Fifty-Ninth
Annual Meeting Program

Integration of Physics, Biology and Epidemiology in Radiation Risk Assessment

Hyatt Regency Bethesda
One Bethesda Metro Center
7400 Wisconsin Avenue
Bethesda, MD 20814

March 27–28, 2023

NCRP Mission:

To support radiation protection by providing independent scientific analysis, information and recommendations that represent the consensus of leading scientists.

@NCRP2023

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Introduction

Integration of Physics, Biology and Epidemiology in Radiation Risk Assessment

Fifty-Ninth Annual Meeting of the National Council on Radiation Protection and Measurements (NCRP)

Welcome to the 2023 NCRP Annual Meeting! We are thrilled to be able to meet face-to-face once again for the first time since 2019. Each year, the theme of the NCRP meeting varies. Sometimes it is designed to inform our members and members of the public of our current activities, other times of a particular challenge. This year, our theme is more aspirational, pointing to an exciting future for radiation protection based on integrating science from a broad realm of disciplines.

Epidemiological studies have been instrumental to our assessment of the effects of radiation exposure in humans. In addition, the findings of those studies often suggest possible mechanisms contributing to the development of cancer and noncancer diseases. Well-designed experiments can identify and quantify the radiogenic, molecular, cellular and organismal lesions that precipitate adverse health effects and the body's responses to those lesions. However, at the low doses and low-dose rates at which many exposures occur, conventional epidemiological tools lose their effectiveness. How then can we quantify the risks of later disease onset after low-dose exposure? Which lesions are generated and which are repaired with full fidelity? What indirect detrimental effects occur? What indicators can be detected that show a step towards disease manifestation has occurred?

NCRP Report No. 186, titled *Approaches for Integrating Information from Radiation Biology and Epidemiology to Enhance Low-Dose Health Risk Assessment*, lays out a framework for establishing biologically based dose-response (BBDR) models that can begin to answer these questions. The Program Committee has selected topics and speakers who will bring this report to life and explore its implications on low-dose science. After the opening Warren K. Sinclair Keynote that will set the tone for the day, speakers on the first day will examine the health risks of radiation exposure through the lenses of epidemiology, biologic mechanisms that underpin both cancer and cardiovascular diseases, and the use of models and extrapolations.

The second day will push the boundaries of our current state-of-the-art technology by examining the integration of epidemiology and biology, featuring a Thomas S. Tenforde Lecture on visualizing cellular mechanisms and how new and innovative technologies may be able to help further our understanding of bioindicators of the disease process. We will then proceed to explore areas where research is needed to fill gaps in knowledge with presentations on the future of epidemiology and computational biology. We close out the meeting by inviting a panel of experts to elucidate how scientists can integrate these technologies to help advance the field of radiation protection.

The Program Committee is hopeful that you will be inspired by what you learn and be introduced to some of the new powerful tools that are available. We hope that you will leave the meeting with ideas for new collaborations and new directions in your research. We are glad you are here and that we can share science and camaraderie in this face-to-face setting!

Established in April 2019, the John D. Boice, Jr., Young Investigator Award is given this year to Michael B. Bellamy from the Memorial Sloan Kettering Cancer Center. This Award is given to recognize an early career professional engaged in some aspect of science pertaining to radiation protection and measurements.

NCRP gratefully acknowledges:

- the U.S. Navy Color Guard who will open our Annual Meeting; and
- Kimberly Jordan of the U.S. Nuclear Regulatory Commission who will sing our National Anthem.

Featured Speakers

The Forty-Sixth Lauriston S. Taylor Lecture will be delivered by Martha S. Linet, a National Institutes of Health Scientist Emerita and Special Volunteer in the Radiation Epidemiology Branch of the National Cancer Institute. Dr. Linet was elected to the Council in 2010 and became a Distinguished Emeritus Member in 2016. She currently serves on Scientific Committee (SC) 8-1 and was a member of SC 4-4.

The Nineteenth Annual Warren K. Sinclair Keynote Lecture will be delivered by Michael M. Weil, Professor in the Department of Environmental and Radiological Health Sciences at Colorado State University. Dr. Weil was first elected to the Council in 2017 and is Co-Chair of Scientific Committee (SC) 1-27 and has served on Program Area Committee 1, SC 1-22, and SC 1-26.

The Sixth Thomas S. Tenforde Lecture will be delivered by Susanne M. Rafelski, Deputy Director at the Allen Institute for Cell Science.

Please Note: The technical program and the Q&A from each session are being recorded. In addition, all areas of the meeting are being recorded and photographed. If you wish to opt-out of videos/photos please visit the registration desk. The photographs will be posted and are publicly available on the NCRP flickr account.

Monday, March 27, 2023

Opening Session

8:10 am **Presentation of the Colors**
U.S. Navy Color Guard

Singing of the National Anthem
Kimberly Jordan
U.S. Nuclear Regulatory Commission

8:15 am **NCRP Welcome**
Kathryn D. Held
President, NCRP

8:20 am **Introduction**
Eric J. Grant, *Program Chair*
Emily A. Caffrey, *Program Vice Chair*

Nineteenth Annual Warren K. Sinclair Keynote Address

8:30 am **Introduction of the Speaker**
Kathryn D. Held

What do Risk Modelers Want? What Can Biologists Provide?
Michael M. Weil
Colorado State University

Setting the Stage with Epidemiology

Lydia B. Zablotska & S. Robin Elgart,
Session Co-Chairs

9:00 am **What Dose-Response Modeling Can, and Cannot, Tell Us About the Biological Mechanisms of Radiation Health Effects**
Dale L. Preston
Hirosoft International

9:20 am **Radiation-Related Cardiovascular Disease: Clinical and Epidemiological Studies**
Andrew Einstein
Columbia University

9:40 am **Overview of NCRP Report No. 186: Approaches for Integrating Information from Radiation Biology and Epidemiology to Enhance Low-Dose Health Risk Assessment**
R. Julian Preston
U.S. Environmental Protection Agency

10:00 am **Break**

Mechanistic Underpinnings: Cancer and Cardiovascular Disease

Sally A. Amundson & R. Julian Preston,
Session Co-Chairs

10:30 am **Low-Dose Effects: Insights from Low and High Linear-Energy Transfer Radiation**
Albert J. Fornace, Jr.
Georgetown University

11:00 am **Using Genomics to Investigate Radiation-Related Thyroid Cancer Following the Chernobyl Accident in 1986**
Stephen J. Chanock
National Cancer Institute

11:30 am **Precision Medicine with Induced Pluripotent Stem Cells and Application in Space Radiation Risk Assessment**
Joseph C. Wu
Stanford Cardiovascular Institute

12:00 pm **Mechanistic Underpinnings for Radiation-Induced Cardiovascular Disease**
Marjan Boerma
University of Arkansas for Medical Sciences

12:30 pm **Lunch**

Models and Extrapolations

Mark P. Little & Robert L. Ullrich,
Session Co-Chairs

2:00 pm **Human Biosamples for Translational Radiation Studies**
Roy E. Shore
New York University Grossman School of Medicine

2:30 pm **An Overview of Approaches for Developing Bioindicators for Risk Estimation at Low Doses and Dose Rates**
Dmitry Klokov
Institute for Radiological Protection and Nuclear Safety, France

3:00 pm **Mathematical Modeling Approaches in Oncology: Can Calculus Cure Cancer?**
Helen M. Byrne
University of Oxford

3:30 pm **Estimating Radiation Risks at Very Low Doses: Radiobiologists, Epidemiologists and Modelers Can Do this Together**
David J. Brenner
Columbia University

4:00 pm **New Technologies Provide Opportunities to Advance Radiation Research**
James A. Lederer
Brigham and Women's Hospital

4:30 pm **Break**

Forty-Sixth Lauriston S. Taylor Lecture on Radiation Protection and Measurements

5:00 pm **Introduction of the Lecturer**
Jerrold T. Bushberg

Cancer Risks and Public Health Issues Across the Radiation Frequency Spectrum: The Long and the Short of It
Martha S. Linet
National Institutes of Health

6:00 pm **Reception**

Tuesday, March 28, 2023

8:15 am **NCRP Annual Business Meeting**

9:30 am **Break**

Sixth Thomas S. Tenforde Topical Lecture

9:45 am **Introduction of the Lecturer**
Eric J. Grant

Towards Evaluating Cell Damage *via* Microscopy Imaging and Analysis of Cell Organization
Susanne M. Rafelski
Allen Institute for Cell Science

Research Needs for Filling the Gaps

Emily A. Caffrey & Eric J. Grant,
Session Co-Chairs

10:15 am **Epidemiology v2.0: Some Ideas for the Path Forward**
Jonine L. Bernstein
Memorial Sloan Kettering Cancer Center

10:30 am **Can Artificial Intelligence Improve Risk Assessment for Radiation-induced Adverse Health Outcomes?**
Issam El Naqa
H. Lee Moffitt Cancer Center

10:45 am	**Computational Biology for Future Modeling of Diseases: Is Artificial Intelligence the Way of the Future?** Afshin Beheshti *Broad Institute of Massachusetts Institute of Technology and Harvard*
11:00 am	**Looking Forward: Where Do We Go from Here?** Simon Bouffler *Public Health England*
11:20 am	**Panel Discussion:** Simon Bouffler, *Moderator* Afshin Beheshti Jonine L. Bernstein Issam El Naqa Susanne M. Rafelski
12:10 pm	**Wrap-Up** Eric J. Grant, *Program Chair* Emily A. Caffrey, *Program Vice Chair*
12:20 pm	**NCRP Vision for the Future and Program Area Committee Activities** Kathryn D. Held *President, NCRP*
12:30 pm	**Adjourn**

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Monday, March 27, 2023

Opening Session

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Nineteenth Annual Warren K. Sinclair Keynote Address

8:30 am

Introduction of the Speaker
Kathryn D. Held

What do Risk Modelers Want? What Can Biologists Provide?
Michael M. Weil
Colorado State University

Biologically based dose-response (BBDR) models are used frequently for assessing radiation associated health risks, particularly for exposure scenarios with limited epidemiological data. This presentation, which draws heavily on NCRP Report No. 186, *Approaches for Integrating Information from Radiation Biology and Epidemiology to Enhance Low-Dose Health Risk Assessment*, will delve into what biological data are needed to provide parameters for BBDR models for cancer risks and the technologies and experimental approaches available to generate these types of data. BBDR model inputs can include the kinetics of clonal expansion and cell loss amongst cells comprising nascent tumors and the rates at which critical mutations and epigenetic alterations are acquired at key steps in the carcinogenic process. The crucial empirical data needed are those that describe how radiation induces or modifies these factors.

A major challenge in deciding which particular biologic data are relevant for incorporation into a BBDR model is that the molecular and cytogenetic signatures of most radiogenic cancers are largely unknown. There are multiple pathways to cancer, but radiation acts only through a subset of them. Knowing which carcinogenic pathway is employed by a particular radiogenic tumor type is requisite to knowing which cells, beginning with the cell of origin, are at risk at key points along the pathway, which mutations must accrue, and how these mutations accelerate or impede subsequent events. Thus, experimental approaches are needed to sort out which pathways are likely to be exploited by radiogenic tumors and which are not. Having molecular and cytogenetic data from tumors arising in irradiated animals can guide this effort.

Another challenge will be in the actual data collection. This will require the use of newly emerging technologies including methodological advances for accurately detecting very rare somatic mutations, single cell sequencing, engineered human tissues and cells, and humanized experimental animals. As noted in NCRP Report 186, these technologies are advancing rapidly. Since technological advancements are often driven by necessity, it is important to clearly define what data are needed. There is an obvious need for methods that can quantify processes such as proliferation and loss *in vivo* in the very few target cells that may eventually give rise to a tumor but are otherwise indistinguishable from other more numerous cells of the same lineage and differentiation stage.

Finally, this presentation will ask what model radiogenic tumors in animals can be used to test how well BBDR models predict risk. Appropriate models will allow exposure conditions, background genetic susceptibility and other factors to be modified resulting in a range of outcomes.

Setting the Stage with Epidemiology

Lydia B. Zablotska & S. Robin Elgart, *Session Co-Chairs*

9:00 am

What Dose-Response Modeling Can, and Cannot, Tell Us About the Biological Mechanisms of Radiation Health Effects

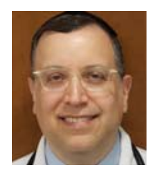
Dale L. Preston
Hirosoft International

Efforts to develop quantitative models for radiation effects on disease rates are largely based on descriptive models with no explicit consideration of biological mechanisms. Most commonly radiation effects are described in terms of the relative rate (ratios of the rates in an exposed group to those in a comparable unexposed population) or excess relative rate (the proportional increase in rates in an exposed group relative to those in an appropriate unexposed population) with some allowance for effect modification and confounding. These models are typically formulated and interpreted without any explicit consideration of biological mechanisms. We will discuss how the multistage model of carcinogenesis suggested by Armitage and Doll in the 1950s has motivated the basic form for the cancer baseline rate models used as a starting point in radiation effect modeling. We will also touch on how Kellerer and Rossi's ideas about dual radiation action influenced the form of most widely used radiation dose response models. Other, rather more sophisticated, biologically motivated models, such as Moolgavkar's two stage model, have also been used to describe radiation effects on cancer rates. While results from these models have occasionally been used to motivate thinking about the implications of the excess (relative) rate patterns that one sees, in our view, they have had little impact on thoughts about biological mechanisms of radiation carcinogenesis. We will talk about the challenges in using the radiation effect models to provide insight into the underlying mechanisms of radiation carcinogenesis, including the limited amount of information on radiation effects in virtually all epidemiological studies; the importance of choosing the right scale (excess rates or excess relative rates) on which to describe effects; and the need to look carefully at the excess risk patterns in providing ideas about mechanisms. We will also touch upon how use of richer classes of models might provide insights into the biological mechanisms of radiation effects. Despite the rapid advances in radiation-biology and, more generally, the understanding of the biology of carcinogenesis and the sophistication and usefulness of many of the descriptive models used in radiation epidemiology, more should and can be done to link those involved in these areas together.

9:20 am

Radiation-Related Cardiovascular Disease: Clinical and Epidemiological Studies

Andrew Einstein
Columbia University



Cardiovascular disease is the leading cause of death worldwide and in the United States. Numerous clinical and pathological studies have demonstrated tissue damage from high-dose ionizing radiation to various cardiac structures, including the coronary arteries, left ventricle, conduction system, valves, and pericardium. This has the potential to lead to a range of corresponding cardiovascular abnormalities, including coronary atherosclerosis and myocardial infarction, cardiomyopathy and heart failure, arrhythmias, aortic stenosis and regurgitation, and constrictive pericarditis, respectively. Understanding of this pathology at high-doses has clinical implications today, impacting screening, diagnosis, and treatment of patients. However, the relationship between ionizing radiation and cardiovascular disease is not limited to high doses, and numerous epidemiological studies of therapeutically, diagnostically, occupationally, and environmentally exposed cohorts at a range of doses and dose rates inform our knowledge of radiation's effects on the cardiovascular system. Some studies suggest a greater risk of cardiovascular disease per unit dose at lower doses and dose rates. In this talk, we will draw upon clinical and epidemiological studies to address cardiovascular diseases, their relationship to radiation exposure across the spectrum of doses, and potential clinical and policy implications.

9:40 am

Overview of NCRP Report No. 186: *Approaches for Integrating Information from Radiation Biology and Epidemiology to Enhance Low-Dose Health Risk Assessment*

R. Julian Preston
U.S. Environmental Protection Agency

NCRP Report No. 186, *Approaches for Integrating Information from Radiation Biology and Epidemiology to Enhance Low-Dose Health Risk Assessment*, derives from previous NCRP reports and commentaries that provide the case for integrating data from radiation biology studies (available and proposed) with epidemiological studies (also available and proposed) to develop biologically-based dose response (BBDR) models. The Report proposes for such models to utilize parameters developed from an adverse outcome pathways (AOP), key events (KE) approach for characterizing radiation-induced cancers and circulatory disease (as the example for a noncancer outcome). The review discusses the current state of knowledge of mechanisms of carcinogenesis, with an emphasis on radiation-induced cancers, and a similar discussion for circulatory disease. The types of the various informative BBDR models are presented along with a proposed generalized BBDR model for cancer and a more speculative one for circulatory disease. The way forward is presented in a comprehensive discussion of the research needs to address the goal of enhancing health risk assessment of exposures to low doses of radiation. The use of an AOP/KE approach for developing a mechanistic framework for BBDR models of radiation-induced cancer and circulatory disease is considered to be a viable one based upon current knowledge of the mechanisms of formation of these adverse health outcomes and the available technical capabilities and computational advances. The way forward for enhancing low-dose radiation risk estimates will require there to be a tight integration of epidemiology data and radiation biology information to meet the goals of relevance and sensitivity of the adverse health outcomes required for overall health risk assessment at low doses and dose rates. (This presentation does not necessarily reflect the views of the U.S. Environmental Protection Agency.)

10:00 am

Break

Mechanistic Underpinnings: Cancer and Cardiovascular Disease

Sally A. Amundson & R. Julian Preston, *Session Co-Chairs*

10:30 am

Low-Dose Effects: Insights from Low and High Linear-Energy Transfer Radiation

Albert J. Fornace, Jr.
Georgetown University

Our laboratory has observed a myriad of responses to damage by low-dose radiation (LDR) in cultured cells and animal models. Many of these effects are magnified with high linear-energy transfer (LET) radiation such as after exposure to high atomic number and energy (HZE) ions, a component of space radiation, or neutrons. Biological damage can be classified into two broad categories: targeted effects (TE) due to direct traversals of cells by ionizing tracks versus nontargeted effects (NTE) caused by release of signals from directly hit cells. Importantly, different radiation types are expected to produce different balances of TE and NTE due to differences in microdosimetric energy deposition patterns and consequent molecular damage profiles. Using omics approaches, we have shown that LDR can affect many tissues *in vivo* and can impact immune function and energy metabolism by inhibiting specific signaling pathways. After either low- or high-LET LDR, we have observed triggering of long-term stress signaling, elevated oxidative stress, increased senescent cells, and induction of a proinflammatory state characteristic of the senescence-associated secretory phenotype. Radiation-induced premature senescence is well known in the field, and it has been shown that even a very small number of senescent cells can result in tissue dysfunction and is probably a prominent mediator of NTE. Interestingly, modeling approaches suggest NTE are more prominent with LDR. Understanding the roles of radiation-induced senescence on metabolism, inflammation, and immune function should help to delineate a systematic view of the physiologic impacts of LDR with practical applications including risk estimation and potential targets for risk reduction.

11:00 am

Using Genomics to Investigate Radiation-Related Thyroid Cancer Following the Chernobyl Accident in 1986

Stephen J. Chanock
National Cancer Institute

The 1986 Chernobyl nuclear accident resulted in increased papillary thyroid carcinoma (PTC) risk for children exposed to radioactive iodine (^{131}I). In a landscape of genomic analyses of 440 PTCs from the Ukraine (359 cases with estimated childhood ^{131}I exposure, 81 unexposed children born after 1986), the findings revealed nearly all were in the Mitogen-activated protein kinase (MAPK) pathway, fusion drivers in PTC were more common in cases exposed to higher radiation dose ($P = 6.6 \times 10^{-8}$) and in those diagnosed at younger ages ($P = 5.4 \times 10^{-9}$) relative to those with mutation drivers. Increased radiation dose was associated with an increase in deletions ($P = 8.0 \times 10^{-9}$) as well as the deletion: SNV ratio ($P = 4.9 \times 10^{-21}$) while simple/balanced structural variants were clonal. Detailed sequence analysis revealed the hallmark of end-joining repair yet no radiation mutational signature in the context of a very low overall mutational burden of PTC. Transcriptomic and epigenomic features were strongly associated with driver events but not radiation dose. Cervical lymph node metastases (cLNM) are well-recognized in pediatric PTC, but not the PTC metastatic process nor potential radiation association. Among 440 PTC, cLNM were more frequent in PTC with fusion (55 %) versus mutation (30 %) drivers ($P = 5.8 \times 10^{-6}$), with heterogeneity by driver gene ($P = 1.6 \times 10^{-19}$; RET-fusion = 71 %, BRAF-mutation = 38 %, RAS-mutation = 5 %). cLNM frequency was not associated ($P > 1.0 \times 10^{-4}$) with other characteristics ($P_{radiation} = 0.31$). Molecular profiling of 47 cLNM revealed driver concordance with matched primary PTCs, and highly concordant mutational spectra. Transcriptome analysis revealed cLNM overexpression of a cluster of HOXC genes (*HOXC10*; $P = 6.4 \times 10^{-23}$). Our results underscore radiation-induced DNA double-strand breaks as early carcinogenic events that subsequently enable the efficient growth of PTC following environmental radiation exposure while highlighting the role of driver alterations in PTC cLNM.

11:30 am

Precision Medicine with Induced Pluripotent Stem Cells and Application in Space Radiation Risk Assessment

Joseph C. Wu
Stanford Cardiovascular Institute

Space radiation is the biggest hurdle for manned space missions, yet the current risk assessment is largely dependent on irradiation experiments or retrospective studies from environmental, occupational or therapeutic radiation exposure. Such terrestrial radiation is distinct from space radiation that contain highly penetrating high-atomic number high-energy atoms continuously exposed at low dose rate. Unlike high-dose radiation exposure, there are significant uncertainties in cardiovascular consequences of low-dose radiation exposure. Emerging evidence suggests that genetics play a significant role in heterogeneous response to radiation exposure, yet conventional risk assessment approach models do not consider genetic diversity or physiological complexities. Human induced pluripotent stem cells (iPSCs) derivatives can serve as an excellent platform for disease modeling by generating isogenic cell types of interest from diverse cohorts, and reconstruction of three-dimensional tissue with iPSC-derivatives can accurately predict the functional and molecular perturbations under external stressors. Over the last decade, we and others have pioneered the efforts to use patient iPSCs to recapitulate the clinical phenotypes by generating diverse cardiovascular cell types and elucidate the molecular mechanisms involved with cutting-edge technologies. For the current session, I will highlight our efforts of cardiovascular disease modeling with human iPSCs and of mitigating space radiation-induced cardiovascular risks.

12:00 pm

Mechanistic Underpinnings for Radiation-Induced Cardiovascular Disease
Marjan Boerma
University of Arkansas for Medical Sciences

Most of what we know about cardiovascular toxicity from ionizing radiation stems from observations in cancer patients who receive high doses of radiation to the heart or vasculature during cancer therapy. However, increased rates of cardiovascular disease are also seen in human populations after exposure to doses of ionizing radiation several-fold lower than in radiation therapy. For instance, studies have shown an increased risk of heart and circulatory disease in Japanese atomic-bomb survivors, nuclear facility emergency workers, uranium miners, radiation workers, and after exposure to low doses of ionizing radiation due to medical treatment. The analysis of these human populations is complicated by several confounding factors such as life-style factors that affect risk of cardiovascular disease. Therefore, studies in animal models have been designed to complement these results by addressing the cardiovascular risk of low-dose radiation and identifying potential mechanisms by which radiation may cause or accelerate cardiovascular disease. Animal models are now available to examine the biological effects of high- and low-dose rates of both high and low linear-energy transfer radiation. While much is still unknown, biological mechanisms by which low doses of radiation may alter the cardiovascular system have emerged.

12:30 pm **Lunch**

Models and Extrapolations

Mark P. Little & Robert L. Ullrich, *Session Co-Chairs*

2:00 pm

Human Biosamples for Translational Radiation Studies
Roy E. Shore
New York University Grossman School of Medicine

An important goal of human biosample studies is to find and verify bioindicators of key events (KEs) in biological pathways of the adverse effects of radiation, in order to improve the assessment of low-dose human risks from radiation exposure. Unlike a biodosimeter, a KE and its associated bioindicator by definition need to be related to radiation exposure level and also predictive of the health outcome or adverse effect of interest. The goal of interrogating human biosamples after radiation exposure can be to evaluate potential bioindicators of KEs that have already been identified in experimental studies, or to conduct an omics search that aims to identify new KEs and bioindicators. A natural sequence of bioindicator studies is, first, to conduct a study comparing the biosamples of a relatively high-dose (*e.g.*, >1 Gy) cohort subgroup to a comparable unexposed subgroup to validate or search for bioindicators. The predictive bioindicators can then be evaluated in low-dose groups where associations are more difficult to ascertain and uncertain.

Informative study designs and procedures are suggested, and characteristics of biosamples from selected cohorts are described. Potential study cohorts with biosamples fall roughly into three categories: groups with radiotherapy exposures (*e.g.*, childhood cancer survivors), those with a large range of whole-body exposures (*e.g.*, Japanese atomic-bomb survivors, Mayak workers), and those with primarily lower-dose exposures (various radiation-worker or environmentally exposed cohorts). More details on cohorts with biosamples are given in NCRP Report No. 186, *Approaches for Integrating Information from Radiation Biology and Epidemiology to Enhance Low-Dose Health Risk Assessment* (2020).

2:30 pm

An Overview of Approaches for Developing Bioindicators for Risk Estimation at Low Doses and Dose Rates

Dmitry Klokov
Institute for Radiological Protection and Nuclear Safety, France

Accurate estimation of risks of adverse health outcomes following exposure of humans to low doses of ionizing radiation is an important, but extremely challenging, goal of radiation protection research. In recent years much attention has been focused on specific and measurable biological parameters that can be indicative of a developing radiation-induced disease. The term “bioindicators,” likely borrowed from environmental toxicology, has been used to refer to such disease predictors. Unfortunately, no validated bioindicators of radiation-induced disease, such as cancer, exist. Therefore, their development is a task that attracts many researchers. Carcinogenesis, although canonically thought of as a mutation driven process, is in fact a very complex biological process that involves a variety of alterations not only at the molecular (DNA) level, but also at cellular, tissular and organismal or systemic levels. If key changes at each of these levels can be identified and connected in a network that reflects experimentally validated causal relationships, a resulting network is called an adverse outcome pathway (AOP). This is a concept that draws much attention of the radioprotection research community as one of the approaches for the identification of bioindicators of radiation-induced disease. Key strategies that can be used for developing AOPs and specifically for the identification and verification of potential biomarkers are discussed. One strategy that involves a systems biology approach towards analyzing complex data sets consisting of multi-omics and clinical readouts from a low-dose experimental animal study is described. Lastly, a summary and a perspective of the utility of artificial intelligence in the identification of bioindicators for radiation-induced cancer is presented.

3:00 pm

Mathematical Modeling Approaches in Oncology: Can Calculus Cure Cancer?

Helen M. Byrne
University of Oxford

The past 25 y have heralded an unparalleled increase in understanding of cancer biology. This transformation is exemplified by the expansion of Hanahan and Weinberg's original Hallmarks of Cancer from six traits to ten! Over this period, mathematical modeling has emerged as a natural tool for unraveling the complex processes that contribute to the initiation and progression of tumors, for testing hypotheses about experimental and clinical observations, and assisting with the development of new approaches for improving cancer treatment.

This talk will focus on modeling approaches that have been used to investigate the growth and response to radiotherapy of solid tumors. These will range from simple, phenomenological models that view the tumor as a homogeneous mass, to more detailed models that resolve the subcellular dynamics of the cell cycle and describe how these dynamics are impacted by fluctuations in oxygen levels, and finally multiscale models that can be used to understand how interactions between subcellular, cellular and tissue scale processes impact a tumor's overall growth dynamics and its response to radiotherapy.

Motivated by Hanahan and Weinberg's decision to expand the Hallmarks of Cancer, I will also reflect on how closer collaboration with cancer scientists and access to experimental data have driven extensions to these models which increase their power to generate qualitative and quantitative predictions about the growth and response to treatment of solid tumors.

3:30 pm

Estimating Radiation Risks at Very Low Doses: Radiobiologists, Epidemiologists and Modelers *Can* Do This Together

David J. Brenner
Columbia University

Estimating radiation risk at very low radiation doses has long been a key goal. Specifically, most large-scale radiation exposure scenarios, both past and projected, involve a (comparatively) small number of individual exposed to high radiation doses, a larger number exposed to low doses, and a very large number of individuals exposed to very low doses.

Lacking a biomarker for radiation-induced disease, radiation epidemiology requires exponentially increasing cohort sizes as the dose of interest decreases; radiobiologists face similar problems as the dose under study goes below centigray levels. Modelers face different, but still hard-to-solve, issues particularly in terms of predicting absolute risks.

However the fact that these three disciplines face different problems at very low doses does open a window of opportunity to combine the best of each to produce credible risk estimates. For example, modeling approaches rely on biological assumptions which can be tested radiobiologically at more amenable doses. And radiation epidemiology can produce risk estimates at doses corresponding to a single radiation track going through a human cell - risk estimates which are much easier for modelers to extrapolate to still lower doses.

From such considerations, I will suggest that, while neither radiobiologists, radiation epidemiologists nor modelers can produce credible very low-dose risk estimates on their own, if these different disciplines appropriately combine forces, this can be done.

4:00 pm

New Technologies Provide Opportunities to Advance Radiation Research

James A. Lederer
Brigham and Women's Hospital

Radiation exposure induces complex acute and chronic injury responses to tissues and cells that varies depending on the exposure dose and location (total or partial body). Moreover, cell damage from radiation initiates both inflammatory and counter-inflammatory reactions that result in altered homeostasis, which predisposes to opportunistic infections and aberrant resolution of radiation injury responses. The advent of next generation RNA sequencing methods (bulk and single cell), mass cytometry [cytometry by time of flight (CyTOF)], and improved proteomics platforms has provided researchers new opportunities to more precisely detect how radiation exposure impacts the immune and tissue landscape. Moreover, high-dimensional data resulting from these technologies has sparked the development of algorithms and platforms that facilitate analysis for clearer biological interpretations of findings. This presentation will provide a review of these advanced research methods and will present examples of how we have used CyTOF to study effects of radiation injury on the immune system and to develop radiation medical countermeasures to protect against opportunistic infections and delayed effects of acute radiation exposure.

4:30 pm **Break**

Forty-Sixth Lauriston S. Taylor Lecture on Radiation Protection and Measurements

5:00 pm **Introduction of the Lecturer**

Jerrold T. Bushberg

Cancer Risks and Public Health Issues Across the Radiation Frequency Spectrum: The Long and the Short of It

Martha S. Linet
National Institutes of Health

Exposures due to environmental, occupational and medical sources of ionizing and nonionizing radiation from frequencies ranging from zero to 1020 Hz are ubiquitous and of substantial public concern. Research findings from studies of these exposures are sometimes controversial. For ionizing radiation, epidemiologic, exposure assessment (dosimetric), and experimental studies since the late 1940s and early 1950s have sought to identify and quantify adverse health risks; the findings have been critically evaluated for decades by radiation protection organizations. For nonionizing radiation, investigations evaluating postulated adverse health effects were initiated in the 1970s, early 1980s, and mid-1990s for ultraviolet radiation (UVR), electromagnetic fields extremely low frequency (powerline frequency) (EMF-ELF), and radiofrequency (RF) (particularly cellular phones) exposures, respectively. Critical assessment of the research on nonionizing radiation began 30 y ago by mostly European-based national and international organizations, more recently by a few U.S. federal government agencies, and only recently by NCRP with the establishment of Program Area Committee 8. This presentation will briefly summarize highlights of epidemiologic and experimental findings on associations of UVR, EMF-ELF, and RF with cancer along with the methodological complexities and research study limitations; the latter include difficulties in estimating exposures and risks, particularly in the context of temporal changes in technologies or behavioral modifications. Analogies will be presented with the challenges for epidemiological studies of low-level ionizing radiation, air pollution, and benzene. Concluding remarks will focus on the need for radiation and public health scientists to address collaboratively scientific questions and public concerns on radiation exposures associated with postulated health risks using multi-disciplinary, methodologically rigorous, and cost-effective research approaches and to use state-of-the-art and proven approaches to communicate findings to the public.

6:00 pm **Reception**

Tuesday, March 28, 2023

8:15 am **NCRP Annual Business Meeting**

9:30 am **Break**

Sixth Thomas S. Tenforde Topical Lecture

9:45 am **Introduction of the Lecturer**
Eric J. Grant

Towards Evaluating Cell Damage *via* Microscopy Imaging and Analysis of Cell Organization
Susanne M. Rafelski
Allen Institute for Cell Science

To understand how a cell, the fundamental unit of life, becomes damaged or abnormal we must first understand what it means for a cell to be normal. A key to understanding the cell is to understand the interplay between cell organization, cell behavior, and cell (molecular) identity. If we can decipher the patterns and rules of how these defining characteristics of a cell work together in space and time then we believe we should be able to "look" at a cell and know what it is doing, what it did, and what it will do. To achieve this, cell scientists require lots and lots of images of cells in real time and then the tools and approaches to transform these images into useful quantitative measurements. The genomics era has provided conceptual approaches and practical tools to data collection and analysis of sequence data and gene expression levels, providing rich datasets on the molecular identity of cells. Likewise, technological improvements in microscopy have made it possible to capture high-resolution three-dimensional (3D) images of healthy, undamaged cells in time. However, cell scientists are now faced with the challenge of developing robust statistical methods for measuring similarities and differences among 3D images of cells and intracellular structures to quantify cell organization and behavior, a task that is conceptually much more complex and requires development of novel image and data analysis frameworks. As we develop these types of novel approaches towards a holistic understanding of the cell, we also aspire to democratize this emerging area of research by sharing our data, analysis algorithms and the reagents, methods, and tools needed to generate them, in an easily accessible way (www.allencell.org).

Research Needs for Filling the Gaps

Emily A. Caffrey & Eric J. Grant, *Session Co-Chairs*

10:15 am

Epidemiology v2.0: Some Ideas for the Path Forward

Jonine L. Bernstein
Memorial Sloan Kettering Cancer Center

As a result of numerous radiation epidemiologic studies, we understand a great deal about the association between exposure to ionizing radiation and adverse human health effects. The focus of these studies has been on the long-term consequences of radiation exposure, primarily: survivors of nuclear and radiation accidents; occupationally exposed workers and the military; patients receiving medical treatment or diagnostic procedures; and populations exposed to elevated levels of natural background radiation, such as radon. Across these studies, the most informative for evaluating radiation-related health risks are those that examine the effects of higher doses and higher dose rates where the evidence is derived from direct measurements. The major challenge today are studies of low-dose exposure risk estimation which are based on dose extrapolation and multiple assumptions. Radiation biology-based data from laboratory animal, cellular and molecular studies elucidate mechanisms underlying radiation-induced damage. Reducing uncertainty in low-dose risk estimation to determine biologic effectiveness requires combining information from experimental studies with observational data from epidemiologic and clinical studies indicating how cells and tissues respond to the damage. The design of the next generation of radiation epidemiologic studies will require cross disciplinary integration of these data, efficient study designs suitable for nested case-control studies and technology for multi-modal integrated analyses. Necessary high quality epidemiologic data involves ascertaining: individual level radiation exposure and risk factor information; detailed long-term follow-up; genetic factors/biospecimen collection; and large sample sizes that include individuals across the lifespan and allow for multiple outcomes. Building on the strength of prior studies, some ideas for how to proceed now will be discussed.

Integration of Physics, Biology and Epidemiology in Radiation Risk Assessment

10:30 am

Can Artificial Intelligence Improve Risk Assessment for Radiation-induced Adverse Health Outcomes?

Issam El Naqa
H. Lee Moffitt Cancer Center

Artificial intelligence (AI) and machine learning (ML) algorithms are currently transforming biomedicine including radiation-related fields in oncology, radiobiology, medical physics, and potentially health physics. AI/ML has been successfully demonstrated to automate complex processes and improve efficiency in areas related to auto-contouring, quality assurance, and treatment planning in radiation oncology. There is also evidence to support better prediction of radiation treatment response including risks of radiation-induced toxicities compared to conventional radiobiology models. Despite this success and the anticipated potentials for health physics, AI/ML applications remain limited in health practice. In this presentation we will present some of these applications and highlight potentials and current challenges. The presentation will further show examples of implementing new approaches to overcome these challenges in health physics from and discuss their implications for the future of AI/ML in the field.

10:45 am

Computational Biology for Future Modeling of Diseases: Is Artificial Intelligence the Way of the Future?

Afshin Beheshti
Broad Institute of Massachusetts Institute of Technology and Harvard

Effective countermeasures/therapeutics for radiation-induced genetic damage are crucial for space health for long-duration exploration missions. Mitigations for the space environment should effectively regulate the increased health risks and should also minimize off-target regulation to reduce toxicity. Computational approaches integrated with systems biology are starting to be effectively utilized for many different diseases and subjects. In this presentation, I will specifically focus on how computational methods are utilized in three different subjects, which include lymphoma, COVID-19, and space biology work, to determine key biology involved for biomarker development with health risks associated with each and rapid development of therapeutics and countermeasures. One focus is studying microRNAs (miRNAs) which are small, noncoding RNA that are part of a cell's natural regulatory system. By combining molecular modeling, bioinformatics, and high-throughput experimental screening to design miRNAs to silence targeted damaged (or mutated) genes, potential applications are wide-ranging from space radiation induced genetic damage to terrestrial genetic disease, cancer, biomarkers, COVID-19, and countermeasure/therapeutic development. In addition, we have utilized novel machine learning techniques to predict potential U.S. Food and Drug Administration approved drugs/small molecules that can provide inhibition of the miRNAs and other key biology involved with increasing health risks with spaceflight, lymphoma, and COVID-19. These methods have broad application to many subjects, which will also be discussed.

11:00 am

Looking Forward: Where Do We Go from Here?
Simon Bouffler
Public Health England

It is self-evident that radiation (bio)physics, radiation biology, and radiation epidemiology each consider the effects of radiation on living organisms at differing levels of biological organization, from fundamental molecular interactions through to population health effects. Traditionally these disciplines have operated fairly independently though all have essentially the same aim - understanding the effects of radiation on health. Perhaps it is over the last decade or so that it has been recognized that integration over the levels of biological organization is required to provide a more complete description of disease processes and ultimately health risk to humans. Organizations such as Multidisciplinary European Low Dose Initiative, NCRP, and the National Academies of Sciences, Engineering, and Medicine have all recognized this in reports and research agendas.

Integration does not happen through chance alone, there is a need to provide mechanisms and support to build interdisciplinary research teams and encourage working at all levels of biological organization. This talk aims to pick up on themes emerging from the presentations at this meeting and consider how interdisciplinary working can be fostered and encouraged at national and international levels. In terms of application of interdisciplinary research for radiation risk assessment, there is a need to generalize research findings which tend to focus on individual disease endpoints in specific models or populations. These challenges are not trivial, especially in a world where radiation research has been in decline.

11:20 am

Panel Discussion:
Simon Bouffler, *Moderator*
Afshin Beheshti
Jonine L. Bernstein
Issam El Naqa
Susanne M. Rafelski

12:10 pm

Wrap-Up
Eric J. Grant, *Program Chair*
Emily A. Caffrey, *Program Vice Chair*

12:20 pm

NCRP Vision for the Future and Program Area Committee Activities
Kathryn D. Held
President, NCRP

12:30 pm **Adjourn**

Program Committee

Eric J. Grant, *Chair*
Radiation Effects Research Foundation (retired)
Ft. Myers, Florida

Emily A Caffrey, *Vice Chair*
University of Alabama at Birmingham
Huntsville, Alabama

Members

Sally A. Amundson
Columbia University Irving Medical Center
New York, New York

Kristin Fabre
National Aeronautics and Space Administration
Houston, Texas

Mark P. Little
National Cancer Institute
Bethesda, Maryland

R. Julian Preston
U.S. Environmental Protection Agency
Research Triangle Park, North Carolina

Robert L. Ullrich
Radiation Effects Research Foundation
Hiroshima, Japan

Michael M. Weil
Colorado State University
Fort Collins, Colorado

Register online: https://ncrp.civdigital.com/2023-annual-meeting/

@NCRP2023

2024 Annual Meeting

Advanced Power Reactor Technology

March 25–26, 2024
Bethesda, Maryland

Annual Warren K. Sinclair Keynote Address

Dr. Michael M. Weil has been selected to give the 19th Warren K. Sinclair Keynote Address at the 2023 Annual Meeting of the National Council on Radiation Protection and Measurements (NCRP). The Address, entitled “What Do Risk Modelers Want? What Can Biologists Provide?,” will be a featured presentation at the 59th NCRP Annual Meeting to be held March 27-28, 2023 at the Hyatt Regency Bethesda, Bethesda, Maryland. The Address will be given at 8:30 a.m. on March 27, 2023. The keynote speaker series honors Dr. Warren K. Sinclair, NCRP's second President (1977 to 1991).

Dr. Weil is a Professor in the Department of Environmental and Radiological Health Sciences at Colorado State University (CSU). His research, which takes advantage of murine models of radiation carcinogenesis and leukemogenesis, is focused on understanding how radiation exposure can lead to cancer and why some individuals may be more susceptible than others. At CSU, Dr. Weil teaches a graduate level course in cancer genetics and lectures in courses on cancer biology, environmental carcinogenesis, principles of radiation biology, and the pathobiology of laboratory animals.

Dr. Weil was first elected to the Council in 2017 and is Co-Chair of Scientific Committee (SC) 1-27 that published NCRP's most recent Commentary No. 32 on Evaluation of a Sex-Specific Difference in Lung Cancer Radiation Risk and Approaches for Improving Lung Cancer Radiation Risk Projection (with a Focus on Application to Space Activities). He has served on Program Area Committee 1, SC 1-22, SC 1-26, and has been a member of Annual Meeting Program Committees in 2021 and 2023. He was also a speaker at both the 2011 and 2021 annual meetings.

Dr. Weil earned his PhD in Microbiology from the University of Texas at Austin and was trained in cancer genetics and radiation biology in the Department of Biochemistry and Molecular Biology and the Department of Experimental Radiotherapy at the University of Texas M.D. Anderson Cancer Center. Dr. Weil is a former Radiation Research Society council member and has served on National Institutes of Health, U.S. Department of Defense, and National Aeronautics and Space Administration grant review panels.

Lauriston S. Taylor Lecture

Dr. Martha S. Linet has been selected to give the 46th Lauriston S. Taylor Lecture at the 2023 Annual Meeting of the National Council on Radiation Protection and Measurements (NCRP). The Lecture, entitled “Cancer Risks and Public Health Issues Across the Radiation Frequency Spectrum: The Long and the Short of It,” will be the featured presentation at the 59th Annual Meeting to be held on March 27-28, 2023 at the Hyatt Regency Bethesda, Bethesda, Maryland. The Lecture will be given at 5:00 p.m. on March 27, 2023. The lecture series honors the late Dr. Lauriston S. Taylor, NCRP Founding President (1929 to 1977) and President Emeritus (1977 to 2004).

Dr. Linet received her BA from Brandeis University, MD from Tufts University, School of Medicine, completed a residency in internal Medicine at Montefiore Hospital in New York, and received an MPH and post-doctoral epidemiology training at the Johns Hopkins School of Public Health.

Currently, Dr. Linet is a National Institutes of Health Scientist Emerita and Special Volunteer in the Radiation Epidemiology Branch of the National Cancer Institute (NCI) where she was Branch Chief (2002 to 2014) and Senior Investigator (1996 to 2019). Dr. Linet authored/coauthored over 400 peer-reviewed journal articles and numerous reviews and commentaries on cancer risks associated with ionizing and nonionizing radiation and on risk factors for hematopoietic neoplasms and brain tumors. She mentored and/or supervised over 40 pre-/post-doctoral fellows. Her many awards include election to the Johns Hopkins Society of Scholars and to the American Epidemiological Society and receipt of the U.S. Department of Health and Human Services Career Achievement Award.

Dr. Linet was elected to the Council in 2010 and became a Distinguished Emeritus Member in 2016. She currently serves on Scientific Committee (SC) 8-1 on Development of NCRP Informational Webpages to Provide Authoritative Information About the Use of Wireless Technology and Current Evidence on Health Effects. She was a member of SC 4-4 on Risks of Ionizing Radiation to the Developing Embryo, Fetus and Nursing Infant and a co-author of NCRP Report No. 174. *Preconception and Prenatal Exposure: Health Effects and Protective Guidance* (2013).

Dr. Linet served on the Nuclear and Radiation Studies Board of the National Academies of Sciences, Engineering and Medicine during 2011 to 2017. She was a member of the Board of Directors and President of the American College of Epidemiology. She serves on the editorial board of the *Journal of NCI* and previously served on the *American Journal of Epidemiology* editorial board.

Thomas S. Tenforde Topical Lecture

Dr. Susanne M. Rafelski has been selected to give the 6th Thomas S. Tenforde Topical Lecture at the 2023 Annual Meeting of the National Council on Radiation Protection and Measurements (NCRP). The Lecture, entitled "Towards Evaluating Cell Damage via Microscopy Imaging and Analysis of Cell Organization," will be a featured presentation at the 59th NCRP Annual Meeting to be held on March 27-28, 2023 at the Hyatt Regency Bethesda, Bethesda, Maryland. The Lecture will be given at 9:45 a.m. on March 28, 2023. The topical lecture series honors Dr. Thomas S. Tenforde, NCRP's fourth President (2002 to 2012).

In December 2020, Dr. Rafelski became the Deputy Director at the Allen Institute for Cell Science which aims to understand the principles by which human induced pluripotent stem cells (hiPSC) establish and maintain robust dynamic localization of cellular structures, and how cells transition between states during differentiation and disease.

Prior to joining the Institute in 2016, Dr. Rafelski was an Assistant Professor in the Department of Developmental and Cell Biology, the Department of Biomedical Engineering, and the Center for Complex Biological Systems at University of California Irvine. She began imaging live cells and visualizing intracellular dynamics in three-dimensions (3D) when she was 17 and hasn't been able to stop since. Her life-long scientific goal is to decipher the patterns and rules that transform the overwhelming complexity found inside cells into functioning units of life. She believes that to do this we must understand the organization of the structures within the cell in space and time. Dr. Rafelski takes an interdisciplinary, quantitative approach to cell biology, combining live-cell image-based assays, molecular genetics, and computational methods.

Dr. Rafelski obtained her BS in Biochemistry and Molecular and Cellular Biology with an additional emphasis in Mathematics from the University of Arizona. She then completed her PhD in Biochemistry at Stanford University, followed by a postdoc at the Center for Cell Dynamics at the Friday Harbor Labs, University of Washington, where she learned computational modeling approaches. Her research focused on integrating bacterial polarity with host-cell cytoskeletal dynamics to understand Listeria actin-based motility. Dr. Rafelski then initiated her current research program on mitochondrial structure-function as a postdoc at University of California San Francisco, where she developed 3D microscopy and image analysis methods to quantify mitochondrial morphology and applied these to investigate mitochondrial size control regulation. As a model system for intracellular organization, the Rafelski lab extended this work to studying the size, topology, and function of mitochondrial networks in budding yeast and mammalian cells.

John D. Boice, Jr., Young Investigator Award

Established in April 2019 by a generous donation by President Emeritus / Director of Science, John D. Boice, Jr., the Young Investigator Award recognizes an early career professional engaged in some aspect of science pertaining to radiation protection and measurements. Dr. Michael B. Bellamy has been selected as the third recipient of the award that includes a travel grant to attend the annual meeting of NCRP where he will be recognized for his accomplishments.

Dr. Bellamy is an expert at applying high-performance radiation transport and internal kinetics algorithms to analyses that support patient, epidemiologic, and occupational radiation safety research and excellence. Currently employed at the Memorial Sloan Kettering Cancer Center, Dr. Bellamy is a member of NCRP Scientific Committee 1-28, Recommendations on Statistical Approaches to Account for Dose Uncertainties in Radiation Epidemiologic Risk Models.

In addition to his ongoing expert dosimetric support of the NCRP Million Person Study on occupational radiation epidemiology, this Georgia Tech graduate has significant radiation protection professional service and affiliations. He serves as a consultant to the International Commission on Radiation Units and Measurements Report Committee 26 (operational radiation protection quantities for external radiation), a corresponding member on the International Commission on Radiological Protection Task Group 90 (age-dependent dose coefficients for external exposures to environmental sources), and a member on the American Nuclear Society Radiation Protection and Shielding Division subcommittees.

Beyond his technical publications in the peer-reviewed literature, Dr. Bellamy has produced numerous federal agency reports [including for the U.S. Environmental Protection Agency (EPA)-Office of Radiation and Indoor Air, U.S. Nuclear Regulatory Commission, Centers for Disease Control and Prevention, EPA-SUPERFUND, and U.S. Department of Energy]. During his time at Oak Ridge National Laboratory (Center for Radiation Protection Knowledge) he worked on cancer risk estimates following inhalation or ingestion of radioactive materials, dose coefficients for external exposure from environmentally distributed radionuclides, dose-rate and dose associated with exposure to patients treated with ^{131}I, neutron dose to the lens of the eye, as well as models and calculations on the relative biological effectiveness of low-energy electrons, photons, and radionuclides, and on other relevant topics of importance for the profession of radiation protection.

Biographies

Sally A. Amundson, Program Committee & Session Co-Chair, is an Associate Professor of Radiation Oncology at the Center for Radiological Research of Columbia University Irving Medical Center in New York, where she is Co-Director of the Center for High-Throughput Minimally-Invasive Radiation Biodosimetry. She holds a doctorate in radiation biology and cancer biology from the Harvard School of Public Health. Her research uses functional genomics approaches to study low-dose radiation and bystander effects, unique effects of space radiation, the development of gene expression approaches for radiation biodosimetry, and the linear-energy transfer dependence of heavy ion radiotherapy.

Prior to joining the group at Columbia, Dr. Amundson worked on molecular radiation biology in the Division of Basic Science at the National Cancer Institute (NCI), where she helped to develop global gene expression profiling techniques, and where she was an Adjunct Investigator in the NCI Radiation Epidemiology Branch. She served on the Science Advisory Committee of the Radiation Effects Research Foundation in Hiroshima from 2009 to 2014 and on the U.S. Environmental Protection Agency Science Advisory Board's Radiation Advisory Committee from 2015 to 2022. She has been a member of the Multidisciplinary European Low Dose Initiative (MELODI) Scientific Advisory Committee since 2016 and has served on the NCRP since 2004.

Dr. Amundson is an Associate Editor of Radiation Research, and has served on the organizing and program committees for numerous meetings, including two of the American Statistical Association Conferences on Radiation and Health, which aim to integrate radiation biology with epidemiology. She is a recipient of the Michael Fry Research Award from the Radiation Research Society (RRS), and served as President of the RRS in 2021 to 2022.

Jonine L. Bernstein, Speaker, is an Attending Epidemiologist at Memorial Sloan Kettering Cancer Center and co-Leader of the institution-wide Population Sciences Research Program. She received a PhD in Epidemiology from Yale University, an MS in Applied Biometry from the University of Southern California, and an AB in Urban Environmental Health (Independent Concentration) from Brown University. Dr. Bernstein's research focuses on genetic and molecular epidemiology, particularly in the etiology of breast cancer and gliomas and the late effects of treatment. She is also spear-heading projects developing and validating radiation-related biomarkers of breast cancer and cognitive impairment. Dr. Bernstein is the principal investigator of the international population-based 25-center Women's Environmental Cancer Radiation and Epidemiologic (WECARE) Study which was specifically designed to examine the interaction of radiation exposure and genetic predisposition in breast cancer, especially radiation-associated contralateral breast cancer. On-going WECARE studies include examining the role of mutations in candidate genes (*e.g.*, ATM, BRCA1, BRCA2, Palb2, Chek2) and pathways (e.g., DNA repair, immune response) as well as tumor molecular markers and risk of developing contralateral breast cancer. At NCRP, Dr. Bernstein is a current Council Member, Co-Chair of Program Area Committee 1, and Co-Chair of the Scientific Committee (SC) 1-28 on Recommendations on Statistical Approaches to Account for Dose Uncertainties in Radiation Epidemiologic Risk Models and was Co-Chair of NCRP SC 1-21 Commentary, *Health Effects of Low Doses of Radiation: Integrating Radiation Biology and Epidemiology*. She also serves as a Scientific Advisory Board Member for the Radiation Effects Research Foundation (in Hiroshima) and is a member of the U.S. Environmental Protection Agency Radiation Advisory Committee. Dr. Bernstein is Past President of the American College of Epidemiology and a past member of the Board of Scientific Counselors Clinical Sciences and Epidemiology at the National Cancer Institute. She is an elected member of the American Epidemiological Society.

Afshin Beheshti, Speaker, completed his PhD from Florida State University in physics and made a transition to cancer, systems biology, space biology, and radiation biology for his postdoctoral training. In 2014 he became an Assistant Professor at Tufts University School of Medicine/Tufts Medical Center where he continued his research as a systems biologist studying various aspects of cancer including microRNAs, aging and cancer, cancer drug targets, and development of novel immunotherapy. In April 2017, Dr. Beheshti joined KBR, National Aeronautics and Space Administration Ames Research Center originally to be part of the GeneLab project assisting with developing the platform. Currently, Dr. Beheshti has several grants where he is conducting his own research on how microRNAs and mitochondria affect space biology, lymphoma, COVID-19 and potential use for countermeasures/therapeutics to mitigate these diseases and responses. Dr. Beheshti currently also holds a Visiting Researcher appointment at Broad Institute of Massachusetts Institute of Technology and Harvard and is the Lead of a nonprofit formed on March 2020 working on COVID-19 called COVID-19 International Research Team.

Marjan Boerma, Speaker, received her PhD in radiation biology with a focus on animal models of radiation-induced heart disease from Leiden University, the Netherlands in 2004 and followed this with a postdoctoral fellowship in the Department of Surgery at the University of Arkansas for Medical Sciences (UAMS). She joined the faculty of the UAMS College of Pharmacy (COP) in 2006 and is now professor and director of the COP Division of Radiation Health. Her research expertise is in animal models of normal tissue injury from ionizing radiation, specifically in the cardiovascular system. Her laboratory uses animal models that address whole-body radiation exposure due to radiological accidents, cardiac side effects of radiation therapy, and cardiovascular effects of low and high linear-energy transfer radiation to mimic exposures during deep-space travel. She has co-authored more than 100 peer-reviewed articles in this area, and her research funding has been provided by the National Cancer Institute, the National Institute of Allergy and Infectious Diseases, the National Aeronautics and Space Administration, the American Cancer Society, and other federal and private funding sources.

Simon Bouffler, Panel Moderator & Speaker, trained as a biologist, receiving a BSc and PhD from the University of Southampton and has worked in the radiation protection field for over 30 y. In his role of Deputy Director for Radiation Protection Sciences at the U.K. Health Security Agency, he has responsibility for all aspects of radiation protection from front-line services and emergency incident preparedness and response through to the underpinning science.

Dr. Bouffler has been involved in many radiation protection research projects, including the current Pianoforte partnership, leading on research infrastructures, and he provided leadership on stakeholder engagement for the earlier European Joint Programme for the Integration of Radiation Protection Research Project. He is Chair of the Multidisciplinary European Low Dose Initiative Strategic Research Agenda working group. Dr. Bouffler has published extensively on radiation cancer and leukemia mechanisms, radio-sensitivity, circulatory disease and eye lens sensitivity with over 130 peer reviewed publications.

In addition, Dr. Bouffler has a number of international advisory roles. He is the U.K. Representative to the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) and a member of the International Commission on Radiological Protection Main Commission. For UNSCEAR he acted as coordinating lead writer for the 2021 report on Biological Mechanisms Relevant for the Inference of Cancer Risks from Low-dose and Low Dose-rate Radiation. Recently he was a member of the U.S. National Academies of Sciences committee, Developing a Long-Term Strategy for Low-Dose Radiation Research in the United States. In 2018, Dr. Bouffler was awarded the Weiss Medal by the Association for Radiation Research.

Biographies

David J. Brenner, Speaker, is the Director of the Columbia University Center for Radiological Research. Founded by a student of Marie Curie, and focusing on new ways to use radiation to better human health, the Center is the oldest and largest radiation biology center in the United States.

Dr. Brenner is the Principal Investigator of the Columbia University program focusing on ultra-high throughput minimally-invasive radiation biodosimetry to respond to a large scale radiological event. Dr. Brenner's team was also the first to quantify the potential issues associated with the rapidly increasing usage of computed tomography scans in the United States. In the radiotherapy field his proposal to use hypofractionated radiotherapy to treat prostate cancer is now standard of care in the clinic. More recently Dr. Brenner has pioneered the use of far-ultraviolet C light as a potentially safe modality designed to sharply reduce airborne viral transmission in occupied public spaces.

Dr. Brenner has published more than 400 peer-reviewed papers and is the author of two books on radiation for the lay person: *Making the Radiation Therapy Decision* and *Radon, Risk and Remedy*. He is a recipient of the Radiation Research Society Failla Gold Medal, and the Oxford University Weldon Prize for mathematical methods applied to biology.

Helen M. Byrne, Speaker, is a Professor of Mathematical Biology at the University of Oxford, with over 25 y experience of developing mathematical models of biomedical systems. She has played a significant role in defining the foundations for mathematical oncology, publishing pioneering work on multiscale and multiphase models of tumor growth and angiogenesis. She was awarded an Advanced Research Fellowship by the U.K.'s Engineering and Physical Sciences Research Council (2000 to 2006) and the Society of Mathematical Biology's Leah Edelstein-Keshet prize (2019) and became a Society of Mathematical Biology Fellow in 2020, in recognition of her contributions to mathematical biology.

She now holds a joint appointment between the University of Oxford's Mathematical Institute and the Oxford Branch of the Ludwig Institute for Cancer Research.

Emily A. Caffrey, Program Vice Chair & Session Co-Chair, is the Program Director and an Assistant Professor for the University of Alabama at Birmingham's Masters in Health Physics Program. She also serves as a scientific consultant to Risk Assessment Corporation. In addition to her consulting and academic roles, Emily is the Editor-in-Chief of the Health Physics Society's (HPS) “Ask The Experts,” the Society's most successful public information and outreach endeavor. Dr. Caffrey also serves on the HPS Program Committee, which develops and manages the technical program of the society's meetings. She has a BS in Nuclear Engineering and a PhD. in Radiation Health Physics and Statistics from Oregon State University. She is also a Certified Health Physicist. Her areas of expertise include dosimetry, statistics, data management and interpretation, and public communication.

She is a recipient of the HPS Elda E. Anderson award for outstanding early career health physicists. In 2019 she was selected as one of 10 recipients of Oregon State's Council of Outstanding Early Career Engineers. This award is reserved for Oregon State Alumni who have distinguished themselves through professional practice, service to Oregon State University, the profession, or society at large.

Stephen J. Chanock, Speaker, is a leading expert in the discovery and characterization of cancer susceptibility regions in the human genome. He has received numerous awards for his scientific contributions to our understanding of common inherited genetic variants associated with cancer risk and outcomes, including the Niehaus, Southorth, Weissenbach Award in Clinical Cancer Genetics, the Jeffrey M. Trent Lecture, and the American Association for Cancer Research-American Cancer Society Award for Research Excellence in Cancer Epidemiology and Prevention in 2021. He is an elected member of the Society for Pediatric Research, the Association of American Physicians, and the American Epidemiological Society. He received his MD from Harvard Medical School in 1983 and completed clinical training in pediatrics, pediatric infectious diseases, and pediatric hematology/oncology and research training in molecular genetics at Boston Children's Hospital and the Dana-Farber Cancer Institute, Boston. From 2001 to 2007, he was a tenured investigator in the Genomic Variation Section of the Pediatric Oncology Branch in the National Cancer Institute (NCI) Center for Cancer Research. In 2001, he was appointed as Chief of the Cancer

Genomics Research Laboratory (formerly Core Genotyping Facility), and in 2007 as Chief of the Laboratory of Translational Genomics, both within the NCI Division of Cancer Epidemiology and Genetics (DCEG). Dr. Chanock co-led the Cancer Genetic Markers of Susceptibility project. From 2012 to 2013, he also served as Acting Co-Director of the NCI Center for Cancer Genomics. Dr. Chanock was appointed Director of DCEG in August 2013.

Andrew J. Einstein, Speaker, is a cardiologist and cardiac imager at Columbia University Irving Medical Center and New York-Presbyterian Hospital. He is a tenured professor of medicine, with appointments in the Departments of Medicine and Radiology, and serves as Director of Nuclear Cardiology, Cardiac Computed Tomography (CT), and Cardiac Magnetic Resonance Imaging (MRI) and Director of the Advanced Cardiac Imaging Fellowship. Born and raised in New Jersey, Dr. Einstein received an AB in mathematics from Princeton University and attended Mount Sinai School of Medicine, where he received an MD as well as a PhD in the Department of Biomathematical Sciences. He also received an MS in patient-oriented research/biostatistics from Columbia's Mailman School of Public Health. After internship and residency in internal medicine at Rutgers Robert Wood Johnson Medical School, he completed cardiology fellowship training at Mount Sinai.

Dr. Einstein's clinical activities are centered on cardiovascular positron emission tomography, single-photon emission computerized tomography, CT, and MRI, and he serves as an attending clinical cardiologist caring for patients with a range of cardiovascular diseases including coronary artery disease, heart failure, valvular heart disease, and arrhythmias. His research, which uses each of these imaging modalities, focuses on improving the use of imaging in cardiovascular medicine, with particular interests and funded projects in radiological protection, amyloidosis, COVID-19, machine learning, and device development. His research is funded by multiple National Institutes of Health (NIH) grants, the International Atomic Energy Agency, and industry. Dr. Einstein is the author or coauthor of over 300 papers and abstracts, in journals including the New England Journal of Medicine, Journal of the American Medical Association, and Lancet. This work has been influential in affecting clinical practice, and has been widely reported in the popular media and cited over 15,000 times in the scientific literature. Dr. Einstein received the Society of Nuclear Medicine and Molecular Imaging's 2022 Hermann Blumgart Award, the American College of Cardiology's Douglas P. Zipes Distinguished Young Scientist Award, and the Lewis Katz Cardiovascular Research Prize for a Young Investigator. Dr. Einstein is a Council Member of NCRP, chair of the Academic Cardiology Section of the American College of Cardiology, and a member of the boards of directors of the American Society of Nuclear Cardiology and the Cardiovascular Council of the Society of Nuclear Medicine and Molecular Imaging. He serves as a member of the Nuclear Regulatory Commission's Advisory Committee for the Medical Use of Isotopes, on the editorial boards of Journal of the American College of Cardiology: Cardiovascular Imaging and the Journal of Nuclear Cardiology, and served as a voting member of the Food and Drug Administration's Medical Imaging Drugs Advisory Committee, on several NIH study sections, and as a coauthor of the International Commission on Radiological Protection Publication 120 on radiological protection in cardiology. Dr. Einstein has served as a mentor to over 40 trainees at stages ranging from high school to junior faculty.

S. Robin Elgart, Session Co-Chair, received her BS in Microbiology from the University of California at Santa Barbara and her PhD in Biomedical Physics from the University of California at Los Angeles in the laboratory of Dr. Keisuke Iwamoto. Her dissertation focused on characterizing the DNA damage response following low-dose radiological exams in patient samples. Dr. Elgart has over 15 y of diverse research experience across multiple life-science disciplines including microbiology, medical physics, and radiation biology. Before joining the Human Research Program as the Space Radiation Element Scientist in April 2020, she served as a subject matter expert specializing in space radiation health risks for the National Aeronautics and Space Administration Space Radiation Analysis Group as well as a Space Environment Officer for Mission Control Center - Houston. As the Space Radiation Element Scientist, Dr. Elgart's primary objective is to develop and execute a robust applied research strategy to meet the agency's goal to safely put the first woman on the Moon and the first humans on Mars.

Biographies

Issam El Naqa, Speaker, is the Chair of the Department of Machine Learning and Senior Member of Radiation Oncology at Moffitt Cancer Center. He has over 20 y of experience in radiation oncology, and is certified medical physicist, researcher, and educator. He is a recognized authority in the fields of machine learning, data analytics, and radiation oncology outcomes modeling and has published extensively in these areas with more than 230 peer-reviewed journal publications and four edited textbooks. He has been a member and fellow of several academic and professional societies including the American Association of Physicists in Medicine and the Institute of Electrical and Electronics Engineers. His research has been funded by several federal and private grants in Canada and the United States and he has served on national and international study sections. He acts as a peer-reviewer and editorial board member for several leading international journals in his areas of expertise.

Kristin, Fabre, Program Committee, joined the National Aeronautics and Space Administration (NASA) Human Research Program as Deputy Chief Scientist in January of 2022. In this role, she works with the Human Research Program (HRP) Management Team and HRP scientists to help drive scientific strategy and scientific portfolio management, working toward the mission of investing in research and technology that mitigates human risk during spaceflight and space missions. Dr. Fabre's previous role was as Chief Scientist at the Translational Research Institute for Space Health (TRISH) from December 2018 to May 2020. At TRISH she led the effort to invest in high-risk, high-reward research and technology for space exploration. She worked with various stakeholders including NASA, industry and academia to adopt and implement outcomes from TRISH-funded project deliverables. Before joining TRISH, Dr. Fabre was the Microphysiological Systems (MPS) Lead at AstraZeneca (AZ) and was part of the MPS Center of Excellence, Drug Safety and Metabolism. Prior to joining AZ in 2016, she was the Scientific Program Manager for the Microphysiological Systems (or Organs-on-Chips) Initiative at the National Institutes of Health (NIH) National Center for Advancing Translational Sciences (NCATS).

Dr. Fabre received her BS in Biology from the University of Wyoming, followed by her MS and PhD from Colorado State University in Cell and Molecular Biology. Prior to joining NCATS, she was at the NIH National Cancer Institute (NCI) as a postdoctoral fellow in the Radiation Biology Branch. During her time at the NCI, Dr. Fabre was highly involved with training programs and was Chair of the NCI Fellows and Young Investigators Steering Committee and created the NCI Fellows Outreach Committee.

Albert J. Fornace, Jr., Speaker, is a Professor in the departments of Oncology; Biochemistry and Molecular and Cellular Biology; and Radiation Medicine at Georgetown University. He was the first recipient of the Molecular Cancer Research Chair at Lombardi Comprehensive Cancer Center, joining Georgetown in 2006 from the Harvard School of Public Health, where he was the Director of the John B. Little Center for the Radiation Sciences and Environmental Health. Earlier, he was Chief of the Gene Response Section at the National Cancer Institute. He is the 2015 recipient of the Radiation Research Society Failla Award.

In the case of radiation research projects, Dr. Fornace leads the multi-institutional National Aeronautics and Space Administration (NASA) Specialized Center of Research in gastrointestinal carcinogenesis by low-dose space radiation. He is also a member of the National Institute of Allergy and Infectious Diseases (NIAID)-funded multi-institutional Center for High Throughput Minimally-Invasive Radiation Biodosimetry which is headed by Dr. David Brenner at Columbia University; he is principal investigator (PI) of a recent NIAID award on metabolomic impairment of immune function by radiation; and PI of a NASA-supported project on mammary tumorigenesis by space radiation. He was also supported in the past by the U.S. Department of Energy's low-dose radiation program. In addition to his research on the molecular pathways involved in radiation signaling, Dr. Fornace has also studied cellular stress responses at broader levels. His laboratory at the National Cancer Institute was the first in collaboration with the National Human Genome Research Institute to assess genome-wide responses to radiation using a transcriptomics approach. His omics studies were then extended to the small molecule level, *i.e.*, metabolomics, and his team along with collaborators developed the field of radiation metabolomics, and have demonstrated low-dose radiation effects at the metabolomic level. Dr. Fornace currently directs the Waters Center of Innovation for Metabolomics at Georgetown and the Georgetown Center for Metabolomic Studies.

Biographies

Eric J. Grant, Program Chair & Session Co-Chair, recently retired from the Radiation Effects Research Foundation (RERF) in Hiroshima/Nagasaki, Japan, where he worked for the past 25 y. Dr. Grant's research focused on solid cancer risks after radiation exposure. He has also published on hormonal changes among women after whole-body exposure, and on the lack of evidence of trans-generational mortality effects of radiation exposure among the children of the atomic-bomb survivors. He continues as a consultant to RERF in the development of their data access infrastructure to improve RERF's ability to collaborate with outside organizations.

Dr. Grant received his BSEE from the University of Michigan and his PhD in Epidemiology from the University of Washington. He worked as a computer programmer for the University of Michigan Medical Center prior to relocating to Japan.

For NCRP, Dr. Grant was most recently a member of the SC 1-27 writing team that produced Commentary No. 32, *Evaluation of a Sex-Specific Difference in Lung Cancer Radiation Risk Projection (with a Focus on Application to Space Activities* (2022). He continues to serve on various societies' committees. He is a member of scientific writing committees and performs independent consulting. He is currently a Special Government Employee with the U.S. Environmental Protection Agency.

Kathryn D. Held, President, became President of the NCRP in January 2019. She held the position of Executive Director and Chief Science Officer from 2016 to 2018. She was first elected to the Council in 2006 and served on the NCRP Board of Directors from 2008 to 2014. She was Vice President from 2011 to 2016 of Program Area Committee 1 on Basic Criteria, Epidemiology, Radiobiology, and Risk. She also served as Chair of the Program Committee for the 2011 Annual Meeting on "Scientific and Policy Challenges of Particle Radiations in Medical Therapy and Space Missions." Dr. Held was a member of Scientific Committee (SC) 1-22 on Radiation Protection for Astronauts in Short-Term Missions and Phase I of SC 1-24 on Radiation Exposures in Space and the Potential of Central Nervous System Effects and an advisor to several NCRP committees.

Dr. Held is an Associate Radiation Biologist in the Department of Radiation Oncology, Massachusetts General Hospital (MGH) and Associate Professor of Radiation Oncology (Radiation Biology) at Harvard Medical School (HMS). At MGH, Dr. Held leads a team that is involved in research on molecular mechanisms for the induction of bystander effects by high energy particles in cells and tissues, characterization of charged particle beam induced DNA damage responses and cell killing, and mechanisms for regulation of DNA damage response by cell-cell communication. Dr. Held also teaches radiation biology to radiation oncology medical and physics residents and graduate students at MGH/HMS and the Massachusetts Institute of Technology.

Dr. Held earned her PhD in biology from the University of Texas, Austin. She has served on review panels for numerous federal agencies including the National Institutes of Health, the National Aeronautics and Space Administration (NASA), and the U.S. Army Medical Research and Material Command programs and other organizations such as the Radiological Society of North America. She is on the Editorial Boards of Radiation Research and the International Journal of Radiation Biology, and has served on committees for the National Academy of Science/National Research Council, NASA, and the American Society of Radiation Oncology. She is a past President of the Radiation Research Society.

Dmitry Klokov, Speaker, received his PhD in Radiobiology (2000, Moscow State University). Currently he is a head of the Laboratory of Experimental Radiotoxicology and Radiobiology at the Institute of Radioprotection and Nuclear Safety (IRSN) in France. He also holds an Adjunct Professor position at the Department of Biochemistry, Microbiology and Immunology of University of Ottawa. Prior to joining IRSN in 2019, Dr. Klokov led a low-dose radiobiology program at the Canadian Nuclear Laboratories since 2007. His postdoctoral studies were at Case Western Reserve University (with Dr. David Boothman), at the British Columbia Cancer Research Centre (with Dr. Peggy Olive), and at the German Cancer Research Centre (with Dr. Jagadeesan Nair). Dr. Klokov's research interests include various domains within the field of low-dose radiation effects, with an overarching goal to understand mechanisms of early genotoxic and molecular responses and how they may contribute to long-term health outcomes, such as cancer, cardiovascular and neurological pathologies, and transgenerational effects. He has published 56 papers and several book chapters, and has given over 12 invited talks. He has also been involved in various international initiatives in low-dose radiobiological research and cooperation, including those coordinated by the United Nations Scientific Committee on the Effects of Atomic Radiation, the Nuclear Energy Agency, the Multidisciplinary European Low Dose Initiative, the U.S. Department of Energy, and others.

James A. Lederer, Speaker, received his PhD in 1991 from the University of Wisconsin - Madison in microbiology, immunology, and pathobiology. He trained as a research fellow in basic cellular immunology until 1995 at Brigham and Women's Hospital (BWH) in the Department of Pathology and then joined the BWH Department of Surgery to develop a new research program built upon using basic immunology approaches to study the immune response to trauma and infections. As such, his research work has been instrumental in founding the trauma immunology research field. Recently, his group has developed trained immunity immunotherapeutic approaches as medical countermeasures for radiation, trauma, and bacterial sepsis in immune compromised individuals. His lab uses innovative approaches like mass cytometry (cytometry by time of flight), RNA sequencing, and proteomics technologies to study the cells and mediators of injury, radiation, infection, autoimmune, and cancer immune responses.

Mark P. Little, Program Committee & Session Co-Chair, joined the National Cancer Institute, Radiation Epidemiology Branch (REB) in 2010 as a Senior Investigator. He studied mathematics at Trinity College, Cambridge and obtained his doctorate in mathematics at New College, Oxford. Over the last three decades he has been analyzing cancer and cardiovascular disease risks in the Japanese atomic-bomb survivors, and in other irradiated populations and offspring. Previously (2000 to 2010), he worked in Imperial College London, and before that (1992 to 2000) at the U.K. National Radiological Protection Board (now part of U.K. Health Security Agency). He is a member of NCRP and Program Area Committee 1, and has served as consultant to the United Nations Scientific Committee on the Effects of Atomic Radiation, to the International Atomic Energy Agency, to the International Commission on Radiological Protection (ICRP) (in particular as member of ICRP Task Groups 91, 119, and 122), to the U.K. Committee on the Medical Aspects of Radiation in the Environment, and to various NCRP committees (those responsible for writing Commentary No. 24 and Report No. 186, also SC 1-28). In REB, Dr. Little is working on assessment of leukemia risk in persons exposed at low doses and dose rates, cancer risk in various cohorts of persons exposed as result of the Chernobyl accident, on risks of various health endpoints in the U.S. cohort of radiologic technologists, and on treatment-related second cancer risks in various populations. He has particular interests in machine learning methods and dose measurement error models, with application to assessment of low-dose and low-dose-rate risk of childhood leukemia, circulatory disease, and cataract.

Dale L. Preston, Speaker, has a BS in mathematics from Humboldt State University, Arcata, California and an MS and a PhD in Biostatistics from University of California Los Angeles. In 1981, after 3 y at Bell Labs, he began working on atomic-bomb survivor studies at the Radiation Effects Research Foundation (RERF) in Hiroshima, where he worked for the next 23 y. While at RERF he developed a class of risk regression models and modeling software that are widely used for dose-response modeling in radiation epidemiology and other areas, took a lead role in the preparation of major reports on radiation effects on cancer and non-cancer mortality and incidence rates in the survivor cohorts, and oversaw the implementation of two new dosimetry systems. He has had a 30 y association with the Radiation Epidemiology Branch of the National Cancer Institute and has worked on studies of the Russian Mayak Worker and Techa River cohorts for more than 25 y. Since returning to the United States in 2004, Dr. Preston has continued to work on the analyses of cancer risks in the atomic-bomb survivors, Mayak Workers, Techa River residents, U.S. radiologic technologists, and other exposed populations. Other professional activities include service as a consultant to United Nations Scientific Committee on the Effects of Atomic Radiation and various Biological Effects of Ionizing Radiation committees, as a member of the International Commission on Radiological Protection Committee 1, and as an associate editor of Radiation Research. He is a fellow of the

American Association for the Advancement of Science and the American Statistical Association and an author of almost 200 peer-reviewed articles.

R. Julian Preston, Program Committee, Session Co-Chair & Speaker, is currently a Special Government Employee (Expert) with the Radiation Protection Division of the U.S. Environmental Protection Agency (EPA). He was previously the Associate Director for Health for the National Health and Environmental Effects Research Laboratory of EPA. He also served as Director of the Environmental Carcinogenesis Division at EPA and as senior science adviser at the Chemical Industry Institute of Toxicology. He has been employed at the Biology Division of the Oak Ridge National Laboratory and has served as Associate Director for the Oak Ridge-University of Tennessee Graduate School for Biomedical Sciences. Dr. Preston's research and current activities have focused on the mechanisms of radiation and chemical carcinogenesis and the approaches for incorporating these types of data into cancer risk assessments by integrating epidemiology and radiation biology. Dr Preston has served on many national and international Committees. He currently serves on NCRP Scientific Committee SC 1-27 and as a member of the National Academy of Sciences Nuclear and Radiation Studies Board. He was a member of a recent Office of Science and Technology Policy Committee on Low Dose Radiation Research. He was also recently co-chair of a National Academies of Sciences, Engineering, and Medicine Committee for a National Aeronautics and Space Administration sponsored project on revising dose limits for astronauts. Dr. Preston was chair of Committee 1 of the International Commission on Radiological Protection (ICRP), a member of the ICRP Main Commission, and the Representative and a member of the U.S. delegation to the United Nations Scientific Committee on the Effects of Atomic Radiation. He served as Chair for the National Research Council's Committee to Assess the Scientific Information for the Radiation Exposure Screening and Education Program and on the Task Group on the Biological Effects of Space Radiation. He is an associate editor of Environmental and Molecular Mutagenesis. Dr. Preston has had more than 250 peer-reviewed papers and chapters published. He received his BA and MA from Peterhouse, Cambridge University, England, in genetics and his PhD from Reading University, England, in radiation genetics.

Roy E. Shore, Speaker, was a Professor and Chief of the Epidemiology Division at New York University Grossman School of Medicine before going to the Radiation Effects Research Foundation in Hiroshima-Nagasaki as Vice Chairman and Chief of Research. He is an author of over 100 radiation-related publications.

He has served on numerous governmental and scholarly committees, including as a long-time member of the International Commission on Radiological Protection and NCRP, and has served on various committees or task groups for the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), the World Health Organization, the National Academy of Sciences, the National Cancer Institute, and the U.S. Environmental Protection Agency, among others. Most recently, he evaluated the projected health effects of the Fukushima radiation accident for UNSCEAR. His interests include the effects of radiation on both cancer and noncancer disease incidence, and understanding the epidemiologic and biological modification of radiation effects by various environmental, genetic and age factors. Recent publications have particularly focused on the effects of low-dose and low dose-rate radiation.

Robert L. Ullrich, Program Committee & Session Co-Chair, is Vice Chairman and Chief of Research at the Radiation Effects Research Foundation. After obtaining his PhD at the University of Rochester, he joined Oak Ridge National Laboratory in 1974 and served as Director of the Radiation Carcinogenesis Unit until 1989 when he became Vice Chair and Director of the Biology Division in the Department of Radiation Oncology at the University of Texas Medical Branch. In 2001, he joined Colorado State University as Professor and Director of the Radiological Health Science and Cancer Research Program. In 2008 he moved back to the University of Texas Medical Branch where he served as the John Sealy Distinguished Chair in Cancer Biology, Professor and Director of the Sealy Center for Cancer Biology and most recently Director of the Cancer Center.

His research over many years has focused on risks and mechanisms of radiation-induced cancer. Initially this work was on the dose-response relationships at low doses and dose rates for radiation-induced cancer in mice. Subsequently, his laboratory developed cell and molecular approaches to study mechanisms in the development of mammary cancer after radiation exposure. His most recent work has been funded by the National Aeronautics and Space Administration (NASA) to establish a Specialized Center of Research in Radiation Carcinogenesis with a focus of studying cancer risks and mechanisms of cancer development following exposure to the unique forms of radiation encountered during space travel.

Dr. Ullrich was first elected as a Council member in 1988 and became a Distinguished Emeritus member in 2006. During his tenure he served on the NCRP Board of Directors from 1996 to 2001 and the Nominating Committee from1993 to 1996 and again in 2002 serving as Chair from 1997 to 1999. He was a member of Scientific Committee (SC) 1-3 which produced Report No. 121, *Principles and Application of Collective Dose in Radiation Protection* (1995) and SC 40 that wrote Report No. 64, *Influence of Dose and its Distribution in Time on Dose-Response Relationships for Low-LET Radiations* (1980) and Report No. 104, *The Relative Biological Effectiveness of Radiations of Different Quality* (1990).

He has served on a number of scientific advisory groups both in the United States as well as internationally. In the United States, Dr. Ullrich served on committees for the National Cancer Institute, the U.S. Department of Energy, NASA, NCRP, and the National Academies/National Research Council. Internationally he served on advisory committees including the International Commission on Radiological Protection, the European Commission, and the International Agency for Cancer Research. He is a member of several scientific societies including the American Association for Cancer Research and the Radiation Research Society (RRS). Most recently the RRS awarded him their highest honor, the Failla Medal, for significant contributions in the radiological sciences.

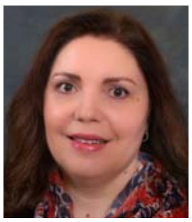
Michael M. Weil, Program Committee & Speaker, is a professor in the Department of Environmental and Radiological Health Sciences at Colorado State University (CSU). His research, which takes advantage of murine models of radiation carcinogenesis and leukemogenesis, is focused on understanding how radiation exposure can lead to cancer and why some individuals may be more susceptible than others. At CSU, Dr. Weil teaches a graduate level course in cancer genetics and lectures in courses on cancer biology, environmental carcinogenesis, principles of radiation biology, and the pathobiology of laboratory animals. Dr. Weil earned his PhD in microbiology from the University of Texas at Austin and was trained in cancer genetics and radiation biology in the Department of Biochemistry and Molecular Biology Biochemistry and the Department of Experimental Radiotherapy at the University of Texas M.D. Anderson Cancer Center. He is an NCRP Council member and a co-author on Commentary No. 23, *Radiation Protection for Space Activities: Supplement to Previous Recommendations* (2014) and Report No. 186, *Approaches for Integrating Information from Radiation Biology and Epidemiology to Enhance Low-Dose Health Risk Assessment* (2020). He currently serves as Co-Chair of Scientific Committee 1-27.

Joseph C. Wu, Speaker, is Director of Stanford Cardiovascular Institute and Simon H. Stertzer, MD, Professor of Medicine and Radiology at Stanford University. Dr. Wu received his MD from Yale University and PhD (Molecular & Medical Pharmacology) at the University of California Los Angeles. He is board certified in cardiovascular medicine.

His lab works on cardiovascular genomics and induced pluripotent stem cells (iPSCs). The main goals are to (1) understand basic disease mechanisms, (2) accelerate drug discovery and screening, (3) develop "clinical trial in a dish" concept, and (4) implement precision medicine for patients. Dr. Wu has published over 500 manuscripts with H-index of 116 on Google scholar. He is listed as top 1 % of highly cited researchers by Web of Science for past 5 y (2018 - 2022).

Dr. Wu has received the National Institutes of Health (NIH) Director's New Innovator Award, NIH Roadmap Transformative Award, Presidential Early Career Award for Scientists and Engineers given out by President Obama at the White House, American Heart Association (AHA) Distinguished Scientist Award, AHA Merit Award, and Burroughs Wellcome Foundation Innovation in Regulatory Science Award. Dr. Wu serves on the Food and Drug Administration Cellular, Tissue, and Gene Therapies Advisory Committee. He is on the Board of the Keystone Symposia. He is President-Elect of the American Heart Association.

Dr. Wu is an elected member of American Society for Clinical Investigation, Association of University Cardiologists, American Institute for Medical and Biological Engineering, American Association for the Advancement of Science, American Association of Physicians, Academia Sinica, National Academy of Inventors, and National Academy of Medicine.



Lydia B. Zablotska, Session Co-Chair, is a Salvatore Pablo Lucia Professor of Epidemiology and Public Health in the Department of Epidemiology and Biostatistics at the University of California, San Francisco, where she serves as the Leader of the Occupational and Environmental Epidemiology Area of Concentration. Dr. Zablotska is a physician and epidemiologist with extensive training and publications in radiation epidemiology, biostatistics, and risk modeling. Her research activities have focused primarily on the examination of risks of radiation exposures in various occupational, medical and environmental settings. Dr. Zablotska's work has clarified the understanding of the effects of occupational radiation exposures on health risks of nuclear power industry workers and workers of the uranium fuel production cycle in various occupational cohorts from the United States and Canada. As a Principal Investigator of the National Cancer Institute-funded Chernobyl studies, she published a number of important publications with the tri-national investigative team which showed that exposures to ingested and inhaled radioactive iodines during childhood lead to increased risks of thyroid cancer similar to risks from external radiation. Study findings redefined the emergency protocols for populations working or living around nuclear power plants and opened a new area of inquiry by showing that exposures to radioiodines increase not only the risks of thyroid cancer, but also of benign thyroid tumors such as follicular adenomas. She served as an expert advisor to the United Nations Scientific Committee on the Effects of Atomic Radiation and was a member of the committee for the National Academies of Sciences, Engineering and Medicine. Dr. Zablotska is an elected Council member of the NCRP.

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