5th EUROPEAN RADIATION PROTECTION WEEK

BILLROTHHAUS, VIENNA, AUSTRIA

22–24 NOVEMBER 2021

Book of Abstracts

Organised by the European Alliance for Medical Radiation Protection Research (EURAMED)

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ERPW Invited Scientific Session I, November 22 09:15–11:15

The Importance of MEENAS in the European Radiation Protection Research and Innovation Scene

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Abstract

The six European radiation protection platforms embody the diversity and multidisciplinarity of the European radiation protection research community. Together we highly value integration and the expression of a common vision to ensure that radiation protection research and innovation maximally respond to the societal needs for radiation protection of human and environment. Therefore, MEENAS, the Consortium of European Radiation Protection Research Platforms, MELODI, EURADOS, EURAMED, NERIS, ALLIANCE and SHARE, was officially established by the undersigning of a MoU on 12 March 2020.

The broad objectives of MEENAS are to:

- Promote the integration and the efficiency of European R&D in radiation protection to better protect humans (public, patients and workers) and environment;
- Advance scientific excellence;
- Further develop and implement the joint R&D roadmap;
- Maintain and develop European research capacity;
- Encourage scientific education and training and foster key research infrastructures in the field of radiation protection; and
- Foster international collaboration and collaboration with sister organisations and networks in a non-exclusive manner by open interaction with the wider research community and stakeholders.

Moreover, by uniting the forces of the individual platforms, we intend to operate as a strong shared-voiced vehicle towards third parties, such as the European Commission (EC), and to enforce the position of radiation protection research in Europe and beyond.

We will shortly present the functioning of MEENAS, its foreseen tasks and future perspectives in shaping European radiation protection R&I. In this context, we will inform how the extended MEENAS group (MEENAS and representatives of several radiation protection institutions in close interaction with entire radiation protection community) prepared, following the EC recommendations, a robust radiation protection co-funded partnership vision document toward the establishment of a partnership for radiation protection research. The final document was transmitted to the European Commission (EC) on 8 January 2021 following a number of iterations with the EC and programme owners and managers (POMs) and platform members.

This vision document and the CONCERT joint roadmap form the basis of our radiation protection R&D community response to the HORIZON-EURATOM-2021-NRT-01-09 call (European Partnership for research in radiation protection and detection of ionising radiation). The involvement of MEENAS in the proposal writing will be explained and our engagement in the future project will be described.

MEENAS expert role as representative for European Radiation Protection R&I is recognised. We are invited to attend the High-Level European Nuclear Roundtable (HLENR) with Commissioner Mariya Gabriel where MEENAS will be able to present the stakes of European Radiation Protection R&I. We will communicate the highlights of that meeting and the (future) role of MEENAS within the HLENR.

ERPW Abstract Session A: Radioecology and Emergency Preparedness
November 22, 11:30–13:00

Modelling the Transfer of ^{137}Cs along a River–Sea Continuum and Application to Accidental Release Scenarios

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Abstract

Numerical models allowing to simulate the transfer of radionuclides at long distance in the environment must take into account the relevant interfaces where bio-physico-chemical processes can modify the fluxes exchanged between compartments. Estuaries are one of such hot spot area, as they can trap contaminated particles or release radionuclides from these particles through desorption. A box-model has been developed and applied to the Rhone River estuary (France) with field data in order to couple a river model (Casteaur) and a sea dispersion model (Sterne) to simulate the transfer of ^{137}Cs along this continuum. This model, also suitable for other estuaries, allows to evaluate the hydrodynamic conditions acting at the mouth (saltwedge into the estuary vs external plume on sea) and the freshwater/seawater mixing. It focuses on dissolved ^{137}Cs and take into account the possible desorption from particles, which is described in the estuary box-model with kinetic rates calibrated from adsorption/desorption experiment in laboratory. This experiment was designed to specifically study the influence of salinity and of the ageing effect. They particularly showed that desorption occurs above a salinity of 3 to 4, and that its importance increases inversely with the duration of the adsorption phase (ageing effect).

Such river-sea continuum modelling can be used to anticipate the dispersion of a ^{137}Cs release in case of accident at one of the nuclear installations along the river. For this, a statistical approach through fuzzy c-mean clustering of a 10 years series of river discharge and wind speed collected at the estuary was set up to explain the variability of the surface plume. The method allows to define 6 scenarios corresponding to the most usual occurrence of these two hydrodynamic forcing, which were used to simulate the extension and dilution of a release fixed at 1 TBq over a time window of 48 h.

Finally, databases reporting on biophysical and socio-economic environments for this area were collected and used to define sensitivity indicators. They were associated to 5 vulnerability classes relating to the impact of a radioactive contamination and aggregated to constitute a final sensitivity basemap. This map was confronted to the simulations of ^{137}Cs release under the 6 hydroclimatic scenarios, for which the seawater activities were converted into fish activities and separated into 4 classes partly based on regulatory limits for food contamination.
This work is in relation with the challenge 1 of the ALLIANCE SRA: predict human and wildlife exposure in a robust way by quantifying key processes that influence radionuclide transfers and exposure. It is linked to the national program ANR-AMORAD.

Spatial Clustering of Contaminated Agricultural Parcels for Efficient Remediation in a Post-Accident Situation

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Abstract

Nuclear accidents may affect large areas through deposition of radionuclides as Caesium-137 and Strontium-90. Given the limited availability of technical capabilities and financial resources, setting priorities of where, how and when to remediate is indispensable. Priority setting is particularly applicable when large agricultural areas and the related food systems are affected whereby the ambition is to return to normalcy as effectively, sustainably, efficiently and rapidly as possible. Multi-criteria decision aiding is a sub-discipline of Operations Research (OR), which is fit for dealing with a wide range of possibly conflicting criteria that are relevant to rank agricultural parcels and remediation technologies according to the urgency of and fitness for remediation. Both questions 'On which parcel to act first?' and 'How to act on a given parcel?' can be addressed sequentially, e.g., by the analytic hierarchy process (AHP), Compromise Programming (CP) or outranking methods like PROMETHEE and ELECTRE. The result is a patchwork of parcels, each with a priority rank for remediation and with a recommended remediation technique. Whereas the resulting recommendations are optimal from an individual parcel's perspective, their practical execution may be hampered by the spatial heterogeneity both with regard to parcels' priorities for remediation and the remediation technique. In this paper we propose a spatial clustering approach to post-process the patchwork of standalone parcels each with its optimal remediation technique into a spatially generalised patchwork which would be more efficient and feasible to remediate. In the approach, CP is used to obtain a priority score for each parcel and each remedial action per parcel. These scores are then combined based on the principles of Region Growing, whereby the stopping criterion for the region growth is based on a maximum allowed deviation of additional parcel score compared to the initial parcel off the cluster. The resulting proposed remediation scheme consists of groups of contiguous or nearby parcels with one single remediation approach. Whereas the resulting solution is suboptimal for individual parcels, from the overall regional perspective it is expected to improve the feasibility of the remediation campaign. We illustrate the approach for a part of the area, consisting of 223 parcels, affected by a hypothetical accident in the Tihange NPP, Belgium. The original patchwork, the most optimal from an individual perspective, consists of 223 uniquely ranked parcels for which 4 remediation techniques are recommended. Compared to the most feasible approach, 1 remediation cluster for the whole region, the post-processed configuration with 13 clusters and 2 remediation techniques improves the overall optimality with 63.0%. While the overall remediation efficient is slightly lower, compared to the original patchwork, great reduction in costs and increase in efficiency can be expected.

The Ecotoxicology of Tritium: Effects on Fish Using Several Endpoints, from Molecule to Individual Responses

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Abstract

Ecosystems are naturally exposed to ionizing radiations. To this natural exposure are added releases in the environment from anthropic activities related to the controlled or accidental releases from the nuclear energy cycle industries. Tritium, a low-energy beta emitter, is one of the radionuclides released during the normal operation of nuclear power plants and nuclear reprocessing plants. It is mainly released in the form of tritiated water (HTO) and integrates into the water cycle, which makes it particularly mobile within ecosystems. Studies conducted using high dose rates have highlighted the developmental and reprotoxic effects of tritium on aquatic vertebrates. However, few focused on molecular/cellular effects. It has been recently proposed that dose rates lower than 10 µGy/h can be acceptable for the protection of ecosystems towards radioactive substances. The application of such benchmark values to tritium is still under debate due to its potential difference in biological effectiveness relative to gamma irradiation.

In this context, this work aimed to characterize the impacts of tritiated water on fish health, as well as its mode of action. Studies focused on the embryo-larval stages of the zebrafish, Danio rerio, and on adults of the fathead minnow, Pimephales promelas. Those species were chosen in order to determine if effects on a model species like zebrafish could be extrapolated to an autochthonous species like fathead minnow. A battery of biological markers of immunotoxicity (ROS production, lysosomal membrane integrity, phagocytosis activity), genotoxicity (DNA damages, gamma-H2AX activity, micronucleus frequency), neurotoxicity (acetylcholinesterase) and oxidative stress (catalase, SOD) was used, as well as measurement of expression of genes involved in these mechanisms, histology of tissues and measurements at the individual level (growth, development, behaviour) were used. Zebrafish were exposed, in the laboratory, to tritium (HTO) at dose rates of 30, 130 and 1300 µGy/h. At the molecular level, a transcriptomic analysis showed the modulation of genes involved in muscle contraction for 24hpf eggs. Analyses from tissular to individual levels showed muscle fiber alterations in 96hpf larvae for all dose rates, and this led to a decrease in swimming velocity after exposure to 130 µGy/h. Fathead minnows were exposed to tritium during 60 days in field and laboratory studies (up to 0,15 and up to 0,65 µGy/h, respectively). These dose rates were established based on the highest concentration of HTO measured at an upwelling on one water body in CNL site in Canada (180 kBq/L). Tritium effects were discriminated from field confounding factors using multivariate analyses. No effects were observed on survival and fish condition for both experiments. However, field and laboratory tritium exposure increased DNA damage and stimulated the responses of the immune and neural systems, revealing that mode of action of tritium was similar under the conditions of both the field and the laboratory studies. These markers can therefore be considered as relevant for studying tritium effects in fish.

On the basis of these results, zebrafish seemed less sensitive to tritium than fathead minnows, as higher dose rates of tritium were necessary to observe similar effects on zebrafish larvae.

Ionizing Radiation, Genotoxic Stress, and Mitochondrial DNA Copy-Number Variation in Caenorhabditis Elegans: Droplet Digital PCR Analysis

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Abstract

Mitochondria are considered vulnerable targets to the effects of ionizing radiation and particularly damage to mitochondrial DNA (mtDNA) has been shown to be more extensive and to persist longer than damage to nuclear DNA (nDNA). Moreover, variation in mtDNA copy number has been proposed as a marker for mitochondrial dysfunction in response to ionizing radiation. In the current study, we developed a high precision and sensitive duplex droplet digital PCR (ddPCR) method for the quantification of the mtDNA/nDNA ratio in the model organism Caenorhabditis elegans. The effect on this ratio after chronic gamma irradiation was investigated at a wide range of doses (0.03 to 72 Gy), in order to identify the dose level of effect. For this purpose, five mitochondrial targets and two nuclear reference genes were amplified pairwise in duplex PCR format (one mitochondrial and one nuclear target per PCR reaction) by both ddPCR and quantitative PCR (qPCR). The results showed that ddPCR but not qPCR enabled detection of a significant increase in the mtDNA copy number (1.6 ± 0.1-fold) for nematodes exposed to high doses (≥24 Gy). Thus, ddPCR provided higher precision measurements compared to qPCR and was more sensitive for the detection of the variation in mtDNA copy number. The ddPCR analysis also showed that chronic exposure of C. elegans to ionizing radiation affected the mtDNA copy number with a Hill type dose-dependent increase and predicted a dose threshold of effect at 10.3±1 Gy. This strongly suggests that chronic genotoxic stress modulates a response on mtDNA replication. In conclusion, the established duplex ddPCR method represents a novel high precision and sensitive tool for the determination of mitochondrial DNA copy number variation and function in C. elegans.

Reference

Maremonti, E., Brede, D. A., Olsen, A. K., Eide, D. M., & Berg, E. S. (2020). Ionizing radiation, genotoxic stress, and mitochondrial DNA copy-number variation in Caenorhabditis elegans: droplet digital PCR analysis. Mutation Research/Genetic Toxicology and Environmental Mutagenesis, 858, 503277.

Training Researchers in Operational Radiation Protection: An Opportunity for Dialogue and Optimization

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Abstract

Introduction: As a general requirement, according to 2013/59/Euratom, workers exposed to sources of ionizing radiation need to be informed and trained about the associated health risks, radiation protection procedures, precautions, etc.

Despite their high level of education in sciences related to nuclear, researchers working with ionizing radiation are not exempted from this requirement.

Although the main goal of this regulation is to learn about the practical implementation of the basic fundamentals of radiation protection, this learning moment could in this case also offer the occasion to both trainer and trainee for a better understanding and integration of each party's experience and expertise.

Challenges: For both trainer and trainee it poses a challenge to translate the fundamental principles of radiation protection into practical guidelines for the research work floor, especially in case of a research environment where next to routine protocols very often "ad-hoc" handlings and temporary installations are used. It is of utmost importance that workers can reflect, together with the Radiation Protection Officer and Expert, about optimizing their conduct and practices.

Opportunity for dialogue and optimization: During these training sessions, radiation researchers learn about the overall system of radiation protection and its practical implementation. As this system is based on decades of radiation research, it allows them to better comprehend the impact of their research. Broadening their view on applications of ionizing radiation and the system of protection might also inspire them to identify new challenges and opportunities and set research priorities. Given their in-depth knowledge, and with the necessary didactic skills, radiation researchers might also be ideal candidates to act as trainers in topics related to radiation protection. This presentation will highlight the opportunities for both trainer and trainee when training researchers in radiation protection.

Radiation Protection and Climate Change: How Do the Dose Response Models Influence the Choices of Solutions to Mitigate Climate Problems

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Abstract

It has become more apparent, even for the most sceptical, that the climate change is real and does present a serious challenge for our infrastructure and our ways of life. Science has also reached a rather broad consensus that one way to mitigate the climate change means to reduce the CO_2 footprint of our society. As nobody is really willing to return to a pre-industrial era (and this would not help much, anyway) and our need for energy production increases, some very serious decisions have to be taken regarding on the ways in which we generate energy. Fossil fuels are by far the most polluting (and not only with CO_2) so this basically leaves us with three main choices: nuclear, hydro and renewables.

Some countries show an extremely strong opposition to nuclear, bordering the irrational, and we are trying to understand why. The obvious answer is the low understanding about how nuclear industry works, what are the safety standards and, most of all, of the real effects of radiation on the human health.

The model used right now for all risk estimations and thus for communicating with the public is the LNT model. Besides the fact that, by now, there is an important body of evidence that suggest that this model is highly inaccurate, the message conveyed by this model is quite threatening for the general public: Every dose carries a risk. The presentation explores the way in which the perception of risk generated by the LNT gives shapes the public response to nuclear energy production. A short study across various media seems to indicate a wide overestimation of the dangers posed by the nuclear industry, a low knowledge of the real environmental impact of the renewables and the underestimation of the risk that a nuclear phase out will pose for the environment The work also presents some ideas about lines of communication with the public in such a way that people will have a better understanding of the real dangers of the nuclear industry (rather that over- or underestimate them) and how does the CO_2 footprint of a nuclear power plant compares to the CO_2 footprint of wind turbines and the solar panels.

Identification and Prioritisation of ALLIANCE SRA Topics Relevant to Medical Radiation Protection Research

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Abstract

The goal of the EURAMED Rocc-n-Roll project (H2020 Euratom) is to propose an integrated and coordinated European approach to research and innovation in medical applications of ionising radiation and related radiation protection, based on stakeholder consensus and existing research agendas and related activities. As part of this, a panel of ALLIANCE members was appointed to identify and prioritise research topics worth being addressed from the ALLIANCE perspective, focussing on aspects of ALLIANCE that can link to the EURAMED SRA.

The panel performed a review and discussion of relevant topics considering different stages of radionuclides application in medicine from radionuclides sourcing, radiopharmaceuticals manufacturing and application to environmental fate. The six topics identified include a compilation and data gap identification of transfer parameter values, studies on the speciation of medical radionuclides and compounds formed in the environment, methods to address data gaps in assessment model parameters, identification and systematic description of environmental exposure pathways for people and environment and cases for demonstration of dose assessment procedures involving medical facilities for the general public and wildlife. The research topics hereby listed were ranked according to relevance, with additional feedback from members of the Alliance SRA Working Group.

The outcome of this exercise will be combined with a similar effort from the NERIS platform, enabling an identification and prioritisation of research within the framework of linking the strategic agendas of ALLIANCE, NERIS and EURAMED. This prioritisation must include not only the level of dose but also the need to demonstrate protection of man and environment in existing and unplanned exposures, especially for pathways that remain uncommon in current radiological impact assessments.

ERPW Abstract Session B: Dosimetry in the Medical Context
November 22, 11:30–13:00

MEDIRAD - Implications of Medical Low-Dose Exposure

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Abstract

The MEDIRAD project, which started in 2017, is nearing completion. It aimed to enhance the scientific bases and clinical practice of radiation protection (RP) in the medical field and addressed the need to better understand and evaluate the health effects of low-dose ionising radiation (IR) exposure from diagnostic and therapeutic imaging and from off-target effects in radiotherapy (RT). MEDIRAD pursued 3 major operational objectives:

- To improve organ dose estimation and registration to inform clinical practice, optimise doses, set recommendations and provide adequate dosimetry for clinical-epidemiological studies of effects resulting from exposures to IR in medicine;
- To evaluate and understand the effects of medical exposures, focusing on two major endpoints of public health relevance: cardiovascular effects of low to moderate doses of radiation from RT in breast cancer treatment including understanding of mechanisms, and long-term carcinogenic effects of low doses from CT in children;
- To develop science-based consensus recommendations for the effective protection of patients, workers and the general public.

This talk will present the key results of the MEDIRAD project, in particular related to dosimetry for CT, and nuclear medicine and cardiovascular impacts of radiotherapy, and provide an overview of the recommendations, which are currently being prepared by the project consortium on the following topics:

- Recommendation 1 (RECO#1): Standardized European procedures for consolidating patient data repositories;
- Recommendation 2 (RECO#2): Further optimisation of ionising radiation-based medical protocols for diagnostics or therapy;
- Recommendation 3 (RECO#3): Further optimisation of radiation protection for patients and medical workers;
- Recommendation 4 (RECO#4): Future research and development priorities.

Acknowledgment
This project has received funding from the Euratom Research and Training Programme 2014–2018 under grant agreement No 755523.

ICRP Approach to Determining Reference Organ and Effective Dose Coefficients for Common X Ray Imaging Examinations

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Abstract

Coefficients between absorbed or equivalent dose to organs at risk and measurable quantities commonly used in X ray imaging procedures have been calculated using Monte Carlo methods for the last 40 years. However, there is no standard reference methodology and consequently many different approaches are used. Most studies have used older style hermaphrodite phantoms as the basis for calculation.

For many years, the ICRP has produced reference dose coefficients for common diagnostic nuclear medicine procedures. The ICRP has now established a Task Group (TG113) to provide reference dose coefficients for radiographic, CT and fluoroscopic X ray imaging procedures. The Task Group is mandated to define and perform Monte Carlo radiation transport simulations on a series of reference imaging examinations and to report the resulting organ absorbed dose and effective dose coefficients.

The scope of this work includes the use of the reference voxel computational phantoms of the ICRP, male and female new-born, 1-year-old, 5-year-old, 10-year-old, 15-year-old, and adult. The work of the Task Group will lead to a series of publications covering adult and paediatric organ and effective dose coefficients within well-defined imaging protocols in radiography and paediatric diagnostic fluoroscopy. Moreover, it will allow for organ dosimetry to be performed in computed tomography for various CT devices. The Task Group has a similar aim for fluoroscopically guided interventional (FGI) procedures, although the complexity of FGI calls for innovative solutions.

To date the Task Group has defined reference projections and performed Monte Carlo simulations for radiographic examinations and has developed a methodology for CT examinations, including automatic tube current modulation. Work on FGI is at an early stage. In this presentation we will review our methodology for radiography and CT and describe how we intend to disseminate the work. We will briefly describe the issues and proposed approach in FGI.

Effectiveness of Five Radioprotective Devices for Staff during Fluoroscopically Guided Procedures: Recommendations from the MEDIRAD Project

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Abstract

Background: During fluoroscopically-guided procedures, staff is exposed to low doses of ionising radiations on a daily basis, eventually resulting in high doses throughout a complete career. Several radioprotective (RP) devices exist; however, their performance can widely vary and is challenging to assess in specific conditions of use.

Purpose: To provide recommendations for evidence-based selection of RP devices, the effectiveness of lead(-free) caps, lead-free aprons, lead(-free) drapes, masks and the zero-gravity suspended system was investigated.

Materials and method: The effectiveness was investigated by means of Monte Carlo (MC) simulations. Numerous irradiation configurations, including beam projections and staff distance from the source, were modelled and different device compositions and designs were considered where applicable. Validation was performed through ad hoc measurements on staff and/or phantoms. Depending on the device, the clinical measurement included from a few tens of procedures up to over 600 while phantom measurements included three common and/or concerning configurations.

Results: According to MC results, a lead(-free) cap could reduce the brain dose by 35% on average. The masks could be more effective (65% average reduction to the brain for the best model) and also protect the eye (25%). However, the irradiation conditions had a strong influence as both devices could become nearly ineffective in specific configurations, particularly when the staff was closer to the X-ray field. Besides, some sensitive brain regions were always left unprotected. Phantom measurements corroborated the results, although with lower effectiveness figures.
The drapes over the patient, whether composed of lead or lead-free material, could significantly decrease the dose to the hands (from MC results: 62% and 30% to the left and right hands on average, respectively) if they were positioned directly above it. No noticeable effect was observed for other organs. Some clinical measurements, however, also showed considerable dose reduction (~50%) to the eye lens which were not predicted by MC results or phantom measurements.
There was no significant difference between the effectiveness of lead and lead-free aprons to protect the organs in the chest region as resulted from the MC and clinical studies.
Of all the devices, the zero-gravity system offered the highest protection to the brain and eye lens according to MC, phantom and clinical results (at least 95%, 66% and 78% on average, respectively), and a protection level comparable to the lead apron for the organs normally covered.

Conclusions: All tested devices showed potential for dose reduction to specific organs. However, the effectiveness of the caps, the masks and the drapes strongly depends on the design, exposure conditions and staff position. In adverse exposure conditions, these devices can become ineffective. Increased independent testing of RP devices, with reference to typical and realistic conditions of use, would therefore be of great help to the staff for selecting such devices. The recommendations derived from the study are being disseminated to the relevant European stakeholders.

Funding
The MEDIRAD project has received funding from the Euratom Research and Training Programme 2014–2018 under grant agreement No 755523.

The Translational Challenge for Medical Radiation Applications and Protection Research: Methodological Approach and Preliminary Results

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Abstract

Background: There have been several translational challenges acknowledged for medical applications of ionising radiation over the years including financial barriers, scarcity of resources, and insufficient access to data; however, these translational bottlenecks have been primarily reported on an ad hoc and study specific basis. Task 5.1 of the EURAMED Rocc-n-Roll project aims to establish a set of consensus statements highlighting the key challenges to clinical translation of medical radiation applications and related radiation protection research.

Methodology: A Delphi methodology has been employed to gain consensus. In the first Delphi round a multidisciplinary panel of 20 individuals was tasked with generating a wide range of statements regarding radiation-specific barriers to translation. Statement prompts were derived from a preliminary literature search and organised across four broad categories: Basic Research, Commercial Development, Clinical Implementation, and Education and Training. Following consolidation, review, and refinement of submissions, 127 unique statements were carried forward.

The second Delphi round drew upon the EURAMED Rocc-n-Roll consortium network alongside the input of eleven prominent international organisations to nominate a broader panel of 130 subject matter experts across all areas of radiation protection research (radiology, nuclear medicine, and radiotherapy). Nominated individuals were asked to rate the extent to which they agreed (or disagreed) with each generated statement as a key translational challenge for radiological research. A SurveyMonkey® collection form was distributed to record respondents' evaluations via 6-point Likert Scale (1 = Strongly Disagree, 2 = Disagree, 3 = Somewhat Disagree, 4 = Somewhat Agree, 5 = Agree, 6 = Strongly Agree). Consensus was defined as median ≥4 with ≥60% of responses in the upper tertile of the scale (i.e., Agree / Strongly Agree). Statements which achieved consensus were progressed forward to a third Delphi round. Additionally, statements on the verge of consensus were further reviewed by the core research team with regard for both the literature and under-represented research areas for inclusion in round three.

Results: Consensus was reached for sixty-one statements following two Delphi rounds. The statements with the strongest agreement from each section were:

- "Robust and efficient database structures that facilitate research across different repositories / platforms through secure data storage and information exchange are needed" (Basic Research; 88.60% (n = 101) Agree or Strongly).

- "Quality assurance is a big challenge for AI based applications, especially with respect to meaningful testing and understanding / evaluating limitations" (Clinical Implementation: 84.26% (n = 91) Agree or Strongly Agree).
- "There is a need for multidisciplinary approaches to education and training that incorporate a team of educators with radiation protection expertise from a range of professions/disciplines" (Education & Training; 83.93% (n = 94) Agree or Strongly Agree).
- "Quality Assurance and Quality Control, with respect to radiation protection principles (justification, optimisation) and other regulatory requirements, need to be better foreseen during the development of novel techniques/technologies and developers must have regard for the accessibility of necessary machine and/or software parts required by the end user to perform QA/QC testing" (Commercial Development; 73.96% (n = 71) Agree or Strongly Agree).

A third Delphi round is currently ongoing, and the final set of core translational challenges disseminated to inform the development of an innovation transfer roadmap.

Conclusion: The final consensus document, arising from task 5.1 of the EURAMED Rocc-n-Roll project, will: identify the key challenges to clinical translation of medical radiation applications and related radiation protection research; facilitate the development of a framework to address these challenges; and inform the implementation of future research and development work.

Inter- and Intra-Individual Variability of Gamma-H2AX in Healthy Volunteers and Clinical Radiotherapy Patients

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Abstract

The gamma-H2AX assay has the potential to be a useful triage tool during large scale radiation accidents or incidents to help identify critically exposed individuals and reassure the worried-well. However, it is important to understand the extent of the inter- and intra-individual variability and consider how these impact dose estimations. Knowing background frequencies of gamma-H2AX foci within a healthy, non-exposed control population is important to determine minimum detectable doses and quantify associated uncertainties. Similarly, inter- and intra-individual variation in the yields and kinetics of radiation-induced gamma-H2AX foci must be considered as important modifiers for uncertainties associated with dose estimations in all scenarios.

339 samples from 32 healthy donors of working age were analysed to determine spontaneous and ex vivo X ray-induced foci yields following exposure to X rays of 0–1 Gy, at 1 and 24 hour post-exposure. Under the US CMCR funded RTGene project, peripheral blood samples were taken with ethical approval and informed consent from a total of 20 patients undergoing external beam radiotherapy for breast, lung, gastrointestinal or genitourinary tumours, and analysed for gamma-H2AX foci just prior to the first fraction, at 11–102 minutes and approximately 24 hours post the first exposure fraction, just prior to the 5th or 6th fraction (between 4 and 9 days post exposure), and just prior to the penultimate fraction (between 17 and 37 days post exposure). Doses were estimated using a previously published bi-exponential model of gamma-H2AX foci repair kinetics, to test this model in vivo, and the data were compared to previously published dose estimated using the dicentric chromosome aberration assay and through modelling the exposed fraction of blood. For healthy normal controls, smoking status, gender and age had no significant effect on spontaneous or radiation-induced gamma-H2AX foci in this small cohort. Residual gamma-H2AX foci following ex vivo radiation exposure were a function of both dose and time (both $p < 0.001$), but not the individual donor, with similar levels of intra- and inter-individual variability observed among these healthy donors.

For the radiotherapy patients, while the doses estimated from the baseline gamma-H2AX foci yields did not vary on an interpatient basis, significant variation in both foci yields and doses estimated using the bi-exponential model was identified. As expected, time of sampling was crucial for dose estimation. However, the previously published bi-exponential model assumes a continued low level of repair in time at a level which was not seen with the radiotherapy patients. As such, this method of dose estimation was not validated in vivo.

We conclude that genetic or environmental factors do not appear to significantly modify baseline and radiation-induced gamma-H2AX foci yields in healthy adult donors. The identified range of variation will be used to refine uncertainties associated with gamma-H2AX-based dose estimations for accidental exposure scenarios. For radiotherapy patients, given the level of interindividual variation in

response between irradiated patients even after the first radiotherapy fraction, the gamma-H2AX assay is not currently recommended for further research in clinical exposure scenarios.

Extremity and Whole-Body Dose Monitoring of Staff with Thermoluminescent and Real-Time Detectors during Treatments of Neuroendocrine Tumours with ^{177}Lu-Dotatate (Luthatera)

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Abstract

Introduction: Luthathera® (^{177}Lu-DOTATATE) is widely used in the treatment of neuroendocrine tumours (NET). Due to its novelty, procedures are not fully standardized, which may result in higher doses to the staff. In addition, ring and wrist dosimeters, typically used in routine practice, often underestimate the maximum dose obtained on the hands and thus require the application of a correction factor. In this work, the Nuclear Medicine staff at our hospital manipulating ^{177}Lu has been monitored with real-time detectors and thermoluminescent dosimeters (TLDs). This work is associated with the SINFONIA project (funded by the EURATOM 2019–2020 research and training programme under the GA No.945196).

Materials and methods: Luthathera (7400 MBq/session) is administered by one physician and one nurse using the gravity infusion method. Extremity dose monitoring was performed during four sessions to the physician with two sets of dosimeters. One set containing five TLDs (MTS-N (LiF:Mg,Ti)) for each hand enabling dose mapping, provided and analyzed by the Belgian Nuclear Research Centre (SCK CEN). The other set containing the official personal ring and wrist TLDs (DXT-RAD (LiF:Mg,Cu,P)) commonly used for clinical risk appraisal by the Spanish National Dosimetry Center (CND), worn on the dominant hand. For real-time monitoring, they were both monitored with a whole-body Tracerco™ personal electronic dosimeter (PED), located at chest level, below the lead apron when worn. This was done for five sessions, the first two without and the last three with a lead apron.

Results and discussion: The TLD set measured 23.7 mSv at the physician's index fingertip for four sessions, 106 mSv at the middle fingertip, and 114 mSv at the ring finger base of the non-dominant hand (left). In his dominant hand (right) the recorded doses were lower, 2.2 mSv at the ring finger base, 4.9 and 5.2 mSv at the tip and base of the middle finger, and 13.7 mSv at the thumb fingertip. In contrast, the CND detectors showed background readings (<0.2 mSv) for the ring, and 0.1 mSv for the wrist dosimeter. This difference can be attributed to the filter cap (3.3 mg/cm thick polycarbonate lens) in ring detectors and to the wrist distance in the other case.
With PEDs, the highest dose rates were recorded during the administration, and the second-highest during the vial exploitation. Physician's mean whole-body doses vary from 10 µSv (no lead apron) to 5 µSv (with lead apron) and the maximum dose rates from 253 µSv/h (no lead apron) to 77 µSv/h (with lead apron). For the nurse, from 23 µSv to 6 µSv and from 376 µSv/h to 142 µSv/h, respectively.

Conclusions: The comparison between CND dosimeters and the dose mapping TLDs shows that the former underestimate finger doses, so their use requires placing them at the most exposed sites. There is room for further optimization at the administration process and vial exploitation if further dose reduction is needed. Besides, using a lead apron reduces the staff doses when manipulating ^{177}Lu, so it is strongly recommended. Nevertheless, more dose monitoring is needed to conclude whether dose limits can be exceeded by performing these treatments more frequently.

Assessment of Blind Scan in Chest CT Examinations

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Abstract

Introduction: As CT is a high dose modality, it has been the subject of many research and optimization studies. Dose outliers and diagnostic reference levels have been thoroughly investigated, as they involve a legal aspect. The extended functionalities of dose management software (DMS) could help to address also other types of quality aspects. In this study, the blind scan in chest CT was investigated. Blind scan is the scanned area that extends outside the localizer borders. In this area no information about the attenuation is available to the scanner, so the tube current modulation (TCM) is not applied in the optimal way.

Method: The chest CT exams of two years (810 inspiration, 865 expiration series) were extracted from the dose management software DOSE (Qaelum, Belgium). The software automatically calculates potential blind scan. This was extracted together with the patient size in terms of water equivalent diameter (WED), scan length and CTDIvol. In order to evaluate the impact of the blind scan on the TCM and the thyroid dose, simulations with an integrated dosimetric tool were performed; first, a theoretical standard chest CT was simulated (no thyroid included). A second simulation was done with the median scan length of the dataset and partially irradiating the thyroid (1/3 of thyroid). Finally, a simulation with the thyroid completely included in the scan range was performed. All settings were simulated both with and without TCM.

Results: The median WED was 27 cm (range: 16–39 cm) and median CTDIvol was 8.3 mGy (range: 2.7–26.1 mGy). The CTDIvol correlated with the WED (Spearman r = 0.82). The scan length ranged from 31–54 cm, with a median of 40 cm. It was observed that in most cases part of the thyroid was included in the scan length.

In 23% of the series, there was blind scan towards the patient's neck, with a median length of 1.4 cm, ranging from 0.1–6.6 cm. In 14% of the cases, the blind scan was more than 3cm, for five series it was equal to or more than 5 cm.

When TCM was used in the simulations, the thyroid dose increased with 13% for partial thyroid irradiation and with 107% for full irradiation, compared to the theoretical standard chest CT. When TCM was not used, the corresponding dose comparisons showed an increase of 49% for partial irradiation and more than 600% for full irradiation.

These findings not only highlight the need to spare the thyroid in chest CT but also show the importance of TCM when used optimally. This function would be compromised in case of blind scan in the neck area, as the TCM would not be properly adjusted to the less dense neck region that follows the highly attenuating shoulder region.

Conclusion: Scanning "blindly" rather than repeating a localizer may have a significant impact on the TCM and therefore on the dose of radiosensitive structures, like the thyroid. Having an advanced dose management system that identifies these cases in a large scale can help to optimize the technique and create dose awareness to the personnel.

ERPW Invited Scientific Session II: Challenges in Research on Individual Radiosensitivity and Susceptibility
November 23, 09:00–10:30

Radiation-Induced Nucleoshuttling of the ATM Protein and the Differences between Radiosensitivity and Radiosusceptibility

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Abstract

The evaluation of the radiation-induced (RI) risks is of medical, scientific and societal interest. However, despite considerable efforts, there is still neither consensual and unified mechanistic models nor predictive assays for describing the three major RI effects, namely radiosensitivity, radiosusceptibility and radiodegeneration. The ATM protein is a major stress response factor that appears upstream most of pathways involved in the three precited RI effects. The rate of the RI ATM nucleoshuttling (RIANS) was shown to be a good predictor of radiosensitivity at high doses and notably after radiotherapy. It also provides a relevant explanation of the linear-quadratic model that links cell survival as a function of radiation dose. More recently, the hyper-radiosensitivity to low dose, the hormesis and the adaptive response phenomena may be also explained by the RIANS model. In the frame of the RIANS model, irradiation induce the monomerization of the cytoplasmic ATM dimers and the diffusion of ATM monomers in nucleus. The resulting nuclear ATM monomers trigger the recognition of DNA double-strand breaks and their repair. In the case of delayed RIANS, DSB can be repair by other pathways than non-homologous end-joining, which may increase the risk of misrepair, cell transformation and cancer. Hence, we will discuss, about a new classification of genetic syndromes based on the RIANS model that would separate the evaluation of radiosensitivity on one hand and the radiosusceptibility on another hand. Interestingly, our conclusions stress the fact that a given tissue may be associated with both radiosensitivity and radiosusceptibility, or else radiosensitivity and radiodegeneration but not radiosusceptibility and radiodegeneration. Our quest for reliable and specific biomarkers should take into account these observations.

ERPW Abstract Session C: Low-Dose Research
November 23, 10:45–12:15

Bone-Marrow-Derived Extracellular Vesicles Influence Radiation-Induced Leukemogenesis

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Abstract

Introduction: Haematological malignancies are considered the main long-term consequences of bone marrow (BM) irradiation. Ionizing radiation (IR) damages the stem and progenitor cells and alters signalling between the stem cell compartment and the BM stroma. The main objective of our work was to investigate extracellular vesicles (EVs)-mediated IR effects on leukaemogenesis after low and high dose irradiation and to study possible underlying mechanisms using an in vivo murine model.

Methodology: Leukaemia incidence was followed in the CBA mouse model either irradiated or treated with EVs isolated from the BM supernatant of irradiated mice or subjected to both irradiation and EV treatment. Changes in leukaemia and inflammation-related gene expression, local and systemic oxidative stress, EV-uptake pattern in the bone marrow were also investigated.

Results and discussion: Compared to spontaneous acute myeloid leukaemia (AML) incidence (1–2%), high dose (3 Gy) irradiation increased the incidence to 19%. EV treatment resulted in 4.5–6% leukaemia incidence with no significant difference between mice treated with EVs isolated from irradiated or non-irradiated animals. The combination of irradiation and EV treatment had an additive effect. Myeloid leukemias had two distinct phenotypes: a classical myeloblastic phenotype with a quick deterioration of the health status of the mice and increased bone marrow infiltration with myeloid blasts and a myelomonocytic phenotype with a slow clinical progression resembling to human chronic myeloid leukemias. Interestingly, EV treatment had a significant impact on leukaemia phenotype. While acute myeloblastic leukaemia comprised approx. 25% of all AML in mice treated with irradiation, this fraction increased to above 60% in mice treated with the combination of irradiation and EV injection.

Apart of myeloid leukemias, lymphoid malignancies were also noted after irradiation and their incidence increased with the dose. Though, in contrary to myeloid leukemias, treatment of mice with extracellular vesicles did not increase the incidence of the disease.

Conclusion: We showed that EVs influenced both the incidence and the phenotype of radiation-induced myeloid leukaemias but not of lymphoid ones. Our results also highlight the role of intercellular signalling mechanisms in radiation-induced leukemogenesis.

Funding
Euratom Research and Training Programme 2014–2018 under grant agreement No 662287 (CONCERT)

Concurrent Live-Cell Imaging of DNA Double-Strand Break Repair and Its Cell-Cycle Status: From Cells to Animal Models

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Abstract

Due to environmental factors such as ionizing radiation and genotoxic chemicals, or endogenous steady-state metabolism, cells are exposed to a large number of DNA damage (hereafter genomic stresses) every day. These genomic stresses trigger recovery from the injury, cell death, and cellular senescence. Thus, the response to such genomic stresses plays an important role in ensuring sustainability of cells. In order to understand and predict the ability of tissues to maintain a steady-state homeostasis in response to the injury at the tissue levels, we are developing quantitative and multi-use technologies for spatiotemporal evaluation of the stress responses.

Among genomic stresses, DNA double-strand breaks (DSBs) are the most severe one, and if they are not repaired correctly, genetic mutations and/or loss of function might occur. A critical early response to DSBs is cell-cycle arrest, which gives an opportunity for the repair response. In a challenge for establishing real-time and quantitative analysis of cell fate triggered by DSBs, we cloned the foci-forming element of mouse 53BP1, one of the DSB repair proteins, and generated a fusion gene connected with a fluorescent protein. We further combined the fluorescent fusion gene with two other fluorescent genes expressing two different cell-cycle indicators (a part of hGmnn and hCdt1) to construct a tricistronic vector, which we named Focicle (Otsuka and Tomita. Sci Rep, 2018). By genome editing using CRISPR/Cas9, we knocked in the Focicle gene into the mouse ROSA26 region, then created a cellular model that allows quantitative live-cell imaging of cell cycle-dependent genomic stress. By time-lapse imaging of a cultured cell line transfected with the Focicle gene, we observed dose-dependent induction and extinction of DSB foci upon irradiation. Also, we found S-phase specific foci induction, suggesting that replication stress in steady-state homeostasis can be evaluated with this technique as well as the evaluation of DNA repair.

Furthermore, to achieve imaging of genomic stress in whole-tissue in mouse, we have succeeded in establishing a new mouse strain, the Focicle mouse, capable of live-cell imaging by knock-in the Focicle gene into fertilized mouse eggs by CRISPR/Cas9. We will introduce an example of organ imaging using this unique animal model and discuss its future application.

Dose Responses for Mortality from Cerebrovascular and Heart Diseases in Atomic Bomb Survivors: 1950–2003

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Abstract

We analyzed the latest publically available Life Span Study (LSS) data for the detrimental health outcome of cerebrovascular diseases (CeVD) and heart diseases. The cohort comprises 86611 Japanese atomic bomb survivors. In the primary analysis (Shimizu et al. 2010), these data were analyzed using a stratified baseline model combined with the LNT model and quadratic, linear-quadratic and linear-threshold models as excess relative risk (ERR) models. Their main results were based on the LNT model. In the present analysis, a larger series of radio-biologically motivated nonlinear dose-response models were applied to the data in combination with a parametric baseline model either as ERR or EAR (excess absolute risk) models. The models were weighted according to their quality of fit using a multi-model inference (MMI) method. It was found that for CeVD, the dose–response curve from MMI is located below the linear no-threshold model at low and medium doses (0–1.4 Gy). At higher doses MMI predicts a higher risk compared to the LNT model. A sublinear dose–response was also found for heart diseases (0–3 Gy). The analyses provide no conclusive answer to the question whether there is a radiation risk below 0.75 Gy for CeVD and 2.6 Gy for heart diseases. MMI suggests that the dose–response curves for CeVD and heart diseases in the Lifespan Study are sublinear at low and moderate doses. The present study used a comprehensive and flexible approach by analyzing the data with a variety of different linear and nonlinear models including those that exhibit flexible threshold-doses without applying artificial cut-points at certain doses and without relying on LNT as a foregone conclusion. Our analysis appeals to the more complex picture that arises from analyzing aggregate endpoints and their possibly different radiobiological mechanisms. Together with the sublinearity this may be a hint that different biological mechanisms may operate at low and medium doses compared to high doses. Our study provides an elegant way to analyze radio-epidemiological data sets, which comprise a number of similar biological endpoints. The MMI method can similarly be applied to other aggregate health outcomes with aggregated endpoints such as all solid cancers or all leukaemias. Because the internationally applied guidelines for radiation protection largely rely on analyses of the LSS data and the LNT model, our findings have important implications for risk assessment of ionizing radiation in the context of medical applications (such as CT scans, radiotherapy and low-dose anti-inflammatory radiotherapy), nuclear energy production, accident-related long-term risks and international radiation protection practices in general.

A Mathematical Model for Analyzing the Effects of Protracted Irradiation on Cancer and Lifespan in Mice

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Abstract

The increased health risk is one of the most important biological effects caused by radiation and is investigated by animal experiments and epidemiological surveys. Statistical analyses are commonly used in the quantitative assessment of these risks based on those experiments and surveys. However, while data are relatively abundant in high dose, data are scarce in low dose range below 100 mSv. As a result, statistically significant radiation effects are observed in the high dose but have not been confirmed in the low dose. It makes the health effects caused by low dose radiation controversial and there are various proposals for them such as linear extrapolation from high dose range, hormesis effects, and bystander effects.

We treat the biological effects of radiation from another point of view, namely, mathematical models. Statistical models determine whether radiation effects are significant or not solely based on data, that is, statistical models are data-based. On the other hand, mathematical models are mechanism-based. In other words, mathematical models describe radiation effects based on their mechanisms. The mechanism-based discussion is important when we need to predict radiation effect in the ranges where data are limited such as high dose with protracted low dose rate radiation.
In this presentation, we propose a mathematical model for radiation-induced life-shortening which is one of the most important health effects caused by radiation. We assume the following mechanism for the radiation-induced life-shortening; radiation effect on cancer results in the life-shortening, i.e., the early occurrences of cancer-related death cause the life-shortening. From this viewpoint, there are two possible factors related to cancer that affect lifespan: early cancer development and the acceleration of cancer progression.

As an example of the application of our model, we analyze experimental data obtained from low dose rate gamma-ray irradiation experiments on mice conducted by Tanaka et al. In the experiments, they irradiated 20 mGy/day gamma-ray to female mice for 400 days from 56 days in age. They analyzed the lifespan of the mice statistically and concluded that the life-shortening in the irradiated group was 119.6±9.6 days in the mean. Our model derives that the life-shortening is 102 days and decomposes the life-shortening into two radiation effects on cancer: 67 days of the early onset of cancer and 35 days of the contraction of the period between cancer occurrence and death. The result shows that the radiation effect on cancer emergence is larger than that on cancer progression. This result is consistent with the experimental condition that the radiation exposure was limited to the early period of mice's total lifespan.

Effect of Caesium-137 Chronic Low-Dose Exposure on Neovascularization Process

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Abstract

Neovascularization is crucial for tissue irrigation adaptation and regeneration in response to pathological conditions such as ischemia. This process consists of the formation of new blood vessels either by angiogenesis, involving endothelial cells (ECs) in pre-existing vasculature, or by vasculogenesis through the recruitment of bone marrow-derived endothelial progenitor cells (EPCs). Recent studies reported that acute exposure to low to moderate doses of ionising radiation, induces an increase of angiogenesis and vasculogenesis (Roza Santos C, 2010; Ministro A, 2016; Lerman O, 2017). Furthermore, nitric oxide (NO) is stimulated in these conditions. However, effects of chronic low dose radioelements, particularly ^{137}Cs, one of the most released in the environment; on neovascularization has so far not been investigated.

We investigated the effect of chronic low dose contamination with ^{137}Cs on NO-dependent neovascularization. C57BL/6 mice received 20 KB/L, 100 KB/L Cs or vehicle for 6 months in drinking water. Three other groups received the same treatment, with addition of 500 µg/mL L-NAME, a NO synthase blocker.

We evaluated angiogenesis with aortic rings sprouting in vitro in matrigel. We also investigated the effect of ^{137}Cs ±L-NAME, on post-ischemic neovascularization. Unilateral hindlimb femoral artery ligation was performed induce surgical ischemia, 4 weeks before the end of treatment. Cutaneous blood flow of the ischemic and non-ischemic (control) limb was measured with Laser Doppler Imaging and capillary density was assessed by immunohistochemistry on hindlimb muscles. Vasculogenesis was assessed in vitro on bone marrow mononuclear cells (MNCs) by measuring their capacity of differentiation into EPCs. We also assessed their ability to form tubular structures in vivo in matrigel after subcutaneous injection into non-contaminated recipient mice. Furthermore, the ability of EPCs to migrate, incorporate into the matrigel and to form tubular structures was also evaluated after subcutaneous injection of SDF-1 into matrigel in control or mice treated with Cs±L-NAME. Our preliminary results indicated a dose-dependent increase of ischemic/non-ischemic blood flow ratio in ^{137}Cs-treated mice, as compared to controls. An increased blood flow ratio was also observed in 20 KB/L ^{137}Cs -treated as compared to control/L-NAME-treated group. A reduction of blood flow was observed in Cs100KB/L - vs Cs100KB/L/LN-treated group. These results suggest a dose-dependent stimulation of post-ischemic neovascularization after ^{137}Cs contamination. Reduction of stimulation in Cs100KB/L -treated group may be due to L-NAME. However, further investigations are necessary to confirm this hypothesis.

The HARMONIC Project: Epidemiological Study for the Assessment of Radiation Doses and Associated Cancer Risks Following Cardiac Fluoroscopy in Childhood

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Abstract

Introduction: Survival rates for congenital heart disease (CHD) have improved markedly in recent decades, leading to increased focus on the long-term complications of treatment. Cardiac fluoroscopy procedures (CFP) used for the management of CHD (diagnosis, monitoring, treatment) often involve prolonged X ray exposure. Estimated organ doses range from close to zero to several hundred mGy. The radiation risks from these doses are unclear. Only 3 epidemiological studies have investigated cancer risks from cardiac CFP in childhood, with discrepant results. Some epidemiological studies on childhood computed tomography (CT), focusing on similar levels of dose exposure, have reported increased radiation-associated risks, mainly of leukemia and brain tumors. However, bias by indication is difficult to rule out, as the indication for the CT scan can be associated to an underlying disease predisposing to the studied outcome. Although far fewer CFPs, compared to CT scans, are performed each year, the epidemiological analysis of cancer risks following these exposures has certain advantages over CT studies. Firstly, CFP is not directly used in the diagnosis, treatment and follow-up of cancer, thus the potential for reverse causality is, in theory, reduced. Secondly, cardiac fluoroscopy is used in the management of very young patients (<5 years) for which current information on the risks from radiation exposure is limited.
The HARMONIC project (Health Effects of Cardiac Fluoroscopy and Modern Radiotherapy in Paediatrics) is a European study aiming to improve our understanding of the long-term health risks from radiation exposures in childhood and early adulthood. The HARMONIC work package (WP) devoted to CFP patients is designed to complement ongoing studies of the cancer risks following CT scans in childhood, including EPI-CT and MEDIRAD projects.

Methods: A pooled cohort of approximately 100,000 patients who underwent CFP in 7 countries, while aged under 22 years, is underway, based on data collection from hospital records and/or insurance claims data. Doses to individual organs will be estimated from dose indicators recorded at the time of examination within a specific WP dedicated to estimation of dose and associated uncertainties. Biological samples are also prospectively collected in Italy to investigate biological mechanisms. The cohort will be followed up using national registries and insurance records to determine vital status and cancer incidence. Information on organ transplantation (a major risk factor for cancer development) and/or other conditions predisposing to cancer will be obtained from national or local registries and health insurance data, when available. The relationship between estimated radiation dose and cancer risk will be investigated using regression modelling.

Results: National cohorts have previously been established in France and the UK. HARMONIC will involve further expansion and extended follow-up of these cohorts, while also establishing new cohorts in Belgium, Italy, Germany, Norway and Spain. Collection of data is underway in each country. Analyses are planned to be performed in 2022.

Perspectives: Results will help to better assess the relationship between low-doses radiation exposure and cancer in early childhood. It will help to better inform patients and parents and reinforce radiation protection knowledge to reduce radiation risks without compromising medical benefits.

The Effect of Low- and High-Dose Rate Brachytherapy on the Immune Phenotype of Prostate Cancer Patients

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Abstract

Introduction: Early diagnosis and personalized treatment of prostate cancer remains challenging due to the lack of reliable prognostic and predictive biomarkers. Radiotherapy can modify the amount and function of different immune cells in peripheral blood and these radiotherapy-induced changes might represent prognostic markers of therapy-response.

Our aim was to perform a detailed analysis of the systemic immune status of prostate cancer patients treated with various radiotherapy protocols in order to mark potential immune-related biomarkers for patient follow-up.

Materials and methods: Blood samples were collected from 21 patients treated with low-dose rate (LDR) brachytherapy before and at 6 time points after seed implantation. So far blood samples of 5 patients treated with high-dose rate (HDR) brachytherapy collected at similar time points to LDR brachytherapy patients were investigated. Phenotypical changes in peripheral blood mononuclear cells were analysed by flow cytometry.

Results and discussion: Circulating total NK cells increased in patients treated with LDR brachytherapy as early as 3 months after seed implantation and remained elevated up to 36 months compared to both pre-treatment values and healthy controls. In HDR brachytherapy patients mature NK cells decreased compared to control group, while degranulating and anergic NK cells levels increased. The level of lymphoid DCs behaved similarly in both patient groups; it was increased in patients before therapy and remained unchanged up to 6 months after therapy initiation. However, it normalized thereafter. Myeloid DCs in HDR brachytherapy patients were at control levels throughout the follow-up period, while in LDR brachytherapy patients myeloid DCs were significantly increased up to 12 months after the start of radiotherapy.

Cancer significantly reduced naïve and activated CD8 cells and increased senescent CD8 and CD4 cells which further elevated after the brachytherapy in HDR patients compared to healthy group. Effector memory T cells increased in HDR-treated patients 3 month after treatment compared to pre-treatment values, T stem cell memory, central memory and terminal memory T cell levels remained below control values up to 36 months.

Conclusion: Significant differences were noted in systemic immune parameters of prostate cancer patients treated with different brachytherapy protocols highlighting the importance of deposition kinetics of ionizing radiation energy in modulating systemic immune responses.

Funding
This work was supported by a Hungarian research grant funded by the National Research, Development, and Innovation Office (NKFI-124879).

ERPW Abstract Session D: General Dosimetry and Various Topics
November 23, 10:45–12:15

Fragmentation Cross-Sections Study of High-Energy ^{20}Ne Ion for Radiation Shielding and Radiotherapy Purposes

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Abstract

The high-energy galactic cosmic radiation offers challenges to space exploration missions. Also, high energy ion like ^{20}Ne provides high RBE and LET characterizations, favorable for radiotherapy. Henceforth, the partial fragmentation cross-sections (PFXS) and linear energy deposition are calculated for ^{20}Ne ions of energy 370 MeV/n in hydrogenous materials. The hydrogenous materials are regarded as the most efficient shielding materials. The $C_5H_8O_2$ (Lucite) and H_2O (water) are used as the target materials. The study utilized the QMD and the INCL++ physics model for simulation to compute the PFXS by the three-dimensional Monte Carlo toolkit Geant4. The comparative analysis is carried out between the simulated outcome of Geant4, the experimental data, and the results generated by the PHITS code system. It is noted that the QMD model offers the best agreement for PFXS with an odd-even effect for fragments of both targets. The INCL++ regenerates results with an inline agreement and a few percent deviations depending on which fragment and target are considered.

Childhood CT Scans and Cancer Risks Estimates: An Update of the French CT Cohort Study

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Abstract

Background: Computed tomography (CT) has been used increasingly worldwide over the last decades. However, concerns have been raised about potentially radiation-related cancer risks, particularly after exposure to CT in childhood, due to the greater radiation sensitivity of children and to their longer life expectancy allowing to develop radiation associated late health effects. Increased risks of central nervous system (CNS) tumours and leukaemia associated with CT exposure during childhood have been reported in recent epidemiological studies. However, no evidence of significant increased risks was suggested in a previous analysis of almost 60,000 patients of the French CT cohort. Methods: The French CT cohort includes patients born after 1994 who received at least one CT scan before the age of 10 years between 2000 and 2011 and had no cancer diagnosis before the first CT.

Examinations and radiological protocols carried out between 2000 and 2011 in the 21 participating hospitals were retrieved to estimate cumulative absorbed doses to the brain and the red bone marrow (RBM). In this work, the cohort was updated in order to extend the follow-up (5 additional years) and to increase the sample size of patients (40,000 new patients with reported vital status). Moreover, the cohort was linked with the National Health Data System (Système national des données de santé, SNDS) to collect CTs performed outside the participating hospitals or after the inclusion period. Hazard ratios (HRs) associated to cumulative organ doses and gender were estimated from Cox models. To rule out the possibility of reverse causation, an exclusion period of 2 years was applied. A latency period was also applied to consider the minimal latency period expected between the exposure and the studied outcome. To address the potential issue of bias by indication, the models were fitted to the restricted sub-cohorts of patients with and without cancer predisposing factors (PFs) separately. Results: The updated French CT cohort includes 103,015 patients followed for 9.3 years in average. 3.1% of patients had PFs. Considering only the CTs performed in the participating hospitals until 2011, mean cumulative doses were 24.5 and 9.3 mGy for the brain and the RBM respectively. Adding the CTs performed outside the participating hospitals or after the inclusion period increased the mean cumulative doses to 27.7 mGy and 10.3 mGy for the brain and the RBM respectively. This study showed statistically significant dose-response relationships for CNS tumours (HR per 10 mGy: 1.05, 95% CI: 1.01–1.09) and leukaemia (HR per 10 mGy: 1.17, 95% CI: 1.09–1.26) for patients without PFs. No evidence of association was observed for lymphoma for these patients and for the three types of cancer for the patients with PFs. Inclusion of additional CTs registered in the SNDS did not impact the HR estimates.

Conclusions: Estimates were compatible with the ones obtained in the previous analysis of the French CT cohort. However, the extended follow-up and the larger sample size of the cohort increased the statistical power, leading to statistically significant dose-response relationships for CNS tumours and leukaemia for patients without PFs.

Determination of Diagnostic Reference Levels and Achievable Doses for Pediatric CT Examinations in the United States and Comparison with International Benchmarks

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Abstract

Purposes: To summarize practice-based diagnostic reference levels (DRLs) and achievable doses (ADs) in the United States (US) from the American College of Radiology CT Dose Index Registry's commonly performed pediatric CT examinations, compare data across examinations with international DRLs, and discuss challenges with such comparisons.

Methods: Dose indices were analyzed across 1,543,535 pediatric CT examinations acquired from 2016-2020 at 1625 registry facilities (66% community hospitals, 16% freestanding centers, 9.5% academic facilities, 3.5% dedicated children's hospitals) representing the 10 most commonly performed protocols. Analysis based on patient age and effective diameter included medians (AD) and 75th percentiles (DRL) for volume CT Dose Index (CTDIvol), dose length product (DLP), and size-specific dose index (SSDE). Results for three common examinations (head without contrast, chest, and abdomen-pelvis (AP) with contrast) were compared with DRLs (CTDIvol and DLP) from 9 recent international investigations (Australia, Belgium, Canada, Finland, Germany, Japan, Korea, Switzerland, Europe).

Results: The most and next most frequently performed examinations were head (57%) and AP CT (28%). CTDIvol and DLP ADs and DRLs in general increased with patient age. The CTDIvol AD and DRL ranged from 19–46 mGy and 23–55 mGy, respectively, for head without contrast examinations. The CTDIvol, SSDE, and DLP DRLs and ADs also increased consistently with increasing patient effective diameter for body examinations. The range of CTDIvol ADs and DRLs for AP with contrast examinations was 2.0–21 mGy and 2.7–26 mGy, respectively. Establishment of age and examination specific pediatric CTs enabled comparisons with the international studies. For head CT without contrast, the 0–<1 yr group U.S. CTDIvol was lower in 67% (6/9), higher in 22% (2/9) and the same in 11% (1) while corresponding DRLs were lower in 56% (5/9), and higher in 44% (4/9) of comparisons. For the 6–18 yr group, U.S. CTDIvol was lower in 22% (2/9), higher in 67% (6/9) and identical in 11% (1/9) of comparisons. For AP CT with contrast in the 0–<1 yr group, U.S. CTDIvol and DLP were lower in 100% (4/4 of those reporting); in the 15–18 yr group U.S. CTDIvol was lower in 1 and higher in the other of two available comparisons. The US DLP was higher than the two international reports available. In general, our results fall within the ranges reported internationally. Difficulties with comparisons included different age classifications, incomplete data across ages, classifications based on weight vs age, potential influences resulting from practice-based reporting, and mapping of CT examination types.

Conclusions: DRLs and ADs as a function of patient age and effective diameter were determined for the 10 most common CT pediatric examinations performed in the U.S. These determinations afford the ability for comparisons with existing, e.g., international, benchmarks and demonstrate the benefits for harmonization in DRL methodology for more productive comparisons and potential practice modifications.

Assessment of Uncertainties Affecting Dosimetric Calculations for the Intake of Radon and NORM

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Abstract

Uncertainties in dosimetry of inhaled radionuclides are arising from different sources. Biokinetic models are used to describe the behaviour of the radionuclide and its progeny in the human body. These models are also used to calculate the number and localisation of decays in the body. Dosimetric models are used to calculate the doses to the target organs by the radiation emitted during or following the decays. The uncertainties of the calculated doses will be studied by propagating the uncertainties of the model parameters through the dose assessment. Fixed parameter values will be replaced by samples from distributions of those and used to estimate the dose. In the project the model parameters will be studied and distributions for the initial parameters based on physiological considerations will be derived and used in an uncertainty assessment. Software tools will be developed to allow the use of the distributions (e.g., by sampling out of those) in the calculations. Besides a global analysis of the uncertainty, these techniques allow also to study the influence of the single model parameters and to identify the most relevant in terms of uncertainty. In this project global uncertainty analysis and sensitivity analysis of exposure scenarios relevant for RADONORM will be performed. It should be noted that the study and treatment of uncertainties in internal dosimetry is still a topic of scientific interest. The biokinetic models provided by ICRP are reference models whose parameters are representative of a reference person. By definition, these parameter values are fixed numbers with no uncertainties. From the literature study so far, it has been observed that the parameters that mainly lead to uncertainties in calculated doses for the intake of radon and NORM are mainly the activity size and breathing rate. Other parameters of interest are the unattached fraction of the aerosol, the nucleation fraction and the target cell parameters.

Sensitivity analysis and the estimation of associated parameter uncertainties in biokinetic models need to be performed to give a better understanding of these models and to estimate the influence of single parameters on the model predictions and hence dose coefficients. The results from this study will provide information about the reliability of assessed doses and indications to sensitive parameters for a better fit of the models to monitoring data; this will be the focus for further studies since this knowledge will be crucial for guiding future epidemiological studies.

Novel Detector for Monitoring Airborne Radioactivity and Fallout during a Nuclear Emergency

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Abstract

Early warning networks are crucial for preparing for nuclear accidents. A comprehensive early warning network enables timely detection of abnormal levels of radioactivity in the atmosphere. The networks currently in use are largely based on stations equipped with ambient gamma dose-rate sensors or gamma-ray spectrometers. These sensor types are well suited for providing an early warning in case a radioactive release plume reaches the vicinity of the detector.

Unfortunately, the current sensors are incapable of distinguishing airborne radioactivity from radioactive fallout. Since radioactive materials are most harmful when inhaled, it is essential to know the amount of radioactivity in the air to determine the right protective measures needed to minimize the possible health effects.

Moreover, the need for monitoring often continues after the first early warning. In previous reactor accidents radionuclides have been released over multiple days. Once the ground around the detector gets contaminated, the current stations will struggle to detect new plumes.

We present a new sensor for early warning networks that can distinguish between airborne radioactivity, radioactive fallout, and contamination of the sensor container box. The sensor is based on the phoswich principle where multiple scintillator elements are instrumented with a common photosensor. Our extensive laboratory and field tests prove that the detector technology works and that the detector can be deployed in field. The presentation summarises the outcome of the four-year research conducted under the DEFACTO project jointly by the Finnish Radiation and Nuclear Safety Authority, Helsinki Institute of Physics, IEM-CSIC Spain and Finnish Defence Forces.

Radio-Biologically Motivated Modelling of Radiation Risks of Mortality from Ischemic Heart Diseases in the Canadian Fluoroscopy Cohort Study

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Abstract

We analyzed the Canadian fluoroscopy cohort study (CFCS) dataset for the detrimental health outcome of ischaemic heart diseases (IHD). This is one of the largest datasets of patients exposed to fractionated low, moderate and high doses of X ray radiation. It includes 63,707 tuberculosis patients from Canada who were exposed to X rays in 1930s–1960s and were followed-up for death from non-cancer causes during 1950–1987. The primary analysis of these data reported significantly increased radiation risks of mortality from IHD with a linear dose–response adjusted for dose fractionation (Zablotska et al. 2014). In the current analyses, the assumption of linearity was scrutinized by analyzing a larger series of radio-biologically motivated nonlinear dose–response models to get a better understanding of the impact of radiation damage on IHD. The models were weighted according to their quality of fit using a multi-model inference (MMI) method. The results indicated an essentially linear dose–response relationship for IHD mortality at low and medium doses (<1.5 gray) with no apparent threshold. At higher doses (≥1.5 Gy), the dose-response from MMI predicted a higher risk compared to the linear no-threshold (LNT) model. At 5 Gy, for example, the estimated radiation risks were fivefold higher compared to the LNT model. The present study used a comprehensive and flexible approach by analyzing the data with a variety of different linear and nonlinear models including those that exhibit flexible threshold-doses without applying artificial cut-points at certain doses and without relying on LNT as a foregone conclusion. Our analyses suggest that different biological mechanisms may operate at low and medium doses compared to high doses and that at higher doses, the LNT model may underestimate the risk compared to the dose response from MMI. Our results should be of particular interest to international radiation protection organizations, which largely rely on analyses of radio-epidemiological cohorts using the LNT model. We conclude that our findings have important implications for risk assessment of ionizing radiation in the context of medical applications (such as CT scans and radiotherapy), nuclear energy production and accident-related long-term risks.

Radiation Protection of Volunteers in Medical Research – A Multifaceted Challenge

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Abstract

Medical clinical research including volunteers in entails ethical issues that must be addressed and the volunteers must be sufficiently protected from possible detriment. Radiation risks must also be taken into account if the volunteers are exposed to ionising radiation. The EU Directive [1] regulates medical exposure, including medical research, and a guidance document [2] has been issued. In Sweden, several regulations have been revised recently to take account of the latest EU directive. The ethical review system has also recently been changed and since 2019 the Swedish Ethical Review Authority (EPM) has replaced the regional ethics committees. These changes prompted an investigation of the system for the radiation protection of volunteers.

The current regulations and guidelines have been reviewed and 100 applications submitted to EPM in 2019 and 2020 have been evaluated. The applications were evaluated in respect of information about the self-assessed societal benefit, radiological method, effective dose, critical organs, age of volunteers, etc. and input from representatives from EPM and researchers was evaluated. The most common application included diagnostic radiology, mostly CT, to evaluate drugs or other treatments. The researchers were affiliated with one of the three largest university hospitals. However, a large share of applications could not easily be evaluated, including e.g., radiation therapy. It was clear that the assessments of effective dose can be improved and the assessment of the societal benefit needs to be harmonized. It is necessary to communicate to concerned parties the use of dose constraint and effective dose.

The investigation also indicates that more collaboration is needed between the researchers and the radiology departments to ensure that an appropriate radiological method is used, radiation protection is optimised and the radiation risk is evaluated in an appropriate way. We also realized that there is a need to clarify the responsibilities of the researchers and the radiology clinics respectively. Optimisation of radiation protection and the use of appropriate radiological methods is a very important part of radiation protection but not an obvious part of the ethics review. We also conclude that some research projects will fall outside the above mentioned regulations as they cannot be classified as medical research or do not use methods to qualify as medical exposure.

One suggestion in order to improve and harmonise radiation protection on a European level is to revise the current guidance Radiation Protection 992 to contain more specific guidance, e.g. how to deal with volunteers in different subgroups such as healthy and terminally ill volunteers and multiple participation by some volunteers. There is also a need to clarify and guide the assessment of societal benefits and how dose constraints relates to the optimisation process.

References

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[2] European commission, Radiation Protection 99, Guidance on medical exposures in medical and biomedical research Directorate-General Environment, Nuclear Safety and Civil Protection 1998

ERPW Invited Scientific Session III: Envisioning the Future of Radiation Protection Research: Big Data, AI and Beyond
November 24, 09:00–10:30

Ethics in Radiological Protection for Medical Diagnosis and Treatment, ICRP TG109

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Abstract

There is a longstanding recognition of the importance of ethical aspects of Radiological Protection (RP), and medical practice has a long history in moral philosophy. ICRP Publication 138 (a) defines the ethical foundations of the System of RP and identifies four core values (beneficence/non maleficence, prudence, justice and dignity) and three procedural values (accountability, transparency and inclusiveness). The ICRP task group (TG) 109 is developing a report specifically dedicated to ethical aspects of RP of patients, intended for medical professionals, patients, families, carers, the public and authorities. The TG 109 report (b), still in draft version, aims to apply the core ethical values and the procedural values in the context of radiological protection of patients. The need to extend the set of values identified in ICRP Publication 138, with those existing in medical ethics, is discussed in TG 109 report, considering the values of precaution, solidarity, autonomy, honesty, and empathy. The report introduces scenarios, adapted from examples in diagnosis and treatment, identifies ethical dilemmas and proposes a method to analyse each scenario from an ethical point of view, on the basis of compliance/non-compliance with the ethical values. The scenarios are meant to provide the individual reader with an approach of reflection and balance, applying the values to answer ethical questions. Depending on multiple factors, including culture and circumstances, the answers may be different in a wide range of situations presented (e.g., pregnancy, elderly, paediatric, end of life).

The report recognises how an effective and balanced RP education and training (E&T) program, that enables patient centered decision-making and helps to achieve the greatest possible benefit at the lowest possible risk, should include content on ethics. A chapter dedicated to E&T of clinicians and health professionals, of relevant stakeholders, and education for the engagement and empowerment of patients, families and carers, addresses the elements of ethical E&T in medical RP. Ethics education of health workers dealing with medical use of radiation should continue throughout their careers. A model is presented to enable the educator to define the student learning outcomes on the basis of the knowledge, skills and competencies (KSCs) necessary for clinicians and health professionals to make carefully considered ethical decisions, giving examples on how KSCs can be defined. The report evidences that a clear understanding of ethical values, together with the principles of RP,

can help address issues of potential conflict in decision making processes when using radiation technologies in medicine.

References

[1] ICRP, 2018. Ethical foundations of the system of radiological protection. ICRP Publication 138. Ann. ICRP 47(1).

[2] F.Bochud, M.C.Cantone, K.Applegate, M.Coffey, J.Damilakis, M.del Rosario Perez, F.Fahey, M.Jesudasan, C. Kurihara-Saio, B.Le Guen, J.Malone, M.Murphy, L.Reid, F.Zolzer (2020). Ethical aspects in the use of radiation in medicine: update from ICRP Task Group 109. ANNALS OF ICRP 49, 1, p. 143–153.

ERPW Abstract Session E: Medical Radiation Protection
November 24, 10:45–12:15

Cell-Type Specific Differences in the Competitive Relationship between Cell Killing and Accumulation of Carcinogenic DNA Lesions Following Fractionated Radiation Exposure

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Abstract

Dose heterogeneity across normal tissue during radiotherapy is a modulating factor for radiation-induced second primary cancers (SPC). This heterogeneity distribution across normal tissue ranges from intermediate to high doses within the in-field volume (usually predicted during treatment planning), to low doses in the out-of-field volume (mainly attributed to scatter radiation). Epidemiological studies, involving dose reconstruction, have indicated an increased risk of certain cancer types in out-of-field regions. Other malignancies are more at risk in the in-field region. The shape of the dose-response relationship, with regards to SPC, still remains unclear, due to problems with dosimetry the limited understanding of the competitive relationship between cell death and the induction of carcinogenic DNA lesions.

We investigated the competitive relationship between cell killing and the accumulation of carcinogenic mutation using two normal cell types (VH10 fibroblasts and AHH-1 lymphoblasts). Dose fractionation schemes were designed based on the cell growth characteristics of each cell type. To simulate the heterogeneous dose distribution across normal tissue during radiotherapy, cells were irradiated at 0.25, 0.5, 1.0, or 2 Gy per fraction. Post fractionated radiation exposure, the effects on cell growth, cell survival, radiosensitivity, and the accumulation of residual DNA damage and genomic instability were analyzed both as a function of dose per fraction and the total absorbed dose.
A dose-dependent decline in cell growth was observed in both cell types during radiation exposure. After the radiation exposure regimen, decreased cell growth was only observed in VH10 and AHH-1 cells irradiated at 1 and 2 Gy/fraction. This lag in cell growth could be attributed to the increased frequency and complexity of DNA lesions at these doses. The accumulation of markers of genomic instability (micronuclei, nuclear buds, and polyploid giant nuclei) also increased as a function of dose per fraction. However, analysis of dose-response relationships as a function of total absorbed dose revealed cell-type-specific differences. Residual DNA damage was present seven days after exposure ended in VH10 cells, while gamma-H2AX foci were more rapidly cleared in AHH-1 cells. Giant nuclei were prominent in AHH-1 cells at 2 Gy/fraction, whereas nuclear buds instead were more common in VH10 cells at all doses/fraction, which was paralleled by similar patterns in cell survival assayed from 10 days post-exposure. Analysis of radiosensitivity (of cells previously exposed to fractionated radiation exposure at doses 0.25, 0.5, 1.0, and 2 Gy per fraction), showed a dose-dependent increase in radioresistance of AHH-1 lymphoblasts, but not VH10 fibroblasts. In conclusion, we demonstrate differential patterns in competition between cell death and induction of carcinogenic lesions, which could aid in our understanding of cell-type-specific differences in the accumulation of mutations in pre-cancerous cells.

Differences of Ex Vivo and In Vivo DSB Repair Capacity in Pbmcs of Patients before and during Radioiodine Therapy

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Abstract

Aim: The aim of the sub-study of the MEDIRAD project was to analyse the DNA double strand break (DSB) repair in isolated peripheral blood mononuclear cells (PBMCs) after an internal ex vivo irradiation of whole blood with [^{131}I]NaI with a nominal absorbed dose of 50 mGy and in vivo during radioiodine therapy. The co-localizing biomarkers γ-H2AX and 53BP1 were used to quantify the induced DSB. Material and Methods: For the ex vivo study, the DSB induction and repair of PBMCs obtained of 18 consenting patients before radioiodine therapy after internally irradiating the blood for 1 h to reach 50 mGy, were analysed 0 h, 4 h and 24 h after irradiation. For the in vivo study, blood of the same patients was taken before and up to 168 h after [^{131}I]NaI administration at multiple time points. For the in vivo study PBMCs were isolated and ethanol-fixed. For the ex vivo repair study, PBMCs were isolated after irradiation and either directly ethanol-fixed, or fixed after 4 h and 24 h in short-time culture. All samples were immuno-stained with γ-H2AX and 53BP1 antibodies and co-localized foci were counted manually by an experienced observer.

Results: The mean absorbed dose of 18 ex vivo irradiated samples was 49.7±2.4 mGy. For all time points of this study (0 h, 4 h, 24 h), the mean average number of RIF after irradiation was (0.65±0.18) at t =0 h, (0.25±0.09) at t = 4 h, and (0.06±0.09) at t = 24 h. In vivo, the mean average number of RIF was (0.38±0.14), (0.64±0.18), (0.43±0.20), and (0.06±0.18) at 1 h, 4 h, 24 h and 168 h after therapy start, respectively. The mean absorbed dose to the blood at the four time points was (16±3) mGy, (61±10) mGy, (191±32) mGy, and (296±52) mGy. The corresponding dose rates are (15.6±2.8) mGy/h, (12.4±1.7) mGy/h, (4.0±0.9) mGy/h and (0.1±0.1) mGy/h at 1 h, 4 h, 24 h and 168 h, respectively. Comparing the ex vivo values to the in vivo results, the number of RIF is similar after 4 h in vivo irradiation at a similar absorbed dose to the blood.

Conclusion: Ex vivo, DSBs decreased 4 h after removing the activity and DSB repair was almost completed after 24 h. Due to the continuous irradiation in vivo, the number of DSBs increased up to 4 h after therapy start and DSBs were only completely repaired 168 h after administration. This study shows that the continuous irradiation with decreasing, however, still relevant dose rates in the patients at late time points leads to altered repair kinetics in vivo, most likely due to dwindling DSB induction competing with DSB repair.

Acknowledgement
The MEDIRAD project has received funding from the Euratom Research and Training Programme 2014–2018 under grant agreement No 755523.

Structural Differences in Tumor and Ablated Tumor Tissue by Measuring Noise Performance Using Artificial Intelligence Method

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Abstract

Microwave ablation (MWA) is one of the most recent techniques in cancer treatment. The technique has advantages for the treatment of solid and even quit large tumours by using high temperature locally. In particular, MWA as a minimal invasive image-guided procedure is a promising technique in liver lesion treatment. Fast ablation time and recovery and long-term survival make it a good choice in comparison to that of surgery [1,2].

Computed tomography (CT) as an interventional image modality system is widely used in the MWA therapy to support physicians for localizing the tumour and finalizing the ablation process. However, the noise in pre-ablation CT scan images cause the very low difference in intensity between the tumour and healthy tissue [3]. Additionally, the required high image resolution causes higher-dose exposure which might be harmful for the patient and the people who are involved during the therapy. Therefore, there is a strong need to visualize the border between the tumour and the healthy tissue for helping the physicians to precisely find the tumour location and completely remove it.

Artificial intelligence (AI), in the area of medical imaging gaining a lot of attention for outstanding noise performance in medical imaging and tissue characterization. Physicians' visual decision making which is based on their expertise and experience can be assisted by AI to make more accurate decision and treatment.

The immediate goal is to find structural data difference in tumour and ablated tumour tissue based on studies of the noise performance behaviour by using AI methods to reduce exposure of patients and staff. In this regard we apply a subset of AI. Deep learning is a method which is used in medical image classification, particularly here in order to accurately classify the tumour and ablated tissue in the presence of noise. Low-dose images produced by adding noise into original CT images are assessed and utilized as input of the network.

The data collection has been performed by using a clinical CT scanner from the University Clinic Magdeburg. In order to assess the noise performance, the noisy images (low-dose) would be fed into the network without accessing to original images [4]. The method classifies the tumour and ablated tumor tissue with the low-dose images. The results can be compared with the original CT images to show the effects of noise on the tumour and ablated tissue.

This talk highlights various research tasks related to low-dose images and consequently noise reduction of the interventional CT images especially associated with quantitative noise measurement with different algorithms for the images [5]. This research contributes to the understanding of tissue characterization for reduction of recurrence rate which results in avoidance of radiation exposure follow-up treatment as well as innovative software demonstrators as a part of APP's for therapy monitoring in an interventional CT setup.

Accurate Estimation of Organ Doses from Chest CT Using Patient-Specific Dosimetry

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Abstract

The aim of this study was to a) provide accurate 3-dimensional (3D) dose distribution and b) provide normalized organ radiation doses for adult chest CT examinations for primarily exposed organs. Chest CT examinations performed on 110 adult patients were included in this study. Patient CT image data were used to create 110 patient models. These models were used as input in an equipment-specific and patient-specific Monte Carlo software (ImpactMC, CT Imaging GmbH, Erlangen, Germany). ImpactMC is a well-validated Monte Carlo code specifically designed for 3D dosimetric evaluation on CT acquired images. The radiation dose was calculated on a per image voxel basis, considering all available physical interactions. A modern CT scanner was modeled (Revolution GSI, General Electric Medical Systems, WI, USA). Monte Carlo simulations were performed on the patient models using the scanner geometry, the energy spectrum of the X ray beam, and the composition and geometrical characteristics of the beam filtration. Following the Monte Carlo simulation of each patient model, an output color-coded image series was generated. These images depict the normalized to free-in-air CTDI (mGy/100 mAs) dose distribution imparted in the patient's body, in voxel-to-voxel correspondence to the input CT image series. Organ tissue dose information was extracted from 3D dose distributions through appropriate delineation. To correlate with organ doses, the water equivalent diameter (WED) was measured at the central axial slice depicting the heart. WED and organ dose correlation was determined through regression analysis. The results consist of normalized organ doses as a function of WED for 3 kVp values. Normalized organ doses correlated strongly with WED ($R2>0.8$ for most cases). Estimation of organ doses from chest CT examinations can be made using correlation equations developed in this study.

Acknowledgment
This study has received funding from the Euratom Research and Training Programme 2014–2018 under grant agreement No 755523 (MEDIRAD project).

Interpretation of Radiation-Induced Aging Based on a Mathematical Model

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Abstract

Increased cancer incidence and shortened lifespan are significant biological effects caused by radiation and are often discussed from the viewpoint of aging. Aging is an intricate process characterized by a progressive loss of physiological integrity, leading to impaired function and increased mortality. One of the causes of the aging is the accumulation of cellular damages, which can also lead to the development of cancer. The integrity of DNA is continuously challenged by exogenous agents including ionizing radiation, as well as by endogenous threats, such as DNA replication errors and reactive oxygen species. We assume that the relation of aging and radiation can be formulated in the same way as that of the endogenous mechanisms.

The age-specific mortality rate is widely used to express the aging process. It was first pointed out by B. Gompertz that the mortality rate increases in geometric progression. In this case, a straight line results when death rates are plotted on a logarithmic scale (Gompertz plot). Radiation-induced aging is frequently categorized as either accelerated aging or premature aging. In the Gompertz plot, the accelerated aging appears as the contraction of the time axis where the premature aging appears as the shift of the time axis. The premature aging has been observed as a result of acute irradiations.

In this study, we discuss the increased incidence and the early development of cancer by incorporating the effects of radiation into a mathematical model based on the Armitage-Doll multistage model of carcinogenesis. Here, we treat the age-dependent cancer prevalence as a measure of aging. We assume that the transition rate from one stage to the next is expressed as the sum of the spontaneous (endogenous) term and the radiation-induced term which is linear in the dose rate. The formula obtained for cancer prevalence shows that radiation dose can be explained in terms of time and provides an interpretation of radiation-induced aging. Our model shows that accelerated aging is related to the dose-rate, whereas premature aging is related to the accumulated dose, giving us a simple and natural interpretation of the radiation-induced aging. We apply the formula to the cancer incidence data in mice chronically exposed to low dose-rate radiation to demonstrate the usefulness of this approach.

Status of the Implementation of the Requirements of the Basic Safety Standards Directive at National Level Regarding Education & Training in Radiation Protection: Results from EURAMED Rocc-n-Roll Project

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Abstract

Introduction: It is widely recognised that Education and Training (E&T) in radiation protection (RP) for health professionals is vital towards a development of an RP safety culture with the objective to protect patients and staff from the dangers arising from the exposure to ionizing radiation.

The International Commission on Radiological Protection (ICRP) supports that professionals involved more directly in the use of ionizing radiation should receive education and training in RP at the start of their career, and the education process should continue throughout their professional life as the collective knowledge of the subject develops.

Also the Heads of the European Radiation Protection Authorities (HERCA) supports that E&T requirements for RP knowledge and skills should cover underpinning science, RP philosophy and principles, management, organisation and practical application techniques and knowledge and skills of applicable legislation and guidance.

It is therefore understandable that, considering all these important and relevant aspects, the European Commission has reinforced the importance of education, information and training in the field of medical exposure, in article 18 of the Council Directive 2013/59 EURATOM, laying down basic safety standards for protection against the dangers arising from exposure to ionising radiation (BSSD), by requiring that European Member States “ensure that practitioners and the individuals involved in the practical aspects of medical radiological procedures have adequate education, information and theoretical and practical training for the purpose of medical radiological practices, as well as relevant competence in radiation protection.”

To understand the status of the implementation of the requirements of the BSSD of E&T in RP in Europe, the project performed a European survey targeting relevant national stakeholders (e.g., national scientific and professional societies; regulators), with interests in medical imaging (radiology, nuclear medicine, hybrid imaging) and radiotherapy.

Materials & Methods: The project designed a survey to assess the status quo of national implementation of the E&T requirements laid down in the BSSD. For this propose the exact text of the article 18 from the BSSD was used in the survey.

For each one of the requirements, the relevant national stakeholders from all European union and EFTA countries and United Kingdom, to whom the survey was sent, were asked to define if they were: a) not implemented; b) partially implemented; c) fully implemented; d) don't know

Results: A total of 550 replies were received from 29 countries, representing several stakeholders: Dentist; Medical Physicist; Nuclear Medicine Physician; Radiation Oncologist; Radiologist; Other Physician; Radiation Biologist; Radiation protection expert; Radiographer; Radiopharmacist; Regulator, Researcher in radiation protection & medical physics.

In general, for all 5 requirements, 14% of the respondents replied that they were not implemented.

Conclusion: Despite the implementation of the BSSD is mandatory in the EU countries and the national legislation should reflect the requirements listed in the BSSD, the project survey shows a huge heterogeneity in the implementation process, calling for an action plan towards harmonization in Europe.

Funding
EURAMED rock-n-roll project is funded by the European Commission, grant nº 899995., under the call NFRP-2019-2020

Early Subclinical Cardiovascular Changes after Radiotherapy for Breast Cancer Detected by Echocardiography: Contribution of the MEDIRAD EARLY-HEART Cohort

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Abstract

Background: Breast cancer (BC) represents a major public health burden worldwide. Significant advances in treatments have been made in recent decades. Among them, radiotherapy (RT) allows reducing local recurrence and deaths resulting from BC. However, RT for BC can lead to cardiotoxicity, resulting in an increased risk of long-term major cardiovascular adverse events (MACE). Consequently, to detect early subclinical cardiac alterations is of primary importance.

Objective: One of the aims of the MEDIRAD EARLY-HEART study is to determine the short-term impact of BC RT on subclinical cardiac function by means of echocardiography and to explore the dose-response relationship.

Methods: Launched in 2017, the ongoing EARLY-HEART study is a prospective multicentre cohort study including women with BC aged 40 to 75 years and treated by RT in the Netherlands, Germany, France, Portugal and Spain. All women were chemotherapy naive. Echocardiographic exams after the RT+6-month follow-up (FU) will be available in September 2021 to determine if significant subclinical cardiac function alterations occurred. A RT+24-month FU is currently ongoing to determine if eventual previous alterations persist. Myocardial deformation analysis was provided by the 2D-speckle-tracking echocardiography. The global longitudinal strain (GLS), its worsening > 10% and the global longitudinal strain rate (GLSR) will be considered to evaluate subclinical cardiac dysfunction.

Results: The EARLY-HEART cohort included 258 women with BC, with a mean age of 58.2±8.1 years, 63.5% with left-sided BC. Presence of pre-existing cardiovascular (CV) risk factors were recorded to allow adjustments in further analyses: obesity was present in 21.0% of the sample (mean body mass index of 26.3±4.6 kg/m²), hypertension in 48.2%, diabetes in 5.4% and 47.8% were current or former smoker. RT total dose varied from 40.05 Gray (Gy) to 50.40 Gy, and 46.1% received a boost (mean boost dose of 11.9±1.9 Gy). Among the 258 patients, 63.9% received concomitant hormonotherapy. Regarding subclinical cardiac investigations at baseline (before RT), 242 patients (93.8%) performed echocardiography exams, yielding a mean GLS of -19.3±3.3%. Full echocardiography analyses after the 6-month FU will be available soon to explore potential alterations of myocardial function between pre-RT time-point, 6-month and 24-month post-RT time-points using paired t tests. Future EARLY-HEART analyses will also provide accurate absorbed dose of cardiac structures (whole heart, right and left ventricles, right and left atrium) based on 3D-dosimetry to explore dose-response relationships using multivariate regressions. Subgroup and sensitivity analyses will be performed. Results of analyses of the relationship between radiation dose and subclinical cardiac function will be presented.

Conclusion: Using strain analysis from echocardiography, the impact of RT on subclinical cardiac function in patients with BC are being explored within the MEDIRAD EARLY-HEART project. Epidemiological data regarding early alteration of GLS could contribute to adaptions in clinical practice about CV monitoring.

ERPW Digital Poster Session
November 24, 13:15–14:00

Salivary Dysfunctions after Radioiodine Treatment (START): Results of a Self-Controlled Study in France

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Abstract

Introduction: The treatment of differentiated thyroid cancer includes generally a total thyroidectomy, followed by a radioiodine (^{131}I) therapy. Due to their ability to concentrate iodine, the salivary glands may present inflammation after administration of ^{131}I, which may be symptomatic, may lead to longer-term chronic abnormalities, resulting in alterations in patients' nutrition and quality of life. The incidence of salivary dysfunctions after ^{131}I therapy varies considerably between studies due to methodological limitations. Also, the occurrence of these dysfunctions may be linked to increased uptake and/or retention of ^{131}I in the salivary glands and/or individual radiosensitivity. However, no clinical or genetic factors have been identified to date to define patients at risk, allowing the delivered activity to be adapted to the expected risk of salivary dysfunctions. The aims of this study are 1) to estimate the incidence of salivary dysfunctions after ^{131}I therapy, 2) to investigate the risk of salivary dysfunctions in relation to ^{131}I dosimeter recorded doses.

Methods: This prospective study included 139 patients, candidates for a ^{131}I therapy in the context of their differentiated thyroid cancer, treated in the Nuclear Medicine Department of the Pitié-Salpêtrière Hospital (45 and 94 patients in 1.1 GBq and a 3.7 GBq dose groups respectively) treated between September 2020 and June 2021. External thermoluminescent dosimeters were placed opposite the salivary glands and at the sternal fork immediately before radioiodine administration and removed 5 days after. The dose precisely received at the salivary glands was established from dosimeter records, physical and computational phantoms.

The follow-up is based on 2 scheduled visits: at inclusion (T_0, immediately before ^{131}I therapy) and 6 months after (T_6). For each visit, questionnaires about salivary disorders (validated French tool) are administered, and individual measurements of the salivary flow (without and with salivary glands stimulation) are performed. Poisson regression models with adjustment for potential confounding factors will be used.

Results: The T6 follow-up started in March 2021 and is still ongoing. Statistical analyses will be set up in October 2021, and results will be presented. Both subjective (questionnaire responses) and

objective (saliva flow rates) indicators of salivary dysfunctions will be analysed, and a combined indicator will be created.

Discussion: It is the first study to investigate the risk of salivary dysfunctions (using both objective and subjective indicators) in relation to organ (salivary glands) doses, based on individual dosimeter records and dose reconstructions. Potential associated risk factors will be investigated. The results will allow the identification of patients at risk of salivary dysfunctions, and thus to propose to clinicians a more adapted follow-up and/or countermeasures to adverse effects.

RadoNorm: Towards Effective Radiation Protection Based on Improved Scientific Evidence and Social Considerations – Focus on Radon and NORM

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Abstract

The RadoNorm project (www.radonorm.eu) has received funding of 18 million EUR from the Euratom Research and Training Programme 2019–2020 and includes 56 partners from 22 EU member states and associated countries. It also collaborates with groups in the US and Canada. The multidisciplinary 5-year project began last autumn and is being coordinated by Germany's Federal Office for Radiation Protection.

The RadoNorm project is designed to initiate and perform research and technical development in support of European Union Member States, Associated Countries and the European Commission in their efforts to implement the EU Basic Safety Standard Regulations (EU-BSS) for protection against the dangers arising from exposure to ionising radiation at the legal, executive and operational level. The project aim is to improve existing and gain new, advanced knowledge, techniques and/or developments related to radon and NORM (a) exposure, (b) dosimetry, (c) risk and effect, (d) mitigation and remediation, and (e) societal aspects. The main focus will be on integrative and innovative solutions to reduce existing uncertainties and ensure better and robust radiation protection with transparent stakeholders involvement. To this end, the project combines biomedical and ecological research with mitigation development and social science research and brings together researchers from national radiation protection entities, universities and SMEs. In a joint effort, the teams from the different participating institutions will contribute to the clarification of the possible effects arising from exposure to ionising radiation emitted by radon and naturally occurring radioactive material or NORM, thus contributing to a better management of risks to human health and the environment. Steps addressed within the project are (a) characterisation of radon and NORM exposures, (b) improving dosimetry, (c) assessing effects and risks for humans and the environment, (d) refining mitigation technologies, (e) raising the understanding for societal aspects, and (f) disseminating achievements. In addition to this, an ambitious pan European E&T programme will contribute to competence building and sustainability of the project findings. These steps are reflected in the respective work packages.

The scientific outputs and technological developments resulting from this project will contribute to a better characterisation of exposure (through the improvement of dosimetry techniques, especially for low dose exposures) and to the risk assessment and mitigation processes. RadoNorm will thus contribute to define safety standards for exposure to ionising radiation, it will also lead to the development of recommendations and protection measures against radon and NORM.

Acknowledgment
This project has received funding from the Euratom Research and Training Programme 2019–2020 under grant agreement No 900009.

Disclaimer
This abstract reflects only the author’s view, and the European Commission is not responsible for any use that may be made of the information it contains.

Continuous Education and Training through a Dose-Management Platform

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Abstract

In recent years, dose-management systems (DMSs) have become invaluable tools of imaging departments to monitor and manage big data resulting from the increased number of imaging exams. A DMS is a software that collects radiation dose indices and other parameters from medical imaging examinations, stores them in a database along with patient demographic and study information, extracts or calculates a large quantity of potentially very interesting dose and quality related parameters and makes the results easily available to the user.

Having access to all the parameters allows for direct insight. Especially in the covid era, DMSs are of tremendous benefit, as direct onsite access to imaging rooms has become even more difficult. Besides monitoring dose and quality, a DMS can be a powerful tool for continuous training of health professionals on optimization and radiation protection. Using actual data and examples from the department is always more stimulating for the attendees. Interesting teaching points can be:

- From standardized dosimetry to individualized dosimetry: phantom dose is not patient dose; explain how the dose changes when patient-specific data are included in the dosimetric calculation. The CTDIvol in CT, which is dose on a standard PMMA phantom, changes to Size Specific Dose Estimate when the patient size is taken into account. Furthermore, effective and organ doses are calculated on anthropomorphic phantoms that match the patient habitus.
- Value of correct positioning in CT: A patient closer to the tube during the localizer view will be considered larger and receive higher dose. In the case of horizontal offset, the bowtie filter will not shape the beam correctly, leading to a non-uniform image quality.
- Skin dose awareness in interventional radiology: it is important to establish a protocol for tracking and following up patients who receive high skin doses with expected skin reactions. Cases can be analyzed and evaluated for optimization purposes (e.g., how changing angulation affects skin dose).
- Compression force in mammography: compression force of a specific range (around 100N) allows for a good quality image; the compression makes the breast more symmetrical and thinner in thickness resulting in a lower radiation burden. It also reduces superimposition of breast structures and increases geometric and motion sharpness.
- Compliance with Diagnostic Reference Levels: one of the major benefits of DMSs is that they can monitor protocols and evaluate the compliance with national and international regulations in a larger scale than previously performed. Creating awareness of the importance of protocol optimization can be an important point of the teaching program.

With a DMS, health professional teachers are given a unique opportunity with valuable information right at their fingertips for different specialties (technologists, radiologists, cardiologists, surgeons)! Setting up a program of continuous education and training can save time and help to avoid mistakes. Different specialties require different competences; a multi-specialties program with different scenarios for technologists, radiologists and medical physicists can be developed. Identifying practical examples and use in house cases improves user engagement and allows for better understanding of quality, optimization and radiation protection.

Cancer-Related Changes in Cells Exposed to Alpha Radiation in Combination with Nicotine

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Abstract

The carcinogenic effect of radon - the second cause of lung cancer - has encouraged the European Commission to fund the RadoNorm project. One of its aims is to reduce scientific uncertainties in all steps of radiation risk management by assessing biological mechanisms underlying radon interaction with other stressors such as smoking. Smoking is the dominant cause of lung cancer; thus, an understanding of the interaction of smoking with radon in inducing lung cancer is required for making a sound risk estimate and establishing a reference level for indoor radon exposure to the general population. Despite the remarkable efforts in determining the radon-smoking interaction, the underlying mechanisms are yet to be identified. Besides, there has been a debate over the issue which compounds in cigarette smoke play an important role in inducing lung cancer. The suggested role of nicotine in reducing DNA repair and enhancing mutations and cell transformation strongly supports the candidacy of this compound as a potential target for study. The present study aims to assess the underlying mechanisms of nicotine interaction with alpha particles. For this purpose, ^{241}Am, having an energy equal to that of ^{222}Rn, is used as the source of alpha particles.

At the outset, set-up experiments were performed. Bronchial epithelial BEAS2B cells were pretreated with 2 µM nicotine for 16 h and then given different doses of alpha particles ranging from 0, 0.5, 1 to 2 Gy. Clonogenic survival assays were run for choosing the optimal dose of alpha particle, alone and in combination, for studying the mechanisms of interaction. Simultaneously, γH2AX analysis has been done to analyze the direct effects on DNA damage response after single exposures or the combination, and differential response patterns were indicated. At the level of gamma-H2AX foci the result indicated the formation of large foci in alpha particle irradiated cells, confirming the formation of more complex damage, while nicotine-treated cells induced a delayed formation of small foci (4–6 h after nicotine exposure ended). The repair kinetic curve showed a biphasic response in response to both alpha particles and combined exposure, with peaks after 1 h and 6 h. However, a faster repair of small foci was indicated in the combination group, as shown by a lower gamma-H2AX level after 4 hours in comparison with alpha radiation alone.

This study is a newly started research project with some preliminary data and will further investigate combination treatments using clonogenic survival, gene expression analysis for radiation-induced DNA damage response genes, as well as proinflammatory marker assays.

Physiologically Based Pharmacokinetic Modelling for Novel Radiopharmaceuticals Using a Multilevel Object-Oriented Modelling Methodology

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Abstract

Introduction: Novel therapeutic radiopharmaceuticals (RPs) are focussing on alpha emitting nuclides. To assess dosimetric impact of these novel radiopharmaceuticals we developed a multilevel object-oriented physiologically based pharmacokinetic (PBPK) model for the treatment of neuroendocrine tumours, based on a PBPK model previously developed by Kletting, et al. In this model, which is implemented in PhysPK, the full chain of events following intravenous administration are included: e.g., extravasation, binding, internalization and release. To study the usefulness of the model for alpha therapy we have performed a simulation to study the results for an alpha emitting nuclide including her progeny.

Material and methods: In this study we have used a pre-therapeutic scan (from literature) which provide patient specific uptake of the RP in healthy and tumorous tissue and simulated a treatment with ^{177}Lu-DOTATATE and ^{212}Pb-DOTATATE. The model including patient specific details is used to simulate therapy with a total administration of 145 nmol DOTATATE of which 10 nmol is labelled with either ^{177}Lu or ^{212}Pb. The dissociation constant and dissociation rate of 0.52 nmol/l and 0.013 min^{-1} respectively are used for both radiopharmaceuticals. Subsequently we compared the amount of radioactive compound accumulated in the liver, spleen, kidney and the tumour at the different sub-tissue levels. For each organ the time integrated activity (TIA) is determined and the fraction located in the vascular, interstitial and cellular space is estimated.

Results: The TIA of ^{212}Pb was found to be between the 20 and 26% of the ^{177}Lu TIA for the evaluated tissues. The distribution of the radiopharmaceutical between the different sub-tissue levels was found to be comparable for each radiopharmaceutical including the progeny. This is expected because both the physiological and pharmacokinetic parameters are equal. However, although the fraction of receptors bound with DOTATATE remains equal, the fraction bound with radioactive DOTATATE declines more quickly for ^{212}Pb and progeny due to differences in decay time. This means that the time in which the total dose is delivered to the tissue is shorter for ^{212}Pb.

Conclusion: Although further validation is needed, the multilevel PBPK model demonstrated to be useful for applications in targeted alpha therapy. One of the subsequent steps to include in the model are the inclusion of different dissociation parameters for different ligands and the impact of recoil. This allows us to conduct dosimetric evaluations of such novel radiopharmaceutical before its actual clinical use.

Dose Variations Using an X Ray Cabinet to Establish Calibration Curves for Biological Dosimetry Techniques

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Abstract

Purpose: X ray cabinets are replacing $^{137}Cs/^{60}Co$ sources in radiation facilities due to advantages in size, handling and radiation protection requirements. However, X ray cabinets are more susceptible to experimental influences than conventional sources due to their different physical properties. The aim of this study was to examine the uncertainties and pitfalls related to the experimental arrangements used to set up calibration curves in biological dosimetry with X ray cabinets.

Materials and Methods: Blood sampling tubes were X ray irradiated in horizontal or vertical position at the beam center with presence or absence of a fan heater. The irradiation was performed with an X ray tube (195 kV, 10 mA, 0.5 mm-thick copper filter, dose rate of 0.59 Gy/min). To evaluate the influence of these experimental settings, a combined approach of physical measurements with thermoluminescence (TL) dosimeters and alanine (dosimeter) pellets and detection of biological effects by quantification of micronuclei (MN) and dicentric chromosomes (DIC) was used.

Results and conclusion: X ray cabinets are user-friendly irradiation units and often applied to investigate biological radiation effects. However, experimental setup components could affect delivered radiation doses extremely. The results of this study revealed that the orientation of blood sampling tubes (vertical vs horizontal) had a significant influence on the radiation dose and thus on the analyzed biological effects. For this reason, a strict dosimetric monitoring of experimental irradiation setups is mandatory for calibration curves established in biological dosimetry. Careful consideration of the experimental setup in close collaboration with physicists is required to ensure traceability and reproducibility of irradiation conditions, to correlate the radiation dose and the number of micronuclei and dicentric chromosomes correctly and to avoid systematical bias influencing the dose estimation in the frame of biological dosimetry.

An Innovative Curriculum Model to Boost the Number of Medical Physicists and Radiation Protection Experts in Medical Radiation

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Abstract

Purpose: In many countries in the world the medical-physics/radiation-protection professions face an acute shortage of entrants owing to the irregular number of physics/engineering graduates and low popularity of two-year master's programmes. Under such conditions of uncertainty the professions would not only fail to grow but inevitably decline, leaving patients and hospital staff without adequate medical-physics/radiation-protection services. A formula needed to be found to: (a) ensure that the potential stock of entrants to the professions would be independent of erratic student numbers in physics/engineering (b) address the paradox of having to reduce the masters programme to one year at a time when the knowledge-skills-competences required for modern medical-physics/radiation-protection practice are expanding rapidly owing to the increasing complexity of medical device technology and clinical protocols.

Method: A survey of medical-physics/radiation-protection education programmes and documentation was carried out and elements of best practice identified. The latter were used to guide the curriculum development process. Stakeholders were consulted and their suggestions implemented in the curriculum.

Results: It was considered that the best way forward would be to opt for an undergraduate inter-faculty programme that combined physics and medical physics/radiation protection. The resulting four-year programme consists of five parallel strands namely physics/mathematics/statistics, medical-physics/radiation-protection, basic-medical-sciences, research and hospital placements. The physics/mathematics/statistics component is sufficiently strong to ensure a strong scientific foundation whilst the medical-physics/radiation-protection component is sufficiently comprehensive to permit the reduction of the Master's in Medical Physics from two years to one.

Conclusions: We are pleased to report that the innovative curricular experiment has been a great success. The combination of pure and applied physics, the inter-faculty nature of the programme (where students share lectures with both physics and healthcare professions students) together with the element of clinical practice have been found to be the most attractive features of the programme. The programme has provided a welcome boost for both the medical-physics/radiation-protection professions and indeed even physics itself.

Response of Current Environmental Dosemeters to New Operational Quantities

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Abstract

Last year, ICRU released the revision of the concept of operational quantities for external radiation. The new quantities, which better correspond to the radiation protection quantities, which are legally regulated, were defined. This change influences the performance of currently used dosemeters. Before implementing of the new quantities as legally binding, instruments must be adapted to measure them adequately. For these purposes, personal and environmental dosemeters calibrated in current operational quantities should be tested and the results analysed. In our work, results on environmental survey monitors and passive dosemeters are discussed. As regards relevant photon energy spectra for ambient monitoring, there is no evident qualitative difference in performance of the dosemeters with respect to the new and old quantities. There are indications that the difference would be greater for lower photon energies <65 keV, for which the dosemeters were not subjected to tests. The difference at higher energies seems to be constant. Therefore, the response could be adapted to the measurement of the new operational quantities using a single factor specific for every dosemeter, at least until the dosemeters are recalibrated or redesigned by manufacturers.

Neutrophil Infiltration in Radiation-Induced Cardiovascular Inflammation

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Abstract

Atherosclerosis is aggravated by cardiovascular risk factors that affect endothelial dysfunction and the migration of leukocytes, including the over accumulation of lipids and fluctuations in cytokine levels. To study the infiltration of leukocytes in radiation-aggravated atherosclerosis, we tested Ldlr-/- mice and C57BL/6j mice after exposure to 0.5 or 1 Gy radiation over 16 weeks. We found that radiation exposure induced atherosclerosis development in Ldlr-/- mice, as demonstrated by increased lipid-laden plaque size, reactive oxygen species levels, and levels of the pro-inflammatory cytokines. Total plasma cholesterol, triglyceride, and LDL cholesterol levels were also increased by radiation exposure, along with cardiovascular risk. We also showed dose-dependent increases in neutrophils and monocytes that coincided with a reduction in lymphocytes in the spleens of Ldlr-/- mice. We concluded that chronic radiation exposure increased the production of pro-inflammatory mediators, which was associated with the migration of neutrophils and inflammatory monocytes into sites of atherosclerosis. Therefore, our data suggest that the accumulation of neutrophils and inflammatory monocytes with the reduction of lymphocytes, contribute to aggravated atherosclerosis in Ldlr-/- mice under prolonged exposure to radiation.

Acknowledgement
This work was supported by the National Research Foundation of Korea (NRF) grants funded by the Korean government (MSIT), grant number NRF2019R1A2C208741613.

Keywords: Atherosclerosis; Radiation; Ldlr-/- mouse; Neutrophil infiltration

Optimization Process in Radiotherapy (OPRORA) Project: Dosimetry Audit on VMAT and IMRT for Prostate and Head and Neck Treatment

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Abstract

The three-year project titled “Optimization PROcesses in RAdiotherapy: clinical and dosimetric audits (OPRORA)” was financed in 2018 by the Italian Ministry of Health to develop and apply a model of parallel clinical (CA) and dosimetry (DA) audits for IMRT and VMAT to selected Italian Radiation Therapy Centers (RTCs). The design of the end-to-end DA will be herein described. Two types of DA were considered: 1) in reference condition, using a PMMA phantom and 2) in treatment condition, to be applied to prostate carcinoma (treated by VMAT) and head and neck carcinoma (treated by IMRT). For DA-2, two different anatomical districts of a Rando-Alderson phantom are employed.

Three different dosimetry systems, calibrated in a ^{60}Co beam at the Italian Primary Lab (INMRI-ENEA), were selected to be used for the audits: alanine dosimeters (FWT-50), TLDs (TLD-100 disk) and gafchromic films (EBT3).

For the DA-1 RTCs are asked to irradiate at the prescribed dose a box-shape volume, inside the PMMA phantom, applying small fields at several angles. In this volume, three alanine dosimeters and a piece of EBT3 film are placed.

In the DA-2, the two parts of the Rando phantom went separately through CT-scanning and contouring, then a treatment plan was created for the two pathologies. In both cases, seven positions for alanine and TLD housing were selected simulating target and organ at risk (OAR) sites, respectively. In each selected target and OAR site a stack of 8 alanine pellets or a stack of 5 TLDs was positioned, respectively. Moreover, for dose distribution evaluation large pieces of EBT3 were sandwiched between two consecutive phantom slices at different tumour positions along cranial-caudal direction. In particular, 2 and 3 positions were identified for prostate and head and neck treatment, respectively. Starting from the common contoured CT-scans and following provided instructions, RTCs are asked to develop a personalized dose planning delivered according to the daily clinical practice. Four centres, not included among the RTCs to be audited and not involved at any level in the project itself, were selected to validate the DA system protocol. The actual audit has been launched in April 2021 and will be concluded in March 2022.

The overall design of a DA, the choice of dosimetry systems and the selection of RTCs, which were herein described, are challenging tasks and critical elements for the success of a DA. The significant number of centres that applied for participation in the project confirms the need of quality management programs in radiotherapy.

Effect of Antioxidant rA1M on Expression of Apoptosis and Oxidative-Stress-Related Genes during ^{177}Lu-Octreotate Treatment of GOT1 Neuroendocrine Tumours

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Abstract

Kidney radiotoxicity during targeted radionuclide therapy with ^{177}Lu-octreotate in patients with neuroendocrine tumours (NETs) limits the administered activity and thereby the therapeutic response. Reducing renal side effects of radiation could allow for higher activity amounts and better tumour control, increasing the cure rate. Co-treatment with the human recombinant antioxidant α1–microglobulin (rA1M) protects against short and long-termed radiation-induced renal damage in mice treated with ^{177}Lu-octreotate. Furthermore, co-treatment with rA1M does not affect the therapeutic effects on tumour volume in human NET GOT1-bearing mice.

Purpose: The aim of this work was to investigate transcriptional regulation of genes related to apoptosis and oxidative stress in GOT1 tumours in mice at one and seven days after administration of rA1M and after treatment with ^{177}Lu-octreotate with or without co-administration with rA1M. Methods: Adult female Balb/c mice with s.c. GOT1 tumours were i.v. injected with either ^{177}Lu-octreotate (30 MBq, n=6), rA1M (5mg/kg, n=6) or co-treatment with both (n=6). A control group was sham-treated with NaCl (n=4). RNA was extracted from tumours sampled at one or seven days after injection. Gene expression of 84 apoptosis and 84 oxidative stress-related genes were evaluated using RNA array plates and RT-qPCR.

Results: RT-qPCR analysis showed higher and similar expression of apoptotic genes in the irradiated groups than rA1M administration alone on day one after injection. Corresponding result after seven days was similar but less prominent. The most affected pro-and anti-apoptotic genes were GADD45A, TNFRS10B, FADD, FAS, CASP4,6,3, BAX and BAG3, BIRC2, BIRC3, BIRC5, XIAP, NAIP, BCL2L10, BCL2L2, IGF-1R, IL-10, CFLAR, respectively. Overall, most oxidative stress genes were not significantly regulated. APOE, DUOX1, HMOX and FOXM1 were some of the most regulated genes in the oxidative stress array. The results were more similar between the irradiated groups than those in the A1M group. CYBG and MB, related to oxygen transportation, were significantly upregulated after ^{177}Lu-octreotate and co-administration, but not after rA1M alone.

Conclusions: The transcriptional regulation of the analyzed apoptosis-related genes may suggest a similar apoptotic response in irradiated and co-treated groups compared to administration of rA1M alone. Antioxidant genes were generally downregulated, indicating that antioxidant defense mechanisms were less prioritized in damaged cells.

Keywords: α1-microglobulin, transcriptional response, GOT1, ^{177}Lu-octreotate, NET, gene regulation

The Questionnaire on GDPR Compliance Developed in the Framework of MEDIRAD Project: Results

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Abstract

The MEDIRAD Project is a 4-year project aimed at enhancing the scientific bases and clinical practice of radiation protection in the medical field; the project has received funding from the Euratom Research and Training Programme 2014–2018 under grant agreement No 755523.

Biomedical and radiation protection research increasingly relies on personal data pertinent for the analysis of exposure/health effects relationships; consequently, the project had to adapt the work procedures involving utilization of patient data for its scientific investigations. Access to and exploitation of such data is now regulated by the General Data Protection Regulation (GDPR) directive, which has been implemented with variations among European countries. For this concern, there is a need for an involvement at national level, as well as for the harmonization and standardization of protocols and techniques at regional level. Relevance is given to the complex multifactorial context that might challenge the final aim. For example, compliance with the new regulation on GDPR will be mandatory. The emergence of variations of regulatory practice for the implementation of GDPR in member states may over time present severe difficulties for the operation of European research projects which require access and exploitation of personal data (epidemiological studies, biobanks, dosimetric & imaging repositories …) as a valid contribution to better understand how to manage the necessity of data patients and to correctly use them for research. For this purpose, it was decided within Task 6.3.2 to administer a questionnaire to the MEDIRAD researchers from the WP 2–5 differently involved in patient data management. The survey aimed to identify the positive and negative experiences encountered in the context of MEDIRAD with respect to GDPR compliance, and to find out how difficulties in this field were overcome. Results allowed elaborating recommendations aiming to help the research community to face future GDPR issues. These MEDIRAD recommendations will target medical researchers, scientific communities and regulatory authorities. The online survey on GDPR Compliance developed by WP6 was launched on 01/02/2021 and closed on 28/02/2021. In total, 37 answers from researchers members of 21 different institutions were collected.

The two most rated recommendations resulting from the survey, with a sum of agree and strongly agree of about 80% of the total responders, were:

- To develop research oriented harmonised European guidance on GDPR compliance in order to reduce divergence of interpretations and practice at national level
- To develop European training courses on GDPR compliance for researchers.

Thus indicating the need of harmonization in the GDPR compliance process and of continuous training on the GDPR subject. The recommendations will aim to facilitate the development of large scale multinational epidemiological studies, proposing guidelines to help European countries to implement at the national level European regulatory requirements on ethics (including compliance with GDPR directive), and to encourage harmonization of regulatory practice notably through the collection of experience gathered through the EURATOM research projects.

Typical Effective Dose Values in Nuclear Medicine Single Photon Emission Imaging in Croatia

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Abstract

Introduction: Dose assessment in diagnostic nuclear medicine is required to optimize imaging procedures, estimate radiation risk, improve radiation safety, and verify compliance of local and national practice with international guidelines. Typical effective dose values for a standard patient related to administered radiopharmaceutical were estimated according to results of a study on national diagnostic reference levels for single photon emission imaging procedures.

Materials and methods: Imaging in nuclear medicine is based on administration of radiopharmaceutical, which is distributed in the patient body. Therefore, International Commission on Radiation Protection (ICRP) has designed a set of mathematical models of the human body to provide estimation of effective dose values delivered by the administered radiopharmaceutical. The methodology proposed by the ICRP assumes that radiation source is whole patient body, and the estimation is based on conversion factors given as radiopharmaceutical specific effective dose per unit of administered activity.

The aim of this study was to estimate typical effective dose values for more than 30 single photon emission imaging procedures performed in Croatia by the application of various radiopharmaceuticals based on the radionuclides ^{99m}Tc, ^{131}I, ^{123}I and ^{67}Ga.

The national practice is represented by typical effective dose values for standard patient with a body mass of 70±20 kg. They were estimated using the median national value of administered activity for each procedure and the corresponding conversion factor. Conversion factors were taken from ICRP publications 60, 80 and 128, except for a few procedures which are omitted from the ICRP publications. Conversion factors for these procedures were taken from respective radiopharmaceutical specification.

Results: Minimum, maximum and typical national effective dose values related to respective administered radiopharmaceutical were estimated. Effective dose values for the procedures of the same type performed at different nuclear medicine departments were rather heterogeneous, demonstrating values that differ over 10 times between minimum and maximum effective dose values for respective procedure. Values of typical effective dose of investigated imaging procedures vary from less than 0.1 mSv to 35.5 mSv. Such large variations can be related to the different administered activity and desired diagnostic outcome, different radiopharmaceutical used and different mathematical model adopted.

In data analysis and comparison of estimated effective dose values different types of uncertainties should be considered. For example, the uncertainty in effective dose estimates from respective radiopharmaceutical vary among patients due to anatomical likeness to the model (mass of organs and distance between organs) and strongly depends on the mathematical model used for the simulation. It is important to note that periodical performance of comprehensive quality control procedures may enable reduction of uncertainties related to administered activity.

Conclusion: Estimation of patient effective dose values allows benchmarking of different nuclear medicine procedures in terms of stochastic radiation risk. It also provides a quantity for comparison of

respective procedure to other imaging modalities based on the application of ionizing radiation. Additionally, information on the number of such procedures enables determination of the contribution of nuclear medicine imaging to the collective effective dose.

Inter-Laboratory Comparison (2021) on the Dicentric Chromosome Assay in the Frame of the European Network of Biological and Physical Retrospective Dosimetry (RENEB)

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Abstract

Inter-laboratory comparisons (ILCs) are regularly performed in the frame of the European legal association RENEB (Running the European Network of Biological and Physical retrospective Dosimetry) network to validate and improve the procedures for various physical and biological assays. The dicentric chromosome assay (DCA) is considered as the "gold standard" for radiation biodosimetry and is an important tool for radiation dose assessment in small and large-scale radiation accidents. For a large-scale accident, where many individuals are potentially exposed to ionizing radiation, the scoring procedure has to be adjusted to handle the large amount of data in a reasonable amount of time and it is crucial to test the performance of the laboratories under conditions simulating a real accident situation.

33 biodosimetry laboratories from 15 European and 7 non-European countries participated in the current RENEB ILC (2021) for the DCA. The general study design included the irradiation of blood samples, blood shipment, sample processing, analysis of chromosome aberrations and dose assessment. Blood from one healthy donor was irradiated in vitro with X-rays and three blind coded blood samples were sent to each participant. The task was to culture samples, to prepare slides and to assess radiation doses based on the observed dicentric yields with reference to an appropriate calibration curve in each laboratory. The main aims were to test the response time of the participants, to determine whether the estimated radiation doses of the participating laboratories were in good agreement with the true doses and to identify potential needs for further training and harmonisation. The participation of laboratories from countries around the world gave the opportunity to compare the results on an international level.

The results of the ILC for the DCA will be presented and the potential and limits of the DCA in the case of a large-scale accident will be discussed. Regular quality-controlled exercises are important to allow the comparison of results obtained in different laboratories and to identify further needs to optimize international networking in the field of biological dosimetry.

Effects of Low-Dose γ Radiation on Atherosclerosis in Apoe(-/-) Mice: Study of Short-Term Effects on Macrophage Polarization and Evaluation of Long-Term Phenotypical and Immunological Effects in the Atherosclerotic Plaque

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Abstract

Effects of low doses of ionizing radiation on atherosclerosis are still a source of many uncertainties, and in particular whether these effects generate anti or pro-inflammatory responses. Furthermore the delay of occurrence of such effects upon irradiation are unknown. Atheroprone ApoE(-/-) mice were exposed to single dose 0, 0.05, 0.5, and 1 Gy of ^{137}Cs (γ) at 10.35 mGy/min dose rate. Short term (24 hours) effects on bone marrow-derived macrophage polarization and long term (100 days) consequences on atherosclerotic plaques were investigated. Cells were treated with Il-4 or INFγ for M2 or M1 polarization, respectively. Polarization was validated by measuring the mRNA levels of polarization markers using RT-qPCR. Also, cell culture supernatants of polarized macrophages were harvested and cytokine expression were determined using ELISA. Challenges in understanding biological mechanisms of LDIR include small size of experimental animal groups, low level changes and data heterogeneity and multimodality. In this study, we report results of applying the fold-change, usually considered a relevant criterion for stating difference and similarity between measurements and a multilevel multivariate approach. We focus on the statistical exploration and analysis of a repeated measurement design using multivariate projection-based approaches such as Partial Least Squares Discriminant Analysis (PLS-DA) (for the identification of indicator variables characterizing each macrophage polarization in low doses).

We found a significant dose-dependent increase of genic expression of Chil-3 and Retnla anti-inflammatory markers in M0 and M2 type macrophages upon 24 hours exposure and no effects on M1types. These effects were associated with a dose-dependent increase of IL-10 and reduction of IL-1 secretions in M0 and M2 and an increase of IL-6 in M1 type macrophages. Circulating pro-inflammatory Ly6CHigh monocytes were reduced at 24 hours and anti-inflammatory Ly6Clow monocytes were notably increased in the spleen 100 days upon irradiation.
Long term exposures to any doses did not affect atherosclerotic plaque size and collagen contents determined by Oil red O and picrosirius red staining respectively. However, a significant reduction of macrophage content by 85% was observed at 1 Gy only.

Taking together these findings show that low to moderate doses of ionizing radiation enhance anti-inflammatory functions of M2 macrophages at short term exposure associated with a reduction of plaque CD68-expressing macrophages at long term exposure in ApoE-/- mice. These results indicate an atheroprotective effect of low to moderate doses of ionizing radiation in an atheroprone mouse model through regulation of macrophages.

European Federation of Organisation for Medical Physics (EFOMP) Perspective on the Current Role and Future Direction of the Physical Scientist as a Medical Physics and Radiation Protection Expert

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Abstract

Medical physicists play a key role in radiation protection of patients, health care staff and public. The role of a properly trained scientist and registered physics expert is recognised in both legislative requirements and day to day practice of radiation protection. The European Federation of Organisations for Medical Physicists (EFOMP) represents 9000 medical physicists in 36 countries. The contribution of the medical physics community extends from fundamental research on the effects of radiation, to proper dosimetry, to equipment and facilities design and optimisation of the benefit risk ratio in both the treatment and diagnosis of disease. EFOMP plays a key role in supporting the European medical physics community in delivering these goals. Key strategic areas in ensuring good radiation protection in Europe feature appropriate training for radiation protection experts and medical physics experts through EFOMP approved national registration schemes, provision of state-of-the-art medical physics training and scientific exchange through is educational platforms, congress and scientific schools. Recently EFOMP updated the core curriculum for medical physicists working in radiotherapy in association with the European Society for Radiotherapy and Oncology (ESTRO). Similar updates have been initiated with European society of Radiology and European Association of Nuclear Medicine (EANM) for the curricula in diagnostic radiology and nuclear medicine. Education and collaboration is key to minimising unintended exposure and unwanted side effects of radiation. This is especially true to the new radiotherapy treatments such as FLASH radiotherapy and proton beam therapy as well as the use of new approaches to planning and optimisation of such therapies.

Recognising that individuals have differing radio sensitivities and that good dosimetry is the key to good radiation protection and successful outcomes, EFOMP recently set up a special interest group in nuclear medicine therapy dosimetry. The working groups of EFOMP produce standards for quality assurance in newer radiation producing technologies as well as recognising the role of the physicist in non-ionising alternatives such as MRI. The working groups also have produced a syllabus on the role of the medical physics expert in clinical trials. Due to the impact that artificial intelligence and big data is beginning to have on radiation protection and understanding of the effects of radiation, an EFOMP working group has recently produced a syllabus on artificial intelligence for the medical physicist. EFOMP recognises that good radiation protection is delivered through collaboration with multidisciplinary teams and have continued to collaborate on areas such as recurrent imaging and patient shielding with aligned organisations involved in patient treatment and diagnosis.

Optimisation Process in Radiotherapy Project: Clinical Audit on VMAT and IMRT for Prostate and Head & Neck Treatment

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Abstract

OPRORA is a three-year project supported by Italian Ministry of Health to implement a reference model of clinical audits (CA) and dosimetric audits (DA) in two Radiation Therapy (RT) advanced techniques, Intensity Modulated Radiation Therapy (IMRT) and Volumetric Modulated Arc Therapy (VMAT). CAs play a relevant role in the development and safety of treatments and in their harmonization at national/international level as demonstrated in countries where CAs and DAs are undertaken on a regular basis with regional audit group networks. The audit role was already stressed in the past and currently required in EURATOM Directive 13/59 transposed in the Italian law as D.Lgs 101/2020.

The CA model has been designed by an Interdisciplinary Committee (IC) and will be carried out in 13 Radiation Therapy Centres (RTCs), homogeneously distributed in Italy. The IC was set up including radiation Oncologists and Medical Physicists from the partners of the Project. CA has been addressed to critical issues of patient radiation protection and to key components of the overall quality system. General aspects and two relevant pathologies, prostate and head & neck tumours, were defined. The IC identified retrospective and prospective indicators (12 for prostate and 15 for head & neck) for areas to be improved. Indicators (belonging to the three categories: structure, process and outcome) have been administered through a Microsoft Excel file.

The CA is taking place as described below:

1. Pilot phase: indicators were administered to the four pilot Radiotherapy Centers; collected data from the pilot phase have been used to improve the first model;
2. Validation phase: the improved version of indicators has then been administered to further four Radiotherapy Centres for a blind validation process (ending at September 2021);
3. Audit phase: the final improved version of indicators will be sent to the recruited RTCs (end of 2021).

An overview of the indicators developed for the two pathologies will be presented at the conference.

The European Metrology Network for Radiation Protection: Benefits and Challenges

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Abstract

The European regulation on ionizing radiation is essentially laid down in the Council DIRECTIVE 2013/59/EURATOM. This Directive implements the basic safety standards for the protection of humans and the environment against the dangers arising from exposure to ionizing radiation.

However, the practical implementation of the European basic safety standards has become more complex due to the lack of consideration of the metrological implications and the adaptation to new technological developments, which lead to new standards, technological innovations, and improved capabilities.

It is therefore of vital importance to create a network that acts as a focal point between the metrology communities and the relevant radiation protection stakeholders, including regulators, standardization bodies, manufacturers, users of radiation sources and international organizations and platforms dealing with radiation protection such as HERCA, IAEA and EURADOS.

The development of such a metrology network under the umbrella of EURAMET was planned by the consortium of the JNP EMPIR project 19NET03 supportBSS. The plan was successfully evaluated by EURAMET and the European Metrology Network (EMN) for Radiation Protection was approved by the EURAMET General Assembly in June 2021.

The EMN for radiation protection will interact with innovative technological developments and has set itself the goal of being the central point of contact in order to cover the metrological needs in radiation protection and to find metrological solutions on a European level.

The main challenges for this goal are in the first step the implementation of a long-term ongoing dialogue between the metrology communities and relevant stakeholder groups and, on the other hand, the development of a joint and sustainable European metrology infrastructure that underpins radiation protection regulation. The first step is visualized in this work.

Acknowledgement
This project 19NET03 supportBSS has received funding from the EMPIR programme co-financed by the participating states and from the European Union's Horizon 2020 research and innovation programme. 19NET03 supportBSS denotes the EMPIR project reference.

Methodologies Used for the Optimisation of Radiation Doses Applied in Stereotactic Radiosurgery of a Brain Tumour

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Abstract

Target audience: This abstract is of interest for researchers in the field of radiation therapy and medical physics, in particular, investigation of optimized radiation dose level in radiation therapy.

Purpose: Stereotactic radiosurgery is a treatment modality applied on patient with single or multiple metastases. Brain metastases were detected approximately in 20–40% of cancer patients and it becomes mainly the reason of high risk of mortality because of various reasons, including factors related to the damage over the risk organs, history of patients, etc. The aim of this study is to study various dosimetry plans and efficiency of Stereotactic Radiosurgery (SRS) for single tumour and multiple metastases in brain and develop novel methodology to optimize delivered radiation doses with the target interest given to the critical tissues and risk anatomies.

Materials and methods: Study was performed on the bases of (n=35) of oncological patients with single tumor (n=0) and multiple metastases (n=23) treated on multiple photon and electron energy TrueBeam and EDGE with the fusion of images of high resolution CT guided simulator and 3T MRI. Size of the target varies from (22 mm) to (29 mm). Age of patients: (42–70). Treatment was conducted with parameters: MV=6FFF, MU=2400, number of fractions=5, total dose=30, total treatment time is approximately (3 min) and Isodose volume VpDGy was (27) and comparable to international standards. QA/QC was performed with the LUCI phantom with setup parameters: PDD, OAR, Scatter factor. Statistical analyses were performed using Box and Whisker analysis and regression models.

Results and discussion: The results of this shows that the single isocenter VMAT radiosurgery technique for the treatment of 1 or more brain metastases produces plans of high clinical quality, including favorable values for both CI and dose GI. CI and HI are evaluated for each target of plan, while a per-plan GI is calculated for each patient. The mean ± standard deviation CI was 1.15 ± 0.12 for all lesions; the mean ± standard deviation per plan GI was 3.37 ± 0.4; the mean ± standard deviation HI for all lesions was 1.446 ± 0.12. For single target plans (n=5), the mean CI was 1.06, the mean GI was 3.04, and the mean HI was 1.48. For multitarget plans (n=9), the mean CI was 1.14, the mean HI was 1.4, and the mean GI was 3.54.

Conclusion: In the settings for the treatment of brain metastasis, local control using the dose levels and delivery in this cohort may be inferior to radio-surgical series. Local control is independent of histology. Careful selection of patients and individual set up protocols remains critical.

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Radiological Component of the Exposome, Multiple Exposures, Risks of Cancer and Other Chronic Diseases in the Constances Cohort (CORALE)

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Abstract

Context: Throughout life, people are exposed to ionizing radiation (IR) at varying levels, via multiple natural and artificial sources, whether in the context of the residential environment, various activities (professional or other such as air travel) or for medical reasons (diagnostic or therapeutic procedures). The carcinogenic effects of IR are well documented at dose levels of 100 milliGrays (mGy) or higher. There is still controversy about the shape of the relationships between exposure and cancer risks at lower doses, called “low doses”. In addition, the quantification of the effects of multi-exposure to IR and other cancer risk factors is poorly documented, with the exception of the interaction between tobacco and radon on lung cancer risk. Similarly, the relationships between exposures to IR at different stages of life (e.g., during childhood, puberty, etc.) and late health effects remain poorly characterized. Potential associations between low doses of IR and non-cancer chronic diseases also require better documentation.

Objectives: The first objective of the CORALE project is to carry out the broadest possible reconstruction of doses of IR from environmental sources (radon, terrestrial and cosmic radiation, food, nuclear installations and other artificial sources), medical (diagnostic and therapeutic procedures) and occupational exposures (nuclear workers but also other industries using radioactive sources, health professionals…) received by participants of the Constances cohort since birth, following the logic of the exposome concept (for its radiological component). The second objective will be to estimate the risks of cancers and other chronic diseases potentially associated with the cumulative doses received (from several sources of IR and over time) taking into account the potential influence of the context of multi-exposures to other risk factors.

Methods: In order to reconstruct the annual doses of IR received by members of the French Constances cohort since their birth, a large number of natural and artificial sources of radioactivity must be considered. Reconstructions related to environmental, medical and occupational exposures will be performed by different units of IRSN in collaboration with the Constances cohort team (Inserm). To do this, a questionnaire will be sent to about 85000 cohort members who have already provided their residential histories. The statistical analyses (e.g., Cox models with time-dependent covariates) will benefit from the expertise of radiobiologists, supporting the exploration of specific hypotheses and interpretations. The use of advanced Bayesian probabilistic models allowing to deal with multi-exposures will be explored.

Perspectives: CORALE is part of a broader long-term research programme, which will include the effects of other multi-exposures (e.g., IR and other environmental exposures) and the study of risks and exposure biomarkers through the Constances biobank.

Cytogenetic Biodosimetry Intercomparison Exercises among Laboratories in South Korea

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Abstract

In order to increase capacity of biodosimetry performance in large scale radiological accidents, standardized protocols and quality assurance of biodosimetry laboratories within networks are required. An intercomparison exercise is a useful tool to validate the performance of laboratories and harmonize the protocols. We launched an intercomparison exercise to harmonize scoring protocol and develop an image repository for education and training. Participating laboratories shared metaphase images previously generated for dicentric and translocation assay. Total 3000 metaphase images were scored according to their own scoring method first. The scoring results and sheets were shared, and inconsistent images were re-evaluated. Metaphase images with agreement were compiled to an image repository, and inconsistent images were used to harmonize scoring protocol. Key issues were analysis of chromosomes with centromeres in terminal position and twisted chromosomes, nomenclature for translocation analysis. This study found the issues required for harmonizing scoring criteria and maintain comparable capacity, which would be further discussed and harmonized in next exercises. This could provide valuable knowledge for standardization of scoring for biodosimetry worldwide, which would further enhance the capacity of national and international biodosimetry networks.

Cytogenetic Aberrations after Partial-Body Irradiation during Fractionated Radiotherapy

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Abstract

Partial-body exposure cases are likely to occur in radiological accident, but studies on the application of biodosimetry have been relatively focused on whole-body exposure. In addition, a direct data of in vivo response to partial-body exposure are limited. In this study, we evaluated the in vivo response of cytogenetic biomarkers to localized and fractionated radiation exposure. Patients (n=12) who received adjuvant radiotherapy after breast conserving surgery were recruited for this study. Their blood samples were taken at various time points during radiotherapy, and dicentric chromosome assay and fluorescence in situ hybridization-based translocation assay were performed. Biological dose estimation was calculated using the results of chromosome analyses. Dicentrics and translocation frequency was increased during radiotherapy. Biological whole-body dose estimates were significantly correlated with calculated equivalent whole-body dose. The partial-body dose agreed quite well with the dose delivered to the tumour after the first fraction of radiotherapy. Taken together, our findings suggest that cytogenetic markers are useful to estimate biological absorbed doses in partial-body and fractionated radiation exposure scenarios.

Cellular and Gene Expression Changes in VH10 and AHH-1 Cells after Chronic and Acute Exposure to Low Doses of Low, High and Mixed LET Ionising Radiation

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Abstract

Background: Ionizing radiation exposures often comprise low doses and dose rates of different qualities, but the shape of the dose response curve for cellular effects is unknown. We aimed at better understanding the effects of chronic low doses and dose rates of distinct radiation qualities in two cell types differing in origin and radiosensitivity.

Methods: Six radiation responsive genes were analysed by qRT-PCR in VH10 fibroblasts and AHH-1 lymphoblasts directly after reaching 50–200 mGy of 1 mGy/h ^{241}Am alphas, 1.6 mGy/h ^{137}Cs gamma or a 1:1 mixed beam chronic exposure. The fold change values were compared to those from cells acutely exposed using 13.4 Gy/h alphas, 4.1 Gy/h X rays, or 1:1 mixed beam to the same doses at 24 h post-irradiation and to 0.1, 0.2 and 1.0 Gy at 4–24 h post-exposure. Additionally, cell viability was determined based on the trypan blue exclusion assay. The potential detrimental effects of selected low doses of chronic radiation were also evaluated in VH10 and AHH-1 cells at the level of micronucleus frequency by standard cytogenetic procedure, and at the level of apoptosis, senescence, cell cycle arrest and oxidative stress by the use of commercially available kits.

Results: Chronic alpha exposure led to a dose dependent upregulation of most genes at doses >150 mGy in VH10. At high dose rates, the magnitude of transcriptional responses was time-dependent, higher at earlier timepoints (4–8 h vs. 24 h), yet lower after acute than chronic alpha exposure in VH10. In AHH-1, chronic exposure did not result in transcriptional changes relative to control. At the timepoint of maximum gene induction, the transcriptional changes in acutely irradiated AHH-1 and VH10 cells were similar, yet with a general delayed alpha response and a more stable effect after X rays and mixed beams in AHH-1. Acutely irradiated AHH-1 cells responded faster to X rays than to alphas, i.e., 4 h versus 8 h, while after mixed beams there was an intermediate gene-dependent response. The pattern regarding radiation qualities was: highest gene expression for X rays and mixed beams and lowest for alpha particles.

Cell growth after 1 mGy/h ^{241}Am chronic alpha particle exposure was reduced as compared to control in VH10, in agreement with the stronger gene upregulation. Preliminary cytogenetic results indicate a reduced micronucleus frequency, apoptotic index and replication index in 100 mGy-alphas irradiated AHH-1 cells as compared to controls. Further experiments are ongoing.

Discussion and conclusion: The transcriptional effect of IR depends on the dose rate, radiation quality, cell type and time point of analysis. The complexity of cellular responses to low doses of radiations of different qualities must be considered in attempts to infer health risks from cell-based studies.

Managing Patients in High-Dose Procedures at Centro Hospitalar Universitário do Porto

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Abstract

Introduction: The quantification of patient's radiation dose and the exposure time of the procedures are a growing concern for the users of ionizing radiation. In interventional radiology good practice recommends the monitoring and dose registration in the clinical record of patients. Being that patients exposed to high doses must be monitored and followed to evaluate the appearance of effects resulting from radiation.

Patient dosimetry is a complex process, and the reports are sometimes a real challenge due to the various units and quantities used.

This work aims to present the management that patients exposed to high dose have at Centro Hospitalar Universitário do Porto (CHUP).

Methods: This evaluation was carried out at CHUP, within the scope of the Committee on Radiation Protection (CPCR). In the presence of a report of an abnormal high dose in patients or professionals, the CPCR triggers a process of investigation the event, monitoring and follow-up. These are achieved by monitoring patient´s dose, maintaining and ensuring the safety of patients and professionals, identifying risk behaviours, continuing education and valuing and recognizing the future consequences of this problem.

Results: Since the implementation of dose notifications in 2018, 98 notifications have been made. All doses of the patients were evaluated by the consultant physicist of the hospital. 55 presented doses above the limits defined in SAFRAD, were contacted and evaluated by the physician and one of these patients was treated for the deterministic effects of radiation.

Conclusions: The attribution to the CPCR the competence to identify, follow-up and evaluate the exposures of marked patients undergoing fluoroscopy procedures allowed to raise the awareness of professionals for the careful management of the dose to the patient and its effects. The implementation of the procedures referred, allowed for better monitoring of patients at risk, greater accuracy in monitoring doses and optimization of protocols.

Occupational Radiation Exposure in Chemoembolizations: Evaluation of Doses in Different Body Regions of Professionals

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Abstract

Introduction: Interventional radiology is an area that exposes medical staff to the highest doses of radiation. The scattered radiation to which medical professionals are regularly exposed to, comes mostly from the patient, therefore staff who remain close to the patient receive highest levels of radiation.

The main objective of radiation monitoring is to ensure that the doses received by professionals do not exceed the values established by Portuguese Decree No. 108/2018. The aim of this study is to investigate radiation exposure profiles in medical staff during an interventional radiologic procedure - hepatic chemoembolization.

Methods: This study was carried out at Centro Hospitalar Universitário do Porto, in the intervention room. We evaluated radiation dose in hepatic chemoembolizations based on four criteria: total exposure time (fluoroscopy time), procedure frequency, air kerma and dose area product (DAP), This procedure was selected considering the potential high dose to medical staff (primary interventionist, assistant, radiographer, nurse, Anesthetist and Anesthetist nurse) due to prolonged exposure to radiation and the difficulty of the procedure.

Results: Each procedure had an average time of fluoroscopy of 11 minutes and 7 seconds, and 36 acquisition frames totalizing a mean DAP of 951976 mGy/cm^2. The dosimetric results of the primary interventionist and of the assistant are markedly superior to the rest of the team due to their proximity to the patient. From our results, we can conclude that work at the intervention room is safe from the point of view of radiation protection.

Conclusions: In our study the dose levels measured indicate that professionals who are properly shielded do not exceed the annual dose limits. The value for the crystalline in these specific procedures will be around 13 mSv which does not exceed the 20 mSv established by the recent European legislation.

QuADRANT: Constant Improvement through Clinical Audit in Radiology, Radiotherapy and Nuclear Medicine — An ESR-Led Project on Behalf of the European Commission

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Abstract

The European Council Basic Safety and Standards Directive (BSSD) 2013/59/Euratom was transposed into National Member State legislation in early 2018. This Directive lays out basic safety standards for radiation protection in radiology departments across EU member states. The revised version further emphasises the core principles of radiation protection with a specific focus on compulsory regular clinical audit 'in accordance with national procedures.'

Several studies evaluating the status of clinical audit in radiology departments across European National Member states have thus far suggested variable levels of compliance with the EC-BSSD and in particular uptake of clinical audit requirements. In many countries clinical audit is not firmly established, and clinical audit infrastructure is poorly developed.

The ESR (European Society of Radiology) and other professional bodies have prioritised improving uptake of clinical audit in radiology departments across National Member states to increase compliance with the BSSD requirements. A key project which was put out to tender by the European Commission in 2019 is named QuADRANT (Constant Improvement in Quality and Safety of Radiology, Radiotherapy and Nuclear Medicine Through Clinical Audit). This 30-month multi-society project is led by the ESR, together with the EANM (European Association of Nuclear Medicine) and ESTRO (European Society for Radiotherapy and Oncology) as consortium partners, on behalf of the European Commission. QuADRANT has the following several core aims:

a) Review the status of implementation of clinical audits in the Member States;
b) Identify good practices in Member States and available guidance and resources for clinical audits, at national, European and international level;
c) Provide further guidance and recommendations on improving the implementation and integration of clinical audits into national healthcare systems;
d) Identify potential for further coordinated EU action on quality and safety of radiology, radiotherapy and nuclear medicine.

In order to meet these aims, QuADRANT is organised into five work packages and involves two conferences and a pan-European survey supplemented by a comprehensive literature review and analysis, including interviews with experts in the field. The project commenced in January 2020, just prior to the onset of the Covd-19 pandemic. The initial conference, work package-WP,2 was held online in December 2020 and provided an overview of background to the project and detail on current guidance, requirements and examples of good practice. WP3 completes over the Summer of 2021, the main survey of member states is a core part of this work package and this and other components of WP3 will inform the second and final conference. WP4 is due to be held early in 2022. These work packages will allow QuADRANT to identify a clear picture of clinical audit process, audit uptake and infrastructure across Europe with the view to identifying guidance and good clinical audit practices that will facilitate improvement in patient experiences and outcomes across Europe in the fields of radiology, radiotherapy and nuclear medicine. Consequently, QuADRANT will provide the European

Commission in the final WP5 with a set of guidances and recommendations to improve clinical audit uptake and BSSD compliance across Europe.

The Current Status of Uptake of European Basic Safety Standard (2013/59/Euratom) Requirements: Results of a Follow-Up Survey in European Radiology Departments

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Abstract

Introduction: The European Council Basic Safety and Standards Directive (BSSD) 2013/59/Euratom, which was transposed into National Member State legislation in early 2018, lays out core radiation protection standards for radiology departments. The Directive mandates regular clinical audit processes which are subject to external inspection. As such, improving BSSD implementation and uptake of supporting processes of clinical audit is a high priority for the European Society of Radiology (ESR) in order to improve departmental compliance with BSSD requirements.

Background: A survey conducted in 2018 amongst the EuroSafe Imaging Stars network demonstrated several shortcomings across the network and variable BSSD compliance across radiology departments. The results of this initial survey highlighted the need for continued promotion of the BSSD and development of appropriate structures and processes to allow effective clinical audit. Following this survey, several radiation protection and clinical audit related initiatives were introduced by the ESR and EuroSafe Imaging to improve compliance, including the development of the ESR Guide to Clinical Audit, Esperanto.

We present a repeat survey undertaken on behalf of the ESR in February 2021, across the EuroSafe Imaging Star department network to reassess compliance with selected key EC-BSSD requirements.

Description of activity and work: A 14-question survey was sent via survey monkey to all 128 imaging departments within the EuroSafe network in February 2021, using selected questions from the original survey, with a closing date of 17th March 2021. Response rate was 61% (78/128). Questions were focussed around the implementation of key BSSD requirements and supporting processes of audit and re-audit. Compared to survey responses in 2018, there was overall a mixed response evident-reduction in positive responses were seen in relation to departmental presence of a clinical audit infrastructure to support BSSD implementation (70.15% in 2021, 81.82% in 2018) and to some areas around justification. Significant improvements were observed in questions relations to monitoring dose limits and occupational exposure to the eye (80% in 2021 and 57.63% in 2018), improvements in re-audit processes were also seen.

Conclusions and recommendations: Survey results demonstrated a mixed picture of compliance with BSSD requirements when compared to the survey results from 2018. This can be explained by the impact of the COVID-19 pandemic which may have diverted resources away from developing clinical audit processes in accordance with BSSD requirements. The survey results indicate the need for further co-ordinated pan-European action. The European Commission initiatives, QuADRANT, led by the ESR, and SAMIRA will help facilitate necessary improvements in implementation of radiation protection and developing a functional clinical audit infrastructure.

Deposition of Ionising Energy Leads to Population Decline via Impaired Meiosis in Caenorhabditis Elegans

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Abstract

Despite the tolerance demonstrated under exposure to high acute doses (> 1 kGy) of ionizing radiation in the nematode Caenorhabditis elegans, adverse outcome at the reproductive level have been observed under exposure of early stages of larval development to low-medium chronic doses (≥ 2.8 Gy). L1–L4 larval stages were shown to be the most radiosensitive stages of development due to adverse effects on gamete production. Specifically, significant sperm reduction and dysregulation of genes related to sperm meiosis and maturation were identified as the main key events (KE1, KE2) causing reduced number of progeny (AO1). Adverse effects of ionizing radiation on proliferative cells were also shown by enhanced germ cell apoptosis (KE3, KE4) in F0 nematodes and significant DNA damage in embryonic cells (F1) of irradiated nematodes, which was corroborated by the dysregulation of genes related to cell-cycle checkpoints, DNA repair, embryonic and post-embryonic development. Increased ROS levels (MIE2) and AODs activation were measured in vivo and by gene expression analysis after chronic irradiation of F0 nematodes. This was not accompanied by any adverse effect on somatic cell viability or any visible phenotypical effect, indicating tolerance of somatic tissue compared to the observed adverse effects shown on the germ cells. The observed redox imbalance suggested a significant contribution of indirect effects, including oxidative damage to DNA (MIE3), and represented the molecular initiating event derived from ionization and excitation of atoms and molecules (MIE1) after chronic irradiation.

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Comprehensive Reporting Solution with Integrated Radiation Dose and Quality Analysis

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Abstract

Objectives: Development of an integrated tool to support structured reporting with automated registration of radiation dose information and additional categorisation of key quality indices for reporting certainty and image quality.

Methods: A web-based system for structured reporting has been developed based in the IHE MRRT profile (Management of Radiology Reporting Templates). Full integration into RIS & PACS environment has been achieved. Different templates have been developed and are in routine use. Major use cases are Cardio-CT, CT for pulmonary embolism or nephro-ureterolithiais, MR of the prostate, PET-CT and others. For all CT examinations, DICOM RDSRs are automatically transmitted to the reporting system. The dose exposure values are registered in the database.
For all reports, there is also the option to document the certainty of conclusions in different categories (>90% consistent with / ~75% suspicious for or probable / ~50% possible / ~25% less likely / <10% unlikely). In addition, the individual assessment of image quality is queried and documented in 5 categories (very low noise / low noise / normal / slightly higher noise / high noise). For certain findings, additional graphical documentation can be performed, e.g., for the location and size of kidney stones, coronary stenoses or prostatic nodules.

Results and conclusions: The acceptance of the reporting solution is high, and the automated recording of dose values allows an immediate correlation of image quality and dose level. The recording of dose, reliability, image quality and all individual aspects of the reporting itself in a database allows a comprehensive analysis with regard to individualized imaging with consideration of general dose reference levels and their adaptation to the patient constitution. Thus, the solution is an important resource for the definition of clinically relevant dose reference levels (DRLs) with respect to different patient groups resp. BMI classes.

Acknowledgement
This development is partly supported by funding from the Euratom Research and Training Programme 2014–2018 under grant agreement No. 755523 (MEDIRAD).

Your Occupational Dose in Your Pocket: Helping to Know Personal Occupational Doses to Improve the Interventional Practices

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Abstract

Purpose: This study presents a smartphone application prototype for occupational dosimetry in interventional practices where the professionals involved who wear an electronic personal dosimeter, can follow their occupational doses received at any time, and can compare them with dose limits and with the other working colleagues.

Methods: Electronic dosimeters worn at chest over the apron, are continuously sending information on dose rate and cumulative Hp(10) each second to hubs located at interventional labs. The hubs also receive information from the X ray system and creates an occupational dose report with the cumulative dose received at each irradiation event to be sent to the DOSIM prototype. DOSIM receives and records information from the occupational dose report presenting the dosimetric information at worker and procedure level. Using their smartphones or a personal computer, personnel involved in interventional practices can review and compare their occupational records with an investigation level, dose limits and the values of their department colleagues (anonymously). A colour code (green, amber, red) indicates if the cumulative dose is well below the dose limits or on the contrary requires optimization. A dosimeter located at interventional C-arm is used as reference dosimeter, recording a cumulative dose in an unfavourable situation (without shielding), receiving the full backscatter radiation form the patient. The ratio between Hp(10) measured by the personal and the reference dosimeters at the C-arm, is presented as an indicator of consistent use of ceiling suspended operator shield. Results extracted from the first months of use are presented.

Results: Seven interventional laboratories and 26 operators (interventionalists and nurses) are being monitored with the DOSIM prototype. The reference dosimeter located at the C-arm (without lead protection) recorded in one of the laboratories 217 mSv during 308 procedures over 5 months, showing an indication of the radiation risk present in an interventional laboratory. The ratio between the personal cumulative dose and the dose at a reference C-arm dosimeter ranged from 0.2% to 1.67% (a factor of 8.5) for different interventionalists. These differences suggest different protection habits among interventional operators, as well as a target for dose reduction.

Conclusions: With this system, professionals have easy access to their occupational dosimetry records using their smartphones, to thereby actively engage in the optimisation process.

Acknowledgements

The authors would like to thank the Economy and Competitiveness Fund (Carlos III Health Institute) and the European Regional Development Fund (ERDF) under the project MEDICI number PI16/01413 and the Spanish National Safety Council under the project EDOCI.

There are no actual or potential conflicts of interest to declare in relation to this paper.

Investigation of Monolithic and Pixelated Detectors and Two-Layer Geometry for Hemispheric PET Systems: A Simulation Study

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Abstract

Positron emission tomography is used for diagnosis and also research on many different brain diseases e.g., tumours, epilepsy, and dementia. Some of these applications require to improve the resolution down to 1 mm potentially increasing the radiation burden. Since the spatial resolution of PET is highly dependent on the system's radius, brain dedicated geometries have been proposed and prototyped during the last years. Several of these brain-dedicated PET systems use a spherical or hemispherical geometry to keep the radius of the scanner at a possible minimum.

In most PET systems most brain dedicated geometries rely on detectors with pixelated crystals. Depending on crystal width and coating thickness, the crystal pitch reduces the volume fraction of the crystals and thereby the detection efficiency significantly which again increases the necessary activity. During the last 10 years detectors using monolithic crystals achieved intrinsic resolutions comparable to pixelated ones. Usage of monolithic crystals might allow to increase the detection efficiency for the same detector size and similar resolution.

Since the intrinsic resolution of monolithic crystal is related to thickness, a second layer of detectors might be used to reach the same total crystal depth as used in pixelated detectors. Additionally, a second layer could cover gaps between adjacent detectors which is inevitable in the one-layer-geometry design. The placement of a second layer might also contribute in improving the detection efficiency of the entire scanner and thus reducing the necessary radiation exposure.

The aim of this study is the investigation of the impact of detector design and placement in hemispheric geometry on the detection efficiency. The investigation was conducted with Monte Carlo simulation using the Geant4 toolkit Gate. Singles and coincidences of monolithic and pixelated detectors in one-layer and two-layer geometries applying the crystal materials BGO, LSO and LYSO are compared. The basic concept of two detector layers is verified. Based on the results geometry and detector design of hemispheric PET systems might be improved.

Effects of rA1M on the Regulation of Apoptotic Related Genes in Kidney Medulla after ^{177}Lu-Octreotate Injection in Mice

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Abstract

Adult patients diagnosed with metastasized neuroendocrine tumours (NETs) are commonly treated with targeted radionuclide therapy using ^{177}Lu-octreotate. The current treatment schedule is seldom curative. Fractionation is used to keep acute side effects of bone marrow low, and the total administered activity limit is set to protect kidneys from late side effects. If higher activity can be administered, without increased radiobiological damage of the kidneys, the cure rate of patients with NETs could be increased. The human recombinant antioxidant α1-microglobulin (rA1M) has been suggested as a potential radioprotector of the kidney. A previous study showed lower expression of some apoptosis related genes in kidneys when ^{177}Lu-octreotate was administered in combination with rA1M than without rA1M. We have previously found tubular damage and different response in kidney cortex and medulla after ^{177}Lu-octreotate and other types of exposure. The major parts of tubular system are in medulla, and the radiobiological response to some extent higher in medulla than cortex.

Aim: The aim of this work was to study the short-term effects of rA1M on the transcriptional level in kidney medulla, when used in combination with ^{177}Lu-octreotate.

Methods: In total, 30 C57BL female mice were divided into 3 treatment groups and 2 control groups (n=6/group). Each mouse received two injections. The treatment groups received 150 MBq ^{177}Lu-octreotate + phosphate-buffered saline (PBS), 150 MBq ^{177}Lu-octreotate + rA1M (5 mg/kg) or rA1M (5 mg/kg) + PBS. The control groups were injected with 2xPBS or PBS + rA1M vehicle solution. Half of the animals in each group were killed after 24 hours, and the other half after 168 hours. Kidneys were dissected immediately and frozen in -80°C. RNA was extracted from kidney medulla. The expression of 84 apoptosis related genes was analysed using RT-qPCR assay.

Results: The number of regulated genes (0.66>FC>1.5) in the mice receiving ^{177}Lu-octreotate or rA1M (5 mg/kg) increased with time, unlike the mice receiving ^{177}Lu-octreotate + rA1M, where the number decreased. In the 177Lu-octreotate group the pro-apoptotic genes were mainly upregulated and the anti-apoptotic genes were mainly downregulated, regardless of time. In the combination group (^{177}Lu-octreotate + rA1M), the pro-apoptotic genes were also upregulated at 24 hours, although the number of upregulated anti-apoptotic genes was higher than in the animals that did not receive rA1M. Furthermore, at 168 hours the number of downregulated pro-apoptotic genes were higher in the combination group than in the ^{177}Lu-octreotate only group, and the number of downregulated anti-apoptotic genes was lower. For the animals injected with rA1M the response was mainly up-regulated pro-apoptotic genes at 24 hours, while at 168 hours all regulated pro-apoptotic genes were down-regulated.

Conclusion: The results indicate that co-administration of rA1M decrease the apoptotic response in the kidney medulla in mice after exposure to ^{177}Lu-octreotate.

The Cytokinesis-Block Micronucleus Assay on Human Cryopreserved Whole Blood and Isolated Peripheral Blood Mononuclear Cells

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Abstract

Purpose: The cytokinesis-block micronucleus (MN) assay is a widely used technique in human biodosimetry studies, occupational genotoxicity studies and in vitro radiosensitivity testing. Fresh whole blood cultures (WBC) are commonly used for these purposes, but the requirement for immediate processing can be logistically challenging. Therefore, we aimed at establishing two novel protocols for the MN assay on cryopreserved whole blood and fresh or cryopreserved isolated peripheral blood mononuclear cells (PBMCs). Additionally, a thorough evaluation of the reliability of these assays for use in biological dosimetry and radiosensitivity assessment was performed.

Materials and methods: The G0 MN assay was performed on fresh and cryopreserved whole blood, freshly isolated and cryopreserved PBMCs from healthy human blood samples. MN yields were scored after irradiation with 220 kV X rays, with doses ranging from 0,5–2 Gy. Additionally, blood samples of 4 patients with a suspected radiosensitive phenotype were analyzed with both protocols. Results: The optimized MN assays on PBMCs and cryopreserved whole blood cultures showed adequate inter-individual and intra-individual variabilities. MN values were significantly lower for fresh PBMCs than for fresh whole blood. Cryopreservation of PBMCs resulted in significant higher MN values compared to fresh PBMCs, while cryopreserved whole blood cultures showed no significant differences in MN yields compared to fresh whole blood cultures. Importantly, after different cryopreservation periods, MN values remained stable for both cryopreserved PBMCs (6 months) and whole blood (1 year). The radiosensitive patients, included in this study, were correctly identified using fresh as well as cryopreserved PBMCs and cryopreserved whole blood.

Conclusions: Our new MN assay protocols on fresh PBMCs, cryopreserved PBMCs and cryopreserved whole blood demonstrate to be reliable tools for biodosimetry and radiosensitivity studies.

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Characteristics of Complete Blood Cell Count among Radiation Workers in South Korea (2014–2019)

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Abstract

Background: Complete blood count (CBC) test is commonly used to monitor health status of radiation workers as a screening test with diagnostic and prognostic objectives for acute and/or chronic diseases. In South Korea, workers who are registered as radiation workers are legally required to check their CBC every year for radiation protection purposes. The aim of this study was to evaluate the characteristics of the hematological parameters of radiation workers using CBC and compare prevalence of abnormal CBC between radiation workers and the general population in South Korea.

Methods: We collected three items of CBC tests (i.e., white blood cell, platelet, and hemoglobin) in 2014–2019 for 20,414 radiation workers from the cohort of the Korean Radiation Workers Study and for general population from the Korea National Health and Nutrition Examination Survey. Age-standardized prevalence ratios (SPR) of abnormal CBC were conducted with gender stratification.

Results: Abnormal prevalences (%) of CBC were 0.56–0.80 for men and 1.60–13.1 for women among radiation workers in 2104–2019. Male radiation workers had significantly lower abnormal prevalences of the CBC items than those of the general population (SPR of white blood cell = 0.41 (95% Cis: 0.39, 0.43), platelet = 0.27 (0.25, 0.29), hemoglobin = 0.18 (0.17, 0.19)). Similarly, female radiation workers had significantly low SPRs of white blood cell (SPR = 0.75 (0.66, 0.85)) and platelet (SPR = 0.72 (0.62, 0.82)); however, a higher SPR of hemoglobin was observed (SPR = 1.62 (1.54, 1.71)), which might be related to screening effects due to periodic workers' medical examinations.

Conclusion: Overall, CBC values of most radiation workers were in normal ranges with lower abnormal prevalence particularly for male workers, compared to the general population. Further studies are recommended to monitor health status of workers with abnormal CBC values and investigate its association with exposure to work-related hazards.

Prediction of Changes in the Frequency of Chromosome Aberrations in Peripheral Blood Lymphocytes after Radiotherapy

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Abstract

In radiotherapy using low-LET radiation of several tens of Gy, the frequency of chromosome aberrations in patients' peripheral blood lymphocytes clearly increases immediately after radiation exposure. This frequency of chromosome aberrations in peripheral blood lymphocytes has been used for biological dosimetry to estimate past radiation doses, not only for medical exposure. Among chromosome aberrations caused by irradiation, it is well known that stable aberrations almost always persist over time, while unstable chromosome aberrations, such as dicentric chromosomes, apparently decrease with time after irradiation. For this reason, it has been considered inappropriate to use unstable chromosome aberrations for evaluation after a long period of time has passed since irradiation or exposure. However, we hypothesized that the WAM model (Whack-a-mole model), which is capable of predicting genetic effects, could be applied to reproduce and predict the decay of the chromosome aberration frequency after radiotherapy.

As so far, we have already shown that the frequency of mutations in the next generation of irradiated individual decays with time after irradiation in past irradiation experiments on various species of animals and plants by use of the WAM model. We have also clearly shown that this variation in mutation frequency over time can be explained by the binomial equation between the production and elimination of mutated germ cells. Here we propose to apply the binomial equation of the WAM model to the variation in the frequency of chromosome aberrations. It is easy to reproduce the successive decrease of unstable chromosome aberrations using the WAM model by replacing the production and elimination of mutant cells with the occurrence and loss of chromosome aberrations. For stable chromosome aberrations, the WAM model can be applied by adding a correction term for lymphocyte proliferation that continues after irradiation. In this presentation, with the parameter sets of the WAM model obtained from some patients' data, we try to reproduce and predict the variation in the frequency of chromosome aberration occurrence in peripheral blood lymphocytes after radiotherapy.

Proposal of New Model Including Proliferation and Irradiation for Cancer Therapy

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Abstract

We propose a challenging model for cancer therapy named SS (Sea Saw) model for biological effects caused by irradiation, which is expressed simply as (24)

$$\frac{dV(t)}{dt} = \big(\lambda - b_1 d(t)\big) V \left(1 - \frac{V(t)}{V_m}\right), \qquad (1)$$

with V(t) and V_m being the volume and the maximum volume of a tumor. The time development of V(t) is controlled by proliferation rate λ and the cell-decreasing rate b_1 caused by irradiation with time dependent dose rate *d*(t). The equation (1) can be solved numerically. If *d*(t)=*d=constant, the* solution is, (51)

$$V(t) = \frac{V_m V(t=0) e^{(\lambda - b_1 d)t}}{V_m + \mathrm{V(t=0)}(e^{(\lambda - b_1 d)t} - 1)} \ . \qquad (2)$$

If ($\lambda - b_1 d$) >0, V(t) increases over time and if ($\lambda - b_1 d$) <0, V(t) decreases with time, which corresponds to cancer therapy. We can recognize the difference between the conventional LQ model and SS model from equation (1). The time-dependent dose rate effect is explicitly treated in the SS model and we never need to introduce such notions as DDREF or BED. Thus, SS model completely overcome the difficulties of the standard LQM method. The calculated results of the SS model can reproduce the existing data of the time dependence of the cancer volume during the cancer treatment. We can clarify how the effect of radiation therapy depends on the cancer stage on the starting time of the radiation treatment. we can treat the fractionation case exactly by taking proper time dependent dose rate. Indeed, we can reproduce increase of V(t) during week-end when the radiation exposure stops. We show additional results using new data obtained from the clinical group of Osaka International Cancer Center. The SS model for radiation therapy dramatically changes the situation of risk estimation of radiation by accounting exact proliferating cancer cells over time. The SS model is expected to provide a great development in cancer-therapy clinical-planning. Also, the model leads us a unified description of radiation therapy and radiation protection, the principle of which has been based on the LQM with the DREF notion.

A Study Using a Mathematical Model on the Radiation Damage Suppression Effect by Stem Cell Competition

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Abstract

The effect of low-dose-rate exposure of ionizing radiation on cancer risk is a major issue of radiation protection. Tissue stem cells are regarded as one of the targets of radiation-induced carcinogenesis. International Commission on Radiological Protection proposed a hypothesis that the effect of radiation may be reduced if damaged stem cells are eliminated by stem cell competition between damaged and intact stem cells. Especially, stem cell competition would be effective under very low-dose-rate conditions, in which only a few stem cells in a stem cell pool may be damaged by radiation. Based on this hypothesis, we constructed a mathematical model to discuss the influence of stem cell competition attenuating the accumulation of damaged cells. In the model, a stem cell pool containing a constant number of cells was assumed. There were two types of cells, intact cells and damaged cells, in the stem cell pool, and the state of the stem cell pool changed through transition event and turnover event. The intact cells turned into damaged cells through transition event which was assumed as the effect of radiation dose. In the turnover event, a single cell was divided, and a single cell was eliminated. The probability of cell division and elimination depended on the properties of cells. The properties of damaged cells were different from that of intact cells. Under very low-dose-rate conditions, the radiation damage was suppressed when the damaged cells were less reproductive and tended to be eliminated compared to the intact cells. On the other hand, the effect of cell competition was smaller at higher dose rates. Furthermore, the size of the stem cell pool affected the reduction in radiation damage. The radiation damage was strongly suppressed when the stem cell pool was large.

Investigation on Coastal Sand as a Fortuitous Dosimeter by Optically Stimulated Luminescence

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Abstract

In a mass-casualty radiological or nuclear (R/N) event the fast triage of individuals into those who are unaffected and those requiring medical help is a high priority. Oftentimes, people who were present during such accident do not own a professional dosimeter and therefore the assessment of their exposure to ionizing radiation depends on fortuitous dosimeters [1,2].

This study focuses on the dose response of coastal sand for doses up to 5 Gy and its possible application as a fortuitous dosimeter in a R/N emergency. Although a noteworthy number of articles regarding the dating of sediments with optically stimulated luminescence (OSL) has been published [3], none investigate the possibility of using them as fortuitous dosimeters.

Moreover, the dose response of coastal sand was studied for three different light stimulations (infrared, blue and both combined) and measured right after irradiation and 24 hours after irradiation in order to determine the signal stability. The obtained data suggests the possibility of using coastal sand as a fortuitous dosimeter since it gave a significant response for all the light stimulations and remained relatively strong even 24 hours after irradiation for several doses and stimulations. Our results, coupled with the rapidity of the measurements, the undemanding sample preparation and user friendliness of the OSL instrument, show that the proposed material could be convenient for a fast categorization of civilians in a R/N accident.

Acknowledgement
This study was supported by NATO Science for Peace and Security Programme (BioPhyMeTRE project (grsant No. G5684)).