放影研 RERF update

Summer
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News and Views

Radiation Effects Research Foundation

Hiroshima and Nagasaki, Japan

Table of Contents

Cover photographs: (left) Public lecture event for citizens in Hiroshima; see page 4
(right) Field investigation portion of RERF workshop on shielding (in front of an air-raid shelter on the grounds of Yamazato Elementary School); see page 15

This newsletter is published twice a year by the Radiation Effects Research Foundation (RERF; formerly the Atomic Bomb Casualty Commission), established in April 1975 as a private, nonprofit Japanese foundation. It is supported by the government of Japan through its Ministry of Health, Labour and Welfare and by the United States through its Department of Energy (DOE), in part by DOE contract DE-HS0000031 with the National Academy of Sciences. RERF became a public interest incorporated foundation on April 1, 2012.

RERF conducts research and studies—for peaceful purposes—on medical effects of radiation and associated diseases in humans, with a view to contributing to maintenance of the health and welfare of the atomic-bomb survivors and to enhancement of the health of all humankind.

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Editorial Policy

Contributions to RERF Update *receive editorial review only and do not receive scientific peer review. The opinions expressed herein are those of the authors only and do not necessarily reflect RERF policies or positions.*

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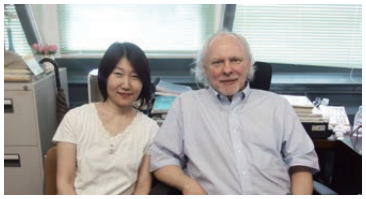
From the Editors

Welcome to the first issue of *Update* for 2014. We had a beautiful cherry blossom (*sakura*) season earlier this year, at the end of March, and as I began this, in May, the azaleas (*tsutsuji*) were blooming and it was time for Golden Week and the Hiroshima Flower Festival. But time has passed and now it is the season of hydrangeas (*ajisai*), at the beginning of June, with the rainy season not far off! We had a mild and generally very nice spring, and it has only now begun to heat up. As usual, we have a full issue of *Update*, with a complement of science articles, a number of introductions of new staff, and other topical news, including reports on the annual meeting of the Scientific Advisory Committee and several recent workshops held at RERF. We are pleased in this issue to welcome a new Technical Editor, Tomoe Sugiyama, who has worked in the Public Relations and Publications Office (former Editorial and Publications Section) at RERF since 2001. She has been helping with previous editions of *Update* and other RERF publications, and is well known as a capable and effective member of the staff—we look forward to working with her in her new role.

One of the things we are thinking about here as we prepare this issue is the increasing transition from print media to online media. We are considering, for example, whether we might try to include materials in the online edition of *Update* that are not feasible to include in the printed edition. With that in mind, you may see a survey of our readers with respect to this change in a future issue of *Update*.



Harry M. Cullings
Editor-in-Chief

Tomoe Sugiyama
Technical Editor

Report on the 41st Scientific Advisory Committee Meeting, 2014

The 41st Scientific Advisory Committee (SAC) review of RERF's research activities was held on March 3–5, 2014, at our Hiroshima facility. The SAC consists of 10 scientists, five each from Japan and the United States. The co-chairs this year were Dr. Marianne Berwick and Dr. Yoichi Gondo. New members of the SAC are Dr. Michiaki Kai of Oita University of Nursing and Health Sciences, Dr. Tomotaka Sobue of the Graduate School of Medicine, Osaka University, and Dr. Anatoly Dritschilo of Georgetown University School of Medicine. They replaced Dr. Kiyoshi Miyagawa, Dr. Kazuo Tajima, and Dr. John J. Mulvihill, respectively, to whom we owe a debt of gratitude for their outstanding, dedicated service to RERF.

It was decided to have more focused reviews of three departments this year: the departments of Epidemiology, Statistics, and Information Technology. To aid the focused reviews, three additional experts were appointed temporarily to the SAC—Dr. Scott Davis, University of Washington (Epidemiology), Dr. Toshimitsu Hamasaki, Osaka University (Biostatistics), and Dr. Divesh Srivastava, AT&T Laboratories (Information Technology). Their insights were very valuable, and it was a great pleasure for us to work with these excellent, perceptive scholars.

RERF Chairman Dr. Toshiteru Okubo opened the meeting with a warm welcome to all. In his report he emphasized how important the SAC's work is to the staff of the RERF. He introduced Dr. Robert L. Ullrich, who was appointed as Associate Chief of Research at RERF as of November 2013. One serious issue that was raised by Chairman Okubo is the need to restructure RERF in order to maintain high-quality science while decreasing the number of overall staff. The rate of attrition mandated by the Japanese government is approximately five workers per year. At this time, there is less than half the staff number that was present at the time of RERF's inauguration in 1975.

Next, Vice Chairman Dr. Roy E. Shore spoke on RERF responses to last year's SAC recommendations and on new research achievements. In

accordance with the 2013 SAC recommendations, RERF has published papers in a number of fairly high impact international journals; published a workshop report on radiation and cardiovascular disease[1]; worked to develop collaborations and affiliations to enhance the global impact of RERF; continued to serve in advisory roles with regard to Fukushima health issues; and increased its training and mentoring of young investigators.

Dr. Shore followed with a description of RERF's major accomplishments during 2013. Among the research achievements were the holding of the International Low Dose Workshop at RERF in December 2013 and multiple publications. Papers that examined radiation effects included those on radiation risk of soft-tissue sarcomas[2]; radiation, immune genes, and risk of gastric cancer[3] or liver cancer[4]; radiation, obesity, and colon cancer risk[5]; radiation, chronic kidney disease, and cardiovascular risk factors[6]; radiation and noncancer respiratory diseases[7]; radiation and glaucoma[8]; and fetal irradiation and chromosome aberration frequency in blood cells compared to mammary cells.[9] He further described the crucial ongoing efforts to consolidate, integrate, and support databases, sample collection, and storage. These efforts were later highlighted in presentations regarding the Information Technology Department and the newly created Biosample Center. Finally, the transparency of the research protocol (RP) review process has been increased, and the Research Priority Committee has been established to provide information on the priority of various research projects, to aid in management decisions.

RERF scientists have continued their active involvement on international radiation-protection and risk-assessment committees, such as the ICRP (International Commission on Radiological Protection), UNSCEAR (United Nations Scientific Committee on the Effects of Atomic Radiation), and the NCRP (U.S. National Council on Radiation Protection & Measurements). They also gave a number of invited lectures abroad and have numerous collaborations with investigators at various institutions in Japan, Europe, America, and Asia.

The SAC provided a written report of its recommendations; a brief statement of the key general recommendations is as follows:

- The justification, prioritization, and overall quality of some of the current research programs are a concern. RPs should assess clearly articulated testable hypotheses that contribute to the overall goals of RERF. Working Groups are encouraged to help prioritize the multiple demands and development of integrated science at RERF.
- Plans for the use of technology (whole genome sequencing, metabolomics, etc.) and bioinformatics resources are encouraged, with prioritization to address critical RERF mission-specific studies.
- The multiple genome-wide studies, next generation sequencing studies, and other high dimensional data analyses require prioritization, with thoughtful planning and coordination among departments.
- Both the new Biosample Center and the data management capacity of the Information Technology Department are critical for development toward becoming a global Center of Excellence for radiation research.
- The development of a database for access to sample identification, location, and other information, which is underway, is critical for biosample-data integration and must be supported by all departments.
- The complete data on every subject ever involved with ABCC-RERF research should be retrievable with ease.
- More high-quality publications are essential for the continued success of RERF. The plans outlined in the Future Plans will assist in this effort.
- Efforts to obtain additional competitive external funds have increased, and the SAC encourages this activity.
- The publication of the "black rain" data represents an opportunity for public education on the strengths and weaknesses of the ability of science to make conclusions about environmental links to health effects.
- The Future Plans are critical to implement, particularly the aspect regarding development of working groups to integrate hypotheses and studies among departments.
- The SAC commends the ongoing efforts related to the holding of seminars and fostering of interactions within RERF. It is suggested that a formal mentoring system be developed to help new investigators at RERF in their professional development.

Selected highlights of the recommendations to the departments with the primary focus include:

- Epidemiology Department: Work closely with colleagues within or outside of RERF to design and implement new studies or additions to ongoing studies that have clear aims and that make maximum use of the Epidemiology Department's stored tissue samples in an efficient manner.
- Statistics Department: The work on non-parametric smoothing in dose-response estimation, especially as it applies to low-dose risk estimation, is new and interesting and is encouraged. The continuation of training and

development of genomic data analysis skills is strongly encouraged, as these skills will increasingly be required in the near future.

- Information Technology Department: RERF has outstanding data sets, but some are not always widely known or accessible to RERF researchers, including old legacy data sets and analytic data sets used in RERF published reports. Meta-data about ABCC-RERF's data sets, including documentation on proper usage, should be improved and made searchable with user-friendly interfaces.

In summary, the SAC highlighted the unique role RERF plays in determining radiation risks and the high continuing potential for studies that make important contributions. The committee urged the prompt development and publication of new results regarding issues of scientific and public-health concern and suggested ways to address new technological challenges in the basic sciences.

RERF Scientific Advisors

Dr. Marianne Berwick, Co-chairperson, Distinguished Professor, Department of Internal Medicine and Department of Dermatology, The University of New Mexico

Dr. Yoichi Gondo, Co-chairperson, Team Leader, Mutagenesis and Genomics Team, RIKEN BioResource Center

Dr. Kazuo Sakai, Director, Research Center for Radiation Protection, National Institute of Radiological Sciences

Dr. Tomotaka Sobue, Professor, Department of Social and Environmental Medicine, Graduate School of Medicine, Osaka University

Dr. Shunichi Yamashita, Director, Vice President, Nagasaki University

Dr. Michiaki Kai, Member of the Board of Trustees, Professor, Environmental Health Science, Department of Health Sciences, Oita University of Nursing and Health Sciences

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Dr. David G. Hoel, Distinguished University Professor, Department of Medicine, Medical University of South Carolina and Principal Scientist, Exponent, Inc.

Dr. Michael N. Cornforth, Professor and Director of Biology Division, Department of Radiation Oncology, The University of Texas Medical Branch

Dr. Anatoly Dritschilo, Professor and Chairman, Department of Radiation Medicine, Georgetown University School of Medicine

Special Scientific Advisors

Dr. Scott Davis, Professor and Chairman, Department of Epidemiology, School of Public Health and Community Medicine, University of Washington

Dr. Toshimitsu Hamasaki, Associate Professor, Department of Biomedical Statistics, Osaka University Graduate School of Medicine

Dr. Divesh Srivastava, Executive Director, Database Research Department, AT&T Labs Research

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Participants of the 41st Scientific Advisory Committee meeting held at Hiroshima RERF

Hiroshima RERF Holds Its Fourth Public Lecture

RERF in Hiroshima held its fourth public lecture for citizens in Memorial Hall of the Hiroshima Peace Memorial Museum, from 14:00 to 16:30 on Saturday, November 30, 2013. The lecture series is designed to enhance communication by conveying information to the general public, including A-bomb survivors and their offspring, about results from RERF's long-standing research on A-bomb radiation health effects.

This most recent public lecture event, titled "Considering Uses for RERF's Stored Samples," was held to obtain feedback from the public about RERF's Biosample Center as well as about possible uses, including in collaborative research, for the center's biosamples. The new organization, established in April 2013, initiated full-scale operations in April 2014. Arranged as a panel discussion, the event was attended by more than 160 people.

The public lecture began with opening remarks by RERF Executive Director Takanobu Teramoto, who offered a glimpse of work and life atop Mt. Hijiyama, where the RERF Hiroshima Laboratory is located, and expressed his gratitude for the participation in the lecture, the aim of which was communication between RERF and the public. Chairman Toshiteru Okubo then explained, among other topics, his belief that the best way to repay the cooperation of the A-bomb survivors of Hiroshima and Nagasaki is full utilization of the many biosamples the foundation has received

Dr. Kazunori Kodama, Chief Scientist and Director of the Biosample Center, giving a lecture during the fourth public lecture held in Hiroshima

from the survivors for research into A-bomb health effects as well as for medical research including into the effects of other radiation exposures.

Presentations by two speakers were then featured, followed by a discussion among the invited panelists. The first speaker, Chief Scientist and Director of the Biosample Center Kazunori Kodama, elaborated on the "Current Status and Uses of RERF's Stored Samples," explaining in detail about the A-bomb survivor samples stored at RERF and the outline of the Biosample Center. The second speaker, Dr. Toshiya Inaba, Director, Research Institute for Radiation Biology and Medicine, Hiroshima University, spoke on the theme "Role of Stored Samples in Radiation Health Effects Research." Dr. Inaba touched on the challenging question of who ultimately owns blood and cancer cells as well as other biosamples that are used in research.

In the panel discussion, the seven panelists—comprising Chairman Okubo and the aforementioned two speakers; Dr. Toshimasa Asahara, President, Hiroshima University, who chaired the discussion; Mr. Sunao Tsuboi, Chairman, Hiroshima Prefectural Confederation of A-bomb Sufferers Organizations; Dr. Masaya Yamauchi, Director of Public Relations and Research, Hiroshima University Hospital; and Mr. Kenji Namba, Chairman, Japan Congress of Journalists Hiroshima—gave their views on the significance of RERF's biosamples. Dr. Yamauchi expressed his desire for assurances of transparency in RERF's approval process for collaborative research proposals. Mr. Namba mentioned his concerns regarding protection of personal information and strict application of guidelines when such collaborative research is conducted. Mr. Tsuboi, an A-bomb survivor, spoke on his support for the idea that the biosamples should be used in collaborative research to learn more about the health effects of radiation.

In the question-and-answer session following the panel discussion, a broad range of opinions were expressed, including doubts about how RERF would be able to continue promoting radiation effects research in the face of a shortage of younger researchers entering the field, the feeling that there is a need for involvement of A-bomb survivors, for example, in RERF's ethics committee, and full-fledged support for RERF to broaden its scope of research by allowing collaborative studies using its biosamples.

The event concluded with closing remarks by Vice Chairman Roy E. Shore, who requested public understanding of the need for RERF to allow use of its stored biosamples in collaborative research to enhance worldwide understanding of radiation's health effects.

Nagasaki RERF Also Holds Fourth Public Lecture

The fourth public lecture event for Nagasaki citizens was held in the Nagasaki A-bomb Museum, from 14:00–16:30 on Saturday, February 22, 2014, under the same theme as in Hiroshima, "Considering Uses for RERF's Stored Samples." Offered as a panel discussion, the event was attended by more than 100 people.

Following opening remarks by RERF Executive Director Takanobu Teramoto, RERF Chairman Toshiteru Okubo explained the aims of that day's public lecture. Then, as the first speaker of the two featured presentations, RERF Chief Scientist and Director of the Biosample Center Kazunori Kodama explained the details of the A-bomb survivor samples stored at RERF and the overview of the Biosample Center under the topic "Current Status and Uses of RERF's Stored Samples." The second speaker, Dr. Yuji Nagayama, Director of the Atomic Bomb Disease Institute, Nagasaki University, spoke on the theme "The Role of Stored Samples in Radiation Health Effects Research." Dr. Nagayama commented that, although A-bomb survivors are the donors of samples used for A-bomb effects research and should ideally be the beneficiaries of the research achievements, such benefits will ultimately be granted to the next generation due to the extensive time necessary to conduct research. He also explained in a straightforward manner the guidelines and procedures concern-

Fourth public lecture held in Nagasaki

ing the handling of biosamples stored at Nagasaki University.

A panel discussion following the above keynote lectures included six panelists: the two speakers, Chairman Okubo, Dr. Shigeru Katamine (President, Nagasaki University, who chaired the discussion), Mr. Koichi Kawano (Chairman, A-bomb-exposed Liaison Council, Nagasaki Prefecture Peace Movement Center), and Mr. Nobufusa Baba (Chief, Executive Editorial Bureau and Chief Editorial Writer of Nagasaki Shimbun), who all gave their views on the significance of RERF's biosamples. Mr. Baba expressed his opinion about RERF from social and historical viewpoints, while Mr. Kawano commented on RERF's role from the standpoint of A-bomb survivors and on the historical and social significance of the biosamples.

In the Q&A session with the audience, many opinions were expressed, including requests that studies using biosamples should be conducted to benefit A-bomb survivors; that RERF should contribute to the relief of A-bomb survivors through its various types of research as well as advocate for the abolition of nuclear weapons; and that efforts should be made to increase RERF's visibility and reliability.

The event concluded with closing remarks by Mr. Teramoto, who expressed his gratitude for the audience's participation in the lecture and valuable opinions expressed by the participants.

RERF Establishes Its Facebook Page

On March 3, 2014, RERF marked its first use of 'social media,' by establishing a Facebook page (Facebook.com/Radiation Effects Research Foundation).

RERF has for years used its web page to communicate with the public about information related to the health effects of radiation exposure from the atomic bombings of Hiroshima and Nagasaki. The area of public affairs, however, has recently seen a dramatic rise in use of different so-called social media platforms, which allow the provider of information and the user to communicate with each other more readily.

Against this backdrop, RERF decided to enter the world of social media using Facebook, with the aim of reaching a broader audience, including younger users, by posting more basic information on the science of radiation health effects and non-scientific news more quickly than is possible on its homepage. The Facebook page is updated weekly, with timely stories involving Fukushima and historical looks at Chernobyl, articles about findings from ABCC-RERF's studies, and reviews of relevant books.

We encourage readers of RERF's *Update* to 'Like' us on Facebook, and by so doing gain access to materials posted there and engage in discussions with followers on such topics as the atomic bombings, radiation and its health effects, and information about nuclear accidents throughout the world.

RERF's recently established Facebook page

PR Specialist Invited to Speak at Hiroshima RERF

On February 7 of this year, in an effort to enhance its public relations acumen, RERF invited a public relations specialist and former journalist to RERF to advise and lecture to interested RERF staff on effective communication with the public and the media in terms of conveying RERF's research results to local and worldwide audiences.

Dr. Masaya Yamauchi, Director of Public Relations and Research (former Assistant Chief Editorial Writer for the Chugoku Shimbun newspaper),

Hiroshima University Hospital, first spoke to a small group of about 12 staff who are directly and indirectly involved in RERF's public relations activities, including five members of the Public Relations and Publications Office. Dr. Yamauchi began the session by asking questions about the issues faced at RERF when communicating with the public and the media, and in response, he provided examples of his own experiences. His insightful advice was based on many years working as a member of the media at the Chugoku Shimbun and in his more recent career at the Hiroshima University Hospital.

After the smaller session, Dr. Yamauchi greeted a large audience at the RERF Auditorium (the talk was broadcast to Nagasaki RERF by teleconference), where he gave a presentation titled "Communicating with the Public and the Media." The presentation focused on ABCC-RERF's public relations history and recent activities, as well as examples of public relations approaches used at the Hiroshima University Hospital. In the talk, Dr. Yamauchi touched on some of the image-management missteps made by ABCC-RERF and listed some of the criticisms the organization has endured. But he also encouraged RERF to continue what he considered to be its important public outreach efforts, emphasizing in particular the public lecture series, in which Dr. Yamauchi participated as a panelist in Hiroshima on November 30, 2013.

A question-and-answer session followed his presentation, with most of the questions involving the manner in which RERF can more effectively transmit its message to the public, including queries about use of social media.

Dr. Masaya Yamauchi, Director of Public Relations and Research, Hiroshima University Hospital, speaking to RERF staff

Dr. Yamauchi's public relations savvy and his unbiased delivery of thoughtful advice provided new ideas about communicating with the public and bolstered the motivation of the public relations staff. RERF hopes for a continued relationship with Dr. Yamauchi as it works to enhance its skills in communicating complex scientific information to the public and the media.

Students of Tokyo Institute of Technology Visit Hiroshima RERF

On the morning of February 28, 2014, 51 students from the Academy for Global Nuclear Safety and Security Agent of the Tokyo Institute of Technology—about two-thirds of whom were foreign-exchange students—paid a visit to RERF's Hiroshima Laboratory under the supervision of Dr. Masaki Saito, Director of the Academy and Professor at the Institute's Research Laboratory for Nuclear Reactors.

The visit to Hiroshima was part of the International Symposium and Seminar on Global Nuclear Human Resource Development for Safety, Security and Safeguards hosted by the Institute. In the RERF Auditorium, the group viewed RERF's promotional video and then sat in on a lecture by RERF Chairman Toshiteru Okubo in English titled "A long-term cohort study on the A-bomb survivors of Hiroshima and Nagasaki: Recent results and future outlook." The visitors then split up into three groups to tour RERF's facilities and listened to explanations that primarily focused on panels describing the Adult Health Study, displays regarding the Cytogenetics Laboratory's biodosimetry systems, and the Biosample Center.

Chairman Toshiteru Okubo, talking to students of the Tokyo Institute of Technology

U.K. Radiation Data Expert Speaks at Hiroshima RERF

Mr. Tony Riddell visited RERF Hiroshima on April 21, 2014, to give a lecture to RERF staff at the culmination of a family trip to Japan, which had included stopovers in Tokyo, Hakone, Kyoto, and Osaka.

Mr. Riddell has worked in some aspect of plutonium-related activities for 27 years. For the first seven years he worked in research and development for British Nuclear Fuels Limited, calculating reactor inventories and designing instrumentation. He then moved to health and safety work, and finally data management for epidemiological studies. He now serves as a data manager at the Epidemiology Department of the Centre for Radiation, Chemicals and Environmental Hazards, Public Health England.

In his lecture, Mr. Riddell gave a detailed review of the setting of radiation protection standards for exposure to plutonium. He reviewed the history of plutonium since its discovery in the early 1940s and the history of studies on its health effects, ending with a discussion of current epidemiological studies underway in worker populations in the U.S. and the former U.S.S.R.

Exposure to plutonium is very different from the direct exposure of the atomic-bomb survivors that is studied by RERF and estimated by Dosimetry System 2002 (DS02). Whereas the DS02 dose estimates involve external exposure to penetrating radiations (neutrons and gamma rays) received almost instantaneously, the typical hazard associated with plutonium involves internal exposure, predominantly to densely ionizing radiation in the form of alpha particles, some of which are received over extended periods of time. Plutonium may be relevant to the atomic-bomb survivors in that some researchers have raised concerns about possible inhalation exposure of survivors in the Nishiyama area of Nagasaki to plutonium that might have been contained in local radioactive fallout from the Nagasaki atomic bomb.

Several questions followed Mr. Riddell's presentation, after which he and his wife and son viewed RERF's introductory video and took an abbreviated tour of the RERF facilities, during which Mr. Riddell expressed particular interest in various aspects of radiation risk communication.

Mr. Tony Riddell, at left, accompanied by his family, taking a tour of Hiroshima RERF. At right is Mr. Jeffrey L. Hart, Chief, Public Relations and Publications Office.

Staff News

Kiyohiro Hamatani's term as Chief of the Cell Biology Laboratory, Department of Radiobiology/Molecular Epidemiology, expired on December 31, 2013. He was reappointed as Adjunct Specialist (research scientist) effective January 1, in order to continue research at the same laboratory. **Nobuko Sera**, Associate Senior Scientist of the Division of Medicine, Department of Clinical Studies in Nagasaki, resigned upon term expiration as of March 31 and assumed the position of Assistant Chief of the Department of Metabolism/Diabetes and Clinical Nutrition, Nagasaki University Hospital on April 1. She was appointed as Part-time Professional of the Department of Clinical Studies in Nagasaki effective June 1 and is expected to continue contributing to RERF research.

The following changes took effect on April 1. **Waka Ohishi**, Acting Chief of the Department of Clinical Studies, was promoted to the post of Chief of the department, **Ayumi Hida**, Assistant Chief of the Department of Clinical Studies in Nagasaki, was promoted to Acting Chief of the department, and **Yoshimi Tatsukawa**, Associate Senior Scientist of the Division of Health Examinations, Department of Clinical Studies, was promoted to Chief of the Division of Medicine. **Michiko Yamada**, Chief of the Division of Health Examinations, Department of Clinical Studies, assumed the position of Chief of the Division of Radiology related to reorganization of the department.

Two new research scientists were hired at RERF. **Kazumasa Sekihara** joined the Department of

Genetics as a research scientist as of December 1, 2013. **Mai Utada** joined the Department of Epidemiology as a research scientist as of April 1.

At RERF, employees who have worked for 10, 20, 30 years are commended for long service in April every year. In 2014, 16 employees—three employees for 30 years of service, five employees for 20 years, and eight employees for 10 years—were commended in Hiroshima. Among this group, the research scientists, commended for 10 years of service, were **Waka Ohishi**, Department Chief, and **Yoshimi Tatsukawa**, Chief of the Division of Medicine, Department of Clinical Studies, **Hiromi Sugiyama**, Research Scientist of the Department of Epidemiology, **Reiko Ito**, Research Scientist of the Cell Biology Laboratory, Department of Radiobiology/Molecular Epidemiology, and **Yasunari Sato**, Research Scientist of the Biochemical Genetics Laboratory, Department of Genetics. In Nagasaki, two general employees were commended for 30 years of service.

The abovementioned two new research scientists introduce themselves in the following section.

Kazumasa Sekihara, Ph.D.

On December 2, 2013, I joined RERF as a research scientist in the Cytogenetics Laboratory of the Department of Genetics, as a temporary employee supported by the MEXT (Ministry of Education, Culture, Sports, Science and Technology Grants-in-Aid for Scientific Research) *Kakenhi* funding.

After graduating from the School of Health Sciences, Faculty of Medicine, University of Tokushima, I received a master's degree from the Graduate School of Medicine, Hokkaido University, and a doctoral degree from the Graduate School of Medical Research, Shimane University. In the master's program, I conducted research on radiation treatment planning, taking into consideration biological effectiveness, under the supervision of Professor Hiroki Shirato (radiology). My doctoral research was on the combined effects of heat shock protein inhibitors and hyperthermia or radiotherapy. That work was supervised by Professor Nobue Uchida (radiation oncology, Tottori Prefectural Central Hospital), Professor Taisuke Inomata (radiation oncology), and Professor Mamoru Harada (immunology). My research work was published and prospects for obtaining my Ph.D. seemed good, and I therefore decided it was time to move on to the next step, which was looking for a research career in radiobiology. Around that time, I learned that RERF was recruiting a research scientist, and I applied for the position. With the help of Dr. Asao Noda, Assistant Chief, RERF Department of Genetics, I was fortunate to be hired.

I got off to a good start in the new workplace about six months ago, and since then I have been enjoying my research work every day at the Department of Genetics. I attribute all this to the kindness and warmth of the people at RERF, which I have experienced since I first applied for the position, and I am truly grateful for that. I am currently working hard on projects to develop green fluorescent protein (GFP) knock-in mice designed for detecting mutations, and to elucidate the mechanism for the repair of double-strand breaks in DNA after exposure to ionizing radiation. I am committed to doing my best to produce good research results during my two-year term at RERF.

This is my first time in Hiroshima since a school trip when I was in elementary school. I have become more familiar with the area since living here and cycling around the city. I like traveling alone, climbing mountains, and exploring places to eat, so I am looking forward to enjoying the nature, culture, and local cuisine of Hiroshima on my time off.

Finally, I feel privileged to be part of the prestigious RERF as one of its research scientists. Since I still have a lot to learn here, I have to ask everyone for continued help. I would really appreciate your ongoing support and guidance.

Mai Utada, Ph.D.

I am Mai Utada. On April 1, 2014, I joined the Department of Epidemiology at RERF as a research scientist. I completed my doctoral studies at the Division of Health Sciences, Osaka University Graduate School of Medicine in March 2014. When I was working on my graduation thesis as an undergraduate student, I was surprised to learn that cancer incidence figures in Japan are not actual figures but estimated ones. This surprising fact triggered my interest in cancer research. While in graduate school, I was fortunate to be given opportunities to get involved in work related to Nagasaki Prefecture Cancer Registry materials and 3-Prefecture Cohort Study data, among others. Through these opportunities, I became interested in engaging in cancer epidemiology research. In the past, I only analyzed well-organized data, and therefore I was rarely aware of the process of how such data were registered and followed up. At RERF, as I am learning the history of cohort studies and the work of the Tumor and Tissue Registry Office firsthand, I now clearly recognize that such data are avail-

able thanks to many people such as study subjects, research scientists, and staff members. Keeping this in mind, I would like to work on my research with further respect and sincerity.

I am from Kure city in Hiroshima prefecture. I attended Yasuda Girls Junior and High Schools in Hiroshima city. Now I am back home in Hiroshima after nine years. I feel very pleased and privileged to be a member of RERF, a foundation with a long and distinguished history, in Hiroshima. Since there are many things I need to learn here, I would really appreciate your continuous support and guidance.

Visiting Student Fellows

Tatjana Bogdanova (Training period: January 14–February 14, 2014)

At RERF, I studied as a visiting student fellow in the Radiobiology/Molecular Epidemiology Department under the guidance of Dr. Tomonori Hayashi.

I graduated from Riga Stradins University in 2011. Now I am working at the Stradins University hospital in the Department of Pathology as a resident pathologist, and also in the same department at the university as an assistant teaching pathological anatomy and pathological physiology to medical students.

I started my doctoral studies in October 2013. My research topic is "Novel morphological and molecular diagnostic parameters and prognosis in cases of gastric cancer."

I grew up in Ludza, which is located in the eastern part of Latvia. Ludza is a small but very beautiful and green country town with a relaxed lifestyle. After graduating from high school, I moved to the capital city of Latvia for my medical studies.

A nice country in which to reside, Latvia has intact and wild nature, as well as very cold and snowy winters and contrasting hot but short summers. Most people love Latvian fall, when trees have colorful leaves, and Sigulda is the most beautiful town in that season.

For a few years now, I have had a great interest in Asian culture, especially that of Korea. Asian countries are different from Europe's (language structure, family ties, traditions), and I find them somehow more exciting. I like to watch Asian movies and typical dramas, from which I learn more about Asian counties and their lifestyles.

I am very grateful for the chance I was given to be trained at RERF and to obtain new experience and knowledge in my area of research. In the course of my work at RERF, I became familiar with some methods for use in my specialty such as cancer tissue microdissection based on observation of cancer cell DNA mutations. Unfortunately, conducting this kind of research in my county requires special equipment.

In more general terms, I learned many things at RERF during the training period, such as how to carry out cell separation with whole blood samples and ROS analysis. I truly enjoyed learning about the multicolor FISH method, which requires that one be a skilled specialist with "good eyes" to find chromosome aberrations. It was very interesting and useful to have access to the data of such a big study cohort of A-bomb survivors, organized according to cancer incidence and radiation dose.

Despite the winter, I truly enjoyed my stay in Hiroshima. I visited wonderful places, like the Peace Memorial Museum, the A-bomb Dome, and Miyajima Island. I will cherish those great memories for the rest of my life.

Svetlana Lakisa (Training period: January 14–February 14, 2014)

As a visiting student fellow, I participated in the collaborative training program offered by RERF and the Hiroshima International Council for Health Care of the Radiation-exposed (HICARE). My home is Latvia—a beautiful country hidden in woods and green fields near the Baltic Sea. Despite the fact that Latvia is a small nation, we have a substantial cultural heritage, with many opportunities to experience this land of folk songs, expansive forests, and Old Riga architecture.

My main field is occupational safety and environmental health, as I continue my work as a researcher at the Institute of Occupational Safety and Environmental Health of Riga Stradins University. During the period 2005–2011, I completed my bachelor's degree studies in public health and obtained my master's degree in health care (both at Riga Stradins University).

I truly appreciated the opportunity to participate in RERF's training program. It was a great experience for me both professionally and in terms of personal growth. Many of the topics that we studied during the training program were completely new to me. Based on this training, I would like to help develop such a scientific/research culture in our research organizations in Latvia.

The amazing places, culture, history, and heritage of Japan were so exciting for me to see. This fantastic experience has the potential to change my life. Naturally, my view on the tragic events of the atomic bombings is different now. Hiroshima is a representation of the world's desire for peace, and I hope to continue pursuing this idea of peace.

I would like to express my gratitude to RERF and HICARE for providing me with the chance to participate in this training program. I am especially grateful to Dr. Tomonori Hayashi and his staff for their contributions to our training and for taking care of us during that unforgettable time.

Eun Kyoung Choi (Training period: February 3–28, 2014)

I am a molecular biology research scientist currently working at the Radiation Medicine Branch, National Cancer Center (NCC) in Goyang, Korea. I came to Hiroshima to participate in the international exchange program of RERF.

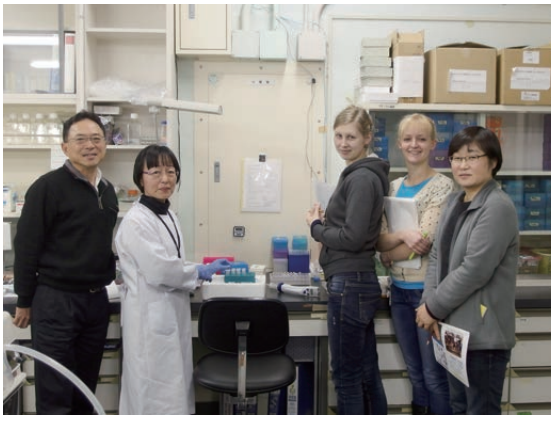
I received a Ph.D. in molecular cell biology from Chonnam National University. I continued to study as a post-doctoral researcher until 2011 at the same university, and then joined the laboratory of NCC in Korea, my current post. I study about the effects of radiation exposure and conduct research related to breast cancer using transgenic mice.

I am glad that the location of my first visit to Japan was the city of Hiroshima. What I knew about Hiroshima was that it had experienced the world's first atomic bombing. I did not know other details about the city. Thankfully, however, I was able to learn many things during my stay here. I would like to say thank you to RERF in Hiroshima and NCC in Goyang, Korea for offering me this wonderful opportunity to participate in this training program.

My first impression about the laboratory was that it is clean, quiet, and very well organized. Furthermore, the institute is located on a hill, which I felt made the environment even more serene. But it had something else that I only discovered during the course of my work. It was the passion with which people conducted their research. I met a lot of people at the institute. And I was surprised that they all showed great passion and strong belief about the research results they had generated over their careers.

While staying in the city, I visited Hiroshima Peace Memorial Park. I saw with my own eyes what happened to Hiroshima in 1945 through the park museum's exhibits and information. I had difficulty envisioning the scene of so many buildings and inhabitants of the city vanishing all at once. I was very surprised. But one of the things that surprised me the most is the resilience of the Japanese, who were able to rebuild their city amidst the debris left by the atomic explosion. I thought that they would have simply given up, but I came to notice that they have a powerful dynamic force behind those restoration efforts. Similarly, I felt that the RERF laboratory also has a mighty energy. I discovered the energy in the enormous amount of data and research results that have been accumulated at the laboratory regarding the atomic-bombing effects. I also felt the amazing strength inherent in the ongoing research. Needless to say, the training program was a great experience for me.

While at RERF in Japan I also met new people and learned about many different things. I see clearly how much it all meant to me, and the special value of such an experience in my life. Thank you once again for the opportunity to work on this interesting program. I want to express my gratitude to the staff of the Department of Radiobiology/Molecular Epidemiology (RME). I am particularly grateful to Dr. Tomonori Hayashi, Assistant Chief of RME, for his help and guidance during the course of the training session. Even after returning to Korea, I will never forget my experiences at RERF.



Dr. Eun Kyoung Choi, Ms. Svetlana Lakisa, Dr. Tatjana Bogdanova, from right, with Dr. Tomonori Hayashi (far left) and Ms. Yukari Morishita, in front of biosamples used in an experiment to measure intracellular reactive oxygen species

RERF International Symposium: The Evaluation of the Effects of Low-dose Radiation Exposure in the Atomic-bomb Survivors

Eric J. Grant, Assistant Chief
Department of Epidemiology, Hiroshima

On December 5–6, 2013, RERF hosted an international symposium titled "The Evaluation of the Effects of Low-dose Radiation Exposure in the Atomic-bomb Survivors." As radiation's effects at low-dose levels remain uncertain, this symposium was organized to refine the epidemiological and statistical methodologies for studies of low-dose radiation effects and to obtain important insights into the biological basis for such effects.

The aims and outline of the symposium were introduced by Dr. Kotaro Ozasa, Chief of the Department of Epidemiology, RERF, who described the Life Span Study (LSS) of atomic-bomb survivors as being a rich source of data for elucidating the health effects of ionizing radiation, while at the same time reminding the group that low-dose radiation effects remain uncertain. The symposium was organized against the backdrop of public concern regarding low-dose exposures, particularly after environmental exposures as seen in the case of the Fukushima nuclear power plant disaster.

On the opening day of the symposium, Dr. Richard Wakeford (University of Manchester) gave a presentation on low-level radiation epidemiology, in which he discussed the current status of the field and explained the difficulties in assessing low-dose radiation risks, and related study designs that are currently yielding helpful results. Dr. Wakeford's talk was followed by an introduction to the current status of low-dose effects research in RERF's LSS by Dr. Ozasa.

The following speakers then made presentations and led discussions aimed at refining methodologies for low-dose effects studies:

- Dr. Tomotaka Sobue (Osaka University) spoke about factors affecting cancer rates in Japan;
- Dr. John B. Cologne (RERF, Department of Statistics) touched on the potential for bias in risk estimates when non-confounding risk factors are ignored in nonlinear models;
- Dr. Eric J. Grant (RERF, Department of Epidemiology) talked about the data that have been collected by ABCC-RERF via questionnaires and interviews since the inception of the LSS that could be used to help model variations in background risks;
- Dr. Harry M. Cullings (RERF, Department of Statistics) spoke twice—the first talk described how the doses calculated by the current RERF dosimetry system depend on the level of detail available regarding shielding conditions at the time of exposure, and the second discussed exposure to residual radioactivity;
- Dr. Ritsu Sakata (RERF, Department of Epidemiology) discussed her recent findings on the effects of fallout rain on mortality and cancer incidence risks;
- Dr. Atsuko Sadakane (RERF, Department of Epidemiology) discussed work that had been done to estimate doses from diagnostic X rays and radiotherapy in the Adult Health Study (AHS) subjects. An LSS mail survey has recently been completed documenting diagnostic and therapeutic radiation exposures;
- Dr. Amy Berrington de González (U.S. National Cancer Institute) spoke about the online radiation-risk assessment tool RadRAT, which estimates the lifetime risk of radiation-related cancer with uncertainty intervals following a user-specified exposure history;
- Dr. Dale L. Preston (Hirosoft International Corporation) discussed the need to consider the choice of comparison group when investigating low-dose risks and the dose-response shape in the LSS data;
- Dr. Kyoji Furukawa (RERF, Department of Statistics) touched on improving dose-response estimation in radiation risk analysis using a Bayesian semi-parametric model; and
- Dr. Nobuhiko Ban (Tokyo Healthcare University) discussed how mathematical models and reality often diverge.

On the second day of the symposium, the topic of estimates of external doses in Fukushima was introduced by Dr. Seiji Yasumura (Fukushima Medical University), who spoke on the methods and results from the Basic Fukushima Health Management Survey, which is an attempt to estimate external radiation exposures for all of the 2.05 million who were Fukushima residents as of 11 March 2011. Various issues related to the biological basis of effects were then discussed by Dr. Ohtsura Niwa (Kyoto University), including the models used for radiation epidemiology and how they relate to mechanistic models. Dr. Nori Nakamura (RERF,

Consultant, Department of Genetics), picking up on the same theme, made the presentation "Breast cancer risk and age at the time of the bombing: A bridge between epidemiology and biology." And Dr. Preetha Rajaraman (U.S. National Cancer Institute), with the last presentation, spoke on the topic of individual differences in radiation sensitivity.

The symposium concluded with a final round-table discussion in which an overall summary of the gathering was delivered and suggestions about the future direction of RERF research by the participants were made.

In conclusion, many complex questions regarding the effects of low-dose radiation exposure remain unanswered. While RERF's LSS is a rich resource for studying the health effects of radiation exposure, we realized that the study cannot provide all of the answers sought by both the scientific community and the public. RERF must continue to publish its results while actively seeking collaborative studies involving other radiation-exposed cohorts. The objective of resolving these complex questions can only be accomplished via a collaborative effort based on a broad collection of expertise.

Participants of the RERF International Symposium: The Evaluation of the Effects of Low-dose Radiation Exposure in the Atomic-bomb Survivors, held at Hiroshima RERF

RERF International Workshop: The Storage and Utilization of Biological Samples for Studies on the Health Effects of Atomic-bomb Radiation

Misa Imaizumi, Chief
Division of Clinical Laboratories
Department of Clinical Studies, Nagasaki
Research Scientist, Biosample Center

On February 10, 2014, RERF hosted an international workshop, "The Storage and Utilization of Biological Samples for Studies on the Health Effects of Atomic-bomb Radiation," at the Hiroshima Laboratory's Auditorium. Increased incidence of solid cancers among A-bomb survivors as a function of their estimated radiation dose is still observed even today, more than 60 years after initial exposure to A-bomb radiation, but most of the molecular mechanisms and biological characteristics underlying this increase remain uncertain. To gain insight into these matters, molecular studies using blood, pathological, and other biological samples are essential. Experts from Japan and overseas participated in the workshop, which was organized to consider RERF's future direction regarding storage and utilization of the unique and valuable biological samples obtained from A-bomb survivors.

We invited Dr. Geraldine A. Thomas, professor of Molecular Pathology, Imperial College London, who launched and now coordinates the Chernobyl

Tissue Bank, to participate in the workshop, as well as four professors from Hiroshima and Nagasaki Universities and two pathologists from local hospitals in Japan.

The event opened with remarks from Dr. Toshiteru Okubo, RERF Chairman. Dr. Kazunori Kodama, RERF Chief Scientist, then defined the aims and outline of the workshop, followed by a special lecture by Dr. Thomas, who delivered an extensive presentation on an overview of the Chernobyl Tissue Bank and approaches to radiation-associated thyroid cancer studies, covering ethical aspects and study findings. The lecture also included reference to methods used at the Chernobyl Tissue Bank for collection and utilization of thyroid tissues and blood.

The next session included the following presentations: "Establishment of the RERF Biosample Center and its role" by Dr. Kodama; "Current preservation status of pathology samples at RERF and development of an archival system for surgical cancer samples from members of the Life Span Study in collaboration with hospitals in Hiroshima and Nagasaki" by Dr. Kotaro Ozasa, Chief, Department of Epidemiology, RERF; "Preservation of fresh thyroid samples obtained from participants of the Adult Health Study" by Dr. Misa Imaizumi, Chief, Division of Clinical Laboratories, Department of Clinical Studies, Nagasaki RERF; and "Storage of biosamples from atomic-bomb survivors at Nagasaki University" by Dr. Shunichi Yamashita, Director and Vice President, Nagasaki University. The presentations reported on the current situation regarding the storage and utilization of biological samples at RERF and Nagasaki University, and the discussion that ensued focused on future directions for storing and using biological samples.

At the session that followed, Dr. Norio Takahashi, Consultant, Office of Associate Chief of Research, RERF, presented "Ethical guidelines for human genome/gene analysis research," which explained ethical issues related to the storage and utilization of biological samples, based on the Japanese ethics guidelines that were revised in February 2013. The findings of studies using tissue and blood samples from A-bomb survivors were then reported by Dr. Yoichiro Kusunoki, Chief, and Dr. Tomonori Hayashi, Assistant Chief, both of the Department of Radiobiology/Molecular Epidemiology, RERF. Their presentations were titled "A molecular oncology study of radiation-associated thyroid cancer among atomic-bomb survivors" and "Immunobiology and immunogenome studies among Adult Health Study participants," respectively. The discussion that followed focused on the current status and future prospects of studies using biological samples.

In a general discussion scheduled for the end of the event, participants actively considered, from both scientific and societal perspectives, the future direction for storage and utilization of biological samples from A-bomb survivors for use in radiation effects studies. This discussion included reference to actual examples from the operation of the Chernobyl Tissue Bank. The workshop concluded with remarks by Dr. Roy E. Shore, RERF Vice Chairman, who expressed his gratitude to the participants.

The workshop was planned by the Biosample Center, sponsored by Japan's Ministry of Health, Labour and Welfare, and carried out with the cooperation of many members from RERF's various departments and the Secretariat. I would like to take this opportunity to express my sincere appreciation to all those concerned for their help in holding a successful workshop.

Participants of the RERF International Workshop: The Storage and Utilization of Biological Samples for Studies on the Health Effects of Atomic-bomb Radiation, held at Hiroshima RERF

RERF International Workshop: Remaining Issues in Shielding Calculations

Harry M. Cullings, Chief
Department of Statistics

On February 19 and 20, 2014, an international workshop was held on remaining issues in shielding calculations for the atomic-bomb survivors. The plan for the workshop was to begin by summarizing the progress that has been made in a project that was recently completed at RERF to provide improved input data on individual survivors' locations and terrain shielding. This work represents several years of dedicated effort and will be described in detail in a manuscript and an RERF report that are now in preparation. Then the program moved to a discussion of remaining issues in the calculation of shielding, particularly for survivors whose doses are currently classified as "unknown" because their shielding cannot be calculated with dosimetry system 2002 (DS02). In addition to a series of presentations at the Hiroshima Laboratory, the workshop included a field trip to sites of interest in Nagasaki that are related to special shielding problems.

Following greetings and an introduction by Dr. Toshiteru Okubo, RERF Chairman, Dr. Harry M. Cullings, RERF Department of Statistics, gave an overview of the work on improved survivor locations and terrain shielding. That project encompassed several methods of using original source documents with new technology to provide improved estimates of location and related terrain data. The first method compared various original source documents such as the Master File, Migration, and Radiation Questionnaires and the 1949 Radiation Census to determine the most reliable estimate of each survivor's location at the time of the bombing, in terms of the coordinates of the 1945 U.S. Army maps that were used at ABCC and RERF from early times up until the present work. Mr. Takashi Oda, Master File Section, RERF Department of Epidemiology, gave the results of a detailed study of the reasons for noted discrepancies among source documents and the related changes in estimated location for certain survivors, a small fraction of which involved large changes in distance from the hypocenter. He also described the restoration of digits representing tens of yards in the U.S. Army map coordinates of many survivors that had been truncated for unknown reasons sometime in the past.

Dr. Cullings then described the creation and use of a key tool in the map work of this project: orthophotographic mosaics of the cities made from pre-bombing aerial photographs. The pre-bombing photographs were geometrically corrected with special software to remove the effect of aircraft altitude, terrain relief, camera angle, and so on, to make them of uniform scale, and were then assembled into a mosaic. Each mosaic was accurately located in the coordinates of the new Japan Geodetic Datum 2000 (JGD2000) using landmarks visible in both the mosaic and accurate new maps, in a geographical information system (GIS). The first use of the orthophotographic mosaics was to align the U.S. Army maps with the mosaics using a "rubber sheeting" method based on a large number of landmarks such as street intersections. This provided mathematical transformations that correct for local distortions in the placement of features on the U.S. Army maps. These transformations were then applied to the U.S. Army map coordinates of the survivors for whom a set of U.S. Army map coordinates represents the only estimate of their location at time of bombing. Dr. Eric J. Grant, RERF Department of Epidemiology, then described an even more accurate method of obtaining improved survivor location estimates for survivors with shielding histories: the neighborhood drawings were aligned with the orthophotographic mosaics using features such as street corners. For more information, see the *Facts and Figures* section by Dr. Toshiteru Okubo, Chairman of RERF, in the Winter 2013 *RERF Update,* Volume 24, Issue 2.

The focus then shifted to remaining issues, with Dr. Cullings and Mr. Tadaaki Watanabe, Master File Section, RERF Department of Epidemiology, describing several cases in which factory shielding was incorrectly classified as wooden house shielding in some early records, and several cases involving special types of terrain shielding such as retaining walls that are depicted in some shielding histories but are not suitable for calculation by the DS02 terrain shielding module.

Dr. Cullings then discussed a possible statistical approach to the "survival bias problem" in calculating doses for survivors in heavy shielding such as concrete buildings and air-raid shelters, by using information about both likelihood of occupancy and likelihood of surviving potential combined injury, as a function of location within a structure. This elaborated on a talk given at the workshop on heavy shielding one year earlier (please refer to "RERF International Workshop: Heavy Structural Shielding," in the *RERF Update*, Summer Edition, Volume 24, Issue 1, 2013). Next, Dr. Stephen D.

Egbert of LEIDOS (formerly Science Applications International Corporation; SAIC) gave a presentation titled "Ideas for Generic Shielding Models That Could Be Used for Monte Carlo Calculations to Support a Sensitivity Analysis of Shielding among Survivors with Currently-Unknown Doses." He discussed requirements for such generic models and how they might be used for various kinds of odd shielding, such as vehicles, large trees, boats, and containers, among others. He also discussed several schema for enhanced calculation of terrain and urban shielding, improved organ doses, and calculation of heavy shielding. Finally, Dr. Grant discussed the information resources at RERF available for construction of three-dimensional models of Hiroshima and Nagasaki that could be used in the future to validate the localized terrain shielding calculations of DS02 by doing a large, full-city calculation of the transport of radiations from the bomb in the air-over-buildings-and-terrain environment.

The second day of the workshop was spent outside in Nagasaki. After an orientation at the RERF Nagasaki Laboratory provided by Mr. Hiroshi Fuchi, Master File Section, Department of Epidemiology, Nagasaki RERF, participants visited a number of locations of air raid shelters and special terrain shielding situations that have been preserved sufficiently for their locations to be reliably and accurately identified in the present-day city and to allow visualization of the spatial relationship between the shielding and the epicenter of the Nagasaki bombing.

RERF International Workshop: Remaining Issues in Shielding Calculations, held in Hiroshima and Nagasaki (here, at Hiroshima RERF)

Fetal Irradiation of Rats Induces Persistent Translocations in Mammary Epithelial Cells Similar to the Level after Adult Irradiation, but Not in Hematolymphoid Cells*

Yoshiaki Kodama

Department of Genetics, RERF

*This article is based on the following publication:

Nakano M, Nishimura M, Hamasaki K, Mishima S, Yoshida M, Nakata A, Shimada Y, Noda A, Nakamura N, Kodama Y: Fetal irradiation of rats induces persistent translocations in mammary epithelial cells similar to the level after adult irradiation, but not in hematolymphoid cells. *Radiat Res* 2014 (February); 181(2):172–6 (doi: 10.1667/RR13446.1)

Study Findings

Examination of rat chromosomes following fetal irradiation showed radiation-induced chromosome aberrations in mammary epithelial cells similar to those found in the mothers, but very few aberrations were observed in lymphocytes. This result demonstrates the presence of tissue specificity with regard to chromosome aberrations following fetal radiation exposure.

Explanation

Previous studies on humans and mice have shown that fetal exposure to radiation fails to induce persistent chromosome aberrations in blood lymphocytes. Such a low level of response to radiation exposure is counterintuitive in view of the generally accepted belief that fetuses are highly sensitive to radiation. In this study, we examined chromosomes of mammary tissues in rats irradiated *in utero* to determine whether or not the same result is observed in other tissues.

1. Objectives

With the aim of determining whether or not the frequencies of chromosome aberration attributable to fetal radiation exposure differ by tissue type, this study examined mammary epithelial cells in rats. In addition, chromosomes of spleen lymphocytes were examined in a subgroup of rats to compare the frequencies of aberration between blood cells and epithelial cells.

2. Methods

Pregnant rats were irradiated at a dose of 2 Gy on day 17.5 of gestation. Mammary tissues were collected from the mothers and their offspring six, nine, and 45 weeks after irradiation. After mammary epithelial cells were cultured, chromosome samples were prepared by a conventional method. To detect translocations, we adopted the fluorescent *in situ* hybridization (FISH) technique to stain chromosomes 2 and 4 green and red, respectively (see Figure), and 800 cells were examined for each rat. The same procedure was followed to examine the chromosomes of cultured spleen lymphocytes.

3. Results

(1) The mean translocation frequency in mammary epithelial cells of rats irradiated *in utero* with a dose of 2 Gy was 3.7% (n = 23). This figure is similar to the mean frequency of 2.9% observed in the mothers (n = 5).

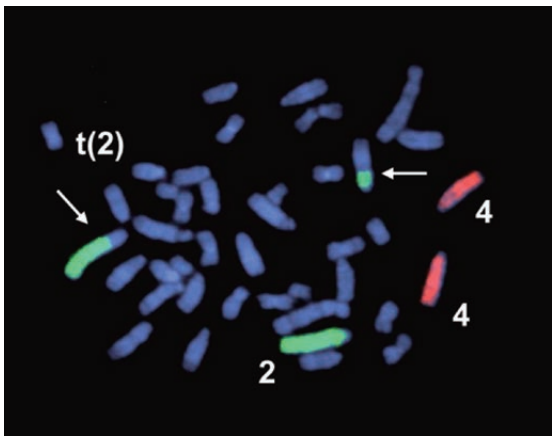


Figure. Detection of translocation (t) by FISH. Chromosomes 2 and 4 are stained green and red, respectively, and the remaining chromosomes are stained blue. Chromosomes stained in two colors (indicated by arrows) are detected as abnormal chromosomes (translocations).

(2) The translocation frequency in spleen lymphocytes was 0.0–0.6% among rats irradiated *in utero* (mean frequency: 0.4%, n = 13), which was significantly lower than the mean translocation frequency of 3.5% observed in the mothers (n = 3).
(3) Translocation frequencies were similar at six, nine, and 45 weeks after irradiation.

As noted above, this study showed that the frequency of chromosome aberrations in the mammary cells of rats irradiated *in utero*, and examined at six to 45 weeks of age, was as high as that in the mothers. In contrast, the translocation frequency in lymphocytes was high in the mothers but considerably lower among rats irradiated *in utero* (about 10% of that of the mothers), supporting the findings in previous studies on mice and humans. These results suggest tissue specificity in the chromosome aberration pattern in fetal exposure. If the translocation frequency is assumed to be an index of the carcinogenic effect of radiation, this study suggests that fetal radiation exposure may induce persistent carcinogenic damage in mammary stem cells and progenitor cells. However, the results of another report showed that fetal exposure in rats did not increase breast cancer risk. No clear reason has been identified that can explain this discrepancy, highlighting the need for further study.

Effects of *IL10* Haplotype and Atomic-bomb Radiation Exposure on Gastric Cancer Risk*

Tomonori Hayashi

Department of Radiobiology/Molecular Epidemiology, RERF

*This article is based on the following publication:

Hayashi T, Itoh R, Cologne JB, Maki M, Morishita Y, Nagamura H, Sasaki K, Hayashi I, Imai K, Yoshida K, Kajimura J, Kyoizumi S, Kusunoki Y, Ohishi W, Fujiwara S, Akahoshi M, Nakachi K: Effects of *IL10* haplotype and atomic-bomb radiation exposure on gastric cancer risk. *Radiat Res* 2013 (July); 180(1):60–9 (doi: 10.1667/RR3183.1)

Study Findings

Our gene structures contain individual differences (called "gene polymorphisms," based upon which are formulated several genotype classifications), with our basic physical constitutions being affected by this genetic variation. Dividing gastric cancer cases among atomic-bomb survivors into intestinal-type and diffuse-type, we examined the association between gastric cancer risk and radiation dose by genotype of *IL10*, an immunosuppressive gene. Although no significant association was found between radiation exposure and intestinal-type gastric cancer risk regardless of *IL10* genotype, the dose dependence of diffuse-type gastric cancer risk varied by *IL10* genotype. This result suggests that *IL10* gene polymorphisms are involved in individual differences in radiation-related diffuse-type gastric cancer risk.

Explanation

Dr. Tomonori Hayashi, Assistant Chief of the Department of Radiobiology/Molecular Epidemiology, Radiation Effects Research Foundation (RERF), and other researchers examined the association between gastric cancer among A-bomb survivors and immune/inflammatory-related gene polymorphisms, using samples collected from immunology studies, carried out since 1981, that followed a portion of the participants in RERF's Adult Health Study (AHS), which is a long-term follow-up study of the health of A-bomb survivors in Hiroshima and Nagasaki. The research team published the results in *Radiation Research*.

1. Study purpose

Gastric cancer is one of the cancers regarding which risks of mortality and incidence are clearly increased for A-bomb survivors. The gastric cancer incidence in RERF's Life Span Study (LSS) population increased with radiation dose (sex-averaged excess relative risk per Gy: 0.28) and remains high even today, more than 65 years since exposure. In this study, we specifically examined the association between risk of gastric cancer (intestinal-type and diffuse-type) and radiation exposure by genotype of the immunosuppressive gene *IL10* to investigate individual differences in gastric-cancer susceptibility to radiation exposure.

2. Study methods

We examined *IL10* gene polymorphisms of 4,690 subjects of the AHS, including 200 gastric cancer cases (93 intestinal-type, 96 diffuse-type, and 11 other cases). *IL10* genotypes can be divided into the following three categories: wild-type homozygotes, heterozygotes, and variant-type homozygotes. Using statistical models (multiplicative and additive), we assessed risks of, and examined the interaction between, different combinations of radiation doses and *IL10* genotypes.

3. Study results

(1) *IL10* genotypes and intestinal-type gastric cancer

After adjustment for sex, year of birth, city, smoking status, and radiation dose, the relative risk (RR) of intestinal-type gastric cancer with *IL10* variant-type homozygotes was significantly high, being 2.2 (95% confidence interval: 1.10–4.25), compared to that with *IL10* wild-type homozygotes. In other words, the variant-type *IL10* gene is considered to be a risk factor of intestinal-type gastric cancer. However, no significant association was observed between radiation exposure and intestinal-type gastric cancer, and no statistical interaction was observed between radiation exposure and *IL10* genotypes.

(2) *IL10* genotypes and diffuse-type gastric cancer

The variant-type *IL10* gene is not a risk factor of diffuse-type gastric cancer, and the excess relative risk (ERR) per Gy of radiation exposure by genotype was statistically significant only for wild-type *IL10* homozygotes (ERR = 0.46/Gy, P = 0.037). On the other hand, the ERR estimate of radiation exposure for variant-type homozygotes was close to 0, with no statistical significance observed. Therefore, variant-type *IL10* might act to reduce risk of diffuse-type gastric cancer due to radiation exposure.

This study of A-bomb survivors suggests that *IL10* genotypes may be associated with the development of radiation-related diffuse-type gastric cancer. There is a possibility, therefore, that immune/inflammatory-related gene polymorphisms may be involved in individual differences in radiation-related cancer risks. Studies are currently underway into the effects of immune/inflammatory-related gene polymorphisms and radiation exposure on not only gastric cancer but also colorectal, lung, hepatocellular, breast, and other cancers.

Radiation Exposure and the Risk of Mortality from Noncancer Respiratory Diseases in the Life Span Study, 1950–2005*

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Pham TM, Sakata R, Grant EJ, Shimizu Y, Furukawa K, Takahashi I, Sugiyama H, Kasagi F, Soda M, Suyama A, Shore RE, Ozasa K: Radiation exposure and the risk of mortality from noncancer respiratory diseases in the Life Span Study, 1950–2005. *Radiat Res* 2013 (November); 180(5): 539–45 (doi: 10.1667/RR13421.1)

Study Rationale

The Life Span Study (LSS) has found that exposure to A-bomb radiation is associated with mortality from noncancer respiratory diseases (hereinafter, simply called respiratory diseases). However, this relationship may be a secondary association caused by the fact that respiratory diseases that can develop at the terminal stage of illnesses such as cancer and circulatory diseases, which have already been linked to radiation exposure, are designated as the cause of death. Considering that the biological mechanisms behind the association between radiation exposure and respiratory diseases are unclear, further examination was necessary before reaching any conclusion about whether the association between radiation exposure and noncancer respiratory disease mortality was genuine or an artifact of disease misclassification.

Explanation

1. Objectives

While the LSS has clarified the association between A-bomb radiation exposure and cancer, attention has also recently been paid to noncancer diseases. The two purposes of the study were (1) to examine the associations of radiation dose with the main subclasses of deaths coded as respiratory diseases on the death certificates; and (2) to determine the degree to which the associations between radiation exposure and respiratory diseases were genuine or were caused by biases due to lifestyle and sociodemographic factors or disease misclassification.

2. Methods

The subjects of the present study were 86,611 people with estimated lung doses from among the 120,321 members of the LSS, which was established on the basis of the Japan 1950 National Census. Based on the International Classification of Diseases, respiratory diseases recorded as causes of death of these subjects were classified into acute respiratory infection, pneumonia/influenza, chronic obstructive lung disease, bronchial asthma, and other respiratory diseases. The present study was based on a follow-up conducted from 1950 through 2005. To determine the degree of association of radiation exposure with mortality from these diseases, excess relative risks (ERR) were estimated using Cox regression analyses.

3. Results

(1) Association between radiation exposure and respiratory diseases

During the study period, 5,515 deaths due to respiratory diseases occurred. The ERR per Gy for all noncancer respiratory diseases was significantly elevated, being 0.17 (95% confidence interval [CI]: 0.08, 0.27). (The ERR of 0.17 here indicates a 17% increase in the risk at 1 Gy of exposure as compared with unexposed subjects, but with a range of uncertainty from 8% to 27%.) The ERR for each of the respective diseases varied, being 0.20 (95% CI: 0.09, 0.34) for pneumonia/influenza, 0.08 (95% CI: –0.14, 0.37) for chronic obstructive lung disease, 0.16 (95% CI: –0.10, 0.52) for bronchial asthma, and –0.16 (95% CI: <0, 0.40) for acute respiratory infection. Adjustments for lifestyle and socioeconomic factors had virtually no impact on the risk estimates. When the study period was divided into shorter intervals (1950–1964, 1965–1979, and 1980–2005), the association between radiation exposure and

respiratory diseases was observed to be stronger in the period 1980–2005. Until the 1970s, most respiratory disease deaths in Japan were from acute infections, but in the 1980s respiratory disease deaths started to be observed primarily as diseases accompanying the terminal stages of cancer and circulatory diseases among the elderly. It was thus plausible that the suggestive association between radiation exposure and respiratory diseases might reflect cancer and circulatory disease in this later period.

(2) Effects of cause-of-death misclassification

Because in the present study information on cause of death was obtained from death certificates, it is important that the underlying cause of death recorded on death certificates be accurate in order to correctly estimate risks. Many patients with cancer or circulatory disease die of respiratory diseases at the terminal stage of such illnesses. Thus, there is a concern that although the actual underlying cause of death is cancer or circulatory diseases, respiratory diseases may be mistakenly recorded as the cause of death. With this in mind, analysis was conducted after excluding subjects with a history of cancer or circulatory diseases from among deaths due to respiratory diseases. As a result, the ERRs decreased by about 35%, and except for pneumonia/influenza, no statistically significant association between radiation exposure and mortality from respiratory diseases was observed.

Care should be taken in interpreting the results of the present study because the study could only partially correct for other causes of death. Some study subjects did not live in Hiroshima or Nagasaki prefectures where our tumor registries could have identified associated cancers, and death certificates often list only one "cause" of death, rather than identifying the important accompanying causes as well, such as cancer or cardiovascular disease. Thus, the apparent associations of radiation with respiratory diseases may have been reduced even more if we had complete ascertainment of the alternative underlying causes. However, the present study indicates that at least part of the apparent association of radiation exposure with noncancer respiratory disease deaths is likely due to reporting artifacts on the death certificates, but not due to sociodemographic or lifestyle biases.

Radiation Effects on Human Heredity*

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Nakamura N, Suyama A, Noda A, Kodama Y: Radiation effects on human heredity. *Annu Rev Genet* 2013 (November); 47:33–50 (doi: 10.1146/annurev-genet-111212-133501)

Summary of Paper

This paper, which offers a review of research results on the genetic effects of radiation, describes classic research using *drosophila* and mice, research with human subjects, and the influence of results of recent human genome sequencing studies. While clear genetic effects of radiation have been observed in animal experiments, no apparent effects have been observed in humans. This paper discusses possible reasons for the difference.

Explanation

This paper consists of the following sections: "Introduction," "Classic studies in laboratory animals," "Studies in humans," "Impact of the human genome study," and "Conclusion." The section "Studies in humans" discusses birth defects, chromosome aberrations, sex ratios, mutations at hypervariable minisatellite loci, cancer incidence, and mortality. It introduces research not only on A-bomb survivors but also on former patients who underwent radiation therapy for childhood cancer as well as workers of nuclear facilities and their families.

Why radiation effects are difficult to detect in studies of human subjects

1. Difference in radiation dose

Although mice are usually irradiated with 3 gray (Gy) or more, such heavy whole-body radiation exposure is extremely rare in humans. However, in the case of radiotherapy for childhood cancer, repetitive localized irradiation to cancer sites causes scattered radiation, which may give rise to gonadal irradiation of accumulated doses of up to 10 Gy or larger when nearby organs are treated.

2. Differences in effects on offspring

In mammalian male germ lines, stem cells continuously divide, with their daughter cells differentiating to become mature sperm. Fertilization occurring soon after radiation exposure is brought about by sperm cells that were irradiated, while fertilization occurring later is brought about by sperm that were irradiated at an immature, stem cell stage. Following exposure to the same radiation dose, the biologic effect on offspring is smaller when fertilization occurs later (i.e., derived from irradiated stem cells) as compared with fertilization that occurs sooner (i.e., from irradiated sperm). The major reason for the difference is thought to lie in the meiotic process (a unique cell-division system whereby chromosome number is reduced by half), which spermatogonia must undergo to differentiate into sperm. On the other hand, female mammals are born with a much larger number of eggs (immature eggs) than necessary in their lifetime, but the number of eggs continues to decrease naturally as they age, with most eggs remaining in an immature state without being released. Only a very limited number of eggs are released after absorbing nutrients in the maturation process. Because there are few examples of conception occurring immediately after radiation exposure, studies of human females focus on the effects of exposure on eggs at immature stages. Here too, the effects on eggs before meiosis are presumed to be small. Unfortunately, however, immature mouse eggs readily die due to apoptosis following exposure to low-dose radiation, and hence no conception is achieved at the higher doses used in studies of mutagenesis and no data are obtained. In contrast, immature human eggs are not susceptible to low-dose apoptosis, so mice cannot serve as a model for human females. In the immature eggs of hamsters, which are resistant to low-dose apoptosis, chromosome aberrations have not been detected in offspring after exposure to 1 Gy of radiation, and it is conceivable that the same applies to humans.

3. Impact of human genomic research

Recent studies reported that numerous "abnormalities" have already accumulated in the human genome. Comparison of two normal people selected randomly shows differences of one base in several million sites, and small deletions and duplications in several hundreds of thousands of sites. On the other hand, the probability that 1 Gy will cause mutation at any gene of a mouse spermatogonial cell is about 1/100,000. Both mice and

humans have about 25,000 genes, and therefore the total number of genes in which mutation occurs is presumed to be 0.25 at the exposure level of 1 Gy. The average dose received by the parents in the studies on birth defects in the offspring of A-bomb survivors is about 0.3 Gy, so the number of genes with mutation is estimated to be 0.075 on average, based on the assumption that radiosensitivity in humans is the same as that in mice. This number, which is much smaller than the number of pre-existing "abnormalities," highlights just how difficult it is to detect radiation effects.

In Memoriam
Dr. Carl Frederick Tessmer

(May 28, 1912–February 2, 2011)

William J. Schull
Former Vice Chairman, RERF

The studies of survivors of the atomic bombings of Hiroshima and Nagasaki are a consequence of a series of recommendations made in the late fall of 1945 by a Japan-U.S. binational committee known as the Joint Commission. One of their recommendations was the initiation, under civilian auspices, of long-term studies to identify the late effects of exposure to the ionizing radiation released by the atomic bombs and to quantitate, to the extent possible, the radiation's effects on human health. Responsibility for the design and conduct of these studies was undertaken by the National Research Council of the U.S. National Academy of Sciences in Washington, D.C. The Council's task was bewildering. There was little scientific information to guide such an undertaking, and the logistics involved in organizing a study of the requisite scope in a war-devastated city some 7,000 miles away were formidable.

These difficulties notwithstanding, a research institution known as the Atomic Bomb Casualty Commission (ABCC), predecessor to the present-day Radiation Effects Research Foundation (RERF), was established in Hiroshima in March 1947 and shortly thereafter in Nagasaki. Leadership of this organization was invested in a temporary Director, Dr. James V. Neel, pending the recruitment of a permanent Director. The initial research program was a cobbling together of several, existing projects including a genetics program conceived and managed by Dr. Neel, several hematological studies, and an investigation of the growth and development of exposed children. While each of the projects had its own merits, together they offered no coherent approach to the overall assessment of radiation-related health risks. It was to Dr. Carl Tessmer, the first permanent ABCC Director, that the task of defining a coherent program fell.

Fortunately, Dr. Tessmer had prior acquaintance with the aims and needs of ABCC. He had taken part in the survey in 1946 organized by Dr. Shields Warren as part of the nuclear weapons tests carried out in the Pacific region known as Operation Crossroads. However, his recruitment was complicated by the fact that he was still an active member of the U.S. Army Medical Corps, and if he was to be involved in ABCC activities, the Surgeon General of the Army had to assign him to detached duty with the National Research Council. A request for such assignment was made to Major General Raymond Bliss, the Surgeon General, by Dr. Lewis Weed, head of the National Research Council, in November 1947. Approval of this assignment was forthcoming, and in March 1948 Lt. Colonel Tessmer was on his way to Japan to serve as Director of ABCC.

Carl Frederick Tessmer was born on May 28, 1912, in North Braddock, Pennsylvania, an eastern borough of the city of Pittsburgh. At the time of Carl's birth, Braddock was a community of 19,000 individuals and the site of the first of Andrew Carnegie's Bessemer furnaces, which revolutionized the worldwide production of steel. His ancestors were Germans who settled in Pennsylvania in the mid-1850s. He received his higher education at the University of Pittsburgh from whence he was awarded a baccalaureate degree in science in 1933. He then enrolled in the University's medical school, which he attended from 1933 to 1935, graduating with a Doctor of Medicine degree in 1935. As was mandatory for licensure at the time, he completed a rotat-

Dr. Carl Frederic Tessmer, when he was Director of ABCC

ing internship at the Pittsburgh Medical Center, and in 1937 served a residency in pathology at the Presbyterian Hospital in Pittsburgh. This was followed by a fellowship at the Mayo Clinic in Rochester, Minnesota, where he continued his study of pathology. Those were difficult years financially for a young physician; the Great Depression, still in full cry, limited career options. Carl accepted a residency at Queen's Hospital in Honolulu. Upon completion of his residency, he became a member of the U.S. Army Medical Corps and was assigned to the medical unit at Schofield Barracks, where he was "Officer of the Day" on December 7, 1941. He served the U.S. Army for 23 years, retiring as Colonel in 1963.

Carl's years as Director of ABCC occurred during the Allied Occupation of Japan. Administratively, ABCC fell under the Supreme Commander for the Allied Powers (SCAP)'s Public Health and Welfare Section, commanded by Colonel Crawford F. Sams (later, Brigadier General Sams). The latter officer had the reputation of being difficult, but Carl managed ABCC's affairs adroitly and successfully. He was responsible for a myriad of details involving personnel, supplies, housing, the contract with the Atomic Energy Commission (AEC), travel, and no end of other miscellany. All of his actions had to be consonant with the numerous regulations promulgated by SCAP regarding interaction between Japanese nationals and members of the Occupation. He presided over the most rapid expansion of staff seen by ABCC (now, RERF). When Carl took office in March 1948, ABCC had 28 employees, and when he retired there were more than 1,000 staff members. He was sensitive to Japanese culture and met regularly with Hiroshima Mayor Shinzo Hamai regarding the siting of the permanent research facility. Indeed, at the formal ground breaking (*Jichinsai*) for ABCC in July 1949 he was actively involved in this traditional *Shinto* ceremony.

From the perspective of research, his tenure encompassed the years when the increase of leukemia among the survivors was noted, and ABCC played a significant role in the 1950 Census of Japan. Indeed, ABCC was permitted to append a short questionnaire to the conventional census form seeking identification of all of the survivors of the atomic bombing of Hiroshima or Nagasaki alive in October 1950. This information was crucial to the later establishment of the fixed cohorts represented by the Life Span Study (LSS) and the Adult Health Study (AHS). Carl was especially active in contesting the recommendation by the Goodpasture committee to terminate the studies in 1950.

On leaving ABCC in early 1951, he was assigned to the United States Army Medical Research Laboratory at Fort Knox, Kentucky as its Commanding Officer. After a three-year stint there, Carl was appointed to serve as Chief of the Radiation Pathology Branch and Chief of the Basic Science Division of the Armed Forces Institute of Pathology in Washington, D.C. He held the latter position for six years and was then reassigned to Japan to become head of the 406th Medical General Laboratory. After his return to the United States and a brief period of duty at the Walter Reed Army Institute of Research in Washington, D.C., he joined the staff of the MD Anderson Hospital and Tumor Institute as Chief Pathologist and Professor of Pathology at the University of Texas Graduate School of Biomedical Sciences in Houston. After 10 years in Houston he would move again, this time to the Olin E. Teague* Veterans Center in Temple, Texas, where he served in a variety of capacities for another decade. Carl retired from academia in 1985 at the age of 73, but continued to be active as a physician and consultant for another quarter of a century. Carl Tessmer died on February 2, 2011, in Belton, Texas, where he had resided for the previous 25 years. He was twice married. His first wife, Maxine (nee Keller), whom he married in 1939, was the mother of his two sons, Jon and David. Maxine preceded Carl in death, as did his second wife, Shizue (nee Murata).

*Olin E. Teague was a much-decorated veteran of World War II and a long-serving member of the United States House of Representatives noted for his legislation on behalf of veterans of the aforementioned war.

Participating in the Health Examination/Consultation Project for A-bomb Survivors Living in South Korea

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The Health Examination/Consultation Project for A-bomb Survivors Living in South Korea has been conducted biannually since 2004 as part of an assistance program for survivors currently residing in that country. The most recent event marked the 20th occasion to hold the project, but it was my first time to participate. As part of a larger effort to assist A-bomb survivors in South Korea, this project is intended to dispel concerns about late effects of A-bomb radiation exposure and to endeavor to enhance the health of A-bomb survivors through health examinations and consultations conducted by physicians and other medical experts dispatched from Japan.

Since A-bomb survivors reside throughout South Korea, the Health Examination/Consultation Project targets cities and regions where a relatively large number of A-bomb survivors are concentrated, such as Seoul, Daegu, Hapcheon, Busan, Masan, Gwangju, Pyeongtaek, Daejeon, Ulsan, Jeju, and Gyeongsangnam-do. Our four-day schedule covered Jeju, Gwangju, and Daejeon from November 10 to 13, 2013 (essentially two days, with the first and last days spent for travel). The project work was carried out by a seven-member team consisting of four internal medicine specialists, one public health nurse from the Nagasaki municipal government, and two employees from the Nagasaki prefectural and municipal governments.

A total of 84 A-bomb survivors participated in this visit: 9 in Jeju, 14 in Gwangju, and 61 in Daejeon. The average age of the participants was 75.3 years, with the oldest being 94 and the youngest 67. Of these individuals, 73 experienced the A-bombing in Hiroshima and 11 in Nagasaki. Since the project time was essentially limited to two days with three locations, the team divided into two groups and worked separately at Jeju and Gwangju on the first two days, and then met at Daejeon to work together there on the third day.

Since I was a member of the Gwangju group, I and the others visited Gwangju on the first day, conducted health consultations there on the next day, and then traveled to Daejeon on the third day. We conducted health consultations with the help of an interpreter, referring to the results of the health examinations that were carried out at local Red Cross hospitals prior to our visit. At the beginning of each health consultation session, we interviewed each of the participants based on a medical questionnaire. Although some participants were good at Japanese, most did not understand or remember the language, and so the interpreters assigned to each physician were of great help. The medical interviews lasted from about 30 minutes to one hour, during which we explained the health examination results and relevant health issues, along with carrying out the medical interview. If called for, we also provided to Korean physicians advice about medical treatment and consultation concerning administrative procedures for A-bomb survivors support programs. At the end of our first day, I found myself completely exhausted, affected as I was by the combination of multiple factors, such as nervousness resulting from my first-time participation in the project, the challenges of providing health consultation through an interpreter, and the fact that I had caught a cold the day before my departure from Japan.

After completing our scheduled health consultations, my Gwangju group traveled by bus to Daejeon to join up with the Jeju group. In Daejeon on the third day, I found that things went relatively smoothly since I had by now achieved a better understanding of how to handle the consultation work and was recovering from my cold. After completing the Daejeon health consultations, the team all together traveled by bus to Seoul, where

At the Gwangju Association of Health Promotion. Dr. Daisuke Haruta is the second person from left in the back row.

we were treated to *yakiniku*, the South Korean specialty of grilled meat, at a dinner hosted by the Republic of Korea National Red Cross. After dinner we enjoyed the night view from the N Seoul Tower, which concluded our itinerary.

Like their Japanese counterparts, many of the South Korean A-bomb survivors interviewed by our team suffer from various lifestyle diseases, such as obesity, hypertension, and diabetes. From what I could discern, there did not seem to be much difference in the medical care provided to A-bomb survivors in Japan and South Korea. We received a pleasant welcome from the survivors in South Korea, and most expressed gratitude and appreciation to us. Employees of the Republic of Korea National Red Cross were also gracious and hospitable and took good care of us for everything, from our mode of transport to our meals. Although we were only able to communicate with a limited number of people in South Korea during the project, I never sensed any of the strain in the relationship between Japan and South Korea that has recently become an issue. If I have an opportunity to participate in this project again, I hope that I can be of help in maintaining the health of A-bomb survivors in South Korea and be part of the effort to establish a bridge of friendship between the two nations.

I would like to express my appreciation to the research scientists and staff members at the RERF Nagasaki Laboratory who supported my participation in this 20th occasion of the Health Examination/Consultation Project for A-bomb Survivors Living in South Korea, as well as to the employees and volunteer staff members from the Korean Red Cross and to our interpreters for their support during our stay in South Korea.

New Terrain Shielding Input Data for the Atomic-bomb Survivors

Harry M. Cullings, Chief
Department of Statistics

As detailed in the last issue of *Update* (volume 24, issue 2, 2013; page 25), RERF recently completed a program of work to provide improved estimates of survivors' locations, to allow more accurate distance input data for dosimetry system DS02 and therefore more accurate dose estimates. As part of that program, it was clear that survivors' terrain shielding would need to be re-evaluated at their new estimated locations. However, it was neither feasible nor desirable to simply emulate the original methods by which terrain-shielding input data were obtained.

To calculate terrain shielding for a survivor, DS02 uses angles of elevation from the survivor's position to the horizon (grazing angles) in five horizontal directions: toward the hypocenter and 45° and 90° to the left and right. For about 315 proximal (<2 km) survivors in Nagasaki called "Globe terrain" cases, the grazing angles were estimated in the 1960s using the elevation contours on the 1945 U.S. Army maps. (No proximal survivors in Hiroshima were considered to have terrain shielding.) For a much larger group of distal (>2 km) survivors, about 3,521 in Hiroshima and 8,242 in Nagasaki, grazing angles were estimated in the implementation of DS02 to account for any shielding that they received by being behind Mt. Hijiyama (Hiroshima) or Mt. Konpira (Nagasaki). Those data were obtained by using digital terrain elevation data on a 50-m horizontal grid, and the survivors were denoted as having "distal terrain" or "mountain" shielding, although many of them turned out to have had little or no terrain shielding, depending on their exact location relative to the mountain and the bomb.

For the new work, more accurate digital terrain elevation data on a 10-m horizontal grid were available from the Geospatial Information Authority of Japan. Furthermore, advances in computational speed made it feasible to estimate grazing angles for all survivors, rather than only for pre-selected groups based on arbitrary criteria. This work was greatly aided by an RERF consultant, Dr. Stephen Egbert of LEIDOS corporation (formerly Science Applications International Corporation; SAIC), who was a main developer of the DS02 terrain shielding module. Notably, Dr. Egbert identified a need, previously unappreciated, to correct grazing angles for the elevation above sea level at the survivor's location. This need arises because each atomic bomb exploded at a particular height above sea level. Therefore, for survivors at a given distance with a given angle of elevation to the horizon, the bomb will be at a lower angle relative to the horizon if the survivor is at a higher elevation.

The Table shows numbers of survivors who have substantial terrain shielding, by distance category, in each city, for both of the old and new methods. Figures 1 and 2 allow the reader to appreciate relative numbers of survivors as a function of both distance and amount of shielding. Some survivors have very heavy terrain shielding, i.e., transmission factors <0.2, i.e., a dose reduction >80%, although most survivors have less dose reduction due to terrain shielding. There is a substantial increase in terrain shielding that is readily seen in the table and figures, because of survivors who were not properly identified as having terrain shielding by the earlier methods. In addition, it was found that many of the original grazing angles estimated in the 1960s were very inaccurate, which is understandable given the difficulty of making such estimates by manual methods with a paper map.

Table. Number and % of survivors with terrain shielding,* by distance category and city

Ground distance (m)		Hiroshima					Nagasaki				
		N	old method		new method		N	old method		new method	
from	to		terrain-shielded	%	terrain-shielded	%		terrain-shielded	%	terrain-shielded	%
0	250	8					0				
250	500	31					8	1	13		
500	750	634					66	5	8	3	5
750	1,000	2,854					405	5	1	2	<0.5
1,000	1,250	5,661					1,588	52	3	103	6
1,250	1,500	7,108					1,565	100	6	221	14
1,500	1,750	7,529			12	<0.5	1,504	171	11	506	34
1,750	2,000	6,373	179	3	157	2	2,459	531	22	759	31
2,000	2,250	7,141	228	3	356	5	2,730	916	34	1,712	63
2,250	2,500	2,842	19	1	124	4	4,131	2,513	61	3,257	79
2,500	2,750	2,109	1	<0.5	70	3	4,825	2,839	59	3,906	81
2,750	3,000	2,418			206	9	1,080	18	2	700	65
3,000	3,250	2,223			183	8	884	2	<0.5	390	44
3,250	3,500	1,489					868			307	35
3,500	3,750	1,025					695			71	10
3,750	4,000	1,141					799				

*gamma-ray transmission factor <0.9

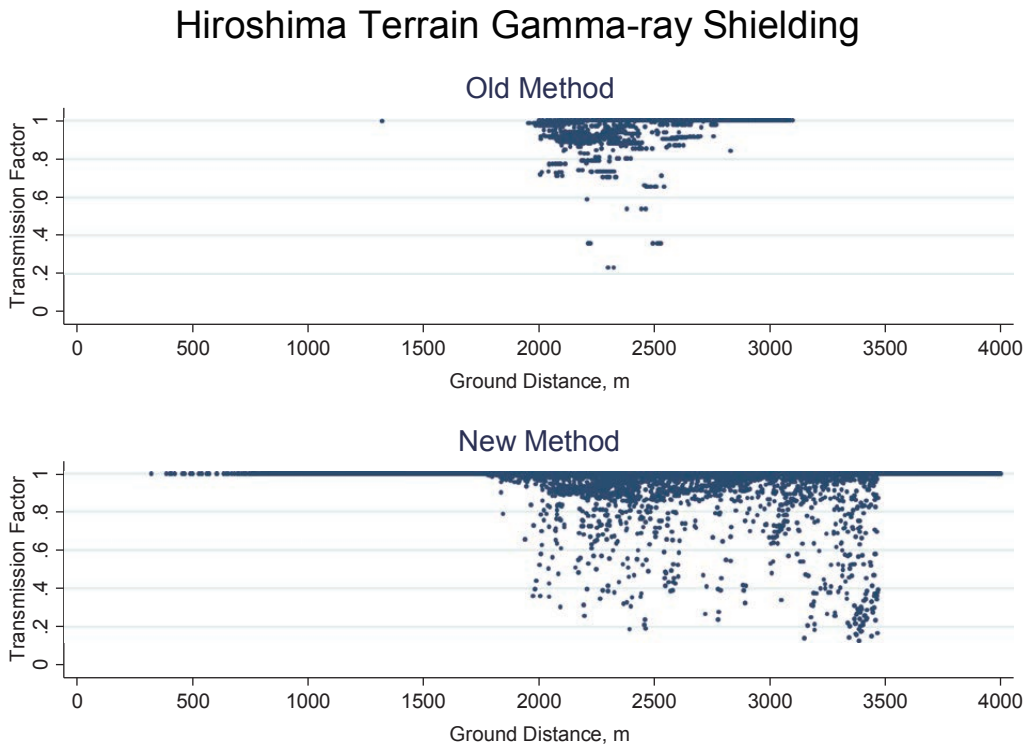

Figure 1. Terrain gamma-ray shielding transmission factor vs. distance, Hiroshima; clearly shown for the "new method" are increased numbers of survivors with calculated transmission factors, and many more survivors with transmission factors considerably less than 1, representing in part those not previously identified as having terrain shielding. (Note: many points representing individual survivors are superimposed. Also, transmission factors less than 1 were not calculated for survivors at distances beyond 3,500 m, where unshielded doses are negligible.)

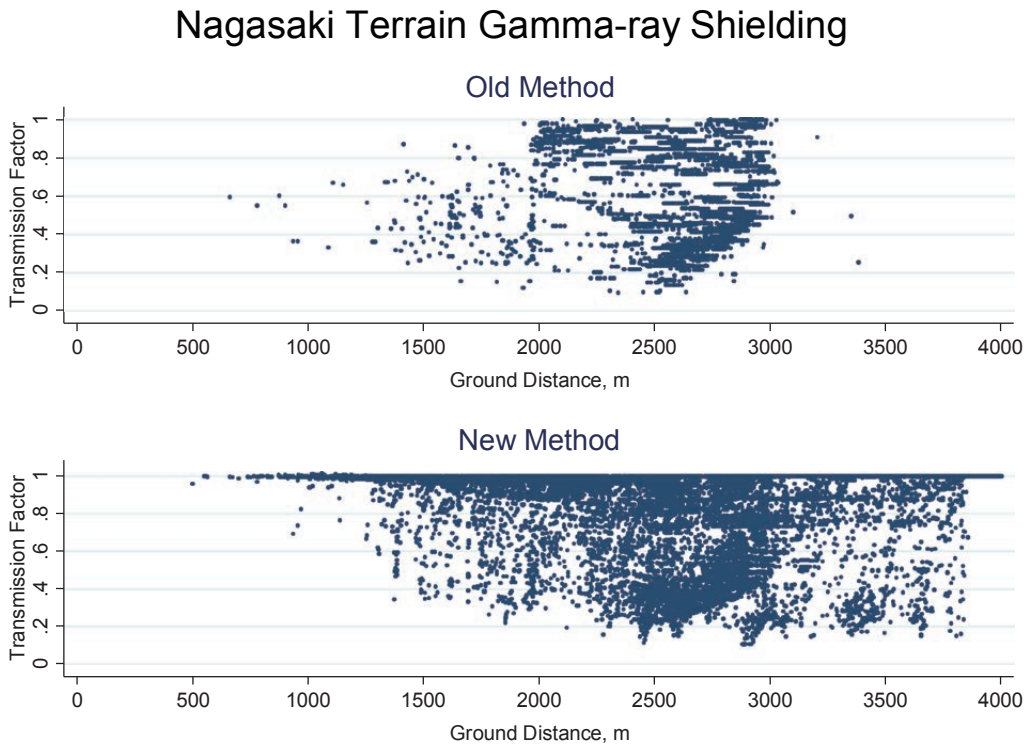

Figure 2. Terrain gamma-ray shielding transmission factor vs. distance, Nagasaki, with increased numbers of survivors with calculated transmission factors, and many more survivors with transmission factors considerably less than 1, due to reevaluation using new method for determination of terrain shielding

Research Protocols Approved in November 2013–April 2014

RP 1-14 A study of the biological significance of the *EML4-ALK* fusion gene in radiation-associated thyroid carcinogenesis using conditional transgenic mice

Hamatani K, Ito R, Taga M, Niwa Y, Kim Y-M, Hayashi Y, Eguchi H, Kusunoki Y

Rearranged anaplastic lymphoma kinase (*ALK*) genes (echinoderm microtubule-associated protein-like 4 [*EML4*]-*ALK* fusion genes), which we found for the first time in papillary thyroid cancer (PTC), are likely to be highly correlated with atomic-bomb (A-bomb) radiation exposure and to occur in a fundamentally exclusive manner in *RET,* neurotropic tyrosine kinase receptor 1 (*NTRK1*), *BRAF*, and *RAS* gene alterations. Interestingly, just as lung adenocarcinoma cases with *EML4-ALK* fusion genes show histological characteristics significantly different from those without the *EML4-ALK* fusion gene, this fusion gene-positive PTC has characteristic solid/trabecular architectures at a high frequency, suggesting that the *EML4-ALK* fusion gene plays a key role in architectural alterations related to the histopathological characteristics of the cancer tissue that concerns our oncology study. We thus hypothesize that the *EML4-ALK* fusion gene plays an important role in causing PTC and is a result of radiation. Function of the fusion gene may be different from *RET/PTC* rearrangements in terms of their pathological consequences. With use of conditional transgenic mice harboring *EML4-ALK* genes, we will test the hypotheses from the following viewpoints: One is to evaluate evidence for generation of PTC from the transgenic mice with this fusion gene. The second is to demonstrate effects of radiation in tumorigenesis in these transgenic mice, i.e., the shortened latency and/or the enhanced aggressiveness of the tumors.

RP 2-14 Study of heart disease in the Adult Health Study population using echocardiography

Takahashi I, Haruta D, Hidaka T, Tsuneto A, Kajimura J, Hayashi T, Furukawa K, Imaizumi M, Hida A, Ohishi W, Kihara Y

There is much evidence that exposure to high dose medical irradiation increases risk of cardiovascular disease. Recent Life Span Study (LSS) reports demonstrated an excess risk of mortality from cardiovascular disease (CVD), especially hypertensive heart disease, heart failure (HF), and rheumatic heart disease after whole-body exposure to atomic-bomb radiation. However, explanations for this relationship between radiation dose and such subtypes of disease incidence are far from convincing because of limitations in death certificate coding of CVD. Using single photon emission computed tomography, other clinical/epidemiologic studies have indicated that medical radiation is associated with dose-dependent perfusion defect in patients treated for breast cancer with radiation therapy, which may be a cause of heart damage. Past experimental findings reported that total body irradiation in rats was associated with development of diastolic dysfunction. We therefore hypothesized that atomic-bomb radiation may cause diastolic dysfunction among the survivors. Based on echocardiograph assessment and blood markers in the Adult Heath Study (AHS) subjects who were 15 years of age and younger at the time of bombings, we will diagnose HF and categorize it into its subtypes. Our main purpose is evaluating radiation effects on diastolic heart failure, one subtype of HF. However, we will also examine as secondary endpoints systolic heart failure, as well as hypertensive, valvular, and ischemic heart disease. Relevant measures for all these types are available from the echocardiograms, conforming to the guidelines and recommendations from the American Society of Echocardiography (ASE). The expected number of subjects for the study is about 2,700 AHS members (including *in utero* survivors) in Hiroshima and Nagasaki who were ≤15 years old at the time of the bombings. We will also measure biomarkers that are thought to play an important role in the development of cardiac dysfunction and fibrosis, as well as remodeling that arises from radiation-related damage-repair processes in cardiac tissues.

Recent Publications

(Japanese): the original article is in Japanese

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Publications Using RERF Data

The following publication represents research done by non-RERF scientists based on the data publicly available from RERF.

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