EURADOS
European Radiation Dosimetry Group e. V.

EURADOS Report 2020-04

Neuherberg, August 2020

Visions for Radiation Dosimetry over the Next Two Decades - Strategic Research Agenda of the European Radiation Dosimetry Group: Version 2020

Jean-François Bottollier-Depois, Isabelle Clairand, Elena Fantuzzi, Paola Fattibene, Roger Harrison, Oliver Hupe, Pawel Olko, Veronika Olšovcová, Werner Rühm, Marco Silari, Rick Tanner, Filip Vanhavere

ISSN 2226-8057

ISBN 978-3-943701-23-4

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Jean- François Bottollier-Depois[1], Isabelle Clairand[1], Elena Fantuzzi[2], Paola Fattibene[3], Roger Harrison[4], Oliver Hupe[5], Pawel Olko[6], Veronika Olšovcová[7], Werner Rühm[8], Marco Silari[9], Rick Tanner[10], Filip Vanhavere[11]

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ISSN 2226-8057

ISBN 978-3-943701-23-4

Imprint

Issued by:
European Radiation Dosimetry e.V.
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D-85758 Neuherberg
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Introduction

The European Radiation Dosimetry Group (EURADOS) comprises a self-sustainable network of more than 70 European institutions and about 600 scientists active in the field of radiation dosimetry. It was founded in 1981, and was registered in Germany as an "e.V." (registered society) in 2008. The aim of the network is to promote research and development and European cooperation in the field of dosimetry of ionising radiation. For this, EURADOS has established Working Groups (WGs) in various dosimetric disciplines such as harmonization of individual monitoring, environmental dosimetry, computational dosimetry, internal dosimetry, dosimetry for medical applications, retrospective dosimetry, and dosimetry in high-energy radiation fields. Complementary EURADOS activities include intercomparisons, bench mark studies, scientific meetings, training activities and an Annual Meeting.

In autumn 2012, EURADOS decided to develop a Strategic Research Agenda (SRA) to identify the future research needs in radiation dosimetry. This SRA was elaborated with input from EURADOS members and with active participation of all the EURADOS WGs. The final SRA was published in 2014 as EURADOS Report 2014-01: "W. Rühm et al., Visions for Radiation Dosimetry over the Next Two Decades – Strategic Research Agenda of the European Radiation Dosimetry Group". The document describes the research needs linked to dosimetry for the years to come, and was organized in five visions, each with different challenges. A summary of the SRA was also published in the Radiation Protection Dosimetry journal[1)]. Based on the SRA, a graphical roadmap was made for each challenge. This means that priorities and a timeline were determined for each of these challenges, including drivers and targets.

The EURADOS SRA is used to direct the research of the EURADOS Working Groups. The SRA is also used in the priority setting of research calls of the European Commission. Moreover, the SRA serves as an input to the Joint Roadmap for European research organized under the CONCERT (EJP) project.

The SRA is not intended to be a fixed document, and periodic revision is needed. The first action taken for this revision was to get input from stakeholder organizations outside EURADOS by means of a stakeholder meeting, which took place in Munich, Germany, in June 2016. More than 20 organisations were represented and gave their view on the EURADOS SRA by addressing different questions on the importance of dosimetry research for their field. The results from this workshop were published as EURADOS report 2017-02: "W. Rühm et al., EURADOS Stakeholder Workshop on June 30th, 2016".

From 2017 onwards, the SRA update continued with input stimulated from the EURADOS WGs, involving as many scientists as possible from all over Europe. A first preparation document was prepared per vision, listing new projects that had taken place or were still running, new important publications, new scientific and technological evolutions. Moreover, the lessons learnt from the stakeholder workshop were listed per vision. A revised and simplified structure was decided, with some new and merged topics. After this, the new SRA was finalized, and feedback from all EURADOS voting members was obtained.

[1)] W. Rühm, E. Fantuzzi, R. Harrison, H. Schuhmacher, F. Vanhavere, J. Alves, J. F. Bottollier-Depois, P. Fattibene, Ž. Knežević, M. A. Lopez, S. Mayer, S. Miljanić, S. Neumaier, P. Olko, H. Stadtmann, R. Tanner and C. Woda. *EURADOS Strategic Research Agenda: Vision for Dosimetry of Ionising Radiation*, **Radiat. Prot. Dosim.** 168, pp.223–234 (2016)

The updated SRA consists of 5 *Visions* which cover the main general fields of radiation dosimetry and its applications. For each *Vision*, more specific *Challenges* are identified. These are the areas which should be addressed if the overall *Vision* is to be achieved. Finally, for each *Challenge*, more detailed *Research lines* are identified. These *Visions*, *Challenges and Research lines* are described in detail below.

Vision 1:
Towards updated fundamental dose concepts and quantities

Challenge 1.1: To improve understanding of spatial correlations of radiation interaction events

The dependence of biological effectiveness on radiation quality is commonly believed to be related to the differences in the energy deposition pattern on a microscopic and nanoscopic scale. For charged particles, this pattern is called the particle track structure, where for heavy particles, such as ions, the energy transfer points are concentrated around the primary particle trajectory. For photon irradiation, the pattern is given by the tracks produced by the electrons (and positrons) liberated in inelastic photon interactions, and for neutrons by the tracks of the recoil protons and nuclear fragments. Identification and quantification of the relevant statistical characteristics of the microscopic spatial pattern of interactions (e.g., spatially correlated occurrence of clusters of energy transfer points) are an essential prerequisite for improvement of present dose concepts.

Micro- and nanodosimetry have provided experimental and computational techniques for the microscopic and nanoscopic characterization of the track structure. The quantity characterizing track structure in microdosimetry is the frequency distribution of the stochastic quantity lineal energy. Traditionally considered target volumes are of few µm in size (i.e. in the order of the magnitude of cell nuclei). In contrast, in nanodosimetry the measurement quantity is the frequency distribution of the number of ionisations produced by a particle track in target volumes of few nm in size.

Objectives

The overarching objective of Challenge 1.1 is the development of a novel, unified concept of radiation quality as a general physical characteristic of the radiation field that would allow separating the physical and biological components contributing to the eventual biological effects of radiation. The aim would be to have a physical 'dose' quantity that in the absence of biological variability would give a unique dose-response relationship. Thus, this new 'dose' quantity would allow a factorization of biological effects of different radiation types and energy spectra into a (measurable) physical component and a component that is only due to biological factors.

Achieving the overall goal will require further investigation into the physical characteristics of particle track structure to identify relevant statistical features that can be exploited for defining the new radiation quality concept and related measurement quantities. Further development of microdosimetric and nanodosimetric detectors along with a likely needed revision of their measurement concepts, and development of a 'gold standard' for track structure simulation codes and their validation by benchmarking with dedicated experiments with be further aims. This will be complemented by the establishment of robust uncertainty budgets for micro- and nanodosimetric quantities obtained by measurement or simulation and identification of the major uncertainty sources.

Research line 1.1.1: Investigation of experimental scaling relations for micro- and nanodosimetry and further characterization of existing detectors

In the historic development of both micro- and nanodosimetry, theoretical density scaling relationships have been exploited for experimentally simulating the (single) microscopic target by an equivalent gas target of macroscopic dimensions. Within the European BioQuaRT project, the

fundamental density scaling hypothesis underlying nanodosimetry has been experimentally tested and verified in the range of operating conditions realized with the three nanodosemeters operational in Europe at that time. The outcomes were 'universal' relationships between the mean ionisation cluster size and the first few elements of the complementary cumulative frequency distribution of ionisation cluster size. The mean ionisation cluster size seems to be related to the radiobiological cross sections for cell inactivation if target sizes are chosen that are well below what used to be commonly considered as relevant dimensions for biological radiation effects. A full understanding of these 'universal' relationships is still missing and hence these must be further investigated by theoretical and simulation studies as well as further characterization of existing and emerging nanodosimetric detectors.

The generic multi-scale approach for characterizing particle track structure by a combination of both microdosimetry and nanodosimetry at different length scales that was developed within the BioQuaRT project has so far only been studied with a prototype detector integrating one of the nanodosemeters in Europe and a silicon microdosemeter. With the ongoing endeavors to extend gas-counter based microdosimetry to target sizes of few 100 nm and even to target sizes below 100 nm and the significant progress made with silicon-based detectors with truly micrometric target sizes (albeit in tissue-inequivalent material), the further investigation of the link between these novel types of microdosimetric information on track structure and its nanodosimetric characteristics is mandatory. This also applies to novel interpretations of nanodosimetric measurands when multiple targets are considered, e.g. in the frame of a potential application of nanodosimetry in radio-oncology treatment planning.

Research line 1.1.2: Research on experimental track structure characterization

In principle, nanodosimetry enables a three-dimensional characterization of the particle track structure including the statistical correlations between different target volumes which may be decisive for biological effects of different radiation qualities. Such a comprehensive characterization of track structure is the prerequisite for an unbiased identification of the biologically relevant target sizes, which may depend on the biological endpoint considered. First promising attempts have been made with existing gas-counter nanodosemeters to measure correlated frequency distributions of ionization cluster sizes for pairs of simulated nanometric targets in close proximity. However, further progress in the field will need track structure imaging techniques, which require the development of novel instruments capable of measuring nanodosimetric track structure information for a complete set of targets along a section of a track. These activities need to be complemented with the experimental investigation of radiation interaction with real nanometric objects in the condensed phase, such as, for instance, nano-droplets of DNA, proteins clustered with water molecules or nano-structured solid-state devices. Apart from laying the basis for the development of detection systems for practical use, the research on experimental track structure characterization also provides a benchmark for the validation of track structure simulation codes.

Research line 1.1.3: Uncertainty estimation for measured track structure quantities

The establishment of uncertainty budgets for measured track structure quantities is a still ongoing challenge that has become even more relevant with the aforementioned novel approaches in microdosimetry and nanodosimetry. This uncertainty budget needs to consider all sources of uncertainty including potential bias introduced through incomplete collection of the charge carriers produced by radiation interactions in the target as well as collected charge carriers produced outside the target region. For this end, the comprehensive modelling of the measurement process and the

determination (by modelling and experiment) of the sensitivity of the measurement outcome on the parameters of the experiment needs to be performed.

Research line 1.1.4: Further development of computational methods for track simulations

Deriving estimates of the uncertainty of nanodosimetric characteristics of track structure is also a major task for the computational methods used for numerical simulation of particle tracks. These numerical methods are, in principle, well suited for studying track formation and for obtaining the probability distributions for micro- or nanodosimetric quantities. Some codes have been developed for this purpose by different groups. Using track structure simulation, first attempts to investigate correlations between nanodosimetric characteristics for different target volumes along the track and between target volumes of different size have been made. The 'multi-scale' characterization of particle track structure and the link between nanodosimetry and microdosimetry strongly rely on such simulations. However, several issues are still not resolved. The two most challenging issues are related to the fact that track structure simulations are mostly based on Monte-Carlo techniques that take into account each individual interaction (step-by-step simulations as opposed to the common condensed-history approaches). The first challenge and potential problem of this approach is that the ionising particles are basically treated as classical particles for which location and momentum can be defined simultaneously (and are used in the simulations). Particularly for electrons with energy below 1 keV, i.e. for the vast majority of electrons produced in ionising interactions, this is in contradiction to the Heisenberg uncertainty principle. A systematic investigation of this issue and a practical workaround still needs to be developed. The second challenge is related to the use of the scattering cross section concept in a context where subsequent interactions occur at average distances in the nm range, so that they cannot be considered as independent events. Some alternative methods for simulating track structure characteristics without using Monte Carlo techniques have been developed which, however, also rely on albeit effective cross sections. Experimental and theoretical investigations into the effect of the presence of additional scattering centres in the vicinity of an atom or molecule where an interaction occurs are needed to assess how the angular distribution changes and to determine the magnitude of changes in absolute cross section values in condensed-phase conditions as opposed to gas phase conditions where atomic and molecular cross section measurements are usually performed. Furthermore, the relevance of using the real interaction coefficients with biological molecules (DNA, proteins, etc.) instead of using cross sections of water as a substitute has already been demonstrated for simple simulation setups. However, most track structure codes are still based on the exclusive use of water cross sections. The impact of this approximation still needs to be investigated in a more comprehensive way. Finally, recent intercomparisons of different codes have shown large discrepancies between results obtained for simple geometrical setups (simulating electron transport in liquid water in all cases) that still need to be resolved. All these issues associated with simulations of microdosimetric and nanodosimetric quantities call for the development of a 'gold standard' for Monte Carlo simulations of track structure with a robust quality assurance scheme based on evaluated databases of cross sections with ascertained uncertainties, implementation in the codes and investigation of uncertainty propagation from cross sections to the final simulation results. This should be complemented by a set of high-quality benchmark experiments that provide a reference for the assessment of the quality of simulation results.

Challenge 1.2: To quantify correlations between track structure and radiation damage

The comprehensive multi-scale characterization of the physical aspects of radiation energy deposition will enable a quantitative investigation of the impact of track structure in terms of biological effects. Track structure has been proven to show a strong correlation with the induction of early biological effects, particularly the occurrence of DNA single and double strand breaks. As later biological endpoints also show dependence on radiation quality, there should also be a correlation of track structure characteristics and the probability of inducing these later effects, such as chromosomal aberrations or cell death. The ability to establish these correlations at the cellular level and to investigate the response at supra-cellular organization level will form the basis for the comprehension of the radiation damage mechanism.

This fundamental knowledge will have a direct impact in addressing current optimization criteria in diagnostics, radiation therapy and radioprotection, such as "biologically weighted" doses delivered in hadron therapy, dose calculation in inhomogeneous irradiations such as those of short-range α- and β- emitters used in nuclear medicine or in the case of internal contamination, risk estimation for low dose exposures, etc.

Objectives

The objective of challenge 1.2 is to investigate potential correlations between the track structure of ionising radiation and the biological radiation damage caused after exposure. To achieve this:

- Radiobiological experiments should be performed with similar metrological methods as those used for challenge 1.1 thereby facilitating the identification of useful connections for further advancements in radiobiological modelling.
- Cell monolayers exposed to single particle tracks represent a powerful model for the study of the geometrical correlation to cellular damage. Radiobiological experiments at the cellular level should improve the knowledge on different possible subcellular structures in the biological target, such as DNA, cell membranes, organelles or even proteins contained in the cells, and their post-irradiation behaviour (i.e. damage induction, recognition, repair, evolution, etc.).
- Automated assays and metrological methods aiming to improve the dependability of radiobiological assays would therefore be desirable.
- The response at supra-cellular organization level must also be taken into account. Dedicated radiobiological experiments and development of methodological approaches are needed to fill the gap between the initial characterization of radiation-induced damage starting from energy deposition and the response of the system as a whole, described with a holistic approach.

Research line 1.2.1: Studies on the geometrical correlation of energy deposition and cellular damage

The method of choice for overlaying particle tracks with cells under controlled geometrical conditions is the microbeam, as it offers targeting capabilities not only for individual cells but also for compartments of cells. Ion microbeams can be used to expose cells to a controlled number of tracks. Alternatives to ion microbeams are methods based on nuclear track detectors and biological assays as DNA damage foci that maintain the geometrical relation between cells and tracks. In these experiments, radiobiological assays are carried out on the irradiated cells to quantify the chosen biological endpoint for a particular radiation quality as well as a particular geometrical arrangement

of the particle track and the irradiated cell. A multi-scale characterization of the track structure can also be carried out using nanodosemeters with multiscale measurement capabilities, and track structure simulation codes that have been benchmarked against nanodosimetric measurements. Statistical cross-analysis would then be carried out to identify, for instance, correlations between results for a particular biological endpoint for different radiation qualities and nanodosimetric probability distributions for various target sizes. Such correlations would then be used to identify the most relevant target size for a particular endpoint. Benchmarking experiments could be performed by exposing cells to "equivalent" combinations of tracks of different radiation quality within these relevant target volumes.

Research line 1.2.2: Automated assays and metrological methods

Technical and methodological developments aiming to improve the detection of radiation-induced biological endpoints in these experiments are also encouraged. For example, TEM (Transmission Electron Microscopy) techniques can be used for a better visualization and description of DNA damage. On the other hand, the stochastic physical nature of the irradiation interaction is certainly at the origin of part of the intercellular heterogeneity response. High throughput analysis techniques as well as recent advances in transcriptomic profiling of single cells can be powerful methods for investigating the intrinsic factors underlying cell-to-cell differences. Systematic studies should be performed for a variety of human cell types, also coming from donors of different age and gender, to obtain information on potential age and sex dependent differences, as well as on individual response to ionising radiation. The goal would be to establish potential weighting functions based on measured track structure characteristics that allow predictions of biological effects. This would be a prerequisite for new dosimetric concepts quantifying radiation effects at the level of individual cells or small tissue compartments.

Research line 1.2.3: Research related to the use of high-Z nanoparticles in radiotherapy

Gold nanoparticles (GNPs) have been used as radiosensitizers in preclinical targeted radiotherapy. The enhanced absorbed doses in the vicinity of multiple GNPs at the cellular and molecular level need a quality assurance that is often performed by Monte Carlo simulations. Furthermore, the radiobiological effects of GNPs shown in in vitro and in vivo experiments need extended Monte Carlo simulations with chemical effect modules as implemented, e.g., in the codes Geant4-DNA and PARTRAC. Another challenge is the observation of X-ray fluorescence released from GNPs irradiated by kilo-voltage x-ray. This provides a new imaging modality for targeted molecular radiotherapy and EURADOS can contribute to this challenge by the simulation of the experimental setup before a prototype is established.

Research line 1.2.4: Research on chemical aspects of the ionising radiation interactions with biological matter

The initial energy deposited by individual inelastic interactions of ionising radiation in biological targets result in early radio-induced damage following a series of complex chemical reactions. A better understanding of the biochemical reactions as well as the role of the chemical environment in the cellular outcome is of great importance for correlating the initial track pattern to the radiation damage. In particular, cell type dependent response to the same radiation quality may originate from both geometrical conditions and differences in the chemical environment. It is therefore necessary to promote experiments and the development of simulation techniques that investigate issues, such as the role of oxygen in DNA damage enhancement and the identification and/or

quantification of different scavenging species in the cell nucleus or cell environment and their impact on radiation damage. These issues also apply to the use of high-Z nanoparticles in radiotherapy, where the functionalization of the nanomaterial not only dramatically influences the cellular uptake but also impacts on the yield of reactive species (e.g. hydroxyl radicals) post-irradiation due to scavenging and/or catalytic effects. Furthermore, as the mechanism of radical production in the vicinity of nanomaterials is not fully understood, there is a need to develop suitable probes for decoding the chemical footprint in the chain of radiation action.

Research line 1.2.5: Studies of temporal correlations of radiation interaction events

Physical and chemical interactions at the basis of biological radiation damage have different reaction times (10^{-18} to 10^{-15} s for physical interactions and 10^{-15} to 10^{-6} s for chemical interactions) and, therefore, in the case of ionising radiation at low fluence rate, different events can be considered as independent: in other words, the physical and chemical interactions of one event are finished when the next event happens in the same volume. However, when high fluence rates are used, or in the case of photon irradiation at high dose rates or flash irradiations (Flash-RT), this simplified description has to be modified. While experiments quantifying the protective effect on normal tissue of Flash-RT can bring insight into such questions, they need to be performed using accurate dosimetry, which is non-trivial as current radiotherapy dosimetry protocols are not designed for such conditions.

Research line 1.2.6: Improvement of Monte Carlo simulations for predicting radio-induced damage in biomolecules

Major advances have been made in the last decades in Monte Carlo simulations for modelling biological response to ionising radiation. These models often include accurate simulation of particle tracks and detailed DNA and chromatin organization. In some cases, water radiolysis and chemical interactions between water radicals and DNA molecule are also taken into account for DNA damage quantification. However, improvements in the chemical stage description and simulation methods are still needed, in particular in order to reduce computing time but nevertheless respecting the accuracy needed for simulating chemical reactions between reactants that cannot be considered as isolated molecules. It is important to acknowledge the limitations that exist in the application of Monte Carlo codes in this context, mainly due to uncertainties in cross sections particularly at low energies and for specific materials as explained in 1.1.4.

Research line 1.2.7: Improvement of risk estimation models

The challenge of risk estimation for low dose exposures requires not only the initial track structure calculations, chemical and effect simulations: the cancer development processes should also be considered in the modeling to obtain an estimation of low dose risk. This can be optimized inside the EURADOS network by combining track structure based nanodosimetry and biologically-based mechanistic modeling and epidemiological data. This can provide insight into the molecular dosimetry for understanding the dose-response relationship at low doses and low dose rates.

Challenge 1.3: To Improve the protection and operational quantities used in dosimetry

The system of radiological protection employs two sets of dose quantities. The protection quantities are based on the energy deposition in exposed persons, weighted for the effects produced, and attempt to quantify the health detriment. However, the protection quantities are not measurable, and so a set of operational quantities are used as estimators for the protection quantities. Whilst the operational quantities themselves are not directly measurable either, they are more closely related

to field quantities such as air kerma and fluence, and their concepts and definitions help to guide the design of measuring devices. Because the protection and the operational quantities are closely related to each other (e.g., personal dose equivalent is designed to provide a (conservative) proxy for effective dose), the consequences of any change in the protection quantities and their use (e.g., for patients) for the proposed operational quantities always requires careful consideration.

Periodic review and revision of the quantities is the responsibility of:

- Protection Quantities: ICRP (the International Commission on Radiological Protection)
- Operational Quantities: ICRU (the International Commission on radiation Measurements and Units).

At time of writing, the publication by ICRU of revised definitions of the operational quantities is imminent.

Objectives

- The overall objective is to improve the utility of the dose quantities in terms of their applicability, their ease of use and their relation to detriment.
- To promote wide understanding of the concepts, application and limitations of the protection and operational quantities. To promote research that supports greater understanding of the quantities.
- To identify opportunities for improving the quantities in future revisions.

These objectives will require dialogue with the radiation protection community together with physical and calculational research.

Research line 1.3.1: To investigate the effects of any change in the protection quantities

Effective dose is a concept introduced by ICRP to relate radiation effects relevant of radiological protection to radiation dose. It is noted that the term "radiation effects" is used here in a more general sense and goes beyond health phenomena known or assumed to be caused by ionising radiation among humans such as cancer, leukemia and heritable diseases. In addition to these effects, the concept of radiation detriment includes factors that are not directly induced by ionising radiation such as a change in quality of life after a disease has manifested (which may be different for different cancer end points), the lethality of such a disease (which may depend on treatment success over time), and years life lost. Any decisions on potential additional health outcomes of relevance (e.g., cardiovascular diseases) to be used in detriment calculation, which may have some influence on the calculation of effective dose, should be complemented by considerations on consequences for the definition of operational quantities. This also holds for any changes in the numerical values of radiation weighting factors and tissue factors used to calculate effective dose.

Research line 1.3.2: To investigate the effects of a change in operational quantities

With the new ICRU proposals for operational quantities, there will be a need to evaluate their impact across a wide range of outcomes. There will also be some scope for identifying and disseminating ideas about how best to apply and accommodate the changes. All research will need to consider the full range of exposure situations and applications (e.g. medical exposures of all types, general industrial, research, nuclear sector, aircrew and space crew) as well as a full range of radiations and energies (photons, electrons, neutrons, cosmic radiation etc.).

- Main differences with existing quantities: a comprehensive analysis of how the operational quantities differ is needed, comparing not only the old and new operational quantities but also their relationships with the protection quantities e.g. effective dose and equivalent dose. For example, the proposed quantities are defined for a wider range of radiation energies and a wider range of radiation types. There are also significant differences for diagnostic-energy X-rays.
- Impact on radiation protection practices and regulation: whilst there are a number of situations in which the adoption of the new quantities will not change the magnitude of the assessed doses, in others there will be significant reductions or increases in dose. Which situations will these be, and by how much will the doses change? These changes are likely to have consequences for regulation, e.g. around dose limitation and national dose registries.
- Impact on dosemeter and instrument design, and associated standards: some instruments/dosemeters will be usable without alteration to measure the new operational quantities; others will require minor adaptations. Still others may require radical redesign or modification, or may even be unusable for the new quantities. A comprehensive survey is needed of the dosemeter and instrument types in current use, to identify where there are problems and where there are none. All existing type test and performance standards will need reviewing and, where necessary, revising.
- Impact on calibration and reference fields, and associated standards: just as some dosemeters and instruments will need redesigning, it is possible that alterations may be needed to optimise the procedures used for their calibration. This could mean alterations to details of the fields used, and will certainly mean the calculation and publication of entire new sets of conversion coefficients. In turn, this will require new set of international standards to be produced.

Research line 1.3.3: To develop appropriate operational and radiation protection quantities for space dosimetry

The assessment of the radiation exposure of astronauts is a task in operational radiation protection which is currently being developed by the ICRP with major space agencies. The dose quantities used up to now for radiation protection purposes are equivalent dose (H_T), effective dose or effective dose equivalent (E) and Gray-equivalent (Gy-Eq.). The first two quantities refer to stochastic effects, the latter to deterministic effects. These quantities are usually calculated applying an environmental model together with a transport model through a spacecraft and the human body tissues using an appropriate phantom model. Gy-Equivalents for organs have to be calculated using depth dose distributions from measurements in human phantoms for the incident radiation field. For space exposures no environmental operational quantities are defined yet. ICRP 123 states that the definition of H*(10) is inappropriate for mixed fields as such as in space. A set of different detectors may be necessary for area and individual monitoring combined with measured depth dose profiles in human phantoms. Monitoring and assessment of doses in the human body is not restricted to effective dose equivalent and needs to include doses to the eye, the skin and extremities, and perhaps other endpoints, due to the specifics in exposure situations.

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

Introduction

Epidemiologic studies are based on the analysis of observed adverse radiation induced medical (health) and biological effects (outcomes, endpoints), and seek to ascertain risks of these effects in comparison with the background/baseline (spontaneous) rates. It is understood that the target population (cohort members or cases and controls) has been identified at the early stage of a study. The subsequent investigations involve the collection of exposure and outcome data and require individual dose estimation. The basis for risk estimates is absorbed dose in the organs of interest for the outcome under investigation in the epidemiological study.

Radiation epidemiological studies are performed among cohorts comprising humans exposed due to medical, occupational and emergency situations. Therefore, the dose evaluation methods strongly overlap with the approaches and methodologies used in each of these domains.

Dose reconstruction is covering a broad range of applications – from retrospective dose assessment starting from the scratch (when information on individual doses is missing) to validation and adjustment of existing dose estimates/records by applying some auxiliary information, in order to adjust all dose estimates of cohort members for comparability and/or producing dose assessments to organs/tissues originally not considered at the time of exposure and monitoring.

Dosimetry for epidemiological studies has some distinctive features, which are expressed in but not limited to:

- assessment of target organ/tissue doses in terms of absorbed doses independently for each quality (say, photons and neutrons separately);
- estimation of doses/quantities/localizations, which originally had not been monitored, in particular - out-of-field doses;
- account of all plausible sources of exposure/pathways or justification of exclusion of the less significant ones (i.e. cross-fire from non-target organs);
- extensive use of historical dose records via their validation (including categorization by the quality/reliability of existing data) and retrospective re-evaluation (including both 'recalibration' and uncertainty estimation);
- collection of auxiliary data (like types of dosimetric equipment, measurement protocols and instruments, conditions of exposure, workloads etc.) to support dose estimation;
- application of dose estimation/reconstruction methods, in particular the ones with high throughput for cohort epidemiological studies.

Dose estimation in epidemiological cohorts is usually a complex task which utilizes the whole arsenal of dose reconstruction, validation and uncertainty evaluation methods on individual or group level depending of epidemiological study design.

Objectives

Dosimetric support accompanying an epidemiological study has three major objectives:

- Provide individual dose estimates with efforts to minimize possible bias for all relevant sources of exposure universally for all members of the cohort under study.

- Provide an appropriate description of the uncertainty for each estimate of individual dose to be incorporated into the stochastic risk analysis.
- Validate the system of dose estimates to the extent possible by independent measurements or strategies (benchmarking).

Thus, the ultimate objective is to provide individual doses involving no bias and as small as possible random errors for different pathways of exposure (i.e. internal and external). The reliability of dose estimates mainly depends on the completeness and quality of cohort-specific initial data and validity of dosimetric models applied. In order to improve risk estimates deduced from the existing and future cohorts, a number of dosimetric improvements are required which are implemented in the following research lines.

Challenge 2.1: To improve dosimetric data for epidemiological studies

Most epidemiological studies on exposed cohorts (A-bomb survivors, environmentally exposed populations in Chernobyl and Techa River, atomic workers and Chernobyl liquidators, medically exposed cohorts) are retrospective in nature and, therefore, doses need to be evaluated a posteriori. These studies are ongoing, and they regularly produce updates of the observed and scored health effects.

Objectives

Recently, some important cohorts were pooled to increase statistical power of the study. Such merging sets a new challenge of harmonization of dose estimates obtained in different countries or parts of the globe. In general, all cohorts need adequate dosimetric support in order to harmonize dosimetric data and to obtain the health risk estimates adjusted for dose uncertainty. Although vast experience has been accumulated, the process of improvement of dosimetric methods and models continues. This process should go along several research lines.

Research line 2.1.1: Estimation of doses to organs and tissues originally not included in dosimetric monitoring and dose assessment

The initial data for dose assessment are significantly different for occupational, environmental and medical exposures. In the latter case, doses to the organs and tissues of interest may significantly differ from values estimated and recorded in course of routine application of respective medical procedures: in-field doses in case of diagnostic and doses to target organs in case of therapy exposure, doses to target organs in nuclear medicine. Moreover, doses to specific non-target organs need to be accurately estimated based on the recorded doses and the details of irradiation protocols. Very often dose assessment is required long after exposure, which means that doses of concern were received in the course of application of outdated equipment and protocols.

In case of internal exposure, crossfire from the organs where activity was deposited should be considered. Also, quite often dosimetric monitoring practice originally does not consider doses/pathways/quantities of epidemiological significance. For instance, whole body dosimetric monitoring of photon exposure is not adequate if doses to the lens of the eye, thyroid or brain, doses due to neutrons or doses to shielded and unshielded organs are in demand from epidemiologists.

In order to address this challenge, both dosimetric methodologies (Monte Carlo transport calculations, biokinetic models, data aggregation), approaches to recovery and use of available initial data (including non-dosimetric) and reconstruction of missing pieces of information (like workloads) should be combined and further elaborated.

Research line 2.1.2: Improvement in the quality and further completion of the initial data used for external and internal dose reconstruction

Historical dosemeter readings are usually used as initial dosimetric data in epidemiological studies on workers. In such cases, the improvement of the data quality can be achieved by retrospective re-evaluation of historical records (including identification of errors based on a review of dosimetric practices and uncertainty estimation) and 'recalibration' of the historical dosemeters (using, for instance Monte Carlo simulations of radiation transport in the workplaces).

Reconstruction of external doses for environmental exposure is usually based on the collected data on radioactive contamination of soil, water and air. However, if historical measurements of outdoor/indoor exposure rate in the sites of interest are available, they are of the greatest importance. Improvement of data quality on the spatial distribution of the involved radiation fields can often be achieved by their validation with the use of luminescent dosimetry methods on samples of building materials.

In this respect, several particular issues must be considered. Firstly, typically doses must be assessed for thousands, tens of thousands or even more subjects. Secondly, life-long and sometimes dose reconstruction on a specific time frame is needed considering periods with varying exposure conditions or varying monitoring data (inter or intra cohorts). Thirdly, important required information (chemical speciation of incorporated radionuclides, value of the detection limits, exposure conditions) is often lacking. Fourthly, a significant percentage of measurements of both external and internal exposures usually fall below detection limits/recording levels. Whatever the quality of the data, each investigated individual can be associated with hundreds or even thousands of data (measurement dates, results of measurements, exposure type/route/time, chemical speciation, etc.).

Expert analysis and sensitivity studies need to be performed systematically, eventually on artificial data sets, to select the best option, and to quantify the impact of these options on dose uncertainty.

Although there are a number of computer codes which allow calculation of external and internal doses from measurement data, none of these codes is able to handle such large cohort data sets. Software programs are designed for use with a specific cohort and cannot be easily adapted for use with others. Therefore, more flexible and adaptable software programs are needed for future epidemiological research. Common dataset standards (i.e. format and content) need to be defined. Such software should not only allow to derive doses from measurement data (as in the case of an incident), but also to link workers' data (e.g. exposure conditions) and other measurement data.

Research line 2.1.3: Improvement of the basic models used for assessments of external and internal doses

The improvement of the dosimetry in epidemiological studies is expected to come from the improved realism of updated biokinetic and dosimetric models.

For instance, new mesh-type reference computational phantoms (MRCPs) for adult male and female have been recently proposed by ICRP. Mesh-type phantoms have several advantages as compared to previous voxel phantoms, including deformability which makes it easier possible to create phantoms in different body sizes (age and constitution) or postures. Another methodology was developed to generate hybrid computational phantoms covering statistical distributions of anthropomorphometry in the paediatric population. Such hybrid computational phantoms

combine voxel-based and simplified equation-based modelling approaches to provide unique advantages and more realism for the construction of anthropomorphic phantoms.

A similar approach has been proposed for the development of dosimetric models of the human skeleton. The construction of hybrid computational phantom libraries for internal radiation dosimetry opens up the prospect of comprehensive calculations of individual doses and their uncertainties for individuals of different ages and diverse anthropometric parameters.

An important aspect of estimation of organ doses from internal exposures is the use of appropriate (case-specific) biokinetic models, i.e. age and gender specific biokinetic models. Other approaches based on the analysis of individual-based measurements should be used for uncertainty assessment.

Along these lines, further research should be conducted to bring the methodologies listed above to the stage of maturity that they can routinely applied for dose assessment in epidemiological studies.

Challenge 2.2: To estimate uncertainties and validate dose results

Until recently, dose uncertainties were accounted for in risk estimates suing some simplified analytical models. Such models include some deficiencies. For example, an increase of dose uncertainty leads to an underestimation of risk factors (i.e., it biases risk estimates downwards). The recent development of stochastic models sets demands for well-established dose uncertainty distributions, which can be used as an input for respective Monte Carlo risk calculation algorithms.

There are various uncertainty models available accounting for various sources of uncertainty. When dosimetric models are concerned, the uncertainty of the estimated internal dose is generally higher than that of external exposure. If dose estimation is based on interviewing human subjects, the so called 'human factor uncertainty' caused by fading memory, recollection errors or intentionally false responses should be considered. In case of environmental or similar time-and-motion dosimetric models, one should distinguish between 'shared' and 'unshared' uncertainties and treat them accordingly.

Objective

A reliable assessment of uncertainty of individual dose estimates within epidemiological studies is expected to improve evaluation of any dose response (e.g. risk) function and enhance the statistical significance of the results obtained.

Research line 2.2.1: Validation of calculated doses by using methods for retrospective dosimetry

Validation of dose estimates by comparison with independent measurements or alternative estimates has proven to be very important for benchmarking (to ensure that any dose estimates are unbiased) and empiric evaluation of uncertainties. Although this approach was extensively used in the past, further improvements are required to bring it to the level of routine and systematic application.

Three instrumental methods for retrospective dosimetry are useful for this purpose: luminescence dosimetry (TL (thermoluminescence) / OSL (optically stimulated luminescence) of quartz extracted from bricks in old exposed buildings, electron paramagnetic resonance (EPR) on tooth enamel, and fluorescent in situ hybridization (FISH) on circulating lymphocytes. Appropriate sampling and storing methods have to be identified and harmonized. Sharing of data and sample banks within the international scientific community should therefore be encouraged.

Biological dosimetry is well established and validated for providing dose estimates following uniform external exposures. In contrast, partial body or internal exposure situations are generally regarded as a challenge for biodosimetry. Work is currently ongoing to investigate whether FISH provides valid estimates of cumulative red bone marrow doses for internal exposures (after incorporation of radionuclides) or for combined external and internal exposures. It will be necessary to characterize further the dynamics of lymphocyte homeostasis and circulation within the human body and the effect of radiation on these processes. Although it is currently accepted that the FISH translocation assay can be usefully applied for detecting internal and combined external gamma and internal doses from internally deposited strontium-90, much work remains to be done to establish and validate dose-response relationships for plutonium-239, as well as other radionuclides.

Research line 2.2.2: Uncertainty analysis in the calculated doses and estimation of their influence on the radiation-risk coefficients

The reduction of dose uncertainties in epidemiological studies is quite challenging. Precise information such as historical data on the work conditions that prevailed at the time must be gathered and verified. Furthermore, subjective uncertainty factors for example after an interview of a worker on the working conditions, or an operator about patient exposures should be analyzed by experts in human sciences, archivists and/or historians. Ultimately, a method, for example a Bayesian network approach, must be developed to combine and quantify the uncertainties resulted from dose calculation and the uncertainties arisen from the propagation of all information available, in a final attempt to quantify their contribution to estimates of radiation–risk coefficients deduced from epidemiological cohorts.

First, starting from the measurement data (including those below the detection limit), data uncertainties should be systematically quantified and harmonized. Second, their influence on the results of different uncertainty models should be analyzed so that any additional uncertainties can be quantified. Once identified, those uncertainties with the largest influence should be reduced by gathering more precise information and, in such a way, reducing the overall uncertainty of the dose estimate. Even with limited resources an extension of historical research on the exposure conditions is worthwhile. For instance, additional information might come from deeper investigations of industry archives.

Quantification of dose uncertainty is an essential component of radiation-induced risk assessment because it is impossible to achieve a point (deterministic) estimate of the true dose for each person. It is now generally accepted that to derive the best, unbiased estimate of health risk, the type, magnitude and interrelationship of the uncertainties of model assumptions, model parameters, and input data used in the associated dose assessment models must be considered. The uncertainty analysis of dose estimates should always distinguish between uncertainty that is specific to each subject (i.e., unshared errors), and uncertainty of doses that are present due to a lack of knowledge about parameter values that are shared to varying degrees by many subjects (or subsets) within the study cohort (i.e., shared errors). Dosimetric uncertainties, particularly those that are shared among subgroups of a study population, can bias, distort or reduce the slope (diminish risk factors) or statistical significance of a dose response curve.

Information on dose uncertainty is provided by Monte-Carlo dose realizations and can be used to adjust risk estimates and their confidence bounds for dose uncertainty. Unshared classical measurement errors bias risk estimates toward zero but can be addressed in dosimetry using regression calibration. Unshared assignment/Berkson errors do not bias risk estimates but impact

risk uncertainty. Failure to adjust shared errors (such as biokinetic model parameters, organ dose conversion factors, released activity, group mean dose etc.) may result in a significant underestimation of uncertainty in risk coefficients. In practice, the error structure of exposure estimation is usually complex and includes various types of errors, although one type usually predominates.

Advanced statistical methods should be elaborated and employed to account for the complex error structures in risk analyses. To date, these methods have been successfully applied in several epidemiological studies, which prove the prospects of their further progression.

Challenge 2.3: To anticipate future epidemiological studies

Although many epidemiological studies per se are retrospective in nature, one should take care of prerequisites for future studies to be launched in coming decades. This is particularly true for investigation of any health effects caused by novel technologies like ion beam therapy.

Objective

In order to establish a solid basis for future epidemiological studies, extensive relevant information should be systematically collected and retained. This will ensure that reconstruction of doses will include rapidly evolving new technologies.

Research line 2.3.1: Prepare future epidemiological studies

There is a need to record doses with detailed description of what they are (which quantity), how they were estimated for all exposure scenarios (medical, accidental, occupational) and which technology was used (dosemeters in occupational/environmental settings, details on the machines and protocols used for diagnostic imaging, etc.). Therefore, the specifications for recording dosimetric and relevant auxiliary data in national dosimetric, and hospital clinical registries should be developed jointly by dosimetrists, epidemiologists, medical physicists and data managers. Special attention in this effort should be paid to personal data protection issues.

Research line 2.3.2: Molecular epidemiological studies

A completely new class of radiation epidemiological studies, so-called molecular studies when endpoints are manifested at molecular, i.e. DNA, rather than tissue, organ or organism level, is emerging. In setting-up molecular epidemiological studies, development of protocols with non-invasive techniques (like saliva or buccal smear sampling) is essential, especially if children are involved, as well as high throughput dose reconstruction techniques in large scale cohort studies. In view of this demand some new standardized dosimetry and scoring methods need to be developed and employed to support harmonisation of dosimetric practices.

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

Introduction

Radiological emergencies are considered a major challenge for modern societies. These emergencies may include the following scenarios:

- Scenario A - incidents that have an impact on large geographical areas (such as the Chernobyl or the Fukushima accident) and lead to exposure of large groups of the general population,
- Scenario B - accidents that involve radiation sources used for example in industry or medicine (usually involving a small number of persons),
- Scenario C - terrorist attacks using either radiological dispersal devices ("dirty bombs"), which contain radioactive materials in addition to conventional explosives, or radiation exposure devices (hidden sources).

In handling such events, many aspects need to be considered, such as information strategies, risk assessment and communication, evacuation concepts, treatment of radiation injuries, etc. which are beyond the scope of the present SRA. In those scenarios, a quick, efficient and reliable estimate of doses to affected individuals or groups of individuals is a prerequisite before any further decisions can be made by the responsible authorities and decision makers. There are quite a few well established, reliable, retrospective methods of dose estimation available. However, dose assessment is complicated by the fact that a number of different exposure scenarios might be of concern, possibly occurring at the same time, including internal exposures from incorporated radionuclides and/or external exposures from various possible sources. Real-time (environmental) monitoring (in the case of nuclear power plant accidents, scenario A) or generally dose-rate measurements by various approaches (manually, stationary, car-borne, air-borne) is usually the first step to assess doses to population groups or groups of individuals and to identify critically exposed sub-groups. Due to the availability of affordable dose-rate meters for the public, citizen networks are becoming an increasingly relevant aspect in the case of scenarios of type A. However, dose-rate data can be incomplete and vary with time, exposure may by heterogeneous and individualized doses calculated from these data can be affected by potentially large uncertainties. An improvement would be the application of methods for individual dose measurement, enabling decision makers a) to rapidly reassure the "worried-well" and b) to identify individuals with high risk of developing radiation-induced injuries, both from external and internal exposure and c) to initiate the most urgent actions, including methods to reduce doses after internal contamination. In scenarios A and C, it is important that the applied methods allow the handling and processing of a large number of samples in a short time, whereas in scenario B an accurate organ-specific dose assessment should be pursued.

Dose assessment is also relevant for the long term and recovery phases, where it should support epidemiological studies to evaluate the possible health impact on affected populations, address the needs of individuals and society, including communication, and support the setting up of health surveillance programs.

Still different is the scope if dosimetry is used for epidemiological studies: in this case sufficient sensitivity of the technique must be assured, to allow dose measurements at or below about 100 mGy, with sufficiently low uncertainty.

For the vision of an efficient dose assessment in case of radiological emergencies the following challenges were identified:

- To quantify doses from internal emitters after accidents.
- To quantify individual doses from external exposure in emergencies
- To improve environmental monitoring in case of an accident, including citizens and mobile networks and harmonization.
- Challenges and opportunities of citizen engagement in dosimetry.

Challenge 3.1: To quantify doses from internal emitters in case of radiological emergencies

Intake of radionuclides as a result of radiation accidents may be associated with a planned situation or may occur as an unexpected event, requiring urgent actions to minimize health effects. In a nuclear emergency, frame priorities are established for fast identification and dose quantification of internal exposures affecting nuclear workers, emergency workers (e.g. first responders) and the population. The first challenge is to proceed with an efficient individual monitoring program according to the intake scenario and a rapid interpretation of monitoring data to estimate internal doses. The initial main concern is a quick identification of people at the highest health risk (Triage). A more reliable dose assessment for the identification of more exposed individuals may be carried out afterwards. The main goal is to transfer the dosimetry data to decision makers to support actions to avoid or minimize tissue reactions based on absorbed dose (Gy) calculations, and to reduce the risk of stochastic effects, based on the results of Committed Effective Dose (Sv). The emergency intake scenario in an early phase generally consists of acute intakes through inhalation of volatile elements or compounds including iodine, caesium, tellurium and inert gases. The emergency intake scenario in an intermediate phase may take account of continuous or incidental ingestion of radionuclides through the food chain. Wound contamination must be considered as well as a potential intake scenario in case of radiation accidents. The final challenge is a reliable quantification of accidental internal exposures that will allow proper epidemiological studies and risk assessments based on well-estimated absorbed doses to the organs and tissues of most interest.

Objectives

- To develop new equipment and methods for in vivo and in vitro monitoring of radionuclides incorporated in the body, for a large number of individuals (workers and members of the public), depending on the intake scenario.
- To develop protocols and computational tools to guarantee a rapid interpretation of monitoring data in an emergency scenario, resulting in reliable estimates of absorbed doses to organs and tissues and committed effective doses of internally exposed persons of different genders and ages.
- To establish proper channels for the transfer of the dosimetry data to decision makers and for the communication with stakeholders, including the civil society involved in or affected by the emergency situation.
- To further develop biokinetic models of decorporating agents administered in the case of significant internal contamination (depending on incorporated radionuclides) and to validate those models with human data.
- To carry out epidemiological studies for estimates of radiation-induced risks during the post-accidental stage, to better understand the health effects (cancer and non-cancer diseases) associated with accidental intakes of radionuclides in case of high levels of exposure. Reference internal dosimetry protocols need to be elaborated and applied with real data of

well-known radiological events that already occurred in the past. Proper estimation of absorbed doses to organs and tissues of exposed persons is required.

Research Line 3.1.1: Improvement of the calibration of in vivo monitoring systems for the measurement of internally contaminated children

The calibration of in vivo monitoring techniques for children has to be improved, including the development and validation of reference calibration physical phantoms scaled by age and the optimization of counting geometries for measurements on children. Studies of the uncertainties involved and the sensitivity of detection need to be carried out. The validation of new methods will be effective through intercomparisons.

Along these lines, new developments of Monte Carlo (MC) methods using computational phantoms (Voxel phantoms, Mesh phantoms) scaled by age will be useful for the calibration of body counters and the assessment of internal doses. Validation of MC results will be possible with proper measurements in the different intake scenarios.

Research Line 3.1.2: Networking, optimization and development of methods for individual monitoring and dose assessment

Networking and optimization of the use of in vivo mobile units, portable devices and other trans-border equipment and tools for individual monitoring and dose assessment in case of accidental internal exposures need to be evaluated and developed as standard, validated, protocols. The involvement of citizens of contaminated areas in establishing and using tools or instruments may be considered for radioactivity measurements. Developing processes and tools for integrating the monitoring results from experts and lay people into a common operational picture (monitoring crowd sourcing) are identified as an important gap that needs further improvement.

New developments on measurement systems are needed for wound monitoring and for dose assessment of exposed populations through wound contamination, based on the application of ISO Standard 20031:2020 *"Monitoring and dosimetry for internal exposures due to wound contamination with radionuclides"* and on "*NCRP Report No. 156, Development of a Biokinetic Model for Radionuclide-Contaminated Wounds and Procedures for Their Assessment, Dosimetry and Treatment"*. Wound measurement protocols are needed, a measurement methodology has to be elaborated and computational tools must be developed for proper interpretation of wound monitoring data for dose assessment for different accidental intake scenarios. These methods should allow for an early estimation of wound contamination, to assess the need for intervention if any (e.g., surgical removal, DTPA /diethylenetriaminepentaacetic acid/ administration, etc.), and will also allow the validation of the NCRP wound model with human data.

The development of more rapid in vitro emergency bioassay methods is required especially for alpha emitters (actinides) and ^{90}Sr, involving measurements of a large number of biological samples of the persons internally exposed. Radiochemistry processes and routine sample turnaround must be shortened, and this needs further development and research. The objective is to establish and validate methods with sufficient sensitivity to meet the requirements for emergency bioassay in typical nuclear accident scenarios.

Further efforts should be made to link internal dosimetry after incorporation of radionuclides with biological dosimetry methods. A EURADOS literature review has been carried out recently including relevant accidents with internal exposures involved where biodosimetry methods were applied.

Lessons learned from this overview will allow proposing a future research program on this topic. The definition of the proper dosimetric quantity to be compared to the biological end-point should be investigated further. Special models need to be developed for reliable blood dosimetry. For dose assessment after accidental internal contamination, in order to handle a large number of dosimetric samples, strategies and methods to increase measurement capacity must be developed. Networking of laboratories has been identified as a very useful approach to get fast and reliable dose estimates.

The development of appropriate and validated software is needed to support interpretation of individual monitoring data for the calculation of committed effective doses (Sv) to the public using age-dependent dose coefficients and for the assessment of absorbed doses to the organs and tissues of interest in different accidental intake scenarios. Software to use for emergency monitoring and dose calculation by on-line free access (e.g. development of Apps for Smart devices (cell phones and tablets)), has to be developed (lessons learned from the CONFIDENCE project).

Dealing with the consequences of a nuclear accident, decision makers will have to rely on estimates of doses received by populations. Research is needed to provide means for a rapid transfer of internal dosimetry data to decision makers and for a more effective communication of internal dosimetry experts with stakeholders and exposed persons. A work plan is needed to include individual dose values e.g. in the JRODOS Platform which should facilitate making proper decisions based on measurement results of exposed population instead of using only model outcomes.

Research Line 3.1.3: Development of new biokinetic modelling for human (e.g. administration of decorporation agents) and non-human biota (wild life dosimetry)

The modelling of biokinetics of chelating agents administered to exposed persons is required for the proper interpretation of bioassay monitoring data in case of decorporation therapy (e.g. development of a DTPA therapy model) to guarantee reliability in dose assessment. In case of high level of internal exposures, bioligands or chelators are commonly administered as treatment to reduce the doses after the incorporation of high radiotoxic radionuclides (notably actinides but not only), e.g. by increasing the excretion of incorporated radionuclides by the contaminated individual compared with standard metabolic behaviour. The objective is to develop biokinetic models that permit a robust interpretation of in vivo, in vitro and wound measurement data affected by the decorporation therapy, resulting in the assessment of reliable dose estimates.

New developments on wildlife dosimetry are needed, e.g. modelling the biokinetics of incorporated radionuclides in non-human biota in different accidental intake scenarios. Not only the biokinetics need improvement, also more phantoms (voxel, nurbs, …) for non-human biota (e.g. animals) are needed to allow better dosimetry from external radiation.

Research Line 3.1.4: New methods for dose reconstruction for epidemiological studies

Absorbed doses to organs and tissues of exposed persons are required but no reference methodology is currently available for internal dose assessments using epidemiological data. Development of a standard methodology and computational tools are required for the calculation and the use of internal doses for epidemiology studies in cases involving internal and internal+external exposures.

Estimations of radiation-induced risks associated with intakes of radionuclides are based on epidemiological studies, which are generally carried out during the post-accidental phase of an emergency situation. For such studies, reliable dose assessment associated with radiation

emergencies including traceability and comparability are indispensable, to better understand any induced cancer and non-cancer health effects.

Challenge 3.2: To quantify individual doses from external exposure in emergencies

In the last ten years, several research projects have highlighted the benefits and limitations of physical markers (EPR/TL and OSL of personal items and biological materials) and biological markers (dicentrics, micronuclei, "omics") of dose assessment. Significant steps forward have been achieved and, indeed, most of the biological dosimetry methods and some of the physical retrospective dosimetry methods are now consolidated within emergency response plans. Methods are standardized and inter-laboratory comparisons, to maintain expertise and answer further research questions, are performed on a regular basis. An ICRU-EURADOS joint report on "Methods of initial phase assessment of individual doses following acute exposure to ionizing radiation", describing the state of the art and giving recommendations, has been published in 2020. ISO standards for several methods are available. However, there is scope for further improvement of all methods and, in the meantime, new methods are also emerging which require validation and standardisation.

Objectives

- To continue to promote standardization of existing consolidated markers through inter-laboratory comparisons, field tests simulating various accidental scenarios and by quantification of uncertainties, from measurement to endpoint.
- To optimize existing markers which need to be improved. Here the emphasis may be, depending on the exposure scenario, on increasing sensitivity (down to about 20 mGy), decreasing uncertainty of the method, improving capacity, decreasing the processing time, etc.
- To identify new markers of radiation exposure, especially for quick identification of individuals in potential danger of short-term deterministic health effects in the early (initial) phase of an emergency/radiation incident. Here the emphasis is on methods for rapid dose measurement with high throughput but not necessarily on high sensitivity (low detection limit).

Research Line 3.2.1: To standardize existing markers and methods

Promote programs of inter-laboratory comparisons

Once a marker and the applied methodology has sufficiently matured, inter-laboratory comparisons should be carried out for standardization. This should be done with the purpose of validating and comparing the methods, to serve as a proficiency assessment of participating laboratories, and to give an estimate of the uncertainties of the dose measurements, which are often larger than inferred from analysis in a single laboratory.

Organize a regular programme of field tests

It is recommended that markers and methods are evaluated under conditions which are realistic and less controlled than inter-laboratory comparisons; for instance, phantoms with attached blood sample tubes and fortuitous dosemeters are exposed to radiation from sealed or dispersed sources in either open fields or closed environments. A further objective of field tests should be the investigation of the potential and limitations of a multi-method approach to reconstruct both doses and exposure conditions (heterogeneous vs. homogeneous) – each field test should address at least one key research question.

Quantification of uncertainties, from measurement to endpoint

There are a number of standardised methods but more tailored methods are needed. These are under development within the community but testing, validation and standardisation is needed here as for the laboratory methods. Training and user-friendly software tools are also needed to facilitate the use of appropriate methods across the retrospective dosimetry community.

Research Line 3.2.2: To improve existing methods

Continue exploring dosimetric properties of existing markers

There is need to continue exploring the still-unclarified properties of the materials which comprise the personal items shown to be the most promising with EPR, TL and OSL, and within new biomarkers including the gamma-H2AX assay and gene expression. Such properties may include the study of the origin of the signals for physical dosimetry, the inter-individual sample variation, the signal stability, and others, depending on the degree of maturity and level of standardization reached by the specific marker.

Study of the dependence of the marker response on radiation quality

There is a need to investigate the response to different photon energies and to neutrons, to make any promising marker identified suitable for a wide range of scenarios.

Dose-to-organ conversion coefficient

Since physical retrospective dosimetry measures dose to (inert) material, for rapid dose estimation, dose coefficients should be predetermined, to convert the absorbed dose in the material to the relevant endpoint (organ absorbed dose, whole body dose etc.), depending on beam quality, carrying positions and exposure conditions. For some materials this has been achieved or is under development but this effort must be continued, especially when new markers or methods have sufficiently been consolidated.

Development of non-invasive measurement approaches

Future research on dosimetry with human tissue samples should use methods which allow for a non-invasive collection of samples. Promising methods should be further explored. For EPR dosimetry with tooth enamel, which is the most sensitive and also the most invasive dosimetry method, a promising approach is based on tooth enamel mini-biopsies (2-5 mg) measured by higher frequency (Q-band) EPR. An interest and potential for mobile systems continues to exist for application in the field: research on in vivo EPR of tooth enamel or nails is focused on development of spectrometers with portable magnets and with different approaches, i.e. continuous wave with low (L-band) microwave frequency or pulsed in the X band frequency range. In vivo OSL measurements of (extracted or separately prepared) dental ceramics has shown that this dosimetry technique is not affected by the major technological and methodological challenges complicating the OSL in vivo measurement of tooth enamel and should therefore be pursued as an alternative. For biological dosimetry, finger prick blood sampling and assessment of biomarker signals in non-blood samples, e.g. in saliva, should also be further explored, to limit the impact on individuals to dose assessment.

Research Line 3.2.3: To identify new markers and develop new methods

Development of destruction-free measurement approaches

Future research should target methods which save the personal item, especially the sensitive items such as the mobile phones. OSL using surface-mount resistors extracted from portable electronic devices (smartphones, flash drives, cameras etc.), as well as EPR with touchscreen glass are currently the most advanced and standardized methods but require destruction of the item, which can lead to low acceptability of this method. EPR or OSL instruments, especially if portable and low-cost, should be developed, or identification of and further research into other components of the device, which can be replaced at low cost, should be pursued.

Widen the field of techniques

In addition to the established luminescence techniques of TL and continuous-wave (cw) OSL, the use of complementary techniques such as radioluminescence, cathodoluminescence, ionoluminescence, photoluminescence and pulsed OSL could widen the range of materials that can be used as a dosemeter or circumvent issues on the materials investigated above when measured with the established techniques (e.g. signal fading, confounding signals). This could also lead to identification of new materials including personal items which are worn close to the body (for example clothing, shoes, bank notes, plastics).

Further development of transcriptional markers

Up-regulation of some genes and non-coding RNAs provide accurate and reliable high-throughput dose estimations in human blood samples irradiated ex vivo and in vivo with dose estimation delivery time now decreased to four hours. Recent inter-comparison exercises using blind blood samples have demonstrated that gene expression is suitable for triage purposes in case of large-scale acute radiation exposure using existing calibration curves.

Investigation of the potential for metabolomic markers

Metabolomic studies of body fluids are also promising exposure biomarkers, potentially indicating tissue-specific radiation exposure. Mitochondrial DNA has also potential as radiation biomarker as its DNA is vulnerable to damage due to its lack of protective histones and an inefficient DNA repair machinery; an increase in common deletion levels after radiation exposure has been reported.

Increasing speed of assays

New, ultrafast technologies will allow the development of portable, high-throughput and cost-effective PCR for example, thus generating new tools for radiation biological dosimetry purposes.

Networking to increase capacity

As the demands in terms of number of dose measurements needed in a large-scale scenario is likely to surpass the capacity of any single laboratory or country, the establishment and maintenance of an international network of experienced laboratories in retrospective dosimetry becomes essential.

Challenge 3.3: To improve environmental monitoring in case of an accident, including citizens and mobile networks and harmonization

New detection systems for environmental monitoring to protect the public in the event of a radiological accident have been developed during the last few years, such as the use of drones or citizens' networks. In addition, novel environmental spectrometric detectors have been

characterized and tested in environmental conditions. From the results of the research it has been concluded that the spectro-dosemeters are suitable for installation in a European early warning network. Some European countries have started to install spectrometers in these networks. These new detection systems will improve the support to governmental decisions in case of radiological emergency. With such an approach an amount of data will be generated that needs a quality control system to provide reliable environmental radiation monitoring. In addition, the harmonization of these data and the assimilation by the different models will be a challenge in the future.

Objectives

- To improve existing dose rate monitors and spectro-dosemeters and develop new instruments for governmental and non-governmental applications.
- To create and implement new algorithms for net dose calculations and spectra analyses for the new detection systems.
- To extend network databases for implementation of harmonization algorithms for all real time data.
- To improve remote sensing (usage of drones and satellites) in the determination of natural and artificial sources of radiation in the environment.

Research Line 3.3.1: To improve aerial measurements using unmanned aerial vehicles

Development of detectors for unmanned aerial monitoring

Suitable detectors to be mounted in unmanned aerial vehicles should be investigated and adapted for their potential use in this research field. These include gamma spectrometric detectors, and the development of alpha emitter detectors in the environment with optical methods. Furthermore, detectors focusing on source localization and imaging will be developed for use in such aerial measurements.

Development of algorithms to calculate dose rate and activity concentrations

The methodologies for the calculation of dose rate at reference levels and activity concentrations in soil and in the radiological cloud should be developed and validated.

Measurement traceability

The development of such measurement systems will increase in the future, therefore calibration and quality control systems should be developed, in order to obtain reliable and harmonized data. Comparison exercises will be necessary in preparation for real scenarios.

Research Line 3.3.2: To improve surveillance networks with novel technologies

Development of the metrology system for non-governmental networks

Calibration and quality control systems should be developed to get reliable and harmonized data.

Implementation of novel spectrometric instruments in surveillance networks

Currently, spectrometric monitors are being progressively installed in the surveillance networks. Therefore, the implementation of the spectral analysis, dose calculations, data harmonization and including the data in the network data bases will be a challenge in the future.

Research Line 3.3.3: To harmonize and improve capacity analysis using novel information

Harmonized on-line in-situ monitoring platforms including new technologies and units in Europe

The huge amount of data including spectra from the new detection systems such as drones and the governmental and non-governmental networks should be harmonized in order to include all the measured data in the radiological picture.

Data analysis

Once the novel information provided by the developed instruments and new technologies have been harmonized, the analysis by combining all this information will be a challenge for the future. Big data and artificial intelligence will play a significant role.

Challenge 3.4: Challenges and opportunities of citizen engagement in dosimetry

With the advancement of digital and miniaturized technologies, there will be an increasing availability of low-cost and easy-to-use radiation detectors. These non-professional tools have created opportunities for citizens to be actively engaged in radiation protection by making their own radiation measurements, either on a self-organized basis or guided by experts, as already widely experienced in other fields of environmental concern.

The above technological advancements, together with a change of attitude in citizens who wish to be increasingly involved in decision making, have led to crowd sourcing and citizen science approaches becoming more and more relevant in the field of radiation protection.

Crowd sourcing is a process where voluntary contributions from a large group of unknown individuals ("the crowd") are collected and used for a purpose, for instance for the creation of collective data maps by sharing geo-localization and measurements. Crowd sourcing can be authority-led or citizen-led, i.e. sprouting spontaneously from the population. The scope of crowd sourcing can be to improve the responses to social, health, or emergency issues, or to contribute to scientific advancement. In the latter case it is called citizen science.

Citizen science can be defined as the active participation of citizens in science. This participation could be during the whole research process or just a part of it, and could include identifying research questions, observing and gathering data, or processing results. Citizen science initiatives often provide benefits both for citizens and researchers, and are currently blooming in many scientific disciplines. Citizen science is also strongly encouraged by the European Commission as a way to democratise science and to bring science-based European policy making closer to the people.

Although some citizen science initiatives already exist in radiation protection, its full potential has currently not yet been exploited. Previous projects such as EAGLE and PREPARE, as well as experience in the aftermath of the Fukushima accident, have highlighted the benefits of enabling and supporting citizens to perform and interpret radiation measurements, both to the scientific community and to the citizens themselves. Furthermore, widespread collections of measurements by citizens during emergency situations could be helpful for decision making and improve the emergency response.

Objectives

The main objectives related to this challenge are:

- Assessing and developing accessible, user-friendly, accurate and reliable tools tuned for citizens to perform their own radiation measurements and compare their measurements with those made both by other citizens and by relevant authorities;
- Providing citizens with clear information that allows them to have a better understanding of radiation, radiation measurements, radiation doses and associated health risks and uncertainties and with clear recommendations, guidelines and instructions that allow them to select the appropriate technology to perform their own radiation measurements, to perform the radiation measurements in a correct way and to interpret the measured values;
- Involving citizens in ongoing research, setting up dedicated citizen science activities and supporting existing citizen science initiatives to ensure their access to the required expertise and background information, and to ensure that the dosimetry is performed as accurately and reliably as possible;
- Bringing together citizens, dosimetry experts, social sciences experts, emergency response experts and authorities in multidisciplinary projects, in order to maximize the impact of citizen science in dosimetry and to increase the understanding and trust between the different stakeholders in radiation protection and emergency response.

Research Line 3.4.1: Evaluation of existing dosimetry tools for citizens and development of new tools

Citizens already have a choice of different technologies to perform their own radiation measurements. Several commercial companies (e.g. Polimaster) and non-profit organisations (e.g. radiation-watch.org) produce relatively cheap and easy-to-use radiation detectors for citizens. Most of these detectors need to be coupled to a smartphone with a dedicated smartphone application. There are also smartphone applications available that allow ionising radiation to be measured using the CMOS sensor of the smartphone camera after covering the lens with black tape (e.g. Gammapix and RadioactivityCounter). Further, there are citizen science networks available with an online platform to collect and visualize radiation measurements by citizens (e.g. Safecast and OpenRadiation).

There is a continuous need for detailed evaluation of existing and new dosimetry tools for citizens. The following questions need to be answered:

- What is the performance (scope, accuracy, reliability, etc.) of these tools?
- In which contexts (e.g. environmental measurements at ground level or on board aircraft, radon, emergency situations, etc.) are these tools useful?
- How can measurements with these tools be used to address scientific questions involving the public and for education purposes?
- How can measurements with these tools contribute to emergency response?
- How user-friendly are these tools?

Answering these questions requires testing of the tools in secondary standard dosimetry laboratories, as well as under more realistic conditions that better match the low dose rate scenarios in which citizens are likely to use them. Benchmarking of the tools should be made by comparing their responses against those of approved and well-calibrated dosemeters and instruments. Input from citizens will be required concerning the user-friendliness of these tools.

One of the most promising recent technologies is the use of the CMOS sensor of smartphone cameras for radiation measurements. It should be investigated how this technique can be further optimized in terms of user-friendliness, accuracy, reliability, calibration and accessibility. There is also

a need for continuous horizon scanning, and to promote and contribute to the development of new technologies that could make future radiation measurements by citizens more accessible, user-friendly and accurate. Very important in any such development of new technologies would be that citizens are actively involved in the process, for instance by consulting panels of citizens, organizing workshops or hackathons, and open-source development. Collaboration with experts in social sciences to determine the best ways for interacting with citizens, and with experts in emergency response to evaluate how measurements by citizens can optimally be integrated into emergency response planning, is also very important to this research line.

Research Line 3.4.2: Set-up an online platform containing information, recommendations and instructions for citizens

Ionizing radiation, radioactivity, radiation measurements, radiation doses and their associated risks and uncertainties are complex topics for non-experts. It is also not straightforward for citizens to find information about good practices to perform their own radiation measurements. There is therefore a strong need for an online platform providing a clear and reliable source of information for citizens, such as:

- Basic information about ionizing radiation, radioactivity, radiation measurements, uncertainties, radiation protection, radiation doses and dose quantities, and the dose-dependent risks associated with radiation;
- An overview of the existing tools that citizens might use to perform their own radiation measurements, with a clear indication of their relative advantages and disadvantages and their inherent limitations;
- Recommendations and clear instructions that citizens can follow in order to perform their own radiation measurements with these tools.

Wherever possible, all the information should be in layman's terms without the use of jargon. Ideally, the information should be available in different European languages such that citizens can consult the website in their mother tongue. The materials on the website should be developed in consultation with social sciences experts and citizens. Furthermore, it will be very important to keep the website up-to-date with information about the latest technology. In order to become the go-to website for advice on radiation measurements for citizens, advertising will be needed, with the precise form of this to be evaluated from a consideration of factors such as target audience and budgetary constraints.

Research Line 3.4.3: Interaction with, and involvement of, citizens and citizen science initiatives

The overall goal of citizen science is to involve citizens in science and to bridge the gap between experts and citizens. Research Line 3.4.3 would explore different ways in which this could best be achieved within the scope of radiation dosimetry. Potential endeavours include:

- Citizens could be involved in ongoing research activities. This involvement might range from informing citizens about the research to actively involving them in the actual research processes, such as by exploring methods in which citizens could participate in data collection and data processing.
- New activities dedicated to citizen science should be considered. For instance, projects could be initiated in which citizens are provided with approved active or passive dosemeters in order to build a detailed environmental dose rate map, or research could be proposed in

which citizens are encouraged to measure cosmic radiation on board aircraft with their smartphones. Such activities would be good for engaging citizens, educating them about radiation and, by focussing on natural radiation, limit the 'scare factor' of ionising radiation. The outcomes of these types of activities would also provide insight into the advantages, disadvantages, possibilities and limitations of radiation measurements by citizens.

- The organization of dedicated outreach activities could be considered, such as online and face-to-face workshops, activities with schools, teach-the-teacher events, etc.
- Proactively reaching out to, and maintaining links with, existing citizen science initiatives related to dosimetry, in order to support their activities and ensure that dosimetry is performed as accurately and reliably as possible.

Where appropriate, such activities should all be developed and advanced in close collaboration with social science experts, as well as other relevant stakeholders.

Citizen science in radiation protection is a multidisciplinary field that needs the involvement of experts in dosimetry, radiation protection, emergency response, social sciences, citizen science, authorities and policy makers. There is a strong need for multidisciplinary projects to further exploit the potential of citizen science in radiation protection.

Vision 4:
Towards integrated personalized dosimetry in medical applications

Introduction

Modern medicine offers a variety of diagnostic methods and tools that include imaging techniques where the diagnosed individual is not exposed to ionising radiation, such as ultrasound and magnetic resonance imaging. In contrast, other methods do involve ionising radiation such as X-ray imaging, CT scans, SPECT/PET and others. In many European countries, for example, the use of CT scans has continuously increased over the last decade and this trend is expected to continue. As a result, even if averaged over the whole population of a certain country, medical exposures are largely responsible for exposure from man-made sources of ionising radiation, and optimization of the received doses is very important.

Additionally, in European countries a considerable fraction of the population will face a cancer diagnosis at a certain time in life, and radiotherapy (using ionising radiation) represents one of the major methods of treatment. Approximately half of all cancer patients will receive external beam radiotherapy at some point in their illness. A large worldwide population of patients is therefore exposed to high target doses in a controlled and well-documented way. The use of therapeutic procedures within nuclear medicine is increasing as well and is attracting worldwide attention. The distribution of dose within the body following radiotherapy (external or internal) varies considerably with many factors: the size and shape of the patient, but also its metabolism, the anatomical location or spread of the target volume, the prescribed dose and the type and energy of radiation (photons, electrons, alphas, hadrons).

The development of dosimetry techniques and the measurement of doses, particularly to radiation-sensitive organs, is an important prerequisite for providing robust dosimetric data for epidemiological studies, ensuring that patients receive optimum doses in both therapy and diagnosis and advancing our understanding of radiation effects on humans. Especially with the current focus towards 'personalised medicine' where patient dosimetry also plays an important role, dosimetry is an important aspect. These goals will need major efforts in the future.

Challenge 4.1: To improve patient and ambient dosimetry in radiotherapy

The optimisation of the dose delivered to the patient in radiotherapy depends on many factors, two of the most important being the normal tissue complication probability (NTCP) and the tumour control probability (TCP). The optimal dose is one which achieves the maximum TCP for the minimum NCTP. As a general estimate, it is usually assumed that the accuracy in dose delivery to the target volume should be $\pm$ 3% ($\pm$ 1 standard deviation). It is self-evident therefore that dosimetry plays a crucial role in achieving this goal and that both dosimetry theory and practice need to keep pace with clinical and technological developments in the field.

The dose at each stage of the treatment chain needs to be monitored, from radiation generation in the treatment machine and associated quality control, to the deposition of dose within the patient. The latter encompasses dose to the target volume and also to outlying critical radiosensitive organs and tissues. There is a need to develop and support the links between nano-, micro-, and macro-dosimetry, and radiobiology and to develop a common conceptual framework. The efficacy and effects of radiotherapy are ultimately tested by clinical trials and epidemiological studies. In support

of this work, the total dose to the organs and tissues from all sources of radiation (therapeutic and diagnostic) is ideally required. In practice, such comprehensive data may not be available and strategies for risk estimation from incomplete dosimetry data are required. More widely, there is a clear need to ensure harmonization and agreement on dosimetry between treatment centres and this requires the development of dosimetry intercomparisons and audit programmes. In addition, ambient dosimetry within, and in the vicinity of, the treatment room is relevant to radiation protection of staff as well as patients.

The elements of this Challenge apply to the developing array of radiation types used in modern radiotherapy, including photons, protons, other particle/ion beams and boron neutron capture therapy (BNCT). There is a need to emphasise dosimetry developments in proton and ion beam treatment techniques, since these pose some of the most challenging dosimetric problems, particularly in mixed radiation fields.

Equally important, dosimetry must be robust in each of the increasing variety of treatment delivery techniques, many of which now implicitly include imaging as a further, if usually small, contribution to the total dose. Examples include Intensity Modulated Radiotherapy (IMRT), tomotherapy, arc therapy, stereotactic radiotherapy, adaptive radiotherapy, Image Guided Radiotherapy (IGRT) and several others. They each have their own particular dosimetric requirements and challenges.

Objectives

- To advance the dosimetry of proton and ion beams.
- To develop dosimetry techniques for quality assurance of radiotherapy, from treatment planning to the delivered dose.
- To develop and support the links between nano-, micro-, and macro-dosimetry, and radiobiology.
- To develop dosimetry in support of radiation effect research and epidemiological studies.

Research Lines

All research lines include the development and application of novel dosemeters, including 2D and 3D detector matrices, detectors for LET and RBE studies (semiconductor micro- and nano-dosimetry, fluorescent nuclear track detectors, 2D/3D dose distributions) and new luminescent materials, techniques and instrumentation.

Research Line 4.1.1: Dosimetry for proton and ion beam radiotherapy

LET dosimetry

Future dosimetry of particle beams should be based on the capabilities to individually determine the position of each primary particle e.g. proton or carbon ion and its LET (energy) for realistic beam intensities. This can be realized using ultra-thin Si or diamond detectors supported by time-of-flight techniques. This technology might be also used for spatially ultra-precise beam delivery systems, for in-phantom dosimetry of protons and heavy ion beams and for 2-D dosimetry for mini- and micro-beam radiotherapy. This should include ion beam dosimetry including radiation quality (LET) specification for treatment planning.

Dosimetry in high dose rate scanning beams and ultra-high dose rates in FLASH therapy and laser-induced proton beams

The short ultra-high dose irradiation (FLASH) was shown to be a promising modality for cancer treatment, reducing damage of normal tissue after the exposure. Dosimetry of such beam is

challenging. The R&D should result in development of reliable active dosemeters dedicated to clinical environment.

Dosimetry in spot-scanning arc therapy (SPArc)

Spot Scanning Proton Arc therapy offers low entrance doses and the highest possible dose conformity in the target. The arcing geometry creates dosimetry challenges when the acceptable limits to delivered dose uncertainty should be maintained. The development of a dedicated active phantom is required to enable acceptable Treatment Plan verification.

Application of detectors and instruments in pulsed neutron fields

Modern proton therapy accelerators such as synchrocyclotrons or laser-induced proton beams produce high intensity, micro- or nano-second pulses, which complicates dosimetry with active instruments. New detectors and associated electronics should be developed.

Improved secondary neutron dosimetry, mixed field dosimetry within the treatment room and inside the patient

Current dosimetric techniques are not sufficiently developed to enable full discrimination between neutron and photon components of the secondary irradiation fields. New methods should be developed which properly measure these components at the therapeutic dose-rates.

Research Line 4.1.2: Dosimetry during treatment and for quality assurance of the treatment process, including inter-centre audit programmes

On-line validation of dosimetry during treatment and to support Quality Control (QC) and in vivo dosimetry (IVD)

This requires the development of dosimetric techniques for checks at all stages of the radiotherapy dosimetry chain i.e. beam production, spatial and temporal dose delivery, in vivo dosimetry and real-time organ dose estimates.

Small field and edge-of-field dosimetry

This involves non-equilibrium dosimetry and the dosimetry of small treatment volumes. Comparison of small field codes of practice and inter-centre applications is required together with determination of the performance characteristics of new detectors in small fields in both photon and ion radiotherapy.

Phantom development

Validation of treatment planning system algorithms and Monte Carlo calculations requires benchmark measurements for selected simulated treatments, for which realistic anthropomorphic phantoms are required. The currently available phantoms will need to be developed further, particularly for treatments carrying a higher risk of late effects, e.g. paediatric phantoms with varying height, weight & fat distribution. Quality Assurance in clinical dosimetry should be supported by cheap, patient specific 3-D printed dosimetric phantoms for dosimetric verifications e.g. specific treatment plans.

Pan-European harmonisation of dose calculations, measurements, intercomparison protocols and audits

It is axiomatic that radiotherapy dosimetry should be harmonised throughout Europe in order to ensure consistent standards of clinical care. This will require the development of inter-centre audit

and intercomparison programmes for emerging treatments (e.g. proton and ion beam radiotherapy) to complement existing programmes for photon radiotherapy.

Dosimetry in magnetic fields

With the development of clinical MRI-linac combinations, work on the performance of detectors in a magnetic field has shown changes to the effective point of measurement of an ionisation chamber and asymmetric dose distributions. Some magnetic field-induced effects are detector dependent. Further work on the effect of magnetic fields in both reference and relative radiotherapy dosimetry is indicated.

Research Line 4.1.3: Dosimetry to develop and support the links between nano-, micro-, and macro-dosimetry and radiobiology

Development and evaluation of models incorporating the radiobiogical aspects into radiotherapy

It is not possible in practice to simulate all radiobiological processes during radiotherapy treatment. Models and dosimetry techniques should be developed to support micro-/nano-dosimetry as a link between physics and radiobiology.

Edge-of-field and high dose gradient dosimetry (i.e. high spatial resolution 3-D and 4-D dosimetry)

Developments in this field (including 2-D dosimetry) are required to enable dosimetry in small tissue and organ volumes (organ sub-volumes), in support of developments in microdosimetry, e.g. in the development of microdosimetric models for incorporated particles.

Research Line 4.1.4: Dosimetry in support of radiation effect research and epidemiological studies

The total dose to the radiotherapy patient

For more accurate input to epidemiological studies, it is necessary to develop and harmonize dosimetry techniques for the measurement and estimation of the total dose to the target and critical organs from all radiation sources (therapeutic and diagnostic) to patients receiving radiotherapy. A metrological framework for dose additivity from different radiation sources needs to be developed. Sources include external beam photon and hadron radiotherapy, brachytherapy, CT, PET and on-board imaging using X-rays. The "total dose" implies that in principle, the dose should be capable of being estimated at all points within the patient. Validation of algorithms for achieving this goal requires the development and harmonisation of techniques for out-of-field dosimetry in simulated treatments using anthropomorphic phantoms, for all treatment modalities and radiation types.

Dose-Risk model evaluation

Dosimetry techniques should be designed to support the development and validation of models of induced cancer and non-cancer (eye, cardiovascular) radiation effects for patients and to provide experimental dosimetric support for the development and validation of Treatment Planning System dose algorithms.

Effective Dose concepts in radiotherapy

For practical clinical purposes, it may be necessary to develop concepts similar to Effective Dose, but modified for radiotherapy to include factors relevant to the radiation protection of radiotherapy patients, e.g. broad dose ranges of irradiated healthy tissue and complex secondary radiation spectra.

Challenge 4.2: Improving patient dosimetry in nuclear medicine

In nuclear medicine, 90% of the procedures are from diagnostic nature. To date, the estimated radiation-absorbed dose to organs and tissues in patients undergoing diagnostic examinations is derived via calculations based on reference models of the human body and the biokinetic behaviour of the radiopharmaceutical. Different software packages (OLINDA/EXM, IDAC-Dose) are available. In 2017, an updated version of IDAC-Dose 2.1 was released, created for diagnostic nuclear medicine reference dosimetry based on standardised anatomical and biokinetic models for patients. Moreover, there are other initiatives, such as the OpenDose collaboration aiming at providing an open database of robust reference S-values generated from different Monte Carlo (MC) software, through an international collaboration. Further improving patient dosimetry in diagnostic nuclear medicine will require a patient-specific quantitative imaging.

There is an increase in the development and use of radiopharmaceuticals (RPs) in Europe for treating cancer in the last few years and the number of molecular radiotherapy (MRT) clinical trials is expected to continue to rise in the future. Although an accurate knowledge of the radiation absorbed dose to critical tissues would provide a more effective targeted use of MRT, most treatments still follow the historical practice of administering a nominal activity of the RP (the "one size fits all" approach). However, it is essential that this problem is addressed, as there is an important focus to move towards personalised medical treatment. One of the main reasons for a reluctance to perform individual patient dosimetry is that the process is complicated and there are currently no standard methods for calibrating or implementing MRT dosimetry in the clinic.

RP dosimetry is a multi-step process. The key steps in obtaining accurate dose estimates are: (1) measurement of the activity to be administered, (2) quantitative assessment of the spatial and temporal activity distribution in cells/tissues and (3) calculation of the deposited energy from the activity distribution in the cells/tissues of interest.

In case of high-LET radiation, the characteristics that make it attractive for targeted therapy also render a number of challenges for the dosimetry of these RPs. The knowledge about the non-uniform distribution of the radionuclides (e.g. due to heterogeneous target expression among (cancer) cells and the diversity of structures in the actual tissues of interest) in combination with the short path length and high-LET of alpha and Auger radiation is important for accurate dosimetry purposes.

The research lines described below aim to contribute to successfully determine dose-response relationships for all existing and emerging radiopharmaceuticals and to the final goal of providing patient-specific dosimetry to allow individual treatment strategies.

Objectives

- To improve the accuracy of activity measurements for gamma, beta and alpha-emitting RPs both in diagnostic and therapeutic procedures.
- To optimise and harmonise quantitative multimodality pre-clinical and/or clinical imaging for gamma, beta and alpha-emitting RPs.
- To gain insights on the validity of available pharmacokinetic models of emerging treatments on individual patient basis.
- To gain insight on the heterogeneity of the deposited energy on micro- and nano-scale in case of high-LET radiation.
- To implement accurate clinical dosimetry methods and determination of uncertainties in the chain from measured activity to calculated absorbed doses.

- To investigate the dose-effect relationships for internal emitters both on cell- and organ-level for beta, alpha and Auger emitting RPs.

Research Line 4.2.1: Internal dosimetry within pre-clinical development and evaluation of RPs emitting alpha, beta and Auger radiation

Determination of heterogeneous activity distribution on cellular level and microdosimetry on in vitro scale

In the development phase of new RPs, they are first tested in vitro on specific cell populations. Evaluating the efficacy of an RP intended for therapeutic use, entails the assessment of biological effects. In literature, however, biological effects are mainly related to the added activity, which is often not a good predictor of biological response. Research is also ongoing to study the influence of the specific part of the cell that is being targeted (e.g. nucleus or cell membrane). In most of these studies, there is no accurate knowledge on the dose given to the cellular targets of interest leading, ultimately, only to rough correlations to biological end points.

On the one hand, there is the need to develop appropriate cellular dosimetry models, implementing realistic cellular features and accurate physics transportation. Whilst on the other hand, radiobiological experiments need to be performed, in order to assess the intracellular activity distribution and relevant biological endpoints. In recent years, many studies investigated biophysical models to predict biological effects based on dosimetric quantities, but only a few of these studies used micro-dosimetric analyses. As targeted alpha therapy (TAT) is gaining a lot of interest, there is an important need to further elaborate dosimetry models that are more representative for the realistic TAT applications. A non-uniform distribution of the radionuclides (e.g. due to heterogeneous target expression among cells) in combination with the short path length and high-LET of alpha (and Auger) radiation results in a non-uniform dose distribution even at cellular level.

Imaging heterogeneous activity distribution on organ level and small-scale (sub-organ) dosimetry on in vivo scale

Accurate dose estimates in pre-clinical models (like mice) have become indispensable to support and explain the results of histological analysis of targeted and untargeted tissues. In this respect, there is still a lot of improvement possible regarding the pre-clinical internal dosimetry of radiolabeled pharmaceuticals. Detailed pre-clinical computational dosimetry is therefore one of the cornerstones of strategies in future clinical trials. General internal dosimetry on organ- or single region-level, following the MIRD schema is based on the assumption of a uniform distribution of radioactivity across the entire organ. The average absorbed dose to the entire organ predicted by such models can misrepresent local regional doses to specific substructures. Accurate dosimetry on sub-organ level will also have to tackle the issue of accurate quantitative imaging at different time intervals at sub-organ level in vivo or ex vivo and can be complemented with non-imaging methods, such as activity determination in for example blood samples. Currently, there is a lack of standardised protocols for pre-clinical testing and quantitative imaging. Additionally, accurate dosimetry requires the development of appropriate and new computational models of organs/tissues of interest, using imaging modalities (eg. µCT and µMRI) with appropriate image contrast and spatial resolution to distinguish between the different substructures within the organ/tissue of interest.

Biokinetics of daughter molecules

In the case of using RPs labelled with alpha emitters, the recoil energy of recoiling daughters is so high that the chemical bonds of the daughter molecule with the targeting vehicle will be lost. The released daughter molecule can be retained inside the tumour, when internalized inside the cell, which will enhance the cytotoxic effect, but it can as well diffuse or be transported to various organs where it can accumulate and cause radiotoxicity of healthy organs. Moreover, radioactive progenies could also be administered to the patient as impurities.

In such cases, it is necessary to determine the biokinetics of the progenies administered as impurities which depend on their chemical form as well as the biokinetics of the progenies produced within the body which are expected to be different from the biokinetics of the parent nuclide. Imaging of the parent nuclide is usually based on imaging the gamma-emitting daughter molecules, but the difference in biokinetics is an important concern hampering accurate dosimetry.

Systematic study of dose-effect relationships for internal emitters (beta & alpha)

Tumour and normal tissues dose-responses for radionuclide therapy have not been studied as extensively as within external beam radiotherapy, the latter one generally described by a linear-quadratic (LQ) model. However, the DNA repair kinetics within internal radiotherapy, are totally different compared to external beam radiotherapy. This has been taken into account by an additional factor G added to the beta term in the LQ equation in case of radionuclide therapy. Generally, quantities used in external beam radiotherapy, such as biologically effective dose (BED – to analyse effect of dose rate), equivalent uniform dose (EUD – to analyse dose heterogeneity) and isoeffective dose are recommended to be applied for radionuclide therapy as well. The justification and verification of applying these quantities in radionuclide therapy need experimental investigations and theoretical simulations.

Moreover, taking into account the stochastic local energy deposition and heterogeneity of absorbed dose distribution, specifically for alpha and Auger emitters, the radiobiological effects, e.g. survival fraction and RBE needs to be related to micro-dosimetric quantities.

As the relationship between administered activity, the absorbed dose and biological effects are not yet well understood, more work is needed on the determination of dose-response relationships within radionuclide therapy. This requires both good biology and dosimetry research and will provide fundamental data that might help treatment planning in NM.

Research Line 4.2.2: Implementation of internal dosimetry in clinical MRT

Dosimetry uncertainties in clinical practice

The European Association of Nuclear Medicine (EANM) has issued guidelines for absorbed dose uncertainty assessment in nuclear medicine. These are based on the ISO Guide to the Expression of Uncertainty in Measurement (GUM), which implemented the law of propagation of uncertainty. This EANM guidance has applied the uncertainty analysis on the MIRD formalism schema for internal dose calculations in nuclear medicine. From the calibration of the imaging system to the patient measurement and dose calculation, a range of uncertainties must be evaluated through specific protocols. These protocols should be further tested, refined and benchmarked. For example, given a set of clinical data, an intercomparison of uncertainty assessment could be carried out with the aim of optimizing and harmonizing practices. However, the EANM guidance does not provide a guidance how to identify the influential parameters in the dose calculation chain. Development of a global

sensitivity analysis (GSA) approach is needed to assess the crucial parameters influencing the uncertainties and then to work on improvement of protocols. Furthermore, development of a Bayesian network approach is needed to incorporate a priori knowledge taking into account ill-defined parameters. These GSA and Bayesian approaches can be applied for assessing the dose uncertainty to patients in nuclear medicine and can be used as complementary approaches to the EANM approach.

Quantitative imaging of radiopharmaceuticals

Patient tailored dose assessment certainly needs detailed knowledge of patient specific biokinetics of RPs. This biokinetic information can be improved by quantitative imaging, namely increasing the number of pre-therapeutic imaging examinations, but also by better calibration protocols. For that purpose, development of new, more realistic calibration phantoms with varying shape and size using 3D printing tools makes it possible to obtain more realistic calibration factors. It is also possible to design phantoms incorporating different levels of activity and to take into account the heterogeneity of activity distribution in organs. A challenge will be to develop or characterize printing material for different kind of tissues, such as representing lung and bone tissue. With the upcoming targeted alpha therapy, quantitative imaging becomes even more challenging due to the low radioactivity levels administered to the patient and the low-emission probabilities of photon energies used for imaging. Research is needed to set-up appropriate protocols for each specific radionuclide and to investigate the challenge in relating macroscopically determined image-based activity to small-scale absorbed doses to sub-organ structures, in particular for short-range particles.

Validation of internal computational dosimetry

Internal dosimetry within nuclear medicine, entirely relates to the calculation of organ doses, based on analytical models, dose kernels or Monte Carlo calculations. To improve the accuracy in the calculation of dose from activity-time distributions the comparison between the different dosimetry approaches, as well as the experimental validation of the computational approaches is needed. The use of 2D and 3D experimental techniques, such as for example gel and film dosimetry in combination with anthropomorphic phantoms is worthwhile investigating.

Research Line 4.2.3: Accuracy of radionuclide activity measurements with radionuclide calibrators

Radionuclide calibrators are used in nuclear medicine to determine the amount of activity in an RP by measuring the current produced through ionisation of the pressurised gas inside the chamber. Their response not only depends on the characteristic emissions of the particular radionuclide, but also on geometrical characteristics of the chamber and sample. The calibration factors are determined in the factory, but several published intercomparison exercises of radionuclide calibrators demonstrated that there is significant room for improvement in the activity measurements of clinical radionuclides. Traceability established by a systematic calibration of the radionuclide calibrator for each relevant nuclide are recommended to comply with the growing need for quantitative accuracy in nuclear medicine and the upcoming more exotic radio-isotopes with more complex decay schemes, used within radionuclide therapy. Moreover, the uncertainty in activity measurements of clinical radioisotopes needs to be assessed, which is caused by source geometry effects. To improve the traceability between primary standards and the accuracy of activities administered to patients and used in pre-clinical research based on radionuclide calibrator measurements, the organisation of intercomparison exercises of activity measurement capabilities in pre-clinical centres and hospitals could be performed.

Research Line 4.2.4: Optimization of patient dose in diagnostic nuclear medicine

Following the position statement of SNMMI (Society of Nuclear Medicine and Molecular Imaging) on dose optimization in nuclear medicine and molecular imaging, "the right test with the right dose should be given to the right patient at the right time". The patient dose to diagnostic radiopharmaceuticals is estimated according to the MIRD/ICRP formalism schema for internal dose calculations by use of the biokinetic data and S-values for reference persons.

However, the biokinetic data of many radiopharmaceuticals commonly used are obsolete, and the S-values are calculated by the stylized computational phantoms. The need of updating the biokinetic data remains as a challenge.

Further, the use of human voxel phantoms and, in the future, the boundary representation phantoms for calculation of S-values is a computational challenge.

With the advanced technical development of image acquisition by PET and SPECT, new precise biokinetic data, especially the rare data for children and adolescents at optimal time points can be acquired and can be used for dose optimization in paediatric nuclear medicine. This challenge will continue because of the growing number of PET procedures in children and it can ensure the reasonable balance between the imagine quality and the radiation risk to the children.

In addition, physiologically based compartmental models may be developed in comparison to the fitting and integration procedures for dose quantification and further risk estimation for age-independent reference persons. An appropriate urinary excretion model of radiopharmaceuticals should be optimally used because a fixed bladder voiding interval has critical impact on the absorbed dose to the bladder wall and proximate organs.

Challenge 4.3: Establishment of reliable patient dosimetry in CT and interventional radiology examinations

Interventional radiology is a fast-growing field of medicine offering minimally invasive treatments where improvement of technology and skills had led to the treatment of more complex diseases. CT is used for diagnosis purposes as well as for treatment planning and patient positioning prior to treatment in radiotherapy. Interventional radiology (IR) and interventional cardiology (IC) are radiation modalities where there are strong dose gradients and doses high enough to potentially cause tissue effects especially if the use of radiation is non-optimized. Repeated CTs also potentially give rise to stochastic effects and in very rare instances tissue effects.

To correctly estimate the dose and the resulting radiation risks, an improved system of dose calculation including dose distributions within organs is needed based on actual patient anatomy for adult and paediatric patients. Currently available generic conversion coefficients from measured quantity to patient (organ) dose cannot be used to accurately determine patient dose. Hence computational methods must be developed based e.g. on predetermined phantom libraries or real patient anatomy. A correct dose estimation would enable improved use of diagnostic reference levels (DRLs), achievable dose levels (ADLs) and skin dose alert (trigger) levels for optimization of patient doses, improved accuracy of skin and other organ doses, and improved accuracy of population dose estimation.

Objectives

- Tools for online and offline skin dose mapping for IR/IC.
- Reliable determination of patient organ doses in IR/IC.

- Efficient use of dose indicators as well as DICOM- RDSR information.
- Harmonization of nomenclature in IR/IC.
- Setting up ADL and DRL.
- Patient-specific dose estimates for CT combined with big data, increased computing power and availability of comprehensive patient data to allow personalized medicine.
- Reconsideration of approaches to image quality assessment and dose optimization.

Research Line 4.3.1: Skin and organ doses in interventional radiology and cardiology

To prevent skin injuries in interventional radiology and cardiology skin dose mapping software are needed to show a real-time dose distribution at patient's skin. Software-based dose mapping tools may provide a more user-friendly and accurate setting of alert levels than presently available, provided that they are well validated and benchmarked against measurements. At the moment independent, scientific validation of software is largely missing.

In addition, suitable software tools are not available in older equipment, and might not even become available in all new equipment. Therefore, the possibility to evaluate the maximum skin dose in real time by other means is of interest. Other possibilities are readily available dose indicators, DICOM RDSR (Radiation Dose Structured Report) information, Monte Carlo based organ dose calculations, and measurements (Gafchromic© films, thermoluminescent dosemeters, semiconductor detectors, …). Nevertheless, measurements are time consuming and expensive and cannot be performed on a regular basis. Research is needed to develop reliable real-time skin dose assessment methods.

Diagnostic reference levels in IR and IC are being set nationally in many countries. However, there is still a need to harmonize nomenclature and investigate the feasibility of trigger levels for maximum skin dose during fluoroscopically guided interventional procedures. The use of online and offline software for dose recording will provide help in setting up ADLs and DRLs.

Indeed, about Monte Carlo simulations employed to determine possible skin injuries during interventional practices, a better description of the skin should be attempted. As a matter of fact, generally, in voxel models the dimensions of the single voxel element is larger than the whole skin thickness (about 1 mm) and the radiation effects on its more sensitive layer (0.07 mm from its external surface) cannot be easily reproduced.

Recently, evidence has been accumulated on radiation-induced effects to cardiovascular system. Especially in IC, the heart can receive a substantial radiation dose and the knowledge of this exposure is needed to prevent adverse effects to the patient. Ideally, these organ dose assessments should be implemented in any dose mapping software. Moreover, mostly a patient is exposed to more than one modality. Therefore obtaining organ doses will be the first step to evaluate the overall exposure of a patient (by all modalities) and therefore its corresponding risk.

Research Line 4.3.2: Patient-specific dose estimates in CT imaging

In CT imaging, a shift from scanner beam dosimetry to patient-specific dose estimates is foreseen. For those estimates (near) real-time solutions to computationally assess and store the patient's organ doses and dose distributions in anatomically realistic settings must be developed and standardized so that the data is available across systems.

Comprehensive phantom libraries are needed to complete the computational phantom outside the imaged region.

Rigorously tested methods to match the image data with the phantom must be developed.

Uncertainty estimates for the computed organ doses should be considered.

In addition, the advances in detector technology (e.g. single-photon counting, spectral acquisition with pixelated detectors, new detector materials) will produce different information than previously encountered. More refined tube current modulation techniques are being introduced, too. To fully exploit this, approaches to image quality assessment and dose optimization together with personalized dosimetry must be reconsidered in cooperation with medical, dosimetry and metrology experts.

Research Line 4.3.3: Multidisciplinary data collection for personalized dosimetry

Big data, deep learning, increased computational power and availability of comprehensive patient imaging data steer toward personalized dosimetry and consideration for individual radiation sensitivity. New approaches are then needed to optimize the imaging protocols on an individual patient basis and to assess the reliability and relevance of the data in a multidisciplinary environment.

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

Introduction

Much research and technical development in radiation protection dosimetry for workers and the public has been carried out, to a large extent within projects funded by the EC. The results of these developments have been transferred to operational radiation protection, including guidelines and technical recommendations. Despite these efforts, a couple of areas exist in which the status is unsatisfactory, necessitating further research. Among others, the following challenges are of importance.

In case of internal contamination it is well known that DTPA (see also Challenge 3.1) increases the excretion of actinides but the dose reduction due to the therapy is currently based on default assumptions that should be improved. Another challenge consists of the reconstruction of the life-long dose estimate for cohorts of workers for whom contamination information is scarce. Models and methods need to be developed to be able to provide reliable dose estimates for both situations.

Most workers are still currently monitored with passive dosemeters. But on-line personal dosimetry is emerging. The mid- or long-term challenge is to allow for a reliable and accurate monitoring of the workers in real time regardless of the protection methods used, and to provide input for the demonstration of compliance to dose limits and the optimal application of the protection principle.

Neutron dosimetry remains a problem, and no good dosemeters are available yet. So improvement in dosimetric characteristics (energy, angular dependence) and field characterisation is needed.

In the field of environmental monitoring one of the challenge is to support the implementation of the EURATOM directive on radon exposure assessment that implies a shift in the focus from the radon activity concentration measurements towards the dose estimation.

In the field of space dosimetry the exposure field must be characterized. For that purpose, space spectrometers should be developed, neutron measurements improved and solar particle events better predicted.

Challenge 5.1: To improve biokinetic and dosimetric models for internal emitters

Internal doses can occur when workers handle unsealed radionuclides, e.g. in the nuclear industry, in the biomedical sector and research, and in nuclear medicine departments. The general public can also incur internal doses if they are exposed to naturally occurring radionuclides such as radon and its progeny, or affected by deliberate or accidental releases of radionuclides. The potential health risk due to incorporated radionuclides is indicated by the assessed committed effective dose. This dose cannot be directly measured or estimated with personal dosemeters. It is thus assessed through measurements of radionuclide activities and the applications of models describing the metabolic behaviour of the contaminants inside the body. The quantification of internal exposures are supported aby in vivo monitoring (measurements of radiation emitted from the body by incorporated radionuclides), in vitro monitoring (measurements of radionuclides in the excreta) or work place monitoring (measurements of radionuclides in air samples). Biokinetic and dosimetric models describe the spatial and temporal distribution of radionuclides in the body and their excretion, and the absorption of energy emitted following their decay. The application of the models

makes it possible to deduce the incorporated activity (intake) from measurements and hence assess the dose. Typically, biokinetic models depend on the radionuclide, the route of intake, the chemical form of the radionuclide, the age of the subject, etc. Dosimetric models in turn depend on the emission spectrum of the radionuclide and on the human anatomy, which is described by reference human models (e.g. developed by ICRP).

The required improvements concern the two main pillars of internal dosimetry: measurements of the incorporated radionuclides and modelling. A specific challenge concerns dose assessment for epidemiological studies and refinement of uncertainty estimates.

Objectives

- *Improvement of in vivo measurements*
  There are still some cases of internal contamination where in vivo measurement techniques could be improved by:
  - Development of specific phantoms.
  - Further development of numerical calibration techniques (e.g. Monte Carlo Methods).
    Development of in situ monitoring approaches for internal dose assessment.

- *Improvement of biokinetic and dosimetric models*
  Modelling the effect of decorporation agents such as DTPA is of interest since there is still no consensus on the method of dose assessment in these cases and the determination of exact dose reduction factors. Any new decorporation models will be also useful for the planning and evaluation of therapies and the development of further decorporation agents.

  The uncertainty of internal doses is largely due to the application of models and other assumptions on the intake and dose assessment (e.g. intake scenario, physic-chemical properties of the contaminants, time of intake, ...). The contribution of the different parts of the assessment to the uncertainty must be better understood, to be able to provide realistic dose uncertainties and to develop methods to reduce these uncertainties.

  The dose due to short-range emitters is heterogeneous and considering their homogeneous distribution within the human body limits the reliability of any deduced dose effect relationships. It is thus of interest to focus on microscopic biokinetics and micro-dosimetry to describe the dose distribution down to the organ levels.

- *Dose and uncertainty assessment for epidemiology*
  Even if there are still some challenges in dose assessment following an internal contamination, when life-long personalized dose assessment has to be done for a cohort of workers the challenges are even bigger. In this field the efforts should concentrate on:
  - Establishing a consensus on the approach to life-long dose assessment.
  - Developing software for life-long dose assessment applicable to various cohorts with different input data available.
  - Establishing a validated uncertainty budget and trying to reduce the overall uncertainties associated with the dose input to epidemiological studies.

Research line 5.1.1: Improvement of in vivo measurement

In vivo measurement systems are calibrated with reference radiation sources implemented in physical models representing the human body or a part of it (phantoms). The distribution of activity within phantoms is in most cases homogeneous and limited to one or two organs. Calibration phantoms mimic the human body but are rough representations, lacking realism and being restricted to only few geometries. Calibration with such phantoms does not induce large uncertainties for homogeneously distributed radionuclides, but there are some specific situations where more realistic phantoms could considerably improve the calibration accuracy. As recent work has shown, 3D printing technology facilitates the production of more realistic calibration phantoms and should be explored further. Manufactured phantoms could be distributed easily and would help in harmonizing measurements.

An alternative to physical calibration is numerical calibration employing mathematical models of the source/detector geometry and Monte Carlo methods to estimate detector efficiency. This technique has proved to be reliable, but it is installation-specific while physical phantoms can be employed in various installations. Efforts to develop physical and numerical calibration should be pursued jointly since both techniques offer complementary advantages. Validation processes are an important matter that should always be considered in these new approaches for in vivo monitoring e.g. by organizing intercomparisons.

Workers exposed to short-lived radionuclides, such as in nuclear medicine departments, need to be monitored very frequently (e.g. every two weeks, weekly or daily) depending on the radionuclide. Due to delay in urine collection and analysis, in vitro bioassay is not an adequate technique and in vivo monitoring cannot be performed at the requested dates since it requires travel of the staff to an offsite monitoring service. The potential solution to this issue is that workers should be monitored in situ using monitoring equipment (e.g. contamination monitors, dose rate meters or even gamma cameras) available at the site/hospital. This allows to characterize the internal exposure at the workplace. The instruments need to be characterized and qualified for this task. A set of reference conversion factors to check, whether a given investigation threshold is exceeded, needs to be developed.

Development of specific phantoms

Lung monitoring is mainly performed for workers exposed to actinides that emit low-energy gamma rays strongly attenuated by the chest wall between the lung and the detector. The attenuation is greatly enhanced by the breast of female workers but no specific calibration phantom exists for women. Breast phantoms that can be fitted to existing calibration phantoms should be developed and distributed in monitoring labs so that calibration can be corrected for female. Recommendations for better monitoring of female workers should be issued based on experience in using these phantoms.

Phantoms enabling the in vivo monitoring of bone seeking radionuclides are very rare and no consensus exists as to their shape. Development of a reference head phantom is a high priority since it is the best location to measure such radionuclides. The research should pursue the following challenges: design and manufacture of a reference phantom based on sound anthropometric data. A bone equivalent material, either 3D printed or moulded, should be developed and tested. The inclusion of a realistic activity distribution is also a technical challenge for the development of such phantoms.

Development of phantoms enabling heterogeneous activity distribution, either distributed in different organs, or distributed inside a single organ is also of interest, since it makes it possible to take into account crossfire contributions of different organs to the detector counts.

Finally, protocols for wound monitoring should be harmonized. For that purpose a devoted simple phantom should be developed, enabling the insertion of radionuclides at different depth under tissue equivalent material. More importantly, a protocol for enabling both depth and activity assessment should be developed, tested and approved on a consensus basis.

Numerical calibration

Several computer libraries of whole body phantoms have been developed but they have rarely been used for systematic studies of the factors affecting in vivo calibration. Such studies do not provide installation-specific calibration factors but explore more general trends so these installations would be able to derive correction factors for specific cases. For a given radionuclide a systematic study should consider (i) the activity distribution in the body at several time intervals after intake (ii) variations in body shape, to obtain calibration factors that can be compared with reference physical calibration factors.

A possible further refinement, using the new generation of deformable phantoms (in MESH or NURBS formats), would consist of varying the monitoring position (sitting, recumbent, reclining in a dedicated monitoring chair) to see which positions require less correction to the reference calibration.

In situ monitoring for short-lived radionuclides (e.g. handled by nuclear medicine staff, comforters, carers and relatives)

In the handling of unsealed short-lived radionuclides, the application of established monitoring techniques is often not feasible. These situations are encountered mainly in nuclear medicine departments, but also in irradiation facilities, where these nuclides might occur as by-products of other processes.

For these nuclides, more frequent in situ monitoring is required to ensure the adequate protection of the exposed persons. Several technical problems must be solved to develop in situ monitoring. Firstly, a low-cost and reliable device would need to be developed (including the detector, a suitable mounting, processing software and user interface). Cost is an important factor: if the proposed solution is considerably more expensive than the existing ones, staff will probably just continue to be monitored as before to save money. Secondly, quality assurance tests and re-calibration should be made as easy as possible to be carried out by users with a limited experience. Thirdly, processing of results should be automated as far as possible, with no need for complex spectrum analysis. Finally, a robust and secure system for archiving results, ultimately in a remote central archive, should be developed. A challenge is to assess the doses to the comforter and carers, who may be exposed to the patients injected with radiopharmaceuticals, for example I-131.

Research line 5.1.2: Improvement of biokinetic and dosimetric models

Biokinetic and dosimetric models can still be improved to describe the effect of perturbations such as decorporation therapies. There has been considerable theoretical and experimental work on this subject but no consensus on therapy protocols, monitoring and the dose assessment, has so far emerged. The most important issue, from the radiation protection side, is monitoring and the dose

assessment following decorporation because reference publications currently contain no information or guidance on this.

Uncertainties in the assessment of internal doses are large, but still not well quantified. Here systematic studies will be required to understand the sources of the uncertainties and to quantify and reduce them for the contributions and the total dose.

The current system of radiological protection relies on the hypothesis of a homogeneous activity distribution at the tissue level. Assessed doses from penetrating radiation emitters such as gamma emitters are relatively insensitive to these assumptions. However, for short-range non-penetrating radiation emitters (alpha-, beta-, Auger emitters) any heterogeneity of activity distribution within tissues would directly translate into heterogeneity in doses. Investigating any direct mechanistic relationship between dose and effects then becomes challenging, or even irrelevant, since the calculated dose does not represent the true biophysical reality. Moreover, there is limited evidence that some radionuclides, like those of uranium or actinides, do have a tendency to concentrate in specific cells.

Decorporation

Following accidental incorporation of actinides DTPA can be administered to accelerate the removal of the radionuclides from the body. The most important issue, from the radiation protection point of view, is the individual monitoring and the interpretation of monitoring data for reliable dose assessments following decorporation. Several biokinetic models have been developed to predict the interaction of DTPA with actinides and, obviously, they all fit the available data (mostly excretion) used to build the model. However, as these models have generally been developed for specific cases their use outside of those cases is open to question. Moreover, due to an overall lack of relevant human data for most organs, there is little information with which to demonstrate the wider relevance of any of these models, and consequently the reliability of dose calculations based on them.

An experimental program that would produce data to enable the identification of a good general model is needed. A better understanding of the action of DTPA in vivo needs to be acquired to provide a physiologically realistic model of decorporation therapy. Dedicated animal experiments studying the spatial and temporal distribution of DTPA in the extracellular fluids need to be planned and conducted. Biokinetic models for the actinides also need to be improved to take into account the physiological basis of their observed behaviour in vivo. Again, dedicated animal experiments will be required. Modern techniques including laser ablation and micro-XRF-imaging would be able to provide information on the tissue/cellular level about the physico-chemical characteristics of the actinide and the DTPA from these experiments. This knowledge can also be useful in the design and development of novel and more efficient (e.g. targeted) decorporation agents or dosimetry models for targeted radionuclide therapy pharmaceuticals and vice versa. Guidelines for monitoring of real cases, which would also provide data useful for biokinetic model development and validation, shall be developed to increase the database available for these purposes.

Uncertainty budget

Internal dose assessment depends on many parameters, some are purely metrological but most are default parameters of the biokinetic and dosimetric models.

The uncertainties of measurement and uncertainties of data-based biokinetic models and human phantoms should be systematically quantified and harmonized, and integrated into the uncertainty

calculation guidance. A global sensitivity analysis should be performed to identify the influential parameters in the complete chain of internal dosimetry calculations. By doing so, uncertainties of components in the measurement and dose calculation can be further specifically investigated, in order to reduce the general uncertainty in the estimated dose.

Microscopic biokinetics and micro-dosimetry

The first step would consist in developing and validating experimental techniques that indeed enable the localization and quantification of radionuclides at the cellular, or at least multi-cellular scale. Promising techniques are laser ablation, and SIMS and SR-XRF, coupled with imaging techniques also offer a longer term prospect. Such techniques would need to be applied to autopsy samples of contaminated animals since micro-distribution should be studied under normal conditions of radionuclides' transport to cells, i.e. in vitro experiments would be irrelevant. Tissue Banks with human tissues, such as the United States National Human Radiobiology Tissue Repository (NHRTR) maintained at USTUR (US Transuranium and Uranium Registries), could also be utilized in these studies. Once the radionuclide distribution at the multi-cellular scale has been obtained, it would be relatively easy to produce dose maps revealing the heterogeneity of doses among cells. It might be sufficient to consider doses at cell level, although application of micro-dosimetric concepts like the one hit distribution might also be useful to quantify the number of events affecting the cells.

Another challenge in micro-dosimetry of internal emitters is studying the microscopic biokinetics at several time points, to study the migration of radionuclides between cells from the extra-cellular space to the cells (and vice-versa).

This work should be carried out with biologists so that the localization of radionuclides or dose can be correlated with biological endpoints.

Research line 5.1.3: Dose and uncertainty assessment for epidemiology studies in workers

Dose assessment for cohorts of workers brings several specific challenges. Firstly, dose must be assessed for thousands, tens of thousands or even more workers. Secondly, life-long dose reconstruction for periods with varying exposure conditions, varying monitoring data (inter or intra cohorts) is required. Thirdly, the information needed (type of compounds, value of the detection limits, exposure conditions) are often lacking. Fourthly, a significant percentage of measurements are usually below detection limits. Whatever the quality of the data for each worker may have, hundreds or even thousands of pieces of information are associated with them (measurement dates, results of measurements, exposure type/route/time, and exposure compound types).

Harmonized Protocols for life-long dose assessment

Currently different methods are used to reconstruct life-long doses. One of the most significant issues is the processing of measurement results below the detection limits or 'censored data'. If set to zero, they will lead to dose underestimates, but set at the detection limit might lead to overestimates. A thorough analysis is needed since much of the available data falls within this category. Expert analysis and sensitivity studies need to be performed systematically, eventually on artificial data sets, to select the best option, and to quantify the impact of these options on dose uncertainty.

Software development for life-long dose assessment

While there are few computer codes which can calculate internal doses from measurement data, none allows handling such large cohort data sets. Software designed for the use with a specific

cohort cannot easily be adapted for use with others. Consequently, more flexible and adaptable software is needed for future epidemiological research. Common dataset standards (i.e. format and content) need to be defined. Such software should not only be able to derive doses from measurement data (as in the case of an incident), but also to link workers' data (e.g. exposure conditions) and other measurement data so that the dose would be calculated using to the correct hypothesis. Such software would permit the implementation of the consensus choices described above. Ultimately, it could also serve to derive uncertainties on assessed doses.

Uncertainty assessment and reduction

As detailed above, there are additional sources of uncertainties when reconstructing life-long doses for workers. The reduction of the dose uncertainties in epidemiological studies is thus even more challenging. Precise information, such as historical research on the working conditions must be gathered and quantified. Furthermore, the subjective uncertainty factors, such as interview of previous workers and answer scoring need to be analysed by experts of human sciences and archivists or experts in modern history. Ultimately, a method, for example a Bayesian network approach, must be developed to combine and quantify the uncertainties resulted from dose calculation and the uncertainties arisen from the propagation of all information available to risk estimation by the epidemiologists.

First, starting from the measurement data, even those below the detection limits, uncertainty resulting from adjustment to biokinetic models should be systematically quantified and harmonized. Second, the sensitivity from the results on different hypotheses that are judged uncertain should be analysed so that additional uncertainties can be quantified. Once identified, the hypotheses that induce the larger uncertainties should be worked on so that more precise information can be gathered. Even if currently the possibilities seem limited, an avenue worth exploring is extending the historical research on the working conditions. For that purpose a precise methodology for interview of "old" workers and answer scoring could be set-up with specialists of human sciences. Other information might come from deeper investigations of the archives of the industries with the help of archivists or experts in modern history.

Challenge 5.2: To develop more accurate and real-time external personal dosimetry for workers

Currently, more than one million workers are exposed to ionising radiations in Europe. The exposure situations are very diverse in terms of type and energy of radiation, as well as regarding the location and size of the body part being exposed (whole body, part of the body, extremities, eye lens).

The challenge is to provide reliable, accurate and real-time personal dosimetry for workers occupationally exposed to external sources of radiation.

The research in the field of personal dosimetry should be able to deliver accurately characterized dosemeters for all relevant dosimetric quantities and in all situations of exposure at workplace, and provide recommendations to derive the limiting dose quantity from the measured operational dose quantity.

The mid- or long-term objective in this field is to be able to monitor the workers reliably and accurately in real-time for all limiting quantities (whole body, eye lens and extremities), regardless of the protection methods used, and to provide input for the optimal application of the protection principle.

Objectives

- "Realtime" dose monitoring of workers should be developed
  - On-line personal dosimetry
  - Active personal dosimetry

- A more accurate dosimetry for specific tissues and organs is needed, especially in case of a heterogeneous field or partial shielding
  - Eye lens dosimetry
  - Extremity dosimetry
  - Brain dosimetry
  - Positioning of the whole body dosemeter on the operator

Research line 5.2.1: "Real-time" dose monitoring of workers is encouraged

On-line personal dosimetry

Recently, new dosemeters associated with connected technologies have become available opening up new opportunities in the field of on-line (real time) personal dosimetry. Such systems should be more developed and adapted to the needs and constraints of personal monitoring. They should be tested and compared to current systems, based on the use of passive and/or active individual dosemeters, to establish their practical impact on individual dosimetry in terms of dose assessment accuracy, data management, quality insurance, compliance with regulations constraints, etc. The impact of such an immediate feedback on the individual dose should also be investigated in terms of change of practices, application of optimization of radiation protection principles (ALARA) and regarding education and training aspects.

In addition, the research in the domain of fast Monte Carlo calculations (GPU based) applicable to individual monitoring should be more developed. The development of real-time individual dosimetry applications based on computer simulations and tracking devices, in addition to conventional "physical" individual dosimetry, or even by replacing it in the long-term, would be of great interest.

Active personal dosimetry

Some work is still necessary on active personal dosimetry. Active personal dosemeters (APDs) can be used in many occupational exposure situations. However, their performance needs to match with conditions in which they are used, which is particularly true for certain medical applications of ionising radiation such as fluoroscopy guided procedures. Consequently, they must be tested for all relevant fields in which they are used. For example, their response on dose rate, response in pulsed fields, as well as angular or energy dependence must be investigated. The procedures to test APDs in realistic radiation fields should be established.

In addition, if dosemeters are used in fluoroscopy-guided procedures for example, calibration procedures or correction factors for personal dosemeters to be worn above the lead apron taking into account the influence of the protective material should be defined. Algorithms for double dosimetry should be proposed to assess both the effective dose and the eye lens equivalent dose taking into account the new ICRU operational quantities for external radiation and ICRP 103 tissue weighting factors.

In general, the questions whether or not APDs can be used as legal dose recorders of whole body individual dosimetry and what requirements for dosimetry systems need to be fulfilled should be raised and solved. These questions are linked to the first topic that concerns on-line personal dosimetry.

Research line 5.2.2: Development of more accurate dosimetry for specific tissues and organs, especially in case of heterogeneous field or partial shielding

Eye lens dosimetry

Eye lens dosemeters, taking into account in particular ergonomic aspects, should be further developed. Tests, comparisons of different eye lens dosemeters and different dosimetry arrangements in terms of dosimetry accuracy and practicality are needed. Moreover, from an operational point of view, there is a need to propose correction factors for the position of the dosemeter and for the attenuation of the eye protection, when used.

Data are still needed for eye lens doses of workers in different fields such as those present in medical applications. In such fields, correlations of eye lens doses with other dose quantities, determination of reference eye lens doses for different procedures, testing and improvement of the efficiency of different protection measures like lead glasses need to be explored.

The reduction in the dose limit for the lens of the eye to make it equal to the whole body dose limit, makes the eye dose potentially the dominant limiting quantity. If the dominant direction of radiation is from the front, even for fields for which neutrons represent a significant component of absorbed dose, eye lens dose limits can be exceeded even before the whole body dose limits are exceeded. Hence, there is an urgent need to assess where eye lens doses are needed across the breadth of applications and industries where radiation protection is required.

Extremity dosimetry

Dosemeters currently available on the market for extremity monitoring do not show sufficient performance at low energies, are not sufficiently ergonomically adapted and, to date, there is no active system that meets the requirements of regulatory dosimetry monitoring.

Besides, the exposure of the extremities in nuclear medicine is an ongoing topic of interest. This topic has been investigated extensively during the ORAMED project (2008-2011), resulting in recommendations which are mainly applicable to the use of F-18, Tc-99m and Y-90. How these recommendations were followed and what their influence is for new radionuclides and new techniques should be clarified. The introduction and/or increased use of new radionuclides (such as Lu-177 or Ga-68) poses additional problems for personal dosimetry and in particular with regard to extremity doses. The impact of such new radionuclides on the adequate assessment of extremity doses, as well as on practices from the radiation protection point of view, should be investigated. Possible aspects in such an investigation are the use of correction factors, the contribution of positrons to extremity doses and the influence of mixed fields.

Brain dosimetry

Among the unshielded organs at risk, in the case of exposure to heterogeneous radiation fields such as working with glove boxes, in interventional radiology or more generally in a situation of partial shielding, the brain is of particular interest. Some papers on possible health effects of the irradiation of the operator's head, performing cardiological and radiological practices, have been published in recent years. The cause of concern was the possible effects generated by the exposure of the brain

during the interventional procedures. As a matter of fact, epidemiological findings show a statistical increase of the risk of brain cancer mortality among medical staff. Even if the exposure to low-dose radiation is only one possible explanation for these increased risks, dose assessment should be improved in this field.

Positioning of the whole body dosemeter on the operator

In case of a heterogeneous field or partial shielding, the operator's head, trunk, waist, upper and lower extremities are exposed to different scattered radiation fields. This implies that the position of the dosemeter on the neck, the trunk, the shoulder or waist, when employed for the whole body dose assessment, can have an effect on the accuracy of the evaluated doses. A study investigating the sensitivity of the dose assessment with respect to the dosemeter positioning and the influence of potential partial shielding can provide relevant information on the dose accuracy.

Challenge 5.3: To develop neutron dosimetry techniques

Neutrons are often regarded as being of secondary importance in workplace radiation protection when compared to photons. However, they form a strong component of the radiation field in many of the higher dose rate workplaces and are the dominant component of the field in commercial aviation. Further, the increasing use of accelerators for medical and research purposes generates neutrons with higher energies than is typical of most nuclear sites. Current dosemeters are not characterized well for such high energies and are expected to perform poorly in those fields.

In its regular intercomparison series, EURADOS has shown that the performance of neutron dosemeters is poor when compared to photon dosemeters. This is in part caused by the wide range of energies that neutron fields include, but also by the rapid change in the neutron conversion coefficients between 10 keV and 100 keV. Further, many types of neutron detectors exhibit poor directional dependence of response, which exacerbates the difficulties in workplaces, where neutron fields are highly scattered.

The need for new, better types of neutron personal dosemeters has long been recognized, but in its neutron dosemeter intercomparisons, EURADOS has seen that personal dosimetry for neutrons is dominated by just two types of dosemeters that have been in use for decades: albedo luminescence dosemeters and etched-track dosemeters. Both have acknowledged deficiencies, so improvements to neutron dose assessment need either novel methods or improvements to the traditional methods. Improved characterization of neutron fields, with a strong focus on the direction dependence of the field, will help greatly in evaluating how accurate neutron dosimetry really is in the workplace.

Prospective determination of the neutron dose rate for designation of controlled areas and for optimization of practice relies on the use of neutron survey instruments. It is widely acknowledged that these instruments do not perform very well in the workplace, with the energy dependence, and to a lesser extent the direction dependence, of their radiation response being strongly variable. Furthermore, pulsed fields from accelerators cause most instruments to under-respond. There is also a correlation between the quality of the dose rate assessment and the mass of the instrument. Instruments that are both lighter and perform better would bring the quality of area surveys closer to the quality currently observed for photon surveys.

Direct estimation of effective dose is increasingly attractive as a method of controlling doses. Online methods for neutrons present particular problems, and the direct estimation of neutron effective dose is a tougher challenge for an instrument than is the estimation of ambient dose equivalent.

However, novel methods that offer the potential for direct estimation of effective dose would provide significant improvements in neutron dose estimation.

Objectives

- Better understanding of neutron workplace fields with a strong focus on the direction dependence of the field.
- Extension of neutron personal dosimetry to novel and high-energy fields.
- New, improved neutron dosemeters.
- Better performance in the workplace from the main types of dosemeters currently used.
- Estimation of neutron risk via direct assessment of effective dose.

Research Line 5.3.1: To evaluate and improve, if necessary, the response of neutron personal dosemeters in high-energy fields

Aircrew dominate all other occupations in terms of collective radiation exposure, but are currently exempted from wearing personal dosemeters. This is in part because the high-energy radiation to which they are exposed causes significant problems for currently available personal dosemeters. Alternative calculational methods of assessing doses are available for aircrew, but workers at research and medical accelerator facilities who are exposed to fields with broadly similar characteristics need personal dosimetry. The rapid expansion of hadron therapy brings high-energy radiation fields with a strong neutron component into the medical area, exposing both workers and the public with neutrons. Research into the radiation fields that people are exposed to, and the correct calibration of dosemeters used in those fields, is needed to ensure that doses to people in such facilities are not underestimated. The development of new personal dosimetry methods for high-energy fields may be extensible to air crew, who are currently not accurately monitored for extreme space weather events.

Research Line 5.3.2: To improve the performance of neutron personal dosemeters in the workplace

Improved methods of performing neutron dosimetry could derive from better personal dosemeters, or from online methods (see also Research Line 5.2.1). Novel neutron dosemeters would ideally give instant readout and provide alarm capability, but accurate passive designs would also be a big step forward, given that an alarm may be available on an active photon device that is also being worn. New methods need to be better in terms of: not under-responding to neutrons with energies in specific ranges, or from important directions; not generating false-positives; having high sensitivity to ensure a reasonable signal-to-noise ratio at relatively low dose rates; good photon discrimination; resistance to environmental factors.

Whilst there are several types of neutron personal dosemeters available, almost all workers are currently monitored by passive devices using albedo dosemeters based on luminescence methods or etched-track dosemeters. Albedo dosemeters have very strong field dependence of response and hence rely very heavily on good knowledge of the field. If the field characteristics are not known, the estimated doses can show very significant biases. For etched-track detectors, the biggest issues are those of material quality. In contrast, the active devices that are available often have a high neutron energy threshold and relatively low sensitivity. Collaborative efforts to resolve these deficiencies are needed, with the quality of material available in Europe for etched-track dosimetry being an area where significant improvements could be achieved.

Research Line 5.3.3: To improve the understanding of neutron workplace fields, with strong focus on the direction dependence of the field

The evaluation of the fluence-energy distribution of neutron fields is well established, though it is less well understood for higher energies. In contrast, the direction dependence of the field is much less well determined although it is very important for the accurate evaluation of the true dose rate and the performance of personal dosemeters. Progress in this area has been made using measurements, but Monte Carlo methods need to be incorporated to achieve better understanding of the direction dependence of the neutron field. Monte Carlo methods can hence be used to complement more traditional methods to produce the basic data required for the evaluation of personal dose equivalent and effective dose in the workplace.

Research Line 5.3.4: Direct estimation of neutron effective dose

Experiments and modelling will be required to directly estimate neutron effective dose in the workplace. Ideally, online methods will be developed involving neutron Monte Carlo methods, although such methods are computationally expensive which makes real-time calculations very difficult. Further, the application of radiation weighting factors in models of workplaces causes problems for direct estimation of effective dose in the Monte Carlo codes that are currently available when applied to voxel phantoms. The new mesh phantoms may make this more feasible. Online dosimetry would ideally be supported by instrumentation that permits direct estimation of effective dose, thereby reducing the dependence on computational modelling.

Research Line 5.3.5: Improvement to neutron dose rate surveying

Neutron dose rate surveys are less accurate than corresponding photon surveys, because the instruments available have poorer radiation response. Neutron dose rate instruments are also very heavy, especially if their response is more acceptable. Consequently, new instruments are required that do not have strong dependence of the response on the neutron energy and direction. These new instruments must be light enough for extensive surveys to be performed in what are often very large facilities. Commonly, accelerator fields are strongly pulsed and high in energy, both of which cause additional problems for instruments. Instruments with acceptable accuracy are needed for all these workplaces with significant neutron dose rates.

Challenge 5.4: To improve environmental monitoring

The implementation of COUNCIL DIRECTIVE 2013/59/EURATOM include challenging tasks involving in some cases drastically reduced exposure limits, like the radon activity concentration in workplaces. Together with the needs defined in the EURATOM treaty it is important to provide sustainable capacities for reliable radiation protection metrology in the environmental field. These capacities, bundled under EURAMET in the form of an European Metrology Network (EMN), can provide a sound base for all environmental measurements in ionising radiation. The new technologies that will be implemented in the environmental monitoring field as described in Challenge 3.3, will require the development and adaptation of infrastructures for the characterization and calibration of such instruments.

Objectives

To support the implementation of the COUNCIL DIRECTIVE 2013/59/EURATOM together with ICRP Publication 137. This will require shifting the focus from the radon activity concentration measurements towards the dose estimation. Therefore the different atmospheric parameters

(aerosol size distribution and concentration, equilibrium factor, …) as well as different individual parameters (breathing rate, breathing volume, transfer factor for the unattached fraction, ...) has to be taken into account. This requires a careful analysis of the ICRP 137 with regard to the European workplaces and homes with a coordinated action with an expert group undertaking traceable field measurements for dose assessments. The calibration and comparison exercises of new technologies will require calibrations in laboratory and in the field. Therefore, infrastructures must be developed or adapted for such objective.

Research line 5.4.1: To improve the environmental monitoring of radon

Analysis of ICRP 137 with regard to the European workplaces and homes including traceable field measurements for dose assessments is needed. ICRP Publication 137 on Occupational Intakes of Radionuclides (OIR), Part 3, gives doses coefficients for the inhalation of radon, thoron and their airborne progeny as well as recommendations for their use for the protection of workers. In special cases, site-specific dose coefficients can be applied and should be investigated in the future.

Inclusion of radon (radon tracer method) in environmental climate networks (like the Integrated Carbon Observation System, ICOS) is needed. The natural radioactive gas radon (^{222}Rn) is being extensively used as a tracer to study a variety of atmospheric processes such as the exchange of greenhouse gases (GHGs) between the surface and the lower troposphere. The use of radon gas as a tracer for GHGs leads to the need of monitoring its atmospheric concentrations with high spatial density and of producing reliable radon flux inventories to be used in inverse modelling validations. Networks of atmospheric stations, such as ICOS, are already including atmospheric ^{222}Rn measurements. In addition, a harmonization of the experimental techniques applied for the measurements of atmospheric ^{222}Rn concentrations and ^{222}Rn fluxes is needed. These efforts can be also useful in order to generate the radon maps required to the European countries in their radon programs for radiological protection.

Research line 5.4.2: To develop and adapt infrastructures for calibration and comparison exercises using novel environmental technologies

In the radon field reference sources and calibration with emphasis on low radon concentrations will be needed in the future.

The use of spectrometric detectors in environmental monitoring for dose calculation and radionuclide identification will increase in the next year (see 3.3.2). Characterization and calibration of these detectors with focus on the inherent background, cosmic radiation and their response to different photon energy fluence will be a need in the future. Infrastructures for such calibrations and comparisons exercises should be developed and adapted.

Aerial sites with both reference point sources and extended contamination will be a need for the characterization and calibration of detectors carried by unmanned aerial vehicles (see 3.3.1).

Data from citizen networks will need a validation (see 3.4) in order to provide reliable data to be used for the development of radiological maps.

Review of the status of passive detectors using in environmental monitoring will be needed, including the implantation of the new ICRU quantities.

Challenge 5.5: To improve dosimetry in space

Leaving the Earth surface towards space, humans have to cope with numerous stressors, such as environmental changes, disrupted circadian rhythms, isolation, microgravity and heightened levels of radiation. Radiation exposure to ionising radiation has been one of the major concerns since the beginning of human spaceflights. Individual doses are usually much higher than on Earth. A lot of efforts have already been undertaken to reduce the radiation load of astronauts and to provide exposure records for human missions.

Radiation in space includes a complex mixture of particles and energies. Space radiation has two primary components: the galactic cosmic rays (GCR) and the solar cosmic rays (SCR). The GCR particle energies range from some eV up to 10^{20} eV. They incident isotropically on the Earth and are very penetrating in nature, difficult to shield and of high biological effectiveness. SCR includes solar proton events (SPEs) which are of particular concern for human space exploration. SPEs consist nearly exclusively of protons with a varying small amount of heavier particles. Their occurrence is infrequent and not predictable. A third source of space radiation, caused by the Earth magnetic field, is the trapped radiation (TR) consisting of charged particles produced in interactions of GCR and SCR with the molecules of the Earth's atmosphere. The radiation field in space is not constant because the energy and fluence spectra are in part modulated by the solar cycle by a factor of two to three, and in addition because there might be sudden increases due to SPEs mostly occurring during periods of increasing and decreasing solar activity. Moreover, the radiation field is modified by planetary atmospheres and surfaces, planetary magnetic fields, spacecraft construction materials and by the interaction with the molecules of the human body. Production of secondary particles in nucleus/nucleus interactions in shielding material adds to the radiation field in a space craft. The challenge is to provide accurate information (energy and particle spectra, dose rates, and microdosimetric quantities) in each exposure situation. The fact that the space radiation field has a quite different radiobiological quality compared to the radiation field in aircraft altitudes complicates the situation.

Exposure situations are quite different within and outside the Earth's magnetosphere, within a spacecraft or on planetary surfaces within habitats, or outside the spacecraft or outside habitats where any astronauts may just be shielded by a space suit. In addition, mass configurations within spacecrafts may change, thereby modifying the radiation exposure of the astronauts.

Objectives

- Development of radiation spectrometers which are able to measure in a mixed high-energy field separately indirectly and directly ionising particles.
- Calibration of measurement devices at reference fields, cross calibration of instrumentation in situ.
- Evaluation of biomarkers as alternative dosemeters.
- Improvement of models to describe the radiation environment and its interaction with space crafts and improvement in predicting solar particle events (time of occurrence, fluence spectra, time evaluation).

Research line 5.5.1: Development of advanced Instrumentation

The International Space Station (ISS) is already equipped extensively with instruments for radiation measurements. However, most of these measurements do not show satisfying results. Up to now tissue equivalent proportional counters (TEPCs) are handled as reference instruments. Comparison

with other instruments like silicon detectors and passive detectors show in most cases a good agreement of the results. One uncertainty is the lack of sufficient knowledge of the shielding around the detector positions. Weak points are also the determination of quality factors using silicon telescopes, where only part of the incident radiation can be used for the determination of an LET spectrum. Available measurements also included determination of depth dose profiles in human phantoms. Efforts are necessary to improve the measurements of particle energy spectra (in particular, neutron energy spectra) by developing and calibrating new instrumentation, in order to reduce uncertainties in dose assessment. Essential is also to develop instruments to record first indications of the occurrence of an SPE, to allow spacecraft crew to enter a radiation shelter. For example, measurements of relativistic electrons could be envisaged as a precursor of a dose increase due to an SPE.

Research line 5.5.2: Calibration of instruments

Evaluation of any dose measurements requires reliable calibration procedures at various reference radiation sources (proton and heavy ion accelerators, reference neutron fields, etc.). Since available instruments are not capable of measuring the radiation of interest over the whole particle and energy range, missing information needs to be substituted by model calculations. Therefore, transport codes need also be validated and optimized using instrumentation and realistic phantoms exposed in reference fields.

Research line 5.5.3: Model development

Knowledge about the radiation environment in space and on the spacecraft/habitat construction are important to be implemented in transport models, to simulate radiation doses for manned spaceflight. Information on the space radiation field needs a continuous upgrade using spectral data provided by particle spectrometry in satellites. Radiation transport models suffer from a lack of cross sections which are critical for the understanding of GCR transport through matter. Providing better cross sections is an important step towards a strong advancement of the models and could result in a significant reduction of uncertainties that are currently present. Measurements of particle fluence and energies or LET distributions and absorbed dose measurements together with model calculations can provide the needed input for an accurate exposure determination. There is a need for a strong improvement of our forecasting capabilities for solar particle events.

Harmonisation and practice

The goal of harmonisation of dosimetric procedures in Europe is central to the overall EURADOS mission. It is obvious that every strategic objective discussed in the Strategic Research Agenda has an element of harmonisation. That is, for all areas of research where dosimetry is required (epidemiology, occupational exposures, environmental monitoring, emergency preparedness, medical applications, etc.) a consistent approach in determining individual doses of exposed subjects and/or ambient dose rates is indispensable.

The principle of "harmonisation" includes delivering standards of dosimetry, and hence of protection, that are equivalent in terms of reliability and overall accuracy. Practices that are harmonised may differ in their details but will deliver results of similar quality. For example, dosimetry carried out in different countries may use different techniques and be subject to different national requirements; but the results should be equally reliable and equally accurate.

Hence, the objective of harmonisation can be regarded as a cross-cutting aspect of continuous improvement. EURADOS aims to continue to promote high levels of harmonisation, and hence reliability and accuracy, across all areas of dosimetry.

Work on harmonisation cuts across the various visions and includes:

- The promotion of intercomparisons, enabling participants to analyse and improve performance and allowing the validation of methods.
- Surveys, enabling the radiation protection community to understand current contexts.
- The publication of agreed recommendations, guidance and interpretations, enabling professionals to improve practice.
- Training and networking, enabling new and current staff to improve their knowledge (see separate section on Training).

More specifically, harmonisation actions are needed for:

- Vision 3 (Towards an efficient dose assessment in case of radiological emergencies):
  - Intercomparisons of retrospective dosimetry methods have taken place and will continue to be useful.
  - Intercomparison of in vivo monitoring and Monte Carlo simulations in case of accidental intakes of radionuclides.
  - In vitro emergency bioassay intercomparisons.
- Vision 4 (Towards an integrated personalized patient dosimetry in medical applications):
  - Harmonisation of methods for nano-, micro-, and macro-dosimetry and their integration with radiobiology (partly also included in Vision 1).
  - Intercomparisons of dosimetry methods in high dose rate and pulsed medical fields.
  - Harmonisation of dose calculations, measurements, intercomparison protocols and audits in radiotherapy especially for new techniques (MRI-linac, spot-scanning arc therapy, FLASH therapy, carbon therapy etc.).
  - Trainings and recommendations on patient radiation protection.
  - Multi-institutional harmonisation of medical imaging codes of practice.
  - Intercomparisons for dose calibrators in nuclear medicine.

- Vision 5 (Towards an improved radiation protection of workers and the public):
  - Intercomparisons should continue to be promoted.
    - The programme of self-sustaining intercomparisons for individual occupational monitoring need to continue. Improvements in participant performance have been made, but there are still deficiencies in some dosimetry systems, especially in the areas of neutron and extremity/ eye lens dosimetry.
    - Intercomparison programmes for internal dosimetry (in vivo and in vitro monitoring and dose assessment) and environmental monitoring have begun and have identified a continuing need.
  - There is still a need for guidance documents and recommendations.
    - Work should be completed on interpretation of ISO17025:2017 for individual monitoring services.
    - The need for other guidance will be assessed, e.g. on choice of dosimetric methods, or on the treatment of uncertainties.
  - These questions and others are likely to entail different surveys on different dosimetric aspects.

- Computational dosimetry
  - Intercomparison exercises have been carried out and areas for improvement identified. Further exercises are needed (e.g., for Monte Carlo simulations, neutron unfolding procedures).

Education and training

Introduction

Education and training (E&T) has always been a key issue in EURADOS activities. By means of training courses, intercomparisons and networking activities EURADOS promotes the maintenance of expertise and hence of sustainability in radiation protection, whose activities are often carried out by small numbers of highly specialised staff.

EURADOS already now organises already quite some E&T activities. On one hand, EURADOS *Winter Schools* are lecture-based and intended for students and those new to the subject area. They have taken place at EURADOS Annual Meetings since 2007. They usually last one or half a day and they provide "refresher courses" on topics relevant to radiation dosimetry. On the other hand, EURADOS *Training Courses* (TC) are mainly meant for training of junior staff or young scientists either on implementation of dosimetry techniques as well as on novel or improved dosimetric methods, related to specific topics in the field of the EURADOS Working Groups. They usually last three to five days, with limited participation to about 40 attendees. In the past, some of the TCs had more than one edition and were slightly updated according to the demand. TCs may include lectures and practical sessions with exercises. In contrast, EURADOS *Scientific Symposia* are a one-day event organized at EURADOS Annual Meetings to enhance discussion on research topics or on results from EURADOS Working Groups or related research projects. Proceedings of the Symposia have been published in peer-reviewed journals.

In addition, since 2012, EURADOS took many efforts to organize series of TC on the implementation of European Technical Recommendations, which were developed by EURADOS within European specific projects funded by EC, both on external exposure and internal contamination. Five TC took places on Technical Recommendations on Individual Monitoring for External Exposure and the first in 2019 on Technical Recommendations on Monitoring Individuals for Occupational Intakes of Radionuclides. Future training actions in this field will be based on this experience and on the input by the individual monitoring service (IMS) community. It is desirable that IMSs will regularly attend the EURADOS Annual Meetings and discuss issues of common interest. In this regard, the analysis of QA/QC surveys organized on a regular basis is a means of identifying topics where training actions might be needed and welcomed by IMSs.

In the field of individual monitoring for external exposure, since 2009 the EURADOS Intercomparison Participant's Meeting have been held, usually at the AM, to report and discuss the overall assessment of the intercomparison exercise.

All these previous EURADOS E&T actions are well described in detail in a paper (J.G. Alves, E. Fantuzzi, P. Gilvin, W. Rühm, et al. EURADOS Education and Training activities. J Radiol Prot, 39, p37-50 (2019)).

Compared to the last SRA, EURADOS started new initiatives like the encouragement of young scientists to collaborate within EURADOS activities. For this, the EURADOS Grant and EURADOS Award were established, the former for the support of research projects developed at laboratories of the EURADOS network and the latter in recognition of excellent work developed within a WG's work programme.

In 2017 the Learning Network was established as a new tool for E&T. The Learning Network takes place during the Annual Meeting and gives participants opportunities to discuss a range of relevant topics on Individual Monitoring.

Recently, coordination with other European platforms for E&T has been promoted and realized within the CONCERT project with the aim of avoiding duplication or overlapping on other EU projects and international organisations activities, promoting collaborations in existing international activities and identifying how, where and what EURADOS can add to the current variety of initiatives.

Several meetings have been held organized by EURADOS together with the radiation protection platforms MELODI (Low Dose Initiative), ALLIANCE (Radioecology), NERIS (Radiological Emergencies), EURAMED (European Alliance for Medical Radiation Protection Research) to present their respective SRA and discuss common topics of interest, including in E&T. The European Radiation Protection Week (ERPW) and ICRP meetings are also examples where updated presentations at E&T sessions were given. In this line, EURADOS contributed to the European Education and Training in Radiation Protection (EUTERP) workshop in 2019.

Training courses were held in collaboration with the ANNETTE network (advanced networking for nuclear education and training and transfer of expertise) where EURADOS experts imparted lectures on specific topics. Collaborations with networks are also expected in order to identify topics needing further development or missing topics (e.g. European Metrology Network).

Additionally, EURADOS supports the dissemination of knowledge in radiation dosimetry by promoting and endorsing conferences such as the individual monitoring (IM) series, the neutron and ion dosimetry symposia (NEUDOS) and contributions to E&T sessions at specific events (e.g. European Radiation Protection Week annually held) and, most recently supporting the participation of Young Scientist to International Conferences (EURADOS Young Scientist Conference Support).

Objectives

EURADOS E&T actions are generally organised to maintain the competence in the field of dosimetry, in Europe, in order to provide training and not to test or recognise competence. Such actions are considered important and will be continued in the future including training on upcoming new dosimetric techniques, in order to guarantee efficient use of techniques in dosimetry in all relevant research disciplines where exposure quantification is needed.

Moreover, EURADOS intends to contribute to a constantly improved information and education of the general public and especially of key figures (physicians, physics teachers, journalists, representatives of local authorities, etc), aiming at a better understanding of ionising radiation technical terms involving radiation and dose, as well as the development of preparedness programmes to face accidents and emergencies.

Coordination with E&T efforts and initiatives of other platforms and organizations will continue addressing the topics of interest to the WGs on radiation dosimetry, the implementation of technical recommendations and good practice in dosimetry in general, representing a contribution to the international E&T actions in radiation protection and dosimetry.

EURADOS will continue and try to support further actions in order to promote the training of young scientists allowing their contribution to the radiation protection community as well as to provide training for specialists on new needs on radiation dosimetry following the results of research studies.

Computational dosimetry

Introduction

In many of the areas of research described in this SRA, computational methods play an important role. The domain of computational radiation physics is not solely reliant on the Monte Carlo method, but also incorporates e.g. deterministic methods that attempt to solve the Boltzmann transport equation, and unfolding methods used to derive neutron energy distributions from experimental data. However, the availability of modern codes and powerful computers has made the Monte Carlo method dominant in radiation protection and dosimetry. Important areas of research where computational methods are needed also include representations of the human body at different scales from macroscopic whole or partial-body representations to the microscopic cellular scale and nanometric DNA level. For example, the operational quantities used in radiation protection are defined in such a way that their values can only be calculated via Monte Carlo simulations. This is equally true for the protection quantities, which are defined in anthropomorphic computational phantoms that cannot be constructed physically but must be simulated. Computational simulations are often also directed at a basic understanding of energy deposition patterns. Another important application is the support that computations can give to the design, optimisation and analysis of experiments.

The availability of Monte Carlo methods contributed in the development of the current system of radiation protection and has as primary task to reduce the variance in the determination of absorbed dose (and its related quantities). Consequently, computational dosimetry is an integral part of the dosimetry research field and further research and development will therefore be needed to maintain that position.

Fields of application with growing needs for computational dosimetry

- ICRU is currently *revising the* operational dose quantities, which will be defined entirely using anthropomorphic phantoms. Computational dosimetry will play a key role in assisting the radiation protection community in adjusting to the changes, such as in the evaluation of the new conversion coefficients and the study of required modifications in the design of current dosemeters. In the longer term, analogous endeavours will be required following future evolutions in understanding radiation risks, such as developing individual monitoring frameworks for dose quantities that are defined in reference to age-dependent phantoms, micro- or nano-dosimetric assessments of radiation damage, or more realistic, structured, or detailed models of the body, skin or eye lens.
- Current research activities are demonstrating the possibility of monitoring individuals' doses in real-time by computational methods. There will be a key role in the development and evaluation of this type of approach as it moves from concept to routine practice, for example in intercomparisons of its usage and assessments of the resulting uncertainties.
- In the medical field, there is currently an important focus to move towards personalized medicine, in which there is also a very important role for patient-specific dosimetry, especially for modalities involving relatively high doses, such as computed tomography and interventional procedures or molecular radiotherapy. In these research domains, computational dosimetry not only plays a crucial and indispensable role, but is also becoming more and more complex. Also in the field of internal dosimetry and, more specifically, the calibration of in vivo measurements with partial body counters, there is a need for an individualised approach to reduce the uncertainties of such measurements. This

can be done by computational phantom development, taking into account individual variability of the persons to be measured. With the *individualized dosimetry approaches* that are more and more envisaged, flexible phantoms of different sizes are needed, as pointed out in the section below.

- With the recent rise of methodologies based on *"artificial intelligence"* such as neural networks, many fields of science have been evolving fast. Radiation protection and dosimetry would also benefit significantly from the use of neural networks. For example, personalized phantoms with realistic anatomies could be constructed from a library of contours, organs, etc., or current Monte Carlo simulations could be (partially) substituted with Convolutional Neural Networks (CNN), which would be the greatest advantage to provide truly real-time dose estimation. Moreover, learning algorithms could be developed from what has already been calculated in order to estimate organ absorbed doses from measurements of biological or non-biological samples.

New developments for Monte Carlo codes

- Recent phantom developments, such as mesh phantoms or NURBS phantoms, permit adaptation of phantoms to the individual personal anatomy. Hence, individual computational dosimetry is, in principle, feasible. However, at present, only few Monte Carlo codes are capable of directly incorporating these types of phantoms without the need of voxelisation. Other codes can deal with this phantom type, but then their performance is slowing down considerably. The capability of dealing with mesh and/or NURBS phantoms with reasonable computing speed needs to be extended to more codes. This could also be achieved if methods would be developed to reduce the number of vertices/splines without degrading too much the anatomical precision. Moreover, in terms of the implementation of MESH and NURBS phantoms in MC codes, the development of new variance reduction techniques (to overcome the problem of computing time with some MC codes) is needed.
- In the framework of real-time computational dosimetry, the implementation of methods to perform "dynamic" calculations in the Monte Carlo codes are needed. For instance, to take into account different postures and movement sequences of the anthropomorphic models would be desirable.
- The need for basic cross section data is fundamental and much remains to be done in this area. For example, the field of individual monitoring will need to match with new developments as the working environment and use of radiation in the workplace evolves. This could include shifts to higher energies as accelerator technology advances, for instance, or to new particle types or radionuclides used in the medical field. Moreover, on the micro- and nano-dosimetry computational side, this implies the implementation of cross-sections for new materials (e.g. gases used in detectors or metals used in their design) in order to be able to directly simulate the experiments and be a useful tool for experimental design. Cross sections (measured and/or modelled) on high Z materials are also needed for specific applications as those involving nano-particle sources.

Uncertainty assessment in computational dosimetry

- Computational dosimetry will further benefit from a thorough evaluation of the uncertainty budget associated to calculation results. For micro- and nano-dosimetry this is of particular importance when dealing with interactions of low-energy electrons. Code *intercomparison and sensitivity analysis* (e.g. variation of results modifying the code physical ingredients) are useful strategies in this sense and can assist new computational development.

- Computational dosimetry greatly enhances the overall quality of radiation dosimetry. Nevertheless, it is important to remember that despite this great utility appropriate *experimental benchmarking* of any calculated data is indispensable. For example, there is a strong need of collaboration with experimental groups (also working on detector development) to provide micro- and nano-dosimetry measurements as benchmarks.

Training in computational dosimetry

- With the large opportunities within dosimetry that exist for the future, by using the progress in computer power, machine learning and Monte Carlo techniques, more and more different codes are in development and in use. The benefits are, however, not for free, as thorough training and experience are needed. It is important for the user to fully understand and study the influence of the variance of input data (geometry, cross sections, physics, etc.) although this may involve considerable effort for standard Monte Carlo codes. The organisation of *intercomparison exercises and training courses* stay an important task for the future. Important problems should be treated using more than one code, as it is most helpful to benchmark problems so that codes may be validated against each other. Overall, comparison of results obtained using different approaches (e.g. condensed-history vs. full track structure or Monte Carlo vs. analytical) will be needed to highlight differences and limitations, also depending on the specific configuration.

Cross references

The dosimetric challenges in radiation protection are divided here according to five different visions. Advances in state of the art in each vision would lead to a significant improvement of radiation protection in the specific domain of that vision.

Of course the general goal remains a better protection of men and environment against the potential hazardous effects of ionising radiation. The division in five visions is somehow arbitrary, and there can be significant overlap between research lines from different challenges, even over different visions.

In the structure of the EURADOS SRA three horizontal activities are identified which are important for all visions: harmonization, education & training, computational dosimetry. These are described in separate chapters.

To stress the importance of the links between different research challenges, the following cross reference table was set-up. This table and the corresponding explanation should highlight the connections that exist.

Three different kind of connections are identified:

- Unrelated research actions (U): independent research actions.
- Complementary research actions (C): these research actions need to be addressed both in parallel and they can influence each other, but they clearly require separate and different research.
- Strongly linked research actions (S): these actions are basically the same or have a strong overlap, but towards different applications. They can tackle the same problem from a different angle but towards the same goal.

VC	1.1	1.2	1.3	2.1	2.2	2.3	3.1	3.2	3.3	3.4	4.1	4.2	4.3	5.1	5.2	5.3	5.4	5.5
1.1		C	U	U	U	U	U	U	U	U	C	U	U	U	U	U	U	C
1.2			C	U	U	U	U	U	U	U	S	C	U	U	U	U	U	C
1.3				C	U	C	U	U	U	U	U	U	U	C	C	C	C	C
2.1					C	U	S	S	U	U	S	C	C	S	S	U	U	U
2.2						C	U	U	U	U	C	C	C	C	C	U	U	U
2.3							U	U	U	U	U	U	U	U	U	U	U	U
3.1								U	C	C	U	U	U	S	U	U	U	U
3.2									C	C	U	U	U	U	S	U	U	U
3.3										C	U	U	U	U	U	U	S	U
3.4											U	U	U	U	U	U	C	U
4.1												U	U	U	U	C	U	C
4.2													U	C	U	U	U	U
4.3														U	U	U	U	U
5.1															U	U	U	U
5.2																C	U	U
5.3																	U	C
5.4																		U
5.5																		

Short explanation of the strongly linked research actions:

- 1.2 and 4.1: The connection between the track structure and the radiation damage is important to improve hadron therapy outcome. Research line 4.1.3 is focussed on the biological effects linked with micro- and nano-dosimetry for hadron therapy. At the same

time 1.2.3 is focussed on a specific type of novel radiotherapy application (high-Z nanoparticles).

- 2.1 and 3.1/3.2: Quantifying doses after accidents is often important for epidemiological studies. More specifically, research line 3.1.4 is focussed on new methods for dose reconstruction for epidemiological studies.
- 2.1 and 4.1: Total body dosimetry in radiotherapy is important for epidemiological studies, because these radiotherapy patients are more and more subject of such studies. Research line 4.1.4 is dedicated to this topic.
- 2.1 and 5.1/5.2: Likewise, also workers are often the topic of epidemiological studies, and improvement in worker dosimetry (both internal and external) is important. Research line 5.1.3 is dedicated to this topic.
- 3.1 and 5.1: Better biokinetic and dosimetric models for internal emitters are needed for routine cases in workers and for accident situations.
- 3.2 and 5.1: Better external dosimetry is needed for routine cases in workers and for accident situations.
- 3.3 and 5.4: Environmental dosimetry can benefit from citizens and mobile networks, both in routine situations as in accidental situations.

Short explanation of the complementary research actions:

- 1.1 and 1.2: Improving the understanding and measurement techniques for the track structures are important to quantify the correlations with the radiation damage.
- 1.1 and 4.1: Track structure characterisation (micro- and nano-dosimetry) is important for hadron therapy.
- 1.1 and 5.5: Space dosimetry is special because of the high-energy particles encountered, so track structure characterisation is an important element of space dosimetry.
- 1.2 and 1.3: The connection between the track structure and the radiation damage is important input to define better radiation protection quantities.
- 1.2 and 4.2: Also in targeted radionuclide therapy the biological effect of high-LET particles is an important research need.
- 1.2 and 5.5: Space dosimetry is special because of the high-energy particles encountered, so the biological effect of these particles is an important element of space dosimetry.
- 1.3 and 2.1/2.3: A change in radiation protection quantities will influence the analyses of epidemiological studies, both in the past and in the future.
- 1.3 and 5.1/5.2/5.3/5.4/5.5: A change in quantities will influence the dosimetry research for the protection of workers and the public.
- 2.1 and 2.2: Improving dosimetric data in existing epidemiological studies and determining the uncertainty go hand in hand and are thus complementary.
- 2.1 and 4.2/4.3: Also patients from nuclear medicine, and from imaging procedures (CT, interventional, …) are often the subject of new epidemiological studies, so good and complete patient dosimetry is very important.
- 2.2 and 2.3: In future epidemiological studies it is important to include a good approach for uncertainty estimation, as this is crucial for a good outcome of the study.
- 2.2 and 4.1/4.2/4.3: Taking account of uncertainties is important in patient dosimetry, this counts in general, but also for epidemiological studies.
- 2.2 and 5.1/5.2 Taking account of uncertainties is important in workers dosimetry, this counts in general, but also for epidemiological studies.

- 3.1 and 3.3/3.4: Citizen engagement and environmental monitoring will help in reconstructing the doses.
- 3.2 and 3.3/3.4: Citizen engagement and environmental monitoring will help in reconstructing the doses.
- 3.3 and 3.4: Citizen engagement will become important in possible future accidents.
- 3.4 and 5.4: Environmental dosimetry can benefit from citizens and mobile networks.
- 4.1 and 5.3: Neutron dosimetry is needed in radiotherapy.
- 4.1 and 5.5: A major part of the doses in space are coming from high Z particles. As such there is a link between hadron therapy and space dosimetry, both in measurement and simulation techniques, and in the links to the biological effects.
- 4.2 and 5.1: Biokinetic models and internal dosimetry can be valid for workers and patients in nuclear medicine.
- 5.2 and 5.3: Neutrons are one of the external exposure situations for workers.
- 5.3 and 5.5: Neutrons are also important in space dosimetry.