2022 MELODI Statement

The purpose of the MELODI Association is to define priority scientific goals and to encourage the implementation of research on health risks from low-dose and low-dose-rate radiation with the aim to improve radiological protection. A robust understanding and quantification of human health risks is the fundamental basis of radiological protection; the system of protection for public, occupational, medical and emergency exposures flows from this basis. The Strategic Research Agenda of MELODI identifies these priority goals and the specific resources, infrastructures and training capabilities needed to further develop low-dose risk research within a time frame of 20 years. MELODI statements aim to inform on priority topics for forthcoming EU and National calls; the EU issued a call for a European Partnership project in 2021, the resulting PIANOFORTE Partnership started in June 2022, and anticipates opening a call for research in March 2023. This Statement should facilitate setting priorities for both the EU and any subsequent European Partnership calls. The high-level priorities of all European radiation protection research platforms have been identified within the CONCERT Joint Roadmap.

The key priority for radiation protection research is to improve health risk estimates for low dose and dose-rate exposures encountered in occupational, medical and public/emergency situations. The approaches will need to be multidisciplinary and innovative, including where appropriate the application of artificial intelligence and machine learning approaches. The integration of expertise outside the conventional fields of radiation research will widen the possibilities to integrate modern health research technologies in the assessment of health risk relevant to radiation protection. The priorities identified for the 2022 – 2027 period listed below take into account the feasibility and impact of the topic area (see MELODI Roadmap document) and the amount of related ongoing work on the topic

Several relevant European projects are ongoing, focused on particular topics. The HARMONIC project investigates short to medium-term health outcomes (endocrine dysfunction, cardiovascular toxicities, second primary cancers and neurovascular damage) in paediatric patients undergoing interventional cardiology or proton therapy. The RADONORM project considers the risks associated with radon and other sources of NORM exposure, the risks arising from combined exposures and elements of radon dosimetry. The SINFONIA project started in 2020 and considers cancer risks associated with medical exposures, including those at low doses.

Priorities for the 2022 – 2027 period:

The overall priority is as given in the Joint Platforms Roadmap (available to download here), Challenge A, *Understanding and quantifying the health effects of radiation exposure.* The following points provide more specific priorities within this overarching aim in light of recent developments:

- To understand the health effects of inhomogeneous exposures, various types of radiation including internal emitters and differences between risks from acute and chronic exposures through the integration of experimental and epidemiological data applying biologically-based risk models. To improve the understanding of the effects of intra-organ dose distribution through observations in patients exposed to inhomogeneous fields and experiments with organotypic tissue models.

- In relation to tissue reaction and stochastic health effects (cancer and other diseases): Characterisation and quantification of variation in response and risk between population sub-groups/individuals due to host factors including genetic and epigenetic factors, sex, co-morbidities, environmental and lifestyle factors, co-exposures and the interactions between these depending on dose levels.
- To evaluate the risks of, and dose-response/dose-rate response relationships for, non-cancer diseases at low and intermediate dose levels (100 - 500 mGy and below): in particular cardiovascular, neurocognitive and immunological effects.
- To define the processes contributing to cancer development in relevant target stem/progenitor cell populations after low-dose/low-dose-rate exposures; including for example the role of microenvironment, cell-to-cell interaction (as mentioned in ICRP publ 131), the role of epigenetics, metabolic status, ageing, and immuno-senescence amongst others, in single and multiple stressor exposure situations.
- To identify, develop, validate and, where feasible, implement the use of biomarkers of exposure, and for early and late effects for cancer or/and non-cancer diseases and variation in susceptibility. The relationship between these radiation biomarkers and those emerging biomarkers of various pathophysiological processes and health outcomes needs to be considered and explored.
- To continue to refine risk estimates for cancers after low-dose and low-dose-rate exposures in occupational, medical and other cohorts. Such quantitative risk estimations are required to inform judgements on risks from acute, chronic and inhomogeneous exposures, and will provide important input to the development of quantitative mechanistic risk models and AOPs, see below.
- To identify, explore and define AOPs for radiation-induced health effects, and determine if those operating at low doses and dose rates are the same as those at higher levels of exposure, and when the triggering of an AOP is sufficient to disrupt normal homeostasis and lead to pathologies.

The current and previous MELODI statements, providing information about short-term research priorities for specific calls, can be found on the MELODI website. The definition of research priorities for the medium and long-term is described in the CONCERT Joint roadmap.

MELODI encourages, where appropriate, (1) the use of archived biological materials from prior EU funded research, (2) the integration of experienced laboratory networks (such as e.g. RENEB), (3) the consolidation and use of important epidemiological studies (both radiological and non-radiological) where feasible, (4) the integration of expertise from outside the conventional fields of radiation research; (5) the use of shared infrastructures and (6) continued availability of targeted education and training opportunities (such as e.g. Student Mobility Support) to share and spread technical skills.