Radiation Protection Dosimetry (2021), Vol. 194, No. 1, pp. 42–56 doi:10.1093/rpd/ncab063
Advance Access publication 15 May 2021

EURADOS STRATEGIC RESEARCH AGENDA 2020: VISION FOR THE DOSIMETRY OF IONISING RADIATION

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Received 7 January 2021; revised 28 February 2021; editorial decision 6 April 2021; accepted 6 April 2021

Since 2012, the European Radiation Dosimetry Group (EURADOS) has developed its Strategic Research Agenda (SRA), which contributes to the identification of future research needs in radiation dosimetry in Europe. Continued scientific developments in this field necessitate regular updates and, consequently, this paper summarises the latest revision of the SRA, with input regarding the state of the art and vision for the future contributed by EURADOS Working Groups and through a stakeholder workshop. Five visions define key issues in dosimetry research that are considered important over at least the next decade. They include scientific objectives and developments in (i) updated fundamental dose concepts and quantities, (ii) improved radiation risk estimates deduced from epidemiological cohorts, (iii) efficient dose assessment for radiological emergencies, (iv) integrated personalised dosimetry in medical applications and (v) improved radiation protection of workers and the public. This SRA will be used as a guideline for future activities of EURADOS Working Groups but can also be used as guidance for research in radiation dosimetry by the wider community. It will also be used as input for a general European research roadmap for radiation protection, following similar previous contributions to the European Joint Programme for the Integration of Radiation Protection Research, under the Horizon 2020 programme (CONCERT). The full version of the SRA is available as a EURADOS report (www.eurados.org).

INTRODUCTION

In 2012, the European Radiation Dosimetry Group (EURADOS) began work on a Strategic Research Agenda (SRA) to identify topics which would influence the development of radiation dosimetry and its applications in a wide range of academic and applied areas for the following two decades, with the fundamental goal of improving radiation protection of radiation workers, patients and the public[1, 2]. As dosimetry is a developing subject, periodic revisions to the SRA are needed. The first revision has now been published[3] and can be downloaded from www.eurados.org. This paper summarises its key points.

Since the first SRA, the EURADOS network has continued to expand and now comprises a self-sustainable network of 80 European institutions (Voting Members) such as research centres, university institutes, reference laboratories, dosimetry services and commercial companies, including over 600 active

scientists in the field of radiation dosimetry. The aim of the network is to promote European cooperation in research and development in the dosimetry of ionising radiation and its implementation in routine practice—drawing upon European, as well as global, developments—in order to contribute to compatibility within Europe and conformance with international practices.

In pursuing these objectives, EURADOS Working Groups (WGs) continue to cover a wide range of various dosimetric disciplines such as individual monitoring, environmental, internal, retrospective, medical, high-energy and computational dosimetry (www.eurados.org).

EURADOS, through its WGs, has the capacity to develop, test and compare novel dosimetric techniques involving a wide range of participating institutions. This expertise also enables problems arising from new applications of ionising radiation to be addressed and thus to contribute to science-based policy recommendations.

Harmonisation, education and training are also key activities for EURADOS, through the organisation of intercomparisons (e.g. in individual and environmental monitoring, internal dose assessment and computational dosimetry methods)[4–9] and training courses[10].

The current revision of the SRA draws upon the expertise and experience of the WGs[11, 12] and incorporates the results of a stakeholder meeting organised in 2016, with input from over 20 organisations within and outside the dosimetric community[13]. The SRA revision has since been discussed at various levels within EURADOS (WGs, Council, Voting Members) by 59 contributors.

EURADOS has been an active participant in the CONCERT project, established in 2014 by the European Commission for the development of a European Joint Programme (EJP) for the Integration of Radiation Protection Research under the Horizon 2020 programme. The objective was to promote the sustainable integration of European and national research programmes in radiation protection. CONCERT operated as a project that brought together research initiatives—and supported SRA development—of several radiation protection research platforms[14]: EURADOS (dosimetry), MELODI (Multidisciplinary European Low Dose Initiative), ALLIANCE (European Radioecology Alliance), NERIS (European Platform on Preparedness for Nuclear and Radiological Emergency Response and Recovery), EURAMED (European Alliance for Medical Radiation Protection Research) and SHARE (Social Sciences and Humanities in Ionising Radiation Research). In conjunction with these platforms, EURADOS has contributed to the publication of the Joint Roadmap for Radiation Protection Research (JRM), drawing upon the cross-cutting and underpinning role of dosimetry and including elements from its first SRA. The revised SRA will also be used in future roadmap and prioritisation exercises in a future post-CONCERT structure.

The EURADOS SRA summarised in this paper is made up of five visions, each of which represents a key area of dosimetry development comprising several challenges and, at a more detailed level, associated research lines. The visions, which demonstrate the breadth of dosimetry topics covered by EURADOS, are: updated fundamental dose concepts and quantities (vision 1); improved dosimetry for radiation risk estimates deduced from epidemiological cohorts (vision 2); efficient dose assessment in the case of radiological emergencies (vision 3); integrated personalised dosimetry in medical applications (vision 4) and improved radiation protection of workers and the public (vision 5). In addition, three additional areas are common to, and underpin, the visions, namely computational dosimetry, harmonisation of practice, and education and training. There are significant links between research lines from different challenges, and even between different visions. These cross-cutting links, and many others, are given in the SRA[3].

More information about EURADOS, including a downloadable version of the full SRA, may be found on the EURADOS website (www.eurados.org).

VISION 1: TOWARDS UPDATED FUNDAMENTAL DOSE CONCEPTS AND QUANTITIES

The biological effectiveness of ionising radiation is believed to be a function of microscopic and nanoscopic energy deposition patterns (particle track structure) involving random interaction events. However, the current radiation protection system is based on protection and operational quantities[15–18] derived from absorbed dose, essentially a ‘point’ quantity, which in practice is averaged over an entire organ or tissue. The overarching objective of this vision is to develop a unified concept of radiation quality which includes the statistical features of track structure. An essential prerequisite for this objective is the identification and quantification of the relevant statistical characteristics of microscopic and nanoscopic spatial and temporal interaction patterns and their correlations with biological damage. This work is, for example, highly significant in the development of hadron radiotherapy and the use of high-Z nanoparticles (see below, and vision 4), but also has a much wider potential influence on dosimetry generally, as described in all five visions. The following three challenges were identified:

Spatial correlations of radiation interaction events

To improve the understanding of spatial correlations of radiation interaction events, it is necessary to develop a novel, unified concept of radiation quality as a general physical characteristic of the radiation field that would allow the separation of the physical and biological components which contribute 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. This will require several lines of research:

- Develop density scaling relationships for micro- and nano-dosimetry[19, 20] using theoretical and simulation studies as well as the characterisation of existing[21] and emerging nanodosimetric detectors[22–24].
- Identify biologically relevant target sizes from a comprehensive characterisation of track structure; develop track structure imaging techniques[25, 26], complemented by experimental investigations of radiation interactions in condensed phase nanometric objects[22, 27, 28].
- Establish uncertainty estimations for measured track structure quantities and develop computational methods for track simulations, including the fundamental challenge of incorporating quantum mechanical descriptions of particle interactions[29, 30].

Track structure and radiation damage

It has been demonstrated that track structure shows a strong correlation with the induction of early biological effects, particularly the occurrence of DNA single and double strand breaks[31–33]. As later biological endpoints also show dependence on radiation quality, correlations between track structure characteristics and the probability of inducing these later effects, such as chromosomal aberrations or cell death, will form the basis of a deeper understanding of radiation damage mechanisms. In general, the prediction of biological effects from track structure characteristics would be a prerequisite for new dosimetric concepts which quantify radiation effects at the level of individual cells or small tissue compartments. Exploration of these correlations suggests several research objectives:

- Study the geometrical correlation of energy deposition and cellular damage using microbeams to target individual cells and small tissue compartments, together with automated assays and metrological methods aimed at improving the detection of radiation-induced biological endpoints[34–36].
- Develop multi-scale characterisation of track structure using nanodosemeters with multiscale measurement capabilities and track structure simulation codes[19, 37, 38].
- Identify the most relevant target size for a particular biological endpoint by using correlations between results for a particular endpoint for different radiation qualities, nanodosimetric probability distributions and target sizes.
- Improve the detection of radiation-induced biological endpoints using experimental developments such as transmission electron microscopy for the demonstration of DNA damage[39].
- Investigate high-throughput analysis techniques and transcriptomic profiling of single cells for investigation of intrinsic factors underlying intracellular differences[40, 41].

A further extensive area of research requires a more comprehensive understanding of biochemical reactions and the cellular chemical environment in the production of radio-induced damage (e.g. the role of oxygen in DNA damage and the understanding of the role of various cellular scavenging species). Monte Carlo (MC) techniques need to be developed to predict radio-induced damage in biomolecules. This research is also relevant to the use of high-Z (e.g. gold) nanoparticles (GNP) in radiotherapy[42–45] (see vision 4). The enhanced absorbed doses in the vicinity of multiple GNPs at the cellular and molecular level require verification that is often provided by MC simulations[46–49] which more generally should be extended to include chemical effect modelling for radiobiological simulations. A further challenge is to simulate X-ray fluorescence as a new imaging modality for targeted molecular radiotherapy in parallel with experimental developments[50].

Recent developments in FLASH radiotherapy at high fluence rates[51]—where the assumption of the independence of physico-chemical interactions may not be valid—has emphasised the need for the investigation of temporal correlations of interaction events (see also vision 4).

Combining track structure-based nanodosimetry, biologically based mechanistic modelling and epidemiological data should provide insights into the molecular dosimetry required for understanding dose–response relationships at low doses and low dose rates.

Radiation protection and operational dosimetry quantities

The system of radiation protection employs both protection and operational quantities[16, 17]. The protection quantities are intended to estimate detriment, whilst the operational quantities are designed to provide measurable, but conservative, estimates of the protection quantities. The success of this system requires periodic review, revision and verification of these quantities in terms of their applicability,

ease of use and relation to detriment. The link between operational and protection quantities would be greatly assisted by making the former relate better to the latter, whilst retaining measurability. However, as the definitions of the quantities evolve, there is a need for the generation of new or revised conversion coefficients as the range of particle types and energies expands, together with the availability of corresponding calibration fields. As concepts change, there is a need to promote research that supports greater understanding of the quantities in the diverse fields in which they are applied. As mentioned in the previous SRA[1], progress in micro- and nano-dosimetry may require revised protection and operational quantities that better reflect radiation damage in the body.

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

In the context of exposure to ionising radiation, epidemiological studies analyse the rates of observed radiation-induced health and biological effects in a target population and derive the risks of these effects in comparison with background or baseline rates. These investigations involve the collection of exposure and outcome data and provide—in the ideal case—individual dose estimates. The current fundamental quantity for risk estimation is absorbed dose in organs appropriate to the outcome under investigation. Studies are performed on cohorts comprising humans exposed, amongst others, to emergency, medical and occupational exposure situations. The dosimetric challenges in these situations are described in visions 3, 4 and 5, respectively. Despite the diversity of exposure conditions, they contain considerable overlapping approaches and methodologies for absorbed dose evaluation. Some of the most important objectives are:

- Assess doses independently for each quality (e.g. in mixed photon and neutron fields).
- Estimate doses which had originally not been recorded (e.g. out-of-field doses in radiotherapy).
- Identify plausible sources or pathways to exposure and exclusion of those less significant (e.g. cross-fire from non-target organs).
- Use historical dose records, including their validation and retrospective re-evaluation.
- Collect auxiliary data (e.g. equipment types, measurement protocols, workloads).
- Apply dose estimation and reconstruction methods, including data reliability, recalibration and uncertainty estimation.

Dosimetric support to epidemiological studies has three major objectives: first, to provide dose estimates with minimum bias for all cohort members and exposure sources; second, to provide uncertainty estimates for all doses; and third, to validate dose estimates by independent benchmarking exercises.

In spite of considerable work in these areas, there are several improvements and developments which need to be made and these are described in the following three challenges:

Improvements to dosimetric data

Most epidemiological studies on exposed cohorts (e.g. A-bomb survivors, Chernobyl and Techa River populations, medically irradiated patients) are retrospective and doses need to be evaluated *a posteriori*, often with sub-optimal data. Also, new dosimetric challenges arise when cohorts are pooled to increase statistical power, since this requires dose estimates from diverse global origins to be harmonised and risk estimates adjusted for dose uncertainties. Several lines of investigation are indicated as follows:

- In a particular retrospective study, doses to organs and tissues may be required which will not have been included in the original dose monitoring or assessment procedures. For example, in medical exposures, doses to the organs and tissues of interest may differ significantly from values estimated and recorded in the course of routine application of the respective medical procedures. Non-target absorbed doses in radiotherapy are also difficult to determine retrospectively from recorded doses. In personal monitoring, whole body dose is inadequate for the estimation of individual organ doses. To address these problems, dosimetric methodologies (e.g. MC transport calculations, biokinetic models, data aggregation), the recovery and use of available initial data and the reconstruction of missing information (e.g. workloads) should be combined and further elaborated.
- In many cases, the quality of the initial data for dose reconstruction requires improvement. For example, personal monitoring data may be improved by re-evaluation of historical records and 'recalibration' of the historical dosemeters using MC simulations. Further problems are associated with handling data from very large cohorts (e.g. tens of thousands), estimating doses over time frames within which exposure conditions may have changed, lack of key data, and dose measurements which may be below detection or recording levels. Software for dose estimation is currently specific to particular cohort studies and more flexible and adaptable

software is needed, particularly for use with very large data sets.
- The development of more realistic biokinetic and dosimetric models would be valuable. These include age- and gender-specific biokinetic models, new mesh-type computational phantoms, hybrid phantoms combining both voxel-based and simplified equation-based modelling approaches and the generation of hybrid computational phantom libraries for internal radiation dosimetry (see also vision 3 and the section on Computational Dosimetry).

Uncertainty estimation and dose validation

The estimation of dose uncertainties has previously used simplified analytical models. However, the recent development of stochastic risk models requires well-established dose uncertainty distributions, which can be used as input to MC risk calculation algorithms. Generally, improvements in uncertainty assessments are likely to enhance the confidence in derived dose–response functions and increase the statistical significance of the results obtained.

Validation of dose estimates by comparison with independent measurements will continue to be important but requires further development, building upon instrumental developments such as electron paramagnetic resonance (EPR) on tooth enamel and fluorescent *in situ* hybridisation (FISH) on circulating lymphocytes. The reduction of dose uncertainties in epidemiological studies is challenging. Systematic quantification and harmonisation of data uncertainties is first required, followed by an analysis of their influence on the results. Statistical methods should continue to be developed to account for the complex nature of errors in risk analyses, following initial successful applications in several studies.

Future epidemiological studies

Finally, it is important to anticipate future epidemiological studies. Although many such studies are retrospective in nature, the prerequisites for future studies may differ, for example in the investigation of health effects caused by novel technologies (e.g. ion beam radiotherapy). Detailed descriptions of doses, their estimation and the technologies used in each exposure scenario are needed to anticipate the data required, together with multidisciplinary development of expanded data registries. The emergence of molecular epidemiology requires new standardised dosimetry and scoring methods to support harmonisation of dosimetric practices.

VISION 3: TOWARDS EFFICIENT DOSE ASSESSMENT IN RADIOLOGICAL EMERGENCIES

Radiological emergencies are a major challenge in modern society. They include three distinct types of incidents:

- Those that have an impact on large geographical areas and lead to the exposure of large groups of the general population such as at Chernobyl and Fukushima.
- Accidents that involve industrial or medical radiation sources, usually involving a relatively small number of victims.
- Terrorist attacks which may involve radioactive materials, either in the form of radiological dispersal devices ('dirty bombs'), containing radioactive materials in addition to conventional explosives, or radiological exposure devices (sealed hidden sources).

Each of these incident types is associated with specific problems in determining radiation doses, identifying individuals who are at the highest risk and deciding the best method to be applied for evacuation, medical treatment and remediation. The dosimetric protocols and techniques employed will depend, in particular, on the number of victims and the severity of the exposure. As a first stage, triage is important, followed by more precise dose investigations of identified exposed individuals.

In most incidents, a quick, efficient and reliable estimate of doses to affected individuals or groups of individuals is a prerequisite for further decision-making by responsible authorities. Dose assessment is complicated by the fact that a number of concurrent exposure scenarios might be of concern, e.g. internal exposures from incorporated radionuclides together with external exposures from various sources. Real-time (environmental) monitoring (in the case of nuclear power plant accidents) or dose-rate measurements by various approaches (manually, stationary, car-borne, air-borne) is usually the first step in assessing doses to population groups and identifying critically exposed sub-groups. Due to the availability of affordable dose-rate metres for the public, citizen networks are becoming an increasingly relevant aspect in cases of public exposure.

Improvements are needed in the application of methods for individual dose measurement, enabling decision makers to reassure the 'worried-well' rapidly, to identify individuals with a high risk of developing radiation-induced injuries, and to initiate the most urgent actions, including methods of reducing doses after internal contamination. Incidents which have an impact on large geographical areas and populations require the handling and processing of a large number of samples in a short time, whereas for those