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European Joint Programme for the Integration of Radiation Protection Research

H2020 – 662287

D 3.3 – Third Annual Joint priority list

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Abstract

Within CONCERT, no extra funding was foreseen for a 3rd call for scientific projects. However the draft EURATOM Work Programme was launched and presented on the EURATOM Fission Info Day in Brussels on 9 October 2017. The topic of interest to radiation protection research in this Work Programme is action NFRP-2018-08.

The Deliverable D3.3 is therefore used to present the joint gap analysis of potential use to project leaders that will submit project proposals to NFRP-2018-08.

This call clearly states that "*this action should seek close cooperation with and complement actions of CONCERT and MEDIRAD*", and that "*this action must take into account prioritization of research in this field reflected in the strategic research agendas of the Radiation Protection Research Platforms MELODI, EURADOS, NERIS, ALLIANCE and EURAMED*".

In addition, the scope of projects answering the call should be based on a "*gap analysis"*, as this will be considered during the evaluation.

Right after the EURATOM Fission Info Day meeting, a meeting of platforms and former Euratom project coordinators took place, to discuss practical arrangements relating to the preparation of proposals answering the NFRP-2018-08 call. This meeting took place on the 9th of November 2018 at the premises of the Representation of Lower Saxony to the European Union.

At this meeting it was (a.o.) decided to provide a gap analysis to be publicly available to the research community: With the information of the SRAs and the past projects in hands, the platforms felt best placed to share their experience and provide such a joint gap analysis.

This deliverable presents the gap analyses provided by the platforms individually as well as a joint gap analysis.

Disclaimer:
The platforms nor the CONCERT WP3 leader can guarantee that this gap analysis is the only valid gap analysis. It is not mandatory to use this gap analysis in project proposals submitted to the Action NFRP-2018-08; rather it is up to the candidate-project coordinators to decide whether this gap analysis is suitable for their projects or not.

Table of Contents

1. Joint gaps agreed upon by the radiation protection research platforms

General note: the gaps are not ordered as a function of importance.

Gap 1. Modelling of the biokinetic behaviour and risk for internal emitters

- In many exposure situations internal exposure to radionuclides is important. Assessment of the health risks associated with internal radionuclide exposure is complex and there remain substantial uncertainties related both to dosimetric aspects and health outcomes. Reduction of these uncertainties will improve risk assessment of internal exposures and hence inform appropriate protection measures.
- Improved modelling for internal doses after accidental situations based on environmental monitoring data and personal monitoring data.

This gap is related to MELODI, EURADOS, NERIS and ALLIANCE.

Gap 2. Improving environmental and health monitoring, particularly by lay people

- Improving environmental and health monitoring by lay people, and new equipment such as drones and a European wide harmonization of such tools and methods and how to integrate this into operational approaches.
- These can be considered as overlapping open topics in both gap analyses, excluding the work to be done in SHAMISEN-SINGS.

This gap is related to EURADOS and NERIS.

Gap 3. Dose optimization in medical exposures

- Development of dose biobanks for benchmarking, establishment of DRLs
- Advanced patient-specific dosimetric methods that accurately estimate radiation dose to each specific tissue/organ of the body. This is needed for Computed Tomography (CT) and interventional radiology procedures as well as for radiotherapy and hadron therapy and radionuclide therapy. This includes non-target organs.
- This is also needed for epidemiological studies.
- Artificial intelligence, machine learning and deep learning can support medical radiation protection (dose estimation, dose management, image quality assessment and especially dose reduction).

This gap is related to MELODI, EURADOS and EURAMED.

Gap 4. Radiation protection approaches based on individual radiosensitivity

- It is important to develop methods to avoid side effects and adverse events by prediction of individual radiosensitivity, to understand the range of radiosensitivity in the population and develop strategies for adjusting doses in medical settings correspondingly.
- Research could investigate new markers and reasons for the individual radiosensitivity
- Projects trying to fill this gap would require research on, *inter alia*, biomarker discovery and validation, individual patient dosimetry, epigenetics and individual susceptibility
- Correlation of nanodosimetry-based characteristics of particle track structure with the biological effectiveness of ionizing radiation may provide useful insights to understand the underlying mechanisms that lead to individual radiosensitivity.

This gap is related to MELODI, EURADOS and EURAMED.

GAP 5. Individualized dosimetry-based activity determination in radionuclide therapy

- Individualized dosimetry based on molecular imaging prior to radionuclide therapy can greatly improve the treatment efficacy and can be applied in everyday clinical practice.
- Empirical activity selection is the most commonly used method but is not an optimal approach. It is important to optimize treatment by anticipating required activity administered to an individual patient.
- Internal micro-dosimetry can support individualized dosimetry in radionuclide therapy.

This gap is related to MELODI, EURADOS and EURAMED.

Gap 6. Biomarkers of exposure, disease and susceptibility

- Biomarkers have the potential to improve estimates of exposure/effect in radiation incidents, epidemiological studies and investigations of radiation impacts on the ecosystem. Biomarkers of disease/effect have the potential to improve epidemiology, early medical diagnosis and the health of non-human species. Susceptibility biomarkers may help refine current population-based approaches to protection.
- Radiation protection measures are based on population average estimates of risk/effect. With an improved understanding of the range of radio-sensitivity within the human population and between species could aid risk assessment and therefore approaches to protection. Variation may potentially be driven by genetic factors, lifestyle factors, age or gender.

This gap is related to MELODI, ALLIANCE and EURAMED.

Gap 7. Radiation impact on the immune system

- The immune system is complex and regulated at multiple levels, and inflammation can affect disease progression.
- A more comprehensive understanding of the immunomodulatory effects of radiation (potentially both inhibitory and stimulatory) could help in determining health outcomes of exposures, particularly in medical and occupational settings. It could therefore be translated

into effective radiation protection measures especially in clinical routine by adjusting exposure to the inhibitory and stimulatory effects

This gap is related to MELODI and EURAMED.

Gap 8. Epigenetic mechanisms of radiation disease/effect

- In recent years a growing appreciation of non-mutational processes that can affect phenotype has been gained. If such processes contribute to radiogenic diseases or effects, notably heritable effects, it will be important to develop an understanding of dose- , dose-rate and radiation quality-dependence.
- Epigenetic status is further known to vary with age. Understanding the dose- and dose-rate dependence will be of particular importance to inform judgements on low dose and dose-rate risk extrapolation.
- To improve understanding of spatial correlations of radiation interaction events and the link with biological effects.

This gap is related to MELODI, EURADOS and ALLIANCE.

Gap 9. Biological and ecological effects of low dose/ low dose rate exposure on humans and biota

- Identification and mechanistic understanding of molecular and cellular processes following exposure to ionising radiation and resulting in adverse effects.
- Understanding variation in radiosensitivity between species at the individual and population levels
- Identification and validation of biomarkers of exposure and effects for use in prospective and retrospective assessments.
- Study the hereditary effects within populations of species, the molecular basis of adaptation (or vulnerability) gained through generations.
- To explore and define the role of epigenetic modifications in radiation-induced adverse effects.

This gap is related to MELODI and ALLIANCE.

GAP 10. Integration of environmental exposure assessment for ionising radiation and other stressors

- Mechanistic understanding of radionuclide dispersion in space and time, and transfer processes.
- Development of process-based models to improve dose assessment predictions, considering both environmental monitoring and personal monitoring data.
- Advanced modelling of process interactions at the various biosphere interfaces at the local, regional and global scales, in different ecosystems (including urban).
- Advanced methods for data treatments to cope with the large amount of data available.
- Integrated holistic modelling approach and advanced methods to identify the most significant sources of uncertainty in radiological impact assessments.

- In reality exposures to radiation rarely if ever occur in isolation, populations are co-exposed to other stressors concurrently. Understanding the interactions between radiation and other potential co-exposures may be relevant to risk assessment if substantial modulation of the radiation effect on humans (including patients) or non-human species is observed.

This gap is related to MELODI, NERIS, ALLIANCE and EURAMED

Gap 11. Optimising emergency and recovery preparedness and response

- Customisation of atmospheric, river, marine, brackish water, terrestrial and urban dispersion models, food chain models and dose assessment models.
- Improvement of monitoring of the different environmental compartments, foods and goods.
- Improvement of dose assessment models for better dose reconstruction and predictions of the impact of an accident.
- Methods and guidance for optimization (residual dose approach, temporal dynamics for the evolution of countermeasures…).

This gap is related to NERIS and ALLIANCE.

SSH as a cross cutting issue

The Social Sciences and Humanities community encourages multi-disciplinary approaches attending also to social and ethical considerations.

Examples are, low dose risk communication, holistic approaches of emergency management, public information and stakeholder engagement, societal aspects of medical applications and so on.

2. Annexes: full texts of individual gap analyses from the radiation protection research platforms and presentations given at the open information day

MELODI statement 2018

Gap analysis

MELODI (Multidisciplinary European Low Dose Initiative) is a European Platform dedicated to low dose ionizing radiation risk research. The purpose of the MELODI Association is to integrate national and European activities in low dose and low dose rate radiation research, to define priority scientific goals and to facilitate effective implementation of research. The MELODI Strategic Research Agenda (SRA) and Feasibility and Impact Analysis (Roadmap) identify these priority goals and the specific resources, infrastructures and training capabilities needed to further develop low-dose risk research. The current draft of the MELODI SRA is available here: http://www.melodi-online.eu/doc/MELODI_SRA_2017_06102017.pdf

Prior to EU research funding calls, MELODI develops a short statement indicating its view on current research needs, which serves as an input to those responsible for defining call topics. In October 2017 the European Commission indicated its intention to open a EURATOM call that includes radiation protection. The proposed work programme includes topics NFRP-2018-8 for research and NFRP-2018-9 for review of previous activities. NFRP-2018-8 specifically indicates that a 'Gap analysis' will be required for each proposal and NFRP-2018-9 could be usefully informed by such an analysis. The SRA Working Group of MELODI consequently has undertaken a review of relevant EURATOM research undertaken (or underway) in Framework programmes 6 and 7 (FP6, FP7) and Horizon 2020 (H2020) identifying their relevance to the six key areas of research identified in the MELODI SRA and roadmap. This informed the identification of gaps that are considered as potential areas for research under NFRP-2018-8 call. A mature reflection and identification of knowledge gaps would require results of all projects to be available; this has not been possible in all cases as some projects have yet to come to completion. We also note that the NFRP-2018-8 call text indicates that the gap analysis included in proposals will be subject to evaluation. The MELODI SRA Working Group anticipates that its gap analysis will be of benefit to those applying to the call.

The areas defined by the MELODI SRA and roadmap that require further research are:

- To explore the shape of the dose-response relationship for radiation-induced health effects (Abbreviation: Shape)
- To understand the potential impact of individual susceptibility on radiation-induced health effects (Abbreviation: Susceptibility)
- To identify, develop and validate biomarkers for exposure, early and late effects for cancer or/and non-cancer diseases (Abbreviation: Biomarkers)
- To explore and define the role of epigenetic modifications in radiation-induced health effects (Abbreviation: Epigenetics)
- To explore the roles of specific target cells for radiation-induced late developing health effects (Abbreviation: Target cells)
- To understand the health effects of inhomogeneous dose distributions, radiation quality and internal emitters (Abbreviation: Inhomogeneity)

Review of FP6, FP7 & H2020 funded projects relevant to low dose risk research

(i) FP6 projects

Project acronym	Title	Primary disease endpoint	MELODI area addressed	Comments
RISC-RAD	**DNA damage responses, Genomic instability and Radiation-Induced Cancer: The problem of risk at low and protracted doses (RISC-RAD)**	Cancer	Shape, Susceptibility, (epigenetics)	This project undertook a wide range of experimental, epidemiological and modelling work addressing cancer dose-response and susceptibility
GENE-RAD RISK	**Radiation exposures at an early age: impact of genotype on breast cancer risk**	Cancer	Susceptibility, Biomarkers	Molecular epidemiological project on DNA repair gene variants and breast cancer risk
RACE	**Radiotherapy for breast cancer and subsequent risk of cardiovascular events**	Circulatory diseases	Shape	Clinical epidemiological follow up of radiotherapy patients for circulatory disease risk
GENEPI-LOWRT	**Genetic Pathways for the Prediction of the Effects of Ionising Radiation: Low Dose**	Cancer, tissue reactions	Susceptibility, Biomarkers, (Shape)	Search for biomarkers of response to low dose exposure in normal and

	Radiosensitivity and Risk to Normal Tissue after Radiotherapy			severe radiotherapy reactors
GENEPI-ENTB2	**GENEtic pathways for the Prediction of the effect of Irradiation-European normal an tumour tissue bank and data base**	Cancer, tissue reactions, circulatory disease	Susceptibility, Biomarkers	Tissue banking from radiotherapy patients. Infrastructural project
ALPHA-RISK	**Quantification of cancer and non-cancer risks associated with multiple chronic radiation exposures: epidemiological studies, organ dose calculation and risk assessment**	Cancer (circulatory diseases)	Shape, Inhomogeneity, Susceptibility	Epidemiological analysis of radon, uranium and plutonium risks
SOUL	**Southern urals radiation risk research**	Cancer, circulatory diseases	Shape, Inhomogeneity, (Biomarkers)	Epidemiological analysis of disease risk in Mayak plant workers and Techa river residents
GEN RISK-T	**Genetic component of the low dose risk of thyroid cancer**	Cancer	Susceptibility, Biomarkers, (Shape)	Experimental study to develop thyroid cancer model
NOTE	**Non-targeted effects of ionising radiation**	Cancer, circulatory diseases	Shape, Epigenetics	Experimental studies to investigate non-DNA targeted actions of radiation

(ii) FP7 projects

Project acronym	**Title**	**Primary disease endpoint**	**MELODI area addressed**	**Comments**
ALLEGRO	**Early and late health risks to normal/healthy tissues from the use of existing and emerging techniques for radiation therapy**	Cancer	Shape, Inhomogeneity	Out-of-field doses to normal tissues delivered by a range of radiotherapy techniques
ANDANTE	**Multidisciplinary evaluation of the**	Cancer	Inhomogeneity, Shape, Target	Study of risks from neutrons in

	cancer risk from neutrons relative to photons using stem cells and the induction of second malignant neoplasms following paediatric radiation therapy		cells	radiotherapy
CARDIO-RISK	**The mechanisms of cardiovascular risks after low radiation doses**	Circulatory diseases	Shape, Target cells, (Epigenetics)	Experimental study of circulatory disease mechanisms
CEREBRAD	**Cognitive and Cerebrovascular Effects Induced by Low Dose Ionising Radiation**	Tissue reactions (cognitive effects), Circulatory diseases	Shape, Target cells, Inhomogeneity, (Epigenetics), (Biomarkers)	Epidemiological and experimental studies of cognitive and cerebrovascular effects of radiation, including in utero
CHILD MED RAD	**Prospective cohort studies of children with substantial medical diagnostic exposure**	Cancer	Shape, Susceptibility	Feasibility study for CT scan risk study in children
DARK-RISK	**Studies on a cohort of Serbian children exposed to x-irradiation to determine the contribution of the non-coding genome to susceptibility at low doses**	Cancer	Epigenetics, Susceptibility, Biomarkers	Epidemiological and experimental studies in *Tinea capitus* cohort; experimental work on Long non-coding RNAs seeking biomarkers of exposure
DoReMi	**Low Dose Research towards Multidisciplinary Integration**	Cancer, Circulatory diseases, lens opacities, tissue reactions	Shape, Susceptibility, (Target cells), Biomarkers, Epigenetics, Inhomogeneity	Large scale project that undertook feasibility studies covering all areas of interest to MELODI
EPI-CT	**Epidemiological study to quantify risks for paediatric computerized tomography and to optimise doses**	Cancer	Shape, Susceptibility, (Biomarkers)	Epidemiological investigation of cancer risk in children undergoing CT scans, includes biomarker

				considerations, dosimetric aspects as well as clinical guidelines
EpiRadBio	**Combining epidemiology and radiobiology to assess cancer risks in the breast, lung, thyroid and digestive tract after exposures to ionizing radiation with total doses in the order of 100 mSv or below**	Cancer	Shape, Target cells, Biomarkers, (Epigenetics), (Inhomogeneity)	Project aimed to integrate radiobiological data with epidemiological data to improve risk assessment for cancer in specific organs
OPERRA-SOPRANO		Cancer, Circulatory diseases	Shape, Biomarkers, Epigenetics,	Systems biological analysis to define the early cellular low dose response and its variation
OPERRA-EURALOC		Cataract (lens opacity)	Shape	Epidemiological investigation of lens opacity amongst medical practitioners
OPERRA-DIMITRA		Cancer	Shape, Biomarkers, target cells	Experimental investigations to determine Cone-beam CT effects of stem cells and to identify salivary biomarkers in children
OPERRA-VIBRATO		Cancer, immune system effects	Biomarkers, Epigenetics, Target cells	Experimental study of immune system gene expression after low dose irradiation
PROCARDIO	**Cardiovascular Risk from Exposure to Low-dose and Low-dose-rate Ionizing Radiation**	Circulatory diseases	Shape, Biomarkers, Target cells, (Epigenetics)	Epidemiological and experimental investigations on cardiovascular disease risk and mechanisms
RENEB	**Realizing the European Network in Biodosimetry**	Cancer	Biomarkers, Shape	Development of a European network for biodosimetry with main focus

				on emergency preparedness but of relevance as resource for low dose risk research and molecular epidemiology
RISK-IR	**Risk, Stem Cells and Tissue Kinetics – Ionising Radiation**	Cancer	Target cells, Shape, Epigenetics	Studies of stem cell responses to radiation at low doses and dose rates
SOLO	**Epidemiological Studies of Exposed Southern Urals Populations**	Cancer, Circulatory diseases	Shape, Inhomogeneity, (Biomarkers)	Epidemiological studies of Mayak plant workers for Pu cancer and circulatory disease risk
STORE	**Sustaining access to Tissues and data from Radiobiological Experiments**	All (potentially)	All (potentially)	Provision of database and archive for materials from radiobiological and epidemiological studies

(iii) H2020 projects

Project acronym	**Title**	**Primary disease endpoint**	**MELODI area addressed**	**Comments**
CONCERT-LDLENSRAD	**Towards a full mechanistic understanding of low dose radiation induced cataracts**	Cataract	Shape, Susceptibility, Biomarkers	Ongoing study into quantitative and mechanistic aspects of low does radiation cataract formation
CONCERT-LEUTRACK		Cancer	Epigenetics, Shape, Biomarkers	Project just starting on role of microvesicles in radiation leukaemogenesis
CONCERT-SEPARATE	**Systemic Effects of Partial-body Exposure to Low Radiation Doses**	Cancer	Epigenetics, Shape, Inhomogeneity	Project just starting on effects of partial body exposure
MEDIRAD	**Implications of medical low dose radiation exposure**	Cancer, Circulatory diseases	Shape, Biomarkers, Epigenetics	Large multi-partner project recently started including

				epidemiological studies of CT risk and circulatory disease risk plus biomarker discovery work

Clearly there have been many projects supported under FP6, FP7 and H2020 that address issues highlighted by MELODI as key areas requiring research to improve low dose and low dose rate radiation health risk assessment. All funded projects align with one or more of MELODI's key areas as identified in the SRA and roadmap. All have contributed to advancement of the field and building the scientific evidence base for low dose/dose rate risk assessment. All diseases/health effects of actual and potential relevance to low dose risk – cancer, circulatory disease, cognitive effects and cataract are considered and a shift in emphasis amongst funded projects towards the non-cancer diseases can be seen. While all projects have made progress in building the evidence base as noted, there remain areas where additional work could be beneficial; these are considered in the gaps described below.

Gap Analysis

Following consideration of the projects listed above it is clear that there are evidence gaps that remain and areas of research that have not been fully considered in the past. On this basis gaps are identified below under each of the key areas identified by MELODI in its SRA and roadmap.

1. *To explore the shape of the dose-response relationship for radiation-induced health effects*
   - Health risk studies amongst populations exposed to background and environmental sources of radiation, and experimental model studies using relevant exposure parameters
   - Studies of second cancers arising in populations treated by radiotherapy, and relevant experimental model studies
   - Health risk and experimental model studies considering co-exposures to radiation and other agents
   - Studies that improve organ-specific cancer risk estimates
   - Studies that will reduce exposure assessment measurement errors in epidemiological analyses
2. *To understand the potential impact of individual susceptibility on radiation-induced health*
   - Studies that lead to the identification and validation of biomarkers of disease risk and/or susceptibility
   - Studies that identify and validate cohorts suitable for molecular/biomarker epidemiological studies
   - Studies of tissue level effects and the role of individual differences in tissue architecture that impact on susceptibility to radiogenic diseases
   - Studies that potentially lead to the identification of biomarkers of resistance to radiation health effects
3. *To identify, develop and validate biomarkers for exposure, early and late effects for cancer or/and non-cancer diseases*
   - Studies that lead to the identification and validation of sensitive, rapid and reliable biomarkers of exposure
   - Studies that lead to the identification and validation of biomarkers of health risk/health risk susceptibility/resistance
4. *To explore and define the role of epigenetic modifications in radiation-induced health effects*
   - Studies that provide clear evidence for or against a role for epigenetic processes operating in radiation carcinogenesis, and dose/dose-rate/radiation quality information

- Studies that provide clear evidence for or against a role for epigenetic processes operating in circulatory diseases/cataract/cognitive dysfunction, and dose/dose-rate/radiation quality information
- Studies that provide clear evidence for or against the operation of ageing/senescence processes in radiogenic disease

5. *To explore the roles of specific target cells for radiation-induced late developing health effects*
   - Studies that identify and quantify the stem/progenitor cell populations at risk for all radiogenic cancer types and non-cancer diseases
   - Studies that provide quantitative information on the processes contributing to radiogenic diseases in relevant stem/progenitor cell populations
   - Studies employing heterotypic 3D cell/tissue/organ culture and animal models to examine radiation effects and sensitivity in stem cells
6. *To understand the health effects of inhomogeneous dose distributions, radiation quality and internal emitters*
   - Studies that consider organ dose in relation to intra-organ dose distribution in relation to health effects
   - Further investigation of sub-cellular dose distribution to elucidate potential targets for radiation action related to health effects other than DNA

MELODI also encourages education and training in disciplines to maintain, develop and improve skills amongst the low dose health risk research community. In this regard it is important to encourage training by those in relevant more fundamental sciences. The skills amongst the MELODI community in data management, data mining and bioinformatics are judged to be suitable for further development.

In terms of infrastructures for research, MELODI encourages, where appropriate, (1) the use of archived biological materials from prior research, particularly where EU funded, (2) the integration of experienced laboratory networks (eg RENEB) improving the robustness of results via intercomparisons, (3) the integration of expertise from outside the conventional fields of radiation research, where appropriate, (4) use of the wider EU scientific infrastructures for, amongst other things genomics, microscopy, structural biology, computing where relevant, (5) where new infrastructures are proposed/developed, the provision of access to the wider community of researchers.

Gap analysis and research priorities from ALLIANCE
15 January 2018

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(The full author list represents the ALLIANCE SRA/roadmap WG. Partners 1, 2, 4 and 5 are also involved in chairing topical roadmap WGs. Persons whose names are in bold are involved in the ALLIANCE bureau; persons whose names are in italic have contributed to this document)

1. Introductive background

The European Radioecology Alliance – the ALLIANCE – was founded in 2009 and officially registered in 2012 (http://www.er-alliance.eu/). Since its creation, the ALLIANCE has progressively grown, going from the 8 founding members in 2012 to 27 members, from 14 countries, in April 2017. The objectives of the ALLIANCE are to coordinate and promote research and recruitment in radioecology and to act as a Research Platform (Definition of priorities and research programmes, Promotion and Communication). The ALLIANCE members recognise that their shared radioecological research can be strengthened by efficiently pooling resources among their partner organisations and prioritising group efforts along common themes of mutual interest[1]. A major step in the prioritisation process was to develop a **Strategic Research Agenda** (SRA)[2] for radioecology. The SRA highlights the required scientific knowledge and methodological/technical know-how for the main components of any human and environmental risk assessment. It identifies three scientific challenges and fifteen associated research lines, consistent with a strategic vision of what radioecology can achieve in the future *via* a prioritisation of efforts. These challenges are:

- Challenge 1 - To Predict Human and Wildlife Exposure in a Robust Way by Quantifying Key Processes that Influence Radionuclide Transfers and Exposure;
- Challenge 2 - To Determine Ecological Consequences Under Realistic Exposure Conditions;
- Challenge 3 - To Improve Human and Environmental Protection by Integrating radioecology.

The SRA is being implemented by **topical roadmaps**[3] that were initiated by the COMET EC-funded project, with the help and endorsement of the ALLIANCE. The development of the roadmaps is driven by the need to provide fit-for-purpose human and environmental impact/risk assessments in support of the protection of man and the environment in interaction with society (interconnected sciences including social sciences and humanities, risk management including communication, economy), for all environmental exposure situations (*i.e.*, planned, existing, emergency). Where appropriate, collaboration between the existing European radiation protection platforms[4] is promoted.

Five scientific areas were selected to launch topical roadmaps:

- Atmospheric radionuclides in transfer processes;
- Marine radioecology;
- Human food-chain modelling;

[1] Muikku, M., Beresford, N.A., Garnier-Leplace, J., Real, A., Sirkka, L., Thorne, M., Vandenhove, H., Willrodt, C. (2018). Sustainability and integration of radioecology—position paper. J. Radiol. Prot. 38, 152-163.

[2] Hinton, T.G., Garnier-Laplace, J., Vandenhove, H., Dowdall, M., Adam-Guillermin, C., Alonzo, F., Barnett, C., Beaugelin-Seiller, K., Beresford, N.A., Bradshaw, C., Brown, J., Eyrolle, F., Février, L., Gariel, J.-C., Gilbin, R., Hertel-Aas, T., Horemans, N., Howard, B.J., Ikäheimonen, T., Mora, J.C., Oughton, D., Real, A., Salbu, B., Simon-Cornu, M., Steiner, M., Sweeck, L., Vives i Batlle, J. (2013). An invitation to contribute to a strategic research agenda in radioecology. J. Environ. Radioact. 115: 73-82

[3] Garnier-Laplace, J., Vandenhove, H., Beresford, N.A., Muikku, M., Real, A. (2018). COMET strongly supported the development and implementation of medium-term topical research roadmaps consistent with the ALLIANCE Strategic Research Agenda. J. Radiol. Prot. 38, 164-174.

[4] EURADOS: www.eurados.org/ for dosimetry; MELODI: http://www.melodi-online.eu/ for low dose risks; NERIS: http://www.eu-neris.net/ for emergency preparedness and post-accidental situations; EURAMED: http://www.eibir.org/scientific-activities/joint-initiatives/european-alliance-for-medical-radiation-protection-research-euramed/ for medical applications.

- Naturally-occurring radioactive materials (NORM);
- Inter- and intra-species radiation sensitivity and transgenerational effects.

Activities planned for a 5-year period within each topical roadmap extend from basic science (mechanistic understanding) to applications that would improve radiation protection (reduce the overall uncertainties), communication with society, assist decision-making processes (including risk mitigation where relevant). The research proposed interlinks the different challenges presented in the SRA.

2. Overview of radioecology research impact in radiation protection over the last decade

References cited throughout the text are some of the major publications. STAR & COMET produced ca. 70+ peer-reviewed articles.

The ALLIANCE activities and associated EC-funded projects or national programmes from ALLIANCE members made important progress in radioecology research over the last decade. This progress has focused on improvement of knowledge and tools to assess environmental radionuclides transfer and subsequent human and environmental exposure and risk assessment[5]. EC-funded projects (STAR, COMET) have developed and improved innovative models for quantifying radionuclide transfer to humans and wildlife and delivered guidance for development and validation of fit-for-purpose models[6]. For accidental situations, effort was dedicated to the characterisation of radioactive particles behaviour in ecosystems[7], and to marine dispersion modelling and marine biota impact assessment[8]. The relevance of studying the complex issue of the influence of multiple stressors in radiological risk assessment was clearly demonstrated through a literature review[9] and simplified case studies (e.g., combination of a stable metal, an organic substance and gamma radiation)[10], and research was initiated on transgenerational effects and epigenetics[11]. There have also been advances in the integration of human and environmental protection frameworks (*e.g.* CROMERICA tool). In addition, the establishment of a series of dedicated observatory sites[12] constitutes a unique opportunity to obtain a better understanding (and modelling) of environmental processes such as the migration and bioavailability of radionuclides, and the resulting exposure pathways and corresponding doses for humans and wildlife. Studying processes in the field, synergistically with laboratory experiments and modelling, is of high added value, notably regarding the complexity of environmental issues (and remediation) associated to long-lasting radiocontaminated sites, such as NORM sites[13]. Although considerable advances have been made since the Chernobyl and Fukushima accidents in predictive modelling to improve exposure estimates[14], there is a need to take into account more realistically key physical, chemical and biological processes in spatio-temporal predictive models. How environmental transfers and subsequent exposure (and dose) of humans and wildlife vary spatially and temporally is a key issue whatever the source term is (either artificial or naturally-occurring radionuclides). Improving the predictive capability of integrated models through comparison of

[5] Beresford, N.A., Wood, M.D., Vives I Batlle, J., Yankovich, T.L., Bradshaw, C., Willey, N. (2016). Making the most of what we have: application of extrapolation approaches in radioecological wildlife transfer models. . J. Environ. Radioact., 151, 373-386

[6] Beresford, N.A., Yankovich, T.L., Wood, M.D., Fesenko, S., Andersson, P., Muikku, M., Willey, N.J. (2013). A new approach to predicting environmental transfer of radionuclides to wildlife: A demonstration for freshwater fish and caesium. Sci. Tot. Environ. 463–464: 284-292; Brown, J.E., Beresford, N.A., Hosseini, A. (2013). Approaches to providing missing transfer parameter values in the ERICA Tool – How well do they work? J. Environ. Radioact. 126: 399-411

[7] Salbu, B., Kashparov, V., Lind, O.C., Garcia-Tenorio, R., Johansen, M.P., Child, D.P., Roos, P., Sancho, C. (2017) Challenges associated with the behaviour of radioactive particles in the environment. J. Env. Radioact., in press

[8] Belharet, M., Estournel, C., Charmasson, S. (2016). Ecosystem model-based approach for modeling the dynamics of 137Cs transfer to marine plankton populations: application to the western North Pacific Ocean after the Fukushima nuclear power plant accident. Biogeosciences, 13, 499-516; Vives i Batlle, J., Aoyama, M., Bradshaw, C., Brown, J., Buesseler, K.O., Casacuberta, N., Christl, M., Duffa, C., Impens, N.R.E.N., Iosjpe, M., Masque, P., Nishikawa, J. (2018). Marine radioecology after the Fukushima Dai-ichi nuclear accident: Are we better positioned to understand the impact of radionuclides in marine ecosystems? J. Env. Radioact. 618, 80-92.

[9] Vanhoudt, N., Vandenhove, H., Real, A., Bradshaw, C., Stark, K. (2012). A review of multiple stressor studies that include ionising radiation. Environ. Poll. 168: 177-192.

[10] Lofts, S., Fevrier, L., Horemans, N., Gilbin, R., Bruggeman, C., Vandenhove, H. (2015). Assessment of co-contaminant effects on uranium and thorium speciation in freshwater using geochemical modelling. J. Environ. Radioact., 149, 99-109; Nascimento, F.J., Svendsen, C., Bradshaw, C. (2015). Combined effects from γ radiation and fluoranthene exposure on carbon transfer from Phytoplankton to Zooplankton. Environ. Sci. Technol. 49, 10624-10631.

[11] Gombeau, K., Bourdineaud, J-P., Ravanat, J-L., Camilleri, V., Cavalie, I., Armant, O., Camilleri, V., Cavalie, I., Floriani, M., Adam-Guillermin, C. (2017). Epigenetic, histopathological and transcriptomic effects following exposure to depleted uranium in adult zebrafish and their progeny. Aq. Toxicol. 184, 14-25.

[12] Muikku, M., Beresford, N.A., Garnier-Leplace, J., Real, A., Sirkka, L., Thorne, M., Vandenhove, H., Willrodt, C. (2018). Sustainability and integration of radioecology—position paper. J. Radiol. Prot. 38, 152-163.

[13] Michalik, B. (2017). NORM contaminated area identification using radionuclides activity concentration pattern in a soil profile. J. Env. Radioact., 173, 102-111

[14] Vives i Batlle, J (2015) Dynamic modelling of radionuclide uptake by marine biota: application to Fukushima assessment J. Environ. Rad 151, 502-511; Calmon, P., Gonze, M-A., Mourlon, (2015). Modeling the early-phase redistribution of radiocesium fallouts in an evergreen coniferous forest after Chernobyl and Fukushima accidents. Sci. Tot. Environ. 529, 30-39.

predictions *versus* observed data, alongside filling knowledge gaps on biogeochemical processes, are the key to reduce uncertainty in human and wildlife exposure estimates for all exposure situations. Marine and watershed radioecological modelling are key-priority domains to tackle. Post-accidental related issues and communication with stakeholders are research priorities clearly shared with NERIS, the social sciences and humanities community, and EURADOS if we refer to refinement of dose assessment.

Understanding biological effects of chronic ionising radiation exposure to low doses and dose-rates is still of major concern for both human and environmental radiation protection, especially with the aim of quantifying the risk to individuals (human and endangered species) and populations. Recently, mechanistic models based on the disturbance of basic metabolism in organisms exposed to ionising radiation have provided insight into the causes of observed effects and represent tools to develop more robust ecological protection benchmarks[15]. COMET proved the relevance of using epigenetic markers in non-human species and started to delineate genetic vs. epigenetic causes of transgenerational effects of chronic exposures[16]. The exploration of "omics" responses to ionising radiation has also been highlighted as a useful approach to unravel basic mechanisms of the biological response to ionising radiation[17]. These concepts could help us understand how co-contaminants/stressors might influence organism radiosensitivity[18]. Exploration of intra- and inter-species causes of variation in radiosensitivity and of the mechanisms of multi- or trans-generational effects[19] is a priority to improve basic knowledge and contribute to the validation of biomarkers as early warning tools (clearly synergistic with MELODI research).

Two projects on radioecology-related topics are ongoing (started January 2017), after being approved in the EJP-CONCERT 1st Call in 2016.
The **TERRITORIES** (To Enhance unceRtainties Reduction and stakeholders Involvement TOwards integrated and graded Risk management of humans and wildlife In long-lasting radiological Exposure Situations) project targets an integrated and graded management of contaminated territories characterised by long-lasting environmental radioactivity, filling in the needs emerged after the recent post-Fukushima experience and the publication of the International and European Basic Safety Standards. A graded approach, for assessing doses to humans and wildlife and managing long-lasting exposure situations (where radiation protection is mainly managed as existing situations), will be achieved through reducing uncertainties to a level that can be considered fit-for-purpose (notably by using existing empirical/experimental data). The overall outcome will be an umbrella framework, that will constitute the basis to produce novel guidance documents for dose assessment, risk management, and remediation of existing NORM sites and of radioactive contaminated sites long-term after an accident, with due consideration of uncertainties and stakeholder involvement in the decision making process. This project will also highlight important factors determining the uncertainty levels that should be focussed on in the future combining experimental and modelling approaches.

Within the **CONFIDENCE** (COping with uNcertainties For Improved modelling and DEcision making in Nuclear emergenCiEs) project, the WP3 addresses key challenges identified in the ALLIANCE Strategic Research Agenda and specifically those of the Human Food Chain Topical Roadmap. The work to be done builds on infrastructures established in the frame of the COMET (COordination and iMplementation of a panEuropean instrumenT for radioecology) project (radioecology Observatory sites like the Chernobyl Exclusion Zone), and will use various appropriate databases (*e.g.* on food chain transfer) held by ALLIANCE members.

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[15] Alonzo, F., Hertel-Aas, T., Real, A., Lance, E., Garcia-Sanchez, L., Bradshaw, C., Vives i Batlle, J., Oughton, D., Garnier-Leplace, J. (2016). Population modelling to compare chronic external radiotoxicity between individual and population endpoints in four taxonomic groups. J. Environ. Radioact., 152, 46-59; Vanhoudt, N., Horemans, N., Wannijn, J., Nauts, R., Van Hees, M., Vandenhove, H. (2014). Primary stress responses in Arabidopsis thaliana exposed to gamma radiation. J. Environ. Radioact. 129: 1-6 ; Lance, E., Alonzo, F., Garcia-Sanchez, L., Beaugelin-Seiller, K., Garnier-Laplace, J. (2012). Modelling population-level consequences of chronic external gamma irradiation in aquatic invertebrates under laboratory conditions. Sci. Tot. Environ. 429: 206-214.

[16] Gombeau, K., Bourdineaud, J-P., Ravanat, J-L., Camilleri, V., Cavalie, I., Armant, O., Camilleri, V., Cavalie, I., Floriani, M., Adam-Guillermin, C. (2017). Epigenetic, histopathological and transcriptomic effects following exposure to depleted uranium in adult zebrafish and their progeny. Aq. Toxicol. 184, 14-25.

[17] Van Hoeck, A., Horemans, N., Nauts, R., Van Hees, M., Vandenhove, H., Blust, R., (2017). Lemna minor plants chronically exposed to ionising radiation: RNA-seq analysis indicates a dose rate dependent shift from acclimation to survival strategies. Plant Sci. 257, 84-95; Song, Y., Salbu, B., Teien, H-C., Evensen, O., Lind, O.l., Rosseland, B.O., Tollefsen, K.E., (2016). Hepatic transcriptional responses in Atlantic salmon (*Salmo salar*) exposed to gamma radiation and depleted uranium singly and in combination. Sci. Tot. Environ., 562, 270-279.

[18] Margerit A., Lecomte-Pradines C., Svendsen C., Frelon S., Gomez E., Gilbin R. (2015). Nested interactions in the combined toxicity of uranium and cadmium to the nematode Caenorhabditis elegans . Ecotoxicol. Environ. Safety, 118, 139–148; Nascimento, F.J., Svendsen, C., Bradshaw, C. (2015). Combined effects from γ radiation and fluoranthene exposure on carbon transfer from Phytoplankton to Zooplankton. Environ. Sci. Technol. 49, 10624-10631

[19] Parisot F., Bourdineau J.-P., Plaire D., Adam-Guillermin C., Alonzo F. (2015). DNA alterations and effects on growth and reproduction in Daphnia magna during chronic exposure to gamma radiation over three successive generations. Aquat. Toxicol., 163: 27–36

In the 2nd CONCERT Call (May 2017) no project directly related with radioecology was approved.

3. Views from international organisations on radioecology science needs released after the last EC-funded radioecology project COMET

The EC-funded COMET project organised its final project meeting from 25-27 April 2017 in Bruges, Belgium in association with the ALLIANCE. At this workshop, key representatives of international organisations were invited and their recommendations and views on progress made in COMET and consequent future requirements were solicited (Table 1).

Table 1. Summary of the main recommendations from international organisations delivered during the final COMET event in Bruges, 2017 (from Garnier-Laplace *et al.,* 2017. D2.4 COMET).

Organisation	Recommendations given to ALLIANCE
UNSCEAR	▸ Effects studies: gain more insight into molecular mechanisms, in synergy with life sciences other than radioecology (From more descriptive research to understanding of basic processes). ▸ Modelling: move toward mechanistic models (From more empirical models to understanding of underlying mechanisms). ▸ Effect studies and modelling depend on each other (Models need to be supported by experimental data and must be able to explain something happening in real world).
ICRP	Focus on an integrated view of all benefits and impacts that includes consideration of protection of people and the environment.
IAEA	There is a lot of common interest between the IAEA MODARIA programme (Modelling and data for radiological impact assessment) and the ALLIANCE topical roadmap working groups and efforts should continue to maximize synergies: ▸ Seasonality of transfer processes and exposure pathways for accidents. ▸ Integration of monitoring and modelling. ▸ Management of exposures from NORM will remain important worldwide. ▸ Realistic evaluation of the importance of exposures to biota for radiation protection. ▸ Strengthen the role of assessments in decision making.
NEA	▸ Prevailing circumstances drive individual and collective behaviours, which drive individual and collective exposures: Models need to address a wide variety of individual and collective circumstances. ▸ Radioecology can contribute SIGNIFICANTLY to understanding cancer mechanisms and markers. ▸ A communications / dialogue strategy is needed to perform research that will appropriately address stakeholder concerns.
IUR	The integration concept proposed today is purely methodology-driven (broadly, same conceptual method applied to man and biota): ▸ Better to start from an integration concept that acknowledges the existing interactions between non-human species and man (i.e. the ecosystem concept). ▸ Need to accept complexity and think in a more ”systems-based” way. Both in experimental work and in modelling.
IRPA	▸ The SRA should specifically address communication with society and enhancement of decision support systems, to improve public communication capabilities and stakeholder engagement. ▸ The SRA may offer young researchers good opportunities to develop their careers in a field that must be maintained, updated and that shall address new challenges. ▸ A challenge not included in the SRA was: keeping and transferring knowledge through the generational replacement. ▸ The implementation of the research roadmaps, will contribute to improve relevant tools and methods for radiation protection of people and the environment.

3. Research needs and priorities

From the ALLIANCE SRA annual priority statement published in 2015, 2016 and 2017, the following research priorities were put forward (no specific order below):

- Environmental availability and impact of radionuclides in terrestrial, freshwater and marine ecosystems (including human food chain) and their interactions with atmosphere, incorporating physical, chemical and/or biological processes. Validated process-based model parameterisation, characterisation of variability and uncertainty, and guidance for fit-for-purpose models**;** ***only partially dealt with under TERRITORIES and CONFIDENCE (R&D focusing on NORM is only initiated under TERRITORIES and the project does not deal with the full range of source types nor with the various affected environments and remediation options)***

- Development of models/tools, and datasets for their calibration and validation and guidance to select and evaluate the effectiveness of different remediation strategies in long-lasting exposure situations (*e.g.* nuclear accidents and/or NORM/TeNORM)**; *only partially dealt with under TERRITORIES and CONFIDENCE. Same note as for the previous priority.***
- Biomarkers of exposure and effects in living organisms as operational outcomes of a mechanistic understanding of intra- and inter-species variation of radiosensitivity under chronic low dose exposure situations, with a focus on the added value for both human and non-human radiological protection**; *not dealt with under the CONCERT calls***
- Multiple stressors and modulation of radiation effects in living organisms; ***not dealt with under the CONCERT calls.***

Such research priorities are to be implemented and adapted to various exposure situations (consistently with those defined to support the joint roadmap under preparation by the EJP CONCERT WP3 (CONCERT D3.4 "First joint roadmap draft", Nov. 2017, 28 pages):

(i) normal operation or accidents of/at various types of nuclear facilities including the nuclear fuel cycle (from uranium mining and milling, to waste management and decommissioning, including research installations),

(ii) medical, industrial and scientific use of ionising radiation sources,

(iii) military use of ionising radiation, such as *e.g.*, fallout from former nuclear weapons, or releases from nuclear-powered vessels,

(iv) activities and legacy related to the use of natural resources, containing naturally occurring radionuclides, that are processed neither for their fissile nor their fertile properties (NORM / TENORM),

(v) contaminated legacy sites, and

(vi) natural radiation as source of ionising radiation: terrestrial and cosmogenic radiation, natural events leading to radionuclide releases.

Given the gap analysis and the on-going research, ALLIANCE proposes the elementary research lines to be focused. ALLIANCE's vision on key-future research priorities is perfectly in line with the research challenges and priorities put forward by the CONCERT on-going joint roadmapping activity. It highlights ALLIANCE own research priorities and their potential links to the common and multidisciplinary challenges as they were defined by the different radiation protection platforms for the purpose of mentioned joint roadmap (see CONCERT D3.4 "First joint roadmap draft", Nov. 2017, 28 pages).

Biological and ecological effects of low dose/ low dose rate exposure on biota (*some of the research lines potentially synergistic with MELODI and/or EURADOS)*

- Identification and mechanistic understanding of molecular and cellular processes following exposure to ionising radiation and resulting in adverse effects at the individual level on population-relevant functions (growth, reproduction and survival, mainly non-cancer effects for non-human species; making use where relevant of state oft heart approaches such as omics, systems biology and trying to find biomarkers or Adverse Outcome Pathway). This may include (i) understanding how effects may modulate for external or internal exposure pathways, and for different radiation types; (ii) revisiting the RBE concept for non-human species by shifting to deterministic population relevant endpoints
- Understanding variation of responses between species at the individual and population levels due to genetic, environmental and behavioural factors and the interactions between these; Exploration of intra- and inter-species causes of variation in radiosensitivity and identification and validation of biomarkers of exposure and effects for use in prospective and retrospective assessments
- Studying hereditary effects within populations of species, the molecular basis of adaptation (or vulnerability) gained through generations and the inter-population effects in the ecosystem; role of epigenetics in genomic instability and inheritance in organisms/cells exposed to radionuclides/ionising radiation and in adaptation of organisms under conditions of a pressure selection
- Mechanistic basis to understand how multiple stressor exposure modifies ionising radiation effects and linking these to risk assessment
- Ecological consequences of exposure to ionising radiation (exposure effects relationships in the field vs. in the laboratory may be modified due to the combination of radiotoxicity effects on growth rate/reproduction

and geographic gene diversity, competition, predation, and abiotic factors including pollutants other than radionuclides)

- Development of advanced methods for fit-for-purpose dose assessment to support and robustly interpret effects studies

Integration and optimization of environmental exposure assessment for ionising radiation and other stressors (*some of the research lines potentially synergistic with Social Sciences and Humanities activities and/or MELODI and/or NERIS and/or EURADOS***)**

- Mechanistic understanding of radionuclide dispersion and transfer processes in and between the various components of the geosphere, biosphere and atmosphere, and associated mechanistic process-based modelling including foodwebs and biokinetics modelling. This mechanistic process-based modelling may integrate physical, chemical and biological processes; taking into account the influence of speciation and bioavailability of individual radionuclides (whatever their origins or the source-terms, including sequences of natural radionuclides constituting decay series in environmental components). This modelling may serve individual realistic human dosimetric assessment along with a better prediction of efficiency of countermeasures when required. This may include calibration and experimental validation of mechanistic models, characterisation of variability and uncertainty.
- Advanced methods to deal with scale extrapolation issues (from molecular processed observed *in vitro* to complete natural (eco)systems)
- Advanced modelling of process interactions at the various biosphere interfaces at the local, regional and global scales such as in (a) marine, brackish, estuarine and freshwater ecosystems, covering the watershed continuum from the source to the ocean and further afield at the global circulation level, and (b) terrestrial ecosystems (agricultural, forestry, natural and urban including NORM landfills); developing landscape-based models. This may include:
    - Interactions between natural hazards and radiologically contaminated areas (e.g., wind resuspension, wildfires or biogenic aerosol emission from contaminated areas or any hydro-meteorological events leading to redistribution of radionuclides through various processes)
    - Advanced methods for data treatments to cope with the large amount of data resulting from elaborated and comprehensive transfer assessment, environmental monitoring and improved dose assessment
    - Improvement /development of innovative methods to characterise the environmental contamination and its evolution in space and time in order to delineate the multiple-hazard footprint (*e.g.*, geostatistical interpretation of environmental, radiological, chemical data) of a site;
    - Integrated holistic modelling approach and advanced methods to identify the most significant sources of uncertainty related to the impact on human and environmental health
- Development of remediation methods and strategies in support of the management of radiocontaminated sites:
    - Innovative modelling approaches for evaluating the effectiveness of different remediation strategies to support decision making at various stages of assessment and remediation
    - Test of remediation strategies including bioremediation based on outcomes of mechanistic studies of radionuclide speciation and transfer in soils, waters and biota
    - Improved risk communication with stakeholders and development of multicriteria decision support tool for optimised remediation and management.

Radioecology-related research for optimising emergency and recovery preparedness and respons (*synergistic with NERIS activities***)**

- Customisation of atmospheric, river, marine, brackish water, terrestrial and urban dispersion models, food chain models and dose assessment models. Improvement of monitoring of the different environmental compartments, foods and goods. This includes the development and combination of different modelling and monitoring techniques (including data assimilation) to improve dose reconstruction and predictions of the impact of an accident.
- Development of more sophisticated parametrizations of processes of high health impact: environmental evolution of iodine speciation, low wind speed conditions, snow and fog events

- Improved understanding of countermeasures (mechanistic process-based models) to better build, select and implement countermeasure strategies at different times (preparedness, response, recovery) and in different geographical areas. This includes:
    - development of new countermeasures and remediation strategies, taking account for selection of level adopted to start decontamination, efficiency of decontamination and waste handling from an accident
    - integration of societal and ethical aspects including environmental characteristics into risk management. This should include methods for identification and priorisatoin of major socio-economical and ecological stakes inventories
    - further development of the participatory processes in emergency and recovery situations (advanced decision science, use of big data, communication strategies during the emergency and in the post-accident phases)

CONCERT WP2/WP3

GAP ANALYSIS NERIS

Version December 22, 2017

The following document provides proposal for research activities based on a first GAP analysis on research activities proposed by the NERIS community and that were not fully visited via national or international research project.

Proposal for research activities based on the GAP analysis

- Improvement of hydrological models, including urban hydrology, surface run-off and marine environment
- Application of foodchain models at the local level to derive sensible countermeasure strategies
- Improvement of dose assessment models considering both environmental monitoring data and personal monitoring data (e.g. personal dosimeters, thyroid measurements, whole body measurements)
- Improved monitoring including lay people, drones and European wide harmonisation of tools and methods
- Methods and guidance to optimise countermeasure strategies: development of measuring strategies to guide practical countermeasure implementation
- Methods and guidance to optimise countermeasure strategies: how to implement/apply the residual dose approach, how to implement fully the guidance from ICRP in terms of simulation and guidance for decision maker
- Research on lifting of countermeasures by developing an integral approach with simulation models and Operational Intervention levels (OIL); improved OILs extending the IAEA approach
- Stakeholder engagement database, better analysis of societal needs for an evaluation of legal instruments and governance frameworks, methods and tools for stakeholder engagement
- “emergency ethics” vs. “normal ethics” to develop guidelines for evacuation and post-accident management, compensation schemes
- Development of health surveillance approaches, dose reconstruction methods, socio-psychological and economic aspects of medical follow-up

First NERIS GAP analysis

The analysis focuses on former EU projects such as EURANOS (2004 – 2009), DETECT (2009 – 2011), NERIS-TP (2011 – 2014), PREPARE (2013 – 2016), HARMONE as part of OPERRA (2015 – 2017), SHAMISEN as part of OPERRA (2015 – 2017) and CONFIDENCE, TERRITORRIES, and ENGAGE as part of CONCERT (2017 ongoing).

The following tables provide the key research areas and if work was performed so far in these projects. It is not exhaustive as most of the simulation models implemented in decision support systems (DSSs) require improvement in various areas.

Research area 1. Challenges in radiological impact assessment during all phases of nuclear and radiological events

Area 1. Key topics	Sub-topics	Work performed
Key topic 1. Improved modelling	Atmospheric transport and dispersion modelling (ATM/ADM)	PREPARE, HARMONE, CONFIDENCE **Missing**: (a) development, sensitivity analysis and incorporation in DSSs of modelling tools for particular source terms (e.g., explosions, two-phase releases, aerosol sprays, fires, etc.), and dispersion of particular forms of substances (e.g., aerosol, phase-changing, particles with spectrum of different size, chemical transformations, etc.), (b) development, evaluation and incorporation in DSSs of fast but accurate modelling tools for dispersion in built-up areas (e.g., urban, industrial sites, etc.) and within large buildings
	Hydrological transport modelling	EURANOS, PREPARE **Missing**: urban hydrology completely missing; Improvements in marine foodchain, run-off modelling, radionuclide behaviour in lakes (behaviour in laces of Fukushima difficult to understand) and long term transport in river networks
	Dose modelling	HARMONE: ERMIN **Missing**: Intercomparison of models for use in a DSS; dose assessment considering both environmental monitoring data and personal monitoring data (e.g. personal dosimeters, thyroid measurements, whole body measurements)
	Radioecological modelling	PREPARE, HARMONE, CONFIDENCE **Missing**: Development of process based models not only for Cs, better customisation approaches for operational application of model also for local conditions, local and national wide application in one model environment

Area 1. Key topics	Sub-topics	Work performed
Key topic 2. Improved monitoring	Monitoring techniques and strategy	DETECT **Missing**: Integrated monitoring strategies with simulation and resource management, international harmonisation
	Data collection	HARMONE **Missing**: Development of guidance for data collection also for lay people and how to integrate this into operational approaches
	Optimization	DETECT **Missing**: Research on new equipment such as drones for dose monitoring and environmental monitoring and LIDAR for optimal use by atmospheric dispersion models
Key topic 3. Data assimilation	Improved source term estimation	PREPARE, CONFIDENCE **Missing**: (a) Link of inverse with in-plant (e.g. FASTNET project) source term estimation methodologies, (b), Further evaluation and improvement of operational aspects of source term reconstruction methods in DSSs, (c) development, evaluation and incorporation in DSSs of inverse methods for estimation of unknown radioactive substances source location (d) methodological research in mathematical procedures, data assimilation techniques and computer methods for complex matrices
	Improved impact assessment	CONFIDENCE **Missing**: Only started in CONFIDENCE and this will address only the basic principles for this related to key uncertainties
	Big Data, Data fusion	PREPARE **Missing**: Methods and tools to analyse the huge amount of calculations performed for preparedness in terms of usability in a real event. First attempt was done with the Analytical Platform, but potential is much bigger

Research Area 2. Challenges in countermeasures and countermeasure strategies in emergency & recovery, decision support & disaster informatics

Area 2. Key topics	Sub-topics	Work performed
Key topic 4. Countermeasures and countermeasure strategies	Countermeasures/management options	EURANOS, NERIS-TP, PREPARE, HARMONE **Missing**: Methods and guidance to develop countermeasure strategies well in advance and for all levels (local to national and international)
	Development of protection strategies or portfolios	**Missing**: Methods and tools for the local level
	Implementation and monitoring of countermeasures, including lifting of	EURANOS, NERIS-TP, SHAMISEN **Missing**: Methods and approaches for lifting of countermeasures, how to monitor the success of a strategy, compensation schemes, how to define OILs (besides the IAEA definition) and how to use them
	Consequence assessment and optimisation of countermeasure strategies	EURANOS, NERIS-TP, PREPARE, HARMONE **Missing**: Methods and guidance to optimise countermeasure strategies, how to implement/apply the residual dose approach, how to implement fully the guidance from ICRP in terms of simulation and guidance for decision maker
Key topic 5. Formal decision support	Robust decision making, including multi-criteria analyses	EURANOS, CONFIDENCE **Missing**: only first attempt in CONFIDENCE for paving the road
	Decisions under high uncertainty	CONFIDENCE **Missing**: only first attempt in CONFIDENCE, in particular which approaches are applicable under high uncertainty
	Methods and tools to support decisions	CONFIDENCE **Missing**: developing suitable tools besides MCDA in the nuclear area, decision making in a group with group performance implications
Key topic 6. Disaster informatics	Analytical platform	PREPARE **Missing**: explore operational value and potential end user, combine with natural disasters
	Knowledge database	NERIS-TP, PREPARE, ENGAGE **Missing**: expand to improved database using the assessments performed for preparedness, combine with big data analysis and extent accordingly to the other exposure situations (medical, post-accident, indoor radon, etc.)
	DSS interface, output and coupling	EURANOS, NERIS-TP, PREPARE **Missing**: coupling with Command and Control (C2) systems for tactical decision making, perform research on the usability of existing DSS, tailor to users need
	Virtual and augmented reality	**Missing**: Development of serious gaming tools to train the emergency actors

Research area 3. Challenges in setting-up a multi-faceted framework for preparedness for emergency response & recovery (with input from all perspectives)

Area 3. Key topics	Sub-topics	Work performed
Key topic 7. Emergency response and recovery framework, including reference levels	Assessment and understanding of risk and vulnerabilities	**Missing**: Vulnerability and risk assessment as starting point for strategy development beyond simple dose or contamination criteria
	Criteria, factors and considerations for protection strategy recommendations and decisions	**Missing**: Add human, societal and ethical factors to the decision making process in preparedness and response (e.g. critical groups)
	Managing the transition to recovery	**Missing**: development of criteria and procedures to lift countermeasures and prepare for the recovery phase, explore the need to change the political framework to properly address the recovery process (e.g. are legal and political structures appropriate to deal with a nuclear disaster?
	Operational issues (resources, capabilities and best practices)	**Missing**: how to use ICRP recommendations beyond the numbers – which is also problematic, optimisation and methods to apply
Key topic 8. Stakeholder engagement, involvement of the public & communication	Stakeholder and public engagement processes	EURANOS, NERIS-TP, PREPARE, CONFIDENCE, TERRITORRIES, ENGAGE **Missing**: Stakeholder engagement database, better analysis of societal needs for an evaluation of legal instruments and governance frameworks, methods and tools for stakeholder engagement
	Citizens Science	ENGAGE **Missing**: how to engage citizens to produce science
	Communication	PREPARE, CONFIDENCE, ENGAGE **Missing**: Role of social media in communication, long-term communication approaches, improved radiation protection culture
Key topic 9. Integrated emergency management – non-radiological aspects (health surveillance, ethical aspects, economic issues, …)	Health Surveillance	SHAMISEN **Missing**: Better health surveillance approaches, dose reconstruction methods, socio-psychological and economic aspects of medical follow-up
	Ethical aspects	**Missing**: “emergency ethics” vs. “normal ethics” to develop guidelines for evacuation and post-accident management, compensation schemes
	Socio-economic factors	PREPARE **Missing**: Methods to better define conditions for social trust, combination of psychological science and RP
	Radiation protection culture for emergency preparedness and post-accident management	ENGAGE **Missing**: Development of tools, methods, processes to build, maintain and transmit RP culture
Key topic 10. Uncertainty and incomplete information handling	Decisions under high uncertainty	CONFIDENCE, TERRITORRIES CONFIDENCE, TERRITORRIES perform research on that topic but are only starting point, so future

Area 3. Key topics	Sub-topics	Work performed
		research can be defined when both projects are completed
	Communication of uncertainties	CONFIDENCE, TERRITORRIES CONIDENCE, TERRITORRIES perform research on that topic but are only starting point, so future research can be defined when both projects are completed

GAP ANALYSES from EURADOS

07-02-2018

INTRODUCTION

EURADOS e. V. is registered in the German Register of Societies as a non-profit association for promoting research and development and European cooperation in the field of the dosimetry of ionizing radiation. Since autumn 2012, the European Radiation Dosimetry Group (EURADOS) has been developing its Strategic Research Agenda (SRA), which is intended to contribute to the identification of future research needs in radiation dosimetry in Europe. The present article summarises—based on input from EURADOS Working Groups (WGs) and Voting Members—five visions in dosimetry and defines key issues in dosimetry research that are considered important for the next decades. The five visions include scientific developments required towards (a) updated fundamental dose concepts and quantities, (b) improved radiation risk estimates deduced from epidemiological cohorts, (c) efficient dose assessment for radiological emergencies, (d) integrated personalised dosimetry in medical applications and (e) improved radiation protection of workers and the public. A detailed version of the SRA can be downloaded as a EURADOS report from the EURADOS website (www.eurados.org).

EURATOM has recently published a new call for Radiation Protection research, NFRP8, with a deadline of September 27th 2018. The call text specifically asks for a gap analyses to be performed in line with the prioritisation o of research in this field reflected in the strategic research agendas of the Radiation Protection Research Platforms:

"This action should seek close cooperation with and complement actions of CONCERT and MEDIRAD projects, strictly avoiding duplication. It aims at pursuing the integrative approach of radiation protection research (of radiation biology, radiation epidemiology, radioecology, medical applications, dosimetry, low-dose risk, emergency preparedness and response, etc.). It should complement the actions undertaken in response to the two above mentioned projects by providing incremental knowledge on the effects of ionising radiation on living beings, dosimetry and management of radiological and nuclear emergency. This action must take into account prioritisation of research in this field reflected in the strategic research agendas of the Radiation Protection Research Platforms. The pertinence and quality of the gap analysis will be considered during evaluation. It is recommended that this work should be undertaken using the working procedures established by the above-mentioned platforms. "

In this framework, EURADOS has performed a gap analyses, comparing the outcome of recently funded projects with the challenges identified in the EURADOS SRA. For this exercise, a list of recent European projects has been made. Only projects that are on-going or were finished after 2013 were included, because the SRA took into account results from older projects. Mainly FP7 funded projects from EURATOM were listed, including OPERRA and CONCERT projects. Also some SECURITY projects were considered. Some EURAMET projects have clear links with the EURADOS priorities and were considered as well, although the focuss was much more on metrological aspects than on radiation protection research.

There was only limited time to perform this gap analyses, and the evaluation of how much a certain project had contributed to the EURADOS challenges was done by members of the EURADOS Council and the Workin Group chairs. Because of this limited time, it was not possible to contact the coordinators of the concerned projects.

VISION 1: TOWARDS UPDATED FUNDAMENTAL DOSE CONCEPTS AND QUANTITIES

The current radiation protection system is based on operational quantities recommended by ICRU and protection quantities recommended by ICRP. Both are derived from absorbed dose using weighting factors to take into account tissue sensitivity and radiation quality on the biological outcome. For radiation quality, defined by particle type and energy spectrum, the weighting factors are too simplistic because the actual biological effectiveness is related to particle track structure, the stochastic pattern of energy depositions, which has a complex relationship to the energy/type of radiation incident on the body/phantom. A novel concept of radiation quality based on measurable properties of this particle track structure, such as microscopic distributions of energy deposition or ionisations, and its experimental realisation with 'dosemeter standards', would allow alternative quantities based on nano- and microdosimetry to be developed for predicting health effects instead of absorbed dose averaged over an organ or tissue.

- **Challenge 1: To improve understanding of spatial correlations of radiation interaction events (priority 12)**

  Detailed numerical simulations of track structures have provided evidence that the dependence of biological effectiveness on radiation quality of early occurring DNA strand breaks is strongly related to target sizes in the range of few nanometres. Trackstructure characteristics for other target sizes may be relevant for later biological end points such as chromosomal aberrations or cell death. Hence, techniques for track-structure characterisation, simulating a range of target sizes on the nanometre scale, need to be developed, and the link between nano- and macrodosimetry must be studied. Experimental investigation of radiation interactions with real nanometric objects in the condensed phase and establishment of uncertainty budgets for measured nanodosimetric quantities are further important tasks. The results of these efforts will provide a benchmark for the validation of simulation codes. Improved track-structure codes must be

developed that overcome the issue of Monte Carlo techniques using classical trajectories and the cross-section concept not being appropriate at the nanometre scale.

GAP ANALYSES:

This topic was not covered at all in any of the previous FP7 projects

- **Challenge 2: To quantify correlations between track structure and radiation damage (priority 1)**

The correlation between track structure and radiation damage must be established in a quantitative way. For this, cells need to be exposed to single particle tracks keeping the geometrical relation between the particle track and the exposed cell. In these experiments, the required radiobiological assays must be improved in terms of statistical power, useable cell types, etc. The physical characteristics of the track structures involved should be explored by using nanodosemeters with multi-scale measurement capabilities or by employing track-structure simulation codes that have been benchmarked using nanodosimetric measurements. Statistical cross analysis should then identify correlations between the yield of a particular biological end point and nanodosimetric quantities characterising the particle tracks. A variety of human cell types of different differentiation and coming from donors of different age and sex should be investigated.

GAP ANALYSES:

This topic was not covered in any of the previous FP7 projects. There was an EMRP (EURAMET) project BIOQUART (Biologically Weighted Quantities for Radiotherapy). The aim of BioQuaRT was to develop measurement and simulation techniques for determining the physical properties of ionising particle track structure on different length scales, and to investigate at the cellular level how these track structure characteristics correlate with the biological effects of radiation. It made some progress in this field, but still a lot of work is needed to come to a better understanding of the correlations between the track structure and radiation damage.

- **Challenge 3: To improve understanding of biokinetics of internal emitters (priority 11)**

Low concentrations of incorporated radionuclides such as alpha and beta emitters are characterised by spatially and temporally inhomogeneous dose distributions within a tissue or organ, e.g. plutonium and strontium isotopes in the skeleton, short-lived radon and thoron progenies in regions of the respiratory tract and Auger emitters such as some radioiodine isotopes in the thyroid. For example, alpha emitters may induce high doses on a local scale that may lead to cell killing, although the mean absorbed lung dose might be low. Hence, characterisation of the spatial inhomogeneity of dose and its effects from individual molecules to the whole body is needed, including benchmarking of track-structure Monte Carlo codes. These efforts must be accompanied by the development of more realistic models of radionuclide deposition in the relevant organs and by describing their energy deposition on a micrometer and nanometer scale to estimate the corresponding local biological effects. The results should be combined with available epidemiological observations. Tissue response may be different from that observed in individual cells, e.g. through bystander mechanisms. This raises the question of whether progenitor cells or also surrounding cells are the primary radiation target. Moreover, it is common practice to assume that cancer initiation is related to cellular transformation in single cells and thus depends on the local dose, while an important promotional factor is inflammation of the irradiated tissue, which is again related to local dose. This again raises the question of which cells in a tissue are the primary targets for initiation and promotion and, consequently, which are the relevant cellular doses.

GAP ANALYSES:

This topic was not covered in most of the previous FP7 projects. The CURE project was dedicated on Uranium exposure for epidemiology. It sought to develop a new study based on modern biological approaches, joint analysis of the main cohorts of workers monitored for uranium exposure, and the latest internal dose calculation models. This three-pronged approach aimed to improve the potential for characterizing the biological and health effects of chronic exposure to low doses of uranium. Also the SOLO project did some work on internal dosimetry for plutonium in the framework of an epidemiology study.

- **Challenge 4: To update operational quantities for external exposure (priority 10)**

Operational quantities should provide a reasonable estimate of the protection quantities, for optimisation and in assessing compliance with the limits. Conversion coefficients for both types of quantities have been published by ICRU and ICRP for photons, neutrons and electrons. ICRP has recently published revised protection quantities in standard male and female adult anthropomorphic phantoms and conversion coefficients for the updated protection quantities including an extension in particle type and energy range. The operational quantities provide a reasonable approximation to the new protection quantities, but with a number of limitations, including the absence of values of conversion coefficients for new particles and for extended energy ranges. Additionally, consideration is needed of operational quantities for the assessment of local skin dose and lens of the eye dose. Further development is required on devices and calibration facilities, as well as the establishment of calibration procedures, to determine the operational quantities.

Progress in nanodosimetry may demonstrate the need for revised protection and operational quantities that better reflect the radiation damage in the body.

GAP ANALYSES:

This topic was not covered in most of the previous FP7 projects. However, since our SRA was written, ICRU has proposed a new approach for the operational quantities. So part of this challenge is addressed, creating of course new actions to investigate the consequences of these proposed changes.

VISION 2: TOWARDS IMPROVED RADIATION RISK ESTIMATES DEDUCED FROM EPIDEMIOLOGICAL COHORTS

Current knowledge of relationships between dose and cancer and non-cancer diseases, and other radioinduced pathologies (e.g. eye lens opacity, fibrosis), depends largely on the analysis of situations where large populations have been exposed either acutely or chronically to ionising radiation. Among occupationally exposed groups, uranium miners, Chernobyl liquidators, Mayak workers, other nuclear workers, air crew, medical staff, etc. are of concern, while other studies include individuals exposed as a consequence of radiotherapy. Cohorts that may become more and more important in the future may include offspring cohorts of exposed parents. Cohorts such as radiotherapy patient populations, for example, are also useful because of the large number of individuals involved, the medium–high doses, and because accurate patient doses can be obtained. Large populations can also be obtained from diagnostic imaging patients. Other efforts include the establishment of national cohorts of individuals of the general populations who may benefit from dosimetric information and the setup of biobanks for physical and biological analyses.

- **Challenge 1: To explore exposure pathways not yet considered or validated (priority 13) and**
- **Challenge 2: To improve retrospective dosimetry for exposure pathways already considered (priority 14)**

It is important to note that whatever the cohort under consideration, development and harmonisation of dosimetry are essential. This is so because the basis for all risk estimates deduced from these cohorts is—among others—the dose. In order to give maximum support for current and future epidemiological and molecular epidemiological studies and to underpin theoretical radiobiological developments, dose distributions in the body following exposures from all known sources of radiation should be quantified and evaluated, in particular for mixed radiation fields that were present, for example, at work places of nuclear workers, or if there were multiple exposures to ionising radiation in medical applications (diagnostics and therapy). Moreover, to reduce bias in retrospective (bio) dosimetry, confounding factors such as chemical or biological contaminants or stressors should be identified and reduced and the age and sex dependence of radiation effects studied. In the past, in most cases, incidence and/or mortality of various cancer types were of major concern, while more recently, cancer diseases following in-utero exposure and non-cancer diseases such as cardiovascular diseases, neurological impairments or eye lens opacities have become of increasing concern. This raises new challenges, and a number of dosimetric improvements are required that include:

(a) Quantification and validation of exposure pathways that have not yet been considered thus far for certain cohorts. This includes doses to certain organs and tissues that need specific attention (e.g. eye lens, blood, brain, foetus), doses to substructures of certain organs (e.g. heart arteries and walls) and determination of the micro-distribution of doses in certain tissues (e.g. in the respiratory tract after inhalation of alpha emitters);

(b) Improvements in techniques of retrospective dosimetry for historical cohorts and validation of the estimated doses (e.g. for Chernobyl liquidators, Techa River populations, atomic bomb survivors, Mayak and Sellafield nuclear workers, uranium miners), which may also include quantification of additional exposures such as those due to residual radiation among the atomic bomb survivors and due to solar particle events among air crew;

(c) Improvement of uncertainty evaluation of doses estimated by retrospective dosimetry techniques.

GAP ANALYSES:

Several EC project have included epidemiological studies, which included a dosimetric studies. Some of these projects have developed further or improved the dosimetry techniques and have reduced the uncertainties, and can as such be considered as contributing to this challenge.

SOLO pooled the Sellafield worker, Mayak andTecha River cohorts to assess risks from exposures in utero and from plutonium in workers. CURE did similar things for Uranium workers, INWORKS forgeneral nuclear industry workers, while COCHER looked at Chernobyl survivors.

The EURALOC project improved the dosimetry for the eye lens with interventional cardiologists.

Several projects used also patient data in their studies, and have contributed to better dose determination at organ level for patient treatments. EPI-CT looked at CT exposure with children. PROCARDIO and CEREBRAD looked at childhood cancer survivors (heart and brain doses respectively). Also MEDIRAD will improve the organ dosimetry of patients undergoing different medical procedures. And ANDANTE improved the dosimetry of peripheral organs during radiotherapy, including neutron doses.

It will stay important to include a major dosimetric workpackage in each project that deals with epidemiology. And the uncertainties on the retrospective dosimetry remain large in all cases (workers, internal doses, patient doses) so that continuous effort is needed to reduce these uncertainties.

VISION 3: TOWARDS AN EFFICIENT DOSE ASSESSMENT IN CASE OF RADIOLOGICAL EMERGENCIES

Radiological emergencies are considered a major challenge of modern societies, including incidents that have an impact on large geographical areas and lead to exposure of large groups of the general population, terroristic attacks and accidents that involve industrial or medical radiation sources. Each of these exposure scenarios is associated with specific problems in determining the radiation doses, identifying individuals who are at the highest risk and deciding the best method to be applied for evacuation, medical treatment and remediation. The needs in terms of dosimetric protocols and techniques depend in particular on the number of victims and the severity of the exposure: at the first stage, triage is of importance, while at the second stage, more precise dose investigations are needed on identified victims.

- **Challenge 1: To identify and and characterize new markers of exposure (priority 8)**

A quick, efficient and reliable estimate of doses to affected individuals is required before any further decisions can be made by the responsible authorities. Moreover, real-time monitoring data might be scarceand rapidly change with time. A number of dosimetric improvements are therefore considered important to enable decision makers to initiate the most urgent actions. For example, rapid identification of individuals with high risk of developing radiationinduced injuries, among hundreds or even thousands of 'worried-well', is essential. Further efforts are needed towards identification of materials of daily life that could be used as fortuitous dosemeters, measureable by electron paramagnetic resonance (EPR), thermoluminescence (TL) and optically stimulated thermoluminescence (OSL). These techniques can also be applied to biological materials such as tooth enamel, finger nails and hairs, preferably by mobile systems for application in the field, which need to be developed. Other objects that were exposed at a certain place could also be used. For the computational techniques applied, automatic direct input of dose rate measurement data into databases, interpolation and extrapolation algorithms and tools for prediction of doses are the main routes of further development of efficient techniques.

- **Challenge 2: To develop strategies and methods to increase measurement capacity (priority 16)**

In order to handle a large number of dosimetric samples, strategies and methods to increase measurement capacity must be developed. One solution is automation of sample preparation and measurement, in particular for analysis of dicentric chromosomes and micronuclei where the evaluation of metaphases should be fully automated. Additionally, methods for high-throughput and cheap measurements should be further developed such as gene expression or protein biomarkers. Web-based scoring of captured images is emerging as a fast and easy method of performing chromosome analysis whilst involving laboratories spread all over the world, and networking of laboratories has been identified as a very useful approach to get fast and reliable dose estimates. Such networks have been or are in the process of being established, but they need to be maintained and their functionality has to be trained and practised.

GAP ANALYSES:

This challenge was an important topic in 2 recent projects. RENEB established a European network in biological dosimetry that will guarantee highest efficiency in processing and scoring of biological samples for fast, reliable results implemented in the EU emergency management. MULTIBIODOSE was a security project that analysed a variety of biodosimetric tools and adapted them to different mass casualty scenarios.

In the recently started CONCERT project CONFIDENCE the uncertainty of radiological data will be investigated and its further propagation in decision support systems and dose estimation in case of accidents. This is also related to this challenge.

Increasing the measurement capability was also an important topic in the 2 recent projects RENEB and MULTIBIODOSE. CATHYMARA adressed the specific topic of thyroid measurements.

Next to these, also other projects adressed and are adressing this important issue indirectly, like SHAMISEN and TERRITORIES, by analysing past experiences and making recommendations. This will be continued in the new CONCERT project SHAMISEN SINGS.

Despites these recent projects, there remains still research to be done for better and faster etimation of doses in case of emergencies, using different physical and biological techniques. The dosimetry in emergencies is still far from ideal.

- **Challenge 3: To quantify doses after accidental internal contamination (priority 3)**

For dose assessment after internal contamination, efforts should be made to link internal dosimetry from incorporated radionuclides with biological dosimetry methods. This would require definition of suitable biological end points, definition of the proper dosimetric quantity to be compared with the biological end point (e.g. blood dose instead of administered activity) and identification of cases for which sufficient biological dosimetry and bioassay data are available to be used for method validation. These studies could also be performed using radiopharmaceuticals. Specific emergency bioassay methods for in vitro monitoring of radionuclides, such as transuranic isotopes, must be either improved or developed, and then validated. For other radionuclides such as radioiodine isotopes, new thyroid phantoms of various sizes should be developed for in vivo monitoring and computational dosimetry. These actions should be complemented by development of counter measures to reduce doses after accidental internal contamination. In particular, for transuranic isotopes, reference biokinetic models under diethylene triamine pentaacetic acid therapy should be developed to improve the reliability of dose assessments in such cases.

GAP ANALYSES:

The first CONCERT call project CONFIDENCE will handle partial aspects of accidental internal contamination, as did SHAMISEN. CATHYMARA adressed the specific topic of thyroid measurements.

Still, there is a lot of work to improve the real dose determination after accidental internal contamination for a whole series of isotopes.

VISION 4: TOWARDS AN INTEGRATED PERSONALIZED DOSIMETRY IN MEDICAL APPLICATION

Modern medicine offers a variety of diagnostic and therapeutic procedures that involve ionising radiation, and consequently medical exposures are largely responsible for exposure from man-made sources of ionising radiation. In European countries, a considerable fraction of the population is being treated by radiotherapy. The distribution of dose within the body following radiotherapy, in particular in healthy tissues outside the tumor, varies considerably with many factors, and doses can vary spatially from tens of gray to milligray. All parts of the dose–risk curve for subsequent cancer induction are therefore involved, from the region where low-dose effects occur, through the region defined largely by the atomic bomb survivors, to the further non-linear region at high doses where cell kill and re-population effects are known to occur.

- **Challenge 1: To establish out-of-field dosimetry for photon and particle therapy (priority 5)**

Epidemiological studies of second cancers following radiotherapy require specification of dose to the patient at the site of the subsequent malignancy, making outof- field dosimetry for photon and particle therapy an important field of dosimetric development, including the development of analytical models for outof-field dosimetry calculations.Moreover, becauseadditional dose contributions may come from diagnostic procedures, epidemiological studies will require quantification of all sources (therapy and/or imaging) for an estimation of combined risk, which must be harmonised and combined. This could be done by means of computational methods supported by the development of novel small-scale detectors for neutrons and photons that could be used to measure the dose distribution within dedicated phantoms irradiated according to typical radiotherapy treatments and modalities. Special attention must be given to paediatric radiotherapy and hadron radiotherapy where high-energy secondary neutrons are produced. As an ultimate goal of this research, calculation of a complete map of doses for each individual patient would be possible.

GAP ANALYSES:

ANDANTE focussed on the neutron exposure in the out-of-field organs. Other projects like PROCARDIO and CEREBRAD looked at secundary effects after radiotherapy for specific organs, and have done some dosimetric work for this. In MEDIRAD work will be done on cardiovascular effects after breast radiotherapy, including an epidemiological study.

Still, a generic study of out-of-field dosimetry, combined with imaging doses, have not been adressed in any project.

- **Challenge 2: To improve dosimetry in modern external beam radiotherapy (priority 6)**

The rapid development in new radiotherapy techniques requires a continuous effort in dosimetry research, not only for out-of-field doses. There is also a need to develop experimental online dosimetry techniques and to improve calibration techniques. Indeed, it is important to be able to check whether the planned dose distribution to the tumour region is accurately administered.

GAP ANALYSES:

This topic was not covered at all in any of the previous FP7 projects. There were some EMPIR and EMRP projects focussing on metrological aspects, like MRgRT (metrology for MR guided radiotherapy), Absorb (Absorbed dose in water and air) and MetrExtRT (metrology for radiotherapy using complex radiation fields).

- **Challenge 3: To improve internal microdosimetry in radiotherapy and medical imaging (priority 15)**

Radiopharmaceuticals have been used in medical imaging and radiotherapy, respectively, to diagnose and to treat cancer and other diseases. The features of cellular and molecular radiobiological effects involved depend strongly on the spatial and temporal distributions of initial physical tracks, on induced chemical radicals and later on dynamical molecular progresses. The analysis should cover alpha and Auger emitters and beta radiation at the levels of molecule, cell, tissue, organ and organism. Furthermore, the potential application of gold or other nanoparticles in medical diagnostic imaging and radiotherapy should be investigated. Molecular biological experimental and theoretical Monte Carlo simulation studies on a micro- and nanometre scale are considered important to reveal the correlation between the experimental biological findings at the cellular level in specific organs, like the lungs and kidneys, and the micrometer and nanometer scale doses of these emitters.

GAP ANALYSES:

This topic was not covered at all in any of the previous FP7 projects

- **Challenge 4: To optimize dose and risk estimations in interventional radiology (priority 7)**

Operational quantities should provide a reasonable estimate of the protection quantities, for optimisation and in In interventional radiology, medical dosimetry is important because the dose to patients can be high, leading even to tissue reactions that may be increased when using low-energy photons below few hundred keV. Thus, an improved system of dose calculation and dose monitoring for adult and paediatric patients needs to be developed (including skin dose measurements, calibration procedures for dose measuring devices, organisation of intercomparisons between clinics and development of online patient dosimetry procedures). This would enable assessment and improved use of diagnostic reference levels (DRLs) and other quantities for optimisation of patient doses, and improved accuracy of skin and other organ doses. The final goal would be patient-specific real-time dose mapping of various dose quantities with known uncertainty and with efficient use of digital imaging and communications in medicine (DICOM) information. Thus, practical systems of patient dose monitoring for local as well as wide-scale evaluation and comparison of patient doses will be available. These systems can be used to estimate and optimise patient doses and radiation- induced risks and to prevent accidents.

GAP ANALYSES:

Two on-going projects cover some parts of this challenge. VERIDIC will focuss on skin doses during interventional procedures. MEDIRAD will look at organ doses during such interventional procedures, and will work on facilitating the retrieval of dose information from the DICOM header.

- **Challenge 5: Establish reliable patient dosimetry in CT examinations (priority 9)**

As for computed tomography (CT) examinations, establishment of reliable patient dosimetry is also important. This could be done by developing automatic systems of dose monitoring (with known uncertainties) and scanner calibration using dedicated phantoms in order to provide easy use of DRLs, improved optimisation of patient doses and improved accuracy of organ doses for risk estimation and population dose estimation. In an effort towards personalised dosimetry, methods of patient dose determination should cope with varying patient sizes. The focus should be on paediatric patients, and dose optimisationmust be considered as key feature of these efforts, especially in view of the rapid development of new CT techniques

GAP ANALYSES:

Similar as for interventional procedures, MEDIRAD will also look at CT examinations. For pediatric examinations, EPI-CT did a lot of work for dose estimations. DIMITRA did the same for dental cone beam CT, while BREAST-CT looked at breast CT exposures.

VISION 5: TOWARDS AN IMPROVED RADIATION PROTECTION OF WORKERS AND THE PUBLIC

- **Challenge 1: To refine, validate and implement new biokinetic models (priority 18)**

The assessment of dose from internal exposure to radionuclides is subject to uncertainty due to activity measurement errors, individual variability, imperfection of biokinetic and dosimetric models and unknown parameters of exposure. Work required will include implementation of the latest biokinetic models including age- and sex-dependent biokinetic parameters. Dose assessment due to administration of (short-lived) radiopharmaceuticals to patients should consider the influence of certain diseases on biokinetic parameters adapted to the short half-lives of the isotopes considered, and the realistic modelling of blood retention and urinary bladder voiding. This is needed to allow modification of standard biokinetic models that were developed for longer-lived radionuclides, based on data from healthy persons. In this context, the availability of databases including autopsy cases should be used to validate any new biokinetic model. The results of these developments should be transferred to operational radiation protection, including guidelines and technical recommendations.

GAP ANALYSES:

This topic was not covered at all in any of the previous FP7 projects.

- **Challenge 2: To develop calibration procedures for partial body counters**

In vivo measurements using partial body counters represent a valuable method in internal dosimetry, providing actual information on radionuclide activity within the body of an individual. However, there is no standard calibration procedure, and suitable anthropomorphic phantoms to assess, for example, the skeletal activity of bone-seeking radionuclides are scarce.To reduce the uncertainties in in vivo measurements, the influence of individual body parameters and phantom characteristics on the detection efficiency must be investigated. Phantom development should include construction of new physical phantoms complemented by their mathematical representation in order to account for individual variability of the persons to be measured.

GAP ANALYSES:

Partial body counters were only adressed in the CATHYMARA project, but this was limited to thyroid monitoring.

- **Challenge 3: To develop accurate and on-line personal dosimetry for workers (priority 4)**

A further challenge is to provide online personal dosimetry for occupationally exposed workers. This requires monitoring of workers in real time for all limiting quantities (including whole body, eye lens, extremities, brain and heart doses). Well-characterised active personal and area dosemeters should be developed for all relevant dosimetric quantities including all relevant radiation fields, especially pulsed fields, with and without shielding, as well as computational tools using advanced tracking technology. Further consideration is needed taking into account their potential for use as official dose record. The inclusion of dosimetry of other potentially radiosensitive organs (brain, heart) might also be needed depending on the outcome of biological research on the brain and cardiovascular risk.

GAP ANALYSES:

For on-line dosimetry, a new CONCERT project PODIUM was approved and started in 2018. Dosimetry of other radiosensitive organs (like heart and brain) for radiation workers is not yet adressed fully in any project. Active dosemeters are still missing for many applications.

- **Challenge 4: To develop neutron dosimetry techniques further (priority 2)**

Neutrons are intentionally used or incidentally created in various scientific and technical applications, and they can dominate the total dose received. Neutron dosimetry is still challenging as neutrons are present in mixed fields and are indirectly ionising particles. Their energy range may cover up to 12 orders of magnitude, they show a wide range of angles of incidence and their conversion coefficients from fluence to dose vary by a factor of 50 over the entire energy range. Some neutron fields represent new challenges, for example, due to strongly pulsed radiation and/or high energy ranges, and proper reference fields are needed. The characterisation of workplace fields is complex and requires sophisticated procedures. Better and easier-to-use methods are needed, allowing the uncertainty of results to be evaluated. The detection threshold of neutron personal dosemeters and their energy and angular dependence remain the main deficiencies of neutron personal dosimetry compared with that for photons.

GAP ANALYSES:

Neutron dosimetry was not covered in recent projects. Only the ANDANTE projects covered the biological aspects of neutrons in the frame of peripheral doses in radiotherapy.

Neutron exposure of radiological workers will be partially covered by the newly started PODIUM project, where computational tools will be used to estimate neutron exposure.

The improvement of neutron dosimetric measurement techniques were not covered in any projects.

- **Challenge 5: To include nuclide-specific information in environmental monitoring (priority 17)**

As for radiation protection of members of the public, permanent and reliable environmental radiation monitoring is indispensable, and nuclide-specific information and data on ground and air contamination levels are of key importance for adequate governmental decisions. Therefore, novel and improved instrumentation for field station use should be developed to allow for measurement of dose rates and collection of nuclide-specific information. New and improved measurement systems based on 'high-resolution' spectrometric detectors require comprehensive scientific investigations of detector features, spectra evaluation and de-convolution methods. These systems could become the core instrumentation of the next generation of environmental radiation monitoring networks in Europe.

GAP ANALYSES:

This challenge will be partially important in the recently started CONCERT project CONFIDENCE, which deals with radiological uncertainties in decision making.

Two recent EURAMET (EMPIR) projects were focussed on the metrological aspects of this challenge: PREPAREDNESS and METROEMR.

Despites these recent projects, there remains still research to be done for improving monitoring including lay people, drones and European wide harmonisation of tools and methods.

CONCLUSION

Following lists gives an overview of the status of the different challenges relative to the EC funded projects of the last years. Included between brackets is the priority of these challenges. These priorities were determined by the EURADOS community, and reflect how important the EURADOS members find these challenges.

It is clear that none of the challenges is completely covered by past projects. There is need for many research projects in the different vision to make further significant progress in dosimetry for radiation protection. Still, because the amount of money is limited in the next EURATOM NFRP8 call, we decided to put forward only the challenges in group A as priorities for this call. For simplification and because they are linked, challenges 1.1 and 1.2 will be combined, as well as 1.3 and 5.1.

A. Challenges not or hardly covered

- **Challenge 1.2: To quantify correlations between track structure and radiation damage (priority 1)**
- **Challenge 5.4: To develop neutron dosimetry techniques further (priority 2)**
- **Challenge 4.2: To improve dosimetry in modern external beam radiotherapy (priority 6)**
- **Challenge 1.3: To improve understanding of biokinetics of internal emitters (priority 11)**
- **Challenge 1.1: To improve understanding of spatial correlations of radiation interaction events (priority 12)**
- **Challenge 4.3: To improve internal microdosimetry in radiotherapy and medical imaging (priority 15)**
- **Challenge 5.1: To refine, validate and implement new biokinetic models (priority 18)**

B. Challenges partially adressed

- **Challenge 3.3: To quantify doses after accidental internal contamination (priority 3)**
- **Challenge 4.1: To establish out-of-field dosimetry for photon and particle therapy (priority 5)**
- **Challenge 1.4: To update operational quantities for external exposure (priority 10)**
- **Challenge 5.2: To develop calibration procedures for partial body counters**

C. Challenges extensively covered

- **Challenge 5.3: To develop accurate and on-line personal dosimetry for workers (priority 4)**
- **Challenge 4.4: To optimize dose and risk estimations in interventional radiology (priority 7)**
- **Challenge 3.1: To identify and and characterize new markers of exposure (priority 8)**
- **Challenge 4.5: Establish reliable patient dosimetry in CT examinations (priority 9)**
- **Challenge 2.1: To explore exposure pathways not yet considered or validated (priority 13)**
- **Challenge 2.2: To improve retrospective dosimetry for exposure pathways already considered (priority 14)**
- **Challenge 3.2: To develop strategies and methods to increase measurement capacity (priority 16)**
- **Challenge 5.5: To include nuclide-specific information in environmental monitoring (priority 17)**

EURAMED
European Alliance for Medical Radiation Protection Research

Gap analysis and possible research topics answering the EC call NFRP-2018-8 January 24, 2018

1. **Background:**

   A preliminary gap analysis was performed to identify research topics which have not been addressed appropriately or at all in the field of medical radiation protection by projects awarded under the 7th Framework Programme or Horizon 2020. The EURAMED strategic research agenda (SRA) document, the CONCERT joint roadmap for radiation protection research, the EURAMED roadmap and the research priority lists ("SRA statements") were taken into consideration to elaborate this analysis. The current document is not intended to be an exhaustive list of gaps, but rather a short list of identified gaps which should be addressed with a high priority and could be possible candidates to be addressed by proposals answering the current EC call NFRP-2018-8 published in November 2017.
   In the above mentioned call, a further integration of European radiation protection research is required, therefore projects helping to close the identified gaps in medical radiation protection research should ideally also foster this integration process between the different radiation protection research areas.

2. **Identified projects within the 7th Framework Programme and their contribution to medical radiation protection research as identified by EURAMED**

   A number of projects have been identified that dealt with exposures related to medical applications of ionizing radiation. These are briefly mentioned in the following list:
   ORAMED concentrated on describing exposures of staff performing medical procedures like for example interventional procedures. Some aspects of optimizing such exposures have been investigated as well, but all were staff-related.
   MADEIRA focused on optimizing the nuclear medical applications of ionizing radiation to patients with a specific emphasis on nuclear medical imaging. The research was carried out developing new systems for image data collection, new time schemes based on biokinetic data sampling and modelling allowing for lower doses or better images as well as new software tools for optimizing image reconstruction based on real patient data.
   ANDANTE focused on biological effects of neutrons especially with respect to pediatric radiation therapy.
   SCOLIO-SEE tried to improve scoliosis diagnostics by improving 3D image processing.
   PEDDOSE.NET looked for dosimetry and health effects of the diagnostic use of radiopharmaceuticals in pediatric patients.
   SEDENTEXCT investigated the possibilities for enhancing safety and efficacy of dental CT procedures.

CHILD_MED_RAD and EPI-CT were projects looking for epidemiological studies about radiation risk especially in cohorts of children exposed in medical applications of ionizing radiation.
ALLEGRO investigated the early and late health effects of radiation therapy also with a focus on pediatric patients.
BREAST-CT developed a dedicated 3D imaging modality for the breast to improve the benefit to risk ratio in mammographic applications.
EUTEMPE-RX was a project to improve education of medical physicists.
EPIRADBIO evaluated cancer risk for exposures below 100 mSv especially for breast, lung, thyroid and the digestive tract as for example resulting from specific medical applications.
PROCARDIO focused on cardiologic effects for various dose ranges of relevance mainly in radiation therapy applications.
DARK_risk looked for epidemiological studies on a pediatric cohort in Serbia exposed to x-rays.
DOREMI and **OPERRA** were large-scale projects, in the development of the medical SRA was initiated (especially in OPERRA). Smaller projects also dealing for example with dental procedures were funded through OPERRA.

3. **CONCERT and MEDIRAD**

Within CONCERT there has been a lot of work ongoing to integrate the strategic aspects of medical radiation protection research into the European framework. The projects funded within CONCERT as far as known so far will not tackle many of the topics identified by the EURAMED SRA, the priority statements or the roadmap documents. Some health risk aspects are covered, which can be related to medical applications of ionizing radiation and there is also some research for dosimetry in the field of medical exposures. However, within CONCERT projects related to medical exposures like PODIUM, the dosimetry is mainly focused on occupational dosimetry and does not deal with optimization. VERIDIC is a dosimetry project to determine skin doses of patients by simulation. SEPARATE uses medical exposure situations to understand low-dose risk, but does not focus on optimizing medical radiation protection in a clinical situation. With ENGAGE, there is a project that deals with stakeholder engagement also for medical applications of ionizing radiation. The LEU-Track project within CONCERT uses patient groups to understand radiation-induced cancer development.

As stated on the official website, “the Horizon 2020 MEDIRAD project on implications of medical low dose exposure aims to enhance the scientific bases and clinical practice of radiation protection in the medical field and thereby addresses the need to understand and evaluate the health effects of low dose ionising radiation exposure from diagnostic and therapeutic imaging and from off-target effects in radiotherapy.” MEDIRAD focuses on reliable dosimetry for clinical-epidemiological studies, on understanding cardiovascular and cancer risk effects related to medical exposures and elaborates recommendations for improved radiation protection.

4. Gap analysis and tasks for potential projects answering the EC call NFRP-2018-8:

As can be seen from the above-mentioned summary, most of the projects performed so far, focused either on exposure determination (only very limited tasks on exposure determination for patients, but mostly occupational radiation dose determination for medical staff) or on potential health detriments related to medical procedures using epidemiological or radiobiological approaches. Only very few projects really tried to understand the full potential for optimizing procedures and translating such results into clinical practice. Therefore, the potential benefit and impact of medical radiation protection research for the European population has not been achieved yet.
In order to address this major, evident gap, EURAMED recommends that projects answering the call NFRP-2018-8 should really focus on the optimization of radiation application for the patients. In that sense, dosimetry, radiobiology, image quality description might be necessary research aspects, but should always be embedded into projects aiming to achieve optimized procedures for the patients and their transfer into clinical practice.
Research is needed to develop optimization strategies in terms of exposure and clinical outcome using modern technologies.
The following text provides key areas for research in the field of medical radiation protection:

a) Fixed activity approach versus individualized dosimetry-based activity determination in radionuclide therapy

Article 56 of the new EU directive 2013/59/EURATOM related to optimization states that 'For all medical exposure of patients for radiotherapeutic purposes, exposures of target volumes shall be individually planned and their delivery appropriately verified taking into account that doses to non-target volumes and tissues shall be as low as reasonably achievable and consistent with the intended radiotherapeutic purpose of the exposure'. In Chapter II, Definitions, it is further stated that 'radiotherapeutic means pertaining to radiotherapy, including nuclear medicine for therapeutic purposes'. This is in line with EURAMED SRA topics 1, 2 and 3.
A large scale randomized trial would be necessary to determine the optimized procedures in radionuclide therapy taking into account survival rates, quality of life, costs etc. Such trials have not been performed in any of the projects mentioned before.

b) Artificial intelligence in medical radiation protection

The goal of this topic is to see if Artificial Intelligence (AI) technology can be used to improve dose optimization by developing algorithms for dose reduction purposes, and for Image quality (IQ) assessment (EURAMED SRA topic 1) in clinical routine (EURAMED SRA topic 3). Ethical aspects have to be discussed i.e. how AI tools could

be implemented into clinical routine (EURAMED SRA topic 4). This topic requires involvement of AI specialists, practitioners, medical radiation physicists and IQ specialists as well as experts from social sciences and humanities.

This topic is not considered in any of the projects mentioned before.

b-1) example: Development of a neural expert system to define the optimum acquisition protocol in medical imaging

In today´s clinical routine, the radiographer still has to manually choose all the technical exposure parameters and adapt them to the examination and patient characteristics, which is provoking errors and avoiding optimization of procedures for the individual patient.
Therefore, there is a need to develop new concepts in medical imaging by integrating neural expert systems, that would define the “most adequate technical parameters” for the exposure, taking into consideration clinical indications and patient characteristics, guaranteeing the needed diagnostic image quality at the lowest exposure.
This topic has never been addressed by FP funding and is related to topic 1, 3 and 4 of the EURAMED SRA.

c) Radiation protection approaches in medical applications based on individual radiosensitivity

As stated by Michel Bourguignon and coauthors (Int. J. of Low Radiation, 2013 Vol.9, No.1, pp.52 – 58) “individual radiosensitivity is a real concern for public health since 5-15% of the population may be concerned and radiosensitive individuals generally show higher cancer risk than the rest of the population.” This is of special importance when irradiating patients. Thus, individual radiosensitivity is a key issue which could be addressed by a research project in the current call. The goal should be to develop methods for medical exposures in diagnostic, minimally invasive or radiotherapeutic procedures based on ionizing radiation to avoid side effects and adverse events by prediction of individual radiosensitivity and develop strategies for adjusting doses correspondingly.

The research could investigate new markers and reasons for the individual susceptibility but should focus on its use in medical applications. In this later aspect, developing methodologies but also their implementation into clinical practice should be addressed. Again, research would be including tasks of the topics 1, 3 and 4 of EURAMED SRA, but would also especially focus on questions related to topic 2.

c-1) example: individual radiation protection approaches in medical applications based on disease- or exposure-related radiation sensitivity of irradiated organs

In many cases, patients are exposed to radiation in a region which is already affected

by a disease. This might be correlated with higher or lower sensitivity to ionizing radiation of the exposed organs. Trying to demonstrate such effects and understand the reasons could allow to optimize radiation procedure sparing specifically sensitive areas or even enhance curing effects of radiation therapy. In addition, e.g. caused by iodinated contrast agents there could be local dose or effect enhancement aspects. Due to Auger electrons in the region directly connected to the iodine there could be dose enhancements on orders of magnitude, which could add on to effects that e.g. iodine might sensitize the region to be investigated
Such research is neither performed in MEDIRAD nor in any of the CONCERT funded projects nor in any project of 7th Framework Programme. Projects trying to fill this gap would require research on individual patient dosimetry (EURAMED SRA topic 1), epigenetics and individual susceptibility (EURAMED SRA topic 2). This topic requires involvement of IT specialists, medical physicists and clinicians for gathering data, for using existing data as well as for showing exemplarily how to use results in clinical practice.

c-1-1) exemplary approach: Establishing Radiomics for individualised medicine and its application in medical radiation protection.

Radiomics could be used together with texture analysis approaches within a project answering the current EC call to look for effects related to individual sensitivity of single organs. Such approaches could also be implemented to develop optimization approaches on an individual patient basis. It should be highlighted that also such a combined approach would need to focus on dedicated applications / diseases in an exemplary way. A clinical transfer would be mandatory.

c-2) example: Effects of low and high ionizing radiation doses on immune system

There is quite some evidence to suggest that high-dose irradiation correlates with immunosuppression, while low-dose irradiation correlates with immunostimulation, at least for quite a number of patients. The high-dose irradiation is mainly mediated by resistant T regulatory cells providing an immunosuppressive profile, while at low-dose irradiation CD8+ and B cells seem to be resistant, resulting thus in immune activation. The immune system consists of a complex regulatory balance of immunostimulation versus immunosuppression. Animal and patient studies are needed to define radiation dose levels that will promote or suppress the development of an antigen specific and/or antigen non-specific immune response. It should also be investigated on how far such mechanisms are depending on individual patient status or whether they are correlated with individual radiosensitivity. Advanced dosimetric methods should accurately estimate radiation dose to each specific tissue/organ of the body. This topic has not been considered in any of the projects mentioned in section 2 of this document and would be related to EURAMED SRA topic 2.

MELODI Multidisciplinary European Low Dose Initiative

MELODI Gap Analysis

NFRP-8 Info Day, 20th February 2018

The process

MELODI Multidisciplinary European Low Dose Initiative

- Prior to EU research funding calls, MELODI develops a short statement indicating its view on current research needs, which serves as an input to those responsible for defining call topics.
- In October 2017 the European Commission indicated its intention to open a EURATOM call that includes radiation protection. The proposed work programme includes topics NFRP-2018-8 for research and NFRP-2018-9 for review of previous activities.
- NFRP-2018-8 specifically indicates that a 'Gap analysis' will be required for each proposal and NFRP-2018-9 could be usefully informed by such an analysis.
- The RP platforms decided to carry out such gap analysis and communicate the analysis openly to the European research community prior to the call.
- The SRA Working Group of MELODI reviewed relevant EURATOM research undertaken (or underway) in FP6, FP7 and Horizon 2020 identifying their relevance to the six key areas of research identified in the MELODI SRA and roadmap
- This informed the identification of gaps that are considered as potential areas for research under NFRP-2018-8 call.

Priority research areas (SRA)

MELODI Multidisciplinary European Low Dose Initiative

1. To explore the shape of the dose-response relationship for radiation-induced health effects **(*Shape*)**
2. To understand the potential impact of individual susceptibility on radiation-induced health effects **(*Susceptibility*)**
3. To identify, develop and validate biomarkers for exposure, early and late effects for cancer or/and non-cancer diseases **(*Biomarkers*)**
4. To explore and define the role of epigenetic modifications in radiation-induced health effects **(*Epigenetics*)**
5. To explore the roles of specific target cells for radiation-induced late developing health effects **(*Target cells*)**
6. To understand the health effects of inhomogeneous dose distributions, radiation quality and internal emitters **(*Inhomogeneity*)**

Projects addressing priority areas

	FP6 (9)	FP7 (18)	H2020 (4)
Shape	5	15	4
Susceptibility	6	4	1
Biomarkers	4	9	3
Epigenetics	1	6	3
Target cells	-	9	-
Inhomogeneity	2	6	1

Conclusions on previous projects

MELODI Multidisciplinary European Low Dose Initiative

- Clearly there have been many projects supported under FP6, FP7 and H2020 that address issues highlighted by MELODI as key areas requiring research to improve low dose and low dose rate radiation health risk assessment.
- All funded projects align with one or more of MELODI's key areas as identified in the SRA and roadmap.
- All have contributed to advancement of the field and building the scientific evidence base for low dose/dose rate risk assessment.
- All diseases/health effects of actual and potential relevance to low dose risk – cancer, circulatory disease, cognitive effects and cataract are considered and a shift in emphasis amongst funded projects towards the non-cancer diseases can be seen.
- While all projects have made progress in building the evidence base as noted, there remain areas where additional work could be beneficial; these are considered in the gaps identified by MELODI.

Gaps remaining

MELODI Multidisciplinary European Low Dose Initiative

Shape

- Health risk studies amongst populations exposed to background and environmental sources of radiation, and experimental model studies using relevant exposure parameters
- Studies of second cancers arising in populations treated by radiotherapy, and relevant experimental model studies
- Health risk and experimental model studies considering co-exposures to radiation and other agents
- Studies that improve organ-specific cancer risk estimates
- Studies that will reduce exposure assessment measurement errors in epidemiological analyses

Susceptibility

- Studies that lead to the identification and validation of biomarkers of disease risk and/or susceptibility
- Studies that identify and validate cohorts suitable for molecular/biomarker epidemiological studies
- Studies of tissue level effects and the role of individual differences in tissue architecture that impact on susceptibility to radiogenic diseases
- Studies that potentially lead to the identification of biomarkers of resistance to radiation health effects

Gaps remaining

MELODI Multidisciplinary European Low Dose Initiative

Biomarkers

- Studies that lead to the identification and validation of sensitive, rapid and reliable biomarkers of exposure
- Studies that lead to the identification and validation of biomarkers of health risk/health risk susceptibility/resistance

Epigenetics

- Studies that provide clear evidence for or against a role for epigenetic processes operating in radiation carcinogenesis, and dose/dose-rate/radiation quality information
- Studies that provide clear evidence for or against a role for epigenetic processes operating in circulatory diseases/cataract/cognitive dysfunction, and dose/dose-rate/radiation quality information
- Studies that provide clear evidence for or against the operation of ageing/senescence processes in radiogenic disease

Gaps remaining

Target cells

- Studies that identify and quantify the stem/progenitor cell populations at risk for all radiogenic cancer types and non-cancer diseases
- Studies that provide quantitative information on the processes contributing to radiogenic diseases in relevant stem/progenitor cell populations
- Studies employing heterotypic 3D cell/tissue/organ culture and animal models to examine radiation effects and sensitivity in stem cells

Inhomogeneity

- Studies that consider organ dose in relation to intra-organ dose distribution in relation to health effects
- Further investigation of sub-cellular dose distribution to elucidate potential targets for radiation action related to health effects other than DNA

Joint gaps with other platforms

MELODI Multidisciplinary European Low Dose Initiative

In common with EURAMED:

- *Susceptibility biomarkers*
- *Immune system*
- *Radiomics (prognostic biomarkers)*

In common with EURADOS:

- *Internal emitter risk*
- *Dose uncertainties as related to epidemiological studies*

In common with NERIS:

- *No common topics identified*

In common with ALLIANCE:

- *Intra-species radiosensitivity (this topic in general common also with EURAMED)*
- *Potential epigenetic mechanisms of radiation disease/effect*
- *Multiple stressor effect on radiogenic somatic disease*

EURATOM NFRP8

GAP ANALYSES
EURADOS

Filip Vanhavere

Munich, February 20th, 2018

EURADOS

Activities of EURADOS (European Radiation Dosimetry Group)

- Founded in 1981

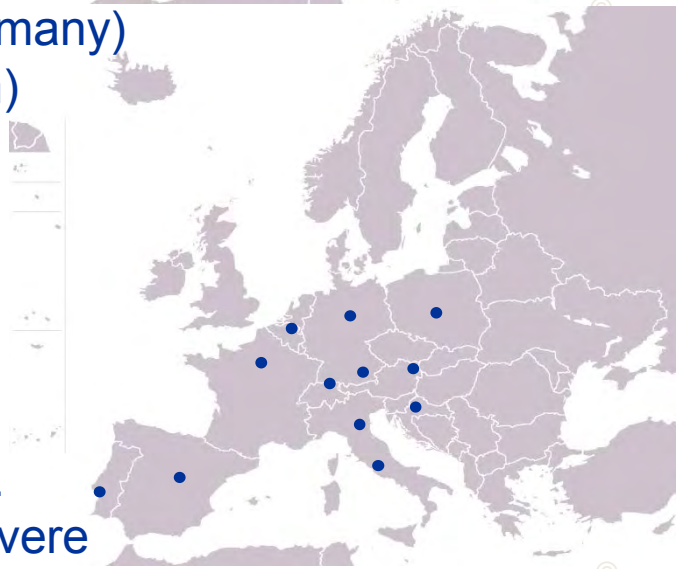
- Aim: To promote European research, development and cooperation in dosimetry

- Activities:
  - coordination of working groups
    - which promote technical development and its implementation in routine work
    - which contribute to harmonization within Europe
  - organization of scientific meetings and training activities
  - organization of intercomparisons and bench mark studies

EURADOS

- **EURADOS General Assembly**
  70 Voting Members (institutions)
  represented by designated individuals

- **EURADOS Board of Officers**
  Chair: W. Rühm (Helmholtz Munich, Germany)
  Vice-Chair: F. Vanhavere (SCK-CEN, Belgium)
  Secretary: JF. Bottollier (IRSN, France)
  Treasurer: H. Schumacher (PTB, Germany)



- **EURADOS Council**
  J. Alves, J.F. Bottollier, E. Fantuzzi, P. Fatibene, M.A. Lopez, I. Clairand, M. Caresano, P. Olko, W. Rühm, H. Schuhmacher, H. Stadtmann, F. Vanhavere

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EURADOS

- **Associate Members**

  Almost 700 active scientists contributing to the overall EURADOS objectives

- **Eight EURADOS Working Groups**
  - Harmonization of Individual Monitoring (P. Gilvin, UK)
  - Environmental Dosimetry (A. Vargas, Spain)
  - Computational Dosimetry (R. Tanner, UK)
  - Internal Dosimetry (B. Bruestedt, Germany)
  - Radiation Dosimetry in Radiotherapy (R. Harrison, UK)
  - Retrospective Dosimetry (C. Woda, Germany)
  - High-Energy Dosimetry (M. Caresano, Italy)
  - Dosimetry in Medical Imaging (Z. Knezevic, Croatia)

EURADOS Strategic Research Agenda – History and Current Status

- **October 2012**
  Council initiates SRA discussion and stimulates input from Working Groups
- **July 2013, Council Meeting**
  Discussion of collected material
- **February 2014, General Assembly**
  SRA presented to Voting Members and input stimulated
- **June 2014:** Publication as EURADOS report
- **Spring 2015**: Summary of SRA published in Rad. Prot. Dosim.
- **Summer 2016**: Stakeholder meeting to comment on SRA

- Voting for priorities by Council and Voting members
  - Used as input for 2 CONCERT Research calls

- **End 2017-2018**: update SRA on-going

EURADOS GAP analyses

- **Comparing the outcome of recently funded projects with the challenges identified in the EURADOS SRA.**
- **list of recent European projects**
  - Only projects that are on-going or were finished after 2013 were included
  - Mainly FP7 funded projects from EURATOM were listed, including OPERRA and CONCERT projects.
  - Some SECURITY and EURAMET projects were considered.
- **Only limited time to perform this gap analyses**
  - Evaluation was done by members of the EURADOS Council and the Workin Group chairs.
  - Because of this limited time, it was not possible to contact the coordinators of the concerned projects.

EURADOS GAP analyses

RANKING PRIORITIES		CONCERT 1			CONCERT 2						OPERRA 1			OPERRA 2		
		CONFIDENCE	LDLENSRAD	TERRITORIES	LEU TRAC ?	PODIUM	VERIDIC	SEPARATE ?	SINGS-SHAMISEN	ENGAGE	SOPRANO ?	EURALOC	DIMITRA	SHAMISEN	CATHYMARA	HARMONE ?
	Vision 1 – Towards Updated Dose Concepts and Quantities															
12	• To improve understanding of spatial correlations of radiation interaction events															
1	• To quantify correlations between track structure and radiation damage															
11	• To improve understanding of biokinetics of internal emitters															
10	• To update operational quantities for external exposure															
	Vision 2 - Towards Improved Radiation Risk Estimates Deduced from Epidemiological Cohorts															
13	•To explore exposure pathways not yet considered or validated											L				
14	•To improve retrospective dosimetry for exposure pathways already considered	M										L				
	Vision 3 - Towards an Efficient Dose Assessment in Case of Radiological Emergencies															
8	•To identify and and characterize new markers of exposure	H														
16	• To develop strategies and methods to increase measurement capacity	M		L					M					L	L	
3	• To quantify doses after accidental internal contamination	H		M										L	M	
	Vision 4 - Towards an Integrated Personalized Dosimetry in Medical Applications															
5	• To establish out-of-field dosimetry for photon and particle therapy															
6	• To improve dosimetry in modern external beam radiotherapy															
15	•To improve internal microdosimetry in radiotherapy and medical imaging															
7	• To optimize dose and risk estimations in interventional radiology						L									
9	• Establish reliable patient dosimetry in CT examinations												L			
	Vision 5 - Towards an Improved Radiation Protection of Workers and the Public															
18	• To refine, validate and implement new biokinetic models															
	• To develop calibration procedures for partial body counters														L	
4	• To develop accurate and on-line personal dosimetry for workers					H										
2	• To develop neutron dosimetry techniques further					L										
17	• To include nuclide-specific information in environmental monitoring	L		?												
	Education and training															

EURADOS gap analyses

VISION 1: TOWARDS UPDATED FUNDAMENTAL DOSE CONCEPTS AND QUANTITIES

Challenge 1: To improve understanding of spatial correlations of radiation interaction events (priority 12)

- This topic was not covered at all in any of the previous FP7 projects

Challenge 2: To quantify correlations between track structure and radiation damage (priority 1)

- This topic was not covered in any of the previous FP7 projects.
- BIOQUART (Biologically Weighted Quantities for Radiotherapy).

Challenge 3: To improve understanding of biokinetics of internal emitters (priority 11)

- This topic was not covered in most of the previous FP7 projects.
- CURE
- SOLO

Challenge 4: To update operational quantities for external exposure (priority 10)

- This topic was not covered in most of the previous FP7 projects.
- ICRU has proposed a new approach for the operational quantities.

EURADOS gap analyses

VISION 2: TOWARDS IMPROVED RADIATION RISK ESTIMATES DEDUCED FROM EPIDEMIOLOGICAL COHORTS

Challenge 1: To explore exposure pathways not yet considered or validated (priority 13) and

Challenge 2: To improve retrospective dosimetry for exposure pathways already considered (priority 14)

- Several EC project have included epidemiological studies, which included a dosimetric study.
- SOLO, CURE, INWORKS, COCHER, EURALOC
- Several projects used also patient data in their studies, and have contributed to better dose determination at organ level for patient treatments: EPI-CT, PROCARDIO, CEREBRAD, MEDIRAD, ANDANTE

EURADOS gap analyses

VISION 3: TOWARDS AN EFFICIENT DOSE ASSESSMENT IN CASE OF RADIOLOGICAL EMERGENCIES

Challenge 1: To identify and and characterize new markers of exposure (priority 8)

Challenge 2: To develop strategies and methods to increase measurement capacity (priority 16)

- This challenge was an important topic in some recent projects: RENEB, MULTIBIODOSE, CONFIDENCE
- Increasing the measurement capability was also an important topic in the recent projects: RENEB, MULTIBIODOSE, CATHYMARA
- Other projects adressed this issue indirectly: SHAMISEN, TERRITORIES, SHAMISEN SINGS.

Challenge 3: To quantify doses after accidental internal contamination (priority 3)

- CONFIDENCE will handle partial aspects of accidental internal contamination, as did SHAMISEN. CATHYMARA adressed the specific topic of thyroid measurements

EURADOS gap analyses

VISION 4: TOWARDS AN INTEGRATED PERSONALIZED DOSIMETRY IN MEDICAL APPLICATION

Challenge 1: To establish out-of-field dosimetry for photon and particle therapy (priority 5)

- ANDANTE focussed on the neutron exposure in the out-of-field organs.
- PROCARDIO, CEREBRAD and MEDIRAD looked at secundary effects after radiotherapy for specific organs

Challenge 2: To improve dosimetry in modern external beam radiotherapy (priority 6)

- This topic was not covered at all in any of the previous FP7 projects.
- There were some EMPIR and EMRP projects focussing on metrological aspects: MRgRT, Absorb, MetrExtRT

Challenge 3: To improve internal microdosimetry in radiotherapy and medical imaging (priority 15)

- This topic was not covered at all in any of the previous FP7 projects

Challenge 4: To optimize dose and risk estimations in interventional radiology (priority 7)

- VERIDIC will focuss on skin doses during interventional procedures.
- MEDIRAD will look at organ doses during interventional procedures

Challenge 5: Establish reliable patient dosimetry in CT examinations (priority 9)

- MEDIRAD will also look at CT examinations
- EPI-CT did a lot of work for dose estimations for pediatric examinations. DIMITRA did the same for dental cone beam CT, while BREAST-CT looked at breast CT exposures.

EURADOS gap analyses

VISION 5: TOWARDS AN IMPROVED RADIATION PROTECTION OF WORKERS AND THE PUBLIC

Challenge 1: To refine, validate and implement new biokinetic models (priority 18)

- This topic was not covered at all in any of the previous FP7 projects

Challenge 2: To develop calibration procedures for partial body counters

- Partial body counters were only adressed in the CATHYMARA project

Challenge 3: To develop accurate and on-line personal dosimetry for workers (priority 4)

- For on-line dosimetry, a new CONCERT project PODIUM was approved

Challenge 4: To develop neutron dosimetry techniques further (priority 2)

- Neutron dosimetry was not covered in recent projects, except partially in PODIUM
- Only the ANDANTE projects covered the biological aspects of neutrons in the frame of peripheral doses in radiotherapy.

Challenge 5: To include nuclide-specific information in environmental monitoring (priority 17)

- This challenge will be partially important in CONFIDENCE
- Two recent EURAMET (EMPIR) projects were focussed on the metrological aspects of this challenge: PREPAREDNESS and METROEMR.

EURADOS gap conclusion

CONCLUSION

- Some challenges were partially addressed by recent projects
- None of the challenges are completely covered
  - No Challenge is “solved”
- There is need for many research projects to make further significant progress in dosimetry for radiation protection.
  - Lack of funding opportunities

- Amount of money is limited in the next EURATOM NFRP8 call
- Only some selected challenges will be put forward as priority for this call

EURADOS gap conclusion

Challenges not or hardly covered

- To quantify correlations between track structure and radiation damage (priority 1)
- To develop neutron dosimetry techniques further (priority 2)
- To improve dosimetry in modern external beam radiotherapy (priority 6)
- To improve understanding of biokinetics of internal emitters (priority 11)
- To improve understanding of spatial correlations of radiation interaction events (priority 12)
- To improve internal microdosimetry in radiotherapy and medical imaging (priority 15)
- To refine, validate and implement new biokinetic models (priority 18)

EURADOS Strategic Research Agenda – Future

Challenges partially adressed

- To quantify doses after accidental internal contamination (priority 3)
- To establish out-of-field dosimetry for photon and particle therapy (priority 5)
- To update operational quantities for external exposure (priority 10)
- To develop calibration procedures for partial body counters

NERIS:
Research Gap analysis

Thierry SCHNEIDER
Chair of NERIS Platform

Open Information and Networking Day of the European Radiation Protection Research Platforms MELODI, EURADOS, NERIS, ALLIANCE and EURAMED

February 20th, 2018. Munich, Germany

Some lessons from Fukushima

- Importance of transparency of the decision-making processes at the local, regional and national levels
- Key role of the access to environmental monitoring at local, national and international levels
- Importance to deal with uncertainties in assessment and management of the different phases of the accident
- Use of modern social media in the exchange of information
- Role of stakeholder involvement processes in both emergency and recovery situations
- Better address societal, ethical and economic aspects
- Need to reinforce Education & Training for various actors

Euratom Research projects of direct interest for NERIS activities (1)

- **PREPARE Project:** Innovative integrated tools and platforms for radiological emergency preparedness and post-accident response in Europe
- **OPERRA Projects:**
  - **CAThyMARA**: Child and adult thyroid monitoring after reactor accident
  - **HARMONE:** Harmonising modelling strategies of European decision support systems for nuclear emergencies
  - **SHAMISEN**: Nuclear emergency situations - Improvement of medical and health surveillance

- **COMET Project:** Coordination and implementation of a pan-European instrument for radioecology

Euratom Research projects of direct interest for NERIS activities (2)

- **CONCERT Projects:**
  - **CONFIDENCE:** Coping with uncertainties for improved modelling and decision making in case of nuclear emergency
  - **TERRITORIES:** Reducing uncertainties in human and ecosystem radiological risk assessment and management in nuclear emergencies and existing exposure situations, including NORM
  - **SHAMISEN SINGS:** Nuclear emergency situations – Improvement of dosimetric, medical and health surveillance – Stakeholder involvement in generating science
  - **ENGAGE:** Enhancing stakeholder participation in the governance of radiological risks for improved radiation protection and informed decision-making (under-negotiation)

NERIS Strategic Research Agenda

3 challenge areas, 10 key topic

- Challenges in radiological impact assessment during all phases of nuclear and radiological events
- Challenges in countermeasures and countermeasure strategies in emergency & recovery, decision support and disaster informatics
- Challenges in setting-up a trans-disciplinary and inclusive framework for preparedness for emergency response and recovery

GAP analysis on research activities proposed by the NERIS community and that were not fully visited via national or international research project
(version 22 December 2017)

NERIS Research Gap Analysis (1)

Challenges in radiological impact assessment during all phases of nuclear and radiological events

- Improvement of **hydrological models**, including urban hydrology, surface run-off and marine environment
- **Application of foodchain models** at the local level to derive sensible countermeasure strategies
- Improvement of **dose assessment models** considering both environmental monitoring data and personal monitoring data (e.g. personal dosimeters, thyroid measurements, whole body measurements)
- Improved **monitoring** including lay people, drones and European wide harmonisation of tools and methods

NERIS Research Gap Analysis (2)

Challenges in countermeasures and countermeasure strategies in emergency & recovery, decision support and disaster informatics

- Methods and guidance to **optimise countermeasure strategies**: development of **measuring strategies** to guide **practical countermeasure implementation**
- Methods and guidance to **optimise countermeasure strategies**: how to implement/apply the **residual dose approach**, how to implement fully the guidance from ICRP in terms of simulation and **guidance for decision maker**
- Research on **lifting of countermeasures** by developing an integral approach with simulation models and Operational Intervention levels (OIL); improved OILs extending the IAEA approach

NERIS Research Gap Analysis (3)

Challenges in setting-up a trans-disciplinary and inclusive framework for preparedness for emergency response and recovery

- **Stakeholder engagement database**, better analysis of societal needs for an evaluation of legal instruments and governance frameworks, methods and tools for stakeholder engagement
- **"Emergency ethics" vs. "normal ethics"** to develop guidelines for **evacuation** and post-accident management, **compensation** schemes
- Development of **health surveillance approaches**, dose reconstruction methods, socio-psychological and economic aspects of medical follow-up

- 25-27 April 2018, Dublin Castle (Ireland)

NERIS

EUROPEAN JOINT PROGRAMME FOR THE INTEGRATION OF RADIATION PROTECTION RESEARCH
CONCERT

Thank you for your attention

www.eu-neris.net

Alliance Gap Analysis and Priority definition for NFRP-2018-8

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www.er-alliance.org

Information Day NFRP-2018-8 – Munich – 20 Feb 2018

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4 radioecology (related) projects

- **STAR** – Strategy for Allied Radioecology (2011-2015)
- **COMET** – COordination and iMplementation of a pan-European instrumenT for radioecology
- **TERRITORIES -** To Enhance unceRtainties Reduction and stakeholders Involvement TOwards integrated and graded Risk management of humans and wildlife In long-lasting radiological Exposure Situations
- **CONFIDENCE -** COping with uNcertainties For Improved modelling and DEcision making in Nuclear emergenCiEs

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SRA-challenges

- Challenge 1 - To Predict Human and Wildlife Exposure in a Robust Way by Quantifying Key Processes that Influence Radionuclide Transfers and Exposure
- Challenge 2 - To Determine Ecological Consequences Under Realistic Exposure Conditions
- Challenge 3 - To Improve Human and Environmental Protection by Integrating radioecology.

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Improvement of knowledge and tools to assess environmental radionuclides transfer and subsequent human & environmental exposure & risk assessment: **progress**

- Developed and improved innovative models for quantifying radionuclide transfer to humans and wildlife
- Guidance for development and validation of fit-for-purpose models
- For accidental situations
  - assessment of radioactive particles behaviour in ecosystems
  - marine dispersion modelling and marine biota impact assessment
- Advances in the integration of human and environmental protection frameworks (*e.g.* CROMERICA tool).
- Establishment of dedicated observatory sites
  - Lab and field investigation of environmental processes is of high added value, especially given the complexity of environmental issues

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Improvement of knowledge and tools to assess environmental radionuclides transfer and subsequent human & environmental exposure & risk assessment: **in progress**

TERRITORIES

- targets an integrated and graded management of contaminated territories characterised by long-lasting environmental radioactivity,
- Graded approach, for assessing doses to humans and wildlife and managing long-lasting exposure situations , risk management and remediation of legacy sites
- Highlight important factors determining the uncertainty levels that should be focussed on in the future combining experimental and modelling approaches

CONFIDENCE

- WP3 addresses Human Food Chain modeling and will make use of Observatoy Sites and appropriate databases (*e.g.* on food chain transfer) held by ALLIANCE members.

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Improvement of knowledge and tools to assess environmental radionuclides transfer and subsequent human & environmental exposure & risk assessment: **needs**

For all exposure situations

- More realistic consideration of key physical, chemical and biological processes Influence of biogeochemical processes in spatio-temporal predictive models
- Spatial and time-dependent environmental transfer and subsequent exposure of humans and wildlife irrespective of source term
- Marine and watershed radioecological modelling
- Communication with stakeholders

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Understanding biological effects of chronic ionising radiation exposure to low doses and dose-rates: **progress**

- Influence of multiple stressors in radiological risk assessment (literature review and simplified case studies)
- R&D initiated on transgenerational effects and epigenetics
  - started to delineate genetic vs. epigenetic causes of transgenerational effects of chronic exposures
  - exploration of "omics" responses to ionising radiation to unravel basic mechanisms of the biological response to ionising radiation
- Initiation of exploration of intra- and inter-species causes of variation in radiosensitivity

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Understanding biological effects of chronic ionising radiation exposure to low doses and dose-rates: **needs**

- Exploration of intra- and inter-species causes of variation in radiosensitivity and of the mechanisms of multi- or trans-generational effects is a priority to improve basic knowledge and contribute to the validation of biomarkers as early warning tools and defining protection standards

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Biological and ecological effects of low dose/ low dose rate exposure on biota *(some of the research lines potentially synergistic with MELODI and/or EURADOS)*

- Identification and mechanistic understanding of molecular and cellular processes following exposure to ionising radiation and resulting in adverse effects at individual and population level
- Understanding variation of responses between species at the individual and population levels due to genetic, environmental and behavioural factors and the interactions between these
- Exploration of intra- and inter-species causes of variation in radiosensitivity and identification and validation of biomarkers of exposure and effects for use in prospective and retrospective assessment
- Hereditary effects within populations of species: molecular basis of vulnerability or adaptation through generations and consequent inter-population effects, role of epigenetics
- Mechanistic basis to understand how multiple stressor exposure modifies ionising radiation effects and linking these to risk assessment
- Ecological consequences of exposure to ionising radiation

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Integration and optimization of environmental exposure assessment for ionising radiation & other stressors (potential *synergism with SSH and/or MELODI, NERIS, EURADOS*)

- Development of advanced methods for fit-for-purpose dose assessment to support and robustly interpret effects studies
- Mechanistic understanding of radionuclide dispersion and transfer processes in and between the various components of the geosphere, biosphere and atmosphere, and associated mechanistic process-based modelling including foodwebs and biokinetics modelling.
- Advanced modelling of process interactions at the various biosphere interfaces at the local, regional and global scales such as in (a) marine, brackish, estuarine and freshwater ecosystems, and (b) terrestrial ecosystems (agricultural, forestry, natural and urban including NORM landfills); developing landscape-based models.
- Development of remediation methods and strategies in support of the management of radiocontaminated sites

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Radioecology-related research for optimising emergency & recovery preparedness and response (*synergism with NERIS*)

- Customisation of atmospheric, river, marine, brackish water, terrestrial and urban dispersion models, food chain models and dose assessment models.
- Sophisticated parametrizations of processes of high health impact: environmental evolution of iodine speciation, low wind speed conditions, snow and fog events
- Improved understanding of countermeasures to better build, select and implement countermeasure strategies at different times (preparedness, response, recovery) and in different geographical areas

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EURAMED

European Alliance for Medical Radiation Protection Research

EURAMED Gap Analysis

Prof. John Damilakis
EURAMED President

- EURAMED is a legal entity since 1 Oct. 2017 (non-profit society registered in Vienna/Austria)
- Before being a legal entity, EURAMED was hosted by EIBIR as a Joint Initiative
- Founding members: EANM, EFOMP, EFRS, ESR, ESTRO
- Management of EURAMED legal entity by EIBIR

Vision

• To lead the European research activities in medical radiation protection and to assume an umbrella function for the harmonisation of practice to advance the European radiation protection safety culture in medicine.

Mission

• To jointly improve medical care through sustainable research efforts in medical radiation protection

• To serve as a platform for medical radiation protection research, linking researchers and clinicians, adopting a harmonized approach to lobbying at European level to impact the European research funding landscape

• **To develop an aligned approach and response to European research calls**

Membership type	Eligibility	Rights & Services	Obligations
Founding members	EANM, EFOMP, EFRS, ESR, ESTRO	• voting right in the General Assembly (GA) • right to nominate representatives to stand for office • possibility to nominate candidates for committee membership	Pay annual membership fee
Full members	institutions or organisations active in the field of medical radiation protection research	• voting right in the General Assembly (GA) • right to nominate representatives to stand for office • possibility to nominate candidates for committee membership	Pay annual membership fee
Associate members	institutions or organisations that do not actively practice medical radiationprotection research, but have a considerable interest in the area of RP	• attend all meetings of the Society	Pay annual membership fee

Corporate members	enterprises interested in the activities and aims of the Society	• attend all meetings of the Society	Pay annual membership fee
Individual members	individuals interested in the activities and aims of Society	• attend all meetings of the Society	Pay annual membership fee

EURAMED Preliminary Gap Analysis: Short list of identified gaps

ORAMED concentrated on describing exposures of staff performing medical procedures like for example interventional procedures. Some aspects of optimizing such exposures have been investigated as well, but all were staff-related.
MADEIRA focused on optimizing the nuclear medical applications of ionizing radiation to patients with a specific emphasis on nuclear medical imaging. The research was carried out developing new systems for image data collection, new time schemes based on biokinetic data sampling and modelling allowing for lower doses or better images as well as new software tools for optimizing image reconstruction based on real patient data.
ANDANTE focused on biological effects of neutrons especially with respect to pediatric radiation therapy.
SCOLIO-SEE tried to improve scoliosis diagnostics by improving 3D image processing.
PEDDOSE.NET looked for dosimetry and health effects of the diagnostic use of radiopharmaceuticals in pediatric patients.
SEDENTEXCT investigated the possibilities for enhancing safety and efficacy of dental CT procedures.

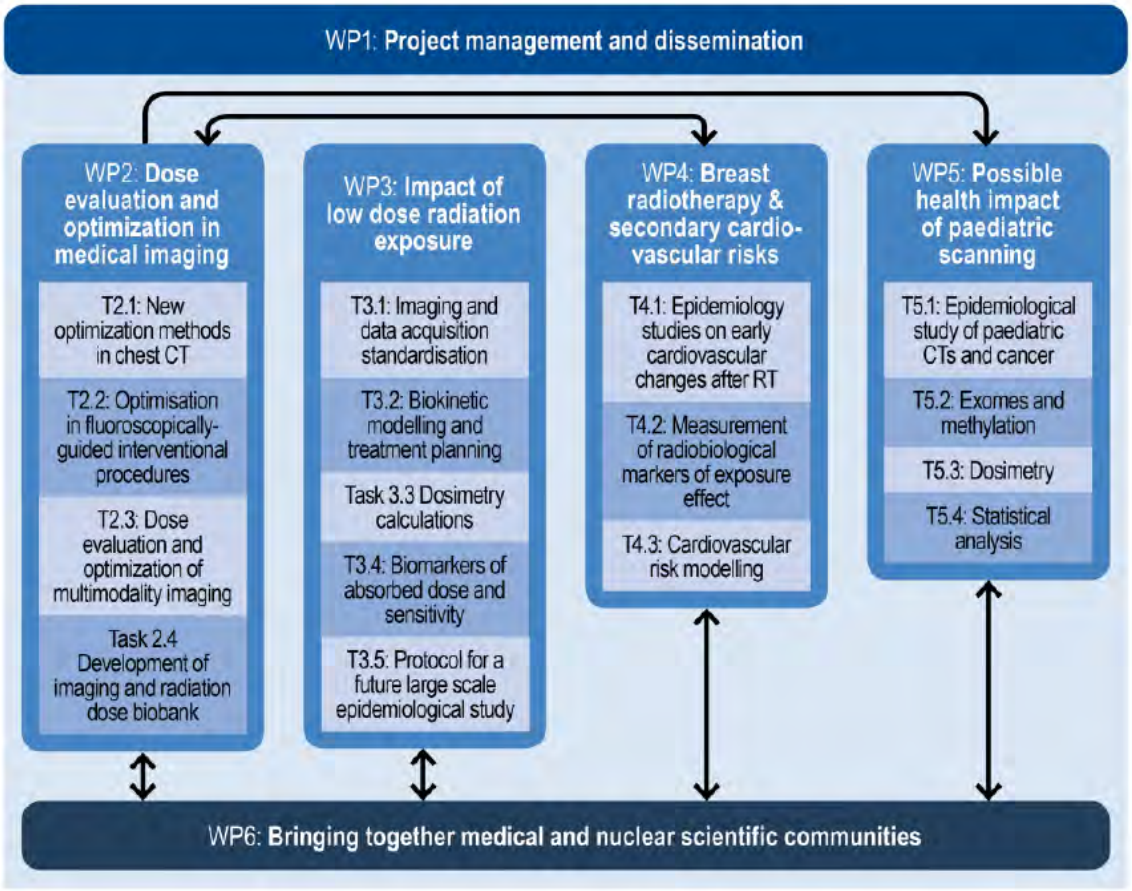
EURAMED Preliminary Gap Analysis: Short list of identified gaps

CHILD_MED_RAD and EPI-CT were projects looking for epidemiological studies about radiation risk especially in cohorts of children exposed in medical applications of ionizing radiation.
ALLEGRO investigated the early and late health effects of radiation therapy also with a focus on pediatric patients.
BREAST-CT developed a dedicated 3D imaging modality for the breast to improve the benefit to risk ratio in mammographic applications.
EUTEMPE-RX was a project to improve education of medical physicists.
EPIRADBIO evaluated cancer risk for exposures below 100 mSv especially for breast, lung, thyroid and the digestive tract as for example resulting from specific medical applications.
PROCARDIO focused on cardiologic effects for various dose ranges of relevance mainly in radiation therapy applications.
DARK_risk looked for epidemiological studies on a pediatric cohort in Serbia exposed to x-rays.
DOREMI and **OPERRA** were large-scale projects, in the development of the medical SRA was initiated (especially in OPERRA). Smaller projects also dealing for example with dental procedures were funded through OPERRA.

EURAMED Preliminary Gap Analysis: Short list of identified gaps

CONCERT
PODIUM
VERIDIC
SEPARATE
ENGAGE
LEU-Track

EURAMED Preliminary Gap Analysis: Short list of identified gaps



MEDIRAD

Fixed activity approach versus individualized dosimetry-based activity determination in radionuclide therapy

Fixed activity approach: prescriptions in radionuclide therapy are based on a fixed amount of activity for all patients

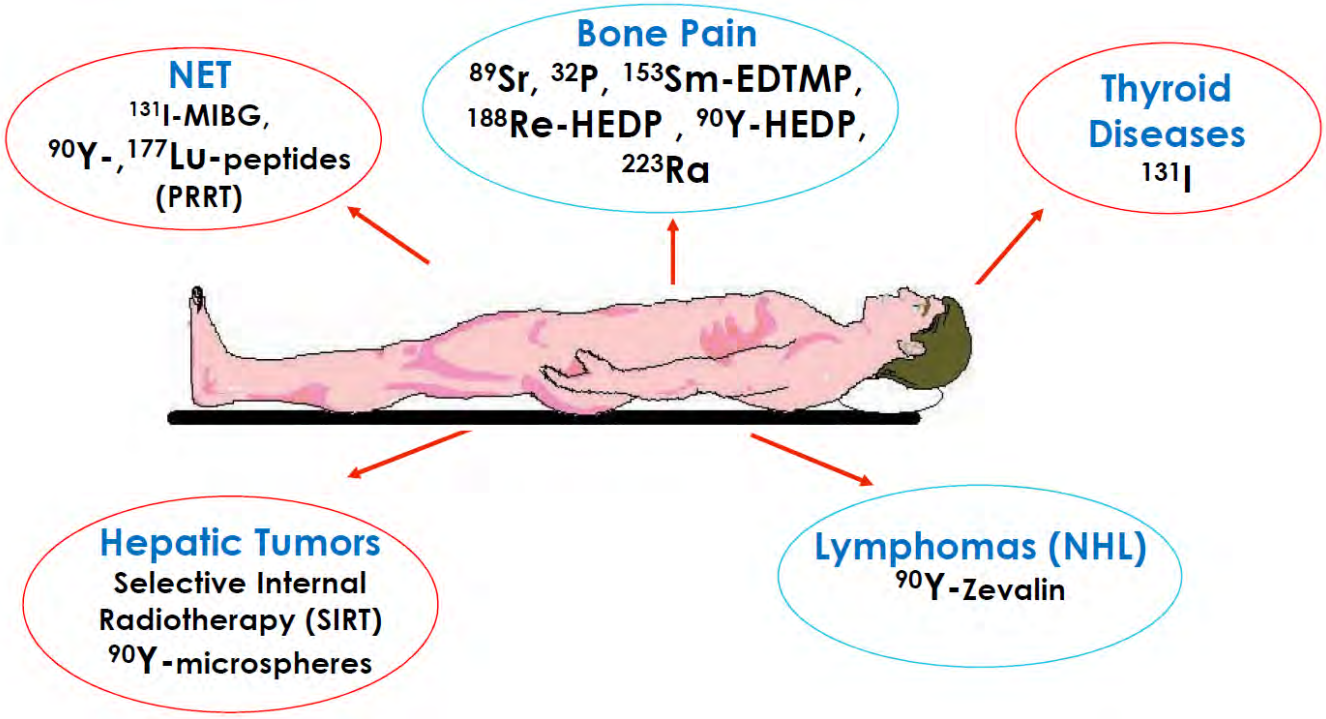
Individualized dosimetry approach in radionuclide therapy: treatment optimization by anticipating required activity to be administered to an individual patient

Fixed activity approach versus individualized dosimetry-based activity determination in radionuclide therapy

"For all medical exposure of patients for radiotherapeutic purposes, exposures of target volumes shall be **individually planned** and their delivery appropriately verified taking into account that doses to non-target volumes and tissues shall be as low as reasonably achievable and consistent with the intended radiotherapeutic purpose of the exposure".
EU directive 2013/59/EURATOM Article 56

'Radiotherapeutic' means pertaining to radiotherapy, including nuclear medicine for therapeutic purposes
EU directive 2013/59/EURATOM Article 4 (Definitions)

Fixed activity approach versus individualized dosimetry-based activity determination in radionuclide therapy



Artificial intelligence in medical radiation protection

Artificial intelligence, machine learning and deep learning can support medical radiation protection (dose estimation, dose data management, image quality assessment, optimization).

Translating approaches into clinical practice, determine drawbacks and limitations, evaluate systems are essential aspects of such approaches and are still missing.

Artificial intelligence in medical radiation protection

Development of innovative software tools on image quality and radiation dose for the determination of optimal protocols in medical imaging. This tool will provide a) image quality information, b) accurate estimation of patient organ doses and c) estimation of radiogenic risk associated with CT, IR and other examinations performed for several clinical indications.

Development of dose and imaging biobanks.

Artificial intelligence in medical radiation protection

Radiomics: a tool to extract quantitative information out of the images. Several software packages provide 'radiomic' features from medical images using data-characterization algorithms. These features have the potential to uncover disease characteristics.

Radiomics could be used together with texture analysis approaches within a project to look for effects related to individual sensitivity of single organs.

Radiation protection approaches in medical applications based on individual radiosensitivity

In many cases, patients are exposed to radiation in a region which is already affected by a disease. This might be correlated with higher or lower sensitivity to ionizing radiation of the exposed organs.

It is important to develop methods for medical exposures in diagnostic, minimally invasive or radiotherapeutic procedures based on ionizing radiation to avoid side effects and adverse events by prediction of individual radiosensitivity and develop strategies for adjusting doses correspondingly.

Research should focus on medical applications.

Effects of low and high ionizing radiation doses on immune system

There is quite some evidence to suggest that high-dose irradiation correlates with immunosuppression, while low-dose irradiation correlates with immunostimulation, at least for quite a number of patients.

Animal and patient studies are needed to define radiation dose levels that will promote or suppress the development of an antigen specific and/or antigen non-specific immune response. It should also be investigated on how far such mechanisms are depending on individual patient status or whether they are correlated with individual radiosensitivity. Advanced dosimetric methods should accurately estimate radiation dose to each specific tissue/organ of the body.

Thank you!

EUROPEAN JOINT PROGRAMME
FOR THE INTEGRATION OF
RADIATION PROTECTION RESEARCH
CONCERT

Social Science and Humanities: Gap analysis for research priorities

Task 2.6 members

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A self-standing Strategic Research Agenda for Social Sciences and Humanities

The SSH strategic research agenda is

a “self-standing” SRA and,

although it has common points,

it is not included as such in other platforms’ SRAs.

From **developing of SSH SRA** to the gap analysis

- Literature review
- Events organised in the framework of EU projects and platforms
  OPERRA, EAGLE, PREPARE, PLATENSO, CONCERT
  - OPERRA Questionnaire

OPERRA
OPEN PROJECT FOR EUROPEAN RADIATION RESEARCH AREA

MELODI

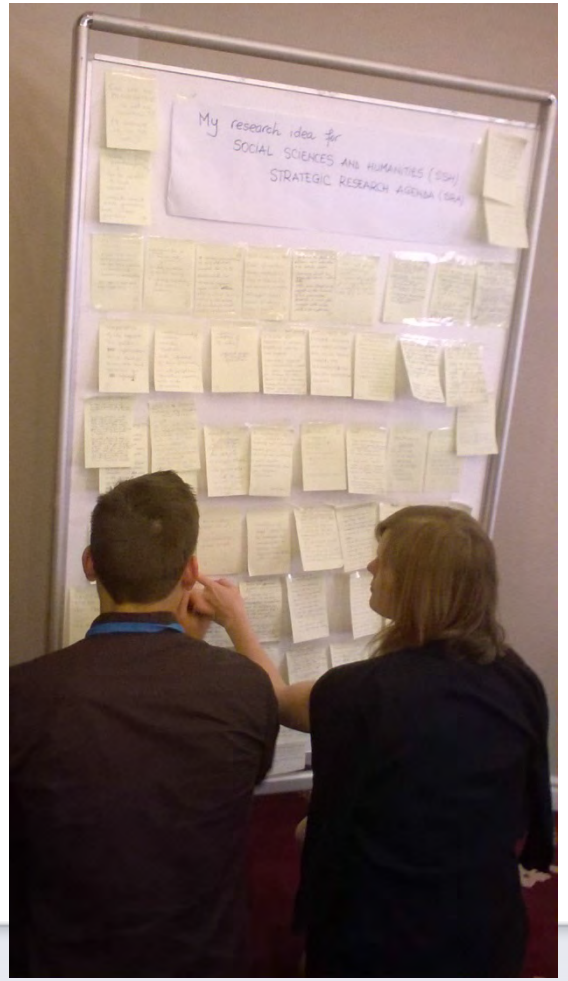
RICOMET 2015
Risk perception, communication and ethics of exposures to ionising radiation

Deliverable 2.2

EUROPEAN JOINT PROGRAMME FOR THE INTEGRATION OF RADIATION PROTECTION RESEARCH
CONCERT

From **developing of SSH SRA** to the gap analysis

11:45 – 12:45	**Open space workshop to collect the input for Strategic Research Agenda (SRA) in Social Sciences and Humanities (SSH) in Radiation Protection** *Coordinated by Michiel Van Oudhesden, SCK•CEN, Belgium*
12:45 - 13:45	*LUNCH and POSTER SESSION*
13:45 - 15:00	*Continuation* **Open space workshop to collect the input for SRA in SSH in Radiation Protection** *Coordinated by Michiel Van Oudhesden, SCK•CEN, Belgium*
15:00 - 15:45	*Plenary* **Brief reporting of collected ideas, delivery to platform** *Chairs: Susan Molyneux-Hodgson, University of Sheffield, United Kingdom and Michiel Van Oudhesden, SCK•CEN, Belgium*



Prioritisation of research topics

Public Health England

Assessment done by the SSH experts out of the CONCERT partners

+

Radiation Protection Week 2016
19 - 23 September 2016

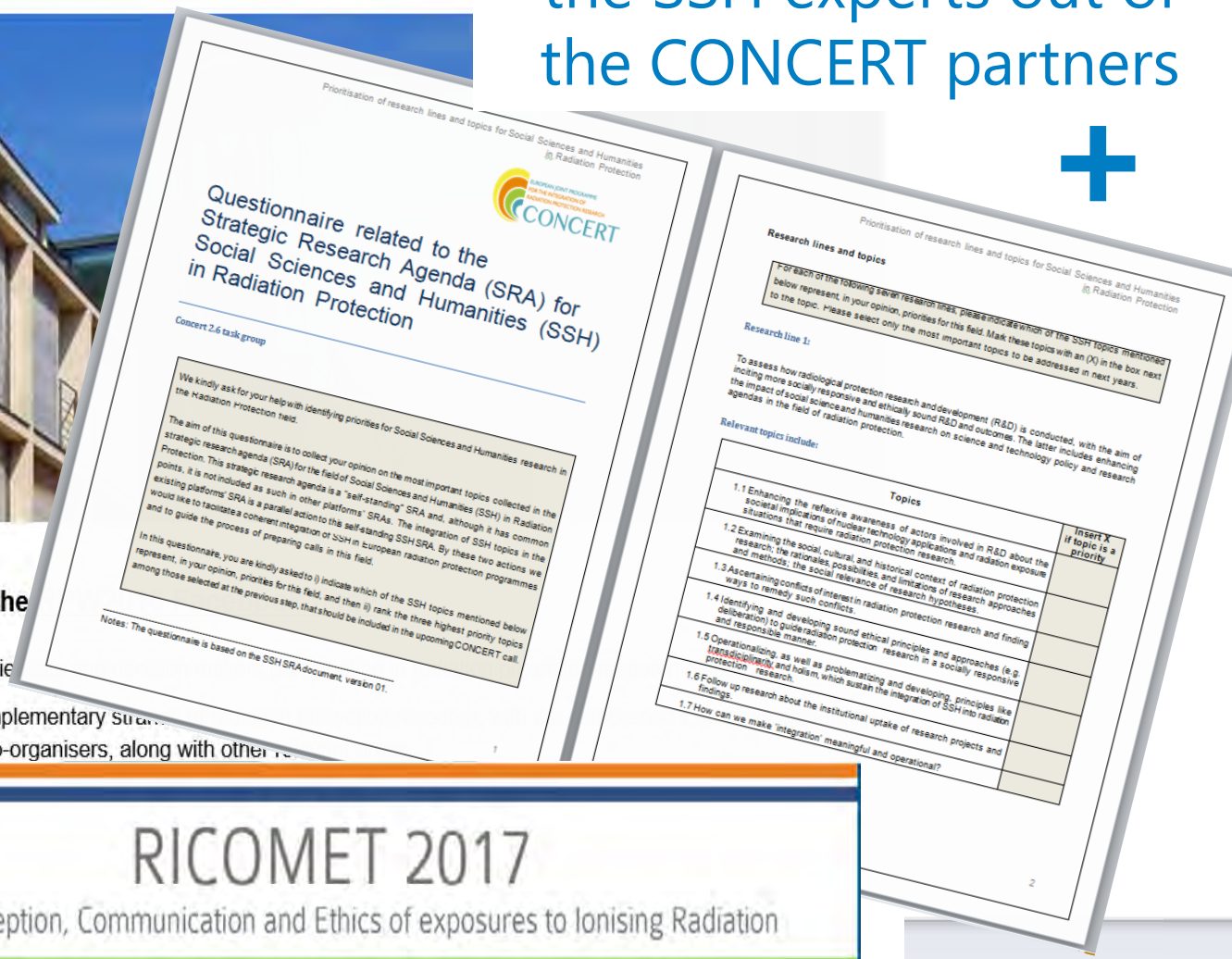
For live updates and news please visit the

The Radiation Protection Week is a 'must' for all scie

For the first time, RPW2016 will bring together complementary st
MELODI, EURADOS, NERIS and ALLIANCE as co-organisers, along with other

Building on and extending the
Protection demonstrated by th

RPW2016 will be held in Oxfo
Observatory Quarter of Oxfor



From developing of SSH SRA to **the gap analysis**

- Analysis of the SSH SRA, the SSH priorities and previous and current projects
  - CONFIDENCE
  - TERRITORIES
  - SHAMISEN
  - SHAMISEN-SINGS
  - PREPARE
  - CONCERT (upcoming)
  - NFRP -9
  - ENGAGE
  - BSS public information & transparency in a radiological emergency

SSH research priorities to be addressed (**gaps**)

- Risk **communication** about radioactivity and radiation protection principles in **medical applications** of ionizing radiation; impact of communication on radiation protection behaviours of practitioners.

- Risk communication about **low doses** and related **uncertainties**.

- **Ethical basis and values** underpinning **risk communication** about ionizing radiation exposures.

SSH research priorities to be addressed (**gaps**)

- The understanding of ionizing radiation concepts, risks and uncertainty by different stakeholders in the context of **medical exposures**, **industrial applications** and **natural radiation**.

- The interplay of **psychological aspects** associated with radioactivity, **social environment** and radiation protection **behaviours**.

SSH research priorities to be addressed (**gaps**)

- Potential and pitfalls of **citizen involvement** in **knowledge production** for radiological risk governance.
- **Socio-economic valuation and multi-criteria decision aid methods** to formally structure the evaluation and integration of radiological and non-radiological factors.
- Enhancing the **reflexive awareness** of actors involved in radiation protection R&D about the societal implications of research.
- **Democratic culture** in radiation protection in order to construct joint actions with institutional and non-institutional actors.

SSH research priorities to be addressed (**gaps**)

- **Mediation, facilitation and representation** on the triangle scientists, public and other stakeholders for different exposure situations.
- **Collaborative framework** for stakeholder engagement in radiation protection research, policy and practice in ways that enhance responsiveness to societal needs and concerns.
- Societal needs for and evaluation of legal instruments and governance frameworks supporting access to **information, public participation and access to justice** in relation with radiation protection issues.
- **Stakeholder and public participation** tools and methodologies for different radiological exposure situations. Roles and rules of stakeholders in the engagement process. Motivational factors, ethics, and link between theory and practice.

SSH research priorities to be addressed (**gaps**)

- Characterization of **radiation protection culture.**
- The role of **RP culture** in the implementation and improvement of the protection system.

To conclude

Apart from addressing one or more of the research activities listed above,

the SSH community encourages **multi-disciplinary approaches** attending also to social and ethical considerations.

Key Gaps in Radiation Protection Research

MELODI, EURADOS, NERIS, ALLIANCE, EURAMED

Open Information and Networking Day of the European Radiation Protection Research Platforms MELODI, EURADOS, NERIS, ALLIANCE and EURAMED

February 20th, 2018. Munich, Germany

Gap 1: Modelling of the biokinetic behaviour and risk for internal emitters

- In many exposure situations internal exposure to radionuclides is important. Assessment of the health risks associated with internal radionuclide exposure is complex and there remain substantial uncertainties related both to dosimetric aspects and health outcomes. Reduction of these uncertainties will improve risk assessment of internal exposures and hence inform appropriate protection measures
- Improved modelling for internal doses after accidental situations based on environmental monitoring data and personal monitoring data

- EURADOS, NERIS, MELODI, ALLIANCE

Gap 2: Improving environmental and health monitoring, particularly by lay people

- Improving environmental and health monitoring by lay people, and new equipment such as drones and a European wide harmonization of such tools and methods and how to integrate this into operational approaches
- These can be considered as overlapping open topics in both gap analyses, excluding the work to be done in Shamisen-sings.

- EURADOS, NERIS

Gap 3: Dose optimization in medical exposures

- Development of dose biobanks for benchmarking, establishment of DRLs
- Advanced patient-specific dosimetric methods that accurately estimate radiation dose to each specific tissue/organ of the body. This is needed for Computed Tomography (CT) and interventional radiology procedures as well as for radiotherapy and hadron therapy and radionuclide therapy. This includes non target organs.
- This is also needed for epidemiological studies.
- Artificial intelligence, machine learning and deep learning can support medical radiation protection (dose estimation, dose management, image quality assessment and especially dose reduction).

- EURAMED, EURADOS, MELODI

Gap 4: Radiation protection approaches based on individual radiosensitivity

- It is important to develop methods to avoid side effects and adverse events by prediction of individual radiosensitivity, to understand the range of radiosensitivity in the population and develop strategies for adjusting doses in medical settings correspondingly.
- Research could investigate new markers and reasons for the individual radiosensitivity
- Projects trying to fill this gap would require research on, inter alia, biomarker discovery and validation, individual patient dosimetry, epigenetics and individual susceptibility
- Correlation of nanodosimetry-based characteristics of particle track structure with the biological effectiveness of ionizing radiation may provide useful insights to understand the underlying mechanisms that lead to individual radiosensitivity

- EURAMED, MELODI, EURADOS

Gap 5: Individualized dosimetry-based activity determination in radionuclide therapy

- Individualized dosimetry based on molecular imaging prior to radionuclide therapy can greatly improve the treatment efficacy and can be applied in everyday clinical practice.
- Empirical activity selection is the most commonly used method but is not an optimal approach. It is important to optimize treatment by anticipating required activity administered to an individual patient.
- Internal micro-dosimetry can support individualized dosimetry in radionuclide therapy.

- EURAMED, EURADOS, MELODI

Gap 6: Biomarkers of exposure, disease and susceptibility

- Biomarkers have the potential to improve estimates of exposure/effect in radiation incidents, epidemiological studies and investigations of radiation impacts on the ecosystem. Biomarkers of disease/effect have the potential to improve epidemiology, early medical diagnosis and the health of non-human species. Susceptibility biomarkers may help refine current population-based approaches to protection.
- Radiation protection measures are based on population average estimates of risk/effect. With an improved understanding of the range of radio-sensitivity within the human population and between species could aid risk assessment and therefore approaches to protection. Variation may potentially be driven by genetic factors, lifestyle factors, age or gender.

- MELODI, EURAMED, ALLIANCE

Gap 7: Radiation impact on the immune system

- The immune system is complex and regulated at multiple levels, and inflammation can affect disease progression.
- A more comprehensive understanding of the immunomodulatory effects of radiation (potentially both inhibitory and stimulatory) could help in determining health outcomes of exposures, particularly in medical and occupational settings. It could therefore be translated into effective radiation protection measures especially in clinical routine by adjusting exposure to the inhibitory and stimulatory effects

- MELODI, EURAMED

Gap 8: Epigenetic mechanisms of radiation disease/effect

- In recent years a growing appreciation of non-mutational processes that can affect phenotype has been gained. If such processes contribute to radiogenic diseases or effects, notably heritable effects, it will be important to develop an understanding of dose- , dose-rate and radiation quality-dependence.
- Epigenetic status is further known to vary with age. Understanding the dose- and dose-rate dependence will be of particular importance to inform judgements on low dose and dose-rate risk extrapolation.
- To improve understanding of spatial correlations of radiation interaction events and the link with biological effects

- MELODI, ALLIANCE, EURADOS

Gap 9: Biological and ecological effects of low dose/ low dose rate exposure on humans and biota

- Identification and mechanistic understanding of molecular and cellular processes following exposure to ionising radiation and resulting in adverse effects.
- Understanding variation in radiosensitivity between species at the individual and population levels
- Identification and validation of biomarkers of exposure and effects for use in prospective and retrospective assessments.
- Study the hereditary effects within populations of species, the molecular basis of adaptation (or vulnerability) gained through generations.
- To explore and define the role of epigenetic modifications in radiation-induced adverse effects.
- ALLIANCE, MELODI

Gap 10: Integration of environmental exposure assessment for ionising radiation and other stressors

- Mechanistic understanding of radionuclide dispersion in space and time, and transfer processes.
- Development of process-based models to improve dose assessment predictions, considering both environmental monitoring and personal monitoring data.
- Advanced modelling of process interactions at the various biosphere interfaces at the local, regional and global scales, in different ecosystems (including urban).
- Advanced methods for data treatments to cope with the large amount of data available.
- Integrated holistic modelling approach and advanced methods to identify the most significant sources of uncertainty in radiological impact assessments.
- In reality exposures to radiation rarely if ever occur in isolation, populations are co-exposed to other stressors concurrently. Understanding the interactions between radiation and other potential co-exposures may be relevant to risk assessment if substantial modulation of the radiation effect on humans (including patients) or non-human species is observed
- ALLIANCE, NERIS, MELODI, EURAMED

Gap 11: Optimising emergency and recovery preparedness and response

- Customisation of atmospheric, river, marine, brackish water, terrestrial and urban dispersion models, food chain models and dose assessment models.
- Improvement of monitoring of the different environmental compartments, foods and goods.
- Improvement of dose assessment models for better dose reconstruction and predictions of the impact of an accident.
- Methods and guidance for optimization (residual dose approach, temporal dynamics for the evolution of countermeasures…)

- NERIS, ALLIANCE

SSH: a cross-cutting issue

SSH community encourages **multi-disciplinary approaches**

attending also to social and ethical considerations.

Examples: low dose risk communication,
holistic approaches of emergency management,
public information and stakeholder engagement,
societal aspects of medical applications, etc.