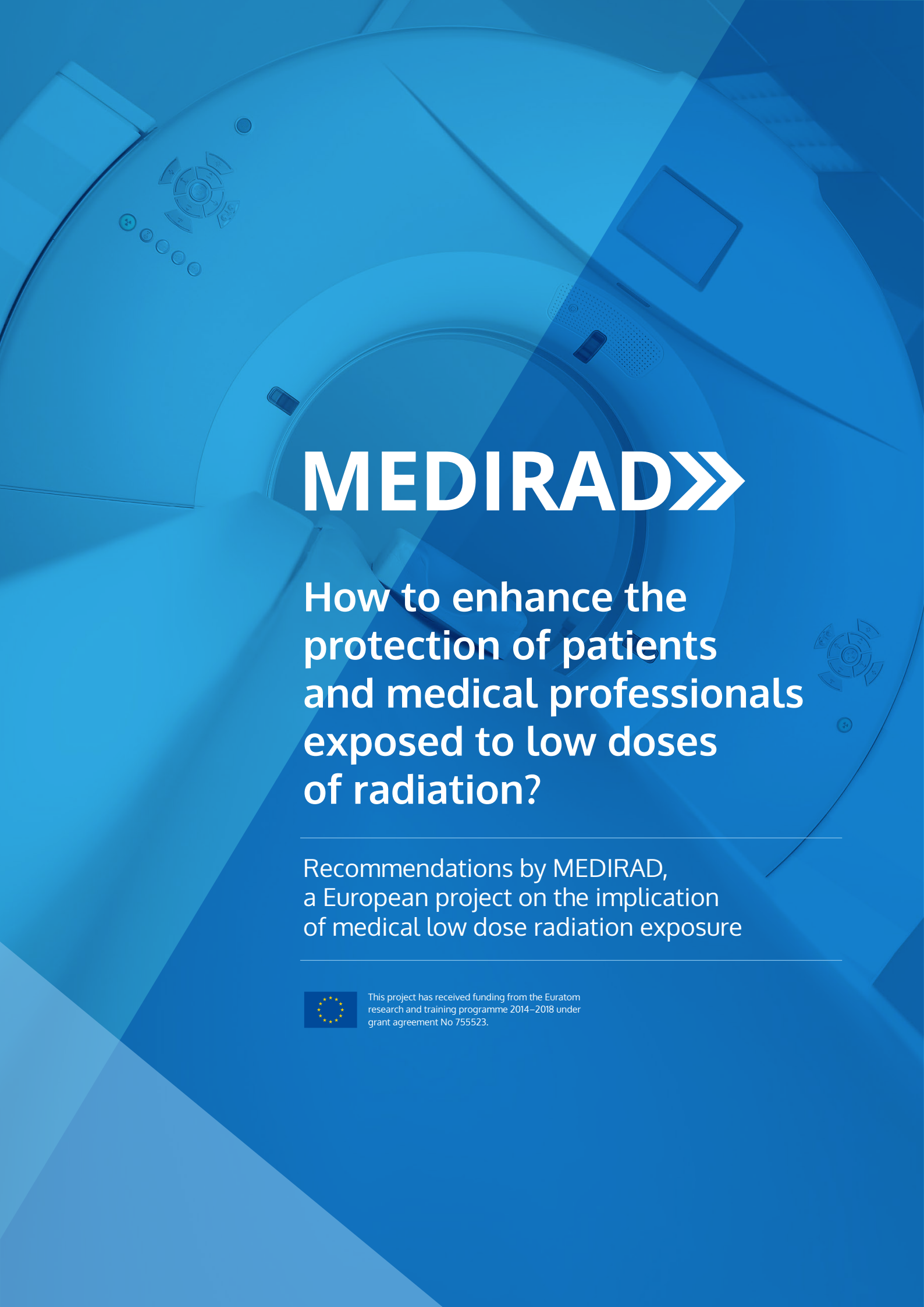


MEDIRAD

How to enhance the protection of patients and medical professionals exposed to low doses of radiation?

Recommendations by MEDIRAD,
a European project on the implication
of medical low dose radiation exposure

This project has received funding from the Euratom research and training programme 2014–2018 under grant agreement No 755523.

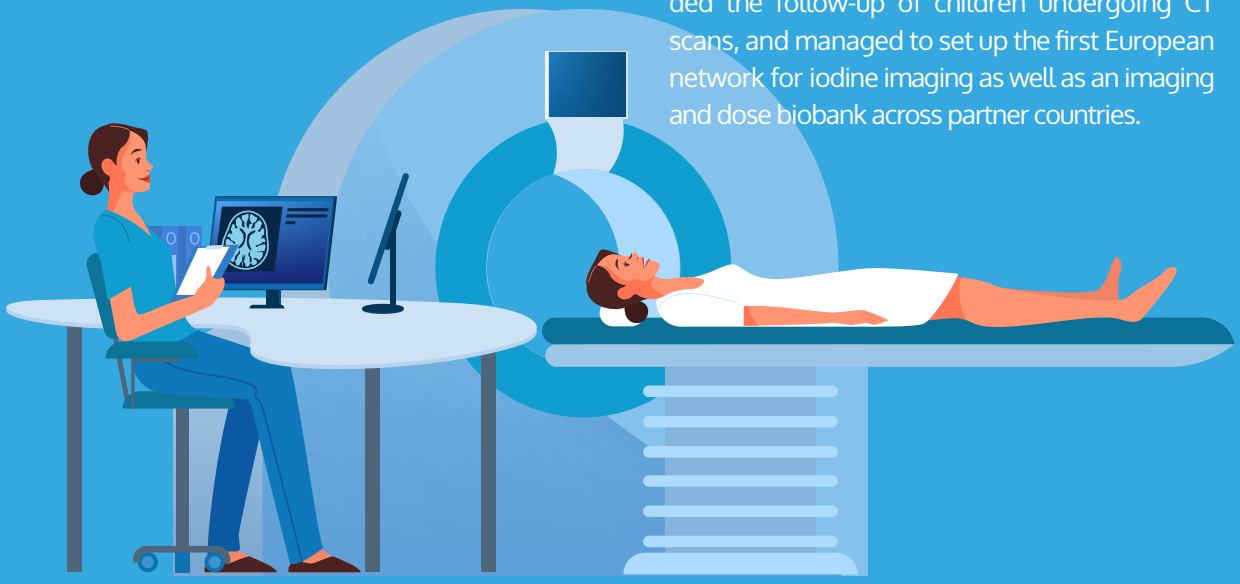
What did MEDIRAD do?

MEDIRAD is a European-funded project with the overall aim of enhancing the scientific basis and clinical practice of radiation protection in medicine, in particular by better understanding and evaluating the health effects of exposure to low-dose ionising radiation resulting from diagnostic and therapeutic procedures.

The multidisciplinary consortium consists of 34 partners from 14 European countries, and its work focused on the three following areas:

First, improving organ dose estimation and registration to inform clinical practice, optimise doses, set recommendations and provide adequate dosimetry for clinical epidemiological studies. Second, evaluating and understanding the effects of medical exposures to radiation, focusing on two major endpoints of public health relevance: cardiovascular effects of low to moderate exposure in breast cancer patients treated with radiotherapy; and long-term cancer risk of low dose exposure from CT in children. Third, developing science-based consensus policy recommendations for the effective protection of patients and staff.

Some of the main outputs of the MEDIRAD consortium include the development of a series of freely-available tools for the scientific and medical communities (such as online tools to determine CT dose and image quality, voxel phantoms, diagnostic reference levels for CT applications in nuclear medicine, dosimetry software packages for molecular radiotherapy), as well as prediction models and imaging biomarkers for identifying radiotherapy-treated breast cancer patients at risk of coronary events. MEDIRAD also expanded the follow-up of children undergoing CT scans, and managed to set up the first European network for iodine imaging as well as an imaging and dose biobank across partner countries.



Going beyond the science

One of the main objectives of the MEDIRAD project was to use the research results obtained throughout the project to develop a series of recommendations that would contribute to improving radioprotection of medical workers and patients across Europe. The added value of these recommendations is that they were drafted after engaging in a substantial dialogue with international and European stakeholders, who were invited to express their needs and expectations, and to comment on the draft recommendations.

The entire consultation process spanned almost five years during which two surveys and two webinars were conducted. It involved a stakeholder board (with ten representatives from European medical associations, radiation protection research platforms, and patient care advocates) and a wider stakeholder forum (from 86 organisations, including health professionals, patients, nuclear scientists, policy makers, competent authorities and representatives from international organisations).

The stakeholder survey revealed 10 top priorities, which, together with 15 priorities identified through MEDIRAD research, were grouped into four major topics: i) consolidation of patient data repositories across Europe; ii) optimisation of radiation-based protocols for diagnostics or therapy; iii) further optimisation of radiation protection for patients and medical workers; iv) future radioprotection research in Europe. For each topic, a series of overall recommendations are given (Table 1), together with an explanation of why they are relevant, specific recommendations on how to implement them, and the audiences concerned.

MEDIRAD recommendations: a summary

1 Consolidation of patient data repositories.

This first set of recommendations underscores the importance of having open **access to an organised collection of clinical image and dose data**, suitably coded to protect the patients' identities, in order to advance radiation protection research, clinical practice, and personalised medicine. Thus, the first overall recommendation is to develop an **interconnected and sustainable system of image and dose repositories at the European level**.

This requires, among other things, the development of standardised coding schemes, reporting templates, application programming interfaces, infrastructure and quality standards for collecting and storing the patients' data. Linking these image and dose data repositories with biobanks through a multisource integrative approach would maximise the utility and impact of the data.

All this cannot be done without harmonising the **implementation of current regulations regarding data protection** (i.e. General Data Protection Regulation) between institutions and countries, or without the **patients' informed** consent to use and share their data.

Specific actions include the use of GDPR guidance documents, training courses, institutional data protection officers, and informing patients and general public of ongoing radioprotection research.

The **Image and Radiation Dose BioBank (IRDBB) built by MEDIRAD** across the 14 partner countries is **proof of concept** that an EU-wide repository for radiological research is feasible, and that these data can be uploaded and accessed from multiple clinical studies and geographic locations using application programming interfaces developed throughout the project.

2 Optimisation of ionising radiation-based medical protocols for diagnostics or therapy.

MEDIRAD developed a free software that identify the optimal Chest CT protocol based on image quality. This methodology can be applied to CT imaging of any region of the body.

The second set of recommendations focuses on optimising the risk-benefit of radiation-based protocols used in diagnostics or therapy. In other words, ensure doses are kept as low as possible while achieving the image quality required for the clinical indication.

2.1. Diagnostics

CT scans are the largest contributor to the European population's collective exposure to medical ionising radiation. Optimising the risk-benefit ratio is **particularly relevant for the paediatric population**, due to their higher radiosensitivity and prolonged life expectancy.

To achieve this, organ dose exposure and image quality parameters have to be determined and documented in a way that **does not add to the workload** of the clinicians, and **dose evaluation should ideally be patient- specific, disease-specific, equipment-specific and protocol-specific**.

Establishing **diagnostic reference levels and image quality reference levels** for each indication will be helpful.

2.2. Molecular radiotherapy

The use of **radioactive substances for treating diseases** is a rapidly evolving discipline. MEDIRAD recommends **developing and implementing patient-specific dosimetry protocols** for treatment planning and verification of doses delivered to target volumes and organs at risk.

Given the limited number of patients treated at single centres, **harmonising data collection and analysis** between centres would greatly facilitate multi-centre and multi-national clinical studies. This requires providing adequate support to centres performing radionuclide therapy.

MEDIRAD has set up the first European network for quantitative imaging of radioiodine for thyroid cancer therapy. The methodologies are applicable to other radiotherapeutics.

2.3. Breast radiotherapy

Radiotherapy plays a pivotal role in the treatment of breast cancer patients, but may induce cardiac damage and subsequent coronary events up to decades after treatment.

MEDIRAD recommends **deploying a EU-wide strategy to better predict and reduce secondary cardiovascular risks** in these patients.

To this end, **multivariable models of normal tissue complication probability** (NCTP) should be applied **to all breast cancer patients**. These models should be **continuously improved** through data collected systematically in a **prospective data registration program** (similar to the European INSPIRE infrastructure for proton therapy). **Long-term follow-up studies** using cardiac imaging and circulating biomarkers will help identify women at risk and develop preventive measures.

Furthermore, **good practices can be actively promoted** to lower radiation doses to the heart at the moment of applying radiotherapy.

MEDIRAD developed multivariable NTCP models that can be used to predict the risk of acute coronary events and identified specific imaging markers and circulating biomarkers that could reflect early cardiac changes.

2.4. Modelling of patient dosimetry

A better estimation of delivered dose to the target organ and neighbouring tissue is key to improving the quality of care and the radiological protection of the patient. It will also allow to optimise protocols for a personalised medicine approach.

Hence, the need to **accelerate the generalised use of modelled total delivered doses to individual patients in clinical practice** within Europe. Providing regular **training on patient dosimetry and use of new technologies** is one of the recommended actions.

The online dose evaluation software tool developed by MEDIRAD in the context of CT exams will contribute to modelling of patient dosimetry.

3 Further optimisation of radiation protection for patients and medical workers.

This set of recommendations addresses three key aspects for improving radiation protection of patients and medical workers. The first concerns patients treated with molecular radiotherapy. Setting up optimised systems for the quantitative imaging of radiopharmaceuticals, irrespective of the gamma camera used, is key to establishing personalised treatment and facilitating multi-national, multi-centre studies.

To achieve this, manufacturers, authorities, practitioners and experts should come together to **establish a roadmap**, enable different imaging systems for quantitative imaging, and use **dose calibrators that can be traced** to a national standard.

Clinical centres, particularly the smaller ones, will need **adequate support** to set up the imaging systems and participate in multi-centre studies.

MEDIRAD results suggest that the set-up process of quantitative imaging can be simplified, but that there is a lack of dose calibrator traceability across Europe.

In addition, patients undergoing radiation-based diagnostic or therapeutic procedures will greatly benefit from a **closer cooperation between the different specialists** involved in their care and follow-up. Actions aimed at building these bridges include establishing **multidisciplinary protocols** to guide the planning, performing and follow-up of high-risk procedures, providing continuous tailored training for medical professionals, and **engaging with patients** and patient associations.

Linking medical professionals from relevant disciplines was identified by MEDIRAD's stakeholder forum as a key factor for improving patient follow-up.

Regarding protection of medical workers, MEDIRAD focused on one of the procedures that account for a significant part of the collective dose received by medical workers in European hospitals: fluoroscopically-guided procedures. Actions identified include developing **appropriate guidance on good practices** for the use of protective equipment at the European-level, **continuous education** of medical professionals, and **independent testing of equipment** in typical conditions of use.

Evaluations performed by MEDIRAD show that lab measurements are insufficient to predict the effectiveness of protective equipment in clinical conditions.

4 Future research on medical radiation protection.

MEDIRAD identifies five key research issues aimed at optimising medical radiation protection. These recommendations do not seek to establish a new research agenda, but rather to stress the strategic significance of providing adequate resources and encouraging close cooperation between medical and radiation research communities.

Further research is needed into the **adverse effects of ionising radiation on healthy tissues**. The adverse outcome pathway framework to help identify relevant molecular and imaging biomarkers of radiosensitivity is strongly recommended. Transfer of these biomarkers into the clinics will help making personalised treatment decisions.

Furthermore, developing **biologically-based models** that integrate biological processes of radiation toxicity and relate them to radiation-induced risk is another key research avenue.

Conducting well-designed, **long-term EU-wide epidemiological studies**, particularly among most at risk populations, will greatly contribute to better understanding and quantifying late health effects of radiation. These studies necessitate adequate funding and infrastructure, including complete patient data registries that can be linked to biobanks (as described in the first set of recommendations).

Optimising radiation-based imaging procedures is a key area of research, since the majority of patients arriving to a European hospital undergo imaging procedures for diagnosis, treatment or staging. Further research on exposure characterisation and appropriate image quality determination will help optimise the benefit-risk ratio of these procedures.

Artificial Intelligence (AI) and machine learning can play a major role in translating large amounts of multisource patient data into clinical decision support. Thus, a EU-wide research strategy to promote the use AI for personalised diagnostic and therapeutic protocols is urgently needed.

Key messages

1. These recommendations were drafted under the overarching principle of optimising the benefit/risk ratio for medical procedures based on ionising radiation.

2. One of the main pillars -and challenges- of radiation protection optimisation and research is having open access to an interconnected and organised collection of image and dose data at the European level. This requires:
   - Harmonising data collection protocols, including information on organ dose exposure and image quality parameters.
   - Addressing heterogeneity in GDPR implementation across countries for efficient data sharing.
   - Linking them to biobanks to maximise the utility of the information.

3. Semi-automated tools that facilitate appropriate dose and image data collection without adding to clinicians' workload need to be developed.

4. Modelling of delivered doses to individual patients needs to be generalised in the clinical practice within Europe.

5. Artificial intelligence and machine learning will play a major role in advancing towards personalised medicine, and is one of the key research avenues identified.

6. Long-term EU-wide epidemiological studies are needed, and participation of small clinical centres in such studies should be supported.

7. Interdisciplinarity (bridging medical specialities, research and patients) is of uttermost importance to harmonise practices and ensure the quality of care and follow-up of patients.

8. Regular training programmes, responding to European standards and tailored to specific needs, should be provided for medical workers and medical physicists.

Concluding remarks

MEDIRAD's recommendations are highly relevant because they draw from research conducted throughout the project and from a sustained dialogue with over 80 relevant stakeholder organisations. The overall conclusion reached by such process is the importance of 'bringing together' (data repositories, protocols, disciplines, communities, EU projects...) to optimise existing radiation-based medical procedures, and explore new technologies and research avenues.

Work conducted throughout the project has provided proof of concept regarding the feasibility of implementing some of the recommendations (eg. the Image and Radiation Dose BioBank) and has developed protocol optimisation tools that are already being used in the clinic.

MEDIRAD invites the different stakeholders to take these recommendations into account: the industry when developing new tools; regulators when upgrading international basic safety standards and national rules; medical associations when considering new guidelines for their members; patient associations when preparing information and advocating for patient protection; clinicians and scientists when planning future research; and policy makers when defining funding priorities.

MEDIRAD consortium members encourage key stakeholders to disseminate these recommendations at the national level, and reiterate their willingness to share all pertinent information to support their implementation.

Table 1

Recommendations to enhance the effective protection of patients and medical professionals, and to identify further research priorities

1

» CONSOLIDATION OF PATIENT DATA REPOSITORIES ACROSS EUROPE

- Develop an interconnected and sustainable system of image and dose repositories at the European level
- Harmonise GDPR implementation in medical radiation protection research
- Enhance awareness regarding radioation protection research among public and patients

2

» OPTIMISATION OF RADIATION-BASED PROTOCOLS FOR MEDICAL DIAGNOSTICS OR THERAPY

- Develop robust tools for optimisation of CT scanning and multimodality imaging
- Develop dosimetry-based protocols for molecular radiotherapy across Europe
- Deploy a EU-wide strategy to better predict and reduce secondary cardiovascular risks in breast cancer patients treated with radiotherapy
- Actively promote good practices aimed at reducing cardiovascular risks after breast radiotherapy
- Accelerate the generalised use in clinical practice of modelled total delivered doses to individual patients within Europe

3

» FURTHER OPTIMISATION OF RADIATION PROTECTION FOR PATIENTS AND MEDICAL WORKERS

- Optimise systems for quantitative imaging irrespective of camera make or model
- Encourage harmonisation of practices through active engagement of health professionals, researchers, health authorities and patients
- Optimise the use of protective equipment to improve radiation protection of medical workers in interventional settings

4

» FUTURE RESEARCH ON MEDICAL RADIATION PROTECTION IN EUROPE

- Conduct further research into adverse effects of ionising radiation on healthy tissues
- Promote a EU-wide research strategy to use AI for optimising protection in radiation oncology
- Develop biologically-based models to evaluate radiation-induced disease risk
- Conduct large-scale clinical epidemiological follow-up of patients to assess late health effects of radiation
- Investigate new and optimise existing medical imaging procedures to improve benefit/risk ratios and personalised approaches

For more information: **www.medirad-project.eu**