaphase dicentric assay is gold standard in cytogenetic biodosimetry, and is the main aberration used for biodosimetry [1,2]. In the mid-1980s a major technical innovation was introduced. This was the method for blocking cytokinesis in cultured lymphocytes by adding cytochalasin B to the medium without inhibiting nuclear division. The so-called cytokinesis blocked (CB) cells [1,3,4] thus produce binucleated cells rather than permitting the two daughter cells to separate. Furthermore, quantification of cell proliferation using the CBMN assay is done by the nuclear division index [5]. The mitotic index (MI) in DIC assay and NDI in CBMN assay is parameters for confirmation of each assay. However, MI and NDI remarkably decrease by cell-cycle delay and arrest in the case of high-dose radiation in peripheral blood culture model. On the other hand, the PCC assay is useful to determine exposure to low doses as well as following life threatening high acute doses of low- and high-LET radiation, because chromosome condensation can be induced in interphase peripheral blood lymphocytes by chemical treatment or by fusion with mitotic cells. Hayata used PCC assay for biodosimetry in the JCO accident in Tokai-mura, Japan [6]. In these cases, metaphase analysis did not work due to low mitotic indices. In this study, a novel parameter, named the cell cycle progression index (CPI), was validated as a novel biomarker for biodosimetry.

2. Experimental design

2.1. Blood collection

Whole peripheral blood from healthy human donors was collected by venepuncture into the vacutainers containing lithium heparin. The informed consent form used was approved by the Uniformed Services University of the Health Sciences' IRB and Hirosaki University. The drown blood was diluted with same volume of RPMI 1640 medium supplemented with 10% FBS, penicillin and streptomycin.

2.2. Ex vivo radiation and blood culture

Whole blood was irradiated with 0, 1, 3, 5, 7, 10, 20 and 30 Gy ^{60}Co γ-rays (0.56 Gy/min) at 37°C using a Robertson Tank, or X-ray (1.0 Gy/min) at room temperature. Two hours after irradiation (DNA repair), lymphocytes were isolated using a density gradient. Lymphocytes equivalent to 0.5 ml whole blood were cultured in 5 ml of PB-MAX Karyotyping Medium (PB-MAX, Invitrogen), which contained a mitogen (phytohemagglutinin, PHA) in a 5% CO_2 at 37°C for 48 h.

2.3. Cell cycle analysis by flow cytometry

BrdU labeling Flow kit (BD Pharmingen) was used for cell-cycle analysis. Isolated normal peripheral lymphocytes were cultured in the PB-MAX in a 5% humidified CO_2 incubator at 37°C for 48 h. 10 nM 5-bromo-2'-deoxy-uridine (BrdU) was added into culture media 30 min before harvesting. After cultivation, cells were harvested and washed with the staining buffer. Cells were incubated with PE-conjugated anti-CD3 mAb on ice for 15 min. After washing with staining buffer, cells were fixed on ice for 10 min. After washing staining buffer, cells were resuspended in freezing medium and stored at -80˚C until use. After permealization, cells were incubated with 300 μg/ml DNase solution at 37 ˚C for 1 hour. Incorporated BrdU was labeled with FITC-conjugated anti-BrdU Ab, and nuclear DNA was stained with 7-AAD. Cell cycle of normal PBL was analyzed using flow cytometry (BD LSRII, BD Biosciences, USA).

2.4. PCC induction, harvest, and spread

PCC assay was performed as described by Miura [7]. Calyculin A (Calbiochem) was used to induce PCC cells. Calyculin A (50 nM) was added into culture media 15, 30 or 60 min before 48-h culture was completed. After hypotonic treatment, cells were fixed in cold 3:1 methanol: glacial acetic acid. Hanabi metaphase spreader or auto spreader PIV (ADSTEC, Japan) was used to prepare PCC spreads. The slides were then stained with 10 % Wright Giemsa (pH 6.8).

2.5. PCC categories and CPI

PCC cells were divided into following 5 categories according to cell cycle stage: non-PCC cells, G1-PCC cells; showing single chromatids, S-PCC cells;

showing both single and sister chromatids, G2/M-PCC cells; showing sister chromatids, and M/A-PCC cells; showing separated sister chromatids. One thousands of well-spreading PCC cells including non-PCC cells were scored and CPI was calculated as the ratio of G2/M-PCC cells to G1-PCC cells.

3. Results and Discussion

3.1. Cell cycle distribution in normal peripheral blood cells after PHA stimulation

PBL does not proliferate in peripheral blood and only CD3+ T cells enter into cell cycle by stimulation with PHA. Cell-cycle distribution changed in each time point after cultivation under PHA-stimulation (data was not shown). In FCM analysis at 48-h cultivation, the frequency of G1 and S cells is about 41.1 ± 0.69% and 41.7 ± 0.58%, respectively (figure 1 left), whereas the yield of G2/M cells is 8%. And the yields of G1-PCC and S-PCC cells were about 5.61 ± 0.24 and 7.6 1 ± 0.41% in PCC analysis, respectively (figure 1 left). However, that of G2/M and M/A-PCC cells was 8 % in PCC stage analysis on normal PBL after 48-h culture. There was no significant difference in the frequency of G2/M cells between both flow cytometric and PCC analysis. The efficiency of G2/M- and M/A-PCC stage (79.6%) in PCC assay is remarkably higher than G1-PCC (13.5 %) and S-PCC (18.2%) cells (figure 1 right). These data indicate that PCC assay enhances the fraction of G2 lymphocytes with premature condensed chromosomes in the PHA 48-hr culture.

3.2. Effect of radiation on cell-cycle distribution in PCC spreads

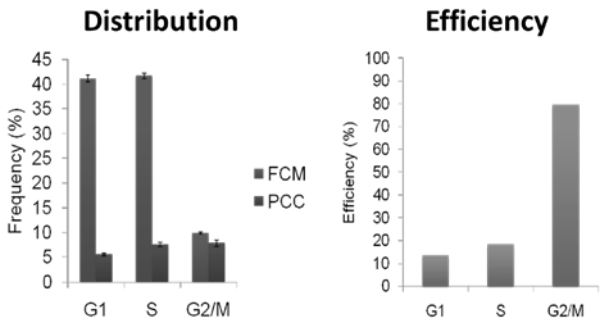

Figure 1. Cell cycle distribution in normal PBL after stimulation with PHA for 48 h.

Chromosomal aberrations are typically measured in blood lymphocytes that have been treated with PHA for 48 hours. Cell-cycle stages in PCC cells were measured based on morphological properties after radiation. The PCC stage distribution remarkably varied between non-irradiated cells and 10-Gy irradiated cells. The G1-PCC cell fraction significantly reduced, and the G2/M-PCC cell fraction increased in 10-Gy irradiated PBL after 48-h culture. This result indicates the dose-dependency for changes in the each PCC index for dose spanning from 0 to 10 Gy γ-rays. There were no significant changes in the fraction of S and M/A phase PCCs over this dose range. However, radiation causes a dose-dependent decrease in G1-PCC coincident with a reciprocal increase in the G2/M-PCC index.

The ratio of G2/M-PCC to G1-PCC, named Cell-cycle Progression Index, CPI, was calculated for dose range from 0 to 10 Gy γ-rays.

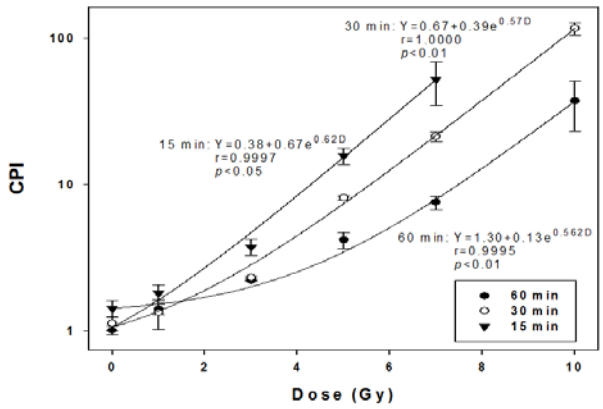

Figure 2. Correlation of CPI with radiation dose in γ-ray irradiated PBL.

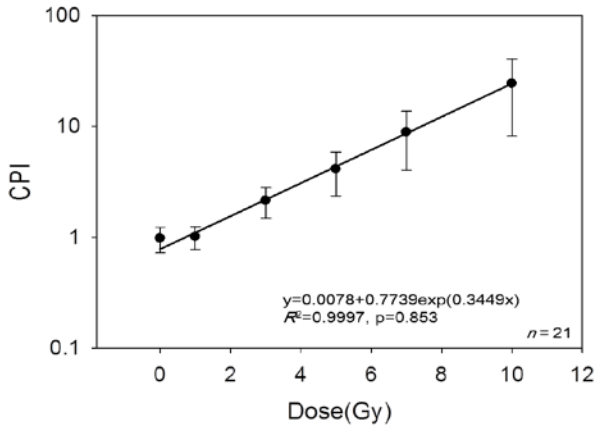

Figure 3. Correlation of CPI with radiation dose in X-ray irradiated PBL.

Progressive dose-dependent increases in CPI were observed for the three calyculin A dosages and reflect the radiation-induced cell-cycle progression delays as measured by relative decreases in G1-PCC and increases in G2/M-PCC with increasing radiation doses (figure 2). An increase in calyculin A treatment time results in a reduction in the CPI levels for controls and irradiation cells and reflect the relative increases in G1-PCC cells. CPI may be useful as an additional index for dose assessment by biodosimetry for dose range from 0 to 10 Gy.

Progressive dose-dependent increases in CPI were also observed in x-ray irradiated PBLs (figure 3). The CPI was significantly correlated with the irradiation dose ($p < 0.05$), and an exponential dose-response curve was obtained with X-ray irradiation [$Y = -0.3743 + 0.9744 \exp(0.3321D)$, $r^2 = 0.999$]. There were no significant individual ($p = 0.853$), age ($p = 0.415$), or gender effects ($p = 0.951$) on the CPI in the human peripheral blood ex vivo x-ray irradiation model. Furthermore, CPI has a predominance that it is calculable in a short time (<20 min/case). These results suggest that the CPI is a useful screening tool for doses ranging from 0 to 10 Gy in radiation emergency medicine.

Summary

1. PCC assay enhances the fraction of G2 lymphocytes with premature condensed chromosomes in the PHA 48-hr culture.
2. The CPI correlates with irradiation dose, and may be useful as a parameter for biodosimetry in PCC assay.
3. There were no significant individual, age, or gender effects on the CPI in the human peripheral blood ex vivo irradiation model.
4. The CPI is a rapid screening tool for doses ranging from 0 to 10 Gy in radiation emergency medicine.

Acknowledgments

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Development of rescue support system for complex disaster with radiation medicine

Hiroyuki Nozaka

Department of Biomedical Sciences, Division of Medical Life Sciences, Hirosaki University Graduate School of Health Sciences, Hirosaki, Japan

Abstract. An unprecedented 9.0-magnitude earthquake was measured in Japan, which struck the Tohoku region of Japan on March 11, 2011. About 19,000 are dead or missing. The Fukushima Daiichi Nuclear Power Plant was caused severe damage, the radioactive material was detected the wide area around Fukushima prefecture. It was not assumed that complex large-scale disaster of earthquake accident and nuclear accident by conventional radiation emergency medicine, large confusion occurred and it was difficult to provide medical care by DMAT. Therefore it was required to medical support system for complex large-scale disaster with radiation accidents. Objective: This study aims to develop the high-speed communication system with portability and easy operativity and rescue support system for radiation disaster medicine. Satellite communication auto positioning system: This system consists of parabolic antenna, 2 axis stepping motor unit, motor controller board and PC. DiSEqC1.2 was used for the control protocol. This system moves in the direction of a communications satellite located on 36,000-km-above ground (geosynchronous orbit), and moving direction is calculated from the latitude and longitude information acquired by GPS. Furthermore, direction adjustment is carried out by field intensity from a satellite. Rescue triage support system for complex disaster with radiation medicine: Database software was used Filemaker Pro 12 and Filemaker Pro 12 server. And we incorporated inspection device applications. The database system is able to register first triage, secondary triage, and radiation triage information of patient. Information is registered with a tablet terminal in radiation emergency medicine operations, and it is possible for a specialist to access and browse information via a satellite network and to carry out medical support. Results: This system was possible to transmit data of patient contaminated with radioactive material to hospital before conveyance, and specialist's advice is obtained via a satellite network. However, it is required to improve in portability and operativity.

Key Words: Radiation Emergency Medicine, Triage support system, Tele-medicine, Disaster Medicine Support system

Introduction

An unprecedented 9.0-magnitude earthquake was measured in Japan, which struck the Tohoku region of Japan on March 11, 2011. About 19,000 are dead or missing. Additionally, a total of 11 nuclear reactors were automatically shut down at the Onagawa plant, Fukushima No. 1 and No. 2 plants and Tokai No. 2 plant after the earthquake. Especially, the Fukushima Daiichi Nuclear Power Plant was caused severe damage, high levels of radiation were detected at the Fukushima No. 1 nuclear powerplant after an explosion, and the radioactive material was detected the wide area around Fukushima prefecture [1, 2].

Emergency Medical Information System (EMIS) is a medical support system which was developed for disaster medicine. This system aims collection of disaster medical information from hospital, and provides medical resource information for patient conveyance. However, when a communications network is destroyed, this system is not able to use for disaster medicine. Furthermore, it was also not assumed that complex large-scale disaster of earthquake accident and nuclear accident in conventional radiation emergency medicine, this

system does not support radiation emergency medicine. Therefore large confusion occurred in the Tohoku Earthquake, and it was difficult to provide medical information or medical rescue by DMAT. For this reason, it is required to develop of medical support system for complex large-scale disaster with radiation accidents [3].

Satellite communication is one of the tele-communication which is useful at the time of a disaster [4]. It provides communication links between various points on Earth. Satellite communications play a vital role in the global telecommunications system. In recent report, Satellite communication was used at the case of the Sichuan "5.12" earthquake in 2008 [5]. It is reported that satellite communication system enabled medical pro-fessionals to coordinate the rescue and relief work after this major natural disaster, at a time when the government emergency response system still had plenty of room for improvement.

This study aims to develop the high-speed communication system with portability and easy operativity and rescue support system for complex large-scale disaster with radiation accidents.

Portable type satellite communication network system

1. System configuration

System configuration was shown in Figure.1-A. This system consists of the following parts.

・Satellite communications antenna (IPSTAR. INC, Thailand)

・Satellite modem (IPSTAR. INC, Thailand)

・Satellite communications antenna tripod(Original design)

・Two axis stepping motor (SMR128G, JAEGER, Taiwan)

・Motor positioner unit (YP-300DR, YURI, China)

・Power generator (Enepo 9i, Honda, Japan)

・Control PC(Let's note C1, Panasonic, Japan)

2. Control system

Program language was used Microsoft visual studio C♯, and communication protocol was used DisEqC (Digital Satellite Equipment Control) 1.2. This protocol is a special communication protocol for use between a satellite receiver and a device such as a multi-dish switch or a small dish antenna rotor. DiSEqC was developed by European satellite provider Eutelsat. DiSEqC relies only upon a coaxial cable to transmit both bidirectional data/signals and power. DiSEqC is commonly used to control switches and motors, and is more flexible than 13/18 volt and 22 kHz tone or ToneBurst/ MiniDiSEqC techniques. Our algorithm was used this protocol for detection of telecommunication satellite (THAICOM 4). After connection of the hardware, this system is initialized, and obtains longitude and latitude information by GPS. Then two axis stepping motor rotate to elevation angle 40°, azimuthal angle 220 ° (Error range ±2°), and detects weak signal from telecommunication satellite. Adjustment of position is carried out by measurement of signal strength, the most suitable direction was selected by DisEqC protocol. Appearance of this system was shown in Figure. 2-B.

Rescue triage support system for complex disaster with radiation medicine

1. System configuration

・Filemaker pro12 (Filemaker. INC, CA, USA)

・Filemaker 12 server (Filemaker. INC, CA, USA)

・Triage tag for radiation contamination (Original design)

・Tablet PC (Let's note C1, Panasonic, Japan)

2. System overview and features

First triage, Second triage, Radiation triage, and vital information (EEG, PCG, US) are able to be registered in this system (Figure.2-A). This system supported Simple Triage And Rapid Treatment (START) method for first triage (Figure.2-B). START method is defined a Simple Triage and Rapid Treatment plan designed for first responders. All vital information is able to register with selection of pull down menu, and judgment is able to be obtained automatically on tablet PC in this system (Fig.2-C). Radiation triage is able to register dose of radioactivity, schema of a contamination part, decontamination disposal, medication and any images of patient with selection of pull down menu on tablet PC. Original radiation triage tag which corresponds to this system was made for complex large-scale disaster (Figure.2-C, D). This system on tablet PC synchronizes with other PC via satellite network, therefore specialists is able to support DMAT or medical staff. Furthermore, this system is able to provide patient information to hospital by E-mail, FAX and EMIS before conveyance.

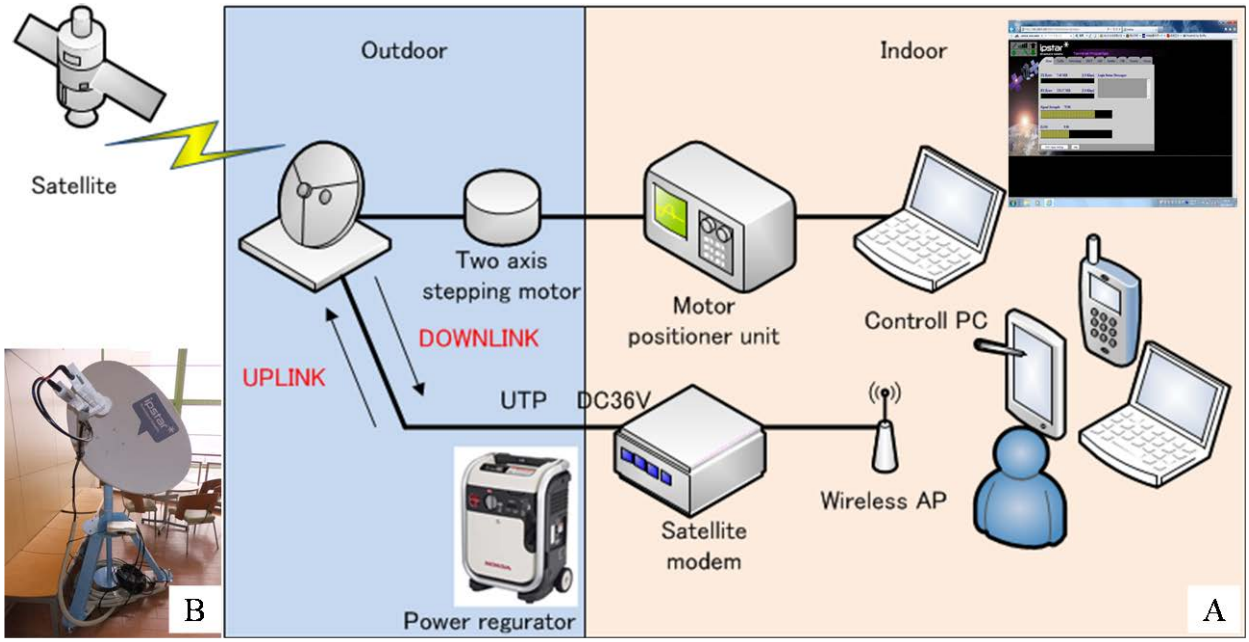

Figure 1. System configuration of auto positioning system

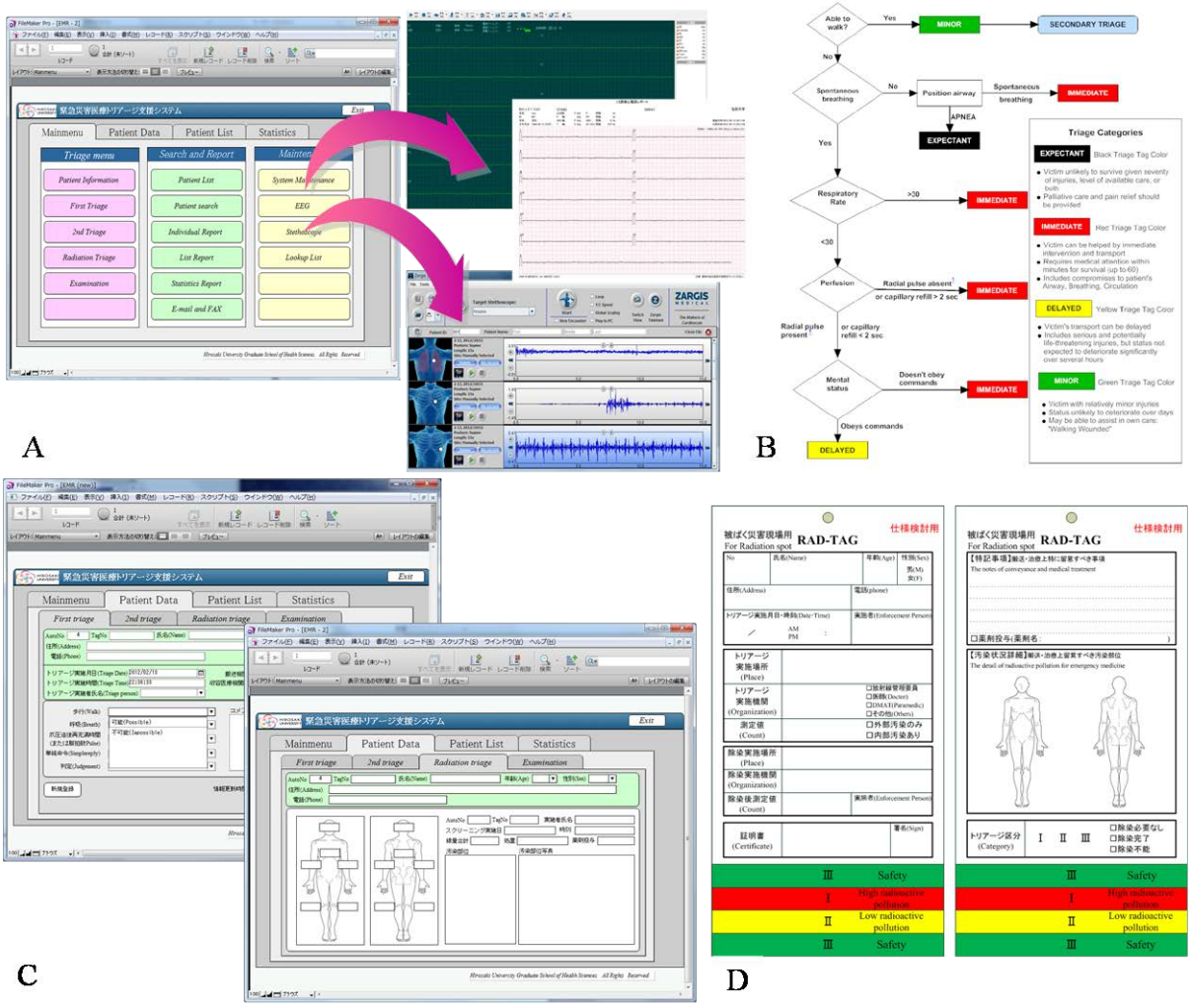

Figure 2. System configuration of rescue triage support system for complex disaster with radiation medicine

System evaluation

1. Accuracy of detection by auto positioning system

We examined detection of THAICOM4 by auto positioning system. The success rate showed 70%. The average time for system set up was 15 minutes. Set up time was shortened to 1/5 as compared with the conventional manual method.

2. Rescue triage support system for complex disaster with radiation medicine

As a result of user input test, it is required less than 1 minute to input for first triage, and less than 3 minute to input for radiation triage.

Conclusion

Our system enables cooperation between medical /rescue professionals at the disaster area and support hospital/medical organization. It is required that system evaluation at the emergency disaster medical training.

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Education of nurses or paramedics in the framework of the management of radio-contaminated or irradiated patients: a very important challenge for the French defence radiation protection service (SPRA)

C Dody[1*], X Michel[1], G Weber-Donat[2], F Entine[1], M Gauthier[3], JC Amabile[1], P Laroche[1].

[1] *French defence radiation protection service (SPRA), Clamart, France*

[2] *Radiology department, Military Hospital Percy, Clamart, France*

3 Military health service Headquarters (DCSSA), Vincennes, France

Abstract. As part of a radiological event, education and training (E/T) is one of the main missions provided by the French defence radiation protection service (SPRA). It concerns all the French military hospitals like Percy, not only as part of the medical management of radio-contaminated and irradiated patients but also for teams' radiation protection. The French military radiological E/T program is built to increase the capability of medical personal, nurses or paramedics to respond effectively to a radiological accident.

Firstly, initial training sessions with the SPRA are regularly organized, especially for the benefit of nurses and technicians. The purpose of this kind of teaching is to demystify radioactivity. Then, a specific training program is realized for medical staffs which are involved in this particular type of management based on practical guidance including practical workshops inside the Centre for the treatment of radio-contaminated wounded (CTBRC). Furthermore, the SPRA is involved in numerous military and civilian training courses coordinated by the French Armed Forces Health Service in order to teach the principles of the medical response organization in the case of a radiological accident. These teachings are dedicated to the Military School of Val-de-Grâce (Paris), the French Navy, the French Air Force, civilian universities of Medicine or for the benefit of foreign students and they conduct in some case to graduate qualification. The French military radiological E/T program underlines systematically the missions of nurses and paramedics in case of a radiological accident.

Keywords: Radiological accident - Emergency medicine - Nurse - Training.

In France, the SPRA is an establishment of the French Armed Forces Health Service (SSA) specialized in radiation protection. In addition to the occupational medicine (medical and radiobiogical supervision of people exposed to ionizing radiation), hygiene and safety (technical controls of installations), regulation and intervention in case of a radiological event, the SPRA provides many hours of training at the staff of the armed forces and also other institutions.

[*] Corresponding to: Christophe DODY, Chief-nurse, French defense radiation protection service (SPRA) – 1bis, rue du lieutenant Raoul Batany 92141 CLAMART CEDEX France E-mail : spra.def@wanadoo.fr

1. The SPRA and Percy hospital

The SSA has three hospitals in Paris and its suburbs.

The SPRA is located on the site of the Percy military hospital in Clamart. This site includes an academic hospital with emergency units, haematology, plastic surgery, physical medicine and rehabilitation, psychiatry, burn care unit, the centre for the treatment of radio-contaminated wounded (CTBRC, figure 1), blood transfusion service. This unique site in Europe is particularly specialized in the care of radiation victims.

2. Teaching at hospital

The training of paramedical personnel is carried out using various methods:

- the lectures are conducted every two months
- practical workshops are conducted every month at the CTBRC
- exercises are performed annually with the civilian's nuclear power plant and public health authorities

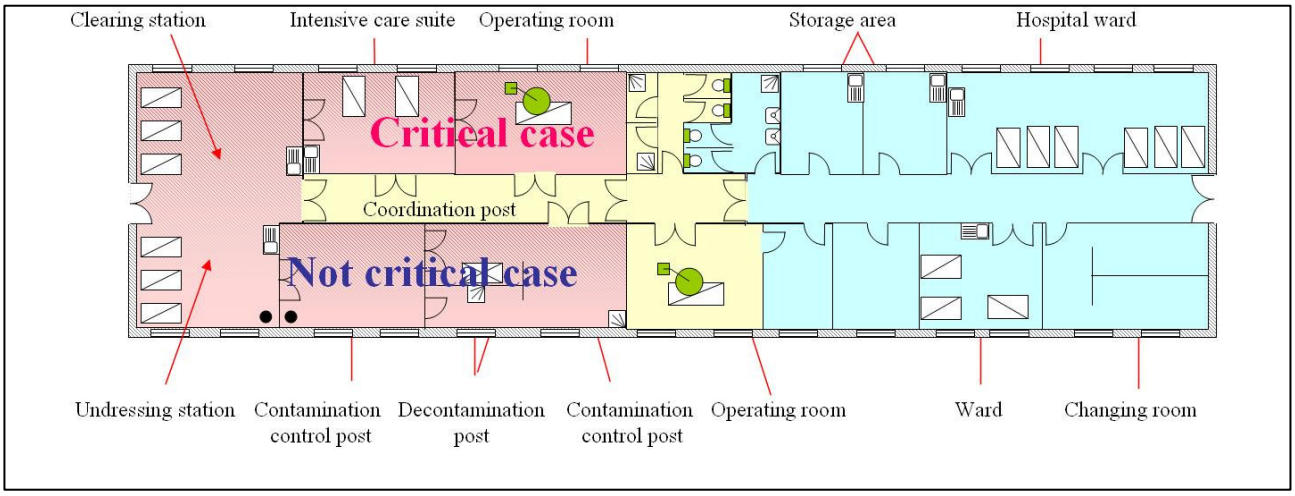

Figure 1: Percy's CTBRC [1]

SPRA provides around one thousand teaching hours per year. Initially organized in two divisions (medical and technical), the SPRA expands in four divisions since October 2012:

- a medical division
- a dosimetry division
- a control division
- a training division

The close relationships between the different units of the hospital have developed different types of trainings in the field of radiological risks management. For example, there are specialized courses done in collaboration with Percy military hospital teams.

2.1. Theoretical courses

Golden rules are the foundation of our education. The importance of these principles is reminded to staffs:

- treatment of life threatening conditions is always the first priority [2]
- limit the spread of the external contamination
- external contamination should not become internal
- treatment of internal contamination is an emergency [3]
- perform detection on a dry skin
- an irradiated patient does not irradiate

The various steps are carried on according to the principle of the forward motion.

A procedure was developed by the SPRA in collaboration with the surgical team in order to avoid the spread of contamination:

- prepare operating theatre (operating room, angiography suite, burn care unit) for direct admissions without shower decontamination step
- assist surgeons for guided surgical resection
- help, at the end of the surgical procedure to manage contaminated wastes (figure 2)

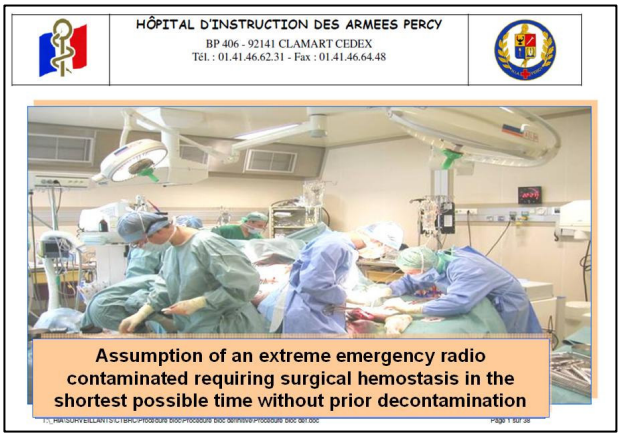

Figure 2: Procedures

2.2. *Practical workshops*

They are made in the CTBRC. They remind students rules for undressing, shower decontamination, contamination control, transfer of decontaminated victims to the hospital and the importance of medico-psychological outcome. The advance principle is respected throughout the chain of care for injured casualties. In that way, the patient is directed firstly to a "dirty" area where decontamination procedures will take place and then admitted to a "clean" area.

Victim undressing is taught on valid and invalid person (figure 3) to prepare students to all possibilities. Whenever possible, clothes are removed without cutting, but cutting clothes is taught to learners. Then the clothes are folded on themselves, from the inside to the outside along the victim.

Figure 3: Undressing victim

The stripping is performed on valid victims and invalid casualties according to the principles established to prevent cross contamination. Clothing which can't be removed easily without risk of transferring contamination are cut. Support victims are done according to established protocols, taking into account the medical aspect of the victim.

The decontamination shower is performed on any type of victim, also taking into account the possible patient injuries (figure 4).

Figure 4: Decontamination shower

Contamination control is carried out by personnel trained in the handling and use of radiometers on a perfectly dry skin so as not to hide residual contamination (figure 5). [4]

Figure 5: Contamination control

Injuries still contaminated after the procedure, will be confined in a dressing impregnated with DTPA prior to performing surgical exploration and resection step (figure 6).

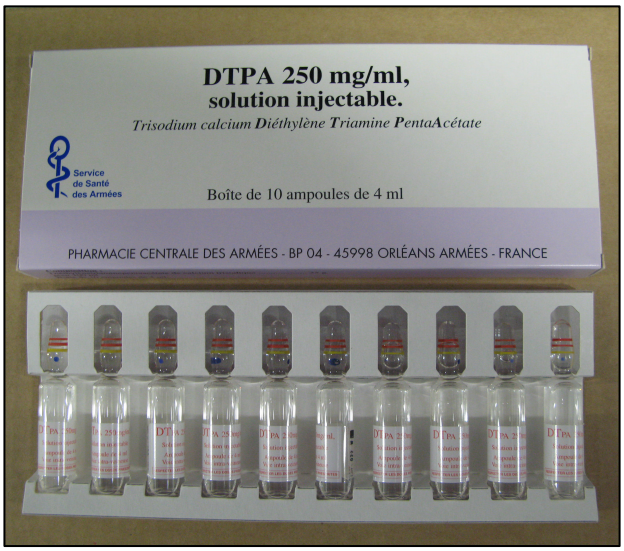

Figure 6: DTPA (diethylentriamene pentaacetate)

The transfer of uncontaminated casualties with conventional injuries and/or external exposure to the hospital is done by ambulance teams.

To prevent Post Traumatic Stress Disorder (PTSD), mental health specialists are trained in psychological interventions.

2.3. Annual exercises

They are performed in collaboration with military and civilian facilities. Technical staffs from nuclear power plants or research centres put the accident scenario into practise at its level and the medical division of the SPRA provides the "medical care" scenario which will cause the activation of management of contaminated patients in the hospital. These exercises can also be controlled by government authorities in connection with the training of the various services entities involved in the management of CBRN risk.

This is an opportunity to validate the direct support procedures for injured victims in appropriate medical facilities without prior decontamination.

Indeed, the preparation of different rooms is an important topic in the training of nurses to optimize radiological care.

We train a maximum of health professionals with different specializations to benefit from their expertise in victims support. For example, physiotherapists are used on positions where the mobilization of affected members will be required as part of the optimization of the management of pain.

2.4. Balance training

On Percy's hospital site, more than half of the staff is trained to take charge of this type of casualties. This strategy allows staff to have at any time a specialized team for radiological emergencies without resorting to a specific group. In addition, the training of all personal seems interesting when there is a long time care. In fact, supporting victims is not limited to a single decontamination chain, and take also into account their care in hospital for the post-decontamination treatment.

3. Teaching outside the hospital

Paramedic training is also made outside the hospital for the benefit of military medical teams. It consists of training in management of casualties from the red zone to the hospital.

In that way, this training concerns air nurse conveyor, submarine medical teams, radiation protection for patients, CBRN post graduate courses, university courses and overseas trainings in aid of foreign forces.

4. Conclusion

Conducting monthly workshops allows personal practice. Furthermore, performing annual exercises with plants' subscribers and specialized homeland services makes operational teams.

For this purpose, training of half of the military hospital staff is sufficient. Indeed, decontamination is only one step of the support. Then casualties benefit from a conventional care in the establishment.

Our aim is to develop procedures in order to allow contaminated victims reception in hospital technical platforms without risk of contamination spread.

We must keep in mind the context of terrorism threats and dismantling of the nuclear industry, which both can be a source of accidents or incidents.

Technical documents are available on military health service website, where we can find for example the practical guide for the management of radiocontaminated casualties by paramedics [5]. Besides, advices from the French nuclear safety authority can also be found in the national guide for medical response to nuclear or radiological event [6].

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The human resource development and training courses on radiation emergency medicine at NIRS

Takako Tominaga[1*], Misao Hachiya[2], Hideo Tatsuzaki[1] and Makoto Akashi[3]

[1] *Department of Radiation Emergency Medicine, Research Center for Radiation Emergency Medicine, National Institution of Radiological Sciences, Chiba, Japan*
[2] *Planning and Promotion Unit, Research Center for Radiation Emergency Medicine, National Institution of Radiological Sciences, Chiba, Japan*
[3] *National Institution of Radiological Sciences, Chiba, Japan*

Abstract. National Institute of Radiological Sciences (NIRS) is the only institution in Japan that has been dedicated to comprehensive scientific research for radiation and human health, and NIRS has been also designated as the tertiary level hospital as well as the national center of radiation emergency medicine in this country. NIRS has conducted a number of domestic training courses on radiation-protection, -measurement, and -emergency medicine since 1960's. Furthermore, NIRS has introduced these training courses and workshops for experts in Asian countries since 2001, in collaboration with international organizations such as the World Health Organization (WHO) and the International Atomic Energy Agency (IAEA). In Japan, the radiation emergency medical response system has been established in 19 prefectures with nuclear facilities; the education and training are provided to personnel in these prefectures. NIRS has accepted personnel from any local government to its training courses regardless of having nuclear fasciitis. Experiences of response to the accident at Tokyo Electric Power Company (TEPCO) Fukushima Daiichi nuclear power plant (NPP) in 2011 revealed that, knowledge of radiation is required for health care providers and first responders in local governments all over Japan. Here, we report details on the training courses for radiation emergency medicine that were carried out at NIRS.

Key Words: radiation emergency medicine, education, training course

Introduction

Definition of a radiation emergency is any unintended event including operating errors, equipment failures or other mishaps, the consequences or potential consequences being not negligible from the viewpoint of protection and safety [1]. After discovery of radiation and radioactivity, radiation is applied in many fields such as industrial, agricultural, medical and other fields. On the other hand, human effects of radiation have been reported since end of 19th century. While radiation gives benefit to human life, radiation could be harmful, suggesting that inappropriate use of radiation leads to deleterious effects. For this reason, the emergency response system for accidental exposure is required.

The education and training are important for plan and preparedness for radiation emergency medicine, since a radiation accident rarely occurs. As the core institute of radiation emergency, the National Institution of Radiological Sciences (NIRS) has held many training courses on radiation protection since 1960's and also conducted courses for medical personnel and first responders since 1980's. Here, we introduce the training courses at NIRS and discuss on demands for education of radiation emergencies after the accident.

[*] Corresponding to: Takako Tominaga, Senior researcher, National Institution of Radiological Sciences, 4-9-1 Anagawa, Inage-ku, Chiba, 263-8555, Japan.
E-mail: tominaga@nirs.go.jp

Education on a radiation emergency medicine in Japan

Among 47 prefectures in our country, only 19 prefectures had preparedness for radiation emergency before 2011 [2]. These prefectures designated primary and secondary radiation emergency hospitals and the medical staff of these hospitals had a chance to attend training course and exercise on radiation emergency. However, the personnel of hospitals which had not been designated had few chances for the education. One of the most important lessons learned from the Fukushima accident is that hospitals could not accept contaminated patients with radionuclides, if they were not trained. Furthermore, the accident also revealed that education/training for radiation emergency medicine was not successful even if the system had been established. Opportunity for the education should be given to medical personnel and first responders, since radiation devices and radioactive materials are anywhere in society. Now the number of local governments without nuclear facilities is increasing which try to make a plan and preparedness for a nuclear/radiation disaster. However, education for medical personnel and first responders in these local governments are not enough.

Training courses at NIRS for local responders

As mentioned above, NIRS has held many training courses on radiation protection and radiation emergency medicine for medical personnel and first responders (Fig. 1). The 3 days course on radiation emergency medicine at hospital are intended for medical doctors, nurses, radiological technologists, and other medical staff. This course includes lectures about radiation basics, biological effects, radiation measurement, biodosimetry, hospital preparedness and management for handling externally and/or internally contaminated patients, dose assessment, and lessons learned from past accidents. Also this course has handling contaminated injuries, use of radiation detectors, its measurement, and table top drill. As of March 31 2011, 813 persons had attended to this course.

The 4 days course for first responders on radiation emergency is held for management at pre-hospital level. This course has lectures about radiation basics, outline of radiation emergency medicine, radiation effects, history of radiation accidents, handling of contaminated patients with injuries on site, and lessons learned from Fukushima NPP accident. This course also has drills of contamination survey, radiation measurement, use of radiation detectors, table top drill, handling of contaminated injuries on site, and zoning. As many as 1883 people attended this training course until March 31 2011.

Before 2011, the numbers of applicants for these training courses were almost once or twice of maximum enrollment. After the Fukushima NPP accident, however, the numbers of applicants for these courses have been increased (Table 1 and Fig. 2). These data suggest that demand for education/training of radiation emergency medicine is being increased in medical personnel and first responders all over Japan.

Workshops and training courses in Fukushima

After the accident in 2011, NIRS has been requested to send experts of radiation measurement or emergency medicine to training courses by local officials or local fire departments in Fukushima. Upon request by the headquarters of Fukushima prefecture, we have also sent 12 experts to the workshops on radiation measurements for officials of municipal and local governments who would be in charge of environmental radiation monitoring in Fukushima. Six workshops were held in Fukushima-, Aizuwakamatsu-, Shirakawa-, Kooriyama-, Minamisouma-, and Iwaki-city with about 270 participants. Fukushima prefecture has 12 local fire departments. Among them, 9 departments had training courses and almost 500 fire fighters and emergency medical technicians took these courses (Table2). NIRS contributed to these courses by sending experts of these fields.

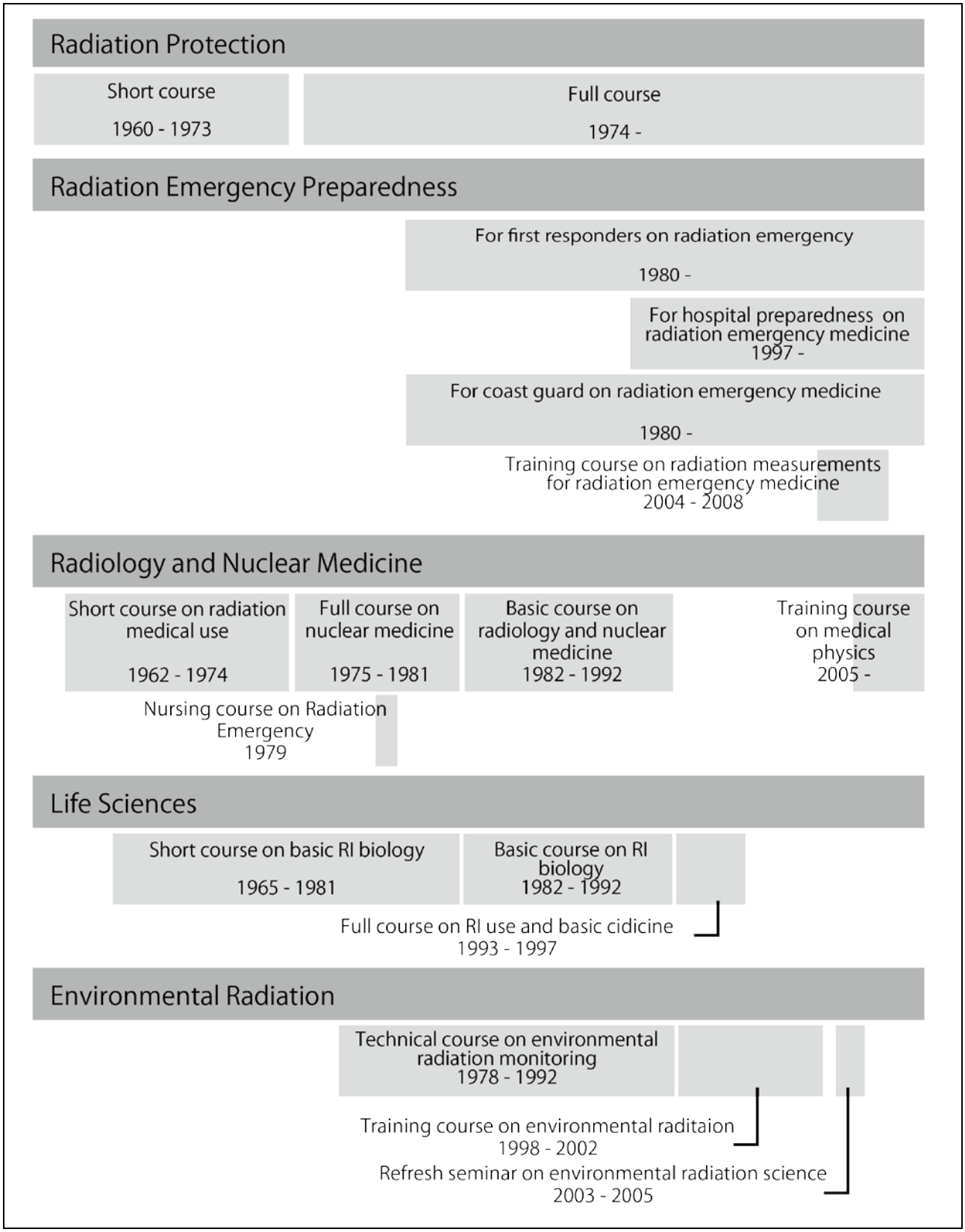

Figure 1. Training courses at NIRS (1960 - 2012)
NIRS has conducted training courses for radiation protection, radiation emergency, health physics, life sciences, and nuclear medicine since 1960's.

Table 1. No. of applicants and participants of training courses on radiation emergency medicine from 2009 to 2012

Training Course		Date	No. applicants	No. participants
Training course on radiation emergency medicine (for hospital staff)	1st	Nov.18-20, 2009	41	25
	2nd	Sep.27-29, 2010	26	26
	3rd	**Oct.12-14, 2011**	**74**	**23**
	4th	**Dec.14-16, 2011**	**73**	**22**
	5th	**Jun.18-20, 2012**	**60**	**41**
Training course on radiation emergency medicine (for leaders)	**1st**	**Sep.7-9, 2011**	**74**	**19**
Training course for first responders on radiation emergency	1st	Feb.8-10, 2010	50	24
	2nd	Dec.13-15, 2010	58	25
	3rd	**Jly.6-8, 2011.**	**45**	**23**
	4th	**Dec.6-8, 2011**	**32**	**21**
NIRS-IAEA-REAC/TS Training course on REM	—	**Aug.23-26, 2011**	**24**	**24**
Workshop on radiation emergency medicine (for nurses of ER at Fukushima Daiichi NPP)	—	**Dec.22, 2011**	—	**11**

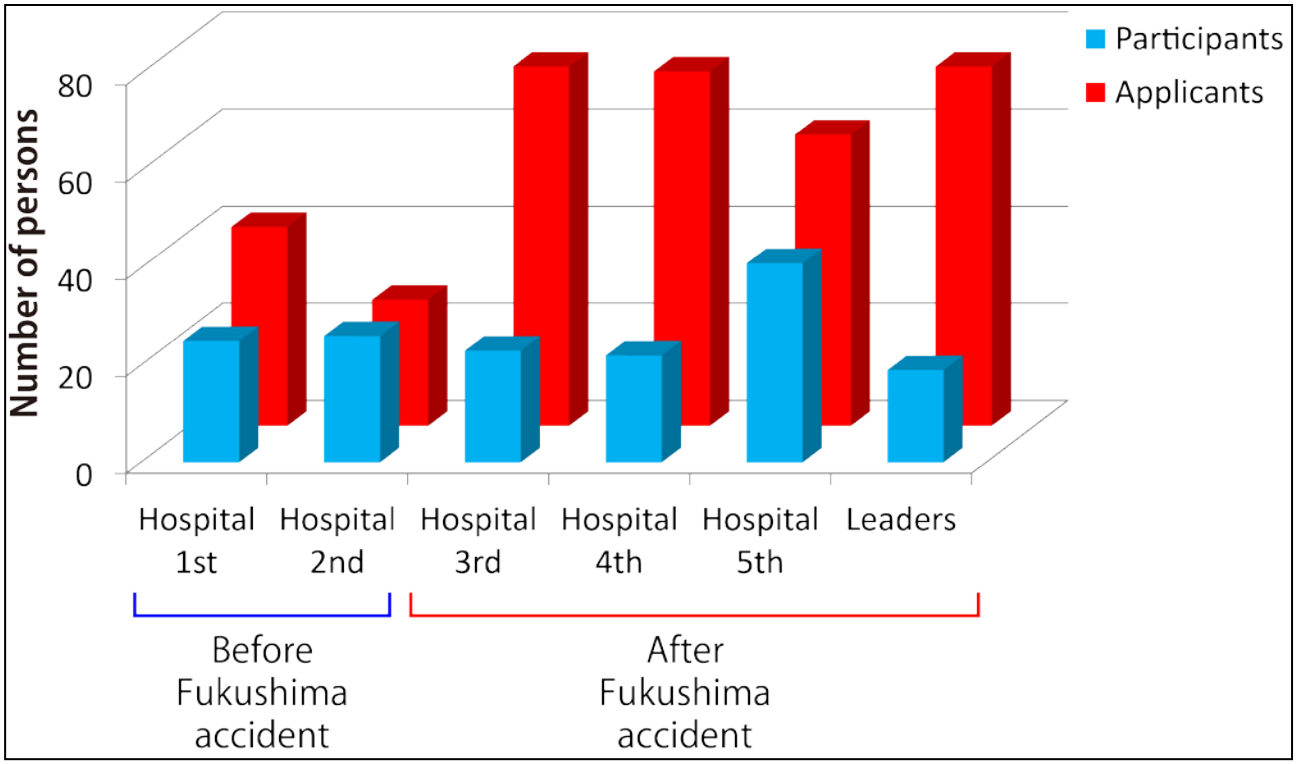

Figure 2. Changes in numbers of applicants and participants of the training course
After the Fukushima NPP accident, the number of applicants for the training courses on radiation emergency has been increased.

Table 2. No. of participants of the training courses for fire departments in Fukushima prefecture

Fire defense headquarters	Date	No. participants	No. experts from NIRS
Futaba fire defense headquarters	Sep.21-22, 2011	83	4
Soma fire defense headquarters	Oct.3-4, 2011	50	3
Iwaki City fire defense headquarters	Oct.28, 2011	32	4
Fukushima City fire defense headquarters	Nov.28-29, 2011	80	5
Fire defense headquarters in Aizu (Kitakata, Aizuwakamatsu, Minamiaizu)	Feb.2, 2011	147	4
Shirakawa fire defense headquarters	Feb.3, 2012	51	4
Date City fire defense headquarters	Mar.16, 2012	50	4

Trainings, workshops, and symposiums for Asian experts

In Asian countries, demands for energy are getting increased with development of industries. Application of radiation for medicine and industrial use are increasing. In order to share information, NIRS has held the training courses, workshops, and symposiums on radiation emergency medicine every year since 2004 (Table3). Totally 345 experts from Asia attended to these training courses.

Discussion

First responders and medical personnel have very few chances for facing the radiation emergency medicine because radiation/nuclear accidents and disasters are rare events. However, unexpected events including malicious ones could occur anywhere. Indeed, the accident which had occurred in the Fukushima NPP was a combined disaster of earthquake, tsunami, and release of massive radioactive materials. Thus, rapid adaptation to unexpected adverse conditions is critical to the successful implementation of any disaster plan. In our country, response system to radiation/nuclear accident was considered independently from other disasters. Response to radiation emergency is important for the comprehensive management system for disaster. Education has to be provided for all medical personnel and first responders to have chance to study radiation emergency.

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Table 3. Training courses, workshops, and symposiums for Asian experts at NIRS

Year	Training course/Workshop/Symposium	In cooperation with	No. participated countries
2001	IAEA/RCA-NIRS Regional Training Course on " Medical Preparedness and Medical Response to Radiation Accidents"	IAEA	12
2004	IAEA/RCA Regional Training Course on " Medical Management for Radiation Accident"	IAEA	11
2005	KIRAMS/NIRS Seminar of "Radiation Emergency Medical Preparedness"	KIRAMS	1
2005	Seminar on "Medical Treatment of Patients Contaminated with α Emitters"		1
2006	WHO-REMPAN Regional Workshop on Radiation Emergency Medical Preparedness and Response in the Western Pacific Asia	WHO, REMPAN	3
2006	International Workshop on Radiation Emergency Medical Preparedness within the Framework of the Asian Nuclear Safety Network	ANSN	12
2006	Symposium on Awareness Enhancement and Confidence Building on Emergency Medical Preparedness in Japan and Asia	NSC, IAEA	12
2007	NIRS Seminar for trainers on Radiation Emergency Medicine in Asia Region		7
2007	NIRS Training Course for Taiwanese Medical Professionals on Radiation Emergency Medical Preparedness		1
2007	NIRS Training Course for Korean Medical Professionals on Radiation Emergency Medical Preparedness	KIRAMS	1
2008	NIRS/ NSC/ IAEA Workshop on Medical Response to Nuclear Accidents in Asia	NSC, IAEA	10
2008	NIRS Training Course for Korean Medical Professionals on Radiation Emergency Medical Preparedness	KIRAMS	1
2008	NIRS Workshop on Cytogenetic Biodosimetry for Asia And NIRS-ISTC Workshop on Cytogenetic Biodosimetry	ISTC	13
2009	NIRS/ NSC Workshop on Medical Response to Nuclear Accidents in Asia	NSC	14
2009	NIRS-KIRAMS Joint seminar on radiation emergency medicine	KIRAMS	1
2010	NSC/NIRS workshop on medical response to nuclear accidents in Asia	NSC, IAEA, WHO	14
2010	NIRS-KIRAMS Joint Seminar on Radiation Emergency Medicine 2010	KIRAMS	1
2011	NIRS-IAEA Workshop on Cytogenetic Biodosimetry for Asia 2011 & NIRS-ISTC Workshop on Cytogenetic Biodosimetry	IAEA, ISTC, WHO	16
2011	NSC/NIRS Workshop on Medical Response to Nuclear Accidents in Asia	NSC, IAEA	13
2011	Symposium on the accident of TEPCO Fukushima Dai-ichi NPS	REAC/TS, IAEA	11
2012	The NIRS workshop on medical response to radiation accidents in Asia 2012 -Lessons learned from TEPCO Fukushima NPP accident-	IAEA	12

IAEA, International Atomic Energy Agency; KIRAMS, Korea Institute of Radiological & Medical Sciences; NSC, Nuclear Safety Commission; ISTC, International Science and Technology Center; WHO, World Health Organization; REAC/TS; Radiation Emergency Assistance Center/ Training Site; REMPAN, Radiation Emergency Medical Preparedness and Assistance Network

The plan of educational program for Certified Nurse Specialist in radiological nursing at Hirosaki University

Yoshiko Nishizawa[1], Yuka Noto[2], Chieko Itaki[2], Toshiko Tomisawa[1], Ruriko Kidachi[3] Tomoko Ichinohe[1], Seiko Kudo[2], and Hideaki Yamabe[1]

[1] *Department of Health Promotion, Division of Health Sciences*
[2] Department of Disability and Health, *Division of Health Sciences*
[3] *Department of Development and Aging, Division of Health Sciences*
Hirosaki University Graduate School of Health Sciences, Hirosaki, Japan

Abstract. The Hirosaki University Graduate School of Health Sciences has worked toward "the development of human resources for radiation emergency medicine" with support from the Japanese Ministry of Education, Culture, Sports, Science and Technology and has accumulated the knowledge and practical ability to educate medical staffs and university students. As a result, we were able to dispatch support staffs to Fukushima following the Fukushima Daiichi Nuclear Power Plant accident. It was disclosed that there were few medical personnel who could support the evacuated inhabitants and treat them properly at the medical institution in the area of the nuclear accident. Therefore, it is necessary to educate medical specialists with higher-level knowledge on radiology, especially nurses who play a central role with physicians in treating patients exposed to radiation and carry out mental health care for the inhabitants. Radiological medicine has various roles including those in radiological examinations and cancer therapy. Therefore, nurses capable of doing consultations for and managing medical radiation exposure are required. However, there are very few subjects on radiation in nursing education, and continuing-education courses are not offered after graduation in Japan. Therefore, it is necessary to educate nurses in Master's degree programs who possess high assessment abilities and practical skills. We planned an educational program for Certified Nurse Specialist in radiological nursing based on our previous experience with a human resources development project focusing on radiation emergency medicine. As a result, we can expect to raise the basic knowledge on radiation for nurses, to improve the practical abilities of the nurses, to ensure proper training for radiation emergency medicine, and to palliate the anxiety of the suffering inhabitants after a nuclear accident or disaster.

Key Words: educational program, Certified Nurse Specialist, radiological nursing

[1] Corresponding to: Yoshiko Nishizawa, Professor, Hirosaki University Graduate School of Health Sciences, 66-1, Hon-cho, Hirosaki, 036-8564, Japan

Introduction

This year, we reorganized the Radiation Emergency Medicine Committee at the Graduate School of Health Sciences by bringing together the Certified Nurse Specialist in Radiological Nursing group. This committee consists of seven university nursing teachers. On behalf of this committee, I would like to introduce the plan of an educational program for Certified Nurse Specialist in radiological nursing (Figure 1).

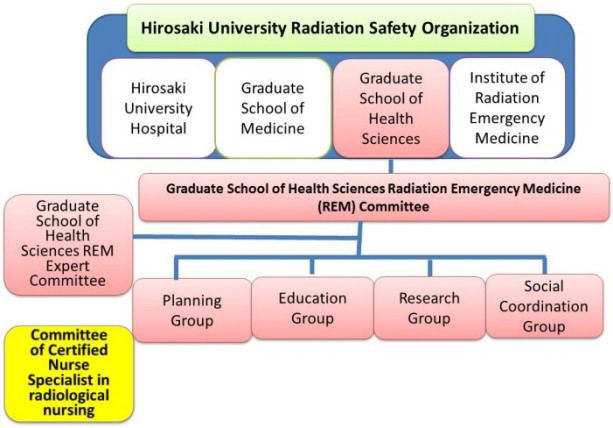

Figure 1 Project Organization and Activity

1. The process for the education of a certified nurse specialist in radiological nursing

From 2008, the Hirosaki University Graduate School of Health Sciences has worked toward “the development of human resources for radiation emergency medicine” with support from the Japanese Ministry of Education, Culture, Sports, Science, and Technology, and has accumulated the knowledge and practical ability to educate medical staffs and university students.

During the first year, we had little knowledge about radiation and limited techniques for educating medical staffs and university students about radiation. Even after receiving training, there were few chances to use it, and our knowledge and skills faded quickly. However, we continued learning about radiation while we wondered if and when we would actually utilize our knowledge and skills.

On March 11, 2011, The Great East Japan Earthquake disaster occurred, followed by the Fukushima Daiichi Nuclear Power Plant accident.

We were able to dispatch support staffs to Fukushima following the Fukushima Daiichi Nuclear Power Plant accident according to our knowledge and practical experience in dealing with radiation. We dispatched 567 talented persons to Fukushima as the Hirosaki University Radiation Exposure Research Team and as members of the Temporary Home Visit Project for evacuated residents.

Many inhabitants around the Fukushima Daiichi Nuclear Power Plant were required to evacuate. Moreover, evacuees had much anxiety because information about radiation was not transmitted quickly and accurately. Therefore, it was necessary to assist evacuees appropriately, and to reduce their anxiety, even if only a little.

However, it was disclosed that there were few medical personnel who could support the evacuees and treat them properly at the medical institution in the area of the nuclear accident. Therefore, it is necessary to educate medical specialists with higher-level knowledge on radiology, especially nurses who play a central role with physicians in treating patients exposed to radiation and carry out mental health care for the inhabitants.

On the other hand, radiological medicine has various roles including those in radiological examinations and cancer therapy. Therefore, nurses capable of doing consultations for and managing medical radiation exposure are needed.

2. The present state of radiological nursing education in Japan

For the basic 3-year nursing course in Japan, the students are required to take 97 units according to the rules of the public health nurse, midwife, and nurse training schools.

However, there are very few subjects on radiation in this basic nursing education. There are only 1 to 2 lectures about radiation in liberal arts and specialized subjects on nursing.

The full curriculum for basic nursing education makes it impossible to add a new subject, although the importance of radiation nursing is recognized.

However, we introduced a course, "Introduction to Basic Radiation," for the first-year undergraduate liberal art students as result of this project at Hirosaki University. This is a required course and is worth 1 unit of study. Another lecture about the risks associated with radiation exposure is a specialized subject, "Medical Risk Management," for third-year students. This is a required subject and is worth 1 unit. However, there are few universities that offer courses in these subjects, and continuing-education courses are not offered after graduation in Japan.

It is difficult to solve these problems only by revising the basic nursing education curriculum. Individuals trained as a Certified Nurse Specialist in radiological nursing who can assist patients and doctors comprehensively are essential. These nurses have specialized knowledge and skills regarding radiation, and they are associated with not only radiation practice and radiation emergency medicine, but also radiation protection and community medicine. In the future, it will be necessary to educate talented, sophisticated individuals who possess assessment ability and who can immediately conduct nursing care and intervention at the Masters level.

3. The present state of Certified Nurse Specialist and the Certified Nurse education in Japan

A Certified Nurse Specialist is an authorized nursing professional that possesses high nursing ability in a particular nursing field. A Certified Nurse Specialist plays the following roles in the professional nursing field.

1) They engage in confluent comprehensive nursing for individuals, families or groups (Practice).
2) They perform educational functions to improve the care activities of nursing professionals (Education).
3) They conduct consultations for the care providers, including nursing professionals (Consultation).
4) Because necessary care is offered smoothly in the professional nursing field, certified nurse specialists coordinate people engaged in health care welfare (Coordination).
5) They also conduct research activities to gain technical knowledge and develop technical improvements (Research).
6) They also coordinate people concerned about ethical problems (Ethical Coordination).

There are now 11 fields in Japan for Certified Nurse Specialists. Unfortunately, the field of radiological nursing has not yet been established. Therefore, we are submitting proposals and filing paperwork for the field of radiological nursing. It is necessary to obtain a Masters-level education, about a 2-year program, to become a Certified Nurse Specialist. Moreover, after the basic nursing education, having 5 years of clinical experience, as well as three or more years of clinical experience in the field of professional nursing are required. They must finally pass the authorized examination conducted by the Japan Nursing Association.

It is a transitional period now for the education of Certified Nurse Specialists in Japan. There are two courses of study. The conventional course has 26 units. The other course comprises 38 units in which students learn physical assessment, clinical pharmacology, and pathologic physiology. This particular course reinforces high assessment and practical abilities. However, all courses will comprise 38 units by 2021, because of the demand for the advancement of Certified Nurse Specialists.

There is a Certified Nurse system in Japan, with 21 fields currently. The conditions of the clinical experience for this system are similar to those of the Certified Nurse Specialist program; however, receiving six or more months and 615 hours of training at an organization that is authorized by the Japan Nursing Association is required. Certified Nurses are not required to have postgraduate education. The fields include "Cancer Chemotherapy Nursing," "Cancer Pain Management Nursing," "Emergency Nursing," and "Radiation Therapy Nursing," among others, and specialized activities have been developed in each field.

Figure 2 shows the similarities and the differences between the specialties on radiation between Certified Nurse Specialists and Certified Nurses.

The specialties of Certified Nurse Specialists in radiological nursing that we planned partly overlap with these types of occupations, but they include all specialties.

The main specialty of conventional radiation nursing is the care of patients who have undergone radiation therapy in medical facilities. Moreover, the specialty of "Certified Nurse in Radiation Therapy Nursing", which started in 2009, includes nursing intervention for cancer patients that are undergoing radiotherapy, instruction and consultation to nursing staffs, and collaboration with other staff members.

It was found from an investigation by members of this committee, that although nursing intervention for the patients who underwent radiotherapy was practiced, the case study meeting, the promotion of the measures for radiation protection, and the preparations for radiation emergency medicine in their institution were not carried out. It was also determined that there were few subjects about radiation nursing in the syllabus for Certified Nurse Specialist in Cancer Nursing course.

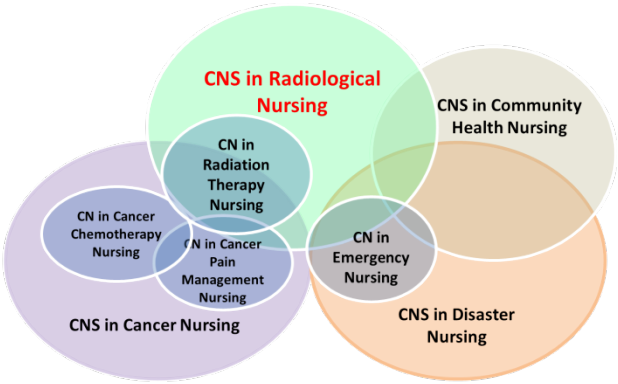

Figure 2 Association with nursing specialties

4. The plan of the educational program for Certified Nurse Specialist in radiological nursing at Hirosaki University

We utilized the results of "the development of human resources for radiation emergency medicine," and planned the educational program for Certified Nurse Specialist in radiological nursing who can perform excellent comprehensive nursing intervention for the radiation nursing as a foundation for the extensive knowledge that is needed for radiation therapy, accidents, and disasters.

"Radiological nursing" is defined as nursing care that is offered during radiographic examinations, radiation therapy, and radiation emergency medicine. A 38-unit course for Certified Nurse Specialists is planned at Hirosaki University. We consider the following six functions essential for Certified Nurse Specialists to accomplish in the plan.

4-1. Aim of education

1) The Certified Nurse Specialist utilizes their expertise in radiation and conducts precise clinical assessment for radiation therapy and radiation emergency medicine. (Practice)
2) The Certified Nurse Specialist utilizes their knowledge and skills as demanded by radiation therapy and radiation emergency medicine and can perform excellent comprehensive nursing intervention for individuals and families. (Practice)
3) The Certified Nurse Specialist can educate or consult medical personnel about the knowledge and skills that are necessary for radiation therapy and radiation emergency medicine. (Education/Consultation)
4) The Certified Nurse Specialist can coordinate the medical radiation exposure and management of the medical staffs necessary for radiation therapy and radiation emergency medicine. (Coordination)
5) The Certified Nurse Specialist makes precise decisions for ethical problems about radiation nursing and can support radiological nursing for solutions. (Ethical Coordination)
6) The Certified Nurse Specialist conducts nursing research to contribute to expertise in radiation nursing and technical improvements. (Research)

4-2. Common subjects for radiological nursing

We also consider the following contents as common subjects for radiological nursing.

a) Radiation expertise
   Learning about the physical and biologic effects of radiation, radiation protection, laws, and regulations. This is becoming the foundation of nursing intervention in radiation therapy.
b) Radiation therapy expertise
   Learning the expertise of radiation therapy, radiation emergency medicine, the acute and delayed somatic effects of radiation, medical radiation exposure, and occupational exposure.
c) Assessment of health problems
   Learning the knowledge, skills, and theories that are necessary to assess and diagnose the health problems in individuals undergoing radiation therapy and radiation emergency medicine.
d) Nursing intervention
   Learning the knowledge and skills to perform comprehensive nursing intervention for individuals undergoing radiation therapy and radiation emergency medicine, to educate or consult medical personnel, and to coordinate the medical radiation exposure and management of the medical staffs.

4-3. Practice

The Certified Nurse Specialist cultivates six types of abilities; prominent practice, education, consultation, cooperation/coordination, research, coordination of ethical problems as a specialist, and learns the role as a specialist in radiological nursing. We planned the following content for the Practice subject.

a) Practice by the Certified Nurse Specialist includes the training of medical staffs that provide radiation therapy
b) Practice by the Certified Nurse Specialist includes the creation of a training record, report or a research paper.

4-4. CNS common subjects; Common subjects, groups A and B

The students choose eight units or more in consideration of the role as a Certified Nurse Specialist in radiological nursing from among common subjects in group A (nursing education theory, nursing management theory, nursing theory, nursing research, consultation theory, nursing ethic, and nursing policy theory).

The students also choose six units from among common subjects in group B (clinical pharmacology, physical assessment, and pathologic physiology) as required subjects for certified nurse specialists. The total number of units is at least 14.

5. The prospective matters for certified nurse specialists in radiological nursing

We can expect to raise the basic knowledge on radiation for nurses, to improve the practical abilities of the nurses, to ensure proper training for radiation emergency medicine, and to palliate the anxiety of the suffering inhabitants after a nuclear accident or disaster.

The nurse who completes the Certified Nurse Specialist in radiological nursing course can act as a nursing manager or a nurse of medical facilities for radiation therapy and radiation emergency medicine.

We can expect that the number of nurses who can assist with radiation emergency medicine will increase steadily by educating Certified Nurse Specialists in radiological nursing as a foundation of radiation nursing.

6. The future prospects for the advancement of radiological nursing

We will be active as a scientific base in the Radiological Nursing Society of Japan because we will strengthen the speciality of the field of certified nurse specialist in radiological nursing. The 1st Annual Meeting, with the main theme "Towards the Advancement of Radiological Nursing," was held in 29 Sept., 2012. There was an announcement about "the need for the certified nurse specialist in radiological nursing and a prospective role" by three symposiasts, and an active discussion was conducted with participants.

We will disseminate our information both domestically and internationally in the near future, with the intention of advancing radiological nursing, by collaborating with the Japanese Society for Therapeutic Radiology and Oncology (JASTRO).

We hope to receive support and cooperation from both domestic and international nursing or radiology professionals

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The 2012 Hirosaki University International Symposium

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