JOINT WORKSHOP QST–CEA-ASNR

4-6 March 2025

Autorité de Sûreté Nucléaire et de Radioprotection (ASNR)

Fontenay-Aux-Roses, France

https://qst-cea-asnr-25.sciencesconf.org/

Context

- NIRS, CEA, and ASNR are three major actors in the fields of radiobiology, radiotoxicology, and dosimetry research worldwide.
- Collaboration agreements exist between these three organizations.
- The previous joint workshop was held in Chiba in 2019.

Aim

- To present and discuss ongoing research projects.
- To provide an opportunity for research teams to meet and get to know each other better.
- To stimulate the emergence of new areas for collaboration.
- To facilitate the establishment of joint research projects by promoting the exchange of students or young researchers and building joint responses to research project calls.

Practical Organization

- Morning and early afternoon sessions will be held in the ASNR Auditorium, with the possibility of remote participation for online Japanese participants.
- Visits to research labs at ASNR and CEA will be organized on the afternoons of days 1 and 2 (limited number of participants).
- Abstracts of all oral and poster presentations will be available on the dedicated website before the workshop.

Organizing committee

- QST/NIRS
  - MORITAKE Takashi — Director, Department of Radiation Regulatory Science Research
  - IMAOKA Tatsuhiko — Director, Department of Radiation Effects Research
  - UCHIHORI Yukio — Director General
- ASNR
  - BENDERITTER Marc – Deputy Head, Division of Research and Expertise on Health
  - DALLENDRE Robert - International Cooperation Manager
  - LAURIER Dominique – Deputy Head, Division of Research and Expertise on Health
  - VARES Guillaume – Laboratory for Radiotoxicology and Experimental Radiobiology
  - BOSC Nathalie – Assistant, Division of Research and Expertise on Health
- CEA
  - BOUSSIN Francois, Head of Institute of Cellular and Molecular Radiobiology (iRCM)/IBFJ, CEA
  - GAUTHIER Laurent, Radiopathology Lab, iRCM CEA
  - LE CLOIREC Aude, Assistant, iRCM

Information and registration
https://qst-cea-asnr-25.sciencesconf.org/

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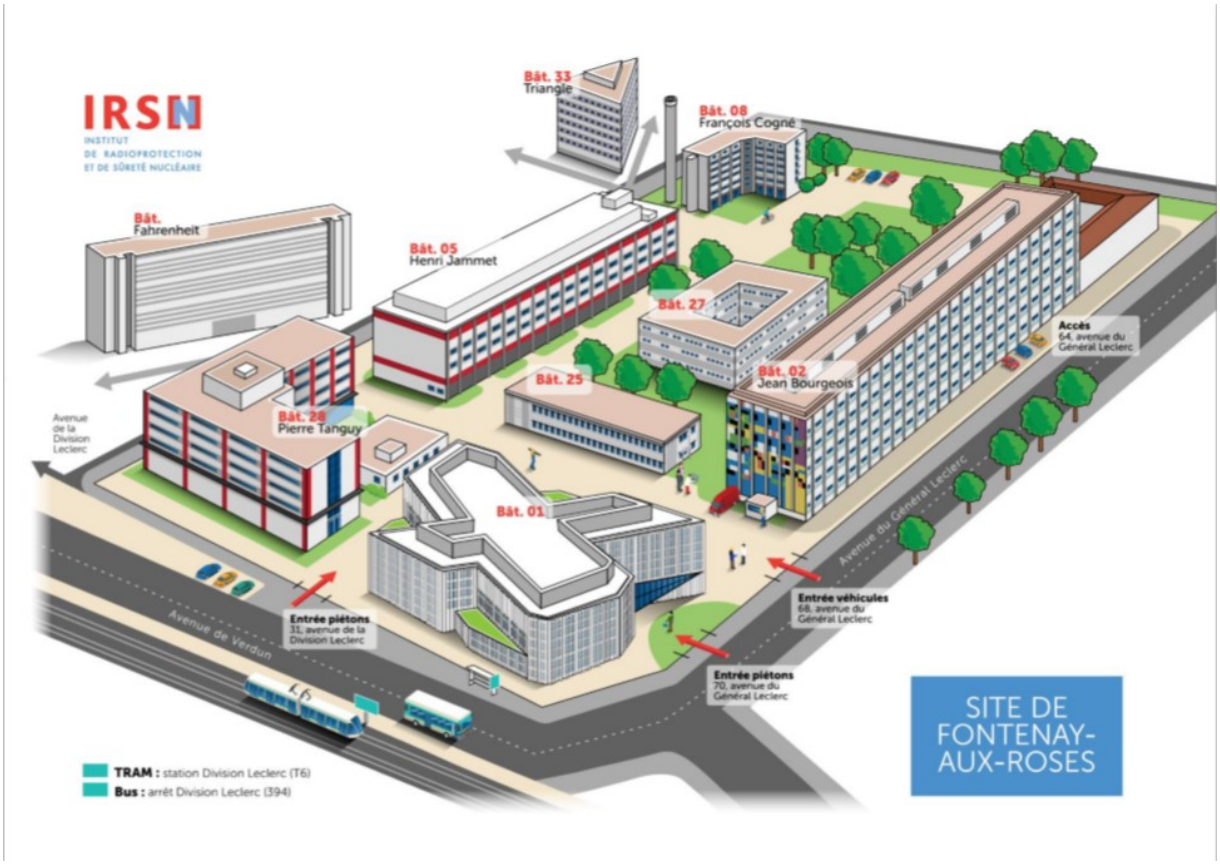
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DAY 1 – Tuesday 4 March 2025

09:15 **Welcome address**

- ASNR – JC. Gariel, Executive Vice-President in charge of the Health and Environment Division (5')
- CEA – R. Veitia, Head of the François Jacob Institute of Biology (IBFJ) (5')
- QST - R. Kanda, Executive Director (5') (*Remote)*

09:30 **Overview of research programs and facilites**

- QST - Y. Uchihori, Director General (10')
- CEA - F. Boussin (10')
- ASNR – M. Benderitter (10')

10:00 **S1: Biological mechanisms of radiation induced carcinogenesis**
Chairs : T. Imaoka, QST – C. Baldeyron, ASNR

- Impact of Lamin B1 dysregulation on DNA repair upon ionizing radiation - P. Bertrand, CEA (10' + 5' Q&A)
- Providing mechanistic basis for low-dose radiation risk assessment: experimental models for molecular and carcinogenesis studies - G. Varès, ASNR, (10' + 5' Q&A)
- Childhood ionizing radiation exposure promotes NASH and hepatocellular carcinoma in mice - Y. Shang, QST (10' + 5' Q&A) *(Remote)*

10:50 *Coffee break*

11:10 **S2: Radiosensitivity and side-effects of radiotherapy**
Chairs: G. Gruel, ASNR – MA. Mouthon, CEA

- Mitochondrial, genetic and behavioural effects of protons on the central nervous system. Microbeam applications - C. Adam-Guillermin, ASNR (10' + 5' Q&A)
- Radiation-induced inflammation and senescence in the irradiated brain – H. Sutcu / A. Chicheportiche, CEA (10' + 5' Q&A)
- Carcinogenesis in mice due to carbon-ion beams and fast neutrons - C. Tsuruoka, QST (10' + 5' Q&A)
- Radiochemical insights into the sparing effect mechanism in ultra-high dose rate FLASH radiotherapy- S. Kodaira, QST (10' + 5' Q&A) *(Remote)*

12:30 *Lunch break*

14:00 **Short presentations #1**
Moderator: G. Varès, ASNR

- Artificial glycan ameliorates radiation-induced intestinal damage – S. Kamimura, QST (5')
- Establishment of a co-operation system for biodosimetry in Japan - K. Ishii, QST (5')
- Development of *in vivo* counter systems at QST – M. Naito, QST (5')
- Survey of cataract and skin injury in orthopedic surgeons - T. Moritake, QST (5')

- Effect of co-exposure to rich Diet and gamma internal low dose irradiation on cerebral and cardiac microvascularisation – M. Chajadine, ASNR (5')
- Effect of co-exposure to high fat diet and acute external low or moderate doses of ionizing radiation on cerebral microcirculation – L. Ould Boukhitine, ASNR (5')
- Innovative biomarkers of therapeutic efficacy and follow-up of localized radiation injury – A. Chemloul, ASNR (5')
- The DNA damage response relies on the characteristics of ionizing particles in myogenic cells – A. Thomas-Joyeux, ASNR (5')
- Effect of photonic / hadronic irradiation of tumor cells on endothelial cell phenotype: impact on the immune system – L. Portier, ASNR (5')
- Mesenchymal stromal cell (MSC) therapy of bladder tissue damage after radiotherapy – AL. Pouliet, ASNR (5')
- Development of micro and nanodosimetric simulations with Geant4-DNA – Y. Perrot, ASNR (5')

15:00 **ASNR Research labs and facilities**

- Presentation of three ASNR Departments: SERAMED, SESANE, SDOS – D. Laurier, ASNR.
- Tour of ASNR labs and facilities (3 groups, limited number of participants):
    - PARISII: Experimental platform for research on the effects of radioactive substances following ingestion or inhalation – D. Denais-Lalième, ASNR.
        - *Poster:* Impact of age on the development of cardiovascular disorders following an external exposure to low or moderate doses of Caesium 137 – TH. Nabet, ASNR
    - PATERSON: High-tech mass spectrometry analytical platform – C. Bouvier-Capely, ASNR.
        - *Poster:* Development of alternative protocols for actinides analysis in emergency situation - C. Bouvier Capely, ASNR
    - Micro-CT and SARRP irradiation platforms – M. Dos Santos, ASNR
        - *Poster:* Impact of the x-ray radiation quality on the radiological burn severity and on the in vivo bone response for retrospective dose estimation at different time points – A. Roussel, ASNR.
        - *Poster:* Improving the therapeutic index after pulmonary irradiation in stereotactic conditions: response of the bronchoalveolar epithelium and role of club cells – S. Bavananthan, ASNR.

17:00 **QST-CEA-ASNR closed meeting**

Identifying topics for possible collaborations.

DAY 2 – Wednesday 5 March 2025

09:00 **S3 - Dosimetry**
Chairs: M. Kowatari, QST - Isabelle Clairand, ASNR

- AI for an automated chromosomal aberration detection in cytogenetic biodosimetry - M. Benadjaoud, ASNR (10' + 5' Q&A)
- Internal dosimetry for occupational exposure and emergency management - D. Broggio, ASNR (10' + 5' Q&A)
- Therapeutic approaches of actinide internal or external contamination using In vivo and ex vivo models - A. Van der Meeren, CEA (10' + 5' Q&A)
- Current status on the development of a population thyroid monitoring system in case of a major nuclear accident in Japan – E. Kim, QST (10' + 5' Q&A) *(Remote)*
- Development of individual monitoring techniques for actinide internal contamination at QST - G. Yang, QST (10' + 5' Q&A)

10:20 **S4 - Effects of radiation exposure on the offspring**
Chairs: C. Adam-Guillermin, ASNR – G. Livera, CEA

- Long-Term Effects of Low-Dose Ionizing Radiation During Pregnancy: Insights and Future Directions in In Vivo Experimental Research – S. Grison, ASNR (10' + 5' Q&A)
- Switching from Homologous Recombination to End Joining allows oocytes to survive radiation – E. Martini, CEA (10' + 5' Q&A)
- Influence of Parents' Eating Habits on Children's Radiosensitivity - B. Wang, QST (10' + 5' Q&A) *(Remote)*

11:10 *Coffee break*

11:30 **S5 - Health effects of low-dose acute and chronic exposures**
Chairs: C. Tsuruoka , QST – D. Klokov, ASNR

- Effects of ionizing radiation on microbiome: a missing link in understanding the mechanisms of health effects of low dose and low dose rate radiation? - D. Klokov, ASNR (10' + 5' Q&A)
- Impact analysis of low ionizing radiation thyroid doses on public health through omics and organoids-based approaches – C. Ory, CEA/ASNR (10' + 5' Q&A)
- Biological mechanisms of dose-rate dependent rat mammary carcinogenesis - K. Nagata, QST (10' + 5' Q&A) *(Remote)*
- High dose radiation induces an early and transient ATM-dependent activation of NF-kB in endothelial cells – S. Candéias, CEA (10' + 5' Q&A)

12:35 *Lunch break*

14:00 **Short presentations #2**
Moderator: L. Gauthier, CEA

- Intravital microscopic thermometry of rat mammary epithelium using a nanodiamond-based quantum sensing technique – T. Imaoka, QST (5')

- Mechanism of radiation carcinogenesis in a novel Brca1 mutation rat model – Y. Nakamura, QST (5')
- Genomic changes in radiation-induced precursor B-cell lymphoma – K. Amano, QST (5')
- Current status on BL14B1 beamline at SPring-8, XAFS analysis and microbeam irradiation for radiological science. – A. Shiro, QST (5')
- Improving radiotherapy by targeting the TRIM33 chromatin reader in myeloid cells, G. Rousselet, CEA (5')
- Compromise stability of mtDNA as a new therapeutic tool to improve cancer radiotherapy, A. Campalans, CEA (5')
- JMY, a new therapeutic target against radiation-induced invasion of glioblastoma stem cells, L. Gauthier, CEA (5')
- NHEJ-dependent mutagenesis at very low and very high dose rates, S. Marcand, CEA (5')
- Safe homologous recombination upon exposure to ionizing radiation through dynamic interplay of Rad51 nucleoprotein filament-associated proteins, E. Coïc, CEA (5')
- Advanced human cerebral organoids as a model for investigating glioma stem cell interactions with microglia and vascular cells and response to radiotherapy, MA. Mouthon, CEA (5')

15:00 **CEA Research labs and facilites**

- Presentation of IBFJ - R. Veitia, CEA
- Tour of CEA/iRCM labs and facilities (3 groups, limited number of participants):
  - CIGEx: Genetic engineering and protein biochemistry – D. Busso, CEA
  - PARI: High-Throughput screening facility – G. Pinna, CEA
  - Irradiation Platform – V. Ménard, CEA

17:00 **QST-CEA-ASNR closed meeting**

Identifying topics for possible collaborations.

19:30 *Dinner in Paris (limited number of participants)*

DAY 3 – Thursday 6 March 2025

09:00 **S6 - Treatment of radiation injury**
(stem cell therapy, decontamination, new drugs, etc.)
Chairs: S. Kamimura, QST - F. Pflumio, CEA

- Advancing the therapy of acute radiation syndrome: Inductive pluripotent stem cells as a new therapeutic tool - A. Chapel, ASNR (10' + 5' Q&A)
- Therapeutic potential of Muse cells in radiation-induced Gastrointestinal syndrome - N. Gault, CEA (10' + 5' Q&A)
- Application of Muse Cells in the Treatment of Radiation-induced intestinal injury - T. Miura, QST (10' + 5' Q&A)

09:50 **Short presentations #3**
Moderator: T. Moritake, QST

- Research on oncometabolites that affect radioresistance – M. Fujita (5') *(Remote)*
- Recent studies on nuclear track detectors for application to medical fields - T. Kusumoto (5') *(Remote)*
- "Single Cell Radio-Biology" project at SPICE-QST microbeam facility — T. Konishi (5') *(Remote)*
- Evaluation of uranium decorporation efficiency in serum using chelating agents by X-ray absorption spectroscopy. - A. Uehara (5') *(Remote)*
- Survey of personal dosimeter wearing rates of medical workers associated with revisions to the law – S. Matsuzaki, QST (5')
- Retrospective dosimetry for the occupational exposure of medical staff - M. Kowatari, QST (5')

10:25 **S7 - Organisation of radiation research**
(Pianoforte, Planet, Collaborating centers, etc.)
Moderator: R. Dallendre, ASNR

- European Partnership Pianoforte - J. Garnier-Laplace, ASNR (10')
- PLANET: Planning and Acting Network for Low Dose Radiation Research in Japan- Y. Yamada, QST (10') *(Remote)*
- Resilience Framework Partnership - Y. Saintigny, CEA (10')
- Discussion (10')

11:05 *Coffee break*

11:25 **S8 - General discussion**
Moderator: JM. Bonnet, ASNR

- Potential topics for collaboration (feedback from closed meetings) (20').
- Support mechanisms for strengthening collaborations (financial support for young researchers and relevant funding for joint France-Japan research activities). G. Veriot, CEA – R. Dallendre, ASNR (15')
- Perspectives for future workshops (10')

12:30 **Closing session**

- QST - Y. Uchihori (5')
- CEA - F. Boussin (5')
- ASNR – M. Benderitter (5')

12:45 *Lunch (limited number of participants)*

ABSTRACTS
Scientific sessions

Impact of Lamin B1 dysregulation on DNA repair upon ionizing radiation

Pascale Bertrand *† [1]

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Our team is developing two research axes: (1) the link between genome stability and nuclear envelope integrity, with a focus on lamin B1, and (2) the link between genome stability, IFN production and immunity, in particular after ionising radiation (IR). In this talk I will present our data on the role of lamin B1 in double-strand break (DSB) repair mechanisms after exposure to IR.
Lamins are essential components of the nuclear envelope. There are two types of lamins: type A lamins and type B lamins. In addition to their essential role in nuclear envelope integrity, lamins are involved in gene expression, replication, DNA repair1, telomere maintenance2 and mitosis3. Deformation of the nuclear envelope is one of the hallmarks of cancer cells. An increase in lamin B1 levels is observed in several tumours and is often associated with their aggressiveness. We are interested in the potential link between lamin B1 and the mechanisms of genome stability, in particular the impact of lamin B1 upregulation on the mechanisms of DSB repair.

We will present published data highlighting the role of lamin B1 in 53BP1 recruitment to DSBs upon IR 1. Indeed, we found that a defect in 53BP1 recruitment upon lamin B1 upregulation is associated with an increased radiosensitivity, a defect in non-homologous end joining and persistence of DSBs upon IR. We will also present unpublished data showing that lamin B1 upregulation also results in a defect in homologous recombination, which is associated with a defect in the RAD51 protein upon IR. If time permits, the consequences of these defects on the induction of inflammation mediated by recognition of cytosolic DNA will be discussed.

1 Etourneaud, Rass et al. Sciences advances (2021)

2 Pennarun et al, Nucleic Acids Res (2021)
3 Picotto et al, on BioRxiv.org (2024)

Keywords: Double, strand break repair, Lamin B1, radiosensitivity, genome (in)stability

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Providing mechanistic basis for low-dose radiation risk assessment: experimental models for molecular and carcinogenesis studies

Sarah Eivers [1], Mélissandre Gomot [1], Arthur Thomas-Joyeux [1,2], Nora Essakhi [1], Clément Codan [1], Quentin Pascal [3], Dmitry Klokov [1], Guillaume Vares *† [1]

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The cellular response to ionising radiation, either naturally occurring or otherwise, involves an intricate and coordinated chain of events. These events encompass activation of DNA damage response and DNA repair pathways via post-translational modification, regulation of transcription and translation, intercellular communication, defining cancer-relevant health outcomes, including apoptosis, genomic instability, proliferation, differentiation, etc. Although the biological response and effects of high doses of ionising radiation are well documented, there is still a level of uncertainty concerning the level of risk and molecular mechanisms involved at the lower dose range. Given the potential implications for human health, we aimed at 1) investigating early molecular effects of low dose ionizing radiation (LDR) exposures, and 2) developing suitable *in vivo* and *ex vivo* models for assessing whether LDR may potentiate the development of cancer. On the one hand, following a combination of molecular and bioinformatic lines of interrogation including RNA-seq, ribo-seq, mRNA stability analysis, ribopuromycylation and γH2AX foci analysis, we present observed changes as a function of time in coordinated transcriptional, post-transcriptional, translational and DNA double-strand break repair pathway responses to low doses of γ-rays in human fibroblast cell lines. On the other hand, we use an inducible colon cancer mouse model with inducible Apc inactivation and Kras activation (KPC:APC) to characterize the effects of medical diagnostic exposures on colon carcinogenesis progression. We established colon organoids from KPC:APC mice to recapitulate colon carcinogenesis in irradiated organoids. Altogether, the consolidation of physiological and molecular data should inform the development of an integrated model for radiation risk assessment.

Keywords: low dose radiation, transcription, translation, carcinogenesis, colon cancer, CT scan

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Childhood ionizing radiation exposure promotes NASH and hepatocellular carcinoma in mice

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The pathological conditions of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) are the major risk factors of hepatocellular carcinoma (HCC). Epidemiological studies and our earlier animal experiments revealed that early-life radiation exposure also leads to an increased risk of HCC, while calorie restriction (CR) effectively delays the onset of radiation-induced HCC. Herein, we aimed to clarify the relevance of NASH to radiation-induced HCC and to the cancer prevention effect of CR. Eight-day-old male B6C3F1 mice were irradiated with 3.8 Gy of X-rays. Then they were fed a standard or 30% CR diet from 49 days of age until a necropsy, which was performed from 56 to 600 days with _˜100-day intervals for pathological and gene expression analyses. We found that early-life radiation exposure accelerated lipid accumulation and NASH-like histopathological changes in the liver, accompanied by early onset of HCC. At the same time, CR ameliorated the changes in the hepatic lipid metabolism and improved the NASH-like pathology, which might contribute to HCC prevention. In addition, gene expression profiling indicated radiation-related activation and CR-related suppression of the peroxisome proliferator-activated receptor γ/CD36 pathway of transmembrane fatty acid translocation before the development of the NASH-like state. Thus, early-life exposure to radiation affects lipid metabolism and induces a steatoinflammatory microenvironment that favors cancer development in the liver. Targeting this pathway by CR or its mimetics would be a promising strategy for preventing HCC related to radiation and possibly other DNA-damaging agents.

Keywords: Childhood exposure, liver

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Mitochondrial, genetic and behavioural effects of protons on the central nervous system. Microbeam applications.

Christelle Adam-Guillermin *† [1], Ahmad Sleiman [1], Kévin Lalanne [1], Mikael Cardot-Martin [1], Guillaume Sevenie [1], Yann Perrot [2], Amokrane Allaoua [1], Francois Vianna-Legros [1]

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About half of all cancer patients will receive radiotherapy during their illness. The therapeutic use of ionizing radiation has been largely guided by the goal of directly eliminating all cancer cells while minimizing the toxicity to adjacent normal tissues. Technological advances in radiation delivery, such as particle therapy, have notably improved tumor dose conformation, thus reducing the dose to the healthy tissues. In this context, proton therapy is the method of choice for treating radio-resistant tumors, which require higher doses of radiation, those close to sensitive organs (optic nerve, brain, spinal cord, etc.) or pediatric cancers. However, despite its ultra-precision, proton therapy can still induce side effects and complications, whose underlying mechanisms are not fully understood.
The work presented here fits into this general framework of side effects of proton therapy treatment of brain tumors, focusing on the mitochondria. Indeed, a wide range of studies have proven the potential of ionizing radiation to alter the mitochondrial function and structure, as mitochondria occupy around 30% of the cellular volume. In addition, recent radiation research revealed that brain irradiation by high-LET carbon ions induces mitochondrial dysfunction and oxidative stress, leading to neurodegeneration and declines in cognitive function.
To study this subject, an integrated radiobiological approach was proposed using the nematode biological model *Caenorhabditis elegans*. The MIRCOM ion microbeam, operated by ASNR, enables to target (sub)cellular compartments of living cells with a predetermined number of charged particles of a certain quality (type and energy), with a resolution ranging from _˜ 2 to 5 μm, respectively for protons and carbon ions. Our data showed that proton central nervous system micro-irradiation resulted in global mitochondrial dysfunction, oxidative stress and induction of the BER pathway with no short-term behavioral consequences. This study confirms the important role played by mitochondria in the biological response to proton irradiation.

Keywords: proton therapy, microbeam, brain, mitochondria

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Effects of photon and proton radiation on the developing adolescent brain

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Adverse neurocognitive outcomes are a major complication of brain radiation therapy. Proton beam radiation therapy (PRT) represents one of the most promising advances in radiotherapy (RT) for pediatric brain tumors. The unique ballistic properties of protons, particularly the Bragg peak, allow for more precise dose delivery, minimizing irradiation of surrounding healthy tissues. Consequently, PRT is believed to better preserve cognitive function compared to conventional X-ray radiation therapy (XRT). However, despite its advantages, PRT still leads to significant neurocognitive impairments in children successfully treated for brain tumors.
To investigate the neurotoxicity of proton and photon radiation on the adolescent brain, we exposed the brains of 21-day-old mice to either proton beam radiation using a cyclotron (IBA) or photon radiation with a 6 MeV linear accelerator (Linac) at an identical dose of 8Gy. The novel object recognition test, conducted four months post-irradiation, revealed memory decline regardless of the irradiation type.

Flow cytometry analyses further demonstrated a significant reduction in bulbar neurogenesis, as indicated by a decrease in cycling neural progenitors within the subventricular zone (SVZ). Histological analysis performed five months post-irradiation showed no clear evidence of astrogliosis in either condition, as assessed by astrocyte morphology in brain sections. Notably, photon radiation induced a more pronounced microglial activation than proton radiation, as evidenced by altered Iba1-positive microglial cell morphology and increased CD68 protein expression in irradiated brain tissue.
These findings were corroborated by single-cell RNA sequencing (scRNA-seq), which revealed that both photon and proton radiation upregulated a gene set associated with microglial activation. Furthermore, gene set enrichment analysis demonstrated that both irradiation types significantly increased pathways linked to inflammatory and immune responses. This persistent upregulation underscores the presence of chronic inflammation in both irradiation conditions, even four months post-exposure.

Keywords: Photon, proton, microglia, senescence, neurogenesis

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Carcinogenesis in mice due to carbon-ion beams and fast neutrons

Chizuru Tsuruoka *† [1], Mayumi Shinagawa [1], Yi Shang [1], Yoshiko Amasaki [1], Masaaki Sunaoshi [1], Takamitsu Morioka [1], Yoshiya Shimada [2], Shizuko Kakinuma [1]

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X-ray radiotherapy is the most common cancer radiotherapy. More precise radiotherapy, such as IMRT and proton and carbon-ion radiotherapies, was later developed, which is characterized by reduced radiation damage to normal tissues surrounding the cancer that appears after radiotherapy. However, low-dose exposure to normal tissues cannot be avoided, and therefore, there remains concern about secondary cancers.The study aims to evaluate the carcinogenic effect, and its age-at-exposure dependence of carbon-ions and fast neutrons, to which normal tissues are exposed during IMRT and particle radiotherapy, using *Ptch1* heterozygous mice. An advantage of this mouse model is that it distinguishes between spontaneous tumors (which have a loss of the wild-type allele by mitotic recombination or non-disjunction) (S-type) and radiation-induced tumors (which have intestinal deletions of the wild-type *Ptch1* locus) (R-type).Age at exposure induced postnatal day (P) 1, 4, and 10, and radiation types used were carbon-ions (0.05 to 0.5 Gy, 13 keV/μm) and fast neutrons (2 MeV, 0.025 to 0.5 Gy). Gamma-ray (0.05 to 0.5 Gy) experimental groups were prepared for comparison. All exposure groups developed MBs most effectively after irradiation at P1. Loss of heterozygosity analysis of MBs was performed to detect R-type MBs, indicating that R-type MBs developed after irradiation during a narrow age window (most strongly at P1 and only moderately at P4, with suppressed tumorigenesis at P10) in all experimental groups. We calculated the RBEs related to exposure to carbon-ions and neutrons. RBEs were about 4 in the carbon-ion irradiated groups at both P1 and P4; this value was higher than the generally recognized RBE of 1–2 for cell killing. RBEs for neutrons irradiated groups were 21 and 7 at P1 and P4, respectively. These results indicate that the perinatal *Ptch1* mice are radiosensitive and support the validity of the current ICRP of radiation weighting factors.

Keywords: Radiation induced medulloblastoma, Carbon, ions, Neutrons

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Radiochemical insights into the sparing effect mechanism in ultra-high dose rate FLASH radiotherapy

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Ultra-high dose rate radiation therapy, commonly known as FLASH, operates at dose rates over 40 Gy/s, which is 1,000 times higher than conventional radiation therapy (approximately 0.03 Gy/s). This method has garnered significant attention due to its potential to reduce side effects on normal tissue while maintaining therapeutic effectiveness. However, the underlying mechanisms of FLASH therapy remain unclear. It is hypothesized that the sparing effect of FLASH may be linked to the yield of water radiolysis products, which contribute to the radiation's indirect action in causing DNA damage. To experimentally investigate the effects of ultra-high dose rate irradiation, we examined the dose-rate dependence of the yields of radiation-induced decomposition products in water. In the presentation, we discuss a possible mechanism of the sparing effect in FLASH radiotherapy from the radiochemical viewpoints.

Keywords: FLASH radiotherapy

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Artificial intelligence for automated chromosomal aberration detection in cytogenetic imaging

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In cytogenetic biological dosimetry, the proportion of chromosomal aberrations in peripheral blood lymphocytes is linked to the dose of ionizing radiation through an adequate calibration curve. Currently, the chromosomal aberration count process relies mostly on human expertise, as this is a difficult object recognition problem. This manual counting is not a satisfying solution in the context of a mass accident, as there is a limited number of human experts. Thus, there is a need for effective automated dicentrics counting tools.
The objective of the presentation is to introduce two automated chromosomal aberration count pipelines based on deep learning developed for Giemsa and Fish cytogenetic imaging modalities. We trained an Unet-based model on a large, annotated GIEMSA database (80k images) to build a high-performing dicentric and fragment detection model by aggregating several instances of the model during its training. Each instance of the model makes an individual decision on the presence of an aberration and a voting threshold is then used to build the global decision. The proposed model strongly reduce overconfident detections on ambiguous objects and significantly outperforms the well-known DCScore Metafer software from METASYSTEMS.
To address the scarcity of annotated data and the class imbalance inherent in FISH imaging translocation detection, we introduced a novel generative approaches based on a large-scale FISH dataset (25k chromosomal patches). Brownian Bridge Diffusion Models, an image-to-image translation framework, were trained to generate synthetic translocations. The quality of the generated data was improved through feature space filtering based on dimension reduction of ResNet-extracted features. This filtering process ensures that the synthetic datasets used for classifier training are both diverse and representative of real-world chromosomal aberrations.
In conclusion, the present work provides promising results about deep learning model deployment for an automated chromosomal aberration detection in cytogenetic imaging.

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Internal dosimetry for occupational exposure and emergency management

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ASNR is in charge, among other things, for research and expertise on civil nuclear activities and radiation protection in France. In the field of radiation protection ASNR develops methods and software to assess internal dose following occupational intake of radionuclides or after an accidental release from a nuclear facility.
Regarding occupational intakes, ASNR has developed the ICARE and MIODOSE tools. ICARE implements and solves the biokinetic and dosimetric model of the ICRP series of Occupational Intake of Radionuclides. MIODOSE integrates ICARE and enables to assess the dose from radio-bioassay measurements. These tools are used when a third-party assessment must be verified but they are also available for radiation protection experts.

Regarding internal dose assessment in case of emergency ASNR dispose of a fleet of mobile units for in-vivo-monitoring of the population. An add-in to this fleet could consist of a system which is modular and transportable and that could be deployed on site for the monitoring of disabled persons or for the monitoring of other subjects in a classical chair geometry.
In case of nuclear emergency ASNR is in charge of collecting monitoring results at the national level. I*n vivo* monitoring results, obtained by the mobile fleet or fixed installations, are transferred to the CRIHOM software and then processed to calculate internal doses. Current developments consist in coupling the results of these measurements with default or calculated source terms to include in the dose assessment radionuclides below the detection limit and other source of exposure, like irradiation by a plume.

Keywords: occupationnal exposure, internal dosimetry, population monitoring, emergency

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Therapeutic approaches of transuranic internal or external contamination using in vivo and ex vivo rat models

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Internal or external contamination by α-emitting transuranic elements (TU) such as plutonium (Pu) is a risk for workers during reprocessing spent nuclear fuel, nuclear facility dismantling as well as for first-responders and public following malevolent or accidental release. In such scenarios, inhalation and penetration via damaged skin or wounds are likely routes of contamination. To limit TU retention and transfer to blood, an early therapeutic handling is essential. Administration by IV or inhalation of the chelating agent Diethylene Triamine Pentaacetic Acid (DTPA) is the recommended treatment to decrease TU body burden and favor urinary excretion of the formed TU-DTPA complexes. However, the efficacy of DTPA is limited by its ability to only chelate ionized TU species and its low biological half-life. Additional research is needed to improve the therapeutic handling of contaminated victims. For such studies, experimental models representative of real contamination cases are required. These include various routes of contamination and physicochemical forms of the TU (poorly soluble compounds for most scenarios).

Our laboratory performs efficacy studies in rats for TU decorporation and decontamination after pulmonary or wound contamination under various physicochemical forms. Different parameters such as route and protocol of DTPA administration or galenic forms are tested.

The presentation will focus on two examples. The first reports on the use of repeated DTPA inhalation as a long-term treatment following lung or wound contamination with TU. Although the efficacy is lower than repeated DTPA IV, this protocol is of great interest, as this mode of administration would be preferable in man. The second example provides evidence of the efficacy of a sterile DTPA-loaded gel for the decontamination of injured skin and deep wounds in rats exposed to Pu or Americium. This topical formulation of DTPA is of practical interest in situation where reducing liquid waste is of crucial importance.

Keywords: Internal contamination, transuranic, decorporation, decontamination

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Current status on the development of a population thyroid monitoring system in case of a major nuclear accident in Japan

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In Japan's guidelines for nuclear emergency preparedness and response, thyroid exposure monitoring targets residents under 19 years of age, as well as pregnant and breastfeeding women, in areas requiring immediate evacuation or temporary relocation. Screening measurements using NaI(Tl) survey meters are typically conducted within approximately three weeks of a disaster, followed by detailed measurements for individuals exceeding the screening level within four weeks. However, conventional NaI(Tl) survey meters are not well-suited for young children due to their short necks. To address this limitation, QST developed and commercialized a portable thyroid spectrometer called "I-Beetle." This lightweight (approximately 300 g), compact device features multiple small, high-energy-resolution GAGG detectors (Gd(Al, Ga)O(Ce)) that are optimally sized and positioned to fit the curvature of a child's anterior neck. The GAGG detector array (1.2 cm × 1.2 cm × 1.2 cm per crystal) ensures accurate measurements, while its thinner probe design (24 mm compared to 38 mm for NaI(Tl) survey meters) enhances usability for infants. This innovative device delivers performance equivalent to existing thyroid monitors, capable of detecting radiation levels as low as approximately 30 Bq under typical background conditions (_˜0.05 μSv/h). Its portability enables rapid deployment and immediate use, making it a valuable tool for improving the accuracy and efficiency of thyroid monitoring during nuclear emergencies. This presentation will discuss the development process of the I-Beetle and its future prospects.

Keywords: Thyroid monitoring, Nuclear emergency, Portable spectrometer

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Development of individual monitoring techniques for actinide internal contamination at QST

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Internal exposure to alpha emitters is likely to bring a relatively high radiation exposure dose even if the intake amount is small. For dose assessment of radionuclides, such as isotopes of actinides, urine and fecal analysis have been used extensively. To provide timely information on the identification of radionuclide type and the dose assessment of the victims in radiation emergency medicine, we have developed rapid bioassay methods to determine U, Pu, Np, Am, and Cm radioisotopes in urinary and fecal samples by means of mass spectrometric (SF-ICP-MS and ICP-MS/MS) and radiometric (alpha spectrometry) techniques (1–5). For method validation, the standard reference materials provided by PROCORAD (Association for the PROmotion of Quality COntrol in RADiotoxicological Analysis), France, were analyzed, and satisfactory results were shown using the performance index of Z-score. The high throughput and high sensitivities of our proposed methods will allow greater numbers of related laboratories to be involved in screening activities for unexpected actinide exposure, such as in the case of a large scale radiological/nuclear disaster.

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Keywords: Actinide internal exposure, Alpha spectrometry, ICP MS/MS, SF ICP MS, PROCORAD, Bioassay

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Long-Term Effects of Low-Dose Ionizing Radiation During Pregnancy: Insights and Future Directions in In Vivo Experimental Research

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Assessing the long-term health risks of low doses of ionizing radiation (IR) is crucial for effective radiation protection, especially concerning prenatal exposures from environmental or medical sources. These exposures can potentially affect offspring and future generations. Although the ICRP considers malformation risks negligible below 100 mGy for in utero exposure, and UNSCEAR finds no evidence of hereditary genetic effects in humans, uncertainties in studies and observable transmissible effects in animal models keep the debate open and necessitate further research, particularly in the low-dose range, to fully understand the harmful effects of prenatal IR exposure.

To enhance our understanding of the multigenerational effects of ionizing radiation, the ASNR has been conducting an in vivo research project based on the DOHaD concept for the past two years. This project aims to evaluate the effects of in utero exposure to low-dose internalized cesium-137 (100 mGy) administered through a drinking solution (3.6 MBq/L/21 days) on the metabolic alteration in offspring of C57BL/6J mice. After weaning, male and female pups were fed either a standard or high-fat diet to study the combined effects of co-exposure to a dietary stressor on metabolism. Analyses focused on young adults (10 weeks) and aged adults (15 months) to identify major developmental effects and functional changes in the nervous, reproductive, and liver systems, as well as molecular imbalances that could predispose individuals to chronic diseases.

Preliminary results show no significant effects on the first generation of mice exposed to cesium-137 in utero throughout gestation. However, some differences in biological responses were observed, which varied based on sex and diet. While no harmful effects have been detected in the first generation so far, future studies should investigate whether functional or molecular changes can be inherited by subsequent generations, possibly through epigenetic mechanisms.

Keywords: In utero, Multigenerational, Cesium 137, Low dose, Offspring, Hereditary

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Switching from Homologous Recombination to End Joining allows oocytes to survive radiation

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During meiosis, homologous recombination (HR) repairs programmed DSBs to form crossovers to ensure that homologous chromosomes segregate properly during the first meiotic division. HR was thought to be the primary DSB repair pathway in meiotic cells. However, recent studies have shown that a subset of DSBs can be repaired by End joining. As opposed to male meiosis which produces new gametes throughout adulthood, mammalian female meiosis produces a unique pool of oocytes that remain arrested in meiotic prophase I until fertilization. Post-natal oocytes are surrounded by granulosa cells to undergo folliculogenesis and generate subsequently primordial follicles (the ovarian reserve) and growing follicles (that mature to be fertilized and end meiotic division). In mammals, primordial oocytes are particularly sensitive to Ionizing Radiation (IR) compared with primary and secondary oocytes. IR mainly triggers functional HR in primordial mouse oocytes but cells are sent to apoptosis by P53 and P63 instead of being repaired. Surprisingly, the same amount of IR also triggers NHEJ in primary and secondary oocytes. We used *Xlf* -/- mice, which lack a component of c-NHEJ, to show that DSB repair by c-NHEJ is in part responsible for the increase in viability of the growing oocytes after IR. These results demonstrate that during folliculogenesis, oocytes switch from programmed HR to NHEJ. This is likely due to a switch from rapid resection of broken ends in primordial follicles to their stabilization in primary-secondary follicles. We are developing oocyte cultures with specific inhibitors to determine the signals involved in this unique and rapid switch of repair mechanism.

Keywords: oocyte, homologous recombination, NHEJ

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Influence of Parents' Eating Habits on Children's Radiosensitivity

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Parental eating habits play a critical role in shaping the health and disease susceptibility of their offspring. Obesity, driven in large part by the Western-style diet-characterized by high calorie and fat intake - has become a pressing global health issue. This condition is strongly linked to various metabolic disorders and long-term health consequences in subsequent generations. Maternal obesity, in particular, has been shown to have profound and lasting effects on offspring, a concept encapsulated in the "developmental origins of health and disease" (DOHaD).
In this study, we explored how maternal consumption of a high-fat diet (HFD) influences the radiosensitivity of offspring. Female C57BL/6J mice were assigned to either an HFD or a standard diet (STD) starting immediately after weaning at 3 weeks of age. At 10 weeks, these females were mated with C3H/He males maintained on an STD. The offspring were nursed by their respective dams and subjected to total body X-irradiation (3.8 Gy) at 7 days postpartum. All offspring, irrespective of their experimental group, were weaned onto an STD at 4 weeks of age.

Our findings revealed that maternal HFD exposure reduced the lifespan of male offspring following X-ray exposure. Notably, maternal HFD alone did not significantly impact the lifespan of male or female offspring. Pathological examination indicated that the reduced lifespan in male offspring was predominantly due to early mortality caused by depletion of bone marrow cells and thymic lymphoma within six months post-irradiation.
To the best of our knowledge, this study is the first to demonstrate that maternal HFD modifies the radiosensitivity of offspring. These results highlight the potential significance of parental dietary habits in influencing offspring responses to environmental stressors such as ionizing radiation.

Keywords: Radiosensitivity, High, Fat Diet, Maternal Obesity, Developmental Origins of Health and Disease (DOHaD), Depletion of Bone Marrow Cells

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Ionizing Radiation and the Gut Microbiome: A Missing Link in Understanding Low-Dose and Low-Dose-Rate Health Effects?

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Nearly a century of research on the mechanistic aspects of ionizing radiation (IR) effects-dating back to H. Muller's groundbreaking *Science* report in 1927-has generated an enormous body of data. Yet, no coherent mechanistic picture has emerged. The dominant mutational paradigm of IR-induced tumorigenesis and carcinogenesis, which underpins the linear no-threshold (LNT) model used in radiation protection, remains insufficient to explain numerous inconsistencies observed in low-dose studies. Given the now-recognized roles of tissue- and organism-level regulatory systems-including the tissue microenvironment, immune status, and the gut microbiome-in systemic health, it is plausible that these factors influence the health outcomes of radiation exposure. The gut microbiome, a key player in host physiology, has been linked to cancer risk through its impact on inflammation and metabolism. Furthermore, the well-established gut-brain axis suggests that microbiome composition may also modulate radiation responses in the brain. This presentation will discuss findings from two our studies: (1) an investigation showing that chronic low-dose gamma and tritium exposure altered the gut microbiome in APCmin/+ mice, correlating with differences in intestinal tumorigenesis and mouse survival; and (2) a study demonstrating that targeted brain irradiation in juvenile wild-type C57Bl/6J mice induced the gut microbiome changes, suggesting a systemic response. Together, these results, along with emerging literature, support the hypothesis that the gut microbiome is a critical factor in shaping cancer and non-cancer risks following radiation exposure in mammals.

Keywords: microbiome, health effects, cancer risk, low doses

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Impact analysis of low ionizing radiation thyroid doses on public health through omics and organoids-based approaches

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This research project developed by the CEA and the ASNR aims to answer questions about the impact of low thyroid doses on human health. We analyze the miRNome and transcriptome of a series of normal thyroid tissues and papillary thyroid cancers (PTC) from Ukrainians unexposed or exposed to radioiodines at high (> 500 mGy) or low (As the ability to respond to the societal debate associated with low thyroid doses also relies on a better knowledge of the molecular mechanisms associated with the exposure, we will explore integrative genes-miRs networks associated with the exposure or etiology signatures. This analysis will be complemented by the development of normal human thyroid organoids reproducing the organization and functions of thyroid follicles, enabling us to explore the effect of ionizing radiation as a function of dose and dose rate. These organoids will also help to answer other scientific questions associated with the thyroid tissue radioprotection, complementing studies carried out in preclinical models, or to estimate the effects of environmental endocrine disruptors on thyroid radiosensitivity.

Keywords: Thyroid, low doses, molecular signature, normal tissue organoids

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Biological mechanisms of dose-rate dependent rat mammary carcinogenesis

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Radiation is one of the factors that causes breast cancer, and the rat is a useful experimental model for studying mammary carcinogenesis. The induction of DNA double-strand breaks (DSBs) is known as the initial event in radiation carcinogenesis. We found that DSBs induced by high-dose rate exposure were more likely to occur in luminal cells than in basal cells of the mammary gland (Nagata et al., 2024. J Radiat Res). However, subsequent mid-term processes leading to carcinogenesis are not well understood at the tissue level. We investigated the dose-rate dependence of cellular dynamics in the mammary gland of female rats for several weeks after irradiation, focusing on cellular dynamics such as cell cycle, proliferation, cell differentiation, cell death, and cell composition in mammary glands. The numbers of Ki-67-positive luminal progenitor cells in tissue sections were significantly decreased by 2-Gy gamma-ray irradiation at high (30 Gy/h) and low dose rate (6 mGy/h) at 2 weeks after exposure. And also, at 2–6 weeks after irradiation, the composition of luminal mature cells was reduced in a dose-rate-dependent manner, and differentiation of luminal cells was suppressed, as shown by flow cytometry. Furthermore, gene expression analysis using tissue RNA at this same time revealed a dose-rate-dependent suppression of the expression of genes related to milk production in mature cells. These results suggest that radiation-induced breast cancer is preceded by persistent inhibition of luminal cell differentiation, creating an environment in which luminal cells mutated by radiation could be exposed to proliferative stimulation.

Keywords: DSB, mammary gland, carcinogenesis, dose rate effect

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High dose radiation induces an early and transient ATM-dependent activation of NF-kB in endothelial cells

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Inflammation is a physiological immune reaction triggered by infectious agents or physical injuries, including ionizing radiation (IR). IR-induced genotoxic stress also activates the Ataxia Telangiectasia Mutated (ATM)-dependent DNA damage response (DDR). The interplay between inflammation and DDR activation contributes to cell fate decisions after irradiation. Interactions between ATM and p53, the main DDR effectors, and NF-kB (Nuclear Factor-kappa B), one of the main transcription factors governing inflammatory responses have been described in different experimental systems. We analysed these interactions in endothelial cells exposed to IR doses ranging from 2 to 10 Gy.
We compared the expression of genes under the control of p53 or NF-kB within the first 24 hours post-exposure. Radiation doses $>$ 5 Gy induce an early and transient induction of inflammatory genes transcription in endothelial cells. This response is dependent on the activation of ATM and NF-kB. In contrast, the transcription of the same panel of inflammatory genes is not induced in irradiated primary fibroblasts, even though they have the ability to initiate an inflammatory response when stimulated by lipopolysaccharide (LPS) or by direct activation of p53.
These results suggest that, after high-dose exposure, primary endothelial cells have the unique ability to modify their immune microenvironment before dying.

Keywords: endothelial cells, ATM, inflammation, DNA damage response

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Advancing Cell Therapy for Acute Radiation Syndrome: Induced Pluripotent Stem Cells as a Novel Therapeutic Approach for Military and Civilian Victims of Nuclear Exposure

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We propose an innovative strategy for hematopoietic transplantation for the treatment of acute hematopoietic radiation syndrome.
This innovative therapy is designed to generate hematopoietic grafts derived from human induced pluripotent stem cells (hiPSC). This protocol has been successfully transposed to a certified production center for Advanced Therapy Medicines (ATMP), resulting in a six-fold increase in production efficiency compared with laboratory-scale methodologies. This transition has led to a sixfold production increase over laboratory-scale methods, significantly enhancing manufacturing efficiency. The resulting preclinical-grade hematopoietic grafts have demonstrated their capacity to restore human hematopoiesis in immunocompromised mice through serial transplantation and are currently undergoing rigorous evaluation in Aachen minipigs.

This advancement marks a significant step toward clinical translation. It paves the way for a cell therapy product with the potential to revolutionize treatment for irradiated patients, particularly in high-risk nuclear exposure scenarios. Additionally, establishing hiPSC banks that are functional, clinically compliant, and diverse in HLA compatibility will enablethe production of ready-to-use universal allogeneic transplants.
By providing a universally accessible, off-the-shelf therapy, this groundbreaking approach holds immense promise for treating individuals exposed to radiation as well as patients suffering from hematopoietic disorders, significantly enhancing the therapeutic landscape for radiation-induced and hematological conditions.

Keywords: Hematopoietic Transplantation, Human Induced Pluripotent Stem Cells (hiPSCs), Acute Hematopoietic Radiation Syndrome (AHRS), Universal Allogeneic Transplants, Radiation, Induced Bone Marrow Failure

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Therapeutic potential of Muse cells in radiation-induced Gastrointestinal syndrome

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Human multilineage-differentiating stress enduring (Muse) cells are pluripotent-like stem cells derived from mesenchymal stem/stromal cells and are known for their regenerative properties. Muse cells are demonstrated a strong ability to promote tissue regeneration across various disease models. In this study, we explored the efficiency of Muse cells, isolated from the Wharton's jelly (WJ-Muse), *in vivo* to repair lethal gastrointestinal syndrome (GIS) induced by high-dose abdominal irradiation (IR), a severe complication following radiotherapy or nuclear accidents. GIS leads to acute loss of intestinal stem cells, impaired epithelial regeneration, and breakdown of the mucosal barrier, ultimately resulting in sepsis and death. Currently, no effective treatment exits to counteract GIS.
In mouse models, we demonstrated that a single dose of 50,000 human WJ-Muse cells, administered shortly after 18 Gy abdominal IR, significantly improved survival by promoting rapid intestinal regeneration and restoring the epithelial barrier. Early cytokine responses (IL-6, MCP-1) triggered by WJ-Muse cells facilitated the recruitment of monocytes and M2-like macrophages, which are critical for tissue repair. Additionally, WJ-Muse cells supported the proliferation of Paneth cells via the IL-6/Stat3 signaling pathway, essential for maintaining the intestinal stem cell niche and supporting Intestinal Stem Cells.
These promising results, obtained across human-mouse barriers thanks to immune-modulation through HLA-G expression, highlight the potential of WJ-Muse as therapeutic strategy for GIS, However the validation of these findings still awaits experiments in larger animals such as pig models to assess their clinical relevance. Furthermore, radiation exposure often results in both gastrointestinal and hematological syndromes. In this talk, i will also discuss future research strategies combining Muse cells with other therapies to treat both types of radiation-induced injuries.

Keywords: high dose irradiation, Muse cells therapy, gastro, intestinal syndrome

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Application of Muse Cells in the Treatment of Radiation-induced intestinal injury

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Purpose: There is still no effective treatment for the gastrointestinal side effects of radiation therapy. Multilineage-differentiating stress enduring (Muse) cells are tissue stem cells that have the ability to spontaneously homing in on injured tissues and repairing them. Several clinical trials have shown that stem cell therapy using human bone marrow-derived Muse (hBM-Muse) cells is effective in treating various diseases, but it is not known whether they are effective in treating radiation-induced intestinal injury. In this study, we investigated whether hBM-Muse cells homing to the radiation-damaged intestine and promote its repair.
Methods and Materials: hBM-Muse cells were injected into the tail vein of mice 2 hours after high-dose total body irradiation. Then, homing analysis, crypt assay, BrdU assay, TUNEL assay, immunostaining, and survival time measurements were performed. In addition, we analyzed the expression of sphingosine monophosphate (S1P), a Muse cell inducing factor, in the mouse small intestine after irradiation. Finally, we investigated whether administration of JTE-013, an S1P receptor 2 (S1PR2)-specific antagonist, inhibits hBM-Muse cells homing to the injured intestine.

Results: S1P expression increased in mouse intestine after irradiation, with hBM-Muse cells homing in on the injured intestine. Injection of hBM-Muse cells after radiation exposure significantly increased the number of crypts, proliferating cells in the crypts, and small intestinal component cells such as intestinal stem cells, inhibited radiation-induced apoptosis, and prolonged mouse survival. Treatment with JTE-013 significantly inhibited intestinal homing and therapeutic effects of hBM-Muse cells. These findings indicate that hBM-Muse cells homed in on the injured intestine through the S1P-S1PR2 interaction to exert therapeutic effects on the radiation-induced intestinal injury.
Conclusion: This study indicates that hBM-Muse cells are effective in treating radiation-induced intestinal injury, suggesting that hBM-Muse cell-based stem cell therapy has the potential to overcome the gastrointestinal side effects that limit the indications for radiation therapy.

Keywords: muse cells, radiation injury

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PIANOFORTE – Advancing Radiation Protection Through Research Integration and Open Call Successes

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The PIANOFORTE Partnership (2022–2029) is a pan-European co-funded initiative dedicated to advancing radiation protection for the public, patients, workers, and the environment across all exposure scenarios. It aims to address critical barriers in human and environmental health risk research associated with ionising radiation while reinforcing evidence-based policy-making. By fostering integration and coordination within the radiation protection community and engaging in structured dialogue with stakeholders, PIANOFORTE ensures that its research outcomes translate into meaningful societal impact.
A cornerstone of PIANOFORTE's approach is the establishment of a robust scientific and technological foundation to support science-based policy recommendations, scalable risk regulation, and safe and optimised practices across diverse sectors that utilise ionising radiation, both energy and non-energy related.

Through its competitive open call mechanism, PIANOFORTE, with more than 110 partners from 26 countries, has significantly expanded and consolidated the European research community, integrating new partners and reinforcing international collaboration. The success of its first two calls has led to seventeen newly co-funded projects launched between early 2024 and early 2025. These projects focus on key areas such as low-dose radiation carcinogenesis, personalised diagnostic and therapeutic applications, and improved preparedness for disasters and emerging threats.
Beyond research, PIANOFORTE actively promotes scientific excellence through open science practices and knowledge dissemination. It is committed to developing a sustainable network of research infrastructures and strengthening the radiation protection workforce through targeted education and training programmes, with a particular focus on early-career scientists.

Keywords: Radiation Protection, Research Partnership, Europe

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RESILIENCE FPA : European Strategic alliance for research, development and innovation onmedical countermeasures against CBRN threats

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The EU is facing security challenges as CBRN threats especially of intended origin. It is thus critical that Europe develops relevant capabilities through medical countermeasures for which today very few are approved for use and available to European armed forces. The RESILIENCE project aims to build a European collaborative ecosystem against currentor future CBRN threats, including research institutes, universities, RTOs, hospitals, industries, mid-caps and SMEs.It will be based on a multiannual action plan of research and development activities established in consultation with relevant authorities leading to effective and efficient medical countermeasures. Such countermeasures would then be industrialized, transferred and used by the armed forces for improving EU preparedness for CBRN military crises and fostering EU sovereignty.The main concept of the RESILIENCE multiannual action plan is based on a time-related deployment of armed forces in a theatre of operations where multiple health conditions requiring MCMs may occur. The action plan is organized around three main pillars of MCMs: Diagnosis, Prevention/Prophylaxis and Treatment which will respond to chemical (nerveagents, yperite, ricin and abrin), biological (pox viruses, viral hemorrhagic fevers, Y. pestis, B. anthracis, B. pseudomallei and Botulinum toxins) and radiological and nuclear threats. Innovative diagnostic tools (e.g., on-field tools), novel vaccines (e.g., antibody-based, vaccine with high cross orthopox protection efficacy) and more efficient treatments (e.g.,decorporating agents, reactivators of cholinesterases, phage therapy) will be developed.By gathering a critical mass of European players who will collaborate to provide European armed forces with novel efficient MCMs, RESILIENCE will contribute to strengthening the autonomy of the European sovereignty, to developing EU autonomous industrial segments and to maintaining the operational capacity of soldiers in the field.

Keywords: CRBN, Medical Countermeasures

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PLANET: Planning and Acting Network for Low Dose Radiation Research in Japan

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The Planning and Acting Network for Low Dose Radiation Research in Japan (PLANET) was established in 2017 in response to the need for an all-Japan network of experts. PLANET prioritizes research needs taking into account the potential of Japan and proposes strategies to improve the estimation of low-dose and low-dose-rate radiation risks. PLANET also proposes a support system for cooperation and collaboration with relevant researchers and research institutions in Japan and aims to promote collaboration with international organizations. PLANET established Working Group 1 (Dose-Rate Effects in Animal Experiments) to consolidate findings from animal experiments on dose-rate effects in carcinogenesis. Considering international trends in low-dose radiation research field as well as the situation in Japan, PLANET updated its priority research areas for Japanese low-dose radiation research in 2023 to include (i) characterization of low-dose and low-dose-rate radiation risk, (ii) factors to be considered for individualization of radiation risk, (iii) biological mechanisms of low-dose and low-dose-rate radiation effects and (iv) integration of epidemiology and biology. In this context, PLANET has established the following three working groups to examine issues in these research areas: Working Group 2 (Dose and dose-rate mapping for radiation risk studies) to identify the range of doses and dose rates at which observable effects on different endpoints have been reported, Working Group 3 (Species- and organ-specific dose-rate effects) to consider the relevance of stem cell dynamics in radiation carcinogenesis of different species and organs, and Working Group 4 (Research Mapping for Radiation-Related Carcinogenesis) to sort out relevant studies, including those on non-mutagenic effects, and to identify priority research areas. These PLANET activities will be used to improve the risk assessment and to contribute to the revision of the next main recommendations of the International Commission on Radiological Protection.

Keywords: low dose, low dose rate, network

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ABSTRACTS
Short Presentations

Effect of photonic / hadronic irradiation of tumor cells on endothelial cell phenotype: impact on the immune system

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Hadrontherapy is a cancer treatment modality using ion beams, which has the advantage compared to conventional photon-based radiotherapy, of using particles with high Linear Energy Transfer (LET) and very precise ballistics. These specific properties make it particularly effective to the treatment of deep-seated tumors while minimizing irradiation of surrounding healthy tissue. Tumors develop within a complex cellular and tissue microenvironment, in which the vascular endothelium plays a key role in the response to ionizing radiation and in the initiation and resolution of immune responses.

To better understand the interactions between tumor cells and endothelial cells, as well as the recruitment of immune cells, we study the influence of tumor cell irradiation with different types of beams (photons, carbon ions) on endothelial cell phenotype and the immune system. For this, tumor cells from head and neck squamous cell carcinoma (HNSCC) were irradiated *in vitro*, and their culture media (so-called conditioned media) were brought into contact with endothelial cells. We evaluated the changes induced by these conditioned media on survival, migration and angiogenesis, as well as on immune cell recruitment (adhesion and transendothelial migration of monocytes) by endothelial cells.

First results showed that conditioned media from irradiated and non-irradiated tumor cells partially inhibit the proliferation, migration and angiogenesis capabilities of non-irradiated endothelial cells, an effect enhanced when endothelial cells are irradiated. From a functional perspective, conditioned media derived from irradiated and non-irradiated tumor cells stimulate interactions between monocytes and endothelial cells and induce a lineage-dependent response on transendothelial migration. These findings indicate that cancer cells influence the phenotype of primary endothelial cells through their conditioned media. Further RNA sequencing analyses of both endothelial and tumor cells are planned for deeper investigation.

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Survey of Cataract and Skin Injury in Orthopedic Surgeons

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The impact of radiation exposure on cataracts and hand skin injuries in orthopedic surgeons remains underexplored. This study aimed to investigate the prevalence of cataracts and chronic hand inflammation and assess their association with radiation exposure.
A cross-sectional analysis was performed on spine surgeons attending academic conferences in Japan. Cataractous changes were classified as none, lens micro-opacity, or cataracts and detailed alongside the prevalence of chronic hand inflammation. Participants were divided into quartiles based on opportunities for hand exposure in the operating and fluoroscopy rooms in 2022. Prevalence ratios and 95% confidence intervals (CIs) of chronic hand inflammation in the upper quartiles compared to the first quartile were calculated using modified Poisson regression adjusted for potential confounders.

The median work experience of the 162 participants was 23 years, and the median number of hand-exposure opportunities was 70 (IQR, 20 to 123) in the operating room and 20 (IQR, 0 to 60) in the fluoroscopy room. The prevalence of cataracts was 20% (32 participants), while the prevalence of cataractous changes, including lens micro-opacity, was 40% (64 participants). Chronic hand inflammation was observed in 62 participants (38%), of whom 52 had longitudinal melanonychia and 23 had hand eczema. The adjusted prevalence ratios of chronic hand inflammation relative to the lowest quartile of hand-exposure opportunities in the operating room were 0.91 (0.50, 1.66) for quartile 2, 0.72 (0.41, 1.25) for quartile 3, and 1.56 (0.97, 2.50) for quartile 4. For fluoroscopy room exposure, the adjusted prevalence ratios were 2.31 (1.16, 4.58) for quartile 2, 2.03 (1.00, 4.09) for quartile 3, and 2.94 (1.51, 5.75) for quartile 4.
This study highlighted significant cataract and chronic hand inflammatory changes in spine surgeons, indicating the effects of both indirect and direct radiation exposure. Therefore, the importance of radiation safety and protective measures must be emphasized.

Keywords: occupational exposure, orthopedic surgeon, cataract, skin Injury, cross, sectional analysis, radiation safety, radiation protection

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Effect of co-exposure to rich Diet and gamma internal low dose irradiation on cerebral and cardiac microvascularization

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Introduction: High-dose ionizing radiation (IR) has been shown to have a major impact on cardiovascular diseases CVD, particularly large-vessel pathologies in which experimental studies show non-deleterious, even beneficial effects. While low-dose IR remains largely unstudied for small-vessel diseases. Epidemiological studies show a potential link between low-dose IR and development of CVD. Moreover, cardiovascular risk factors like dyslipidemia, known for its role in microvascular disease, could potentiate the effects of IRs. Our study focuses on the impact of low-dose internal 137 Cs contamination, in combination with a current risk factor - a high fat diet HFD - on cerebral and cardiac micro-vascularization.

Methods: C57BL/6JRj mice on normal diet ND, C57BL/6JRj mice on HFD, C57BL/6JRj mice internally contaminated with 137 Cs (500Kbq/L) and C57BL/6JRj mice co-exposed to HFD and 137 Cs were used. Experiments included dosimetry, metabolic parameters, cardiac echo-doppler and RT qPCR RNA extractions.

Results: The HFD induced a highly significant decrease in 137 Cs accumulation in mouse whole body (200mGy), muscle and adipose tissue compared to the ND group (400 mGy). 137 Cs contamination had no impact on weight gain whatever the diet, but improved glucose tolerance on ND; this result was not observed on HFD. Cardiac echo Doppler showed that HFD induced ventricular dysfunction, and that 137 Cs impacted carotid, ventricular and aortic flow and pressure without potentiating co-exposure. In the hippocampus, 137 Cs on a ND induced endothelial dysfunction and changes in hypoxia and angiogenesis parameters.

Conclusion: the HFD appears to be involved in the accumulation of 137 Cs in mice, which in turn appears to be involved in the regulation of glucose tolerance. Internal contamination with low-dose 137 Cs showed for the first time an impact on cardiac and cerebral function, suggesting potential vascular rarefaction. These results represent a medical and industrial interest on low-dose IR context.

Keywords: low dose internal Cs137 contamination, high fat diet, cardiac and cerebral microvascularization

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Development of micro and nanodosimetric simulations with Geant4-DNA

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With the continuous developments and the increasing complexity of irradiation techniques in radiotherapy, the current risk models for the irradiation of healthy tissues need to be reviewed. An understanding of the mechanisms of occurrence of the biological effects at the basis of these risks is thus necessary to update them and adapt to these changes. In this frame, Monte Carlo Track Structure (MCTS) codes are indispensable tools to improve the knowledge of the links between the physics of ionizing radiation and its biological consequences which have their origin at molecular level.

In this context and as a member of the collaboration developing the Geant4-DNA open-source code (1,2,3,4), ASNR has been contributing for many years to the development of multiscale computational tools for predicting radiobiological response, validated with experimental data obtained under controlled conditions.

The following discussion will address the issue of Monte Carlo simulations on this scale, with the presentation of the tools developed and utilised at the LDRI: the dsbandrepair simulation chain to compute DNA damage for a cell nucleus (5,6) and MINAS-TIRITH, an extension to pass from a single cell to the cell population level (7,8).

These tools allow to make progress in the understanding of the mechanisms at the origin of the biological effects. All the developments are intended to be integrated into the open-source code Geant4-DNA.

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Keywords: Monte Carlo simulations, radiobiology, Geant4, DNA

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Mesenchymal stromal cell (MSC) therapy of bladder tissue damage after radiotherapy

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Chronic radiation cystitis (CRC) is a complication of pelvic radiotherapy, characterized by chronic inflammation of the bladder, associated with pain, haematuria and incontinence. Therapeutic approaches are limited and often resistant to conventional treatments. Previous studies have demonstrated the efficacy of mesenchymal stromal cells (MSCs) in bladder pathologies such as interstitial cystitis, suggesting their potential as a therapeutic alternative for CRC. This project is part of the ASNR's efforts to characterize and prevent the side effects of ionizing radiation.
A preclinical rat model of CRC has been developed to assess the effect of MSC treatment. The entire bladder is locally irradiated with a total dose of 40 Gy, using the Small Animal Irradiation Platform (SARRP). To optimize therapeutic efficacy, repeated intravenous injections of MSCs are performed prior to the development of chronic radiation cystitis. Analyses, including physiological, histological, transcriptomic and protein approaches, were conducted.

At the physiological level, MSC treatment appeared to reduce urinary incontinence and bladder vascular lesions as early as 6 months post-irradiation.

Histological studies of the bladder wall show that treatment reduces hyperplasia (abnormal increase in the number of basal cells in the urothelium) at the start of the chronic phase. MSC treatment also promotes the differentiation of basal cells into superficial cells, thereby restoring the impermeability of the urothelium.

At transcriptomic level, the study of urothelial cell marker expression confirms the restoration of bladder wall integrity.
The results show that MSC cell therapy could be a promising approach to slow the progression of the chronic phase of CRC by reducing inflammation, vascular damage and fibrosis. These preclinical data support a relevant strategy for treating the side effects of radiotherapy to improve patients' quality of life.

Keywords: Radiation cystitis, Mesenchymal stromal cells, Radiotherapy

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Effect of co-exposure to high-fat diet and low or moderate doses of ionizing radiation on the cerebral microcirculation

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Epidemiological studies on cohorts of workers suggest a relationship between exposure to low and moderate doses of ionizing radiation (IR) and the risk of cerebrovascular diseases and dementia (Gillies et al, 2017; Laurent et al, 2023). Microvascular alterations which are strongly associated with cerebrovascular pathologies, have mainly only been studied at high dose ranges. Furthermore, established risk factors such as obesity and dyslipidemia increase the incidence of microvascular diseases. This study aims at identifying the response of cerebral microcirculation to acute exposure to low-to-moderate doses of IR, associated or not with a lipid-rich diet.

8-week-old male C57BL/6J mice fed either with a high-fat diet or a normal diet, were acutely exposed to total-body irradiation by an external source of gamma IR at doses of 300 mGy and 1 Gy. Sacrifice and analysis were conducted at 4 time-points post-irradiation, spanning both short term (24 hours and 15 days) and long term (3 and 6 months) periods. Microvascular density in the hippocampus was assessed by immunostaining of vascular markers in brain slices. Expressions of genes related to processes like endothelial dysfunction, hypoxia and angiogenesis were evaluated by RT-PCR.

We show that exposure to IR alone, at any dose, has no impact on the density of cerebral vascularization, nor does the lipid-rich diet. The same applies to the exposure to the lipid-rich diet combined to the irradiation at 300 mGy. However, co-exposure to a lipid-rich diet and to irradiation at 1 Gy induced an increase in hypoxia and angiogenesis processes in the short term, and a rise in vascular density at 3 months post-exposure, compared with control groups.
Co-exposure to high-fat diet and moderate dose (1Gy) of gamma IR increase vascular density in the brain hippocampus, a process probably following hypoxia-induced angiogenesis.

Keywords: microcirculation, brain, high fat diet, low dose radiation

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Development of in vivo counter systems at QST

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In vivo counting is one dosimetric approach for assessing internal contamination during the initial phase of accidents. The National Institutes for Quantum Science and Technology (QST) has introduced a new in vivo counter system, designed for multi-mode use of whole-body counting (WBC) and specific-organ counting. The system consists of three identical high-purity germanium detectors with a flexible configuration mechanism for the various modes.
We have evaluated the performance of the new system using two standard phantoms of BOMAB for the WBC and LLNL for lung counting as well as through the Monte Carlo calculations (Tamakuma et al., 2023, Naito et al., 2024). For the WBC mode, while the 137Cs peak efficiencies varied depending on the detector position, these variations were minimal when the middle detector was positioned above thorax and abdomen of the phantom. The calculated results presented consistent peak efficiencies with the measurements within differences of 5%.
For the lung counting mode, the system demonstrated minimum detectable activities (MDAs) for 239Pu and 241Am comparable to those of our previous lung counter, which consisted of two ACT-II units (Canberra Inc., USA). Meanwhile, the total sensitive area of the new lung counter is _˜15% smaller than that of the old system. These results suggest that an optimization of detector configuration improved the performance of the new lung counter. We also evaluated the identification of Pu isotopes during interferences from 241Am in scenarios simulating internal contamination from nuclear spent fuels, i.e., the Pu isotopes and 241Am are simultaneously detected. Calibration curves for identifying the Pu isotopes and their MDAs were obtained as a function of 241Am activity in the lung. For low levels of 241Am contamination, the Pu MDA was the lowest using the 17.2 keV peak. However, 241Am contamination exceeding _˜1,000 Bq made the best peak selection the 20.2 keV one.

Keywords: whole body counter, WBC, lung counter, internal dose assessment

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The DNA damage response relies on the characteristics of ionizing particles in myogenic cells

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DNA integrity is crucial for proper cellular function, yet it remains a primary target of radiotherapy to induce tumor cell death. As advanced radiotherapy techniques increasingly utilize charged particles, their impact on healthy tissues, including skeletal muscle, remains a concern. This study investigates the DNA damage response (DDR) in myogenic cells after microbeam irradiation with protons and α-particles.
Using the murine immortalized C2C7 cell line, we induced localized DNA damage in myoblasts and myotubes by a microbeam irradiation approach of protons or α-particles. Thus, we analyzed the recruitment kinetics of key DDR proteins in proliferating myoblasts and differentiated myotubes. Our results demonstrate that myoblasts engage both non-homologous end-joining (NHEJ) and homologous recombination (HR) for DNA double-strand break (DSB) repair, with the balance between these pathways influenced by the type of ionizing particle, energy deposition, and time after irradiation. In contrast, postmitotic myotubes exhibit a reduced DDR.
Interestingly, α-particles-induced DNA damage is predominantly repaired by NHEJ, whereas protons-induced DNA lesions are processed more rapidly by HR, suggesting a differential DNA repair pathway recruitment. This difference may have critical implications for radiotherapy protocols, particularly in minimizing long-term muscle tissue damage in cancer patients.

Keywords: DNA damage response, skeletal muscle, charged particles, ion microbeam, non, homologous end, joining, homologous recombination.

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Innovative biomarkers of therapeutic efficacy and follow-up of localized radiation injury

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In case of a radiological event of industrial, medical, or malicious origin (CBRN threat), a potentially large number of individuals may be exposed to high doses of ionizing radiations (IR), leading to the development of a localized radiation injury (LRI), with the severity, kinetics and progression depending on the absorbed dose. Initially after exposure, the LRI appears as a transitory erythema, followed by a latency phase. The LRI then gradually develops from erythema to dermatitis and desquamation, and in the worst cases, into ulceration and necrosis. The medical management of victims involves four phases: identification, prognosis and diagnosis, treatment, and follow-up. Identifying biomarkers that allow fast and non-invasive analysis of patients could improve the prognosis, diagnosis, and medical monitoring of LRI.
Using a preclinical model of hindlimb irradiation in C57BL/6 mice, we recently identified molecular diagnostic signatures of plasmatic microRNA (miRNA) and metabolites associated with LRI severity. These signatures could distinguish irradiated from non-irradiated mice, as well as segregate those with severe from moderate injuries. More interestingly, we identified prognostic plasma miRNA signatures that can predict the development and severity of LRI before appearance of clinical symptoms.

The aim of this project is to demonstrate the relevance of plasma miRNA and metabolites as biomarkers of treatment efficacy and therapeutic follow-up.

Using a preclinical murine model of LRI on both male and female Nude mice treated by injection of mesenchymal stromal cells (MSC) based therapy , blood samples will be collected at different timepoints to perform multi-omics analysis and to confirm the relevance of the biomarkers. The data will be correlated with clinical parameters including injury score, skin barrier function and cutaneous perfusion. Results will be used as input data for mathematical models to assess the effectiveness of treatments and identify biomarkers for therapeutic follow-up.

Keywords: Localized radiation injury, MicroRNA, Tissue repair, Mesenchymal stromal cells, Metabolites

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Establishment of a co-operation system for biodosimetry in Japan

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In Japan, the government has designated six institutes-Hirosaki University, Fukushima Medical University, QST, University of Fukui, Hiroshima University, and Nagasaki University-as Advanced Radiation Emergency Medical Support Centers. In the event of a large-scale nuclear disaster, it is crucial for these institutes to collaborate effectively. To facilitate this, we are developing domestic cooperation networks utilizing an AI-assisted biodosimetry system. We have identified three cooperation patterns: (i) sending blood samples between institutes, (ii) sending chromosome preparations, and (iii) sending chromosome images. As a first step, we conducted a drill for blood sample transportation and confirmed that samples can be transferred without coagulation or loss of cell viability during winter. For the second step, we are working on harmonizing the methods for chromosome preparation and fluorescence *in situ* hybridization. Standardizing these methods will ensure that the samples are uniformly prepared, enabling the AI-assisted biodosimetry system to accurately detect and classify chromosomes. We will retrain the AI model using chromosome images generated by the harmonized methods.

Keywords: biodosimetry, cooperation network, FISH

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Proposal for research of developmental engineering and radiobiology

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Radiation effects on early embryos have been extensively studied, focusing on their impacts on subsequent embryonic development. Meanwhile, investigating the radiation response of artificially manipulated embryos using developmental engineering techniques may reveal novel reproductive mechanisms that cannot be observed in naturally fertilized embryos. This approach provides a unique opportunity to uncover new insights into embryogenesis, potentially reshaping our understanding of developmental biology and radiation biology. Somatic cell nuclear transfer (SCNT) is only developmental engineering technique that can produce individuals with the same genetic copy as a donor by injecting donor somatic cells into enucleated oocytes. The developmental efficiency is significantly lower than that of fertilized embryos, and the reasons for this are not well understood. In this presentation, we will discuss the use of SCNT embryos to uncover previously uncharacterized reproductive mechanisms. By exposing these embryos to controlled doses of radiation and analyzing their subsequent developmental process, we aim to elucidate the interplay between radiation- induced damage and the embryo's innate repair system and differentiation capabilities. This study is expected to provide new insights into embryonic resilience and adaptability, contributing to both the understanding of early developmental processes and advancements in radiation biology. These findings may provide potential applications, including the development of improved radiation protection strategies.

Keywords: Radiation effects, Radiation, induced damage, Embryonic development, Repair mechanisms, Somatic cell nuclear transfer

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Mechanism of radiation carcinogenesis in a novel Brca1 mutation rat model

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BRCA1 is involved in homologous recombination repair. Female heterozygous carriers of a pathogenic *BRCA1* mutation have a high incidence of breast cancer. We have established a heterozygous *Brca1* mutant rat model, in which the incidence of mammary carcinoma is significantly increased after exposure to 2 Gy of gamma-rays at 3 weeks of age. No inactivation of the wild-type *Brca1* allele has been observed in mammary carcinomas of rats, suggesting that this model recapitulates the Brca1 haploinsufficiency carcinogenesis. Here, we analyzed genomic aberration in carcinomas to clarify the mechanism of radiation carcinogenesis based on Brca1 haploinsufficiency. Genome DNA was extracted from mammary carcinomas developed in untreated and irradiated wild-type and *Brca1* mutant rats, and whole-exome sequencing was performed. Then, somatic single nucleotide variants (SNVs) and insertions and deletions (InDels) were detected using VarScan2 (Ver. 2.2.4), and the copy number variants (CNVs) were identified by Control-FREEC (Ver. 10.8). As a result, there were no significant differences in the numbers of SNVs and InDels and the pattern of SNVs between carcinomas from *Brca1* mutant rats and wild-type rats. Nonsynonymous mutations and CNV regions specific to carcinomas developed in *Brca1* mutant rats were not identified. Cancer-driver mutations in carcinomas were significantly fewer in irradiated *Brca1* mutant rats than in irradiated wild-type rats. Furthermore, most carcinomas from irradiated *Brca1* mutant rats had no driver mutation. These results suggest that oncogenic mutations that unable to be detected by whole-exome sequencing analysis, such as epigenetic mutations and fusion genes, may occur in irradiated *Brca1* mutant rats.

Keywords: Brca1, Breast cancer, Carcinogenesis

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Effect of ionizing radiation on mitochondrial function. Compromise stability of mtDNA as a new therapeutic tool to improve cancer radiotherapy.

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A major challenge in radiotherapy is to enhance tumor cell sensitivity to radiation while minimizing damage to healthy tissues. Ionizing radiation (IR) induces mitochondrial DNA (mtDNA) alterations that can impair mitochondrial function and cell survival. Since mitochondria play a key role in tumor cell proliferation, they represent a promising therapeutic target for cancer treatment. We have characterized the impact of different IR sources on mitochondrial function in radioresistant cancer cells. Our findings revealed several adaptive responses that may contribute to radioresistance, including increased mtDNA content, mitochondrial mass, enhanced activity, and hyperfusion of the mitochondrial network. The use of mitochondrial-targeted G-quadruplex (G4) ligands, which block mtDNA replication and transcription, disrupted these responses, reducing cancer cell survival in an mtDNA-dependent manner. These results demonstrate that mitochondrial adaptations contribute to radioresistance and highlight mitochondria as a novel target for the radiosensitizing effects of G4-ligands, extending their potential beyond telomere destabilization.

Keywords: radiosensitivity, G4, mitochondria

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Intravital microscopic thermometry of rat mammary epithelium by fluorescent nanodiamond

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Quantum sensing using the fluorescent nanodiamond (FND) nitrogen-vacancy center enables physical/chemical measurements of the microenvironment, although application of such measurements in living mammals poses significant challenges due to the unknown biodistribution and toxicity of FNDs, the limited penetration of visible light for quantum state manipulation/measurement, and interference from physiological motion. Here, we describe a microenvironmental thermometry technique using FNDs in rat mammary epithelium, an important model for mammary gland biology and breast cancer research. FNDs were injected directly into the mammary gland. Microscopic observation of mammary tissue sections showed that most FNDs remained in the mammary epithelium for at least 8 weeks. Pathological examination indicated no obvious change in tissue morphology, suggesting negligible toxicity. Optical excitation and detection were performed through a skin incision. Periodic movements due to respiration and heartbeat were mitigated by frequency filtering of the signal. Based on these methods, we successfully detected temperature elevation in the mammary epithelium associated with lipopolysaccharide-induced inflammation, demonstrating the sensitivity and relevance of the technique in biological contexts. This study lays the groundwork for expanding the applicability of quantum sensing in biomedical research, providing a tool for real-time monitoring of physiological and pathological processes.

Keywords: quantum sensing, fluorescent nanodiamond, thermometry, laboratory animal, mammary gland

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Current status on BL14B1 beamline at SPring-8, XAFS analysis and microbeam irradiation for radiological science

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SPring-8 is a large-scale synchrotron radiation facility in Japan that produces extremely bright X-rays for advanced research in various fields, including radiological science. QST holds two contract beamlines, BL11XU and BL14B1, at SPring-8, shared for collaborative research. BL14B1 offers capabilities for various diffraction experiments and X-ray absorption spectroscopy (XAS) spectroscopy in the energy range of 5–90 keV for monochromatic beams and 5–150 keV for white beams. Taking advantage of the features of the light source, we have utilized the beamline for two primary purposes. First, we have employed X-ray absorption spectroscopy (XAS), a widely used analytical technique to obtain detailed local geometric and/or electronic structure information of the central atom, for decorporation of radionuclides. The primary purpose of XAS in this context is to investigate the decorporation efficiency of actinides in human serum by evaluating chelating agents considered as potential drugs to reduce internal exposure. The use of a 36-element solid-state detector enabled low-concentration XAS measurements to investigate the chemical forms and their concentrations of radionuclides. Second, we are developing an irradiation system for mammalian cells and organoids for radiobiological studies relevant to radiation health risks and therapy. Irradiation experiments have already been carried out using monochromatic X-rays around the absorption edge of iodine. The dose rate of monochromatic X-rays at approximately 33.2 keV was determined to be 0.099 ± 0.006 Gy/s using an optical stimulated luminescence detector. The incorporation of iodine effectively sensitized cell inactivation and DNA double-strand break induction in cells, confirming our expectation that it would act as a radiosensitizer in cancer therapy. Our next aim is to develop a microbeam irradiation system to investigate the biological effects, not only DNA damage induction and repair but also other sub-cellular damages that may contribute to genomic instability.

Keywords: Synchrotron radiation, XAS, Irradiation system

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Improving radiotherapy by targeting the TRIM33 chromatin reader in myeloid cells

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Radiotherapy exerts its effects not only through the direct killing of tumor cells, but also through stimulation of an anti-tumor immune response. The radio-induced immune response might lead to tumor shrinkage outside the irradiated field. This so-called abscopal effect is therapeutically favorable, but very rarely observed in the clinics. Improving the immunogenicity of radiotherapy without decreasing its direct cytotoxic effects is a major goal in the design of novel therapeutic approaches coupling immunotherapy and radiotherapy.
Interferon beta (IFN-β) is a crucial molecular step in the induction of an immune response by radiotherapy. Briefly, ionizing radiations damage DNA, eventually leading to the presence of DNA in the cytoplasm. This cytoplasmic DNA triggers the cGAS/STING pathway, culminating in IFN-β secretion. IFN-β then activates both dendritic and T cells, participating in the stimulation of a full-blown anti-tumor immune response.
Building on previous work showing a role for the chromatin reader TRIM33 in controlling IFN-β expression in activated macrophages, we now report that TRIM33 acts as a checkpoint of IFN-β expression in irradiated macrophages. This is also the case for macrophages treated with irradiated tumor cells. Accordingly, radiotherapy is more efficient in mice carrying a deletion of *Trim33* in myeloid cells, as shown in different pre-clinical models. The increased efficiency of radiotherapy depends on the IFN pathway, and on CD8+ T lymphocytes. In addition, cured mice are resistant to a secondary tumor challenge, demonstrating the acquisition of a memory of the primary response. We propose that the presence of macrophages devoid of TRIM33 during radiotherapy increases the radio-induced immune response. This observation paves the way for a strategy targeting TRIM33 to boost the immunotherapeutic effects of radiotherapy.

Keywords: interferon beta, trim33, radiotherapy, myeloid cells

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No Specific Impact of Ultra-High Dose Rates on Radiation-Induced Chromosome Rearrangements

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Ionizing radiation generates DNA double-strand breaks (DSBs) that challenge DNA repair mechanisms and drive mutagenesis, chromosome rearrangements, and cell lethality. These features underlie its application in cancer therapy. DSBs arise from direct DNA ionization or the indirect action of reactive oxygen species (ROS) generated by energy deposition events. While distinct particle-matter interactions are considered independent during standard irradiation timescales, the impact of extreme dose rates - comparable to ROS half-lives - remains unclear. Here, we used a chromosome fusion capture (CFC) assay in budding yeast to quantify radiation-induced chromosome rearrangements under varying conditions. We validated the assay's sensitivity and observed results consistent with prior studies regarding oxygen enhancement ratios and photon energy effects. Importantly, we found that X-rays delivered at extreme dose rates produced chromosome rearrangements at frequencies indistinguishable from standard irradiations. These findings suggest that ultra-high dose rates do not alter the nature or frequency of radiation-induced DSBs, providing insights for FLASH-irradiation protocols.

Keywords: Ionizing radiations, FLASH irradiation, Chromosome, DNA Repair, NHEJ, Mutagenesis, Dicentric

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JMY, a new therapeutic target against radiation-induced invasion of glioblastoma stem cells

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Glioblastomas (GBMs) are severe primary brain tumors with a median survival of no more than 15 months, despite aggressive multimodal treatment combining surgery, chemotherapy, and radiotherapy. This therapeutic resistance, which clinically results in systematic recurrences, is largely attributed to the presence of glioblastoma stem cells (GSCs) within the tumor. GSCs share certain properties with normal neural stem cells, such as the expression of membrane markers and the ability to self-renew and differentiate, allowing them to regenerate tumors. They are also particularly resistant to treatments.

Using various experimental models, we have demonstrated that sublethal irradiation can enhance the migration and invasion of human GSCs, potentially facilitating their escape from the irradiated tumor area. Genetic inactivation and the use of specific pharmacological inhibitors have revealed that this radiation-induced migration/invasion involves the nuclear accumulation of HIF1α, which stimulates the transcription of the Junction-Mediating and regulatorY protein (JMY). Through its ability to nucleate actin monomers, JMY is thought to promote radiation-induced GSC migration/invasion. JMY may also play a crucial role in GBM pathophysiology by facilitating the formation of intercellular cytoplasmic extensions rich in actin, known as tumor microtubes. These protrusions enhance the invasive capacities of GSCs and their resistance to treatments.

Expression of different mutated forms of JMY indicates that forcing its localization to the nucleus suppresses radiation-induced GSC migration. Using JMY-deficient GSCs or GSCs expressing different JMY variants in novel invasion models within cerebral organoids should provide a better characterization of this radiation-induced invasion and, ultimately, help develop new therapeutic strategies to improve radiotherapy efficacy and more effectively prevent GBM recurrences

Keywords: Glioblastoma Stem Cells, Radiation, Induced Invasion, JMY, Cerebral Organoid

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Genomic changes in radiation-induced precursor B-cell lymphoma

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Epidemiological studies of atomic bomb survivors have shown an increased risk of acute lymphoblastic leukemia (ALL) related to radiation dose. ALL is a malignancy of B-cell or T-cell precursors, and the majority (> 70%) of human ALL is precursor B-cell origin. Our group has revealed an increased risk of precursor B-cell lymphomas (pBLs) after radiation exposure in some animal experiments.
In this study, we aimed to determine the genomic features of murine pBLs developed after gamma-ray or heavy-ion irradiation.

Male and female B6C3F1 mice were left non-irradiated or irradiated with 4 Gy of gamma rays or 0.2, 1, or 2 Gy of heavy ions (carbon, silicon, argon, or iron ions) at 1 or 7 weeks of age (infancy or young adulthood, respectively). pBLs developed in mice were subjected to array comparative genomic hybridization (array-CGH) and whole-exome sequencing.

The array-CGH analysis revealed that hemizygous interstitial deletion of chromosome 8 (del8) was characteristically found at high frequency in gamma-ray-induced pBLs (7/19 cases, 37%). Two known tumor-suppressor genes were located in the commonly deleted region of del8. Whole-exome sequencing identified a loss-of-function mutation in one of the genes in one pBL with del8, which showed the earliest onset among the pBLs with del8, highlighting the role of this gene as a tumor suppressor. On the other hand, hemizygous interstitial deletion of chromosome 19 (del19) was prevalent in pBLs from carbon- and silicon-irradiated groups (6/18 cases, 33%). Three known tumor-suppressor genes were located in the commonly deleted region of del19. Whole-exome sequencing identified frequent mutations in two of these three genes in pBLs from all groups.
These results suggest radiation-type-dependent mechanisms involved in the development of pBLs after radiation exposure.

Keywords: heavy ion, space radiation, mouse, lymphoma

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Safe homologous recombination upon exposure to ionizing radiation through dynamic interplay of Rad51 nucleoprotein filament-associated proteins

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Homologous recombination (HR) is a conserved process that plays an important role in genome stability. As a mechanism for repairing DNA gaps and double-strand breaks, it is importantly involved in the cellular response to ionizing radiation. However, unscheduled HR can induce genome rearrangements and unprocessed HR intermediates can interfere with DNA replication. The potential toxicity of Rad51 filaments was revealed in yeast cells deficient in the DNA helicase Srs2, a negative regulator of Rad51 filament formation. Uncontrolled Rad51 filaments create conflicts with primordial processes such as DNA replication, leading to a marked sensitivity to IR. We found that these conflicts are the result of excessive stabilization of Rad51 filaments due to their association with the main loader of Rad51 on DNA, Rad52. Interestingly, Rad52 association with Rad51 filaments protects functional Rad51 filaments from Srs2 disassembly activity. To fully understand the consequences of Rad52 association with Rad51 filaments, we elucidated the structure of the Rad52-Rad51 complex at high resolution. This allowed us to define key mutations that disrupt the interaction and to measure their impact on HR efficiency and Rad51 filament dynamics in vivo using a functional Rad51-GFP construct. Two other protein complexes composed of Rad51 paralogs, Rad55-Rad57 and SHU, are also positive regulators of Rad51 filament formation. We designed a model of their organization with Rad51 filaments using the Alphafold2 software and generated mutations specific for each interaction domain. Our study shows how they affect Rad51 filament formation, stability and toxicity.

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Advanced human cerebral organoids as a model for investigating glioma stem cell interactions with microglia and vascular cells and response to radiotherapy

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The recent development of human brain organoids from induced pluripotent stem cells (IPSCs) enables the modeling of brain biology and pathophysiology, such as gliomas. However, most models lack vascular and/or immune systems, both of which play essential roles in maintaining brain health and in pathophysiological mechanisms. We have established a new method for generating vascularized complex cerebral organoids (CCOs) containing microglial cells (brain-resident macrophages) by incorporating bipotent hematopoietic/endothelial progenitors derived from the same IPSC lines during the early stages of development. This approach led to the formation of extensive vascular-like structures with blood-brain barrier characteristics, which were perfused upon transplantation into immunodeficient mice. Additionally, microglial cells exhibiting typical phenotypes and functionalities also developed within the CCOs. By coculturing CCOs with glioma stem cells, we demonstrated that this model effectively recapitulates the tumor niche of glioblastoma, showing vascular co-option, reprogramming of microglia into tumor-associated macrophages, and recurrence after radiotherapy. In conclusion, our vascularized and immunocompetent CCO model will be invaluable for understanding human brain development, exploring how this process is disrupted in diseases like gliomas, and discovering new therapeutic strategies. Advanced human cerebral organoids as a model for investigating glioma stem cell interactions with microglia and vascular cells and response to radiotherapy

Keywords: brain organoids, glioma

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Evaluation of uranium decorporation efficiency in serum using chelating agents by X-ray absorption spectroscopy

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Uranium is considered to be a chemical and radiological toxic metal that accumulates in the kidneys and bones after the incorporation. The decorporation therapy using chelating agents has been treated to reduce the health effect by the internal exposure. X-ray absorption spectroscopy (XAS) provides detailed information about the electronic state and local structure around a specific atom, such as bond lengths and coordination numbers. In the present study, uranium chemical form in serum was analyzed by XAS in the presence and absence of chelating agents to study decorporation effectiveness of human body exposed to uranium. XAS spectra of uranium L3 edge were measured at BL14B1 beamline of SPring-8, Japan. The chelating agents used were 1-hydroxyethane 1,1-bisphosphonate (EHBP), inositol hexaphosphate (IP6), deferoxamine B (DFO), and diethylenetriaminepentaacetate (DTPA). About 150 μL of the serum sample containing uranium and chelating agent was placed in a hole on an acryl cell with 10 mm thickness, and sealed by Kapton poly imide tape. XAS spectra of uranium in serum changed depending on the concentration of the chelating agents, resulting that XAS spectra in the presence of chelating agents were distinguished with those in the absence of the chelating agents. The main ligands forming complexes with uranium in the serum were estimated as follows: IP6 $>$ EHBP $>$ bioligands $>$ DFO $>>$ DTPA when the concentration ratio of the chelating agent to uranium was 10(1). XAS measurements were employed to investigate the uranium chemical forms and their concentrations in serum with aim of assessing the decorporation efficiency for the appropriate treatment using chelating agents in the human body(2).
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Keywords: Decorporation therapy, Uranium, X ray absorption spectroscopy, Chelating agent

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"Single Cell Radio-Biology" project at SPICE-QST microbeam facility

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SPICE-QST microbeam is a focused vertical microbeam system designed for sub-cellular target irradiation of adherent mammalian cells. The microbeam delivers 2-μm diameter microbeams to target individual cells with a defined number of 3.4 MeV protons at a high-throughput irradiation rate of 300-400 positions/minute (1). Leveraging the advantages of microbeam technologies, such as sub-cellular target resolution and precise dose control, which enable single-cell analyses, we have initiated an international collaboration to investigate the role of radiation-induced defensive intra- and intercellular communication. This collaboration aims to address fundamental questions in radiation biology. Traditionally, DNA has been considered the primary target of radiation in radiation biology. However, numerous phenomena observed in recent decades cannot be fully explained by this classical paradigm. These findings suggest the existence of non-DNA/secondary targets that may activate intra- and inter-cellular signaling pathways. Our objective is to utilize microbeam technology to identify these non-DNA/secondary targets and to investigate their involvement in cellular response. Specifically, we have studied intra-cellular response induced by cytoplasmic damage, focusing on the activation of the oxidative stress response pathway, which appeared as protective response (2).As for studies on intercellular responses, we have investigated the bi-directional response between targeted cancer cells and non-targeted normal cells, resulting in the "rescue" of targeted cells, a phenomenon described as a facet of the radiation-induced bystander effect (3). This presentation will summarize the findings from these investigations. SPICE take in part of IAEA-CRP F11024, "Sub-cellular Imaging and Irradiation using Accelerator-based Techniques." and PIANOFORTE (PI: C. Adam-Guillermin, ASNR).

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Research on oncometabolites that affect radioresistance

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Metabolic reprogramming is recognized as part of cancer malignancy, and the role of abnormally accumulated oncometabolites in cancer aggressiveness have been attracting attention. Recently, some intermediate metabolites of the TCA cycle, traditionally considered crucial for ATP production, have been reported to act as one of the upstream regulators of epigenomic changes. These epigenomic changes are linked to various phenotypic alterations associated with cancer malignancy, leading us to hypothesize that they may also contribute to the radioresistance observed in some malignant cancers. To investigate this, we focused on intermediate metabolites of the TCA cycle to determine their impact on shifting the phenotype of cancer cells toward increased radioresistance. Treatment of pancreatic cancer cells with cell-permeable oncometabolites up-regulated gene expressions relating to cancer malignancy, such as enhanced epithelial-mesenchymal transition (EMT), increased cell motility, and elevated stress tolerance, including reactive oxygen species (ROS) scavenging systems. Additionally, the results of MeDIP-chip microarray analysis, which examines DNA methylation changes in the CpG islands of gene promoter regions, revealed significant methylation changes in some genes having role in EMT, cell motility, and stress tolerance, including ROS scavenging systems. Importantly, when these oncometabolite-treated cells were exposed to X-ray irradiation at doses of 2, 4, and 6 Gy and subjected to a colony formation assay, the cells were altered their phenotype toward increased radioresistance to X-rays. Overall, our research indicated the significant role of these metabolites in altering the radioresistant phenotype of cancer cells. These findings not only deepen our understanding of cancer metabolism but also provide potential therapeutic targets for overcoming radioresistance in cancer treatment.

Keywords: radioresistance, oncometabolites

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Recent studies on nuclear track detectors for application to medical fields

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We are tackling dosimetry using fluorescent nuclear track detector (FNTD), which is made from aluminum oxide doped with carbon and magnesium (Al2O3; C,Mg) and enables to detect any radiation. In the presentation, recent advances of dosimetry using FNTD will be presented concerning the following application fields;

- Detection of Auger electrons, aiming at understandings of the contribution of low-energy electrons for biological effectiveness.
- Identification of incident energy of incoming ions (protons and alpha particles) for nano- or micro- scale dosimetry.
- Beam size measurements for evaluating the density of ion tracks in SPICE-QST facility.

FNTD technology is applicable various application fields, not only above three branches, so that the authors wish discussing new topics, which bring us to new collaborative research.

Keywords: FNTD, dosimetry

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Survey of personal dosimeter wearing rates of medical workers associated with revisions to the law

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Following the International Commission on Radiological Protection (ICRP) recommendation to lower the equivalent dose limit for the lens of the eye, Japan's laws and regulations, the Regulation on Prevention of Ionizing Radiation Hazards, were amended. This amendment was promulgated in April 2020 and effected in April 2021. However, it is unclear what impact this amendment to the laws and regulations has had on medical workers' wearing personal dosimeters. Therefore, in this study, we surveyed the changes in medical workers' wearing of personal dosimeters before and after the amendment to the laws and regulations.

The survey covered the wearing of personal dosimeters by medical staff working in radiation-controlled areas (such as X-ray fluoroscopy rooms and operating rooms) at medical institutions. Surveyors were recruited from the website, targeting Radiological technologists. Surveyors conducted visual inspections and submitted the results by post or as an email attachment. The survey period was from 1st February to 31st March 2020 (control period), 2021 (promulgation period), and 2022 (enforcement period). The personal dosimeter wearing rate was calculated as the ratio of people wearing personal dosimeters to the number of people surveyed about their personal dosimeter wearing status.

The personal dosimeter wearing rate was 64.3%, 71.1%, and 77.3% during the control, promulgation, and enforcement periods, respectively ($p < 0.001$). On the other hand, physicians' personal dosimeter wearing rate was lower than that of other medical workers throughout the entire period, at 35.1%, 55.1%, and 61.1%, respectively ($p < 0.001$). These results show that the personal dosimeter wearing rate has improved due to the revision of laws and regulations. However, it has not yet reached 100%, and further measures to improve the situation will be required.

Keywords: personal dosimeter, wearing rate, the amendment to the laws and regulations

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Retrospective dosimetry for the occupational exposure of medical staff

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Aims: Our group attempts to develop a retrospective model to estimate cumulative doses for healthcare workers who are not adequately monitored by personal dosemeters. Our group revealed that for orthopaedic surgeons have a low rate of wearing legal personal dosemeters during their procedures. Even if radiation-induced diseases might occur to surgeons as a result of overexposure, no causal link can be established without properly measuring and recording doses. A retrospective dose estimation model should be established to give the best estimate of cumulative doses for highly exposed orthopaedic surgeons who are not fully monitored during they were engaged in their procedures.
Methods: As the simplest model, a cumulative dose is considered the product of an assumed annual dose (mSv) of a surgeon and the number of years (years) that a surgeon was engaged in medical procedures. A model that estimates a surgeon's cumulative dose from an estimated dose (μSv) per procedure and an estimate of the total number of procedures performed to date is also simple. To provide a more accurate dose estimate for surgeons, we are developing a retrospective dose estimation model that takes into account the doses per procedure for different categories of medical procedures, and the annual number of procedures, considering the different careers of individual orthopaedic surgeons.
Results and discussion: A survey of orthopaedic surgeons was carried out. The procedures performed by orthopaedic surgeons were categorized into eight main categories in terms of whether they or not involve a high radiation dose. The number of procedures performed per year for each category was summarized in relation to the number of years since the medical license was issued. The annual number of procedures ranged between 50 and > 200 depending on the year after obtaining the license. Details will be discussed in the presentation.

Keywords: dosimetry, medical staff, X, rays, occupational exposure, radiological protection

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ABSTRACTS
Posters

Impact of age on the development of cardiovascular disorders following an external exposure to low or moderate doses of Caesium 137

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Populations living near contaminated areas following nuclear accidents are chronically exposed to low doses (LD) of ionizing radiation (IR), the consequences of which, at the cardiovascular level, remain poorly evaluated. Epidemiological findings suggest a relationship between age and the onset of cardiovascular diseases (CVD) with higher cardiovascular morbidity and mortality rates in elderly subjects than in young subjects of the exposed populations. Our aim is to examine the effect of low to moderate doses of gamma rays on the development of late CVD, especially vascular remodeling, while highlighting the age-related health effects.
15 months-old male C57Bl/6J mice were exposed total body to gamma rays' doses ranging from 0.1 to 0.5Gy to mimic cumulated doses of chronic exposure to IR. The experiments were carried out at 24-hours, 15-days and 3-months time points post-IR. The effects of radiation on the vascular system were assessed by doppler ultrasound and Millar probe for functional parameters, by histological labelling for morphology and by western blotting for the molecular mechanisms.

24h post-exposure (PE), the results show a modulation in the expression of proteins involved in calcium signaling, notably a significant decrease in total phospholamban, a regulator of intracellular calcium, at 250 and 500mGy, and in the sodium-calcium exchanger NCX at 100 and 500mGy.
15 days PE, an enhanced heart rate followed by a decrease in left ventricular ejection fraction at 100mGy were observed. Systolic pulmonary artery pressure was significantly increased at 100 and 250mGy. However, no significant changes were observed at 500mGy.
These results show that exposure to low-intensity IR (< 500mGy) induces molecular and functional alterations that could participate in the vascular pathologies observed in elderly people living in contaminated areas. Histological analyses, notably immunolabeling and clearing of the heart and lungs, are ongoing to identify markers of these alterations.

Keywords: Cardiovascular, age, heart lung axis, low dose radiation, gamma rays

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On-line analysis based on chromatographic separation and ICP-MS detection: Application for the analysis of actinides in urine.

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In the event of a nuclear accident or a terrorist attack, radionuclides may be released into the atmosphere. Alpha emitters such as actinides are of particular concern as they can cause severe health effects. Current protocols, used especially for the individual monitoring of nuclear workers are based on the actinides analyses in urine by alpha spectrometry after urine mineralisation and actinides separation on chromatographic columns. The detection limits are very low and the methods are accurate and sensitive, but it takes 7 to 15 days to get an acceptable result regarding ICRP recommendations and dose regulations. This means that it cannot be used in case of an emergency where many potentially contaminated people and thousands of samples need to be processed. Emergency protocols have already been developed with reduced sample volumes and shorter counting times for alpha spectrometry. However, the detection limits achieved are much higher than those for routine protocols. In its mass spectrometry platform PATERSON, the Laboratory of Research in Radiochemistry, Speciation and Imaging has developed a rapid analytical protocol for the actinides determination in urine by coupling a chromatographic column with ICP-MS analysis. These developments, funded by the Institute for Radiation Protection and Nuclear Safety and the Ministry of Defence, are based on the use of a specific chelating agent, a calix(6)arene molecule with hydroxamic acid groups, incorporated into a polymer resin. The use of this calix(6)arene-based column allows the simultaneous extraction of 97% of plutonium, 81% of americium and 61% of uranium from mineralised urine. This good performance combined with the rapid ICP-MS detection allowed the on-line analysis of 238U, 239Pu and 241Am in urine in less than 6 hours, including urine mineralisation. With detection limits of around ten mBq.L-1 per radionuclide, this calixarene column and ICP-MS coupling method is perfectly suited to a crisis situation.

Keywords: actinides, urine, emergency, online analysis, ICPMS, calixarene

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Impact of the X-ray radiation quality on the radiological burn severity and on the in vivo bone response for retrospective dose estimation at different time points

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Although the use of ionizing radiation is often controlled, radiological accidents can occur and lead to localized overexposures. Care of victims requires an accurate estimation of the dose absorbed by the tissues. However, depending on the X-ray quality involved, the dose deposit in matter varies as the more predominant the photoelectric effect is, the more heterogeneous is the energy deposit. This study aims to determine the impact of X-ray quality on the lesion severities, the absorbed dose to the bone, and the quantity of radio-induced free radicals (RIFR) at different time points by EPR spectroscopy.
Localized paw expositions of C57Bl6/j mice were performed at 30 Gy (Kair) with 4 voltages: 50kV, 80kV, 220kV, and 10MV. Lesion severity was quantified until six months post-irradiation using a lesion score, transepidermal water loss (TWL) and cutaneous blood perfusion measurements. Irradiated tibias were collected for EPR spectroscopy analysis at six time points (D0 to D168). Lesion scoring shows a lesion peak at D21 for low-energy X-rays, and less intense lesions between D14 and D21 for high-energy. TWL and cutaneous blood perfusion significantly increased at the lesion peak. EPR measurements estimate an initial bone dose (D0) of 152.2 ± 14.3, 103.5 ± 7.9, and 33.8 ± 11.3 Gy respectively for 50kV, 220kV, 10MV expositions (197.8 ± 26.7 Gy for 80kV). Then, the quantity of RIFR decreases over time depending on the quality of the X-rays. The higher the voltage, the faster the decay.
The absorbed bone dose depends on the X-ray quality, which is related to the predominance of the photoelectric effect. The lowest bone doses are associated with high-energy X-rays that lead to less severe burns. EPR measurements for bones collected at interest time points show variations in RIFR's quantity decrease depending on the X-ray quality, suggesting different behaviors of bone renewal processes.

Keywords: Retrospective dosimetry, EPR spectroscopy, Radiological injuries, X, ray

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Response of the Broncho-Alveolar Epithelium to Pulmonary Irradiation under Stereotactic Conditions: Focus on Club Cells

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The LRMED has developed a preclinical model of small-volume lung irradiation in mice to mimic stereotactic pulmonary radiotherapy protocols. The study focuses on the broncho-alveolar epithelium's response, particularly the role of club cells in radiation-induced lung injuries.
First, a chemical depletion model of club cells, either transient or sustained, is used to determine their impact on the development of radiation-induced lung injuries. Second, we use single-cell RNA sequencing to track gene expression profiles of bronchiolar epithelial cell populations in response to ionizing radiation.

In C57Bl6/J mice, depletion of Club cells is induced by intraperitoneal injection of naphthalene (NA) (or corn oil, CO, the vehicle). Irradiation is performed using the SARRP system, using a collimated 3x3 mm^2 beam delivering a single 80 Gy dose in an arc to the left lung, causing focal acute inflammation and fibrosis. Mice receive irradiation either three days post-NA injection (when club cells are at their lowest) or 14 days later (after repopulation). Chronic depletion is maintained through repeated NA injections post-irradiation. Lung tissues are analyzed one month (inflammation) and six months (fibrosis) post-exposure using CT scans, histopathology, immunohistology, and gene expression studies.

One-month post-exposure, CT scans reveal reduced opacification and a decrease in poorly aerated lung volumes (< -435 HU, Hounsfield units) in the absence of club cells, indicating more diffuse tissue damage, though with significantly greater septal thickening. Gene expression analysis shows a less inflammatory lesion area. Irradiation after club cell repopulation eliminates these differences, suggesting repopulation by functional cells. By six months, all differences observed are faded. Club cells appear to modulate the early development of radiation-induced lesions, but it remains unclear how the lesion evolves in their presence.
This project also studies chronic depletion's impact on lung lesions and a fibrosis-resistant mouse strain. Single-cell RNA sequencing is ongoing for both models.

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