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Joint RERF-ICRP Workshop on Health Risk of Radiation and the System of Radiological Protection

Sunday, October 9, 2016

Organised by Radiation Effect Research Foundation (RERF)
and the International Commission on Radiological Protection (ICRP)
with support from the Nippon Foundation

Abstracts

Radiation Effects Research Foundation
A Cooperative Japan-US Research Organization

INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION

Joint RERF-ICRP Workshop on

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The University of Tokyo

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Background

RERF is a world-leading research institute on radiation effects. Their studies of atomic bomb survivors are considered the gold standard in epidemiological research on the health effects of radiation exposure, and are often cited by UNSCEAR. ICRP has worked with RERF scientists for many years, as the work of RERF is considered a key element in the scientific foundation of the system of radiological protection. This joint workshop provides an opportunity to continue to exchange information between RERF and ICRP in an open forum on the most advanced research from RERF for the purpose of using scientific findings for the protection of people from the risks of radiation.

Objectives

RERF and ICRP welcome this opportunity to discuss the current work with Japanese scientists, covering radiation related topics including: the risk of hereditary effects, cancer and non-cancer. In addition, the future of radiation health risk science and the system of radiological protection will be discussed.

Symposium venue

Room number 221, Faculty of Engineering Build. 2, Hongo Campus, The University of Tokyo
Access: http://www.t.u-tokyo.ac.jp/soee/access.html

Program

13:00 – 13:05: Opening address

By Christopher Clement (ICRP) (5 min)

13:05 – 13:55: Session 1: Risk of hereditary effects

Chair: Yoshiya Shimada (NIRS)

Speaker:

Nori Nakamura (RERF): "Hereditary effects of radiation in men and in mice" (30 min)

Questions and answers (20 min)

13:55 – 14:55: Session 2: Dose response of radiation associated cancer and DDREF

Chairs: Ludovic Vaillant (CEPN), Michiaki Kai (ICRP)

Speakers:

Eric Grant (RERF) on "Dose response of solid cancer in atomic bomb survivors" (20 min)

Werner Ruehm (ICRP) on "Current ICRP stance on DDREF" (20 min)

Questions and answers (20 min)

14:55 – 15:55: Session 3: Risk of non-cancer: current controversy on the disease type

Chairs: Kazunori Kodama (RERF), Mark Little (NCI)

Speakers:

Kotaro Ozasa (RERF) on "Current research on non-cancer diseases in atomic bomb survivors" (20 min)

Tamara Azizova (ICRP) on "Circulatory disease in Mayak workers" (30 min)

Questions and answers (20 min)

15:55 – 16:10 Coffee break

16:10 – 17:30 Round table discussion on "Futures of Health Risk Research and the System of Radiological Protection"

Discussion leaders:

Robert Ullrich (RERF) on "Future of radiation research at RERF" (15 min)

Nobuhiko Ban (ICRP) on "Future of radiation protection" (15 min)

Comments from the floor

Hereditary effects of radiation in men and in mice

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Abstract–Ionizing radiation is a mutagen capable of inducing heritable genetic damage in various species. In humans, however, clear evidence for the increased risk of genetic damage represented by chromosome aberrations, malformations or Mendelian disorders in the offspring of exposed parents (either atomic-bomb survivors or childhood cancer survivors) has not been observed. Our past study in mice indicated that the mutation induction rate in spermatogonia cells was of the order of 10^{-6}/DNA fragment/Gy when about 1,000 sites in the genome were screened with the two-dimensional electrophoresis (2DE) technique of DNA. More recently, over 1,000,000 sites were screened with the array-based comparative genomic hybridization (aCGH) technique. The results indicated that the mutation induction rate was even lower, of the order of 10^{-7}/probe site/Gy. Compared with the mean induction rate of the order of 10^{-5}/locus/Gy with the classic specific-locus tests at 7 genes, it appears that the mean mutation induction rate decreased with the increase in the number of genes or sites examined per genome. These results indicate two possibilities; one is that deletions are induced evenly in the genome but many of them are not recovered as viable F1 due to loss of haploid sensitive genes in the deletion. Alternatively, DNA breaks may not occur randomly in the genome.

Solid cancer incidence among the Life Span Study of atomic bomb survivors: 1958–2009

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Abstract–This analysis of all solid cancer incidence among the Life Span Study (LSS) cohort of atomic-bomb survivors adds eleven years of follow-up data since the last report and includes updated dose estimates and adjustment for smoking. 105,444 cohort members who were alive and had no known history of cancer were analyzed from 1958–2009 using Poisson regression methods. Risk estimates are reported for a person exposed at age 30 years with attained age 70 years. 22,538 incident first primary solid cancer cases were identified. For females, the dose response was consistent with linearity with an estimated excess relative risk (ERR) of 0.64 per Gy (95% CI: 0.52 to 0.77). For males, significant upward curvature was observed and therefore a linear-quadratic model was used, which resulted in an ERR of 0.20 (95% CI: 0.12 to 0.28) at 1 Gy and an ERR of 0.010 (95% CI: −0.0003 to 0.021) at 0.1 Gy. In conclusion, solid cancer risks remained elevated more than 60 years after radiation exposure. Smoking adjustment had little or no impact on the shape of the dose response. At this time, uncertainties in the shape of the dose response preclude definitive conclusions to confidently guide radiation protection policies.

Current ICRP stance on DDREF

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Abstract–In the ICRP 103 Recommendations, the International Commission on Radiological Protection (ICRP) confirmed the use of a Dose and Dose Rate Effectiveness Factor (DDREF) with a numerical value of 2, which had been introduced by ICRP in the earlier ICRP 60 Recommendations. This factor is used by ICRP to rescale risks of radiation-induced solid cancers obtained from the cohort of atomic bomb survivors, which were exposed to higher dose and dose rates as compared to workers who are usually exposed to lower dose and dose rates. Other international bodies such as the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), the BEIR VI Committee of the American National Academy of Sciences, or the German Radiation Protection Commission (SSK), however, suggest alternative approaches or propose other numerical values for the DDREF. Currently, members of ICRP Task Group 91 are reviewing the scientific literature on sub-cellular and cellular effects relevant for carcinogenesis, combine animal data from various studies, and analyse most recent epidemiological data from cohorts exposed to ionizing radiation. The present paper gives an overview on the current activities of this Task Group.

Current research on non-cancer diseases in atomic bomb survivors

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Abstract–Radiation-associated risks of non-cancer diseases among atomic bomb survivors have been evaluated by the Life Span Study (LSS) and the Adult Health Study (AHS). Information regarding non-cancer diseases in the LSS is obtained only from death certificates while precise and detailed information is obtained in the AHS, a sub-cohort of the LSS, of which members are clinically examined biennially. But, such information was obtained by medical procedures that were available for limited participants in selected periods, so that the results might not be generalized in comparison with the LSS. In addition, mortality and morbidity trend and pathogenesis of non-cancer diseases in Japan has changed over the long follow-up period since the devastated post-war through economic development and lifestyle westernization. Radiation-associated risk of cardiovascular disease may be mediated by radiation-associated hypertension as hypertension was a major basis of cardiovascular disease in Japan. Atherosclerotic predisposition was slightly elevated with radiation exposure, but it remains unclear how strong the elevation affected the pathogenesis of cardiovascular disease among atomic bomb survivors. Radiation-associated mortality risk was apparently observed for cardiovascular and non-cancer respiratory deaths potentially accompanied with uncertain conditions at death, which made the interpretation of results complicated and inconclusive.

Circulatory diseases in the cohort of Mayak PA workers occupationally exposed to radiation

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Abstract–The study was aimed to investigate incidence and mortality from circulatory diseases (CDs) including ischaemic heart disease (IHD), cerebrovascular diseases (CeVD) and lower extremity arterial disease (LEAD) in Mayak workers occupationally exposed to low dose rate radiation. The cohort included 22,377 individuals first employed in 1948–1982 and followed up to 2008. 8,717 cases and 1,578 deaths from CeVD, 7,225 cases and 2,848 deaths from IHD, 943 cases of LEASO and 5,010 deaths from CDs were registered. A significant linear association of IHD, CeVD and LEAD incidence was found with dose from external gamma-rays adjusting for non-radiation factors and dose from internal alpha-radiation. Significant increasing linear trend in IHD and CD mortality with increasing gamma-dose was observed. Dose-response analysis for internal alpha-radiation due to incorporated plutonium showed a significant linear association of IHD and CeVD incidence with total absorbed dose from internal alpha-radiation to the liver including adjustments for non-radiation factors and dose from external gamma-rays. Significant increasing linear trends in mortality from IHD, CeVD and CDs with increasing dose from internal alpha-radiation were revealed only for a subcohort of workers who were Ozyorsk residents exposed to internal alpha-radiation at total absorbed dose to the liver < 1.0 Gy.

Future of radiation research at RERF

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Abstract–A unique characteristic of research at RERF is the opportunity to conduct multidisciplinary studies in a single setting taking advantage of the LSS and AHS cohorts. Such studies can be used to quantify radiation effects as a function of dose as well as approach underlying mechanisms of direct applicability to basic radiation biology. Such basic research, in combination with epidemiological and clinical studies, also provides essential information with respect to effects of ionizing radiation at low doses, which are often difficult to directly measure. At present an important new activity is aimed at quantifying and characterizing heritable effects of radiation exposure in the children of the atomic bomb survivors using next generation sequencing. In previous studies previously conducted at RERF, heritable mutations have been undetectable using a variety of endpoints. More recently, observations in a mouse model using CGH have indicated that the frequency of new mutations in offspring was substantially lower than would be expected based on the specific locus test. Integrated multidisciplinary studies on effects of radiation exposure on the incidence and underlying mechanisms of organ-specific cancers and non-neoplastic effects (principally cardiovascular disease) are also being developed. Such studies take advantage of the RERF biobank as well as animal models with an emphasis on "omics" approaches.

Future of radiation protection

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Abstract–The objective of radiological protection for human health is to prevent deterministic effects and reduce the risks of stochastic effects to the extent reasonably achievable. This principle is based on the premise that deterministic effects are due to injury in population of cells at high doses and that stochastic effects arise from mutation of somatic cells or germ cells. While the notion has a solid base, accumulating data suggest there are challenges to be overcome. One of the emerging issues is tissue reactions, particularly increase in the risk of circulatory disease after moderate exposure. It is not a typical deterministic effect that is attributed to radiation-induced cell killing/malfunction in individual tissues, but a tissue reaction that is caused jointly by radiation and other factors involving multiple tissues. Consequently the threshold is obscure, and the contributing dose could be unclear in non-uniform exposure. These features raise a question about the classification of effects and the shape of dose response curve for this type of effect. As to stochastic effects, recent epidemiological data indicate the dose-rate effect may not be significant in cancer induction, and there is doubt and criticism about the use of dose and dose rate effectiveness factor (DDREF). On the other hand, review of the studies on tissue stem cells suggest long-term kinetics of target/stem cells in the tissue may modify the dose response in the case of protracted exposure. While it may take long before reconciling these opposing views, looking into each class of cancer will be a necessary step towards resolution. Biologically it is little wonder that the tumorigenic process differs between cancer types, and response to radiation may not follow a simple rule. In this context, analyses and experiments on the basis of cancer site/type is desirable for realistic assessment. At the same time, modifying effects of sex, age and lifestyle factors should not be dismissed since they often have a great impact on sensitivity and the baseline risk. Addressing these issues does not necessarily mean future radiological protection will be more elaborate and complex. Rather, we have to make best efforts to integrate recent findings into a simple, robust and practical system. Careful examination of the available data and promotion of strategic research on priority issues are needed toward this end.