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D2.7 Synergies between the medical SRA and the SRAs of MELODI and EURADOS

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Abstract

In parallel to the CONCERT project there has been a large effort by the European medical associations dealing with ionizing radiation based on the memorandum of understanding between EURADOS, MELODI and these associations and partly initialized by OPERRA to generate a Strategic Research Agenda (SRA) which is now ready and can be found using the link:

<http://www.eibir.org/scientific-activities/joint-initiatives/european-alliance-for-medical-radiation-protection-research-euramed/euramed-sra/>

Based on the SRA, EURAMED has formulated a list of five priorities for radiation protection research in the medical context.

1. Patient-tailored diagnosis and treatment: full exploitation and improvement of technology and techniques with clinical and dose structured reporting
2. Individual patient-related radiation sensitivity and early biomarkers of response and morbidity
3. Individualised patient dosimetry for medical use of radiation
4. Improvement of use of evidence-based guidelines for medical imaging procedures: risk-benefit assessment and communication
5. Infrastructure for quality assurance: data coding, collection and management for a comprehensive medical imaging database and biobank

Many of the objectives of the EURAMED SRA are closely linked with the objectives of MELODI for low dose risk and the objectives of EURADOS for dosimetry of medical and occupational exposures. The objective of this deliverable is to explore and highlight the synergies between the medical SRA and the SRAs of MELODI and EURADOS. SRA synergies between EURADOS and other research platforms have been previously discussed in a workshop “EURADOS Contributions for CONCERT WP2.7” on June 30th, 2016, at the Helmholtz Center Munich in Neuherberg where international organisations were invited as stakeholders (see Annex). However, EURAMED was not formally established at that time and MELODI could not participate in the workshop. This report provides a first analysis of synergies based on the SRAs. The analysis of synergies will be deepened after joint discussions in a workshop planned for month 22 (March 2017), using this document as discussion paper.



Synergies between MELODI, EURADOS and EURAMED strategic research agendas

The generation of strategic research agendas within the different platforms MELODI; EURADOS and EURAMED as the youngest member of such platforms dealing with radiation protection research issues in Europe, has a completely different history. Nevertheless it was intended by the memorandum of understanding between MELODI, EURADOS and the five medical associations EANM, EFOMP, EFRS, ESR and ESTRO to identify also synergies and common interests between the platforms MELODI and EURADOS and the medical radiation protection research community. Since the EURAMED SRA is the newest of the three SRAs it is logical to start from this document to identify synergies and common interests. This is done in the first part of this document. This deliverable also aims at identifying possible further synergies which have not yet been identified or prioritized, which will be named in the second part of this document.

1. Synergies which can already be identified in the SRAs:

There are very obvious synergies / interests between EURAMED and EURADOS as well as between EURAMED and MELODI. The most obvious example for synergies between EURAMED and EURADOS is certainly the topic 1.1. (chapter 3.1.1.) of the EURAMED SRA entitled: Characterisation of exposure. Here there are various subtopics of interest all of which are also of interest to EURADOS:

- „Calibration of dosimeters for medical applications is currently performed using secondary standards non-specific to the radiation fields used in medical application of ionising radiation leading to undefined measurement uncertainties. Therefore, exact measurements require calibration against radiation fields specific to medical applications.
- There is a limited availability of dosimeters for use inside the human body, this implies, that currently simulations of radiation transport and deposition are necessary, e.g. using Monte-Carlo (MC) methods (6,7), and normalise them to measured quantities.
- Real-time measurement of doses is relevant to reduce doses to staff. Therefore, the development of specific dosimeters is required; allowing real-time monitoring e.g. of eye structures and extremity/finger doses from interventional radiology/cardiology and nuclear medicine. The existing dosimeters are either not for online measurements or they suffer from technological limitations in terms of highest dose rates as in pulsed radiation fields or size or practicability.
- Non-uniform spatial (3D) and temporarily varying (4D) dose distributions can lead to differences of up to several orders of magnitude in local dose distributions (8). Therefore, micro-dosimetric measurement devices and techniques for use within and between cells, the anatomical structures of organs and the human body are necessary, e.g. for dosimetric use with regard to individual structures in the eye, the brain and the heart, and also other organs depending on the basis of future research results.
- Different types of radiation (photons, electrons, protons, heavy ions, secondary neutrons) are used for and/or associated with medical purposes. Correct

determination of doses to and dose-distributions within patients at different levels of spatial resolution is necessary depending on the required purpose in terms of radiobiological questions or optimisation of procedures. Also mixed fields and energy spectra need to be taken into account for reliable measurements and calculations of dose-distributions.

- Knowledge on track structure and/or microdosimetry of internal emitters (alpha, beta, Auger) is a prerequisite to predict the associated biological effects (9). Therefore, computational methods need to be further developed and connected to the results of corresponding research on measurements and calibration procedures (see above).
- Development of updated or alternative quantities and concepts for describing the anatomical dose distributions within organs, tissues and the body as the basis for predicting health effects, rather than mean absorbed doses (e.g. dose averaged over an organ) or dose volume histograms.
- Methodologies have to be developed for determination, description measurement and calculation of doses outside the planning target volume (PTV) for radiation therapy i.e. the peripheral dose. This is urgently required to build and optimise prediction models for secondary tumours, but also tissue effects, and to enable comparison of different techniques and/or technologies.”

Except from the 3rd bullet point all aspects also have a direct influence on radiobiological research performed on patient groups or data gathered from such patients and can be seen as prerequisites for such research as intended by MELODI. The 3rd bullet point matches well with a EURADOS priority.

In addition, the aspects listed as topic 1.2 (chapter 3.1.2) entitled “individual dosimetry” is of extreme importance to optimise radiation application in medicine on a per patient basis. Thus, there is a tremendous need for common development of methods with EURADOS on such topics, namely:

- Development of computational methods for dose distribution calculations based on patient-specific and equipment-specific characteristics for all medical procedures using ionising radiation, including for example CT, interventional and nuclear medicine procedures as well as radiotherapeutic procedures avoiding different dose indicators for different types of procedures in order to get comparable meaningful information about organ doses of individuals.
- Development of optimal measurement protocols in nuclear medicine for accurate estimation of absorbed doses using patient-specific and equipment-specific characteristics. Refinement, validation and implementation of new biokinetic models for dosimetry in molecular radiotherapy using for example physiologically-based pharmacokinetic (PBPK) models for the individual assessment of biokinetics (13), including uncertainty budgets (14).
- Development of methods to estimate or measure the actual delivered radiation dose in radiotherapy.
- Development of a unique dose indicator that describes the absorbed dose to organs in order to perform risk assessment.

Especially the subtopics described under bullet points 2 and 4 are of great importance also for the radiobiological and epidemiological studies as of interest to MELODI. On the other hand the outcome of such radiobiological and epidemiologic studies is very meaningful for risk assessment and communication as stated in the EURAMED SRA under chapter 3.4.1 (topic 4.1).

Especially when dealing with patients there are large factors of uncertainties in the determination of dose distributions. To determine such uncertainties and draw conclusions for risk estimates and epidemiological studies is a key question to be answered using methods of uncertainty and sensitivity analysis besides the determination of the best and most effective way for optimisation in medical radiation protection as stated in the EURAMED SRA (topic 1.4 – chapter 3.1.4). That means regarding this topic there are synergies with both platforms (MELODI, EURADOS).

There is a lot of radiobiological research which would be of great importance for the research topics proposed in EURAMED. Such research as well as epidemiological studies can influence the research under topic 2 “Normal tissue reactions, radiation-induced morbidity and long-term health problems” in its total (chapter 3.2). Various topics that require multidisciplinary approaches as proposed by MELODI have been identified such as

- Exposure-associated cancer risk: dose, dose-distribution, and dose-rate dependence
- Non-cancer effects in various tissues and radiobiology-based effect models for individual morbidity endpoints
- Individual patient-related radiation sensitivity and early biomarkers of response and morbidity
- Radiobiological mechanism of radiation-induced side-effects and protective strategies

All of these topics are key questions determined in the MELODI SRA as well. In the EURAMED SRA the patient specific approaches are the main focus, but a strong overlap of interests, methods and approaches is to be stated.

In addition, the research proposed by the EURAMED SRA under chapter 3.3.3 – topic 3.3 “Clinical and dose structured reporting” would allow much better and more standardized descriptions of patients in terms of clinical aspects and exposure characterisation for inclusion / exclusion and evaluation in epidemiological studies for risk estimation.

On the other hand, the whole topic 4 – chapter 3.4 “Justification of the use of ionising radiation in medical practice” is relying on better understanding of radiation induced effects, which can be especially found in the subtopic description of chapter 3.4.1. This understanding of radiation induced effects and the individual sensitivity of single patients is of major importance to many aspects of personalisation as a tool to optimised radiation protection of patients and the harmonisation of this process throughout Europe.

As both other platforms, EURAMED states in its SRA the importance of infrastructures. Existing radiobiological infrastructures or those to be newly developed would need to be broadened in terms of the data to be collected and its underlying mechanisms due to the importance of integrating image and medical data but on the other hand defining accordance with privacy

protection on a very high level. However, if this can be achieved, then there would be additional research options for all platforms.

Also, training and education is highlighted in all of the SRAs. In the medical field a difference is seen in the education and training between professionals in health care and those working in medical radiation protection. However, all researchers working with clinical data for radiation protection purposes or radiobiology/dosimetry/epidemiology with patient data could benefit also from parts of the training and expertise from the health care professionals in such areas.

2. Further potential synergies not yet mentioned explicitly

As it can be seen from the description in part 1 there are already many synergistic approaches and ideas for research for the benefit of dosimetric improvements, radiobiology questions and general understanding as well as patient and staff protection for medical applications described and identified. In addition, it would be of great interest for optimising medical radiation applications in terms of radiation protection on a per patient basis to investigate how individual patient sensitivity even on an organ level could be identified fast from investigations done basically just for diagnostic purposes or how to develop specific characterising procedures that allow fast optimisation of medical applications in clinical practice.

In terms of dosimetry, it would be of interest also to develop fast applicable methods of dose determination as well for patients as for staff and also for local dose determination for the modern technologies like proton / ion or neutron therapy. In addition the description as well as the effect determination for very strongly localized dose distributions would be an additional possible synergistic interest.

Discussions on synergies will be continued in the joint workshop of EURAMED, MELODI and EURADOS during spring 2017.

ANNEX

SRA Synergies between EURADOS and other Research Platforms

W Rühm on behalf of EURADOS

EURADOS Contributions for CONCERT D2.7

This report summarizes the synergies of the EURADOS research interests with those of other European platforms. The synergies with MELODI, ALLIANCE, and NERIS are rather clear and already included in the formulation of the first and second CONCERT Call text (based on actions performed within the OPERRA project, and documented in various OPERRA reports). For this reason, besides continuing the discussions with MELODI, ALLIANCE and NERIS, more recently EURADOS has focused to establish links to medical European associations and on the recently founded EURAMED platform.

Development of EURADOS SRA

Since autumn 2012, the EURADOS WGs have collected proposals for topics related to dosimetry which are believed to be important to the future of radiation research. During the EURADOS Annual Meeting in February 2013 in Barcelona, Spain, EURADOS Council established an SRA Editorial Group who put together all collected information and began to draft the EURADOS Strategic Research Agenda (SRA). The developed document has been discussed in detail at various levels (Working Groups, Council, Voting Members), and presented at various occasions. Thereafter the document was finalized and published as the EURADOS Strategic Research Agenda (first version) on the EURADOS website (www.eurados.org), as EURADOS Report 2014-01 “Visions for Radiation Dosimetry over the Next Two Decades - Strategic Research Agenda of the European Radiation Dosimetry Group”. The authors of this report were the members of the SRA task group, EURADOS Council, and EURADOS Working Group Chairs. In early 2016, a condensed version of the EURADOS SRA was prepared by the same authors and published in *Radiation Protection Dosimetry* (Radiat. Prot. Dosim. 168, 223-234, 2016).

EURADOS Stakeholder Workshop

It was acknowledged from the beginning that the EURADOS SRA was a moving target and that continuous efforts are needed to improve and update the SRA. At its meeting in July 2015 in Braunschweig, Germany, the EURADOS Council decided to organize a one-day workshop where relevant stakeholders should be invited and asked to provide their view on the current version of the EURADOS SRA, and to identify potential synergies. The workshop took place on June 30th, 2016, at the Helmholtz Center Munich in Neuherberg, Germany, and international organizations were invited who are expected to be interested in an improved dosimetry of ionizing radiation. Among those 24 organizations who accepted the invitation and sent

representatives were MELODI, ALLIANCE, and NERIS. Because EURAMED was not yet formally established at that time, five European medical associations were invited and the following associations sent representatives: European Association of Nuclear Medicine (EANM), European Federation of Organizations for Medical Physics (EFOMP), European Society of Radiology (ESR), and European Society for Radiotherapy and Oncology (ESTRO).

Currently, a summary report of this meeting is being prepared by EURADOS highlighting the synergistic interests among these organisations. Once agreed by all participants this report will form the basis to update the current EURADOS SRA.

Synergies with NERIS and ALLIANCE

Meeting EURADOS-NERIS-ALLIANCE in February 2016

At the EURADOS Annual Meeting at Politecnico in Milano, Italy, on February 9th 2016, a meeting took place between members of EURADOS, NERIS and ALLIANCE. MELODI was also invited but no one could attend the meeting. The purpose of this meeting was to help each of the three platforms to improve their understanding of the other platforms' expertise and to explore synergies between their respective Strategic Research Agendas (SRAs), in order to identify common research priorities and to create stronger links among the three platforms.

Vision 3 of the EURADOS SRA is "Towards an Efficient Dose Assessment in Radiological and Nuclear Emergencies" and involves four EURADOS working groups:

- WG3 Environmental monitoring
- WG6 Computational dosimetry
- WG7 Internal dosimetry
- WG10 Retrospective dosimetry

This vision includes a number of challenges which, from the EURADOS point of view, contain topics that might be of mutual interest for EURADOS and NERIS. In particular, NERIS highlighted two challenges of the EURADOS SRA:

- Strategies and methods to increase measurement capacity (it was noted that EURADOS is focussed on people but that there is a need also for screening environmental samples, food, etc.)
- Nuclide specific information in environmental monitoring

One of the key objectives of NERIS is the development and improvement of decision support systems (DSS) and one of the key elements in achieving this is the acquisition of good monitoring data. This is the type of work being undertaken by EURADOS WG3. In particular, under the subject of monitoring, a number of research questions were identified by NERIS including

- Development of environmental monitoring strategies (methodology, tools, ...)

- Integration of new monitoring techniques, especially use of drones, smartphone apps and small devices for radiation measurement
- Integration of public measurements in monitoring strategy, including technical and societal/ethical aspects

Furthermore, in order to assess and reduce uncertainties in dose evaluations, nuclide specific information, or particle size distribution of breathable aerosols are relevant, and there is a common interest on these. EURADOS has some experience on this field, also about the measurement methods of physical and chemical parameters of aerosols.

Other topics of joint interest identified included

- Determining individual doses as well as population doses to cover both radiological and nuclear accident scenarios
- Rapid methods for determining internal contamination
- Uncertainties in modelling and measurement data

ALLIANCE evidenced that EURADOS can contribute in the wildlife dosimetry (internal dosimetry, MC calculations, voxel phantoms of animals), with a special attention to: Simple biokinetics for groups of animals to calculate doses due to internal exposures (retention/excretion functions, dose coefficients); Monte Carlo simulation of in-vivo monitoring using Voxel phantoms of animals (equipment, counting geometries, calibration factors,...); markers of exposure, i.e. environmental biodosimetry and retrospective dosimetry.

Synergies with EURAMED

From the beginning it was clear that the European platforms should use their respective SRAs also to identify scientific synergisms and common scientific interests. Accordingly, the EURADOS SRA was structured in a way that should facilitate identification of potential synergies also with medical associations. More specifically, chapter 3.4 in the EURADOS SRA is dedicated to application of dosimetry in the medical field. This chapter describes the vision of EURADOS towards an integrated personalized dosimetry in medical applications. The chapter includes five challenges, which each are worked out in more detail by means of specific research lines. The challenges are:

- To improve out-of-field dosimetry for photon and particle therapy,
- To improve dosimetry in modern external beam radiotherapy,
- To improve internal microdosimetry in radiotherapy and medical imaging,
- To optimize dose estimations in interventional radiology, and
- To establish reliable patient dosimetry in CT examinations

We note that other visions formulated by EURADOS may also include topics of potential interest for EURADOS. These may include

Vision 1: Towards updated fundamental dose concepts and quantities

- To improve understanding of radiation-induced effects from internal emitters

Vision 2: Towards improved radiation risk estimates deduced from epidemiological cohorts

- To improve exposure pathways not yet considered or validated
- To improve retrospective dosimetry for exposure pathways already considered

Vision 3: Towards an efficient dose assessment in case of radiological emergencies

- To quantify doses after accidental internal contamination
- To rapidly identify individuals with highest doses

Vision 5: Towards improved radiation protection of workers and the public

- To implement new biokinetic models for intake of radionuclides
- To develop accurate and on-line personal dosimetry for workers

We also note that this list might not be complete and EURAMED might identify additional topics of mutual interest.

Actions of collaboration initiated with EANM

Kick-off Meeting EURADOS – EANM in February 2016

This meeting was organized by EURADOS during the EURADOS Annual Meeting in February 2016 in Milano, Italy. The meeting was initially proposed by Vere Smyth, University of Pavia. From EANM, members of their Dosimetry Committee participated while from EURADOS about 15 interested members from various Working Groups participated.

All participants were welcomed by W Rühm, who also expressed the interest of EURADOS in collaborating with EANM, contributing towards a better understanding on the dosimetry in nuclear medicine. He reminded that MELODI and EURADOS have signed a memorandum of understanding with five European medical associations including EANM that expresses the interest of these organizations to cooperate.

Vere Smyth gave an introduction to the subject; he explained his motivation to initiate a potential collaboration between EANM and EURADOS. He mentioned the MetroMRT (Metrology for molecular radiotherapy) collaborative project, part-funded by the EC through the European Metrology Research for three years, which ended in 5/2015. The overall aim of the project was to provide the science for development of a protocol for calibrating and verifying clinical dosimetry measurements in MRT. A new follow up project funded by EURAMET (2016-2019) will start in June 2016 on clinical implementation of MRT dosimetry including radionuclides such as ^{90}Y or ^{166}Ho . He also mentioned an IAEA working group set up to produce a text book on MRT dosimetry. Vere raised the question whether EURADOS could install a new working group on dosimetry in nuclear medicine and motivated all participants to think of what the role of EURADOS could be. At present MRT is not covered within EURADOS and there are no EANM members in EURADOS.

EANM was presented by Klaus Bacher who is a member of EANM Dosimetry committee: EANM has 15 committees among other on dosimetry, physics, radionuclide therapy; these cover expertise needed to work on dosimetry in nuclear medicine.

EURADOS activities were presented by the chairs of the working groups that could contribute to a joint collaboration: WG6 on computational dosimetry (R. Tanner), WG7 on internal dosimetry (M.A. Lopez), WG9 on Dosimetry in Radiotherapy (R. Harrison), and WG12 on Dosimetry in Medical Imaging (Ž. Knežević).

The following discussion revealed a number of topics where a joint collaboration would be beneficial (if necessary, links to hospitals could be provided by EANM):

- Microdosimetry and computational dosimetry (e.g., bone marrow dosimetry)
- ^{90}Y dosimetry with a link to doses to the skin and the lens of the eye
- Combination of radionuclides with external beams
- Dosimetry of nuclear medical imaging
- Dosimetry of new pharmaceuticals (e.g. using alpha emitters)
- Joint training actions

The following actions were identified, to be realized on a step-by-step basis:

- A technical cooperation between EURADOS and the EANM Dosimetry Committee should be established
- EURADOS will identify a number of colleagues (“core group”) who will be in charge to contact EANM and discuss with them (D. Nosske, L Struelens, W. Li)
- EANM offered to organize a satellite EANM/EURADOS workshop before or after their annual meeting (to be held in Barcelona, Spain, from 15th – 19th October 2016). Both EANM and EURADOS agreed that this would be very useful and should be done, as a first step in a longer lasting joint collaboration.
- EURADOS may consider – on a long term – to form a task group or even a working group on “Dosimetry in Nuclear Medicine”.

EANM - EURADOS meeting in October 2016

This meeting was organized by EANM during the EANM Annual Meeting in October 2016 in Barcelona, Spain. The meeting was decided at the kick-off meeting in Milano, Italy (see above). From EANM, the following members participated: Mark Konijnenberg, Klaus Bacher, Carlo Chiera, Jonathan Gear, Glenn Flux, Michael Lassmann, Uta Eberlein, Lidia Strigari, Nora Hocine). From Eurados the following individuals participated: Weibo Li, Tiffany Beaumont, Jochen Tschiersch, Lara Struelens. In addition Vere Smyth participated.

In the meeting EURADOS informed about EURADOS activities. In particular, a questionnaire has been sent around EURADOS members to gather information about research activities related to nuclear medicine that are performed within their institutes. Twenty-one reports from 17 institutes from ten countries were received. EANM informed about activities of their Dosimetry Committee.

In the discussion it became clear that the common ground between EANM and EURADOS is the organization of training, development of guidelines and the harmonization of practices. It could be interesting to share resources that are present from both sides, e.g. patients, phantoms, contact to companies. It was noted that EANM consists of medical centers, mostly with interest in clinically related research and codes of practice, while EURADOS consists of research institutes, universities, medical centers and some companies. Radiation protection and staff monitoring has been identified as a clear overlap between both organizations. Radiation protection of staff is part of the EANM Radiation Protection Committee (president: Michael Lassmann). It was also clear that the exchange of information is the most important aspect. Attending each other's meetings is a good approach, and organizing joint sessions at EURADOS Annual Meetings and at EANM congresses can be a good starting point.

Actions decided were a) organization of a more thematically focused joint meeting at the next EURADOS Annual Meeting in 2017 at KIT in Karlsruhe, Germany. The meeting will take place from Monday February 27 – Thursday March 2, 2017. The EURADOS Winter School held on this occasion will focus on the topic “Internal Dosimetry in Radiation Protection and Medicine”. The joint session could be organized on Friday morning, March 3. Topics to be discussed will be clinical dosimetry, radiation protection, microdosimetry, bio-dosimetry, the implementation of the EU directive. In total three to five presentations of each group on the chosen topics will be given. It was also suggested to organize a joint session at the next EANM congress, and to organise a Do.MoRe session.