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.