Summary Report

Conexus International workshop on "Advances in Radiation Biology, Radioecology, Epidemiology, and Low-Dose Radiation Risk Modeling and Communication"

Dates: 2025-November 17-18

Venue: Algonquin College, Ottawa, Ontario, CANADA

Format: Hybrid (in-person and virtual) participation, including established researchers, regulators, early-career scientists, and undergraduate/graduate students)

Organizing Institution: Conexus Nuclear Inc.

Sponsors: Conexus Nuclear Inc.; International Association for Radiation Research; International Union of Radioecology

Organizing Committee: Ralph Stube, Carmel Mothersill, Edouard Azzam

Executive Summary

This interdisciplinary two-day workshop was convened to assess the current state of knowledge on the biological and health effects of low-dose and low dose-rate ionizing radiation, with the goal of identifying scientific advances, persistent uncertainties, and research priorities relevant to radiation protection and public health. The program was intentionally structured to integrate mechanistic, epidemiological, ecological, and communication perspectives, reflecting the multifaceted nature of low-dose radiation science and the need for cross-disciplinary dialogue.

Sessions I–VIII spanned a wide range of experimental systems, exposure scenarios, and analytical approaches. Presentations addressed cellular and molecular mechanisms, dose–response relationships, sex- and tissue-specific effects, epidemiological evidence, and the application of emerging technologies such as omics, advanced imaging, artificial intelligence, systems biology, as well as risk communication approaches. Together, these sessions highlighted both progress in detecting subtle biological responses at low doses and the challenges of extrapolating findings across biological scales and exposure contexts.

The workshop also devoted focused attention to ecological effects of radiation, emphasizing non-human biota and ecosystem-level considerations that extend beyond human-centric risk models. Radioecological case studies, long-term field investigations, and conceptual frameworks illustrated ecosystem resilience, context dependence, and the limitations of reductionist approaches in predicting environmental outcomes. These discussions reinforced the importance of aligning measurement endpoints with ecological protection goals.

National and international coordination featured prominently, with presentations outlining structured efforts to harmonize research strategies, share data and infrastructure, and strengthen the policy relevance of low-dose research. Initiatives such as the Nuclear Energy Agency (NEA) High-Level Group on Low-Dose Research and the Canadian Radiation Research Network were highlighted as mechanisms for advancing coordinated, evidence-based approaches at both national and global levels.

The program included a panel discussion and dedicated open forums that encouraged active exchange among participants, fostering critical reflection on uncertainty, risk assessment, and communication challenges. An end-of-day dialogue on Day 1 allowed themes to be synthesized across sessions, revealing areas of consensus and divergence and helping to frame subsequent discussions. In addition, student poster presentations showcased developing research across biodosimetry, radiobiology, epidemiology, ecology, and space radiation, underscoring the importance of training and sustaining a diverse, highly skilled workforce. Collectively, these components provided a comprehensive platform for advancing understanding, collaboration, and strategic direction in low-dose radiation research.

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Workshop sessions

Session I: Radiation Exposure: From Dose to Biological Impact in Mammalian Systems

Chair: **Amy Kronenberg** (Lawrence Berkeley National Laboratory, USA)

Speakers: **Susan Bailey** (Colorado State University, USA)
Tatjana Paunesku (Northwestern Feinberg School of Medicine, USA)
Sally Amundson (Columbia University, USA)
Dmitry Klokov (Nuclear Safety and Radiation Protection Authority, France)

Brief overview: Talks in this session explored mechanistic pathways linking radiation exposure to biological outcomes. Transcriptomic analyses continued to reveal reproducible low-dose gene expression signatures despite an expected variability between datasets. New findings also underscore the importance of the gut-brain axis, showing that localized brain irradiation induces long-lasting shifts in gut microbiota and systemic immunity. A presentation on biomarker discovery highlighted how radiation quality, dose rate, exposure type, and analytical techniques shape biomarker profiles and temporal responses. A summary of NASA's Twins Study illustrated how multi-omics and physiological data from long-duration spaceflight inform research relevant to aging, immunity, ocular health, and performance under prolonged stress.

Overall, the presentations highlighted the following: i) Low-dose effects are real, measurable, and mechanistically rich, and are not experimental noise; ii) Qualitative differences between low- and high-dose responses recur across a wide variety of biological outcomes including transcriptomics, telomere biology, dose-rate effects, system-level and non-targeted effects (*e.g.*, bystander signaling, gut–brain axis, immune modulation). The dose response relationships challenge typical monotonous dose-response models that are common for moderate to high dose and dose-rate exposures, and also challenge organ- and hit-centric models; iii) Temporal dynamics matter (*e.g.*, early vs. late responses; delayed microbiome changes; post-flight telomere collapse); iv) Integration of advanced tools (multi-omics, synchrotron imaging, 3D tissues, AI) is no longer optional but essential to properly describe physiological and neurological outcomes at low doses and dose-rates.

Presentations

- In the first talk titled "Twins, Telomeres & Tourists – in SPACE!", Dr Susan Bailey discussed how long-duration spaceflight affects human biology, focusing on telomere dynamics as an integrated biomarker of aging, radiation exposure, and physiological stress. The talk centered on results from NASA's landmark Twins Study, in which astronaut Scott Kelly spent nearly one year aboard the International Space Station, while his identical twin, Mark Kelly, remained on Earth as a matched ground control.

Dr Bailey outlined the broader hazards of spaceflight, including microgravity, isolation, altered circadian rhythms, limited diet, and chronic exposure to the space radiation environment. She emphasized that the current era of space exploration, driven by both government and commercial enterprises, necessitates a deeper understanding of long-term health risks.

A major focus of the talk was the multi-omics approach pioneered in the Twins Study, coordinated with contributions from Chris Mason and colleagues. These efforts included genomic, transcriptomic, proteomic, metabolomic, microbiome, cardiovascular, immune, and cognitive assessments, representing one of the most comprehensive longitudinal studies ever conducted in astronauts.

Dr Bailey presented compelling evidence that average telomere length increased during spaceflight, contrary to the initial hypothesis that space stressors would accelerate telomere shortening. This telomere elongation was consistently observed using multiple independent methods (qPCR, telomere FISH, DNA sequencing) and across multiple missions, including shorter commercial flights such as Inspiration4, the first all-civilian, privately funded commercial orbital spaceflight. However, upon returning to Earth, astronauts experienced rapid telomere shortening, resulting in a higher burden of critically short telomeres than before flight, likely reflecting the cumulative effects of spaceflight-related stressors.

Mechanistic analyses suggested that these changes do not reflect a "rejuvenation" effect but rather shifts in cell population dynamics, radiation-induced cell killing, chronic oxidative stress, persistent DNA damage responses, and activation of alternative lengthening of telomeres (ALT)-like phenotypes. Supporting this interpretation, Dr Bailey described persistent chromosomal inversions, satellite associations, and heterogeneous sister telomere lengths following spaceflight: genomic instability signatures also observed in other irradiated cohorts, including cancer patients and non-human primates.

The talk concluded by framing spaceflight as a potential model of accelerated aging, particularly within the hematopoietic and immune systems. Dr Bailey emphasized the importance of ongoing longitudinal monitoring for individuals engaged in long-term missions but also for the growing number of individuals engaged in short-term commercial spaceflight missions, integration of astronaut data into public resources such as the Space Omics and Medical Atlas (SOMA), and the need to develop effective mitigation strategies as humans prepare for longer missions beyond low Earth orbit.

<u>Key Takeaways</u>

1. Spaceflight induces dynamic telomere remodeling: Telomeres lengthen during spaceflight but shorten rapidly after return, leaving astronauts with more short telomeres, an indicator of increased long-term health risk.

2. Longer telomeres in space do not imply rejuvenation: The findings of the Twin Study support a model of altered cell population dynamics, radiation-induced stress, and selective survival rather than true biological youthfulness.
3. Low-dose, low–dose-rate space radiation, in combination with other space environment stressors, is associated with measurable genomic effects: Persistent chromosomal inversions and telomere abnormalities suggest long-lasting genome instability after flight.
4. Telomere length is a sensitive integrative biomarker: Telomere length dynamics (changes over time) capture the combined effects of radiation, oxidative stress, inflammation, microgravity, and lifestyle stressors in astronauts.
5. Findings generalize across mission durations and astronaut populations: Similar telomere responses were observed in missions ranging from days to a year, including commercial civilian flights.
6. Immune and hematopoietic systems appear particularly vulnerable: Decreased white blood cell counts, altered neutrophil-to-lymphocyte ratios, and lymphocyte radiosensitivity point to increased aging risks.
7. Spaceflight may model accelerated aging on Earth: Insights from astronaut studies may inform understanding of aging, cancer risk, cardiovascular disease, and neurocognitive decline.
8. Multi-omics and open data are essential for future progress: Resources like SOMA and the NASA Open Science Data Repository enable broader discovery and cross-cohort comparisons.
9. Long-term health outcomes remain an open question: Cancer and other late stochastic effects require decades of follow-up, underscoring the need for sustained astronaut health surveillance.
10. Results directly inform deep-space mission planning: Understanding biological changes and mechanisms is critical for developing countermeasures and ensuring crew safety on Moon and Mars missions.

- In the second talk titled “Pursuit of Biomarkers of Radiation Exposures”, Dr. Tatjana Paunescu discussed the conceptual and practical challenges of identifying biomarkers of radiation exposure, in contrast to identifying biomarkers of chemical exposures. Her talk combined philosophical framing with experimental examples drawn from radiation biology, bio-nanotechnology, and synchrotron-based imaging.

Dr Paunesku began by questioning the premise of biomarker simplification. Radiation exposure is not a single, uniform phenomenon but varies by radiation type, dose, dose rate, delivery method (external vs. internal emitters), biological model system, and time since

exposure. Given this heterogeneity, she argued that no single biomarker can universally capture "radiation exposure," though partial or context-specific indicators may still be valuable.

She first described laboratory efforts to use DNA damage markers, notably γH2AX and 53BP1 foci, as biomarkers. Using a custom-built, microbeam-style focused X-ray system developed in-house, her group irradiated cultured cells and organoids in defined stripes, allowing precise control of dose and dose rate. These studies demonstrated that while DNA damage foci can reflect radiation exposure, their interpretation depends strongly on dose rate, biological context, and the timing of post-exposure measurements.

The second major component of the talk focused on the utility and challenges of studying archival irradiated tissues, including rodents, dogs, and non-human primates exposed decades ago to internal radionuclides such as plutonium and strontium under U.S. Department of Energy–funded programs. These paraffin-embedded samples, now housed at Northwestern University, are largely incompatible with modern molecular techniques such as mRNA profiling due to degradation. However, Dr. Paunesku emphasized that synchrotron-based X-ray fluorescence microscopy (XFM) allows direct, non-destructive elemental imaging of such tissues.

Using synchrotron facilities at Brookhaven National Laboratory and Lawrence Berkeley National Laboratory, her team localized alpha-particle–emitting plutonium in tissues, confirmed its chemical identity via X-ray absorption near-edge structure (XANES), and mapped tissue architecture using small- and wide-angle X-ray scattering. Complementary elemental analyses (*e.g.*, iron, zinc, calcium) revealed highly heterogeneous elemental distributions associated with specific tissue structures and pathologies, including radiation-associated lung tumors.

Dr Paunesku proposed that complex elemental signatures, rather than single molecular endpoints, may serve as future biomarkers of radiation exposure or radiation-induced disease. By integrating elemental maps with pathology, computational clustering (*e.g.*, UMAP), and eventually AI-based analysis, such multidimensional datasets could reveal exposure- or disease-specific patterns that precede overt pathology. She concluded that biomarker discovery in radiation biology must embrace complexity and integration across techniques, rather than relying on overly reductive single-marker approaches.

<u>Key Takeaways</u>

1. Radiation biomarkers will not be universal or simple: Radiation effects depend on radiation type, dose, dose rate, delivery route, biological system, and time since exposure and will share features with alterations associated with oxidative stress.
2. DNA damage markers are informative but context-dependent: γH2AX and 53BP1 foci reflect radiation exposure but are influenced by dose rate, repair kinetics, and cell type.

3. Microbeam-style X-ray systems enable precise mechanistic studies: Spatially patterned irradiation allows investigation of dose-rate and partial-exposure effects in cells and organoids.
4. Archival irradiated tissues remain scientifically valuable: Even decades-old paraffin-embedded samples can yield new insights when analyzed with modern imaging techniques.
5. Synchrotron X-ray fluorescence microscopy is a powerful tool: SXRFM enables direct visualization of radionuclides and elemental distributions without molecular extraction.
6. Elemental heterogeneity may signal radiation-induced pathology: Abnormal distributions of metals (*e.g.*, iron, zinc, calcium) correlate with tissue structure and disease states.
7. Future biomarkers are likely multidimensional: Integrated elemental, structural, and computational signatures may outperform single molecular endpoints.
8. AI and data integration will be essential: Advanced analytics are needed to link complex elemental patterns to radiation exposure and health outcomes.
9. Biomarker research must accept biological complexity: Effective radiation biomarkers will emerge from combining multiple techniques rather than oversimplifying exposure biology.

- The third talk titled "Biological Responses to Low Dose Radiation Exposure: Insight from Transcriptomics" by Dr Sally Amundson provided a high-level overview of how transcriptomics has transformed understanding of biological responses to low dose ionizing radiation. Drawing on her pioneering work and more recent studies from the literature, she emphasized that gene expression profiling offers mechanistic insight and practical opportunities for biomarker development that are not accessible through classical radiobiological endpoints alone.

Dr Amundson began by explaining that transcriptomics captures dynamic, genome-wide responses to radiation, revealing pathways related to damage sensing, signaling, stress response, and cell fate decisions. Early work from her group demonstrated that low-dose responses are highly time-dependent, often peaking earlier than responses to high doses. Importantly, gene expression changes at low doses do not simply scale down from high-dose responses; instead, they can follow qualitatively different dose–response relationships, as illustrated by genes such as CDKN1A ($p21^{Waf1}$).

Addressing criticism that low-dose transcriptional signals merely reflect dying cells, Dr. Amundson showed analyses normalizing gene induction to lethal events, demonstrating that low-dose gene expression changes cannot be explained by cell death alone. She then highlighted the role of dose-rate, showing that some genes (*e.g.*, GADD45, CDKN1A) are strongly dose-rate

dependent, while others (*e.g.*, MDM2) remain relatively resistant to dose-rate reduction, pointing to distinct underlying signaling mechanisms.

Moving beyond monolayer cultures, Dr Amundson described studies using 3-dimensional (3D) human skin models, which better approximate tissue architecture. These experiments revealed an earlier maximum for transcriptional response after low doses compared with high doses and identified HNF4A, a transcriptional factor that regulates the expression of genes involved in liver development and metabolic homeostasis, as a previously unrecognized radiation transcriptional hub preferentially activated at low dose. Differences in timing and phosphorylation state suggested that low- and high-dose radiation engage distinct regulatory networks, rather than differing only in magnitude.

A major portion of the talk focused on bystander effects of radiation exposure. Using spatially restricted irradiation in 3D tissues, her group observed wave-like, oscillatory gene expression patterns that varied with both time and distance from the irradiated region. Transcriptomic analysis of bystander cells revealed the dominance of signal transduction pathways, particularly NF-κB-centered networks and G-protein–coupled receptor signaling, in contradistinction to the cell-cycle-dominated responses seen in directly irradiated tissues.

Dr Amundson concluded by reviewing human biodosimetry and population studies, showing that even very low doses, such as those from CT scans, can induce reproducible gene expression changes *ex vivo* and *in vivo*. Studies in high natural background radiation areas, radiation workers, and the Mayak Production Association cohort demonstrated persistent transcriptional alterations years after exposure, suggesting the feasibility of transcriptomics for dose reconstruction and long-term exposure assessment. She closed by emphasizing future directions, including single-cell and spatial transcriptomics, organoids and tissue-on-chip models, multi-omics integration, and AI-driven analysis, to better link early molecular responses to long-term health outcomes.

<u>Key Takeaways</u>

1. Low-dose radiation elicits real, measurable biological responses: Transcriptomic changes occur at doses well below 0.1 Gy and are very likely not experimental noise.
2. Low- and high-dose responses are qualitatively different: Gene expression at low doses cannot be inferred by extrapolation from high-dose data.
3. Timing matters critically: Radiation-induced transcriptional responses are highly dynamic, with low doses often peaking earlier than high doses.
4. Dose rate modifies gene expression in gene-specific ways: Some genes are dose-rate sensitive, while others are relatively resistant, implying distinct signaling pathways.
5. Responses are not driven solely by cell death: Normalization to lethal events shows that low-dose transcriptional changes reflect active biological regulation.

6. Tissue context reshapes radiation responses: 3D tissue models reveal regulatory networks and transcription factors (*e.g.*, HNF4A) not evident in 2D cultures.
7. Bystander effects involve propagating signaling waves: Non-irradiated cells show oscillatory, distance-dependent gene expression dominated by NF-κB and related signaling pathways.
8. Transcriptomics supports low dose biodosimetry: Small gene sets can reconstruct dose in blood without isolating specific cell subtypes.
9. Gene expression changes can persist long term: Studies of exposed populations show stable transcriptional signatures after years of chronic exposure.
10. Future progress depends on integration and scale: Single-cell, spatial omics, advanced models, and AI are essential to link early transcriptional responses to disease risk.

- The fourth talk titled "The Gut Microbiome as a Mediator of Ionizing Radiation Effects: Lessons from Brain-Targeted Exposure" by Dr Dmitry Klokov who began by introducing ASNR, a newly formed French authority combining regulatory, advisory, and research functions under one organization. Despite its regulatory mandate, ASNR maintains an active research portfolio closely integrated with academia, supporting translational radiobiology relevant to medicine and radiation protection.

The scientific core of the talk addressed how localized irradiation of the brain, without direct gut exposure, can induce long-term changes in the gut microbiome, highlighting the systemic nature of radiation effects. The study was motivated by pediatric medical scenarios, such as neonatal stroke diagnosis and intervention, where brain doses of several hundred mGy to ~1 Gy or more may occur during imaging or angiographic procedures. Survivors often experience long-term cognitive and neurological deficits, raising questions about how radiation contributes to these outcomes.

Using a mouse postnatal irradiation model and a small animal radiation research platform (SARRP), Dr Klokov's team delivered either whole-brain irradiation or highly localized irradiation to the dentate gyrus (DG) of the hippocampus, a neurogenic region critical for learning and memory. Doses ranged from 250 mGy to 2 Gy, with most biological effects emerging at 1 Gy, a dose relevant to pediatric clinical practice.

The investigators first characterized brain and systemic inflammatory responses, measuring cytokines in neural tissue and blood. They found that irradiation volume mattered: targeted DG irradiation often elicited stronger and more heterogeneous inflammatory responses than whole-brain exposure. Notably, systemic immune alterations, including increased white blood cell counts, persisted for months, indicating long-term immune modulation after early-life brain irradiation.

The central novel finding relevant to impacts of radiation on the gut-brain axis came from 16S rRNA sequencing of fecal samples, which revealed that brain-only irradiation altered the gut microbiome. While within-sample diversity (alpha diversity) showed only trends that were not statistically significant, while between-sample diversity (beta diversity) demonstrated statistically significant dysbiosis following whole-brain irradiation and, at later time-points, DG-targeted irradiation. These changes emerged months after exposure, indicating delayed but persistent microbiome remodeling.

Taxonomic analysis showed that Firmicutes were the most affected bacterial group, with distinct compositional shifts depending on whether irradiation was given to the whole-brain or if it was administered in a focal manner to the DG. These results demonstrate that different brain regions can differentially influence the gut microbiome, even in the absence of direct intestinal irradiation.

Dr Klokov emphasized that this was an exploratory, descriptive study, not a mechanistic one. However, he proposed plausible signaling routes via the gut-brain axis, including neural pathways (vagus nerve), endocrine signaling, and immune mediators such as cytokines. Importantly, feedback from microbiome alterations could, in turn, influence neuroinflammation, behavior, and long-term brain health, potentially contributing to previously observed cognitive effects following the same irradiation.

Placing the findings in context, Dr Klokov noted that microbiome disruption is well documented after high-dose radiotherapy, but low- and moderate-dose effects remain poorly studied. Emerging data, including his group's work, suggest that microbiome changes can occur even at doses ≤100 mGy, though effects at these lower doses are often subtle.

He concluded by highlighting the clinical and radiation-protection relevance of microbiome research. Because the microbiome is accessible, measurable, and modifiable, it may serve as both a biomarker of exposure and a therapeutic target to mitigate radiation-induced health effects, especially in vulnerable pediatric populations.

<u>Key Takeaways</u>

1. Brain-only irradiation can alter the gut microbiome: Significant microbiome changes occurred despite no direct intestinal exposure, demonstrating systemic radiation effects.
2. Radiation effects depend on irradiated brain volume and region: Targeted dentate gyrus irradiation often produced stronger or different responses than whole-brain exposure.
3. Microbiome changes are delayed and long-lasting: Dysbiosis developed months after exposure and persisted, highlighting long-term consequences of early-life irradiation.
4. Firmicutes are particularly radiation-responsive: This major bacterial group showed consistent compositional changes following brain irradiation.

5. Inflammation links brain irradiation to microbiome effects: Altered brain and systemic cytokine profiles correlated with microbiome remodeling.
6. Gut–brain axis signaling likely mediates the effects: Neural, immune, and endocrine pathways may transmit signals from the irradiated brain to the gut.
7. Moderate doses (~1 Gy) are biologically relevant and clinically realistic: The doses producing effects overlap with those encountered in pediatric diagnostic and interventional medicine.
8. Low-dose microbiome effects remain understudied: Evidence suggests changes can occur at ≤100 mGy, but systematic studies are scarce.
9. Microbiome offers translational opportunities: As a modifiable system, it could serve as a biomarker and intervention target for radiation-exposed individuals.
10. Radiation biology must adopt a system-level perspective: Localized exposures can have organism-wide consequences, challenging organ-centric models of radiation risk.

Session II: Low Dose-Rate Effects in Mammalian Systems: Scientific Perspectives and Regulatory Views

Chair: **Badri N. Pandey** (Bhabha Atomic Research Centre, India)

Speakers: **Christopher Thome** (Northern Ontario School of Medicine, Canada)
Nicholas D. Priest (Université Laval, Canada; Middlesex University, UK)

Brief overview: The presentations in this session complemented Session I's transcriptomic, telomere, and systems biology evidence and strengthened the case that the workshop addresses foundational assumptions in radiation protection. They provided direct experimental and epidemiological evidence that i) Low-dose and low–dose-rate effects cannot be inferred by scaling down high-dose data; ii) dose–response relationships are often nonlinear, sometimes exhibiting threshold-like behavior; and iii) background radiation itself may play a biologically relevant, homeostatic role. Research conducted at SNOLAB under controlled radon exposures demonstrated that suppression of natural background radiation can impair cellular function, while chronic radon inhalation studies refine dose-response relationships at low dose rates. Studies using plutonium, radium, radon, and thorium isotopes revealed complex, often non-linear dose-response patterns and organ-specific thresholds, underscoring the limitations of single relative biological effectiveness (RBE values) for risk estimation.

Presentations

In his introductory remarks, Dr B. N. Pandey framed the discussion around the growing scientific and regulatory importance of understanding radiation effects at doses and dose rates

relevant to environmental, occupational, and public exposures. He emphasized the need to leverage insights into low dose radiation biological effects to strengthen health risk assessment for low level exposures, while also recognizing their potential relevance for therapeutic applications.

- In the opening presentation titled “Biological Impacts of Chronic Low Dose Radiation: Mechanistic Insights from SNOLAB and Controlled Radon Exposure Studies”, Dr. Christopher Thome, described the multidisciplinary research program at NOSM University focused on chronic low-dose and low-dose-rate radiation exposures. The talk centered on two complementary experimental platforms: (1) sub-background radiation studies in deep underground laboratories, and (2) controlled radon inhalation studies using novel animal exposure chambers.

Dr Thome first described experiments conducted at SNOLAB, a deep underground research facility providing extreme shielding from cosmic and terrestrial radiation. By culturing biological systems under sub-background radiation conditions, the group directly tested the effects of reducing ionizing radiation exposure to levels below those found at the Earth’s surface on biological fitness. Across multiple model systems, sub-background radiation conditions were associated with evidence of impaired biological function following the removal of natural background radiation.

Using human CGL1 hybrid cells (a non-tumorigenic but transformation-sensitive model), prolonged culture under sub-background conditions led to increased alkaline phosphatase expression, a marker of neoplastic transformation. Importantly, this effect was reversible when cells were returned to normal background radiation levels. Parallel studies using desiccated yeast, including DNA repair–deficient strains, demonstrated reduced survival and metabolic activity after long-term incubation underground, with effects most pronounced in repair-deficient cells. These findings suggest that background radiation contributes to maintaining genomic stability and normal cellular function.

The second part of the talk addressed radon gas exposure, a public health concern. Dr Thome described the development of a state-of-the-art small-animal radon exposure chamber capable of reproducing residential and occupational radon levels (hundreds to thousands of Bq/m^3) while controlling particle size and equilibrium factors. Short-term rat and mouse studies (up to several weeks) showed no adverse effects on lung physiology or inflammation, and in some cases revealed anti-inflammatory responses at moderate radon concentrations ($\leq$1000 Bq/m^3). These findings align with reports of anti-inflammatory effects observed after low-dose external irradiation and underscore the need for systematic investigation of the health consequences of chronic, long-term radon exposure, including potential cumulative effects on lung tissue, immune regulation, and cancer risk, which remain key uncertainties in radon risk assessment and public health policy.

Ongoing and planned studies will extend radon exposures to chronic durations (up to six months) and evaluate cancer incidence, lung function, systemic effects, microbiome changes, transcriptomic and epigenomic alterations, and blood-based biomarkers. The program is expanding internationally, with multiple underground laboratories and radon facilities collaborating to address reproducibility and variability across sites.

The talk concluded with a discussion on experimental challenges, including inter-facility variability, strain differences, environmental confounders, and the need for matched controls at each site. Participants highlighted the potential regulatory implications of this work, particularly for occupational radon monitoring and evidence-based threshold setting.

Key Takeaways

1. Low-dose and low-dose-rate radiation responses differ from high-dose effects: Biological outcomes at low doses may not be reliably inferred by linear extrapolation from high-dose data.
2. Natural background radiation appears biologically relevant: Removal of background radiation impaired cellular function, increased neoplastic transformation markers, and reduced survival in multiple model systems.
3. Effects are reversible upon return to background radiation levels, suggesting that maintaining normal environmental radiation levels may help preserve normal biological function in human cells.
4. DNA repair capacity modulates low-dose sensitivity: Repair-deficient yeast showed heightened vulnerability under sub-background conditions.
5. Mechanistic radon studies are experimentally feasible: Novel radon chamber at SNOLAB enables controlled, biologically relevant animal exposures while accounting for the influence of background radiation beyond radon.
6. Short-term radon exposure showed no adverse lung effects: At residential-to-moderate occupational levels, radon did not impair lung physiology and may reduce inflammatory signaling, but systematic studies of chronic, long-term exposures are needed to determine potential cumulative effects on lung function and inflammatory responses.
7. Chronic radon effects, including cancer risk, remain the critical endpoint: Long-term studies are underway to assess carcinogenesis and systemic outcomes.
8. Reproducibility across underground laboratories is a priority: International, multi-site studies aim to strengthen confidence in low-dose findings.
9. Regulatory and public health implications are substantial: Results may inform radon monitoring policies concerned with protecting populations from long-term exposure risks.

- In the second talk titled “Challenging-Observations on the Relative Biological Effectiveness and Low-Dose Toxicity of Alpha-Emitting Radionuclides in Experimental Animals and Man”, Dr Nicholas D. Priest critically examined uncertainties in alpha-particle cancer risk estimation, with particular emphasis on relative biological effectiveness (RBE/relative toxicity) and the shape of dose–response relationships. The talk challenged several simplifying assumptions used in radiation protection, especially the use of a single radiation weighting factor of 20 for alpha particles, as recommended by the International Commission on Radiological Protection.

Dr Priest began by reviewing decades of animal and human studies of internally deposited alpha emitters, including radium, plutonium, americium, radon, thoron, and thorium-based agents. He argued that while alpha emitters are clearly carcinogenic at sufficiently high doses, major uncertainties remain in (1) how alpha risks compare quantitatively with low-linear energy transfer (LET) radiation, and (2) whether cancer risk at low doses follows a strictly linear relationship.

To address uncertainties in relative toxicity, Dr Priest described a landmark animal study designed to overcome the methodological flaws of previous alpha–beta comparisons. Instead of comparing chemically dissimilar radionuclides with different biodistributions, his team used calcium-45 (β-emitter) and curium-242 (α-emitter), matched for half-life and immobilized on identical fused clay particles. These particles were injected into mice, producing nearly identical spatial and temporal dose distributions, an experimental condition rarely achieved in radiobiology.

The results showed strong tissue specificity in alpha effectiveness at inducing cancer. Relative toxicity ratios (alpha divided by beta) ranged from <1 (malignant lymphoma) to ~6 (liver carcinoma), with whole-body carcinoma averages around 2–3. When benchmarked against cobalt-60 γ radiation rather than beta emitters, the inferred alpha-to-gamma risk ratios varied widely by tissue, from ~1.5 to ~16, with a typical average closer to 6, substantially lower than the ICRP default of 20 for stochastic risk.

Dr Priest then turned to the shape of alpha-particle dose–response curves, drawing on epidemiological data from radium dial painters, Thorotrast patients, nuclear workers, and long-term animal studies in dogs and rodents. Using linear–quadratic models with intercept terms, he demonstrated that many datasets fit better to nonlinear models exhibiting apparent thresholds rather than simple linear relationships. Across seven human studies and eight dog studies, threshold-like behavior was observed consistently, with mean estimated thresholds of approximately 1.2 Gy in humans and 0.7 Gy in dogs for alpha-induced cancers.

To explain these findings biologically, Dr Priest proposed that alpha-particle carcinogenesis is not driven solely by random DNA damage. Instead, high local doses from alpha emitters cause cell killing and chronic inflammation, leading to macrophage and neutrophil infiltration, oxidative stress, fibrosis, and ultimately cancer promotion-mechanisms analogous to

those established for asbestos-induced lung cancer. Supporting this interpretation, he showed that fibrosis incidence closely tracked cancer incidence in alpha-exposed dogs and that fibrotic tissue can physically shield bone surfaces, reducing dose rates at very high exposures and producing downturns in dose–response curves.

In concluding remarks, Dr Priest proposed a more nuanced framework for alpha risk assessment:

- Tissue-specific relative toxicity factors should be used wherever possible.
- Where no tissue-specific data exist, a default alpha-to-gamma factor of ~6 may be more appropriate for risk estimation than 20.
- For internally deposited alpha emitters such as radium and actinon elements, cancer risk below ~100 mGy appears negligible based on available evidence.

  Dr Priest also cautioned that confounding inflammatory lung exposures, including smoking, diesel exhaust, asbestos, silica, thoron, and historical practices such as McIntyre Powder inhalation in Canadian miners, must be considered when interpreting radon epidemiology.

<u>Key Takeaways</u>

1. A single alpha weighting factor is biologically oversimplified: Alpha-particle cancer risk varies widely by tissue and exposure scenario.
2. Experimentally matched alpha-beta comparisons reduce major uncertainties: Studies using identical dose distributions show much lower average alpha effectiveness than assumed by the ICRP.
3. Typical alpha-to-gamma risk ratios cluster around ~6, not 20: Whole-body averages are far below current radiation weighting factors.
4. Dose–response relationships for alpha emitters are often nonlinear: Linear–quadratic models with thresholds fit human and animal data better than linear models.
5. Threshold-like behavior is consistently observed: Estimated cancer thresholds are ~1 Gy in humans and ~0.7 Gy in dogs for internal alpha exposure.
6. Inflammation and cell killing are central to alpha carcinogenesis: Alpha radiation acts similarly to asbestos by inducing chronic inflammation that promotes cancer.
7. Fibrosis is both a marker and modifier of risk: Fibrotic tissue correlates with cancer incidence and may reduce dose rates at high exposures.
8. Low-dose alpha risk from internal emitters appears very small: Below ~100 mGy, available data suggest negligible cancer risk.
9. Epidemiological studies of occupational radon exposure should consider potential confounders, including smoking, thoron, silica, asbestos, diesel exhaust, and McIntyre Powder.

Session III: Human Radiation Epidemiology at Low Doses and Dose Rates

Chair: Paul Demers (University of Toronto, Canada)

Speakers: **Dominique Laurier** (Nuclear Safety and Radiation Protection Authority, France)
Mark P. Little (Northwestern University, USA; Oxford Brookes University, UK)
Paul Villeneuve (Carleton University, Canada)
Rachel Lane/ Tim Prendergast (Canadian Nuclear Safety Commission/Health Canada)

Brief overview: Updated epidemiological analyses reaffirmed modest excess cancer risks at doses ≤100 mGy, while highlighting uncertainties in circulatory, ocular, and neurological outcomes at low or moderate exposures. New findings from Canadian nuclear power plant worker cohorts emphasized challenges related to confounding and exposure misclassification, and also considerations related to outcome ascertainment using record linkage methodologies. The expansive CANRAD cohort of >860,000 workers, with extended follow-up, offers significant potential to refine long-term risk estimates.

In summary, while the mechanistic and animal studies in Session II suggested nonlinearity, thresholds, adaptation, and system-level effects, the presentation on human cancer epidemiology largely supported linear or near-linear models, within its resolution limits. The non-cancer epidemiology sits in between: plausible signals, but with major uncertainties. Across all presentations, Session III emphasized that future progress depends not just on larger datasets, but on i) better bias control, ii) improved exposure reconstruction, iii) more precise outcome ascertainment, iv) integration of socioeconomic and lifestyle proxies, and v) transparent uncertainty characterization

Presentations

- In the first presentation titled "Overview of Recent Epidemiological Findings on Cancer Risks at Low Doses", Dr Dominique Laurier provided a state-of-the-art overview of cancer risk evidence at doses <100 mGy and low dose rates, drawing on large epidemiological cohorts published over the last two decades.

Dr Laurier emphasized that while epidemiology has long supported cancer risk estimation at moderate-to-high doses, recent large-scale and pooled studies (outlined below) now provide statistically significant evidence in the low-dose range, improving confidence in risk estimates relevant to radiation protection.

Atomic Bomb Survivor studies

The Hiroshima and Nagasaki Life Span Study remains a cornerstone of radiation risk assessment. Although some survivors received high acute doses, approximately 80% received <100 mGy, making this cohort informative for low-dose analyses. Updated cancer incidence data

(>22,000 cases) show i) a significant excess relative risk (ERR) per Gy, persisting when doses >100 mGy are excluded; ii) no evidence for a dose threshold, consistent with a continuous dose–response relationship; iii) emerging evidence that the shape of the dose–response varies by sex, age at exposure, time since exposure, and cancer site, suggesting that pooling all solid cancers may obscure biologically relevant heterogeneity.

Nuclear Worker Studies

Dr Laurier next discussed occupational cohorts exposed chronically to low-dose radiation, focusing on the multinational INWORKS study (France, UK, USA; >300,000 workers; >34 years follow-up). Results demonstrate the following:

- A statistically significant increase in solid cancer mortality with cumulative dose, even when analyses are restricted to <100 mGy.
- Leukemia risk (excluding CLL) showing a stronger dose–response than solid cancers, with linearity persisting after excluding doses >300 mGy.
- Broad consistency across worker cohorts, including comparisons with studies of nuclear power plant workers and medical radiation workers.

  Dr Laurier contextualized these findings by translating risk estimates into absolute terms: among 1,000 workers with exposure profiles similar to INWORKS, approximately one excess cancer death would be attributable to occupational radiation exposure, illustrating that low dose does not mean zero risk, but excess risk remains small.

Pediatric CT Scan Studies

Medical exposure studies were highlighted as another critical source of low-dose data. The European EPI-CT cohort (>600,000 children) showed:

- Significant associations between cumulative CT-related doses and brain cancer and hematological malignancies, with mean organ doses well below 50 mGy.
- Estimated attributable risks of roughly 1 excess cancer per 10,000 exposed children.

Dr Laurier noted that bias by indication and reverse causation remain key challenges in CT studies. He highlighted the recent study on Risk of Pediatric and Adolescent Cancer Associated with Medical Imaging (RIC study; Canada/USA; >3.7 million children), which incorporated detailed clinical indications for imaging and identified high-risk conditions (*e.g.*, Down syndrome), thereby substantially strengthening causal interpretation. This study also found significant dose–response relationships for hematological cancers at mean red bone marrow doses ~14 mGy.

Synthesis and Implications

Drawing on pooled analyses, meta-analyses, and very large cohorts across different exposure scenarios, Dr Laurier concluded that:

- Evidence for cancer risk below 100 mGy has substantially strengthened over the past 20 years.
- Observed dose–response relationships at low doses are broadly consistent across populations and exposure types.
- There is no persuasive epidemiological evidence for a departure from linearity or for a meaningful threshold within the observable dose range.
- If thresholds exist, they are likely below a few tens of milligray, beyond current epidemiological resolution.

  Dr Laurier stressed that low-dose epidemiology remains complex, with unavoidable uncertainties, confounding factors, and heterogeneity across studies. Nonetheless, the overall evidence base is now far more robust than in the early 2000s, with important implications for radiation protection and risk assessment.

<u>Key Takeaways</u>

1. Epidemiological evidence at low doses has markedly improved: Large, pooled cohorts and meta-analyses now demonstrate statistically significant cancer risks below 100 mGy.
2. Atomic bomb survivor data remain central but are no longer the sole foundation: Nuclear workers and medical exposure studies independently support low-dose risk estimates.
3. No clear dose threshold has been demonstrated: Cancer risk appears to increase continuously with dose, consistent with linear or near-linear models.
4. Low dose does not mean zero risk, but excess risk is small: Absolute attributable risks are low (*e.g.*, ~1 excess cancer per 1,000 workers or per 10,000 pediatric CT patients).
5. Leukemia shows a stronger dose-response than solid cancers: This pattern is consistent across multiple cohorts and exposure settings.
6. Cancer site, sex, age, and time since exposure matter: Heterogeneity in dose–response shape suggests the need for site-specific analyses rather than aggregated “all solid cancer” models.
7. Bias control is critical, especially in medical exposure studies: Studies with detailed clinical indication data (*e.g.*, RIC) provide stronger causal inference.
8. Evidence does not support a deviation from the LNT model at low doses: While uncertainties remain, epidemiology does not justify abandoning linear extrapolation.
9. Radiation protection relevance is high: Findings inform DDREF, occupational standards, medical imaging justification, and public risk communication.
10. Remaining uncertainties lie at very low doses (<10-20 mGy): Epidemiology currently lacks power to resolve risks at the lowest environmental exposure levels.

- In contrast to cancer-focused epidemiology, in the second talk titled "Non-Cancer Effects of Ionizing Radiation in Directly Exposed Individuals, Especially Circulatory and Ocular Diseases", Dr Mark Little addressed non-cancer outcomes associated with ionizing radiation exposure, concentrating on cardiovascular disease (CVD), ocular disease, and neurodegenerative disorders. Drawing on decades of epidemiological work across atomic bomb survivors, nuclear workers, medical cohorts, and environmental exposures, he emphasized both emerging evidence and persistent uncertainties at low doses and low dose rates.

Cardiovascular Disease

High-dose radiotherapy studies have long established radiation-induced cardiovascular effects. Over the past two decades, epidemiological evidence has expanded to lower doses, including occupational and environmental exposures. Data from nuclear worker cohorts (including subsets of the INWORKS collaboration), Mayak workers, and historical tuberculosis patients exposed to repeated fluoroscopy suggest positive dose–response relationships for ischemic heart disease and stroke, often below ~0.5 Gy.

Although the excess relative risk per gray (~10%) is smaller than for cancer, the high baseline incidence of cardiovascular disease means that the absolute attributable risk may be comparable to cancer risks, making CVD highly relevant for radiation protection. Meta-analyses show statistically significant associations for most circulatory endpoints, though results are complicated by heterogeneity across cohorts, possible curvature or biphasic dose–response shapes, and residual confounding (*e.g.*, smoking).

Ocular Disease

Radiation-induced cataracts are one of the earliest recognized non-cancer effects, first observed in atomic bomb survivors and occupational cohorts. Recent studies show excess risks at moderate and lower doses, particularly for posterior subcapsular and cortical cataracts. Evidence comes from atomic bomb survivors, Mayak workers, Chernobyl liquidators, and U.S. radiologic technologists.

Some cohorts suggest detectable increases even below 100 mGy, though this finding is not universal. In contrast, glaucoma and macular degeneration generally show little or no consistent association, with the possible exception of normal-tension glaucoma, observed in a few cohorts.

Neurodegenerative Diseases

Evidence for radiation-associated neurodegenerative disease remains limited and inconsistent. Animal studies show neuropathological changes following high-energy ion exposure, but similar effects are not seen with conventional X-rays. Epidemiologically, there is emerging but mixed evidence for Parkinson's disease, including positive findings in Mayak

workers and pooled occupational analyses. Evidence for Alzheimer's disease or dementia is weaker and inconsistent across cohorts, including atomic bomb survivors and nuclear workers.

Overall Perspective

Dr Little emphasized that while non-cancer effects of radiation are increasingly supported at moderate doses, robust epidemiological evidence below ~0.1 Gy remains scarce, particularly for cardiovascular and neurological endpoints. Methodological challenges (heterogeneity, exposure misclassification, competing risks, and confounding factors) remain major obstacles to definitive conclusions.

Key Takeaways

1. Cardiovascular disease is a major non-cancer concern: Even modest relative risks may translate into meaningful absolute risks due to high baseline incidence.
2. Evidence supports CVD risks at moderate doses (<0.5 Gy) and low dose rates, but data below 0.1 Gy are sparse and noisy.
3. Cataracts show the strongest and most consistent non-cancer association, especially posterior subcapsular and cortical types, with some evidence extending into the low-dose range.
4. Glaucoma and macular degeneration show limited evidence, aside from possible signals for normal-tension glaucoma in certain cohorts.
5. Neurodegenerative outcomes remain uncertain: Parkinson's disease shows emerging signals; evidence for Alzheimer's disease is weak.
6. Heterogeneity across studies is substantial, complicating pooled risk estimation and interpretation.
7. Absolute risk, not just relative risk, is critical for radiation protection decisions involving non-cancer outcomes.
8. Overall, non-cancer radiation risks are increasingly plausible at moderate doses, but clear conclusions at very low doses (<100 mGy) remain elusive.

- In the third presentation titled "Low-Dose Radiation and Neurodegenerative Disease: Insights and Possible Biases from Recent Analysis of Canadian Nuclear Power Plant workers", Dr Paul Villeneuve discussed emerging evidence linking low-dose occupational ionizing radiation exposure to dementia, drawing primarily on analyses of Canada's National Dose Registry (NDR). He also emphasized the methodological complexities inherent in studying neurodegenerative outcomes using large administrative datasets.

Dr Villeneuve began by highlighting the substantial public health burden of dementia, with annual costs in Canada estimated at approximately $40 billion, largely driven by caregiving. He reviewed proposed biological mechanisms linking radiation exposure to neurodegeneration, including oxidative stress, DNA damage, neuroinflammation, and vascular injury, noting overlap with pathways implicated in cardiovascular disease.

He summarized prior epidemiological evidence, noting that many studies of radiation and dementia have relied on mortality data, which substantially under-ascertain dementia cases. A previous systematic review led by his group reported an ~11% increase in dementia risk per 100 mSv, but results across studies have been heterogeneous and inconsistent, partly due to outcome misclassification and broad neurodegenerative disease definitions. These limitations were echoed in a recent Radiation Research Society workshop review led by Dr Lydia Zablotska, which called for improved outcome ascertainment and exposure-response modeling.

Dr Villeneuve then presented new findings from an incidence-based study conducted within the NDR, led by his PhD trainee Brianna Frangioni. Restricting the cohort to Ontario workers enabled linkage to provincial health administrative databases, allowing identification of incident dementia cases rather than deaths. He highlighted the importance of using incidence outcomes rather than through death registrations where dementia outcomes can be missed. Using an internal cohort design, the study observed a ~50% increased risk of dementia in the highest cumulative dose category, with a statistically significant trend across exposure categories. Flexible modeling using cubic splines suggested an increasing exposure–response relationship at lower doses, although estimates at higher doses were unstable due to small numbers.

He emphasized that while these findings suggest that low-dose occupational radiation may increase dementia risk, they must be interpreted cautiously due to multiple potential sources of bias. The major focus of the talk was confounding, particularly from unmeasured lifestyle and health factors, such as smoking, physical activity, cardiovascular disease, air pollution, psychosocial stress, and sleep disturbance, which are strongly related to dementia risk but largely absent from occupational radiation registries.

Dr Villeneuve also discussed outcome ascertainment and record linkage biases, demonstrating that dementia mortality rates differed substantially depending on whether linkage was conducted at the provincial (Ontario) or national (Statistics Canada) level. Importantly, the magnitude of the risk estimates also varied. Differences in available identifiers (*e.g.*, social insurance numbers nationally versus probabilistic linkage provincially) appeared to influence case capture, raising concerns about comparability of risk estimates across jurisdictions.

In concluding, Dr Villeneuve argued that future progress in radiation–dementia research will require better bias assessment, richer covariate data, and methodological innovations such as nested case–control studies, ancillary data linkage, and quantitative bias analysis, paralleling approaches previously developed for air pollution epidemiology. He also highlighted the need for validation studies for record linkage of occupational cohorts to better understand possible biases.

<u>Key Takeaways</u>

1. Dementia is a major and growing public health burden, making even modest radiation-related risks potentially important at the population level.

2. Incidence-based studies are essential: Reliance on death certificates substantially underestimates dementia occurrence and obscures exposure–latency relationships.
3. New NDR evidence suggests increased dementia risk with occupational radiation exposure: Ontario-based analyses show a ~50% higher risk in the highest exposure group, with a positive exposure–response trend.
4. Dose–response modeling indicates possible effects at low doses, but estimates at higher doses are unstable due to small numbers.
5. Confounding is a central challenge: Key dementia risk factors, including cardiovascular disease, smoking, physical inactivity, air pollution, and psychosocial factors are largely missing from administrative radiation datasets.
6. Outcome ascertainment and record linkage can strongly influence results: Differences between provincial and national linkage approaches can produce materially different dementia mortality rates and risk estimates.
7. Bias assessment must be explicit and quantitative: Selection bias, confounding, and outcome misclassification can meaningfully distort associations if unaddressed.
8. Lessons from air pollution epidemiology are directly relevant: Indirect confounding adjustment and use of ancillary datasets may help address missing lifestyle data in occupational cohorts.
9. Future studies should incorporate enhanced data collection strategies: Options include nested case–control designs, linkage to health surveys, and improved capture of individual risk factors.
10. Overall conclusion: Occupational radiation exposure may contribute to dementia risk, but methodological rigor—not larger datasets alone—will determine the credibility of future findings.

- The final presentation titled “The CANadian RADiation Workers Cohort (CANRAD) Study” addressed the scientific, technical, and logistical foundations underpinning contemporary radiation epidemiology in Canada. In this presentation, Dr Rachel Lane and Mr Tim Prendergast described efforts to resolve longstanding data limitations in the National Dose Registry (NDR) and to create a robust, research-ready national cohort (CANRAD) capable of supporting long-term studies of cancer and non-cancer outcomes at low and moderate doses.

Dr Lane began by explaining how anomalously high excess relative risks observed for Canadian workers in early multinational nuclear worker studies (notably the IARC 15-country study) prompted closer scrutiny of Canadian data. These investigations identified missing or incomplete historical dose records, particularly from Atomic Energy of Canada Limited (AECL), as a likely source of bias. As a result, Canada was excluded from the INWORKS study, motivating sustained efforts to identify, verify, and correct historical dose and employment data.

The National Dose Registry, maintained by Health Canada, was described as the core data source. Established in 1951, the NDR contains occupational radiation dose records for approximately one million workers across sectors including nuclear power, mining, medical, industrial, accelerator, and research environments. The speakers emphasized the complexity of integrating facility-based historical cohorts such as AECL workers and uranium miners from Eldorado and Ontario mines into the NDR, particularly when early records were incomplete or destroyed (*e.g.*, the 1958 fire that eliminated pre-1956 AECL records, including those from the 1953 NRX reactor accident).

A major focus of the talk was the resolution of data-quality issues in the NDR. These included:

- Incorrect dose-year defaults (*e.g.*, doses assigned to 1900),
- Duplicate dose entries,
- Negative doses arising from legacy "logical delete" practices,
- Ambiguities surrounding reported zero doses versus unmonitored workers or reporting thresholds.

Through extensive cleaning, deduplication, and verification, these issues have largely been resolved, significantly improving confidence in cumulative dose estimates.

Dr Lane then detailed the record linkage strategy used to create the CANRAD cohort, leveraging Statistics Canada's new Social Data Linkage Environment (SDLE). This two-stage process separates personal identifiers from analytical data to protect confidentiality while enabling linkage to:

- National mortality records (1926–2020),
- Cancer incidence data (1969–2019),
- Tax files (for vital status and follow-up),
- Employment and dose histories.

From an initial dataset of ~1 million records, approximately 860,000 individuals (≈90%) met inclusion criteria and were successfully linked for analysis. The cohort is nearly sex-balanced, enabling investigation of sex-specific radiation risks, and remains largely alive, with mortality and cancer incidence expected to rise substantially as the cohort ages.

Descriptive results showed strong sectoral and sex differences in exposure, with higher cumulative doses concentrated among male workers in mining and nuclear sectors, and lower doses predominating among female workers in medical occupations. Cancer and circulatory diseases together accounted for ~64% of deaths, underscoring the relevance of both cancer and non-cancer endpoints.

The speakers concluded by outlining ongoing and future research, including:

- An expanded Canadian Uranium Worker Study (~80,000 workers),

- Verification and update of the historic AECL cohort (including ~880 newly identified NRX cleanup doses),
- An updated Canadian Nuclear Power Worker Study,
- External and internal dose–response analyses by academic collaborators.
- An updated CANRAD linkage, incorporating dose and work histories through 2023, improved identifiers, restored Quebec and Nova Scotia cancer incidence, and new family income deciles (as proxies for lifestyle factors), is expected to be available for researchers in the near term.

Key Takeaways

1. Early Canadian radiation risk anomalies were largely data-driven: Apparent excess risks in international studies prompted discovery of missing and incomplete historical dose records, particularly from AECL.
2. The National Dose Registry has undergone major quality improvements: Errors related to dose year, duplication, negative doses, and zero-dose interpretation have been systematically identified and corrected.
3. CANRAD is now one of the largest and most comprehensive occupational radiation cohorts worldwide: ~860,000 workers with long-term follow-up for mortality and cancer incidence.
4. Modern record linkage methods substantially enhance cohort validity: Statistics Canada's SDLE (Social Data Linkage Environment) allows high-quality linkage while preserving confidentiality.
5. The cohort enables study of sex, industry, and dose-pattern differences: Near-equal representation of males and females and wide variation in exposure profiles across sectors.
6. Cancer and circulatory diseases dominate mortality outcomes: These outcomes may reflect combined effects of radiation exposure and other factors, including aging, supporting continued evaluation of both cancer and non-cancer radiation risks.
7. Historical exposure reconstruction remains critical: Newly identified AECL and NRX cleanup doses materially improve early-period dose estimation.
8. Geographic and temporal gaps in cancer incidence remain a challenge: Past limitations (*e.g.*, Quebec and Nova Scotia data) are being actively resolved.
9. Socioeconomic data will strengthen confounding control: Newly linked income deciles provide surrogate measures for lifestyle-related risk factors.
10. Canada is now positioned for renewed leadership in radiation epidemiology: The strengthened CANRAD cohort provides a foundation for addressing key uncertainties in low-dose and low-dose-rate health effects.

Session IV: New Nuclear Technologies: Safety, Waste Management, Emergency Preparedness, and Regulatory Reform

Chair: Brent J. Lewis (Royal Military College of Canada)

Speakers: **Brett Rosenberg** (NV5 Training Academy, USA)
Ricardo Dick (Canadian Nuclear Laboratories, Canada)
Nicholas Dainiak (Yale School of Medicine, USA)
Larry Kapustka (LK Consultancy, Canada)

Brief overview: Overall, the presentations in Session IV i) connected science to operational reality. They reviewed updated biokinetic and dosimetric models that influence current regulatory assumptions. They emphasized that biokinetic and dosimetric models have advanced beyond what many regulators currently use, creating real-world implications for compliance, worker safety, and internal dose assessment. ii) An overview of CNL's waste management strategy demonstrated how engineering controls and regulatory oversight translate into tangible reductions in environmental exposure, providing concrete examples of science-informed risk mitigation. iii) The presentation on emergency medical response evaluated hematopoietic cytokines for radiological mass-casualty settings. The presented data illustrated that human health response to radiation exposure is complex and requires evidence-based, *pre-planned* approach to interventions. They emphasized differences in countermeasures dosing, stability, and patient experience. iv) The session concluded with a discussion of polarized public views on nuclear technologies and the need for inclusive, transparent engagement grounded in postnormal science, where evidence is developed and decisions are made transparently in the presence of uncertainty, competing values, and high societal stakes, and in consensus-based frameworks. Key messages included the importance of early stakeholder engagement, trust, transparency, and adaptive solutions, lessons applicable to low-dose regulation, risk communication, and public health policies.

- In the opening presentation titled "Evolution of Biokinetic Models – Impacts on Regulations and Operations", Dr Brett Rosenberg examined the historical evolution of biokinetic and internal dosimetry models and highlighted their practical consequences for radiation protection, operational decision-making, and regulatory consistency. His central message was that scientific advances in biokinetic modeling have outpaced regulatory adoption, particularly in the US, creating inconsistencies that directly affect dose assessment and compliance outcomes.

Dr Rosenberg traced the development of internal dosimetry from ICRP Publication 2, which introduced permissible internal doses based largely on radium experience and simple non-recycling "catenary" compartment models, through ICRP 30, which remains the basis for U.S. Nuclear Regulatory Commission (NRC) regulations. These early frameworks assumed fixed

aerosol sizes (1 μm AMAD), broad solubility classes (days, weeks, years), and identical biokinetics for parent radionuclides and their progeny, an assumption that has been superceded by advances in modern science.

Subsequent advances, reflected in the recommendations of ICRP 60 publication and more recently, in ICRP Publication 130 on occupational intakes of radionuclides, represent a substantial conceptual shift. Modern models incorporate:

- Recycling of radionuclides within the body, rather than simple one-pass clearance;
- Independent biokinetics for radioactive progeny, critical for actinides and decay chains;
- Process- and chemical-form–specific biokinetics, replacing coarse solubility classes;
- Updated respiratory tract models and expanded tissue representation;
- Long-term dose integration (50 years) rather than annual reassessment.

Dr Rosenberg emphasized that these changes are not academic refinements but materially alter intake estimates and dose coefficients, sometimes by orders of magnitude for the same bioassay data. As a result, whether an exposure is classified as a regulatory exceedance may depend more on the biokinetic model used than on the underlying measurements themselves.

A key theme was the diversity of regulatory authorities and statutory mandates. In the United States, the NRC continues to rely on ICRP 30–based models, while the Department of Energy (DOE) largely aligns with later ICRP recommendations. Meanwhile, most of the international community has transitioned to ICRP 60+ frameworks, leaving U.S. practice increasingly misaligned with global standards. Dr Rosenberg argued that this disconnect is especially problematic given emerging technologies, such as advanced reactors, fusion systems, novel fuels, and metal tritides that are poorly addressed by legacy models.

He also highlighted evolving concepts in radiation and tissue weighting factors, noting that increased granularity and conservatism partly compensate for large uncertainties in intake estimation and biokinetics. The growing recognition of previously underappreciated tissues (e.g., extra-thoracic airways) further underscores the need to modernize dose assessment approaches.

Through practical examples (*e.g.*, cesium and plutonium intakes), Dr Rosenberg demonstrated that model choice can change compliance determinations, reinforcing his conclusion that consistent, science-based adoption of modern biokinetic models is essential for credible radiation protection in an era of expanding nuclear technologies.

<u>Key Takeaways</u>

1. Biokinetic models have evolved dramatically, from simple non-recycling compartments to chemically specific, recycling, long-term dose models.
2. Regulatory frameworks vary, particularly in the U.S., where NRC and DOE rely on different generations of models.
3. Model choice can dominate dose estimates, leading to different regulatory outcomes for identical bioassay data.

4. Independent progeny biokinetics matter, especially for actinides and complex decay chains.
5. Modern ICRP models improve realism but increase complexity and data requirements.
6. Emerging nuclear technologies expose gaps in legacy internal dosimetry approaches.
7. Conservatism in weighting factors partially reflects uncertainty, not just biology.
8. Harmonization with international standards is needed to ensure worker protection, regulatory credibility, and operational clarity.

- In the second presentation titled "Advances in Waste Management Exposure at Canadian Nuclear Laboratories", Mr Ricardo Dick provided an overview of the historical evolution and current practices of radioactive waste management at CNL. Focus was placed on radiation exposure control, environmental protection, and the development of the Near Surface Disposal Facility (NSDF).

Mr Dick began by outlining the scope of waste management operations at CNL, emphasizing that current efforts are centered on safe interim storage, waste handling, and preparation for eventual transfer to the NSDF. He described how waste management strategies at CNL have evolved in response to early operational experience, regulatory requirements, and increased understanding of environmental pathways and exposure risks.

CNL currently manages nine waste management areas, divided into operating facilities and legacy (non-operating) facilities. Operating facilities, including Waste Management Areas B, D/H, G, and H, handle a range of low-level, intermediate-level, bulk, containerized, and fuel-related wastes, sourced from on-site operations, decommissioning activities, and external vendors. Legacy facilities, such as Waste Management Areas A, C, E, and F, date back to the early years of Canada's nuclear program and reflect earlier disposal practices, including sand trenches and liquid waste dispersal, which are no longer considered acceptable.

A central theme of the talk was the progressive improvement of exposure control measures. Early disposal methods, which posed risks of seepage and environmental migration, were gradually replaced by engineered solutions, including asphalt-lined trenches, concrete bunkers, tile holes, and above-ground containment systems. These engineering controls were complemented by strengthened administrative controls, such as improved signage, enhanced environmental and radiological monitoring, routine sampling, worker training, and close regulatory oversight by the Canadian Nuclear Safety Commission (CNSC).

Mr Dick then introduced the Near Surface Disposal Facility (NSDF) as the next major step in CNL's waste management strategy. The NSDF is designed as a large-scale, multi-barrier disposal system, covering approximately one million square meters, intended primarily for low- and intermediate-level radioactive waste. Key components include the Engineered Containment Mound (ECM), a wastewater treatment plant, and a vehicle decontamination facility. The multi-

layer containment system is engineered to minimize radionuclide migration, protect groundwater, and ensure long-term isolation of waste for hundreds of years (~500 years).

Finally, Mr Dick emphasized that the NSDF reflects a process of continuous improvement, incorporating lessons learned from historical CNL facilities, other Canadian projects (such as Port Hope, Ontario), and international waste disposal experience. He concluded by reaffirming CNL's commitment to ALARA (As Low As Reasonably Achievable) principles, continuous monitoring throughout the facility life cycle, regulatory compliance, and responsible stewardship of radioactive waste.

Key Takeaways

1. CNL waste management practices have evolved substantially, moving from early trench-based disposal to modern engineered containment systems.
2. Radiation exposure control is achieved through layered defenses, combining engineering controls, administrative measures, monitoring, and training.
3. Operating waste management areas support ongoing operations, decommissioning, and interim storage pending transfer to NSDF.
4. Legacy waste facilities reflect historical practices and underscore the need for modern disposal solutions.
5. The Near Surface Disposal Facility (NSDF) represents a major advancement, using a multi-barrier design to limit environmental release and protect groundwater.
6. The NSDF integrates wastewater treatment, vehicle decontamination, and long-term monitoring as part of a comprehensive safety system.
7. Regulatory oversight by the CNSC and engagement with communities and Indigenous groups are integral to facility development and operation.
8. The NSDF design reflects lessons learned from Canadian and international experience, supporting sustainable, long-term radioactive waste management.

- In the third presentation titled "Hematologists' Approach to Cytokine Administration in a Mass Casualty Radiologic/Nuclear Emergency", Dr Nicholas Dainiak addressed the current evidence, limitations, and practical challenges associated with cytokine therapy as medical countermeasures (MCMs) for radiation-induced hematopoietic syndrome. His central message was that, despite significant progress, critical gaps remain in optimizing cytokine selection, timing, and deployment for mass-casualty radiation events.

Dr Dainiak began by identifying three major unmet needs:

(1) Closing knowledge gaps in radiation hematology and cytokine biology;

(2) Development and approval of new MCMs, as no single "magic bullet" exists; and

(3) Clarification of cytokine use, drawing on hematologists' real-world experience in treating radiation injury victims.

To frame cytokine action, he reviewed the hematopoietic hierarchy, from self-renewing hematopoietic stem cells through common lymphoid and myeloid progenitors to mature blood cell lineages. He then mapped the sites of action of key cytokines:

- G-CSF (filgrastim/pegfilgrastim) primarily stimulates granulocyte production;
- GM-CSF (sargramostim) has broader effects on myeloid, monocytic, dendritic, erythroid, platelet, and T-cell populations;
- Romiplostim targets the megakaryocyte–platelet lineage, with possible erythroid effects.

A major portion of the talk emphasized the complex immuno-hematopoietic feedback loops involving T cells, dendritic cells, regulatory T cells, and cytokines such as GM-CSF, IL-3, IL-10, TGF-β, IL-17, and IL-22. These interactions highlight that radiation injury affects not only marrow recovery but also immune regulation, gut integrity, and infection susceptibility, underscoring the complexity of therapeutic intervention.

Dr Dainiak then presented results from a systematic review and meta-analysis of cytokine use in radiation injury, drawing from 13 eligible studies (9 non-human primate [NHP] studies and 4 reviews of human cases). Key findings included:

- G-CSF improved survival in only 1 of 4 studies, often requiring transfusion support and associated with leukocytosis and bone pain.
- Pegfilgrastim (pegylated form of recombinant human G-CSF) improved survival in 1 of 2 studies, with similar limitations.
- Sargramostim (recombinant human GM-CSF) improved survival in 4 of 5 studies, notably without transfusion support, despite inducing non-infectious leukocytosis.
- Romiplostim, alone or combined with pegfilgrastim, showed improved survival, with combination therapy reaching statistical significance in recent studies.

Detailed NHP data demonstrated that GM-CSF significantly reduced mortality, including deaths from sepsis, hemorrhage, and cardiac complications, the principal causes of death after radiation exposure. Importantly, GM-CSF remained effective when administered up to 96 hours post-exposure, contrasting with other cytokines that require initiation within 24 hours.

Dr Dainiak also addressed logistical and operational considerations critical for emergency response: cytokine stability, dosing frequency, route of administration, and field usability. Sargramostim was highlighted as being stable across temperature, radiation, and light conditions, though it requires daily injections for 14 days. In contrast, GM-CSF, pegfilgrastim, romiplostim (a recombinant protein drug used to stimulate platelet production), and biosimilars are less stable and must be administered early, often within 24 hours.

In closing, he stressed the importance of cytokine stockpiling, pre-established clinical protocols, and pre-designed clinical studies to enable rapid data collection and evidence-based decision-making during radiation mass-casualty incidents. He emphasized that cytokines are only one component of a broader therapeutic strategy, which may also include antibiotics, blood

products, chelating agents, and -when cytokine therapy fails- stem cell transplantation, including peripheral blood and umbilical cord blood, as used in past nuclear accidents.

Key Takeaways

1. Cytokines are essential but incomplete MCMs for radiation-induced hematopoietic injury; no single agent addresses all aspects of damage.
2. Hematopoietic recovery is biologically complex, involving stem cells, immune regulation, and gut integrity.
3. GM-CSF (sargramostim) shows the most consistent survival benefit in NHP models, often without transfusion support.
4. Timing matters: many cytokines require administration within 24 hours, whereas GM-CSF remains effective up to 96 hours post-exposure.
5. Operational feasibility is critical -stability, dosing frequency, and ease of administration influence real-world effectiveness.
6. Non-human primate data are central to FDA approval, but human data remain limited.
7. Cytokine-induced leukocytosis is often non-infectious, particularly with GM-CSF.
8. Combination cytokine therapy (*e.g.*, romiplostim plus pegfilgrastim) may offer added benefits.
9. Preparedness requires stockpiling, protocols, and pre-planned studies, not ad hoc decision-making.
10. Cytokines should be integrated into a broader treatment framework, including transfusions, antimicrobials, decorporation agents, and stem cell transplantation for non-responders.

- In the closing presentation titled “Advocacy for and Opposition to Nuclear Power: Can the Differences be Bridged?”, Dr Larry Kaputska addressed the persistent stalemate surrounding nuclear energy and other high-stakes environmental issues, focusing not on technical risk, but on how decisions are made, communicated, and socially legitimized. His central thesis was that many controversies in nuclear and environmental policy are “wicked problems” -issues that cannot be resolved by technical evidence alone and therefore require structured, inclusive, and value-aware decision processes.

Dr Kapustka began by observing that positions on nuclear power have become increasingly polarized, with proponents and opponents selectively using evidence to reinforce pre-existing beliefs. This selective framing leads to dialogue failure, where stakeholders “talk past each other” rather than engage meaningfully. Drawing on Malcolm Gladwell’s concept from Blink, he emphasized that human decision-making is often rapid, intuitive, and emotionally driven, not the result of exhaustive rational analysis -an evolutionary trait that complicates complex risk governance.

He argued that although environmental and risk assessments integrate vast multidisciplinary data, decision-makers rarely synthesize all inputs, often defaulting to economics or engineering considerations. To overcome this limitation, Dr Kapustka advocated for formalized decision frameworks, highlighting ASTM consensus-based environmental decision-making guidelines. These frameworks emphasize early identification of decision-makers and stakeholders, clear project boundaries, explicit goals, agreed-upon rules for disagreement, and realistic timelines and budgets.

A major theme was the importance and fragility of the social license to operate. Public acceptance, while informal, exerts powerful influence through political pressure, consumer behavior, and opposition campaigns. Trust can take years to build and be lost instantly through perceived manipulation or lack of transparency. Effective engagement, therefore, must be early, continuous, honest, and adaptive across the entire project life cycle. Using examples such as the stalled Mackenzie Pipeline project, Dr Kapustka illustrated how failure to engage stakeholders early can derail projects for decades.

Dr Kapustka stressed the ethical responsibility of scientists and engineers to provide information that is verifiable, transparent, and free of undisclosed bias. He cautioned against normative science (embedding value judgments into supposedly objective analyses) and stealth advocacy (framing evidence to favor a predetermined outcome). He emphasized that scientists do not possess superior insight into societal values and must clearly distinguish measurements from models, while openly communicating uncertainties alongside certainties.

He further challenged the “deficit model” of science communication, which assumes public opposition arises from lack of knowledge. People may fully understand technical arguments but reject them because they conflict with deeply held values. Decisions are often emotional, symbolic, or cultural, not purely rational -an insight illustrated by everyday consumer behavior and public reactions to technologies.

The concept of wicked problems, introduced by Rittel and Webber, framed the latter part of the talk. Such problems lack consensus definitions, have no stopping rules or objectively “correct” solutions, and differ across social and geographic contexts. Attempts to impose elegant, technical fixes often fail. Instead, Dr Kapustka advocated for “clumsy solutions” that are inclusive, transparent, cross-disciplinary, and iterative approaches that accommodate multiple value systems and evolve over time.

In closing, he urged humility in confronting complex socio-ecological systems. There are no magic solutions, only adaptive pathways that acknowledge what is known, unknown, and unknowable. Long-term success depends on trust, inclusion, honest communication, and respect for societal values, particularly in contentious domains such as nuclear energy, radiation risk models, and climate policy.

<u>Key Takeaways</u>

1. Many nuclear and environmental controversies are “wicked problems”, not solvable by technical evidence alone.
2. Polarization is reinforced by selective use of information, causing stakeholders to talk past each other.
3. Human decisions are often intuitive and value-driven, not purely rational or analytical.
4. Formalized, consensus-based decision frameworks can help overcome cognitive and institutional limitations.
5. Early, continuous stakeholder engagement is essential; late engagement increases cost, delay, and opposition.
6. Social license to operate is fragile and can be lost quickly through perceived bias or lack of transparency.
7. Scientists must avoid normative science and stealth advocacy, clearly separating facts, models, assumptions, and values.
8. Public resistance is not simply a knowledge deficit; values and trust play decisive roles.
9. Uncertainty should be communicated openly, alongside what is well established.
10. Effective solutions are often “clumsy,” adaptive, and context-specific, requiring humility, inclusion, and extended dialogue.

End of Day I:

Open Discussion

Moderator: Edouard Azzam (Conexus Nuclear Inc., Canada)

The closing dialogue of Day 1 took the form of an open forum, encouraging participants to engage speakers on unresolved questions and emerging themes before transitioning to the poster session. Discussion centered on tissue repositories, low-dose radiation research, dosimetry challenges, biological variability, education and training, and emergency preparedness.

A major focus was the value and vulnerability of tissue archives. Participants emphasized the need for repositories that are sustainable, low-cost, and independent of continuous funding, while still enabling future analytical advances. Speakers highlighted ongoing challenges in long-term funding, governance, and accessibility, noting that many irreplaceable samples from past low-dose and space-related studies risk being lost without demonstrated user demand. Calls were made for researchers to actively express interest to funding agencies to justify continued support. New and emerging repositories at CNL, NASA Ames, and Canadian Space Agency-linked facilities were noted, with emphasis on maintaining active, shared-use tissue banks rather than passive “museums.”

Scientific discussion turned to low-dose and low-dose-rate effects, particularly on the immune system. Speakers highlighted the importance of variable dose-rate models that better

reflect occupational and environmental exposures and noted that facilities such as CNL in Chalk River enable well-controlled chronic and variable dose-rate experiments. Advanced techniques, including single-cell RNA sequencing, were cited as promising but challenged by the subtlety and variability of low-dose responses.

A recurring theme was the difficulty of *dosimetry* at low doses, especially at cellular and subcellular scales. Participants stressed that inadequate reporting of dosimetry undermines reproducibility and interpretation, and that many researchers lack sufficient understanding of how doses are delivered in their own experiments. The discussion underscored the need for closer integration of biology, physics, and dosimetry, and for improved training pathways to bridge these disciplines.

Broader conceptual issues were also raised, including inter-individual biological variability, underlying disease states, and the lack of clear quantitative endpoints for radiation damage. Speakers questioned whether protection standards should be based on average responses or the most sensitive individuals, noting that regulatory thresholds always reflect policy decisions rather than purely scientific ones. The group acknowledged that variability is intrinsic to living systems and must be embraced rather than eliminated.

The session concluded with comments on medical preparedness for radiation mass-casualty events by Dr Nicholas Dainiak who highlighted the U.S. Radiation Injury Treatment Network (RITN) model, emphasizing coordinated patient triage, transfer to transplant centers, reliance on limited biodosimetry capacity, and the critical role of medical countermeasure stockpiles, particularly cytokines. Comparable efforts in Europe were noted, with encouragement for Canada to further formalize national preparedness.

Overall, the discussion reinforced that low-dose radiation research, preparedness, and regulation remain works in progress, requiring sustained infrastructure, interdisciplinary training, transparent dosimetry, and coordinated international planning.

Reception, Continuing Dialogue, Poster Session

Student Posters:

1. **Development of New Optical Techniques for Rapid Biodosimetry**
   H. Flemming[*], P. Riarh[*], M. Ghasemi[*], C. McNairn[*], S. Subedi[†], V. Chauhan[‡], J. L. Inman[§], and S. Murugkar[*]
   [*] Department of Physics, Carleton University, Ottawa, Canada
   [†] Department of Mathematics and Statistics, Carleton University, Ottawa, Canada
   [‡] Radiation Protection Bureau, Health Canada, Ottawa, Canada
   [§] Biological Systems and Engineering, Lawrence Berkeley National Lab, Berkeley, USA

2. **Chronic Low-Dose Ionizing Radiation Induces Minimal Immune Alterations: Insights from Single-Cell Transcriptomics**

Bryan Marr[1], Holly Laakso[2], Melinda Blimkie[2], Andrew Cao[1], Uche Nworah[1], Seung-Hwan Lee[1, 3*], and Abrar U. Khan[1*]
[1] University of Ottawa, Ottawa, Canada,
[2] Canadian Nuclear Laboratories, Chalk River, Canada,
[3] University of Ottawa Institute of Systems Biology, Ottawa, Canada
* Co-correspondence

3. **Investigating the Role of Prostaglandin System Dysregulation in Radiation Resistance of Triple Negative Breast Cancer Cells**

Noah Dickinson[1,2], Emma Mageau[1], Alyssa Murray[1,2], Ronan Derbowka[1], Jessica Dougherty[2], Wuroud Al-Khayyat[1], TC Tai[2], Tom Kovala[2], Christopher Thome[2], Natalie Lefort[2], Sujeenthar Tharmalingam[2]
[1] Laurentian University, Sudbury, ON, Canada
[2] NOSM University, Sudbury, ON, Canada

4. **Investigating the Role of PTGS2 (Prostaglandin Synthase 2) Overexpression in Radiation Resistance and Metabolic Alterations in Triple Negative Breast Cancer Cells**

Emma Mageau[*1], Noah Dickinson[1], Alyssa Murray[1], Megan Davis[1], Kaitlyn Marshall-Bergeron[1], Jessica Dougherty[2], Wuroud Al-Khayyat[1], Ramya Narendrula[1,2], Maggie Lavoie[1], Ronan Derbowka[1], Tom Kovala[1,2,3], Douglas R. Boreham[1,2], Natalie Lefort[1,2], Tze Chun Tai[1,2,3], Christopher Thome[1,2,3], and Sujeenthar Tharmalingam[1,2,3]
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[2]Medical Sciences Division, NOSM University, 935 Ramsey Lake Rd., Sudbury, ON P3E 2C6, Canada
[3]Health Sciences North Research Institute, Sudbury, ON P3E 2H2, Canada

5. **Sub-background effects on growth in *S. cerevisiae* yeast: exploring the role of natural background radiation**

Reaume, H.[1], Lapointe, M.[1,2,3], Laframboise, T.[1,2], Robinson, D.[2], Tharmalingam, S.[1,2], Boreham, D.[1,2], Thome, C.[1,2]
[1]Laurentian University, Sudbury, ON, Canada
[2]NOSM University, Laurentian Ontario, Sudbury, ON, Canada
[3]SNOLAB, Lively, ON, Canada

6. **BRIGHT-Canada - Bringing Radiobiology Innovations to Grow the Highly Trained workforce in Canada**

Marcelo Vazquez[1], Marie-Claude Grégoire[1], Aaron Goodarzi[2], Cornelia Hoehr[3], Guy Trudel[4], Mary-Ellen Harper[4], Odette Laneuville[4], Pierre Billon[2], Rowan Thomson[5], Seung-Hwan Lee[4], Susan Lees-Miller[2], Tommy Alain[4], Jean-François Couture[4]
[1]Canadian Nuclear Laboratories, Chalk River, ON, Canada
[2]University of Calgary, Calgary, AB, Canada
[3]TRIUMF, Vancouver V6T 2A3, BC, Canada
[4]University of Ottawa, Ottawa, ON, Canada
[5]Carleton University, Ottawa, ON, Canada

7. **Sex-specific responses to combined low dose five-ion galactic cosmic radiation simulation exposure and hindlimb unloading in brain and behavior of male and female mice**

S. Puukila[1,2], S.D. Mhatre[3], J. Iyer[3,4], S. Tabares Ruiz[2], C.G.T. Tahimic[5], M. Burke[6,7], M.A. Brekker[8], A. Klein[9], O. Siu[9], Z. Feinstein[7], A.M. Paul[2,10], A. E. Ronca[11], J. S. Alwood[12]
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[2]Blue Marble Space Institute of Science, Seattle, WA, USA
[3]Amentum, Chantilly, VA; 4 Universities Space Research Association, Washington, DC, USA
[5]Department of Biology, University of North Florida, Jacksonville, FL, USA
[6]Houston-Methodist Research Institute, Dept of Neurosurgery, Houston, TX, USA
[7]Weill Cornell Medical College, Dept of Systems and Computational Biomedicine, New York, NY, USA
[8]Boston University, Department of Biochemistry and Cell Biology, Boston, MA, USA
[9]SLSTP, NASA Ames Research Center, Space Biosciences Division, Mountain View, CA, USA
[10] Embry-Riddle Aeronautical University, Department of Human Factors and Behavioral Neurobiology, Daytona Beach, FL
[11] Wake Forest Medical School, Dept of Obstetrics & Gynecology
[12] NASA Ames Research Center, Space Biosciences Division, Mountain View, CA

8. **New optical methods for identifying biomarkers of radiation exposure in lung cancer cells irradiated at clinical doses**

Justin R. Gagnon[1], Ngoc Vuong[2], Danicia Flores[2], Teresa Buragina[1], Edouard I. Azzam[3], Vinita Chauhan[2], Sangeeta Murugkar[1]
[1] Carleton University, Department of Physics, Ottawa, Ontario, Canada
[2] Health Canada, Consumer and Clinical Radiation Protection Bureau, Ottawa, Ontario, Canada
[3] Department of Radiology, Rutgers New Jersey Medical School, Newark, NJ, USA

9. **Development of an Automated Calyculin-A-Induced Premature Chromosome Condensation (PCC) Assay for Biodosimetry**

Hailey Adams[1,2,3], Kevin Pham[1], Ruth C. Wilkins[1,2], Lindsay A. Beaton-Green[1,2]

[1] Consumer and Clinical Radiation Protection Bureau, Health Canada

[2] Carleton University, Ottawa, Canada

[3] University of Ottawa, Ottawa, Canada

10. **In Vivo microRNA Signatures Induced by Acute and Chronic Low-Dose Radiation of Varying Quality**

Ronan Derbowka[1], Christopher Thome[2], Sujeenthar Tharmalingam[2]

[1] Laurentian University, Sudbury, ON, Canada

[2] NOSM University, ON, Canada

11. **Low-Dose Ionizing Radiation Modulates Translation Efficiency in Human Lung Fibroblasts**

Rosette N. Tamaddon [1,2,3], Martin Roffe [2], Antonella Bertucci [1], Dmitry Klokov[3,4], Yi Wang [1,3], Tommy Alain [2,3]

[1] Canadian Nuclear Laboratories, Chalk River, Canada.

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[3] Department of Biochemistry Microbiology and Immunology, University of Ottawa, Ottawa, Canada.

[4] L'Autorité de Sûreté Nucléaire et de Radioprotection (ASNR), 31 avenue de la Division Leclerc, 92260 Fontenay-aux-Roses, France

12. **Effects of amphiregulin on the radiation response in intestinal epithelial cells: a potential mitigator of gastrointestinal injury**

Taylor Laframboise[1,2], Alex Jameus[1,2], Sujeenthar Tharmalingam[1,2], Christopher Thome[1,2]

[1] Northern Ontario School of Medicine, Sudbury, ON, Canada

[2] Laurentian University, Sudbury, ON, Canada

13. **Hematological and gene expression changes in A/J mice after exposure to fractionated doses of gamma rays or neutrons**

Marcelo Vazquez[1], Lindsey Bertrand[1], Martin Roffe[1,2], Sebastian Tattenberg[3,4], Alex Hands[3], Camille Bélanger-Champagne[4], Andrew Minchinton[5], Cornelia Hoehr[4], Edouard I. Azzam[1,6]

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Overall Observations from Student Posters

1. Technological Innovation: Strong emphasis on advanced assays, optical techniques, and omics for biodosimetry and mechanistic studies.
2. Low-Dose Radiation Focus: Subtle biological changes at chronic or fractionated low doses are a recurring theme.
3. Cancer & Radiation Therapy: Students investigated mechanisms of resistance and potential protective interventions.
4. Environmental & Space Applications: Studies highlight the ecological and space-relevant implications of radiation.
5. Interdisciplinary Approach: Most projects combine physics, biology, and computational/statistical analyses.
6. Capacity Building: Dedicated attention to training the next generation of radiobiologists through coordinated programs.

Conexus Poster

A poster describing Conexus excellence and innovation through collaborative work was also displayed during this session.

DAY II

Session V: Diagnostic Radiology: Balancing Risks and Benefits

Chair: **Douglas R. Boreham** (NOSM University, Canada)

Speaker: **Cynthia McCollough** (Mayo Clinic, Rochester, MN, USA)

In her talk titled "CT radiation dose, risk, and benefits: What the data say?", Dr Cynthia McCollough addressed risk-benefit considerations in CT imaging, noting that while cohort studies show associations between pediatric CT exposure and cancer incidence, causality remains uncertain. Absolute excess risks must be weighed against substantial clinical benefits. She stressed justification of imaging (CT scans should only be performed when medically warranted), careful dose optimization (maintaining image quality while minimizing radiation exposure, and the importance of *clear, patient-centered risk communication* of small absolute risks.

In summary, CT imaging provides substantial clinical benefit by enabling earlier and more accurate diagnoses; however, some patients who could benefit from CT scanning may hesitate or decline imaging because concerns about radiation exposure and challenges in understanding very small risks influence their decisions. At CT-level doses, radiation risks remain uncertain and are best communicated with clarity, simplicity, and honesty, emphasizing that decisions should be based on overall net benefit rather than risk alone. Clinicians often need support in discussing these issues, as inconsistent or overly cautious messaging can lead patients to decline necessary imaging. Effective communication should use relatable comparisons, visual aids, and patient-centered language, while professional and regulatory bodies work toward harmonized guidance. Ultimately, clear and balanced risk-benefit communication by medical professionals is essential to ensure that patients receive medically justified imaging without undue anxiety.

Key takeaways:

1. CT scans provide major clinical benefits, but risk communication remains challenging: i) CT imaging is indispensable and often lifesaving; however, some patients' perceptions are dominated by fears of radiation exposure; ii) People tend to overestimate radiation risks and underappreciate the diagnostic value and potential to prevent harm.
2. Overestimation of risk stems from cognitive biases and difficulty with very small numbers: i) Patients who would benefit from CT scanning struggle to interpret low-probability risks (*e.g.*, <1 in 10,000); ii) messages like "all radiation is bad" are easier to grasp than nuanced explanations of small or uncertain risks.
3. There is uncertainty regarding low-dose radiation risks, and honest communication is essential: i) At CT-level doses, epidemiological evidence is limited; risk estimates depend

on modeling assumptions; ii) Communicating uncertainty accurately is crucial so patients can make informed decisions.

4. Decision-making should be framed around "net benefit," not risk alone: i) The appropriate question is rarely "Is there risk?" but rather "Is the health benefit of performing this CT greater than the potential risk?"; ii) avoiding a necessary CT can lead to delayed or missed diagnoses with far greater clinical consequences.
5. Physicians and radiologists need support in explaining radiation risk: i) Many clinicians lack confidence or time to discuss radiation doses or risk models; ii) providing simple, standardized language and tools improves patient understanding and shared decision-making.
6. Effective risk communication must be simple, contextual, and visual: i) Use relatable comparisons (*e.g.*, background radiation), avoid scientific jargon, and emphasize the patient's clinical situation; ii) visual aids help bridge numeracy gaps and reduce misunderstanding.
7. Public messaging about radiation should be balanced and actionable: i) Current broad statements (*e.g.*, "minimize radiation") can inadvertently increase anxiety or lead patients to refuse beneficial scans; ii) messages should distinguish between unnecessary imaging (which should be avoided) and clinically justified imaging (which is beneficial).
8. Policymakers and professional groups should develop consistent communication strategies: i) Fragmented messages from different agencies undermine trust; ii) harmonized guidelines and risk-communication frameworks can improve both public understanding and clinical practice.
9. Research and outreach should focus on understanding patient values: i) Risk communication is not only about numbers; it must reflect fears, values, and personal risk tolerance; ii) engaging with patients early improves trust and facilitates informed choices.

Session VI: Risk Modeling in Radiation Protection

Chair: Sally Amundson (Columbia University, USA)

Speakers: **Francis Cucinotta** (University of Nevada, USA)
David Brenner (Columbia University, USA)

Brief overview: This session highlighted innovative approaches to radiation risk modeling, particularly for low-dose, low-dose-rate, and high-LET exposures. Presentations focused on the limitations of traditional dose–response assumptions, emerging datasets for chronic exposures, and advanced computational methods including causal machine learning (CML) and multiscale AI-driven modeling, tools that estimate causal effects without assuming predefined dose–response models. In the first presentation, analyses of A-bomb survivors and nuclear worker cohorts showed encouraging concordance between CML and traditional analyses. The second

presentation introduced a track structure–based excess relative risk model using high-LET particle data, offering a gamma-independent method relevant for space radiation risk projections and demonstrating notable departures from quality-factor–based predictions.

Overall, the session emphasized that emerging datasets and computational methods can overcome some limitations of traditional radiation risk modeling, particularly for chronic, low-dose, and high-LET exposures relevant to occupational and spaceflight scenarios. Advanced analytical techniques, including CML and AI-integrated multiscale modeling, offer promising avenues for refining risk assessment and guiding regulatory and mission-planning decisions.

- In the first talk titled "Regulatory Dose Limits: New Data Sets, New Analysis Techniques", Dr David Brenner discussed the challenge regulators face in setting appropriate low-dose radiation limits, given that traditional epidemiology provides reliable risk estimates only at moderate to high doses. Current occupational and public dose limits are derived almost entirely from the atomic bomb survivor data, an acute, instantaneous exposure scenario, yet regulators must now consider evidence from large, high-quality cohorts with *prolonged*, low-dose, low-dose-rate exposures. Dr Brenner emphasized that prolonged exposures produce different biological effects due to repair kinetics and should not be treated as equivalent to acute bursts. He highlighted newly accessible datasets (*e.g.*, DOE worker cohorts in the Comprehensive Epidemiologic Data Resource - CEDR) and proposed causal machine learning (CML) as a complementary analytical method that avoids assumptions about dose–response shape (*e.g.*, LNT) and focuses on causal inference rather than simple associations. Early results applying CML to A-bomb survivor data suggest the method is viable and may help with a reassessment of occupational dose limits. He concluded that current limits (50 mSv/year) may need reconsideration when applied to prolonged exposures but stressed that the work is preliminary.

Key Takeaways:

1. The central problem: low-dose risk is hard to quantify: i) Epidemiology provides clear results at high/moderate doses, but not at low doses relevant for regulation; ii) Multiple dose–response models fit existing data but diverge drastically at low dose.
2. Current regulatory limits rely heavily on acute A-bomb data: i) Occupational limit (50 mSv/year) is derived exclusively from instantaneous A-bomb exposures; ii) public limits simply scale this down using "acceptance factors," not new data; ii) this approach predates availability of large, well-characterized prolonged-exposure cohorts.
3. Prolonged exposure ≠ acute exposure: i) Radiobiology shows that extending exposure time allows repair of DNA damage and reduces biological impact; ii) therefore, applying A-bomb data where exposure was acute to chronic occupational exposures may need to be revisited.

4. New high-quality chronic-exposure data sets are now available: i) DOE worker cohorts (*e.g.*, Oak Ridge, Hanford) in CEDR are large, long-followed, and publicly accessible; ii) these offer opportunities for more realistic risk estimation at low dose rates.
5. Causal machine learning (CML) as a new analytical tool: i) Avoids the need to assume LNT or any specific dose–response form; ii) attempts to estimate causal effects rather than correlations; iii) already extensively validated in other fields (economics, social sciences); iv) preliminary radiation applications show results consistent with traditional analyses.
6. Regulatory relevance: i) CML may allow evidence-based re-evaluation of occupational dose limits without being trapped in LNT debates; ii) Dr Brenner suggests the 50 mSv/year limit warrants reconsideration for long-term exposures.
7. CML methodology provides an opportunity to study cohorts chronically exposed to low-dose, low-dose-rate radiation without pre-specifying the mathematical shape of the dose response relationship.
8. Dr Brenner acknowledges uncertainties and ongoing methodological development, emphasizing the need for peer review and community feedback in applying CML to assess ionizing radiation exposure limits for occupationally-exposed workers and for the general public.

- The second talk titled "Flying Without a Net: High LET Risk Predictions without a Gamma-Ray Basis" was delivered by Dr Francis Cucinotta, who presented a comprehensive analysis of high-LET radiation risks, emphasizing how complex DNA damage, particularly clustered and non-DSB lesions, differs fundamentally from damage induced by low-LET radiation and, as a result, how such damage contributes to major uncertainties in current risk models. He demonstrated that high-LET radiation produces qualitative biological effects, including distinct tumor spectra, enhanced metastatic potential, epigenetic changes, and pronounced non-linear dose responses at very low particle traversals. These phenomena challenge standard NASA and NCRP cancer risk models, which rely heavily on atomic-bomb epidemiology and separate "quality factor" and "Dose Rate Effectiveness Factor (DREF)" ratios. Dr Cucinotta argued that these frameworks may underestimate space radiation cancer risks, especially when non-targeted effects are included, potentially raising Mars-mission risk predictions by two- to three-fold. He outlined an alternative "direct excess relative risk" model derived from animal data and introduced a new AI-driven strategy to harmonize omics, mechanistic, and tissue-level datasets for improved low-dose risk estimation.

<u>Key Takeaways</u>

1. Clustered DNA damage dominates high-LET effects: i) High-LET radiation produces complex clustered DNA damage (including tandem lesions and non-DSB clusters) at far greater frequencies than low-LET radiation; ii) new imaging and modeling suggest non-

DSB clusters vastly outnumber DSBs and can persist for days, driving ROS, delayed DSB formation, and mutagenesis.

2. Standard risk models are constrained by low-LET assumptions: i) Traditional NASA/NCRP models rely on epidemiology-based parameters (quality factors + DREF) that may not capture qualitative differences in radiation action; ii) RBE estimates vary widely across tumor types, largely due to inconsistencies in low-LET reference radiation.
3. High-LET radiation causes qualitatively different tumor biology: i) Mouse tumor studies show distinct dose-response shapes and tumor spectra following heavy-ion exposure; ii) high-LET radiation leads to more aggressive cancers and increased metastatic potential compared to gamma rays or protons; iii) cytogenetic and epigenetic profiles after heavy-ion exposure differ markedly from low-LET patterns.
4. Non-targeted effects often produce non-linear responses at very low doses: i) Multiple datasets (chromosomal damage, transformation, Harderian gland tumors) show steep upturns in effect per unit dose when exposures fall below one particle traversal per nucleus; ii) these effects cannot be explained by cell killing or delta-ray dose and may substantially elevate risk estimates; iii) including non-targeted effects in models increases predicted Mars-mission cancer risks by 2-3 folds.
5. Alternative Model: Direct Excess Relative Risk (DERR) from animal data: i) Dr Cucinotta proposes replacing dual-ratio models with a relative-risk approach derived directly from heavy-ion and neutron animal studies; ii) saturation-type dose–response models fit high-LET tumor data better than linear models.
6. Future direction: AI-integrated multiscale modeling: i) New work aims to integrate single-cell sequencing, pathway analyses, and clinical patient datasets using AI approaches; ii) a major challenge is technological heterogeneity across omics datasets; AI harmonization is essential; iii) the goal is to create mechanistically informed models that accurately predict radiation risks at very low doses.

Session VII: Risk Communication of Radiation Health Effects

Chair: **Marie-Claude Grégoire (Canadian Nuclear Laboratories, Canada)**

Speakers: **Margot Hurlbert** (University of Saskatchewan & University of Regina, Canada)
Paul Locke (John Hopkins Bloomberg School of Public Health, USA)

Brief overview: This session explored key challenges in communicating radiation risks to workers and the public. Discussions highlighted persistent issues including technical overemphasis, limited communication training among radiation professionals, inconsistent messaging, and reliance on outdated “deficit model” approaches. Participants emphasized that effective risk communication must integrate scientific data, social context, and audience values, with trust-building at its core.

Presentation: Rather than having formal presentations by the speakers, this session consisted of a dialogue among the Chair, the Speakers and the Audience. The Chair highlighted key challenges in communicating radiation risks to the public. In response, the speakers emphasized persistent issues, including overreliance on technical models, limited communication training among radiation professionals, and inconsistent messaging across disciplines. The public often views radiation risk through the lens of source, control, and trust, which differs from the dose-focused perspective of experts. The outdated "deficit model" -simply providing more scientific facts was shown to be ineffective. Speakers stressed the need for modern, engagement-focused communication approaches, careful use of risk comparisons, and the selection of credible messengers, ideally scientists and engineers who are properly trained to communicate clearly and respectfully.

In summary, the consensus was that effective radiation risk communication requires integration of science, social context, and interdisciplinary collaboration. Building and maintaining public trust, preparing for emergencies, and ensuring transparent governance are essential for protecting health, supporting nuclear technology adoption, and addressing societal concerns.

<u>Key Takeaways</u>

1. Research & Risk Integration: i) Need to combine low- and high-dose radiation data to inform workers and the public; ii) integrating research, industry experience, and public perception; iii) probabilistic risk models, such as "Probability of Causation," could quantify exposure–effect relationships; iv) interdisciplinary research is critical, covering occupational safety, medical exposures, environmental monitoring, and long-term waste management.
2. Worker Concerns: i) Workers and families seek clear information on reproductive health, cancer and non-cancer risks, and radiation exposure; ii) providing clear, accessible educational materials for home and work is essential; iii) worker advocates can facilitate communication and ensure concerns are addressed.
3. Public Perception & Trust: i) Public understanding is shaped by conflicting messages (e.g., radiation causes and treats cancer); ii) age influences trust: older adults are generally more trusting; younger populations are often unsure or unfamiliar with scientific concepts; iii) cultural context matters, including ethical and environmental perspectives, especially for Indigenous communities.
4. Communication Strategies: i) One-off presentations are insufficient, ongoing engagement and dialogue build trust; ii) interaction should be two-way, allowing audiences to ask questions and participate; iii) social context is as important as scientific content; presenters should research audience concerns in advance; iv) practical tools (tone, language, process, visual cues) are critical, particularly in emergency preparedness; v) resources like NCRP's emergency risk communication guidelines provide structured support.

5. Industry & Governance Considerations: i) Organizations or professionals who use or generate ionizing radiation in the course of their work should provide information but should not dominate messaging; ii) local scientists, academics, and interdisciplinary teams help increase credibility and trust; iii) clear communication on accountability, governance, and long-term waste management is essential; iv) lessons from past initiatives (e.g., Saskatchewan nuclear projects) highlight the need for proactive, transparent strategies.

International and National Coordination in Low-Dose Radiation Research

Chair: **Ralph Stube** (Conexus Nuclear Inc., Canada)

Speakers: **Dominique Laurier** (ASNR, France)
Vinita Chauhan (Health Canada)

Dr Dominique Laurier presented a brief overview of the work of the NEA High-Level Group on Low-Dose Research (HLG-LDR), which was established in 2019 by the OECD Nuclear Energy Agency (NEA) under the Committee on Radiation Protection and Public Health (CRPPH). The HLG-LDR aims to promote international coordination through a structured research database (http://www.oecd-nea.org/ldr), the development and integration of adverse outcome pathways (AOPs) with current examples including five endorsed AOPs (AOP #272; AOP #470; AOP #478; AOP #482; AOP #483), and policy-oriented communication. He stressed that the emphasis is on aligning research priorities and sharing methodologies across countries to address uncertainties in low-dose radiation effects.

Dr Vinita Chauhan described Canada's initiative of establishing the Canadian Radiation Research Network (CRRN), envisioned as a coherent, multidisciplinary network that leverages the expertise of Canadian researchers and regulators to address key knowledge gaps related to low-dose radiation exposure. She emphasized that a well-coordinated CRRN will reduce duplication of efforts, promote collaboration, enable sharing of resources and infrastructure, identify research gaps, and facilitate data and information sharing to maximize the value of funded research. By consolidating Canadian research capacity and integrating emerging methodologies, the CRRN will strengthen Canada's ability to address scientific and regulatory challenges related to low-dose radiation exposure and ensure that research outcomes translate into robust, evidence-based policies that protect the health of Canadians.

Both NEA HLG-LDR and CRRN initiatives underscore the importance of structured collaboration, harmonized approaches, and technology integration in advancing low-dose radiation science. These coordinated efforts help inform regulatory decision-making, improve risk assessment, and position Canada and its international partners to address key scientific and policy challenges.

Panel Discussion

Moderator: **Edouard Azzam** (Conexus Nuclear Inc., Canada)

Panelists: **Mark P. Little** (Northwestern University, USA; Oxford Brookes University, UK)
Ruth Wilkins (Health Canada & Carleton University, Canada)
Margot Hurlbert (University of Saskatchewan & University of Regina, Canada)
Larry Kapustka (LK Consultancy, Canada)
David Rowan (Canadian Nuclear Laboratories, Canada)
Paul Locke (John Hopkins Bloomberg School of Public Health, USA)

The panel discussion brought together experts from radiation biology, radioecology, epidemiology, risk modeling, and science communication to discuss emerging science and ongoing challenges in understanding low-dose radiation effects, with a strong focus on translating complex data into actionable insights for policy, workers, and the public. Participants emphasized that while substantial progress has been made in mechanistic research and in applied risk assessment, important uncertainties remain across biological scales -from molecular pathways to human populations and ecological systems- and that improving communication of these nuances to policymakers and the public is essential.

Discussions highlighted the complexity of translating findings from cellular and organismal studies into meaningful population-level predictions for both humans and ecosystems. Although research has characterized many molecular and cellular responses to low-dose radiation, these effects do not always scale predictably to tissues, organisms, or communities. In ecological protection, for example, current measurement approaches focus heavily on organism-level endpoints, while protection goals emphasize populations, communities, and ecosystem services. Because population dynamics depend on non-linear interactions -births, deaths, immigration, emigration, density dependence, and habitat constraints- organism-level data often cannot reliably predict ecological outcomes. Participants noted parallels with climate-change modeling, where complex, multi-scale interactions also introduce uncertainty that must be explicitly acknowledged and continually refined.

Human epidemiological research faces similar challenges. Although large cohort studies provide critical evidence for radiation-related disease risks, detecting effects at very low doses is statistically problematic. The workshop underscored the need for sustained support of long-term cohorts, improved dosimetry, harmonized international datasets, and methods that integrate biological understanding with epidemiological observations. Advances in high-throughput technologies, biomarker discovery, and systems biology offer opportunities to strengthen mechanistic evidence and inform risk models but require coordinated investment and careful validation.

Across all domains, participants viewed artificial intelligence and machine-learning approaches as promising tools; particularly, for integrating diverse datasets, identifying non-

linear patterns, and quantifying uncertainty. However, AI was not seen as a simple solution. Its outputs are only as reliable as the underlying data, and automated models must be paired with expert interpretation, transparent assumptions, and rigorous quality control. Machine learning methods do not eliminate the problems of bias that may result from unmeasured confounders. Quantum computing may further enhance complex modeling capabilities in the future, but similarly demands caution, expertise, and interdisciplinary collaboration.

A recurring theme throughout the workshop was the central importance of communication. Scientists must engage on regular basis with stakeholders and clearly articulate not only what is known, but also the scope and sources of uncertainty, the limits of extrapolation, and the rationale underlying risk-management decisions. Effective communication fosters trust: It supports evidence-based policy and helps the public and decision-makers understand how scientific knowledge informs protection standards.

Overall, the dialogue emphasized that meaningful progress in low-dose radiation science will depend on integrated research across disciplines; improved measurement and modeling approaches at relevant biological and ecological scales; responsible and transparent use of advanced computational tools; and a *strong commitment to communication that conveys both scientific advances and remaining uncertainties*.

Key Takeaways:

1. Worker Concerns Are Diverse: Workers often ask about personal health risks, reproductive safety, and connections between occupational exposure and cancer, as well as other health risks. Risk communication must address these concerns clearly and credibly.
2. Low Dose Radiation Effects Are Not Communicated Effectively: There is widespread confusion among both workers and the public about low vs. high dose radiation, emphasizing the need for precise terminology (*e.g.*, low-dose ionizing radiation) and context-specific explanations.
3. Probability-Based Risk Models Are Needed: Industry stakeholders highlighted the value of integrating low- and high-dose data into risk models (*e.g.*, probability of causation tools) to support informed decision-making and legal clarity.
4. Public Trust Requires Interdisciplinary Communication: Trust is shaped by who delivers the message and how. Scientists, regulators, engineers, and community representatives must collaborate, considering social, cultural, and historical contexts.
5. Age and Demographics Affect Trust: Older individuals tend to be more trusting of scientific sources, while younger audiences often respond with uncertainty or “don’t know” answers, highlighting the need for tailored engagement strategies.
6. Preparedness Is More Than Technical: Effective risk communication for accidents or emergencies must be proactive, structured, and supported by resources that guide response, messaging, and social engagement.

7. Community and Cultural Sensitivities Matter: Indigenous perspectives, environmental stewardship, and local ecosystem dependencies must be incorporated into both protection strategies and communication plans.
8. Industry Communication Needs Transparency: Vendors must be prepared to discuss not only successes but also risks and contingencies. Local and trusted institutions (*e.g.*, national labs, universities) play a critical role in bridging gaps.
9. Learning From History Is Crucial: Past missteps, including poorly communicated nuclear projects and public safety misunderstanding, emphasize the importance of trust, accountability, and proactive planning to enhance readiness for public communication.
10. Education and Capacity Building Are Essential: Academic institutions, social scientists, and regulatory bodies should equip communicators with frameworks, tools, and training to respond effectively to public inquiries, even in complex or high-stakes scenarios.

In summary, the panel stressed that our radiation protection guidelines are robust, and progress in low-dose radiation research and protection requires integrated science, transparent communication, and culturally aware engagement. Success depends on bridging biological, epidemiological, ecological, and social dimensions to inform policy and maintain public trust.

Session VIII: Radiation Dose and Biological Responses in Non-Human Ecosystems

Chair: **Jennifer Olfert** (Canadian Nuclear Laboratories, Canada)

Speakers: **David Rowan** (Canadian Nuclear Laboratories, Canada)
Marilyne Stuart (Canadian Nuclear Laboratories, Canada)
Larry Kapustka (LK Consultancy, Alberta, Canada)

Brief overview: This session examined the ecological and biological impacts of radiation on non-human systems, ranging from ecosystem-level effects at contaminated sites to sex-specific molecular responses in animals and conceptual approaches for improved ecological protection. Presentations emphasized long-term, multidisciplinary research, nuanced interpretation of low-dose effects, and advanced modeling for risk assessment.

The first presentation examined ecological impacts of radiation across species and ecosystems. Studies at the Chalk River Site found no adverse ecological effects in sediment, mayfly populations, or sensitive fern gametophytes, even at the most contaminated areas, with evidence of hormetic increases in viability up to ~10 Gy. The second presentation demonstrated sex-dependent hepatic transcriptional responses to organically bound tritium. The third argued for expanding beyond the Reference Animal and Plant (RAP) approach toward ecosystem-level frameworks that better align with ecological protection goals.

- In the first talk titled “Assessing Ecological Effects of Legacy Contamination on the Chalk River Site”, Dr David Rowan presented a comprehensive assessment of ecological effects associated with historical radioactive releases at the Chalk River site, Canada’s oldest nuclear facility. His talk focused on whether long-term operations and past accidents have resulted in measurable biological effects in aquatic and terrestrial ecosystems, and how such evidence informs remediation decisions.

The primary aquatic case study examined the Ottawa River near the Chalk River process outfall, where historical releases, particularly of cesium-137, had raised concerns about risks to biota. Dr Rowan described an extensive ecological risk assessment centered on *Hexagenia* spp., a burrowing mayfly widely used as a sensitive indicator of sediment quality. This species is ecologically important, forms a key component of aquatic food webs, and serves as prey for endangered sturgeons.

Sampling involved 217 sites and approximately 1,000 sediment dredges, generating a robust dataset of population and community metrics, including abundance, frequency of occurrence, and biomass. Comparisons among upstream, adjacent, and downstream locations showed no statistically meaningful differences in *Hexagenia* populations despite localized sediment contamination near the outfall. These findings indicate no detectable present-day ecological effects from more than 70 years of site operations. Importantly, Dr Rowan noted that similar conclusions were reached in a pioneering 1948 radioecological study at Chalk River, highlighting long-term consistency in ecological observations.

To address whether effects may have occurred historically, sediment cores were analyzed to reconstruct temporal contamination profiles using lead-210 dating. These records revealed elevated radionuclide concentrations during earlier periods, notably following the 1952 NRX reactor accident and releases in the 1970s. Dose reconstruction using the ERICA Tool indicated that peak dose rates to *Hexagenia* reached approximately 500 $\mu Gy\ h^{-1}$ during the 1970s, which is near the lower boundary of “possible effects” for non-human biota, but not clearly within ranges associated with adverse ecological outcomes. Present-day doses are substantially lower.

Based on the absence of demonstrated ecological harm, Dr Rowan explained that remediation decisions favored natural attenuation rather than disruptive actions such as dredging, allowing clean sediment deposition and radioactive decay to reduce risks over time.

The talk also addressed terrestrial ecosystems, using sensitive fern (*Onoclea sensibilis*) gametophytes as bioindicators of genotoxicity in contaminated waste management areas. Field dose rates ranged from background (~60 $\mu Gy\ h^{-1}$) to elevated levels (~900 $\mu Gy\ h^{-1}$), corresponding to growing-season doses up to ~4 Gy. Laboratory dose-response studies showed no effects at field-relevant doses, with reproductive failure occurring only at much higher exposures (~10 Gy). Evidence of hormesis at low doses was also noted, consistent with observations in many plant species.

Overall, Dr Rowan concluded that even at the most contaminated locations examined, no population- or species-level ecological effects were detected. He emphasized that from a radioecological perspective, effects on ecosystems generally require substantially higher doses than those observed at Chalk River. Comparisons with sites such as Chernobyl and Savannah River reinforced the idea that ecosystems can remain functional at contamination levels that are of concern for human exposure, particularly once human disturbance is removed.

Key Takeaways

1. No detectable ecological effects were observed in aquatic or terrestrial ecosystems at Chalk River, despite historical radioactive releases.
2. Sentinel species, particularly *Hexagenia* sp. mayflies, provide powerful, ecologically relevant indicators for assessing radiation effects in natural systems.
3. Historical dose reconstruction showed peak doses near, but generally below, thresholds associated with adverse effects in non-human biota.
4. Natural attenuation was scientifically justified as a remediation strategy, avoiding unnecessary ecological disruption.
5. Field-based radioecology often reveals greater ecosystem resilience than predicted by laboratory or human-centric risk models.
6. Ecological impacts typically require much higher doses than those encountered at most regulated nuclear sites.
7. Comparisons with highly contaminated sites (*e.g.*, Chernobyl) underscore the importance of dose rate, exposure duration, and ecosystem context.
8. The work highlights the value of long-term, multidisciplinary radioecological studies in guiding evidence-based environmental management.

- In the second talk titled "Sex Differences Affect Hepatic Transcriptional Responses in Mice Exposed to Organically Bound Tritium", Dr Marilyne Stuart presented an omics-based investigation into the biological effects of chronic, multigenerational exposure to organically bound tritium (OBT) in mice. The study leveraged archived tissues from a long-term multigenerational experiment, enabling advanced transcriptomic analyses to probe subtle biological responses at environmentally relevant dose rates.

The broader study followed four generations (G0–G3) of mice chronically exposed to tritium in different organically bound forms, either tritiated amino acids or tritiated fatty acids, administered through diet or drinking water. G0 exposures began early in life and continued across generations, including *in utero* exposure for later generations. The work presented in this talk focused on second-generation (G2) mice, which experienced lifelong exposure across three successive generations.

Tritium dose rates in G2 mice were extremely low (~4×10^{-4} Gy/day, or ~0.02 μGy/h), comparable to environmental exposure scenarios near nuclear facilities or post-accident settings

such as Fukushima. Dosimetry showed that approximately 50–60% of the absorbed dose originated from organically bound tritium, confirming biologically relevant internal exposure. Biomarkers such as γ-H2AX and changes in fatty acid composition verified that exposure occurred, despite the very low dose rates.

Phenotypic assessments revealed sex-specific physiological responses. Female mice exposed to tritiated amino acids exhibited increased body and liver weights relative to controls, while males exposed to tritiated fatty acids showed a modest but significant decrease in body weight. Importantly, liver-to-body weight ratios were unchanged, indicating modulation rather than overt toxicity.

Hematological and blood chemistry analyses identified only subtle changes, all remaining within normal physiological ranges. Females showed reduced mean platelet volume and decreases in alkaline phosphatase (ALP) and creatinine, suggesting metabolic modulation. Males displayed changes in white blood cell and lymphocyte counts in the amino acid group, and alterations in ALP, calcium, and sodium levels, indicating possible immune and metabolic responses. These findings pointed to adaptive rather than pathological effects.

To better understand underlying mechanisms, liver RNA sequencing was performed (~25,000 genes analyzed). Transcriptomic profiling revealed a strong separation by sex and by OBT form. Females exposed to tritiated amino acids exhibited widespread gene expression changes consistent with anabolic metabolism, cell cycle progression, and reduced apoptosis. In contrast, males showed a limited transcriptomic response dominated by stress-adaptive pathways, including DNA damage response, mitochondrial energy regulation, and detoxification processes. Responses to tritiated fatty acids involved more similar numbers of differentially expressed genes in both sexes, suggesting that OBT chemical form influences metabolic pathway engagement.

Overall, the study demonstrated that chronic low-dose tritium exposure does not produce overt toxicity, but instead induces sex-specific, exposure-form–dependent molecular and physiological adaptations. Dr Stuart emphasized that sex differences exceeded exposure-related differences, underscoring the importance of biological context in low-dose radiation risk assessment. The work raises key questions about dose metrics (dose rate vs cumulative dose), generational persistence of effects, and integration of omics data with traditional toxicological endpoints.

<u>Key Takeaways</u>

1. Environmentally relevant, chronic low-dose tritium exposure produced measurable biological responses without overt toxicity.
2. Organically bound tritium contributed most of the internal dose, underscoring its importance in radiological risk assessments.
3. Sex-specific responses dominated outcomes, often exceeding differences between exposure groups.

4. Females exhibited anabolic and growth-associated transcriptomic responses, while males showed stress-adaptive and checkpoint-related responses.
5. Physiological and biochemical changes were subtle and within normal ranges, consistent with adaptive modulation rather than harm.
6. The chemical form of OBT matters, influencing metabolic pathways and gene expression profiles.
7. Transcriptomics revealed effects invisible to traditional endpoints, demonstrating the value of omics approaches in low-dose radiation biology.
8. The study raises important questions about appropriate dose metrics, intergenerational effects, and integration of molecular and phenotypic data in radioecology and radiobiology.

- In his talk titled "Ecological Considerations in Radiation Safety", Dr Larry Kapustka concluded the session with a conceptual and critical examination of how ecological systems are assessed and protected within environmental and radiological risk frameworks. Drawing on decades of experience in ecology and environmental protection, he argued that current regulatory approaches systematically underestimate ecological complexity and therefore risk misunderstanding (or misrepresenting), real ecosystem responses to stressors, including ionizing radiation.

Dr Kapustka began by recalling the robust radioecological research conducted in the 1950s–1960s following nuclear weapons testing, particularly in North America. He noted that political and regulatory priorities subsequently shifted toward human health protection, leading to the assumption that protecting humans would automatically protect ecosystems. This assumption was formalized through the Reference Animal and Plant (RAP) approach, modeled after the "reference Man" concept. Dr Kapustka argued that both assumptions are fundamentally flawed, as they ignore ecosystem dynamics, species interactions, and emergent properties that arise at higher levels of biological organization.

A central theme of the talk was the mismatch between protection goals and measurement endpoints. Regulatory goals typically focus on populations, ecosystem function, and services, yet most studies measure organism-level endpoints under simplified laboratory conditions, often involving single species and single stressors. While organism-level studies are reproducible and statistically robust, Dr Kapustka emphasized that they are the least relevant for predicting ecosystem-level outcomes. Conversely, ecosystem-level studies directly address protection goals but are inherently complex, context-dependent, and difficult to generalize.

Dr Kapustka illustrated the limits of prediction using conceptual food-web models of increasing complexity. In simple linear systems, responses to stressors can often be predicted. However, even modest increases in connectivity and feedback loops rapidly erode predictive capacity. Ecological systems operate through nested positive and negative feedback loops across multiple spatial and temporal scales, making outcomes highly contingent and often non-intuitive.

Critically, management tends to focus on fast, easily measured variables, whereas ecological stability is frequently governed by slow variables operating over decades or longer.

He further demonstrated how incomplete conceptual models can lead to entirely incorrect conclusions. Using examples involving symbiotic associations, Dr Kapustka showed that the dominant exposure pathway, and thus the most affected organisms, can shift dramatically depending on ecological context. Without understanding such foundational system properties, risk assessments may be "100% wrong."

To navigate this complexity, Dr Kapustka outlined three complementary approaches that can improve ecological risk assessment:

1. Hierarchical Patch Dynamics, which situates focal endpoints within broader contextual levels while linking them to mechanistic processes at lower levels.
2. Systems Perspectives, aided by visualization tools, which treat ecosystems as complex (but not merely complicated) networks and encourage examination of interactions beyond single nodes.
3. Bayesian Network Models, which integrate multiple stressors, endpoints, and uncertainties to produce probabilistic -not deterministic- outcomes, allowing iterative updating as new data become available.

Dr Kapustka emphasized that Bayesian approaches are particularly valuable because they explicitly incorporate uncertainty, allow sensitivity analyses, and can be run "backwards" to explore plausible causal pathways, an important feature in regulatory and legal contexts where causality is often contested. However, he cautioned that these models are only as sound as their underlying conceptual structure.

The talk concluded with a discussion of "wicked problems", complex decision-making situations with no single correct answer, where choices involve tradeoffs and outcomes depend on societal values such as balancing environmental goals, costs, or species protection priorities. Dr Kapustka stressed that scientific assessments should align with community concerns and that scientists must be transparent about uncertainty. He closed with a call for intellectual humility, careful conceptual modeling, and rigorous vetting of study designs before data collection - advocating for "mental experiments" as an essential but increasingly neglected step in ecological science.

<u>Key Takeaways</u>

1. Protecting humans does not automatically protect ecosystems; ecological systems have distinct dynamics and vulnerabilities.
2. Reference Animal and Plant approaches oversimplify reality and cannot reliably predict ecosystem-level effects.
3. There is a fundamental mismatch between regulatory protection goals (ecosystems, populations) and measured endpoints (organisms).

4. Ecological systems are governed by feedback loops and emergent properties, making outcomes difficult to predict from reductionist studies.
5. Slow variables, which operate over decades, often control ecosystem stability yet are rarely the focus of monitoring or management.
6. Incomplete or incorrect conceptual models can lead to entirely wrong conclusions, regardless of data quality.
7. Hierarchical patch dynamics, systems thinking, and Bayesian networks offer practical tools for addressing ecological complexity.
8. Bayesian models are valuable because they integrate uncertainty, evolve with new data, and provide probabilistic outcomes, not false certainty.
9. Many environmental problems are wicked, with no objective solutions; decisions depend on societal values and priorities.
10. Scientists must practice humility, transparency, and rigorous study design, recognizing what is known, unknown, and unknowable.

Key Insights and Path Forward:

This workshop provided an interdisciplinary assessment of the biological and health effects of low-dose and low dose-rate ionizing radiation, integrating mechanistic, epidemiological, ecological, and communication perspectives. Across Sessions I–VIII, speakers highlighted significant advances in experimental models, high-throughput technologies, and analytical tools, while emphasizing persistent challenges in extrapolating findings across biological scales, exposure scenarios, and populations. Strengthening the integration of mechanistic and epidemiological evidence emerged as a central priority for improving low-dose risk assessment and regulatory relevance. Dedicated discussions on risk communication further emphasized the need for engagement-based, culturally aware, and interdisciplinary approaches that address worker concerns, public perception, and emergency preparedness.

An open discussion at the end of Day 1 enabled candid dialogue among speakers and participants, allowing key themes to be synthesized across sessions. This exchange highlighted areas of convergence, particularly regarding uncertainty at low doses, the interpretation of non-linear responses, and the need for improved experimental design, data integration, and stringent dosimetry. The discussion also reinforced the value of sustained, cross-disciplinary interaction in refining research priorities and identifying gaps not apparent within individual presentations.

The panel discussion further underscored the complexity and uncertainty inherent in low-dose radiation science, particularly when translating cellular and organismal responses to population- and ecosystem-level outcomes. Participants emphasized the potential of artificial intelligence and advanced computational approaches to integrate diverse datasets and address non-linear relationships, while cautioning that these tools must be applied transparently and

supported by high-quality data and expert interpretation. Clear communication of both scientific advances and uncertainties was identified as essential for informing policy and maintaining public trust.

Sessions on national and international coordination highlighted the importance of structured collaboration through initiatives such as the NEA High-Level Group on Low-Dose Research and the Canadian Radiation Research Network. These efforts promote harmonized methodologies, shared resources, and regulatory-relevant research priorities, strengthening Canada's leadership and global engagement in radiation protection science.

Student poster presentations showcased innovative research in fields including biodosimetry, radiobiology, epidemiology, ecology, and space radiation, underscoring the vitality of the field and the importance of workforce development. Overall, the workshop identified key research priorities, fostered new collaborations, and reinforced the need for integrated science, coordinated research infrastructures, and transparent communication to advance evidence-based radiation protection and public health.