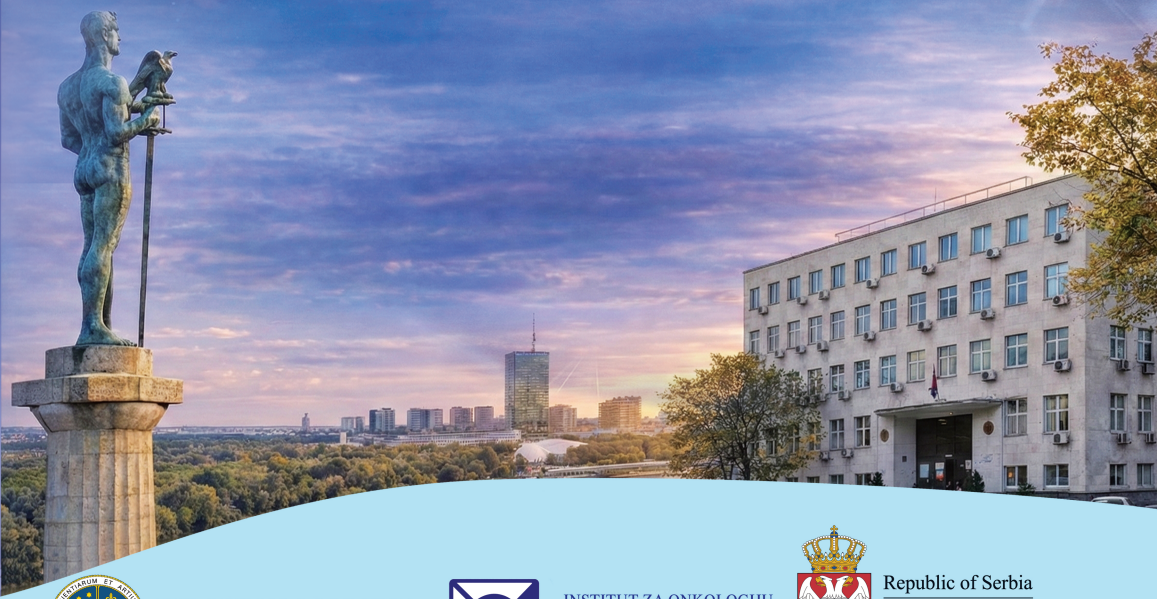
Belgrade
21–22 September 2026
Belgrade Art Hotel

1st Serbian International Congress “From Basic Radiobiology towards Radiogenomics”



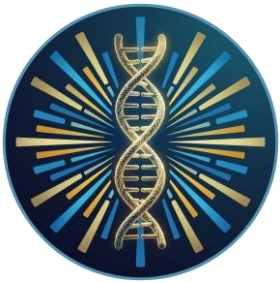
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INSTITUT ZA ONKOLOGIJU I RADIOLOGIJU SRBIJE
NATIONAL CANCER RESEARCH CENTER

Republic of Serbia
MINISTRY OF SCIENCE, TECHNOLOGICAL DEVELOPMENT AND INNOVATION

1st Serbian International Congress

“From Basic Radiobiology towards Radiogenomics”



ABSTRACT BOOK

Belgrade on 21–22 September 2026.

The Institute for Oncology and Radiology of Serbia (IORS),
in cooperation with the
European Academy of Sciences and Arts (EASA)
Belgrade Art Hotel (Radisson)

Letter of Welcome

Dear Colleagues,

On behalf of the Organizing Committee, it is my great pleasure to welcome you to the 1st Serbian International Congress "From Basic Radiobiology towards Radiogenomics", held in Belgrade, Serbia, on 21–22 September 2026.

Organized by the Institute for Oncology and Radiology of Serbia under the auspices of the European Academy of Sciences and Arts (EASA), this inaugural Congress provides a forum for scientists, clinicians and researchers to exchange knowledge and discuss current developments in radiobiology, radiogenomics, radiation oncology, proton therapy, artificial intelligence and translational cancer research.

The scientific program reflects the multidisciplinary nature of contemporary radiation research, bringing together internationally recognized experts and emerging investigators to share recent findings and promote collaboration between basic, translational and clinical sciences.

We are grateful to all invited speakers, authors, reviewers, sponsors and participants for their contribution to the success of this Congress. We also acknowledge the support of our institutional partners and collaborators, whose commitment has made this meeting possible.

We hope that the discussions initiated during these two days will encourage new collaborations and contribute to further advances in radiation research and precision oncology.

Welcome to Belgrade, and thank you for being part of this first edition.

Tatjana Stanojković, research professor
Chair of the Organising Committee



Letter of Welcome

Dear Colleagues,

It is my great honor to welcome you to the 1st Serbian International Congress "From Basic Radiobiology towards Radiogenomics."The European Academy of Sciences and Arts (EASA) is dedicated to promoting scientific excellence through interdisciplinary research and international collaboration, building bridges between disciplines and nations. The scientific vision of this Congress reflects these values by bringing together experts from fundamental and clinical sciences to address one of the most rapidly evolving areas of modern oncology. The integration of radiobiology with radiogenomics is transforming precision radiation oncology. Advances in molecular biology, genomics, biomarker discovery, artificial intelligence, and advanced radiotherapy including proton/hadron therapy, are improving our understanding of individual radiation response and creating new opportunities for personalized cancer treatment. Translating these scientific advances into clinical practice requires close collaboration between basic scientists, clinicians, medical physicists, and computational researchers. The participation of distinguished speakers from across Europe highlights the international significance of this meeting and the importance of multidisciplinary cooperation in addressing the complex biological challenges of cancer. This Congress represents an important step toward establishing a sustainable European platform for collaboration in radiobiology and radiogenomics, strengthening scientific partnerships in Serbia, South-East Europe, and the wider European Research Area. The members of EASA's Class II from Serbia have made valuable contributions to the Academy's scientific activities, and I am confident that this Congress will mark the beginning of a lasting partnership between the European Academy of Sciences and Arts and the Serbian scientific community. I wish you a successful Congress, inspiring discussions, productive collaborations, and scientific achievements that will contribute to the continued advancement of precision oncology.

Thank you,
Professor. Dušan Šuput, MD., PhD
Dean Class Medicine
European Academy of Sciences and Arts



CME accreditation

The international congress “From Basic Radiobiology towards Radiogenomics,” organized by the Institute for Oncology and Radiology of Serbia, serves as a continuing education program focused on the latest advancements in radiobiology, radiogenomics, proton therapy, and the use of machine learning in radiation oncology.

The congress has received accreditation from the Serbian Medical Chamber (Srpska lekarska komora) and the Health Council of Serbia (Zdravstveni savet Srbije) as an international event, under accreditation number A-1-1005/26. The congress has been accredited as a continuing medical education event for physicians, pharmacists, biochemists, molecular biologists, and physicists. Attendance at the congress carries 10 CME credits for participants and 15 CME credits for invited speakers.

The program aims to integrate cutting-edge knowledge across these disciplines, emphasizing the translation of scientific research into clinical applications. It brings together leading experts in molecular oncology, radiobiology, epidemiology, biomedical engineering, and artificial intelligence, providing participants with a thorough understanding of current trends and future prospects in the field.

One thematic session will focus on radiogenomics, exploring the genetic and multi-omics factors that influence radiosensitivity and radioresistance. Speakers will discuss modern models of genetic predisposition, epidemiological techniques, and the development of predictive biomarkers for the personalization of radiotherapy. This segment is aligned with current guidelines for translating radiomics and molecular markers into clinically applicable tests—an essential step toward precision oncology.

The second session will cover the biological effects of radiation on normal tissues, including DNA damage mechanisms, inflammatory responses, and models of genotoxicity. Significant emphasis will be placed on radioprotective strategies and their potential clinical applications. This portion of the program connects foundational radiobiological processes with practical challenges in radiotherapy planning and delivery.

The third thematic session will showcase the application of machine learning in radiobiology and radiogenomics. Presentations will focus on models for predicting treatment responses, integrating large biomedical datasets, and optimizing radiotherapy protocols. Particular attention will be given to model

interpretability and their possible clinical uses, reflecting contemporary principles for developing reliable AI tools.

The fourth thematic session highlights Serbia's research capabilities in radiobiology, radiogenomics, and oncology. Findings from national projects, international collaborations, and translational studies will be showcased to promote the growth of the local scientific community. This segment seeks to foster networking and stimulate new research initiatives.

The fifth session will explore proton therapy and its advanced therapeutic avenues, including the radiobiological nuances of protons and heavy ions, relative biological effectiveness (RBE), and clinical experiences from leading European centers. Participants will gain insights into current indications, controversies, limitations, and innovations in heavy-particle therapy, especially regarding the advantages of protons in treating complex anatomical sites and various tumor pathohistological types.

Through these five thematic sessions, the program equips participants with the advanced knowledge and skills crucial for modern oncology practice, translational research, and the development of personalized therapeutic strategies



Acknowledgments

The Organizing Committee for the 1st Serbian International Congress titled "From Basic Radiobiology towards Radiogenomics" would like to express our appreciation for the ongoing assistance from the Institute for Oncology and Radiology of Serbia and the European Academy of Sciences and Arts.

We are also deeply thankful to the following sponsors for their financial backing of the congress:

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Program

Day 1	
08:00 – 08:15	Opening Ceremony ***Ass. Prof. Milan Žegarac***, Director of the Institute for Oncology and Radiology of Serbia (or representative) Minister of Science, Technological Development, and Innovation of the Republic of Serbia (or representative) ***Prof. Dušan Šuput***, Dean Class II European Academy of Sciences and Arts, Salzburg, Austria, and Professor Faculty of Medicine, UL, Ljubljana, Slovenia Opening welcoming speech: EASA and Challenges of the future of medicine
Session 1: Radiogenomics – Clinical Perspectives Chairs: Alexandros Georgakilas and Tatjana Stanojković	
08:15 – 08:45	***Prof. dr Anca-Ligia Grosu,*** *FACR Director Department of Radiation Oncology, University of Freiburg, Germany* Title: Peripheral immune response after WBRT with and without hippocampal avoidance
08:45 – 09:15	***Prof. dr Catharine West,*** *Professor of Radiation Biology, University of Manchester* Title: Omic approaches for discovering biomarkers of radiotherapy response
09:15 – 09:45	***Dr Ana Vega,*** *PhD, Hospital Clínico Santiago de Compostela 15706, Santiago de Compostela, A Coruña, Spain* Title: Clinical Impact of Genetic Variants on Radiotherapy Toxicity and Treatment Response
09:45 – 10:25	Discussion
10:25 – 10:40	Coffee break

Session 2: Radiobiology - Effects of Radiation on Normal Tissue Chairs: Marina Nikitović and Ester Orlandi	
10:40 – 11:10	***Prof. dr Barbara Jereczek-Fossa,*** *Chair of Dept. of Radiation Oncology, IEO, Full Professor of Radiation Oncology, University of Milan, Italy, President Elect of the European Society for Radiotherapy and Oncology (ESTRO)* Title: The potential of radiation oncology: from biological insights to technological innovation-ESTRO perspective
11:10 – 11:40	***Prof. dr Maja Čemažar,*** *Head of the Research and Education Division at the Ljubljana Institute of Oncology and Head of the Department of Experimental Oncology; Full professor at the Faculty of Health Sciences, University of Primorska* Title: Electroporation-Based Therapies Combined with Radiotherapy
11:40 – 12:10	***Prof. dr. Rob P Coppes,*** *Department of Biomedical Sciences, FB30 Department of Radiation Oncology, University Medical Center Groningen, University of Groningen, Netherlands* Title: Difference in inflammatory and regenerative responses in normal tissue-derived organoids
12:10 – 12:40	***Prof. dr Igor Belyaev,*** *Head of Department of Radiobiology, at Biomedical Research Center Slovak Academy of Sciences, Bratislava* Title: Integrated Cytogenetic and Molecular Markers of Radiation-Induced Genetic Instability: From Biodosimetry to Radiation Risk Assessment
12:40 – 13:10	***Prof. dr Alexandros Georgakilas,*** *PhD, Professor of Radiation Biophysics, School of Applied Mathematical and Physical Sciences National Technical University of Athens (NTUA), Greece*

	Title: From DNA Damage Complexity to Radiogenomic Signatures: Mechanistic Determinants of Cellular Fate and Therapy Response
13:10 – 13:40	Discussion
13:40 – 14:30	Lunch
Session 3: Machine Learning in Radiobiology and Radiogenomics Chairs: Igor Belyaev and Niklas Wahl	
14:30 – 15:00	***Prof. dr Habib Zaidi,*** *Head of PET Instrumentation and Neuroimaging Laboratory (PINLab) Geneva University Hospital* Title: The promise of artificial intelligence in computational nuclear oncology and theranostic digital twins
15:00 – 15:30	***Dr. Tiziana Rancati,*** *PhD, Senior Researcher, CMON Lab Data Science Unit Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy* Title: From population constraints to personalized risk: a bio-physical framework for NTCP modelling and iso-side-effect planning
15:30 – 16:10	Discussion
16:10 – 16:20	Industry-Supported Lecture
16:20 – 16:30	Industry-Supported Lecture
16:30 – 17:30	Visit to the Clinic for Radiation Oncology - IORS
Day 2	
Session 4: Research in Serbia - Experiences and ongoing collaborative research Chairs: Tatjana Stanojković and Marina Nikitović	
08:00 – 08:30	***Asst. Prof. Aleksandar Tomašević****, MD, PhD, Faculty of Medicine, University of Belgrade, Head of the Clinic for Radiotherapy, Institute for Oncology and Radiology of Serbia*



	Title: The Institute for Oncology and Radiology of Serbia: Radiotherapy Clinic Overview and Clinical Experience
08:30 – 09:00	***Prof. dr Marina Nikitović,*** *MD, PhD, Full Professor of Oncology and Radiology, Chairman of the Expert Committee for Oncology, Republic of Serbia, Deputy Director for Research and Education, Institute for Oncology and Radiology of Serbia* Title: Current Aspects of Radiobiology in Institute for Oncology and Radiology of Serbia - road to RadExIORSBoost
09:00 – 09:30	***Asst. Prof. Aleksandar Stepanović,*** *MD, PhD, Research Associate, Faculty of Medicine, University of Belgrade, Institute for Oncology and Radiology of Serbia* Title: Decoding Radiotherapy Response in Brain Tumors: The Role of MicroRNAs
09:30 – 10:00	***Dr. sc. med. Katarina Kopčalić,*** *MD, PhD, Research Associate, Institute for Oncology and Radiology of Serbia* Title: Biomarkers as a predictor of radiotoxicity in prostate cancer patients
10:00 – 10:30	***Asst. Prof. Mladen Marinković,*** *MD, PhD, Research Associate, Faculty of Medicine, University of Belgrade, Institute for Oncology and Radiology of Serbia* Title: Radiobiology of rectal cancer - insights from the STEPUPIORS Horizon Europe project
10:30 – 11:00	Discussion
11:00 – 11:15	Coffee break
Session 5: Proton Therapy Chairs: Aleksandar Stepanović and Igor Belyaev	
11:15 – 11:45	***Dr. Ester Orlandi****, Head of Clinical Department of the CNAO Foundation (National Center of Oncological Hadrontherapy) of Pavia, Italy*

	Title: Advancing precision in particle therapy: from biomarker-driven trials to enhanced quality of life
11:45 – 12:15	***Dr. rer. Nat. Niklas Wahl**, PhD, Ruprecht-Karls-Universität Heidelberg, Germany, conducted in the Department of Medical Physics in Radiation Oncology, German Cancer Research Center – DKFZ* Title: Towards the Direct Integration of Multimodal Outcome Prediction Models
12:15 – 12:45	***Prof. dr Cai Grau,** Head of Research, Heading the interdisciplinary radiotherapy research at the Danish Center for Particle Therapy (DCPT) at Aarhus University Hospital in Aarhus, Denmark* Title: Proton Therapy towards 2030: Progress, Challenges, and Future Directions
12:45 – 13:25	Discussion
13:25 – 13:35	Industry-Supported Lecture
13:35 – 13:45	Industry-Supported Lecture
13:45 – 14:00	Closing remarks
14:00	Lunch

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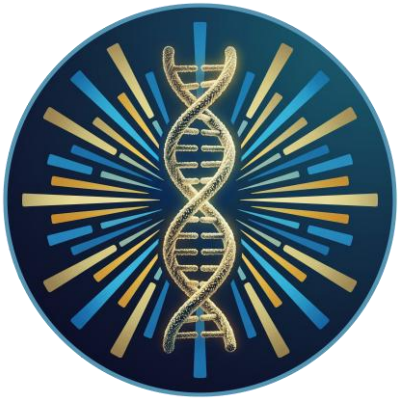
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Session 1: Radiogenomics – Clinical Perspectives



Peripheral Immune Response after WBRT with and without Hippocampal Avoidance (HA)

Anca-L. Grosu

Department of Radiation Oncology, University Medical Center Freiburg, Freiburg, Germany

Hippocampus-avoidance whole-brain radiotherapy (HA-WBRT) improves neurocognitive outcomes in patients with multiple brain metastases (HIPPORAD-Study). We investigated whether sparing the hippocampus also influences the systemic immune response.

This prospective secondary analysis of the randomized HIPPORAD trial compared HA-WBRT plus simultaneous integrated boost (SIB) with conventional WBRT plus SIB in patients with 4–10 brain metastases. Peripheral blood mononuclear cells were collected longitudinally at baseline, at the end of radiotherapy, 6 weeks, and 3 months post-treatment. Multiparameter flow cytometry was performed to assess T cell and NK/NKT cell subsets, proliferation, exhaustion markers, and cytokine production.

Overall survival and progression-free survival did not significantly differ between treatment arms. Relative T cell frequencies remained stable, although transient reductions in absolute $CD4^+$ and $CD8^+$ T cell counts were observed at treatment completion.

HA-WBRT was associated with increased IFN-γ production in $CD8^+$ T cells at the end of radiotherapy. Moreover, NK and NKT cells in the HA-WBRT group showed elevated IFN-γ, TNF-α, and granzyme B expression during follow-up, suggesting enhanced cytotoxic activity. In contrast, WBRT was associated with reduced NK cell frequencies and diminished TNF-α expression at later time points. T cells in both groups predominantly exhibited a $PD\text{-}1^+$ non-terminally exhausted phenotype.

Hippocampal sparing during dose-escalated whole-brain radiotherapy may modestly enhance systemic immune functionality without compromising tumor control.

Omic Approaches for Discovering Biomarkers of Radiotherapy Response

Catharine West

Division of Cancer Sciences, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, United Kingdom

Omic approaches (genomics, transcriptomics, proteomics) underpin radiotherapy biomarker research. Radiogenomic studies identified germline genetic variants that support the use of DNA samples (blood, saliva) to derive polygenic risk scores to predict the risks of radiotherapy toxicity. The work was supported by international collaboration via the Radiogenomics and REQUITE Consortiums to enable genome-wide association studies in large radiotherapy cohorts. Transcriptomic studies identified molecular signatures to assess radiosensitivity and predict benefit from combining radiotherapy with other interventions. While less widely studied, new proteomic methods, such as nano-proteomic profiling of plasma proteins, enable the identification of low-abundance biomarkers of radiotherapy response. Next steps in omic discovery programmes in radiotherapy must focus on clinical translation and evaluate the use of biomarkers in interventional studies. There is also a need to engage non-academic partners at an early stage to redress our community's limited track record in successful commercial translation.

Clinical Impact of Genetic Variants on Radiotherapy Toxicity and Treatment Response

Ana Vega[1,2]

[1] Genetics in Cancer and Rare Disease Group, Galician Public Foundation of Genomic Medicine, Santiago de Compostela, Spain;

[2] Health Research Institute of Santiago de Compostela (IDIS), Santiago de Compostela, Spain

Interindividual variability in radiotherapy toxicity and tumour response has long suggested an underlying genetic component to clinical radiosensitivity. Over the past two decades, radiogenomics has sought to identify inherited genetic variants associated with radiation response, initially through candidate gene studies focused on DNA damage response and repair pathways, and subsequently through genome-wide association studies (GWAS). These efforts have provided proof-of-principle evidence that common genetic variation contributes to normal tissue toxicity and treatment outcomes. Large collaborative initiatives such as the Radiogenomics Consortium have enabled validation of reproducible associations, including the *ATM* rs1801516 variant, and have established the polygenic nature of radiotherapy response. Recent advances in germline genetic testing and next-generation sequencing have shifted attention towards rare pathogenic variants in DNA damage response and repair (DDR) genes, including *BRCA1*, *BRCA2*, and *ATM*. These variants are increasingly recognised as determinants of cancer biology and treatment outcomes, although their impact on radiotherapy efficacy and toxicity remains poorly defined. Given the central role of DNA repair in radiation response and the well-established radiosensitivity observed in inherited DNA repair syndromes, there is a strong biological rationale to investigate their clinical relevance in patients receiving definitive radiotherapy. Emerging data from high-risk prostate cancer cohorts treated with definitive radiotherapy will be presented, further supporting the hypothesis that pathogenic DDR variants may define distinct radiosensitivity phenotypes with potential implications for treatment efficacy, toxicity risk, and clinical decision-making.

Understanding how inherited defects in DNA repair pathways influence both treatment efficacy and toxicity may enable biologically informed patient stratification, personalised treatment selection, and more precise radiotherapy delivery, moving the field beyond traditional radiogenomics towards clinically actionable precision radiation oncology.

Session 2: Radiobiology - Effects of Radiation on Normal Tissue



The Potential of Radiation Oncology: From Biological Insights to Technological Innovation – An ESTRO Perspective

Barbara Alicja Jereczek-Fossa[1,2]

[1] Department of Oncology and Hemato-Oncology, University of Milan, Milan, Italy;

[2] Division of Radiation Oncology, European Institute of Oncology IRCCS, Milan, Italy

Radiation oncology is evolving through the integration of biological knowledge and technological innovation, strengthening its role in precision cancer care. Advances in tumor biology and normal tissue responses are guiding personalized radiotherapy strategies, while modern technologies enable their accurate clinical translation. Image-guided, adaptive, and stereotactic techniques, together with particle therapy, enable tailored dose escalation or de-escalation, optimizing tumor control and minimizing side effects. Translational research also supports the rational combination of radiotherapy with systemic therapies, including immunotherapy. From an ESTRO perspective, translational research is key to bridging science and clinical practice, fostering multidisciplinary collaboration, innovation, and sustainability. By aligning biology with technology, radiation oncology continues to deliver effective, safe, and patient-centred treatments across Europe and beyond.

Electroporation-Based Therapies Combined with Radiotherapy: Preclinical Studies in Murine Tumor Models

Maja Čemažar[1,2]

[1] Institute of Oncology Ljubljana, Ljubljana, Slovenia

[2] University of Primorska, Faculty of Health Sciences, Izola, Slovenia

Electroporation-based therapies are emerging as effective strategies for enhancing the local and systemic efficacy of cancer treatments. By transiently increasing cell membrane permeability, reversible electroporation has been used in electrochemotherapy (ECT), where electroporation is used for enhanced uptake of chemotherapeutic drugs and in gene electrotransfer (GET), where electroporation is used to facilitate the uptake of nucleic acids leading to either the expression of therapeutic proteins or gene silencing effect. Several preclinical studies have addressed the potential of combining ECT or GET with radiotherapy. In several murine tumor models, the combination of ECT with single or fractionated radiotherapy led to significantly improved therapeutic outcomes. An even more pronounced therapeutic effect was obtained when radiotherapy was combined with intratumoral interleukin-12 (IL-12) GET. Furthermore, the abscopal effect was achieved when IL-12 GET was performed intramuscularly. In addition, GET of antiangiogenic gene therapy has been investigated in combination with radiotherapy. Targeting tumor vasculature through GET sensitizes tumors to irradiation by impairing vasculature and modifying the tumor microenvironment.

Collectively, studies performed in different tumor models showed that the combinations can lead to improved local and systemic tumor response, partly due to complementary mechanisms of action including direct cytotoxicity, vascular disruption, and enhanced immunogenic cell death.

Differences in Inflammatory and Regenerative Responses in Normal Tissue-Derived Organoids

Rob Coppes

Department of Radiation Oncology and Biomedical Sciences, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

Radiotherapy inevitably involves co-irradiation (IR) of normal tissue, often leading to side effects that limit the dose to the tumour and/or reduce the quality of life for cancer survivors. The response of normal tissues to IR mainly depends on the survival and regenerative potential of tissue stem cells and is influenced by inflammatory processes, vascular damage, altered neural innervation, and fibrosis. In fact, transplanting tissue-specific stem cells has been shown to restore tissue homeostasis and prevent late radiation effects. However, radiation-induced senescence, fibrosis, and chronic inflammation can disrupt the stem cell niche, creating an unfavourable environment for the regenerative capacity of tissue stem cells. Recently, we have developed several methods for culturing murine and patient-specific tissue-like organoids. These organoids include all glandular lineages, can self-renew extensively, and, upon transplantation, restore glandular function—thereby facilitating the study of radiation responses. Using these models and approaches, including single-cell RNA sequencing and replating potential, we demonstrated that proton IR induces an increased antiviral immune response, inflammation, and regenerative response compared to photon IR. Furthermore, this response varies across different glandular tissues. The data suggest that an additional component of protons may support normal tissue regeneration, but irradiation in general may also influence carcinogenesis.

Supported by the Dutch Cancer Society (KWF, grant No. 10650 and 12092) and The Netherlands Organisation for Health Research and Development (ZonMw, Grant nrs. 11.600.1023 and 40-43600-98-14003)

Integrated Cytogenetic and Molecular Markers of Radiation-Induced Genetic Instability: From Biodosimetry to Radiation Risk Assessment

Belyaev Igor[1], Durdik Matus, Gulati Sachin, Jakl Lukas, Kochanova Dominika, Kosik Pavol, Markova Eva, Martinka Karol, Skorvaga Milan, Vigasova Katarina, Vinnikov Volodymyr, Zastko Lucian

[1] Department of Radiobiology, Cancer Research Institute, Biomedical Research Centre, Slovak Academy of Sciences, Bratislava, Slovak Republic

Accurate assessment of radiation effects requires integration of molecular and cytogenetic endpoints across exposure scenarios. We present a comprehensive framework linking DNA damage response (DDR), chromosomal instability, and leukemogenic risk for applications in biodosimetry, personalized radiotherapy, and occupational radiation protection.

Low-dose irradiation induced γH2AX responses comparable to extrapolated high-dose data, whereas prolonged persistence of 53BP1 foci revealed altered DSB repair dynamics not detectable by γH2AX alone. Imaging flow cytometry enhanced the sensitivity of γH2AX foci and pan-staining detection, improving discrimination of early apoptotic and DDR-related events. Chronic low-dose exposure in radiological workers was associated with increased chromosomal aberrations and MLL gene amplification, demonstrating cumulative genomic instability beyond transient DDR markers.

We established and validated joint dose–response curves combining dicentrics and interphase cell survival in human lymphocytes. Linear–quadratic modeling and the exponential parameter D_0 enabled accurate reconstruction of uniform and partial-body exposures, strengthening cytogenetic biodosimetry for megavoltage photon irradiation.

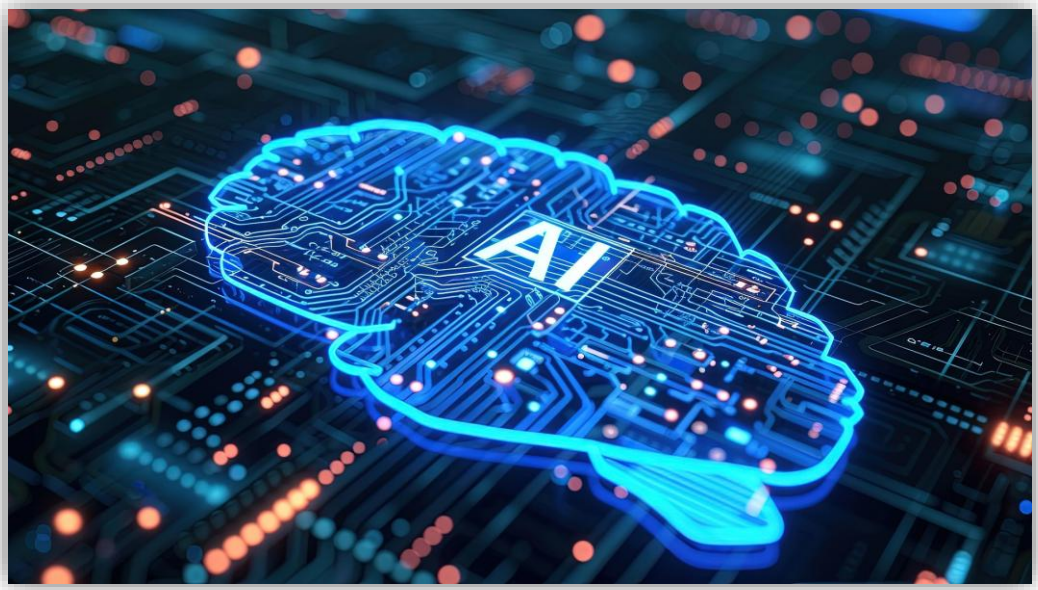
In hematopoietic stem/progenitor cells, low-dose radiation induced BCR-ABL at very low frequency without selective enrichment of AML-related fusion genes, refining current concepts of radiation-induced leukemogenesis. Increased γH2AX/53BP1 foci and EDA2R upregulation identified molecular signatures of individual radiosensitivity.
Taken together, these results define an integrated dose–response platform bridging mechanistic radiobiology and applied radiation risk assessment.

From DNA Damage Complexity to Radiogenomic Signatures: Mechanistic Determinants of Cellular Fate and Therapy Response

Alexandros Georgakilas
Department of Physics, School of Applied Mathematical and Physical Sciences, National Technical University of Athens, Athens, Greece

Advances in radiation biology have revealed that biological outcomes are not determined solely by dose, but also by damage complexity, replication stress dynamics, and the cellular DNA damage response (DDR). This lecture will discuss how clustered DNA lesions, chromatin context, and persistent DDR signaling shape genomic instability, senescence, and immune modulation. Particular emphasis will be placed on the mechanistic transition from classical radiobiology endpoints to radiogenomic profiling, integrating molecular biomarkers, transcriptomic signatures, and systems-level modeling. By linking physical track structure to genomic response patterns, radiogenomics provides a framework for personalized radiation risk assessment and therapy optimization. Understanding these mechanistic layers is essential for improving the therapeutic ratio and predicting normal tissue and tumor responses.

Session 3: Machine Learning in Radiobiology and Radiogenomics



The Promise of Artificial Intelligence in Computational Nuclear Oncology and Theranostic Digital Twins

Habib Zaidi[1,2]

[1] Division of Nuclear Medicine and Molecular Imaging, Geneva University Hospital, Geneva, Switzerland;

[2] Faculty of Medicine, University of Geneva, Geneva, Switzerland

The role of multimodal precision imaging in the management of cancer patients is well-established. A new concept in the field of radiopharmaceutical therapies (RPTs) for cancer, referred to as computational nuclear oncology, involving the use of theranostic digital twins (TDTs) and in silico virtual clinical trials, which is the central topic of this talk, has recently emerged and is expected to result in a major breakthrough in theranostics. Computational models, such as DTs—virtual patient replicas created from but not limited to imaging and clinical data, have emerged as tools to generate synthetic data and simulate radiopharmaceutical kinetics to guide in silico treatment planning. This talk presents the fundamental principles and major applications of artificial intelligence (AI), in particular deep learning approaches, in multimodality medical imaging and computational modeling in theranostics. It will inform the audience about a series of advanced developments recently carried out at the PET Instrumentation and Neuroimaging Laboratory of Geneva University Hospital and other active research groups. Novel deep learning techniques are revolutionizing clinical practice and are now offering unique capabilities to the clinical medical imaging community. Future opportunities and challenges facing the adoption of deep learning approaches and their role in molecular imaging research are also addressed.

From Population Constraints to Personalized Risk: A Biophysical Framework for NTCP Modelling and Iso-Side-Effect Planning

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The transition toward precision radiotherapy requires moving away from population-based dose constraints and toward personalized risk prediction models. The main approach involves a two-part strategy: pinpointing the exact biological scale of radiation response and integrating it with comprehensive multi-omic profiling of the patient's baseline condition. A critical component of modern modeling is the transition from whole-organ and single-organ analysis to a more granular understanding of the biological entities at risk. This involves identifying whether clinical toxicity is driven by the organ as a whole, specific, organ subunits, or the complex cooperation between multiple organ systems. In parallel, the framework seeks to define valuable dosimetric descriptors that go beyond simple volume thresholds and capture synergistic effects of dose distribution that traditional metrics often overlook. The predictive value of these models is anchored in the systematic integration of the patient's biological profile, combining the purely clinical variables with high-dimensional biological modifiers. Central to this is the role of genetics and transcriptomics in identifying germline variations and dynamic gene expression patterns that govern DNA repair and pro-inflammatory pathways. Furthermore, the framework can incorporate the systemic influence of the microbiota-mediated radiation response. These molecular layers are complemented by imaging, which can provide additional biological information. This integrated biophysical modeling enables a superior approach to treatment optimization, facilitating "iso-side-effect" planning. In this context, treatment intensity is dynamically adjusted to maximize therapeutic gain while strictly adhering to a personalized risk profile.

Session 4: Research in Serbia - Experiences and ongoing collaborative research



The Institute for Oncology and Radiology of Serbia: Radiotherapy Clinic Overview and Clinical Experience

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Institute for Oncology and Radiology of Serbia (IORS) is a leading healthcare and scientific institution in Serbia dedicated to the diagnosis, treatment, and research of malignant diseases. Located in Belgrade, the Institute plays a key role in the national oncology care system and serves as a referral center for the most complex cases across the country. The Institute's activities include modern diagnostic methods such as radiology, pathohistology, and molecular diagnostics, as well as various treatment approaches, including surgery, radiotherapy, and chemotherapy. Approximately 4,500 patients receive radiotherapy annually at IORS. Radiotherapy represents one of the core components of modern cancer treatment at the Institute. The Department of Radiotherapy operates eight advanced linear accelerators and uses sophisticated treatment planning systems, enabling the application of state-of-the-art techniques such as IMRT, VMAT, IGRT, total body irradiation (TBI), as well as modern MRI-based brachytherapy. These techniques allow highly precise tumor irradiation while maximizing sparing surrounding healthy tissue, resulting in improved disease control, higher cure rates, and reduced radiation-induced side effects. A multidisciplinary team of physicians, medical physicists, and radiologic technologists plans and delivers individualized treatment for each patient. Continuous education and adherence to modern standards ensure high-quality care and improved treatment outcomes. The Institute is also actively engaged in scientific research, participates in international studies, and continuously works on improving treatment standards. Education and training of healthcare professionals remain an important part of its mission through specializations, courses, and professional meetings.

Current Aspects of Radiobiology at the Institute for Oncology and Radiology of Serbia – Road to RadExIORSBoost

Marina Nikitović
Institute for Oncology and Radiology of Serbia

Radiobiology has become necessary for advancing personalized radiotherapy. At the Institute for Oncology and Radiology of Serbia, translational radiobiology research has been systematically developed since 2016, focusing on inflammatory mediators, cytokine expression, microRNA profiles, and genetic variants associated with radiotoxicity. RadExIORSBoost represents the next developmental stage of this program. RadExIORSBoost as a comprehensive platform aims to strengthen the institutional capacity for predictive radiobiology by integrating clinical and radiation oncology and molecular research. Within the Horizon Europe framework, members of the radiobiology team, radiation oncologists and experimental oncology researchers participate in specialized workshops and hands-on training hosted by partner institutions including Heidelberg University, Mannheim Medical Faculty, Department of Radiation Oncology, Germany; Medical University of Vienna, Department of Radiotherapy, Austria; Institute of Oncology Ljubljana, Slovenia; University of Leicester, United Kingdom. These activities enhance methodological expertise, support the adoption of advanced analytical approaches, and accelerate the translation of radiobiological findings into clinical decision-making. Through RadExIORSBoost, the Institute is building a sustainable pathway towards the implementation of validated biomarkers in routine clinical practice, improving patient selection, minimizing toxicity, and shaping the future of personalized radiotherapy in Serbia.

Decoding Radiotherapy Response in Brain Tumors: The Role of MicroRNAs

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MicroRNAs play a significant role in glioblastoma. They are involved in tumor growth, biological behavior, and disease progression. MicroRNA-10b and miR-21 are known as oncogenic microRNAs, and are frequently overexpressed in glioblastoma. In contrast, microRNA-34a is a significant tumor suppressor and is often downregulated in glioblastoma. Previous studies have shown that overexpression of miR-10b and miR-21 promotes tumor invasion of glioblastoma cells and suppresses apoptosis. In addition, these microRNAs have been shown to affect radioresistance and chemoresistance in patients with glioblastoma. Ionizing radiation further modifies miRNA expression, influencing major pathways such as EGFR/PI3K/AKT and p53-mediated DNA damage response. Because these molecules reflect dynamic cellular adaptation under treatment pressure, microRNAs have emerged not only as potential predictors of radiosensitivity and early toxicity but also as possible prognostic markers linked to disease course. MicroRNAs-10b/21/34a are not limited to tumor cells only, as they regulate different fundamental cellular processes such as apoptosis, DNA repair, oxidative stress responses and inflammatory signaling. These same processes are key to the development of toxicity. The question arises whether these microRNAs associated with tumor aggressiveness may also reflect susceptibility to toxicity. In our prospective study we observed that miR-34a showed a significant increase at the 15th fraction in patients who developed acute toxicity, while miR-10b was

associated with both toxicity occurrence and grade. MiR-21 correlated with toxicity grade. These findings are consistent with broader evidence that specific miRNA signatures may indicate treatment response and clinical outcome.

Biomarkers as Predictors of Radiotoxicity in Prostate Cancer Patients

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Radiotherapy plays a significant role in the multidisciplinary approach to treating prostate cancer patients. However, some of these patients may develop severe adverse effects after receiving radiotherapy that negatively affect their quality of life. Radiotoxicity may manifest in the lower gastrointestinal (GI) tract, or genitourinary (GU) tract. The probability of complications in normal tissue increases as the delivered radiation dose is increased. However, there are patients with satisfactory dosimetric parameters who develop radiation toxicity and vice versa. Prediction models that take into account additional parameters to identify patients most susceptible to developing toxicity may serve as essential factor toward a personalized radiotherapy. The factors that may affect radiosensitivity are individual, clinical characteristic, but the existing and known factors are not sufficient for understanding of the development of radiotoxicity. One of the challenges of modern radiotherapy is the identification of biological factors such as changes in cytokines levels and microRNA that can be connected with the occurrence of gastrointestinal and genitourinary radiotoxicity. A prospective cohort study of prostate cancer patients treated with radiotherapy (definitive and postoperative), without prior hormonal therapy was performed at Institute for Oncology and Radiology of Serbia from January 2016 to

February 2020. Level of cytokine such as IL-1β, IL-2, IL-6, IFN-γ i TGF- β1 in serum of patients before treatment, several times during treatment and one month after radiotherapy is determined. Also, there were determined changes levels of mi-R 21, mi-R 146a and mi-R 155 in peripheral mononuclear cells (PMNC). Given the need to identify novel biomarkers associated with individual normal tissue radiosensitivity and to provide the ability to predict the risk of developing radiation toxicity for each PC patients with the aim of personalized approaches to RT, we continued our research within Horizon Europe project RadexIORS boost in which we participate with our partner institutions from abroad. In this project we investigate Radiation-induced lymphocyte apoptosis assay (RILA), Radiation-induced DNA damage and DNA repair activity detection by comet assay and γ-H2AX assay, Transcriptome and miRNome analysis of peripheral blood mononuclear cells, in order to validation of biomarkers and models for predicting radiosensitivity with the aim of increasing the efficiency of radiotherapy and ensuring a better quality of life in prostate cancer patients undergoing radiotherapy.

Radiobiology of Rectal Cancer – Insights from the STEPUPIORS Horizon Europe Project

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Treatment for locally advanced rectal cancer (LARC) involves neoadjuvant chemoradiotherapy (nCRT) followed by surgical resection of the tumour. However, clinical response to nCRT varies from complete clinical response to a lack of response. The mission of the EU-funded STEPUPIORS project was to identify prognostic and predictive biomarkers in LARC by analysing the molecular profile of patients at diagnosis and during treatment using omics approaches. The obtained results contribute to evidence-based patient selection for tailored treatment protocols, thus minimising adverse effects and overall treatment costs, and improving patients' quality of life.

Session 5: Proton Therapy



Advancing Precision in Particle Therapy: From Biomarker-Driven Trials to Enhanced Quality of Life

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The landscape of particle therapy, particularly involving protons and carbon ions, is rapidly evolving towards a model of high-precision, biologically optimized oncology. This program outlines a multifaceted strategy designed to bridge the gap between technical innovation and clinical outcomes. A primary objective is the enhancement of quality of life for long-term survivors, shifting the focus from mere tumor control to the minimization of late-term toxicities and functional preservation. Central to this evolution is the development and validation of biomarkers, utilizing AI-driven approaches and radiomics to predict individual patient responses. These biological insights will be directly integrated into optimized strategies for particle therapy planning, ensuring maximum dose conformity and healthy tissue sparing. Furthermore, the implementation of biomarker-driven clinical trials will allow for more personalized treatment pathways. The research also explores the synergistic potential of combining particle therapy with immunotherapy, aiming to leverage the unique immunogenic effects of high-LET radiation. Finally, the programme seeks to advance Boron Neutron Capture Therapy (BNCT) as a selective cell-level treatment for complex cases. Together, these initiatives represent a comprehensive commitment to advancing the efficacy and safety of particle-based treatments.

Towards the Direct Integration of Multimodal Outcome Prediction Models in Photon and Proton Radiotherapy

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Recent advances in machine learning have enabled increasingly sophisticated outcome prediction models that combine imaging, clinical, and dosimetric information. These multimodal models hold promise for moving beyond surrogate dose-centric planning prescriptions and enabling treatment planning that directly optimizes clinically relevant outcomes such as toxicity and tumor control. However, integrating such models into the treatment planning process poses substantial challenges.

From a computational perspective, most machine learning models are not readily compatible with treatment planning optimization frameworks. Issues such as model differentiability, stability of gradients, and computational cost complicate their direct use within iterative optimization algorithms. Furthermore, the representation and curation of training data become critical: dose distributions, spatial dose metrics, and emerging dosiomic descriptors can strongly influence model behaviour and introduce biases if not handled carefully.

Beyond these computational aspects, fundamental biological uncertainties remain, especially for particle therapy. Proton and ion beams produce complex patterns of energy deposition and ionization clustering that are only partially captured by conventional dose-based metrics. This raises questions about how outcome models should incorporate physical and biological descriptors that better reflect the underlying radiation-matter interactions.

Proton Therapy towards 2030: Progress, Challenges, and Future Directions

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Proton therapy has attracted significant clinical interest because of its favorable dose distribution, which may improve tumor control while sparing surrounding healthy tissue. Since its introduction in 1954, more than 300,000 patients have been treated with ion beam therapy. Despite extensive technological progress, however, high-level clinical evidence demonstrating clear superiority of protons over photons remains limited. How will proton therapy evolve towards 2030?

Ongoing phase II–III trials are central to defining clinical benefit, particularly in emerging indications such as re-irradiation and select tumor sites including esophageal and head-and-neck cancers. In the United States, several randomized trials have been reported, but insurance-related biases continue to be of concern. In contrast, Europe has seen rapid growth, with the number of proton centers doubling between 2017 and 2020 and more than 30 interventional trials currently recruiting.

Looking ahead, progress in proton radiobiology, including improved relative biological effectiveness modelling, and the potential clinical adoption of FLASH and spatially fractionated proton therapies show promise for enhanced normal tissue sparing. Continued technological innovation, especially AI-driven planning, novel delivery techniques such as proton arc therapy, and large-scale prospective data registries, will be critical, although challenges in robustness, data governance, and long-term funding remain.

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