PIANOFORTE Partnership

European Partnership for Radiation Protection Research

Horizon-Euratom – 101061037

D6.5 – Information on projects selected for funding - call 2

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Reviewer(s): Members of the Executive Board

Work package / Task	**WP6**	**T6.2**
Deliverable nature:	**Report**	
Dissemination level: (Confidentiality)	**Public**	
Contractual delivery date:	**Month 29 | 31 October 2024**	
Actual delivery date:	**Month 32 | 16 January 2025**	
Version:	**1.0**	
Total number of pages:	**22**	
Keywords:	**open call, research projects, radiation protection, radiation-induced cancer, nuclear technologies, radiation therapy, emergency preparedness**	
Approved by the coordinator:	Month 32**| 17 January 2025**	
Submitted to EC by the coordinator:	Month 32**| 22 January 2025**	

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1. Second call for research projects

1.1 Call documents and research topics

Four research topics were approved during the General Assembly meeting held on Tuesday 5th December 2023 in Budapest, Hungary.

Topic 1: Developing a knowledge base for a better understanding of disease pathogenesis of ionising radiation-induced cancer to improve risk assessment, was retained from the list for the 1st call for proposals by the General Assembly decision also for the 2nd call as only one project was selected for funding under the 1st call (see Deliverable 6.4).
Three further research topics with the highest priority were proposed by WP2 (Task 2.1 Set up the research priorities for 3 open calls) based on the prioritisation procedure including ideas and reflecting needs and interests of POMs, research platforms, stakeholders and the PIANOFORTE Advisory Board:

Topic 2: Ensure readiness and scientific knowledge to support Environmental Impact Assessment and emergency preparedness and response for novel nuclear technologies;

Topic 3: Development of techniques and methods to go beyond effective dose in case of internal exposure following a nuclear or radiological emergency;

Topic 4: Implementation of new and optimized radiation therapy approaches for better targeting to protect healthy tissues better against detrimental effects of incising radiation.

1.2 Important dates

The second open call for proposals has been launched on Tuesday 23 April 2024. The deadline for submission was Tuesday 23 July 2024 (15:00 CEST). The second call for research projects has been accomplished during PIANOFORTE General Assembly meeting (Brussels, Belgium) on Wednesday 11 December 2024, where the results of the project proposals evaluation have been presented and selected research projects approved for funding.

1.3 Dissemination of information about the Call

All documents related to the 2nd call for research proposals, namely the Call text, Guidelines for applicants, Auxiliary Proposal Template, Auxiliary Financial Excel Sheet and CV template were published on PIANOFORTE website at the moment when the 2nd call for proposals has been launched on Tuesday 23 April 2024. The announcement was disseminated also in the News section on the PIANOFORTE web and by means of social media (LinkedIn and X network).

Administrative, legal and financial conditions of the PIANOFORTE Open Call 2024 were presented during the Call Infoday organised online on Tuesday, 14th May 2024. The presentation was followed by answering questions from the meeting participants. A video replay of the webinar was posted on the

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PIANOFORTE YouTube channel (https://www.youtube.com/watch?v=CDCkWT5bgjo) and the presentation from the online meeting (General information (PDF)) was made available on the PIANOFORTE website together with "Frequently Asked Questions" (mainly information about consortium composition and budget aspects in PDF format, version 13.05.2024 and addendum version 04.06.2024). Further, information about the Call has been disseminated also by means of social media (LinkedIn and X network).

1.4 Call evaluation procedure

The call evaluation procedure was identical as for the 1st call for proposals and is summarised in Figure 1. Project coordinators submitted full proposals before the call deadline on Tuesday 23 July 2024. As a whole, 22 proposals have been submitted. First, all projects were checked for their eligibility. Afterwards, the evaluation by independent international reviewers took place. The final scoring and ranking by the independent experts have been agreed during a Project Review Panel (PRP) meeting organised as online meeting by the National Center for Research and Development, Poland.

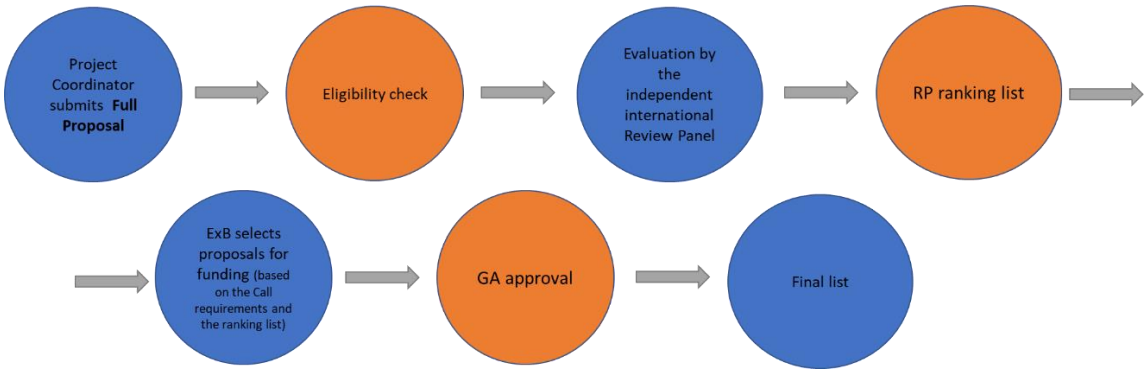

Figure 1: Scheme of the call evaluation procedure.

1.5 Evaluation criteria

Evaluation criteria were the same for all submitted project proposals with equal weight of each criterion:

- **Excellence (threshold 3/5)**

Clarity and pertinence of the project's objectives, and the extent to which the proposed work is ambitious, and goes beyond the state of the art.

Soundness of the proposed methodology, including the underlying concepts, models, assumptions, inter-disciplinary approaches, appropriate consideration of the gender dimension in research and innovation content, and the quality of open science practices, including sharing and management of research outputs and engagement of citizens, civil society and end-users where appropriate.

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- **Impact (threshold 3/5)**

Credibility of the pathways to achieve the expected outcomes and impacts specified in the work program, and the likely scale and significance of the contributions from the project.
Suitability and quality of the measures to maximize expected outcomes and impacts, as set out in the dissemination and exploitation plan, including communication activities.

- **Quality and efficiency of the implementation (threshold 3/5)**

Quality and effectiveness of the work plan, assessment of risks, and appropriateness of the effort assigned to work packages, and the resources overall.
Capacity and role of each participant, and the extent to which the consortium as a whole brings together the necessary expertise.

Reviewers were asked to evaluate the submitted proposals using whole numbers and halves based on the following evaluation scores:

Score	Grade	Definition
0	The proposal fails to address the criterion or cannot be assessed due to missing or incomplete information (unless the result of an 'obvious clerical error').	
1	Poor	The criterion is inadequately addressed, or there are serious inherent weaknesses.
2	Fair	The proposal broadly addresses the criterion, but there are significant weaknesses.
3	Good	The proposal addresses the criterion well, but with a number of shortcomings.
4	Very good	The proposal addresses the criterion very well, but with a small number of shortcomings.
5	Excellent	The proposal successfully addresses all relevant aspects of the criterion. Any shortcomings are minor.

1.6 Call results

In total, 22 project proposals were submitted within the 2nd call. One application was not eligible for evaluation due to formal reasons (not fulfilled conditions on budget limits) and 10 proposals were not recommended by PRP for funding (threshold not reached). The other 11 proposals were ranked according to their overall scores. Eight projects with the best evaluation scores fitted into the Call 2 total budget of 13 MEUR and were proposed to the PIANOFORTE General Assembly to be selected for funding. The second call for proposals has been successfully accomplished and 8 research projects were approved by the PIANOFORTE General Assembly on Wednesday 11 December in Brussels, Belgium.

The overall representation of countries in the submitted proposals is shown in Figure 2. It is obvious that the countries are also widely represented in the funded projects (Figure 3). In total, 95 entities (Beneficiaries, Affiliated entities, etc.) were involved in the submitted proposals and

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52 entities participate in 8 funded projects. Three of eight project coordinators are female (38 %).

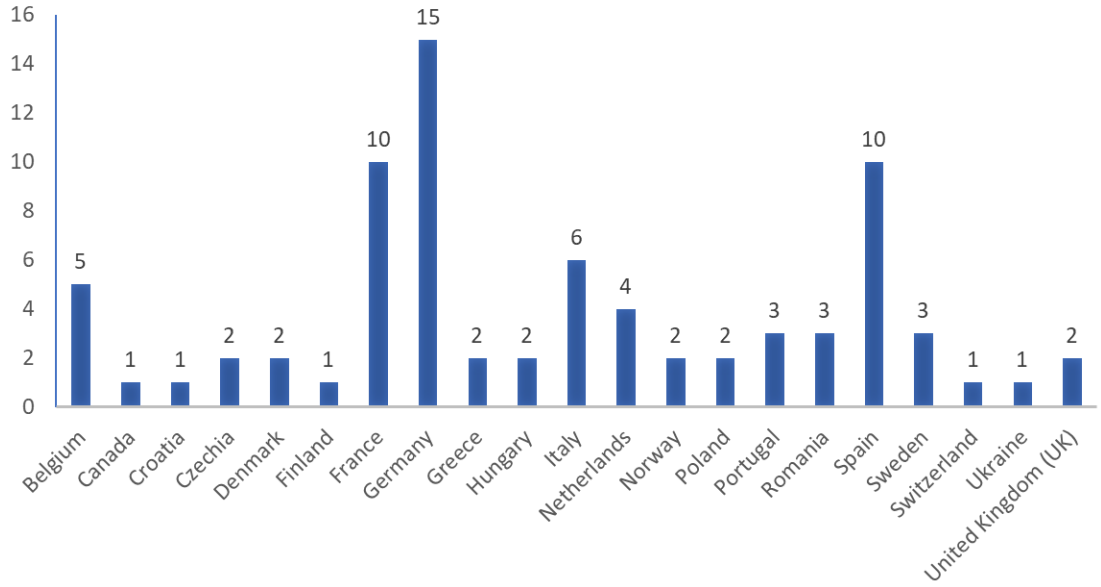

Figure 2: Country distribution in submitted proposals.

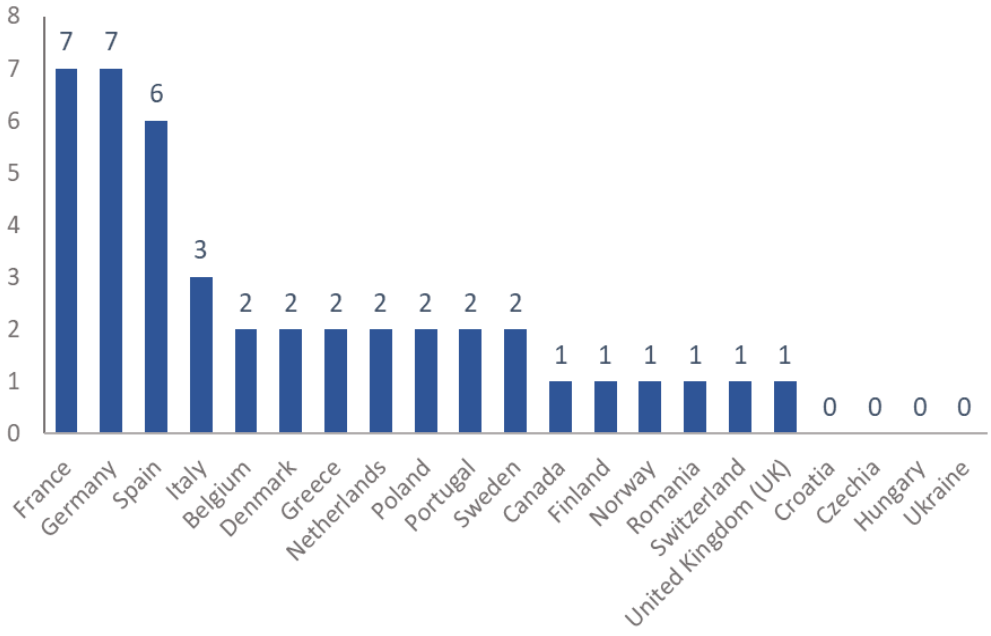

Figure 3: Country distribution in funded proposals.

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2. Selected research projects

The 8 projects approved for funding are:

Topic 1: Developing a knowledge base for a better understanding of disease pathogenesis of ionising radiation-induced cancer to improve risk assessment

CORNET - deCiphering the rOle of micRoenvironment after low-dose exposure for coloN carcinogenEsis and radiaTion risk
MIRAMARE - Mechanisms of the inversed relationship between menarche age and radiation-induced breast and endometrial cancer
UBT-Rad - Unraveling brain tumor formation after low dose irradiation exposure

Topic 2: Ensure readiness and scientific knowledge to support Environmental Impact Assessment and emergency preparedness and response for novel nuclear technologies

CATAPULT - Comprehensive Assessment and Preparedness for Emerging Nuclear Technologies
GIROSCOPE - Guidance for Innovative Reactor Off-Site Consequences, Planned and Emergency

Topic 3: Development of techniques and methods to go beyond effective dose in case of internal exposures following a nuclear or radiological emergency
No proposal selected

Topic 4: Implementation of new and optimized radiation therapy approaches for better targeting to protect healthy tissues better against detrimental effects of incising radiation

DOSELIA - Computing whole-body radiation dose distributions and subsequent cancer risks from modern radiotherapy techniques in paediatric patients
EMPATHY - Evaluation and optimization of proton arc therapy
KAYAC+ - Knowledge on outcome of adolescent and young adults with cancer

2.1 CORNET - deCiphering the rOle of micRoenvironment after low-dose exposure for coloN carcinogenEsis and radiaTion risk

Project coordinator: Prof. Siamak Haghdoost, University of Caen Normandy, ABTE laboratory, AE4651, France

Project partners (5):

- IFC CNR, Italy
- ASNR, France
- INSERM, France
- BfS, Federal Office for Radiation Protection, Germany
- CEA, France

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Abstract:

The risk of developing colon cancer (CC) has been associated with medical and environmental exposures to ionizing radiation (IR), as seen within the A-bomb survivor cohorts. While a mutational component of sporadic CC development has been extensively studied, less is known about the role of non-mutational processes, such as alterations in tissue microenvironment (TME). Whether low dose radiation (LDR) can induce changes in TME contributing to CC remains unknown. We hypothesize that LDR can alter secretion and the cargo of extracellular vesicles (EVs) produced by colonic epithelial and tissue-resident immune cells leading to the establishment of a pro-tumorigenic and immunosuppressive milieu driving promotion and progression of CC. Macrophages and tumor-initiating epithelial cells are the key players in this process. To test this hypothesis we will utilize an innovative systemic approach consisting of in vivo, in vitro and in silico studies. We will use the inducible KPC:APC mouse model of human CC which allows the study of CC in the intact immune system context. The mice will be exposed to sham, 25 or 250 mGy of X-rays and carcinogenesis will be assessed by histological analyses. Concurrently, we will characterise secreted EVs, their proteome and miRNAs. TME will further be characterized by immunohistology and spatial transcriptomics. The level of oxidative stress will be assessed. We will also generate colon organoids from the KPC:APC mouse to conduct mechanistic studies to understand the precise role of EVs in the communication between different cell types and how LDR affects those to promote neoplastic transformation. This will also be achieved by experimenting with co-cultured cells, isolated and/or manipulated EVs. Key findings will be validated in human-derived colon organoids and CC tumoroids to assess the transfer of knowledge to humans. Our in silico study will utilize a Systems Biology approach to carry out multimodal and multiomics data integration to refine mechanistic results. The last and the key part of the study will use Biologically-Based Risk Modeling to integrate existing knowledge on the association of LDR and colon cancer from human epidemiological studies with mechanistic knowledge and experimental results providing an ultimate validation of our results for human CC risk assessment following LDR exposures.

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Figure 4: CORNET project presentation at social media.

2.2 MIRAMARE - Mechanisms of the inversed relationship between menarche age and radiation-induced breast and endometrial cancer

Project coordinator: Prof. Andrzej Wojcik, Stockholm University, Department of Molecular Biosciences, the Wenner-Gren Institute, Sweden

Project partners (3):

- UCampania, Italy
- Silesian University of Technology, Poland
- CEA, France

Abstract:

The risk of radiogenic breast and endometrial cancer is highest following exposure around puberty. This is explained by the developing breast and endometrial tissue, driven by oestrogen. However, what is puzzling is that age at menarche (the first menstrual period) is a strong modifier of risk irrespective of the age at exposure: for any age at exposure the relative risk of radiation-induced breast and endometrial cancer is highest for women who had menarche at an early age. The increase of risk with decreasing menarche age is, on average, 24% for breast cancer and 31% for endometrial cancer per year of decreasing menarche age. The mechanisms are not understood but one factor responsible for early menarche age is obesity. It is possible that the inversed correlation between menarche age and

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cancer results from the interaction of obesity-related factors, sex hormones and radiation. The aim of MIRAMARE is to test this hypothesis in in vitro cell model systems, representing a novel approach. Normal breast and endometrial cell lines will be used as the breast and endometrium cell models. The impact of obesity will be studied by pre-treating irradiated cells with the obesity hormone leptin. The impact of sex hormones will be studied by pre-treating irradiated cells with oestrogen and progesterone. Combinations of the hormones will be tested. Cells will be exposed to radiation acutely and chronically. The rational for chronic radiation exposure is to test if the effect of obesity and sex hormones is also detectable under conditions of low dose rate exposure scenario. Analyses will include cancer-related changes at the level of the epigenome, genome, stem cell-ness, senescence and immune response. Short and long-term responses will be compared. Data will be integrated and exploited by bioinformatics tools that will use artificial intelligence techniques including data mining to identify gene sets specific to radiation responses, menarche age, ageing and obesity. Education and training activities and social science investigations reaching out beyond the radioprotection community will be carried out. The study will provide new insights into the mechanisms of the individual radiogenic cancer risk modifiers obesity and menarche age following acute and chronic radiation exposure, contributing to cancer prevention for women.

Figure 5: MIRAMARE project presentation at social media.

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2.3 UBT-Rad - Unraveling brain tumor formation after low dose irradiation exposure

Project coordinator: Dr. Samuel Valable, CNRS - Imaging and Therapeutic Strategies for Cancers and Brain Tissue – ISTCT, France

Project partners (5):

- University of Caen Normandy, France
- BfS, Federal Office for Radiation Protection, Germany
- CEA, France
- EEAE, Greece
- Mainz University Medical Center, Germany

Abstract:

The incidence of pediatric brain tumors follows a constant increase. Among the risk factors in children and adolescents, high dose ionizing radiation (HDIR) are the strongest documented. There are a few established risk factors for CNS tumors in children and adolescents, including inherited disorders and ionizing radiation. The EPI-CT study suggest a linear increase in the relative rate of cancer with radiation dose to the brain from CT examinations. However, many factors, including age, gender, lifestyle, environment, and genetic backgrounds may influence the radiosusceptibility. Here, we hypothesize that low dose irradiation (LDIR), received in children could be a driven factor of the neoplastic acquisition and promoted by genetic mutations. We also aim to explore other mechanisms that may modulate brain tumor formation on focusing on three main topics: brain microenvironment, immune reaction, and redox status. Last, we aim to identity and inhibit factors that would disable tumor progression. The present study has been designed around six WPs. Firstly, we will work in vitro on the initiation of tumor formation from neural stem cells and astrocytes that will be initiated following genetic modifications (NBS1/TP53/PTEN). Once prepared, these cells will be irradiated and neoplastic transformation will be measured (WP2). Therefore, WP2 will correspond to the identification of intrinsic mechanisms underlying LDIR-induced brain carcinogenesis. WP3 will correspond to the identification of the role of the brain microenvironment (microglia, astrocytes, endothelial cells) using in vitro (cocultures and supernatant transfer) and ex vivo (organotypic slices) approaches. WP4 will correspond to in vivo assessment the effects of LDIR exposure on brain tumor incidence, survival animal and the identification of early biomarkers (relative to HDIR) as a function of age and sex and in or out-of-field irradiation (whole-brain, hemibrain or brainless whole-body). WP5 will consist of teaching and education on effects of LDIR-induced carcinogenesis and WP6 will correspond to dissemination. WP1 will be dedicated to project coordination. The UBT-Rad project is therefore design to comprehensively understand the brain tissue reaction occurring after low dose irradiation exposure and to identify factors that could in turn be inhibited to disable brain tumor formation.

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Figure 6: UBT-Rad project presentation at social media.

2.4 CATAPULT - Comprehensive Assessment and Preparedness for Emerging Nuclear Technologies

Project coordinator: Dr. Fabrizio Gabrielli, Karlsruhe Institute of Technology, Institute for Neutron Physics and Reactor Technology (INR), Germany

Project partners (12):

- STUK, Finland
- UEF, Finland
- HZDR, Germany
- ASNR, France
- RIVM, Netherlands
- NRG, Netherlands
- SCK CEN, Belgium
- Raten, Romania
- IFA, Romania
- Merience SCP, Spain
- CIEMAT, Spain
- CAFAC – Lusófona University, Portugal

Abstract:

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The objective of CATAPULT is evaluating and extending the state-of-art methods for the Environmental Impact Assessment (EIA), the Emergency Preparedness and Response (EP&R), and the risk communication when applied to Small (water-cooled) and Advanced Modular Reactors. Modular reactors pose challenges for both EIA and EP&R. Being envisioned to be located in urbanised site-locations, the region affected by an accidental release is expected to be largely smaller than in large water cooled-reactors, leading to a potential higher impact in the near field from a radiation protection perspective. Furthermore, specific physical and chemical characteristics of the emissions are expected for Gas- and Lead-cooled reactors – so far hardly included in current assessment models, because of the use of coolants, fuels, and materials different than in traditional water-cooled reactors. Therefore, an accurate EIA and EP&R for modular reactors is essential. With this goal, CATAPULT brings together 8 institutions with a wide interdisciplinary expertise in EIA and EP&R as well as in technical, regulatory, social, and ethical aspects. By a large engagement of the stakeholders, CATAPULT aims at building a comprehensive guidance for EIA and EP&R with tight cross-links between technical and social aspects. In CATAPULT, the state-of-art methods for the radionuclide transport and uptake in the environment and for the dose assessment is reviewed and adapted - if needed - to the specific needs required by the modular reactors considered in the project and a roadmap for future developments is assessed also based on the stakeholders' needs. Such activity will support the development of a guidance for EIA by the close involvement of the end-of-users responsible for reviewing applications submitted by prospective licensees, i.e., authorities and their Technical Safety Organization. CATAPULT will employ such technical activities to address the social dilemma related to the impact of such new nuclear technologies on the society (or Not In My Backyard -NIMBY - syndrome) and to actively engage lay citizens in codesigning the Risk Communication in the framework of the EIA process and documentation. This community-driven approach will also provide an implementation guidance for effective risk communication about EIA.

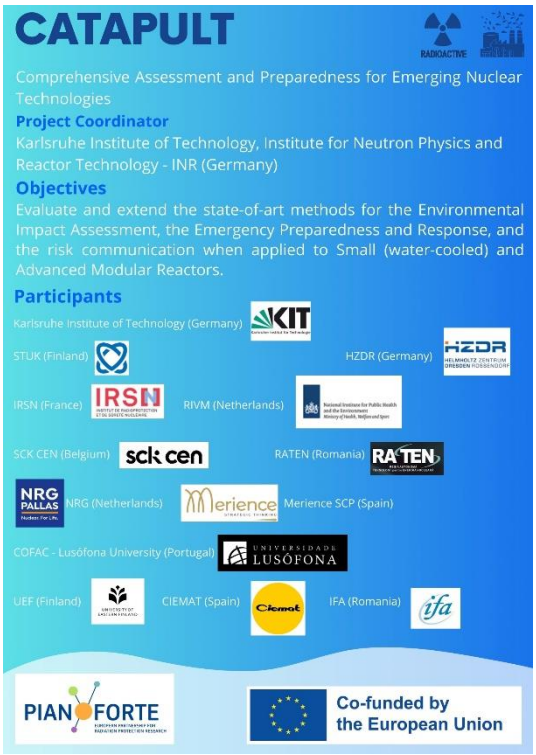

Figure 7: CATAPULT project presentation at social media.

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2.5 GIROSCOPE - Guidance for Innovative Reactor Off-Site Consequences, Planned and Emergency

Project coordinator: Dr. Anna Wawrzynczak-Szaban, National Centre for Nuclear Research, Department of Nuclear Energy and Environmental Studies, Otwock-Swierk, Poland

Project partners (11):

- CIEMAT, Spain
- NMBU, Norway
- BfS, Germany
- University of Gothenburg, Sweden
- CEPN, France
- ASNR, France
- CNL, Canada
- APA, Portugal
- UK HSA, United Kingdom
- NCSRD, Greece
- NERIS platform

Abstract:

The GIROSCOPE project is being proposed to provide a robust scientific platform and framework for emergency preparedness and response (EP&R) and Environmental Impact Assessment (EIA) for novel nuclear reactors (NNRs). Innovative reactor designs are being considered not only for electricity generation but also for heat and power supply to industrial plants, in the vicinity of urban areas as well as in remote or hard-to-reach areas. These diverse reactor designs and applications, combined with minimal pre-existing experience of how the technology will perform throughout its life cycle, introduce radiation protection challenges requiring a comprehensive understanding and novel solutions. To meet these challenges GIROSCOPE brings together 12 institutions with a broad expertise in EP&R including, nuclear reactor design and assessment, transport modelling, EIA, and covering technical, safety and security and societal aspects.

GIROSCOPE will thoroughly characterize the source terms of the three types of NNRs: High-Temperature Gas-cooled Reactor (HTGR), Compact Molten Salt Reactor (CMSR), and Small Light Water Reactor (SLWR). It will evaluate NNR types and their potential locations, focusing on the future requirements these sites may impose, and evaluate societal perceptions and related concerns. The project will also review radionuclide environmental transport models and demonstrate their applicability to NNR technologies. Advanced models and novel concepts (e.g., employing AI) for environmental transport of radionuclides will be developed and tested to determine the impact in complicated environments.

GIROSCOPE will provide guidelines targeted at decision-makers in nuclear safety. Supported by stakeholder engagement, the project will provide a framework for NNR assessment, a scenario

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database and recommendations that address the needs identified in IAEA and other international guidelines. The project's outcomes will provide substantial added value and a forward-looking guide for all European countries interested in investing in NNR technologies. By delivering scientifically sound and practical guidance, the project will support the safe and effective deployment of innovative nuclear reactors, ensuring that EIA and EP&R measures are robust and fit for purpose.

Figure 8: GIROSCOPE project presentation at social media.

2.6 DOSELIA - Computing whole-body radiation dose distributions and subsequent cancer risks from modern radiotherapy techniques in paediatric patients

Project coordinator: Dr. Charlotte Robert, Gustave Roussy Radiotherapy, U1030, Villejuif, France

Project partners (10):

- ASNR, France
- CEA, France
- INSERM, France
- University of Caen Normandy, France
- Aarhus University, Denmark
- Aarhus University Hospital. Denmark
- LMU Munich, Germany
- WPE, Germany

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- University Hospital Essen, Germany
- SÚRO, Czech Republic

Abstract:

The DOSELIA project aims to significantly enhance the assessment of whole-body doses and the risk of subsequent primary cancers in paediatric patients undergoing external beam radiotherapy (EBRT). Recent technological advances in EBRT have drastically improved irradiation precision, making it crucial to optimise treatment delivery to minimise exposure to healthy tissues, especially in children who are more vulnerable to long-term side effects. Current treatment planning systems cannot accurately calculate out-of-field doses or do not incorporate risk projection models specifically tailored to paediatric patients.

DOSELIA represents a major advancement in paediatric radiation therapy by integrating cutting-edge AI technology with rigorous scientific methodology to protect the healthy tissues and enhance the long-term health outcomes of young cancer patients. The project will develop a new AI-based software prototype capable of providing rapid and accurate whole-body dose distributions. This software will include modules for assessing doses from therapeutic irradiation (photons and protons) and imaging processes (planning and positioning), as well as risk prediction models for subsequent primary cancers. The study will develop and validate the algorithms using existing research infrastructures and data, particularly from the EU-funded HARMONIC project.

The dosimetry and risk projection models will leverage the latest scientific insights from biological and epidemiological research, along with advanced statistical methods, to offer comprehensive risk evaluations. Applied prospectively, this tool could help clinicians determine the optimum treatment plan or modality—such as photon irradiation strategy or photons versus protons—and evaluate the impact of image-guided radiotherapy schemes. The proposed tools will be developed in collaboration with medical professionals, including physicians, radiation oncologists, medical physicists, and other stakeholders, to ensure adequation with user's needs and effective risk communication.

DOSELIA software is designed to facilitate its integration into clinical practice to improve decision-making and patient safety. The expected result is a reduction in the effects of radiation, including the incidence of secondary malignancies on healthy tissue in paediatric patients receiving modern radiotherapy.

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Figure 9: DOSELIA project presentation at social media.

2.7 EMPATHY - Evaluation and optimization of proton arc therapy

Project coordinator: Dr. Carles Gomà, Research Foundation Clínic Barcelona, Biomedical Research Institute (IDIBAPS), Translational genomics and targeted therapies in solid tumours, Spain

Project partners (8):

- HZDR, Germany
- HCB, Spain
- SJD, Spain
- VHIO, Spain
- CIEMAT, Spain
- SCK CEN, Belgium
- KU Leuven, Belgium
- TUD, Germany

Abstract:

Radiotherapy (RT) is an established modality for cancer treatment and broadly used for every second cancer patient. In the vast majority of treatments high-energy X-rays are used. Still, photon therapy (XRT) is irremediably limited by the physics of X-rays, depositing a lot of dose upstream and

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downstream of the target volume. In contrast, protons focus most of the dose in a well-determined area in the target. Compared to XRT, for the same dose in the target, proton therapy (PT) deposits about 50% less dose in the patient. This is particularly interesting in pediatric cases where it is of utmost importance to minimize the irradiation of healthy tissues to lower the risk of radiation-induced secondary cancers. In certain aspects, PT still lags behind XRT, compromising its dosimetric superiority. This concerns essential hardware and software components, for example on-board imaging with quantitative image information of sufficient precision tailored to the requirements of PT and the possibility of adapting the treatment according to the anatomy of the day. While in XRT it has become standard to irradiate while continuously rotating the beam around the patient (arc therapy),
in PT usually only a few fixed beam directions are used. Fortunately, technologies are rapidly evolving in PT. Proton arc therapy and online adaptive PT will become reality with commercial solutions in the next couple of years. They will allow even better restriction of the dose to the target.
However, the introduction of these technologies leads to the emergence of new challenges: the combination of adaptive PT and proton arc therapy is not obvious, due to the considerable complexity of proton arc treatment planning. In addition, the dispersion of low doses over larger volumes of tissue and the more intensive use of X-ray imaging is a challenge. The reduction of imaging dose is of particular interest for pediatric patients. Our objective is to enable a major technological and clinical leap for PT, with the association of arc delivery, online treatment adaptation, and novel imaging modalities (photon counting CT), without eluding practical and implementation considerations. With a strong focus on the expected toxicity, with a thorough optimization of all irradiation sources, we will very likely and relevantly improve treatment outcome for pediatric cases, both short and long term.

Figure 10: EMPATHY project presentation at social media.

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2.8 KAYAC+ - Knowledge on outcome of adolescent and young adults with cancer

Project coordinator: Prof. Esther G.C. Troost, TUD Dresden University of Technology, Faculty of Medicine, OncoRay - National Center for Radiation Research in Oncology, Dresden, Germany

Project partners (19):

- UMCG, Netherlands
- IFJ PAN, Poland
- Centre Léon Bérard, France
- CEA, France
- HZDR, Germany
- SCK CEN, Belgium
- KU Leuven, Belgium
- RIVM, Netherlands
- Aarhus University, Denmark
- Aarhus University Hospital, Denmark
- Scandionkliniken, Sweden
- Stockholms Universitet, Sweden
- INFN, Italy
- CNAO, Italy
- PSI, Switzerland
- Institut de Recerca Sant Pau, Spain
- CIEMAT, Spain
- Glowny Instytut Gornictwa (GIG), Poland
- SÚRO, Czech Republic

Abstract:

Annually, cancer is diagnosed in 150.000 adolescents and young adults (AYAs) aged between 15 and 39 years in Europe and in 1.2 million AYA worldwide. Alarmingly, the age-standardized incidence was found to be highest in AYA in Western European countries [1]. The malignancies encountered mostly originate from the breast (15%), thyroid (15%), cervix, testicles (8%), central nervous system 8%), bone or soft tissues (8%) as well as lymphoma (19%) [cancer.gov].

Many of those malignancies are treated with a combination of surgery, systemic therapy, and irradiation. Although a high cure rate is achieved, it is lower than for the paediatric counterparts. Of note, the risk of secondary tumours in survivors of AYA cancer 35 years after treatment ranges between 11.9% (breast cancer) and 26.6% (Hodgkin's lymphoma) with an excess proportion of lung cancer [2]. In part, these secondary tumours may be caused by therapeutic interventions potentially affecting the DNA of cells in non-cancerous tissues. Novel radiation modalities are increasingly being utilised in European centres, facilitated by image-guidance and online-adaptive approaches. Particles, e.g. protons or carbon ions, are characterised by an energy-dependent point of maximum dose deposition, the so-called Bragg peak, followed by a sharp dose-gradient to zero dose. Also, the relative

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biological effectiveness of particles is higher compared to that of photons. Both characteristics enable sparing of normal tissues, thus reducing the incidence of side-effects and in theory of secondary tumours.

Within the pan-European KAYAC+ study, we will address various scientific questions of photon and particle therapy in AYA cancer patients. These include: differences in radiation treatment plans, dose from secondary particles and imaging, the induction of treatment-induced second tumours as well as the incidence of side-effects and their costs, and the contribution of radiation modalities, comorbidities, and lifestyle factors to secondary tumours. These questions will be assessed by two PhD students, one with a background in medicine or epidemiology, the other in the field of (medical) physics. The KAYAC+ database, which will be the nucleus for the pan-European database on particle therapy, will facilitate this project as well as future translational research.

Figure 11: KAYAK+ project presentation at social media.

3. Research projects start

Most of the research projects will start in January 2025. The questionnaire prepared for 1st Call research projects coordinators in order to gather information on expected results and their dissemination, planned education and training efforts, data management and infrastructure use by each project will also be distributed to coordinators of projects funded within the 2nd Call. Available PIANOFORTE tools and resources will be provided to research teams in order to maximize the scientific impact.

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4. Conclusions

The second call for proposals was prepared through the collaboration of all PIANOFORTE work packages: research topics formulation and prioritisation, preparation of the Call documents (Call text, Guidelines for applicants, Auxiliary proposal template, Auxiliary financial excel sheet), online Infoday for applicants, etc.

The evaluation procedure of submitted proposals was led by WP7 independently of the PIANOFORTE coordinator and beneficiaries. The second call for proposals has been successfully accomplished and 8 research projects were approved by PIANOFORTE General Assembly on Wednesday 11 December 2024 in Brussels, Belgium.

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