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D6.6 Publishing the web-handbook including protocols issued from harmonization procedures

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Abstract

This deliverable deals with the final version of the web-handbook made from the ordered compilation of all the infrastructures that have been collected and whose visibility has been reinforced through the 40 issues of the Bulletin AIR² (**A**ccess to **I**nfrastructures for **R**adiation protection **R**esearch). Some others have been included at the end of the web-handbook as an add-on due to few special issues published recently. Its proposed structure is issued from three initial working groups, which have proposed categories and subcategories in order to also build easily the database AIR²D² (**A**ccess to **I**nfrastructures for **R**adiation protection **R**esearch **D**ocumented **D**atabase) and their evolutions due to the data collection during 3 years.

Infrastructures have been classified into three categories: (1) exposure platforms and contaminated sites, (2) databases, sample banks and cohorts, (3) analytical platforms, models and tools.

In order to build the subcategories, "Exposure Platforms" has been subdivided into (a) Low dose and low dose-rates, (b) Microbeams, (c) Particular radiation qualities: ions, neutrons, alpha…, (d) Internal contamination, (e) Observatory sites and (f) Metrology exposure platforms. The category "Databases, Sample banks, Cohorts" has been divided into "Databases", "Sample banks" and "Cohorts" and finally the category "Analytical platforms, Models & Tools" into "Analytical platforms" and "Models & Tools".

The document comprises five sections:

1) Introduction,
2) The CONCERT's Infrastructure Web-handbook,
3) Protocols issued from harmonization procedures,
4) Conclusions and perspectives,
5) Final version of the web-handbook with organized and compiled infrastructures' articles. (Annex)

This web-handbook compiles the articles of 120 infrastructures published in the Bulletin AIR², with 45 exposure platforms and contaminated sites, 35 databases, sample banks and cohorts and 40 analytical platforms, models and tools.

The tables and all individual infrastructures' articles are compiled into the connected (with hyperlinks) attached pdf file, which will permit building a real web-handbook from which every researcher will easily identify suitable infrastructures related to their needs.

Observing that some infrastructures can be classified in more than one subcategory and that those subcategories may evolve, this version could be revised and extended considering future activities "post-CONCERT". The final host website has not yet been defined by the CONCERT Management Board.

Acknowledgements

This version of CONCERT's infrastructure web-handbook is out and we are both proud and happy for it!

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The numbers speak for themselves:

40 issues, 120 infrastructures, more than 20 countries and 50 institutes represented and 1000 monthly readers of AIR^2! Thank you all!

This work has also resulted in 2 additional Special Issues dedicated to infrastructures and 11 Special Issues focused on CONCERT projects or ongoing European projects related to the radiation protection field.

Finally, special thanks are also due to all the indirect contributors to AIR² and AIR²D², technicians and researchers working to maintain and expand the quality and potential of infrastructures and to make them available to the radiation protection community.

Summary

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  In situ analytical techniques applied in the field (NMBU)
  References for 'In situ analytical techniques applied in the field'

- **Chapter 4: Protocols issued from harmonization procedures**
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  Recommendations about archive materials (SCK•CEN, HMGU)
  Development of Youtube tutorials focusing on the main biodosimetry techniques (CEA)

  - Conclusions and perspectives (CEA)

  - Cross tables (CEA)
  - Index (alphabetical order) (CEA)

  Annex (web-handbook pdf file) (CEA)

Introduction

CONCERT, the European Joint Programme for the Integration of Radiation Protection Research, is operating as an umbrella structure based on the strategic research agendas already prepared in the fields of low dose risk research (MELODI), radioecology (ALLIANCE), nuclear emergency preparedness (NERIS), dosimetry (EURADOS), medical radiation protection (EURAMED) and finally of the newly formed European platform for Social Sciences and Humanities related to ionizing radiation (SHARE). CONCERT aims at attracting and pooling national research efforts with European ones in order to make better use of public R&D resources and to tackle common European challenges in Radiation Protection more effectively by joint research efforts in key areas.

Coming to CONCERT WP6- Access to Infrastructures, its major focus is to increase the visibility of high quality infrastructures available to perform cutting-edge research in any of the disciplines related to Radiation Protection, and to facilitate access to these facilities for researchers and students in the field. The term "infrastructures" comprises so-called large infrastructures such as exposure platforms, including those for animal and plant experiments (both laboratory and field facilities), epidemiological cohorts, sample banks, databases, analytical platforms such as biological dosimetry facilities and 'omics platforms and e-infrastructures as well as models and tools. The necessity to focus on infrastructures in the Radiation Protection field has been highlighted by the HLEG (High Level Expert Group) in 2009. Since then, large EURATOM projects (e.g. DoReMi, STAR, OPERRA…) have included specific WPs and tasks dedicated to infrastructures. Surveys performed in former projects have revealed that the prevailing opinion is that most necessary infrastructures are already available although, not at the bench of each user. Indeed, besides the funding of experiments, the access to state-of-the-art infrastructures is a major bottleneck. Therefore, CONCERT WP6 started listing the infrastructures and provided a description of recommended criteria, both common ones (general information about the facility, its owner and the access rules) and technical ones, tailor-made for each infrastructure category. In order to best utilize existing resources, emphasis was put on promoting the visibility, using "mature" infrastructures to avoid unnecessary costs and duplication and aiming at sustainability.

To this end, two main tools have been developed by the WP6: the database **AIR²D²** (**A**ccess to **I**nfrastructures for **R**adiation protection **R**esearch **D**ocumented **D**atabase) and CONCERT's monthly bulletin (10 issues/year), **AIR²** (**A**ccess to **I**nfrastructures for **R**adiation protection **R**esearch). Since October 2015, AIR² serves for the dissemination of the information available on infrastructures related to Radiation Protection research and has now reached its 40th Issue with 120 infrastructures. The bulletins and the database are housed on the CONCERT website: https://www.concert-h2020.eu/en/Concert_info/Access_Infrastructures.

AIR² consists of 5 pages: The 1st page includes the editorial of the WP6 leader (Dr Laure Sabatier, CEA) and the section "The floor to …", in which leaders of the CONCERT WPs, presidents of the European platforms MELODI, EURADOS, ALLIANCE, NERIS, EURAMED, CONCERT grantees, POMs and national contact points related to infrastructures are invited to highlight their work through the infrastructure binocular. The next three pages are dedicated to presenting infrastructures: one infrastructure from the category "Exposure platforms" (page 2), one from the category "Databases, Sample banks, Cohorts" (page 3), and one from the category "Analytical platforms, Models & Tools" (page 4). These three pages are structured in the same way, i.e. with a text featuring the infrastructure, written by its owner, two spaces for images/photographs/schemes, a photo of the author, two key references of work involving the infrastructure, and an ID card which provides key information of the infrastructure at a glance. Finally, page 5 resumes the list of infrastructures published to date, those to be featured in the next issue and a list of CONCERT courses and future events related to Radiation Protection E&T and research, together with their respective hyperlinks. It was decided to use the colours of the CONCERT logo for the bulletin, with one colour per page: "Exposure platforms"= **green**, "Databases, Sample banks, Cohorts"= **orange**, "Analytical platforms, Models & Tools"= **yellow**.

The third tool developed as instrument of visibility to facilitate the future set-up of projects in the radiation protection field is the present web-handbook. It is issued directly from the efforts made to create and to sustain AIR² and AIR²D². All the pages featuring infrastructures (pages 2, 3 and 4 of the AIR² bulletin) are assembled; differently listing all the published infrastructures. This web-handbook includes 120 infrastructures of the 3 aforementioned categories, each of which is divided into new subcategories, e.g. Exposure Platforms are subdivided into (a) Low dose and low dose-rates, (b) Microbeams, (c) Particular radiation qualities: ions, neutrons, alpha…, (d) Internal contamination, (e) Observatory sites and (f) Metrology exposure platforms; the category "Databases, Sample banks, Cohorts" is divided

into “Databases”, “Sample banks” and “Cohorts” and similarly the category “Analytical platforms, Models & Tools” into “Analytical platforms” and “Models & Tools”. To enrich the web-handbook, each category and subcategory has been introduced by a dedicated short text to describe the current landscape under visibility. Included in the Chapter 3, a special focus part entitled “In situ analytical techniques applied in the field” has been added.

Besides this introduction, this document comprises also a short chapter entitled “The CONCERT’s Infrastructure Web-handbook”, where the principal parts extracted from the web-handbook are shown: definitions, a categories and subcategories table, the three cross tables corresponding to the three categories “Exposure platforms”, “Databases, Sample banks, Cohorts” and “Analytical platforms, Models & Tools” including the 11 subcategories with a first classification of the 120 infrastructures published till September 2019 also shown in the 40 issues of AIR².

A new Chapter 4 entitled “Protocols issued from harmonization procedures” has been added describing various efforts that have been made to diffuse protocols mainly focusing on biodosimetry techniques. Protocols have also been developed concerning STORE and data archiving from CONCERT’s projects and from older results issued from previous radiation protection research activities.

The “Conclusions and perspectives” section of this deliverable considers the actual landscape and compares all these highlighted infrastructures to others legitimate that could and/or should be introduced. It analyses also its strengths and weaknesses, possible improvements and potential developments.

Finally, a connected (with hyperlinks) pdf file constitutes the final version of all infrastructures for the web-handbook and is provided in the annex.

This version of the web-handbook comprises:

- How to use this web-handbook
- Definitions
- A table of categories and subcategories
- Three cross tables corresponding to each chapter with hyperlinks and containing labels/tags for each infrastructure
- An index

How to use this web-handbook

The present web-handbook consists of the following parts:

- Detailed **"Definitions"**, explaining which infrastructures correspond to each category and subcategory. Namely, the terms *Exposure platform*, *Low dose and low dose rates*, *Microbeam*, *Internal contamination facility*, *Observatory site*, *Metrology exposure platforms*, *Databases*, *Sample Banks*, *Cohorts*, *Analytical platform* and *Models & Tools* are clearly defined.

- 1 **blue context table** providing an overview of the chapters to follow. Hyperlinks to all the main chapters and subchapters are provided in order to facilitate the reading.

- 1 **green content table** for the 1st Chapter, Exposure platforms, including the subcategories of (a) Low doses and low dose rates, (b) Microbeams, (c) Particular radiation qualities: ions, neutrons, alpha…, (d) Internal contamination, (e) Observatory sites and (f) Metrology exposure platforms. All the 45 infrastructures presented until September 2019 in the 40 issues of AIR^2 are attributed to their corresponding subcategories and hyperlinks that redirect the reader to the respective article are provided.

- 1 **orange content table** for the 2nd Chapter, Databases, Sample banks, Cohorts, including the subcategories of (a) Databases, (b) Sample banks, (c) Cohorts. All the 35 infrastructures presented until September 2019 in the 40 issues of AIR^2 are attributed to their corresponding subcategories and hyperlinks that redirect the reader to the respective article are provided.

- 1 **yellow content table** for the 3rd Chapter, Analytical platforms, Models & Tools including the subcategories of (a) Analytical platforms (b) Models & Tools. All the 40 infrastructures presented until September 2019 in the 40 issues of AIR^2 are attributed to their corresponding subcategories and hyperlinks that redirect the reader to the respective article are provided.

- The 3 main Chapters: **1. Exposure platforms**, **2. Databases, Sample banks, Cohorts** and **3. Analytical platforms, Models & Tools** in the form of AIR^2 individual articles. The infrastructures are presented in respect to the order of appearance of the main subcategory that they belong (see the 3 content tables).

In order to facilitate the navigation of the reader and provide more information, hyperlinks are provided throughout the web-handbook. Just click the underlined words! Enjoy reading.

Definitions

Exposure platform:
A facility where organisms, samples or instruments may be irradiated under controlled conditions in which dosimetric characteristics are well defined and measured under a quality control system. The traceability is guaranteed by a continuous chain of calibrations to the highest references in ionizing radiations, built through the International System of Units (SI) (see also BIPM website).

Low dose and low dose rates:
An ionising radiation dose of <100 mGy and a dose rate of <0.1 mGy/min averaged over 1 h (corresponding to 6 mGy/h) (UNSCEAR 2012).

Microbeam:
A small collimated beam, with micrometre or sub-micrometre dimensions. Together with integrated imaging techniques, they allow precisely localized radiation damages.

Internal contamination facility:
Facility where animals (or plants) are exposed to radiation *via* ingestion, inhalation or by wounds. Organisms are kept under controlled conditions.

Observatory site:
Natural site contaminated by radionuclides (NORM: Naturally Occurring Radioactive Materials or anthropogenic) *via* industrial activities or accidental releases.

Metrology exposure platforms:
Metrology is defined by the International Bureau of Weights and Measures (BIPM) as "the science of measurement, embracing both experimental and theoretical determinations at any level of uncertainty in any field of science and technology". They are facilities dedicated to well define and quantified radiation beams or radioactive sources to irradiate, to test and/or calibrate measurement devices aiming to ensure that the produced results and their uncertainties during research projects are confident, reliable, and traceable to SI system.

Databases:
Organised collections of data.

Sample Banks:
Collection of biological samples (e.g. humans, animals, or plant samples…) and inert samples (soils, water, …)with a relation to radiation topics (e.g. nuclear workers, irradiation during childhood with low doses, irradiation during a radiological accident…) and generally associated/connected to databases.

Cohorts:
Grouping of information and/or data about one particular population in radiation research areas (e.g. nuclear workers, irradiation during childhood with low doses, irradiation during a radiological accident…). Generally applied for epidemiological and or health studies can be linked to a sample bank.

Analytical platform:
Depending on the endpoints, dedicated analytical platform should be selected to investigate irradiated or potentially irradiated samples in order to define the received dose or to study biological alteration in the sample due to the irradiation (e.g. expression of proteins or genes, post-translational modification of proteins, activation/inactivation of regulatory and other biological pathways, DNA damage and repair 'omics platforms).

Models & Tools:
Predictive or analytical software or processes, as well as biological model (such as animal or plant model).

Table of categories and subcategories

CONCERT's Infrastructure Web-handbook structure		
Chapter	**Category**	**Subcategory**
1	Exposure platforms	(a) Low doses and low dose rates (b) Microbeams (c) Particular radiation qualities: ions, neutrons, alpha… (d) Internal contamination (e) Observatory sites (f) Metrology exposure platforms
2	Databases, Sample banks, Cohorts	(a) Databases (b) Sample banks (c) Cohorts
3	Analytical platforms, Models & Tools	(a) Analytical platforms (b) Models & Tools

Table 1: Attribution of labels for categories and subcategories

Chapter 1: Exposure platforms

Exposure platforms are facilities where organisms, samples or instruments can be exposed to ionizing radiation under controlled conditions with well-characterized dosimetry and traceability. They include laboratory facilities that are capable of carrying out *in vivo* exposure of animals and plants or *in vitro* exposures of tissues, organs or cells, as well as field facilities and observatories. Based on criteria developed within CONCERT WP6 (Deliverable 6.2), a list of infrastructures has been created to provide a database of facilities mainly located in Europe. Recognizing that facilities have a range of applications and can utilize different exposure scenarios, varying in field, beam size, radiation quality and exposure route (external and internal), the exposure platforms have been divided into different categories, covering:
Low doses and low dose rates - facilities with ionizing radiation dose of <100 mGy and dose rates of <0.1 mGy/min averaged over 1 hour (UNSCEAR 2012);
Microbeams – facilities with small collimated beams of micrometre or sub-micrometre dimensions.
Particular radiation qualities – an overview of the facilities that allow exposure to radiation of different qualities;
Internal contamination - facilities where animals or plants are exposed to radiation *via* ingestion, inhalation or by wounds;
Observatory sites - natural sites contaminated by radionuclides (NORM or anthropogenic) *via* industrial activities or accidental releases and;
Metrology exposures - facilities dedicated to well-quantified radiation beams or radioactive sources to test and/or calibrate measurement devices.

Each subcategory is described shortly in the following subchapters, which give an overview and short description of platforms described in AIR^2, either as a table or a list of relevant platforms.

(a) Low doses and low dose rates

Low dose and low dose rate facilities allow the irradiation of a range of samples from cells to whole organisms, primarily to external gamma irradiation [1]. Table 2 lists the major features of facilities described in AIR^2 issues. The list (in order of increasing dose rate) is not exhaustive, and other gamma irradiation facilities can be found in AIR^{2}D^2. Most of the listed facilities use a ^{137}Cs source, and are focusing on external gamma irradiation, while in some cases, other radiation types besides photons are available at the same location. For larger facilities, simultaneous irradiation to controls and a range of doses can be attained by exposing samples at different distances to the source, while other facilities use shielding of the source to vary dose ranges.

The available facilities cover a wide dose range for low dose rate scenarios, including underground facilities that can achieve very low experimental dose rates through natural radiation shielding. This makes it possible to carry out systematic investigations and comparisons of doses and dose rates, covering sub-background, background and enhanced doses. With respect to the below underground facilities, in addition to the Gran Sasso National Laboratory (LNGS) in Italy there are several other low level labs in the world presently involved in biological studies [2].

Facility (AIR^2 issue)	Location	Radiation source	Dose rate (mGy/h)	Biological samples
PULEX-COSMIC SILENCE ***(Issue 3, December 2015)*** *Facility located inside a tunnel with 1400 m rock overburden: negligible contribution by directly ionising cosmic rays and neutrons*	LNGS-INFN Assergi, Italy	Environmental radiation (mostly γ-rays) *(muon and neutron fluxes of $3*10^{-8}$ & $3.78*10^{-6}$ respectively)*	~ $2*10^{-5}$ ~ $0.5*10^{-5}$ *(with Fe shielding)*	Cells and small animals (*e.g. Drosophila melanogaster*)
LIBIS ***(Issue 11, October 2016)***	ISS Rome, Italy	Cs-137	$2*10^{-3}$ – $2*10^{1}$	Cells and small animals (*e.g. Drosophila melanogaster*)
MICADO'LAB ***(Issue 19, July 2017)***	IRSN Saint Paul Lez Durance, France	Cs-137	$5*10^{-3}$ - 10^{2}	Model organisms in ecotoxicology (nematode, daphnid, zebrafish, plants)
AMBIC ***(Issue 39, July 2017)***	IES Rokkasho, Aomori Japan	Cs-137	$4.2*10^{-2}$ & $8.33*10^{-1}$ 8.33 & 16.67 $4.56*10^{4}$	Rodents (mice & rats) and cells
FIGARO ***(Issue 1, October 2015)***	CERAD, NMBU Norway	Co-60	$4*10^{-1}$ - $3*10^{3}$	Cells and small animals (small rodent, fish, amphibians, invertebrates) plants, GMO*
LOW DOSE RATE FACILITY ***(Issue 16, April 2016)***	Stockholm University, Sweden	Cs-137	1 - 50 (cells) 1 - 70 (mice) *(with lead shielding)*	Cells and small animals *(4 cages, 5 mice/cage)*
SCRS-GIG ***(Issue 9, July 2016)***	Główny Instytut Górnictwa Katowice, Poland	Photons (Cs-137; X-rays) *Neutrons (Am-Be) Beta (Sr-90) Radon*	γ-rays (collimated) $1*10^{-3}$ - $1.87*10^{2}$ γ-rays (panoramic) $1.5*10^{-1}$ - 1.7 X-rays (collimated) up to $4*10^{4}$ *Neutrons (panoramic)* $3*10^{-2}$ *Beta (collimated) 50 - $3*10^{3}$ Radon in air up to 10 kBq/m^3*	Easily adaptable to expose living organisms (cell culture and small animals, plants) to different radiation types
MICROTRON LAB ***(Issue 12, November 2016)***	Nuclear Physics Institute of the CAS Reź, Czech Rep	Electron and gamma beam, *Neutrons*	$6*10^{2}$ - $6*10^{8}$	Cells and small animals (fish, rodents etc) plants …

*GMO: Genetically modified organisms.

Table 2: List of the low dose and low dose rate facilities (in order of increasing dose rate)

(b) Microbeams

Microbeams are valuable instruments for the exploration of radiobiological response mechanisms. The strength of microbeams lies in their ability to deliver precise doses of radiation at a cellular and subcellular scale with an accuracy of one or a few micrometres. Together with integrated imaging techniques, they can enable assessment of localized radiation damages. These abilities have led to the development of a range of microbeam facilities around the world allowing the delivery of precisely defined beams of charged particles, X-rays, or electrons.

An overview of the facilities currently in operation, dedicated to biology or shared with analytical experiments, is presented in table 3 below.

Facility	Location	Particle	Energy range
RARAF (Columbia University)	New York	protons, alpha	1–5 MeV
SPICE (NIRS)	Chiba	Protons	3.4 MeV
Ion Beam Centre (University of Surrey)	Guildford	protons, alpha up to Ca	1–12 MeV
IMP	Fudan	protons, alpha	6 MeV
PTB	Braunschweig	protons, alpha	2–20 MeV
RIKEN	Wako	protons, alpha	3–4 MeV
SNAKE	Munich	protons, alpha, Li, O, Si, Cl, I	4–28 MeV 1–10.5 MeV/u
GSI	Darmstadt	protons, alpha, C to U	1.4–11.4 MeV/u
JAERI	Takasaki	A, C, Ne, Ar	12.5–17.5 MeV/u
LIPSION (University of Leipzig)	Leipzig	H, He	2.25 MeV
Microbeam (PNNL)	Richland	Electrons	Variable energy
MIRCOM	Cadarache	protons, alpha up to C	Up to 8-12 MeV

Table 3: Microbeam facilities currently in operation (updated from [3])

(c) Particular radiation qualities: ions, neutrons, alpha,…

The health risks of radiation exposure depend not only on absorbed dose, but also on radiation quality. For radiation protection purposes, radiation weighting factors are applied to account for the effects of radiation quality which is strongly related to the spatial pattern of energy deposition at the subcellular scale [3]. The existence of radiation weighting factors implies that there is a strong evidence base showing the different biological and health consequences due to different radiation qualities. However, there is a lack of mechanistic understanding of how radiation qualities affect risk, while the exact values of radiation weighting factors are also debated.

The inhomogeneous spatial pattern of energy deposition is a real feature of many environmental, medical and occupational exposures. In addition, it is gaining further importance because of the more wide-spread availability of external beam hadron therapy, the perspective of longer duration space travel (as well as space tourism) in the future, and the increasing clinical use of radionuclides [4].

Much of the information on the effects of radiation quality is obtained from studies on internal exposures, which adds an additional complexity to understanding the effects of radiation quality. In many cases, internal exposures feature three main differences compared to, for example, the radiation field that A-bomb survivors were exposed to. Besides the differences in radiation quality, dose rate and intra-organ distribution, the super-cellular distribution of energy deposition can also be very different, making it difficult to separate health effects of radiation quality from the effects of dose rate and from the effects of inhomogeneous distribution of radionuclides. Although it is possible to test the effects of radiation quality alone at the single cell level, it provides very little information on how radiation quality modulates radiation risk. On the other hand (and at the other end of biological organization), exposure of multicellular organisms is more useful for risk assessment, but in most cases it also involves effect modifying factors other than radiation quality.

The infrastructures listed in the webhandbook under the title ”Particular radiation qualities” include photon, neutron (BIO, FRM II), light (AGOR, alpha particles irradiator, IRRAD, FAIR, HIT, TIFPA), and heavy ion (CIRIL, FAIR) sources as well as exposure to different radionuclides (Radon Exposure Chamber, GSI). Exposures to mixed fields (CERF, Mixed alpha and X-ray exposure facility) and changing dose rate (Changing dose rate exposure facility) are also available. While PULEX Cosmic-Silence (photons, cosmic rays, neutrons), SCRS-GIG (alpha-, beta-, gamma-, radon), and B3 (actinides) are listed in other chapters of the web-handbook, they are also suitable to study the effects of radiation quality. Many of these infrastructures are available for both cell culture and small animal studies. However, some others are mainly used for dosimetry purposes (CERF, FRM II, IRRAD) along with those listed under the Metrology exposure platforms (Laboratory for retrospective radon and thoron dosimetry, MELAF). The detailed description of these infrastructures can be found at the hyperlinks.

Given the challenges described above and in the Second joint roadmap for radiation protection research (CONCERT D3.7) (Challenge A and B in particular, [5]) the understanding of the effects of radiation quality requires the maintenance of a large network of research infrastructures, and strong collaboration between research groups within and outside Europe.

(d) Internal contamination

Seven facilities are registered as potential laboratories, which can manage internal contamination mainly for small animals (rodents) but also cells and plants, showing that this capability is now relatively rare. The objectives are to study the consequences of a chronic exposure to low activity concentrations of radionuclides issued for example from nuclear activities or accidents, and from the environment (Rn, NORM). The classic way of incorporation of radionuclides is through ingestion or inhalation. Associated with the internal contamination facilities, generally supporting labs are available: radiochemistry, cell culture, dissection… and of course instrumentation to measure radioactivity.

To evaluate the consequences of those uptakes/intakes of radionuclides, the chronic exposure should be quantified as doses. To obtain that information, it is the role and interest of the internal dosimetry. So, this particular link could be highlighted here with three analytical platforms also registered in this web-handbook and given in Table 4.

Internal dosimetry consists in the assessment of internal exposures by interpreting the monitoring data of incorporated radionuclides in terms of intake (Bq) and committed effective dose E(50) (mSv). Measurements of the content of internal X-ray and gamma emitters retained in the body can be obtained by *in vivo* monitoring in body-counters (activity (Bq) in total body or in an organ is obtained) and by *in vitro* bioassay measurements of excreted radionuclides in biological samples (typically activity concentrations Bqd^{-1}, BqL in urine or in faeces are obtained). The activity that is incorporated by an exposed person can also be estimated from the results of air samplers (activity concentration (Bq/m^3) in the environment) e.g. in a workplace.

The assessment of E(50) from measurement results is carried out by applying the correct and current ICRP retention and excretion models and dose coefficients, depending on the intake scenario and exposure conditions. Software tools are available for such dose assessments, developed by reference institutions in Europe e.g. PHE-UK (IMBA, Taurus), IRSN-France (MIODOSE), RPI-Ukraine (IMIE), and from outside Europe (e.g. AIDE software by Los Alamos Nat. Lab. in US, MONDAL-MONDES by NIRS in Japan). ICRP is in the process of updating biokinetic models and dose coefficients through the OIR (Occupation Intakes of Radionuclides) series of reports (Parts I-IV already available, Part V in process) in agreement with ICRP Publication 103. An electronic Annex is provided (and updated) through ICRP website as “Data Viewer” that allows the access of all the OIR relevant data needed for dose evaluations, for most common radionuclides at risk to be incorporated by workers in a workplace.

Facility (AIR² issue) Analytical Platforms Models and Tools	Location	Radiation source	Dose	Biological samples
CIEMAT Whole Body Counter Internal Dosimetry (Issue 33, December 2018)	Madrid Spain	Gamma emitters inside the body: In total body (e.g. ^{137}Cs, ^{60}Co,…) In thyroid (radioiodine e.g. ^{131}I, ^{125}I) In lungs (Actinides e.g. ^{235}U, ^{241}Am)	Measurement of activity content (Bq) of radionuclide in total body or in specific organs (interpretation of monitoring data in terms of committed effective dose E(50)	Exposed workers Exposed population
CIEMAT In vitro Internal Dosimetry Laboratories ***(Issue 38, June 2019)***	Madrid Spain	Alpha emitters in excreta samples (urine and faeces), typically U, Am, Pu Beta emitters in urine, typically ^{3}H and ^{90}Sr	Measurement of activity concentration (Bq.d^{-1}, Bq L^{-1}) in excreta samples (urine and faeces) (interpretation of monitoring data in term of committed effective dse E(50)	Exposed workers Exposed population
ŒDIPE – Nuclear Medicine ***(Issue 26, April 2018)*** https://www.irsn.fr/EN/Research/Scientific-tools/Computer-codes/Pages/OEDIPE-Personalised-dosimetric-evaluation-tool-3443.aspx	IRSN, Fontenay -aux- Roses France	Radiopharmaceuticals for diagnosis and therapy (e.g. using ^{131}I, ^{90}Y, ^{177}Lu, ^{223}Ra,…)	Dose assessment in nuclear medicine: Absorbed dose and biologically effective dose considerations	Nuclear medicine patients

Table 4: Three analytical platforms doing internal dosimetry

Recently, the European Commission has published the RP188 Report (Radiation Protection series) in which technical recommendations are given for monitoring individuals with occupational intakes of radionuclides. This internal dosimetry reference document in Europe was developed by EURADOS Working Group 7 members as a outcome of the TECHREC Project supported by EC-DGENER.
Another aspect of internal dosimetry is the patient exposure in a nuclear medicine frame, by using radiopharmaceuticals for diagnosis and therapy. An important tool for such dose assessments (OEDIPE code) is presented in the table above, developed by IRSN (France) for absorbed dose evaluation and biologically effective dose considerations.

(e) Observatory sites

The Observatory sites are radioactively (and chemically) contaminated field sites, first presented in a OECD/NEA report [6], which represent a powerful tool to integrate research activities done in different disciplines of radiation protection (radioecology, radiation biology, environmental toxicology, ecotoxicology and ecology, among others), through common studies, shared data, etc.

Presently four sites have been selected as radioecological Observatory sites by ALLIANCE, three of which have been published in the AIR² bulletin:

- Chernobyl Exclusion Zone, Ukraine (Issue 17, May 2017)
- Forest observatory site in Yamakiya, Japan (Issue 26, April 2018)
- Belgian NORM Observatory Site (Issue 27, May 2018)
- Upper Silesian coal basin, Poland (https://radioecology-exchange.org/content/upper-silesian-coal-basin).

Table 5 summarizes the major features of the three observatory sites selected by ALLIANCE published in the AIR² bulletin (including a link where more information can be obtained).

The Chernobyl Exclusion Zone and the Forest in Yamakiya observatory sites offer a radiation contamination gradient, in which relevant amounts of non-radioactive pollutants are almost absent.
The Belgian NORM Site and the Upper Silesian coal basin observatory sites offer a mixed radioactively-chemically

contaminant situation, in which naturally occurring radionuclides (i.e. U-238 and/or Th-228, and their decay products Ra-226, Rn-222, Pb-210 and Po-210) and heavy metals (i.e. As, Cd, Pb, Zn, etc.) are present.

Observatory sites offer a unique opportunity for E&T activities. The ALLIANCE has organised in the past field courses in The Chernobyl Exclusion Zone and in the Upper Silesian coal basin (Poland).

Feature	Chernobyl Exclusion Zone	Forest in Yamakiya	Belgian NORM Site
Type of ecosystem contaminated	Terrestrial and freshwater (and urban)	Terrestrial semi-natural forest	Terrestrial - forest
Compartment of environment contaminated	All sample types	Soil, water, sediments, plants, animals	Soil, sludge, vegetation
Contamination source	Mainly: Cs-137, Sr-90, Am-241, Pu-isotopes, U-isotopes, I-129, C-14, Tc-99 (also as 'hot particles')	Radiocaesium (major source of contamination) Pu, Sr-90 are also present	Naturally occurring radionuclides present in the sludge: U-238,Ra-226, Pb-210 and Po-210
Radioactivity or dosimetric characteristics	Activity concentrations and dose rates	NA	Activity concentrations and dose rates
Total contaminated area	➢ 4,700 km^2	953 km^2 (>20 $mSv \cdot y^{-1}$)	Approximately 0.07 Km^2
Species exposed/ present in the site	400 species of vertebrates including: 73 mammals, 251 birds, 7 reptilians, 11 amphibians, 67 ichthyoids	Animals: earthworm, frog, newt, mouse, wild boar, etc. Plants: Japanese cedar, pine and broad-leaf trees, fern, bamboo, sasa plant	Trees, shrubs, herbs, grasses, insects, etc.
Presence of an associated contamination	No significant evidence for this	N.A.	Co-contaminants such as As, Cd, Cr, Pb and Zn
Supporting lab	Basic laboratory facilities are available in the Chernobyl Exclusion Zone	Institute of Environmental Radioactivity (IER) of Fukushima University supports sampling, pretreatment and analyses	No laboratory infrastructure available on site. SCK•CEN laboratories can be made available (subject to agreement)
Access	Require permission - achieved through a local collaborator	Permission from IER is required	Permission via SCK•CEN is required
Link	https://radioecology-exchange.org/content/chernobyl-exclusion-zone	https://radioecology-exchange.org/content/fukushima-radioecological-observatory-yamakiya	https://radioecology-exchange.org/content/belgian-norm-site

Table 5: Summary of the major features of the three Observatory sites selected by ALLIANCE published in the AIR^2 bulletin

In addition, three other contaminated sites, which could be used as observatory sites, have been published in the AIR^2 bulletin:

- IRSE Experimental Farm (Issue 35, March 2019), sited in the Semipalatinsk Test Site in Kazakhstan. Is a territory of 18,500 km^2 of steppe semi-desert environment contaminated with radionuclides (cesium, strontium, transuranium elements, tritium, among others) and heavy metals (http://irse.nnc.kz/).
- Phosphogypsum stack at Barreiro, Portugal (Issue 36, April 2019), is a territory of around 55,000 m^2 of phosphogypsum stack, contaminated with natural radionuclides (Ra-226 and Pb-210), heavy metals and rare earth elements (http://www.baiadotejo.pt/en/park/barreiro).
- ZATU (Zone Atelier Territoire Uranifère) in France (Special Issue 10, April 2020), is a watershed area of around 5 km^2, contaminated with natural radionuclides (U, Ra, Rn, Po) and heavy metals (As, Pb, …) (https://zatu.org/).

(f) Metrology exposure platforms

Metrology exposure platforms are facilities dedicated to well defined and quantified radiation beams or radioactive sources to irradiate, to test and/or calibrate measurement devices and rarely cells. These aim to ensure that the produced results and their uncertainties during research projects are confident, reliable, and traceable to SI systems. A summary of the facilities listed within the AIR² bulletins is provided in Table 6, which is a very weak sample among a large potential of laboratories in each European country (i.e SDOS, IRSN France – LNHB, CEA, France - , PTB, Germany – METAS, Switzerland – BEV, Austria – ENEA, Italy, CIEMAT, Spain….). As the highest level of accuracy for dosimetry measurements is associated with the best uncertainties, they give a high quality services and a guarantee through their accreditation ISO 17025. They are the most often related to EURADOS activities and connected together through the EURAMET association (network). Harmonization of protocols and methods and intercomparisons are for them essential activities to maintain the consistency of dosimetric quantities through Europe.

Name	Location	Irradiation type	Dose rate
Laboratory for retrospective Radon and Thoron dosimetry	Sofia University, Bulgaria	Alpha particles	^{222}Rn: 1-2000 kBq/m^3 ^{220}Rn: 2-1800 kBq/m^3
Radon Calibration Laboratory	BfS, Germany	Alpha particles	^{222}Rn: 0.5 - 100 kBq/m^3
MELAF	PTB, Germany	γ rays Electrons	0.01- 100 mGy/h
Laboratory for Dosimetry Standards (NDS)	JSI, Slovenia	γ rays X-rays	0-0.1 Gy/min
Calibration & Dosimetry Laboratory (INTE-UPC)	Polytechnic University of Catalonia, Spain	Photons γ X-rays Beta particles	γ: 1 µGy/h- 54 mGy/h X-rays: 0.1 mGy/h -10 Gy/h β: 4 mGy - 0.5 Gy/h
Radiation Metrology Laboratory (DOS)	STUK, Finland	γ rays X-rays Beta particles Neutrons	700 nGy/h - 40µGy/h
Calibration Laboratory (CALLAB)	CERN, Switzerland	γ rays X-rays Beta particles Neutrons Mixed field γ+n	0.36 - 360 µGy/h
Calibration Laboratory at KIT	KIT, Germany	γ rays Electrons Neutrons	2 µGy/h - 80 mGy/h
The Nuclear Metrology Group (NMG)	NPL, United Kingdom	Mixed field γ+n γ rays	1 µGy/h - mGy/h
Neutron irradiation facility (UNIPI-AmBe)	Pisa University, Italy	γ rays Neutrons	γ: 0.53 mSv/h n: 9.4 µSv/h
Laboratory for nuclear Calibration (LNK)	SCK•CEN, Belgium	γ rays X-rays Beta particles Neutrons	Few mSv

Table 6: The eleven metrology exposure platforms listed within AIR² issues

This proposed classification depending the irradiation type shows that two platforms are dedicated to Rn metrology, however the labs have generally a large offer of possibilities with beams and radioactive sources. Just on the front line (behind National Metrology Institutes, NMI, that establish standards) for the diffusion of the best dosimetric

quantities through calibrations. They are essential for all dosimetric measurements systems and for all exposure platforms to guarantee that all experiences and results could be comparable and compatible.
Regarding the existing chain of NMI in ionizing radiation through Europe and their calibration labs, this sample of 11 platforms is very small and this first inventory is far from a complete overview of the existing potential. It is probably a sign that the best physical dosimetry is not well connected to numerous applications in the radiation protection research multidisciplinary field.

References Chapter 1

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Chapter 2: Databases, Sample banks, Cohorts

As part of the 40 regular issues of the AIR² bulletin, a total of 36 infrastructures listed in the "Databases, Sample banks, Cohorts" category have been covered. This includes 8 databases, 19 sample banks and 24 cohorts. Special issues of AIR² also covered additional databases, either already existing or being constructed. It must be outlined that a few "double counts" had to occur across subcategories, since some sample banks are attached to cohorts and these are sometimes - but not always - considered as separate infrastructures. As a result, some biobanks attached to cohorts were either presented in the same issue of AIR² as the source cohort, or not. In addition, whether some infrastructures had to fall into the "Sample banks" or the "Databases" category was not always a clear cut. Finally, one might also reasonably consider that a cohort is, first, a database - and might therefore fall into a more general "database" category. Actually, cohorts are simply specific types of databases, which have been treated separately because of their major role in human radiation protection research and of their specific requirements regarding individual data protection.

The other databases identified cover a broad spectrum of purposes and uses, from collections of pure environmental data (e.g. levels of radionuclides in the marine environment) and parameters (e.g. mineral-specific sorption data), to data on transfer of radionuclides to organisms and finally ionising radiation-induced effects in various non-human biota. Of course, STORE, a platform for resource sharing covering all kinds of radiation research, which enables users to locate data or bioresources, has been presented, as well as the FREDERICA database devoted to radioecology. Both databases were produced under EC funded projects. The availability of legacy datasets and biological materials resources still mainly depends on uncoordinated, often institutional, initiatives to curate and archive them, yet there are still few stable platforms for their preservation, sharing, and reuse [1]. This is why CONCERT Subtask 6.2 included efforts to maintain the STORE and FREDERICA databases.

Drs Maria Gomolka and Paul Schofield provided their expert views on the sample banks and databases covered by the AIR² bulletin, and described additional infrastructures that could not be covered whatever the reasons (see the introductions of the dedicated subchapters). Regarding cohorts and sample banks at least, it appears that the most well established radiobiology and radio-epidemiological datasets available in the European Union have been covered by AIR². Some major infrastructures located outside of the European Union have also been covered (e.g. in Japan, USA, Russia, Kazakhstan). This includes for instance the Life Span Study of Japanese Atomic Bomb survivors, the American JANUS and NASA radiobiological archives, the Mayak and Techa River cohorts and biobanks, and more.

In summary, although exhaustive coverage of existing infrastructures for radiation research worldwide in only 40 issues was of course impossible, the AIR² bulletin provided a very useful overview of major databases, sample banks and cohorts available for radiation protection research. This helped reaching the WP6 goal of increasing the visibility of these infrastructures and provided solid grounds for the continuation of this work, as part of MELODI and other European platforms for radiation research.

(a) Databases

Background

Radiobiology was one of the first disciplinary areas to start generating very large structured datasets in the biological sciences. From the 1940s onwards the collection of accidental and experimental exposure data globally has been a major undertaking, and its archiving and dissemination has been a significant challenge for a variety of reasons. More recently, the collection of epidemiological and environmental data, either routine monitoring or post-incident follow-up has added to the importance of data archiving and retrieval. In addition to these large-scale, and in some areas long-duration, experiments and monitoring and epidemiological exercises, the production of data from hypothesis-driven experimentation has accelerated enormously and the archiving, sharing and reuse of this data present particular challenges. Existing public repositories either do not cater for the high-resolution metadata needed for radiation biology or cannot accommodate coherent large datasets. The ongoing nature of data collection and curation also means that in contrast to the archiving and sharing of legacy datasets, sustainability of the infrastructure and user training are of critical importance. The reader is referred to a recent paper surveying the international landscape of radiation biology and epidemiology for a comprehensive temporal, geographical and thematic overview of the current state of play and Table 1 of this paper is a useful summary of the findings [1]. 23 major databases and data resources were described and many also have comprehensive entries in the AIR² infrastructures bulletin series. This section of the web handbook will therefore deal at summary level with the current strengths and challenges in the data landscape for radiation biology and epidemiology.

The issues of data archiving and reuse have been under considerable scrutiny in recent years, resulting in the formulation of the FAIR guidelines for Open Data [2]. Resulting from extensive consultation between funding agencies, journals and scientists, these guidelines have been adopted by many major funding agencies, the European Commission and formally by the countries of the OECD and G20 group of nations [3, 4]. Findability, Accessibility, Interoperability, and Reusability represent the four principles of Open data and are essential for effective data governance and management [5]. The advantages of data sharing are overwhelming, amongst which are improved reproducibility, accountability, and the added value, both scientific and financial, of reusing data for purposes for which it was not originally intended; aggregating with other datasets, or conducting novel analysis in the light of new methods or paradigms [6]. For the individual this also provides increased recognition and often collaborations or further developments of studies that they had not anticipated.

The problem of data availability has recently been raised by Beresford et al. [7] and reflects a common issue about the provision of summary data alone, or in some cases no primary data at all. Withholding of primary data not only slows the progress of science, for example withholding unique contamination datasets, but also makes intercomparison and aggregation of datasets impossible. This adds to the uncertainty about reliability of conclusions where it is impossible to replicate the analysis. Where this kind of problem impacts on regulatory activities and safety assessments, with potentially huge implications for humans and environmental safety, as well as major economic impacts, there is an additional imperative for the community to ensure that the highest standards are met.

The development of very large datasets in recent years has increased the willingness to share, though there are still some issues, common with other disciplines [8-10] that inhibit full and free sharing. These include protectionism, concerns that flaws in analysis might be revealed, lack of time, expertise or funding for preparation of data for upload, lack of appropriate sharing platforms, concerns over intellectual property protection, and loss of “ownership”. These are common to many disciplines and, respondents in a recent survey of data sharing in a large European radiobiology project, CONCERT, the responses received broadly reflected these common findings [11].

Increasingly funding agencies, and specifically the European Commission, have adopted a policy of free and open data sharing. A comprehensive list of international data sharing requirements for funding agencies, journals and institutions is available on from the FAIR sharing project. The requirement for data management plans (DMPs) will become mandatory in the next EC Framework programme, however it is not yet clear what level of accessibility and discovery will be acceptable as Data sharing, nor have the monitoring and compliance process been articulated. The latter is extremely difficult and so far other funding agencies have taken a sampling and audit approach rather than an explicit confirmation that sharing goals in the DMP have been met. The generation of machine actionable and dynamic DMPs might in the future be a way of checking assertions that data has been shared but as yet these approaches have not been implemented to our knowledge [12].

During the course of the project we found several examples where data was purportedly shared, and yet despite protracted efforts was unavailable. This was either because of unresponsiveness of contacts, change of personnel and lack of continuity, or most often institutional reorganisation and loss of funding. This underlines the importance of using strategic sustainable databases rather than providing data access through individual investigators and their home institutions. Secondly, we found problems with explicit policies on the lifetime of data sharing: how long should data be shared for, how long should it be retained, how should it be made available? In principle, these should be addressed by data management plans, but in the course of the STORE project we saw no data management plans which adequately dealt with these issues, and none which complied with the basic principles of a DMP as laid down by the UK DCC, accepted as being the gold standard under H2020. We were not made aware of any systematic mechanisms for the assessment of DMPs for H2020 or CONCERT internal funding calls.

We identify the following challenges:

- Provision of a sustainable database at scale structured to deal with the volume of data generated and appropriate for legacy data. Attention to detailed metadata is required in order for data to become truly discoverable, consistent with FAIR guidelines.
- Requirement for DMPs and their oversight
- Education and training in appropriate community norms and the technical aspects of data sharing
- Human subject data

These challenges are not unique to the radiation biology community, although in some cases the solutions maybe rather particular.

A sustainable platform for data sharing

The STORE database has begun to address some of the issues concerning a platform for sharing and archiving radiobiology, radioecology and epidemiology data. This is in principle sustained by the generous commitment of the BfS, but cannot at present undertake the expansion to scale required to be commensurate with requirements. STORE is complementary to existing large-scale repositories, for example those run by ELIXIR as core resources, but current implemented structures, themes and metadata standards in these databases do not sufficiently encompass Radiation biology to make discovery and sharing of data possible. The development of a formal ontology for radiation biology metadata is currently in progress in collaboration with the NASA Ames Laboratory in the USA.

Data Management Plans

Currently the Commission is advising DMPs for H2020, as discussed above, but these are not uniformly required by the major funding agencies and institutions across Europe and recognition of the importance of data science in support of the biological sciences is only slowly taking place, in a large part promoted by international membership of the ELIXIR bioinformatics network.

Education

Education in community norms for data management and that use of public data resources has emerged as a critical bottleneck for developing an international radiobiology commons. Targeting young scientists and early stage researchers is the most important area, but increasing awareness of FAIR issues amongst established investigators is also important if we are to change attitudes and compliance in the community. Along with this goes increasing awareness of data available, which might help in the design of execution of projects or even be the basis of new projects and at the moment this very positive aspect of data sharing is not widely leveraged.

Human subject data

Specific challenges exist for radiobiology and epidemiology research data concerning human subjects. While the collaborative and international sharing of data on human subjects has always been subject to appropriate legal and ethical constraints, the development of new international legal governance structures, particularly the European GDPR, and successful challenges to existing mechanisms for international data sharing, which potentially impact on the EU-US safe-haven concept for health data [13][1], have occurred at a time when new analytical techniques and international collaborations require large-scale data aggregation and integration to support the analysis of Big Data in the health sciences. The recent requirement for FAIR data archiving to facilitate sharing and reuse has intersected with acute regulatory concern about the reproducibility of epidemiological studies and transparency of drug trials [14, 15][2], leading to a complex set of ambiguities and contradictions in complying with these new obligations, particularly in Europe, made more difficult by investigators having to ensure compatibility with research ethics requirements concerning informed consent. While GDPR allows researchers to seek consent for participation in scientific studies within accepted ethical norms for the discipline, it is not yet clear whether, under some interpretations of GDPR requirements, this is sufficient for compliance, especially where consent is sought in broad terms.

Intrinsic to the aims of data sharing and reuse is the explicit intention that data be reanalysed and used in ways not foreseen when the data was collected. This is particularly the case where data is collected in the aftermath of a nuclear incident where the type of analysis to which that data might be subjected, or datasets with which it might be integrated or co-analysed, cannot be foreseen. In principle, this conflicts with GDPR provisions for specifying the defined processes for which the data is collected. Fortunately, the GDPR allows for a scientific research exemption, subject to Article 89(1) protections, which is designed to be broadly compatible with current ethico-legal frameworks for the conduct of scientific research. Article 9(2)(j) and Article 89 mean that researchers can retain patient health data long term, use data from one research project for others, and for legitimate areas of scientific research so long as they have appropriate ethical approval [16]. Recital 162 allows an exception for the statistical processing and processing for scientific reasons of personal data enabling the big data analytics and machine learning tools and facilitating data retention and reuse. It is not therefore expected that dataset archiving and reuse will be a problem for human subject data. However, the sharing of data for reanalysis and movement of data across national borders presents more complex potential problems.

A recent report from the European Parliament Panel for the Future of Science and Technology (STOA) has comprehensively addressed the impact of GDPR on the conduct of research on human subjects and personal data. The implementation of GDPR is as yet in its infancy and it is very hard as yet to assess the impact on either the feasibility of some types of research, or the administrative and financial overheads it might entail. Integration of GDPR into national legislative frameworks in Europe has already generated national heterogeneity as research exceptions and derogations may be introduced into national law by member states under Articles 89(2) and (3) of GDPR [17]. The impact of GDPR additionally potentially interacts with human rights legislation and the UN charter on human rights, which puts an obligation for the support of medical research on governments. Article 12 of the ICESCR requires states to “prevent, treat, and control epidemic, endemic, occupational, and other diseases to achieve the full realization of the highest attainable standard of physical and mental health”. This entails “fostering recognition of factors favouring positive health results, e.g., research”. In addition, there are complex interactions with intellectual property legislation discussed in [18] and [19], the consequences of which are yet to be worked through.

Strategies for dealing with these problems are being developed. For example the BBMRI ERIC is producing a unifying Code of Conduct for Health Research, which will address the interpretation and implementation of GDPR, and other strategies have been mooted such as blockchain-based data tracking and more recently international database federation. The CINECA consortium has recently launched an infrastructure for the sharing of 1.4 million personal genomes, where data are geographically distributed but discoverable and/or accessible in a unified manner.

[1] Court of Justice of the European Union; Judgment in Case C-362/14 Maximillian Schrems v Data Protection Commissioner, 6 October 2015

[2] https://www.ema.europa.eu/en/documents/other/european-medicines-agency-policy-publication-clinical-data-medicinal-products-human-use_en.pdf

Radiation epidemiology datasets like those in other disciplines fall into the two main categories of exposure outcome estimation and clinical procedure or drug trials. More unusually several major occupational health datasets are proprietary and the impact of recent UK data subject legislation and GDPR is yet to be assessed on datasets where analysis is already published and data collection ongoing. With regard to epidemiology data discovery and access, the model currently adopted in STORE is that of describing the dataset metadata in as fine detail as possible and maintaining public contact details for the Data Controllers. In this way STORE hopes to support data reuse and reanalysis together with collaborative efforts without handling the data directly; at least until legal and ethical issues are resolved.

There remains a problem in addition to that of legal constraints on data sharing in the wide range of approaches and procedures adopted locally by clinical trial and epidemiological units, e.g. [20]. There is a clear need for community-wide homogenization and policy recommendations to ensure adherence to consistent best practice to ensure maximization of data sharing and exploitation. Hopefully, the BBMRI recommendations may go some way to developing a benchmark in this area.

In summary, we find that the implementation of FAIR sharing in the radiation science community lags behind other communities for cultural and practical reasons. Some of this practicality concerns adequate and sustainable provision of dedicated data platforms but also allocation to research projects of additional funding dedicated to data management. Training and education with a strong policy drive are also clearly important.

Issues with sharing human data are very similar to those in other epidemiology and clinical trial studies, but in the case of radiation epidemiology large datasets are often collected as part of ongoing monitoring with rather broad analytical intent and in most cases the intention is to store the data for extended period of time. These problems are likely to be resolved as the accepted implementations of GDPR in particular are agreed, but there is currently a risk that national divergence from GDPR through national derogations might generate more problems for sharing and integrating datasets. This needs to be addressed by policy-makers and investigators on a coordinated basis; especially where knowledge-based international regulatory activities are involved.

(b) Sample banks

Available Biobanks for Radiation Research

Biobanks are the cornerstone for any molecular epidemiological research in humans. What makes a biobank a real treasure chest is the combination of high quality biological material with high quality data concerning exposure assessment of the included individuals (not only radiation exposure), life style, health and medical data, as well as epidemiological data.

Biobanks for occupational and accidental radiation exposure

Extensive biobanks, in view of numbers and available information, exist from individuals exposed to radiation in the occupational context. Here first of all the nuclear workers from Russia. Here three Biobanks (Biobank of Mayak PA worker cohort, Russian Human Radiobiological Tissue Repository, Database of Mayak workers´ families) for Mayak workers (see table) and also of their relatives are available harbouring several thousands of individuals with more or less quality of the available biosamples. But also, a huge biobank is available in Siberia (The Bank of Biological Materials of SBRC) and for uranium miners in Germany (German Uranium Miner Biobank). These biobanks are precious in respect to their composition – just a normal population cross section, in respect to the exposure assessment and the received dose (usually higher doses than from environmental exposure). The biobanks are especially suitable to follow up individual radiation susceptibility, especially to lung cancer, to investigate non-cancer induced radiation diseases, such as cardiac diseases and radiation specific fingerprints in tumour material. But also individuals exposed to accidental exposure such as the Chernobyl accident and the contamination in the Techa river (The Techa River Cohort Biobank). The Chernobyl Tissue Bank has already proven to be a highly valuable tool to investigate radiation marks in radiation induced thyroid tissue.

Biobanks for medical radiation exposure

Individuals exposed to medical radiation doses are also followed up for acute and late radiation effects after radiation therapy. Here a highly valuable biobank is the output from the REQUITE study, including more than 4,000 individuals mainly from Europe but also from the USA. If the biobank from the ISE cohort is included already in the REQUITE biobank was not stated. A small biobank BACCARAT study from just 114 patients exists also in France but with the advantage that only breast cancer patients are included that receive radiotherapy but no chemical treatment. Another prospective biobank is on the way to be set up from patients with chronic degenerative inflammatory joint diseases. This biobank (IMMO-LDRT01) may also be very precious to analyse effects on the immune system after low radiation dose exposure. Defined numbers of already included or envisaged individuals are not given.

Biobanks for childhood radiation exposure

Radiation side effects are of growing interest in individuals irradiated in their childhood. Here the ISIBELa biobank, the Portuguese Tinea Capitis Biobank and the French Hemangioma Biobank are available to follow up radiation induced effects. Biobanks for children receiving diagnostic radiation dose are on the way to be set up, but are not depicted in the bulletins.

Biobanks to analyse disease markers in population-based biobanks

Analyses of disease markers for adverse effects should best be investigated in huge population based biobanks existing now worldwide. The Biobank of Eastern Finland is highly remarkable since there are all essential health data available, but also the Biobank of the CONSTANCE cohort and the French longitudinal study of children (ELFE).

What is missing are huge already existing biobanks in Austria (Biobank Graz), Asia (Zhangjiang Biobank, Biobank Japan), UK (UK Biobank), Australia (Victoria Cancer Biobank), Canada (Canadian Partnership for Tomorrow Projects), the USA (“All of Us” biobank), FINNGEN Biobank, EuroBioBank network, Germany (German National Cohort Biobank) and Qatar Biobank to name the world largest biorepositories. These biobanks may also be useful in analysing e.g. radon associated risks.

Biobanks from non-human species

Two repositories do exist: the JANUS animal radiobiology archive which do contain material from large mouse and dog experimental studies and biospecimen from NASA´s sponsored life science experiments.

Biobank	Type of Samples	Size	Localization of Biobank	Cohort/Data	AIR² Bulletin
Wismut Biobank	Peripheral blood lymphocytes, blood DNA, blood RNA, plasma, PAXgene tubes, DNA and RNA from tumour and non-tumour FFPE lung tissue	442 high/low exposed workers >400 lung cancer cases of workers 81 children of workers	Munich, BfS, Germany	Wismut Cohort, partially also included in cohort, uranium workers blood samples were collected between 2008-2012; exposure stopped 1990	Issue 1 (October 2015)
French Hemangioma Biobank	Peripheral blood lymphocytes, DNA, cytogenetic slides from T- and B-cells	369 individuals	Paris, CEA, France	French Hemangioma Cohort (Hemangioma patients treated with radiotherapy in childhood, currently 42-75 years old	Issue 4 (February 2016)
Portuguese Tinea Capitis Cohort	Blood DNA (400 cases), oral mucosa cells, lymphocytes, plasma, serum, tumour and normal tissue DNA from thyroid and basal cell carcinoma From patients An age-matched non irradiated control group is also available	1,375 cases	Porto, Ipatimup/Cancer Biology, Portugal	Portuguese Tinea Capitis Cohort – Evaluation of lon term effects of childhood LDR exposure	Issue 7 (May 2016)
French longitudinal study of children (Elfe)	Maternal urine, blood, milk and hair at birth, cord blood and meconium stools and hair from newborns, urine and stools from children	For a subgroup (~400?)	https://www.elfe-france.fr/en/the-research/publications/academic-journals/	18,000 children involved in the cohort, children followed from birth to adulthood, Radon study included and medical irradiation	Issue 8 (June 2016)
JANUS Animal Radiobiology Archive	FFPE tissue from different animal species (mice, dogs) irradiation experiments		NASA and US Department of Energy http://janus.northwestern.edu/janus2/index.php Northwestern University, USA	Animal lifespan, diseases and time of death from animal studies between 1950-1990	Issue 11 (October 2016)

Biobank of Eastern Finland	FFPE tissue samples, Frozen tissue samples, plasma and serum, blood, DNA	250,000 samples from 100,000 individuals	https://ita-suomenbiopankki.fi/en/researchers/ North Savo Hospital District, the South Savo Social and Health Care Authority, Siun sote – the Joint Municipal Authority for North Karelia Social and Health services, the Eastern Savo Hospital District, and the University of Eastern Finland	Hospital integrated Biobank – each new patient is asked to donate biosamples	Issue 13 (Decembeer 2016)
Chernobyl Tissue Bank	Frozen tissue, DNA and RNA extracted from frozen tissue, blood samples, DNA from blood, serum, sections from FFPE tissue	4,500 cases	London, Coordinating Centre: CTB secretariat, Department of Surgery and Cancer, Imperial College, UK	Cases of thyroid cancer and adenoma from exposed Chernobyl fall out areas of Ukraine and Russia and also from non-exposed areas. Part of the samples are included in the Ukraine-American Cohort	Issue 14 (February 2017)
The Techa River Cohort Biobank	Cells, DNA, fixed slides	30,000 individuals in cohort, but how many biosamples is not clear	Chelyabinsk, Urals Research Center for Radiation Medicine, Russia	Techa River Cohort (Cohort study of general population exposed on the Techa River) – population exposed to radionuclide (^{99,90} Sr, ^{137} Cs release in water/river sediments	Issue 23 (December 2017)
The Bank of Biological Materials of SBRC	Blood, blood DNA, tissue samples (normal and tumor), ethanol/acidic acid cell suspension	20,000 samples from 10,000 individuals	Seversk, Seversk Biophysical Research Center, Russia	Siverian Group of Chemical Enterprises (SGCE), the world´s largest nuclear industrial complex, residents of Seversk	Issue 26 (April 2018)
Biobank of Mayak PA worker cohort	Tumour and non-tumour tissue fixed in formalin and embedded in paraffin, blood components, DNA	22,000 (from 13% biological material available) ~ 2860 individuals?	Ozyorsk, Southern Urals Biophysics Institute, Russia	Mayak PA Worker Cohort	Issue 28 (June 2018)

Russian Human Radiobiological Tissue Repository (RHRTR)	Organs and tissues fixed in formalin and embedded and stored as paraffin blocks and histology slides	350,000 samples from 9,560 individuals	Ozyorsk, Southern Urals Biophysics institute, Russia	Mayak PA Worker Cohort	Issue 29 (July 2018)
ISIBELa, KIKme	Fibroblasts, Saliva	104 cases of secondary neoplasm; 377 cases no SPN; 137 sex and age matched controls	Mainz, University Mainz, Germany	The ISIBELLA Cohort (an interdisciplinary study on radiation induced second cancer) – childhood cancer 0-15 years of exposure	Issue 33 (December 2018)
The ISE cohort	DNA, RNA	476	Heidelberg, DKFZ, Germany	The ISE Cohort (Individual sensitivity to radiotherapy for breast cancer)	Issue 34 (February 2019)
NASA´s sponsored life sciences experiments	Various Biospecimen (human, animal, plant, bacteria)	7,000	https://lsda.jsc.nasa.gov/Biospecimen	NASA experiments	Special Issue 4, February 2019
Database of Mayak workers´ families	Tumour and non-tumour tissues (formalin-fixed, paraffin embedded tissue blocks, histological slides), blood and its components?, DNA	11,030	Ozyorsk, Southern Urals Biophysics Institute, Russia	Mayak PA worker Cohort (Unclear which material is available for family members	Issue 35 (March 2019)
CONSTANCES	Blood, urine	200,000		CONSTANCES (population-based cohort in France from 2012-2019) 18-69 years	Issue 36 (April 2019)
IMMO-LDRT01 Cohort	Serum, Plasma, frozen PBMC	N?	Erlangen, Germany	IMMO-LDRT01 CORHORT (Cohort of locally low-dose irradiated patients with chronic degenerative, inflammatory joint diseases) prospective study in Erlangen	Issue 37 (May 2019)

BACCARAT	Plasma	114	Paris, IRSN, France PI: Dr. Sophie Jacob	The BACCARAT Study (Early cardiotoxicity after radiotherapy for breast cancer): only Radiotherapy patients without chemotherapy included, 2 years prospective study	Issue 38 (June 2019)
REQUITE	Blood DNA (N = 4,400), RNA (N= 1,837), PAXgene tubes (1,202)	4,438	Data and Biobank centralized in Manchester, UK	REQUITE (Mainly European, USA included): Radiotherapy Patients (lung cancer, prostate cancer, breast cancer	Issue 40 (September 2019)

Table 7: Overview of existing biobanks and cohorts

(c) Cohorts

Cohorts are essential infrastructures for human radiation protection research. Although many health effects of ionizing radiation exposure on human health (mostly on cancer) have been strongly established, it is still relevant to use a variety of cohorts in order to study the potential health effects of exposures occurring at ever decreasing doses, including cancer but also non-cancer outcomes. Linking these cohorts with biobanks is essential to determine biological pathways from radiation exposure to radiation-related diseases, in order to better communicate judgements on the causal nature of observed associations, improve predictions and possibly to identify biomarkers that would be useful for prevention and monitoring of radiation-related risks.

One of the reasons why so many cohorts are needed (beyond the obvious desirability to replicate and validate findings across study setting), is also to evaluate whether the various modalities of radiation exposure (e.g. particle types, internal versus external exposures, dose levels, dose rates) yield health effects that are compatible with hypotheses retained by the ICRP to define radiation protection standards, and evaluate whether any change is necessary. The various characteristics of study populations (children versus adults, men versus women, people with different genetic backgrounds or lifestyles) also justify the conduct of studies in cohorts contrasted on these characteristics in order to study radiosusceptiblity and radiosensitivity [21].

Essential criteria for quality and informativeness of cohorts have been reviewed by UNSCEAR [22]. This notably includes adequate dosimetry, information on potential confounding factors, absence of selection bias, sufficient follow-up and size in order to get enough statistical power for analysis.

The cohorts presented in the AIR² bulletins cover a variety of radiation exposure situations: medical, occupational, and environmental (including post-accidental) exposures. They cover external exposure at various doses and dose rates (from low dose to high doses delivered for radiotherapies) and internal exposure to a wide array of radionuclides. Various age at exposures have also been considered.

Most well-established radio-epidemiological cohorts available (at least in part) in Europe have been covered. This notably includes large international projects such as the EPI-CT cohort of CT scans or the INWORKS study of radiation workers. When such international studies have been covered, no further focus on national datasets included in these international analyses have been made. Some cohorts located outside of the European Union (e.g. in Japan, USA, Russia, Kazakhstan) have also been presented.

Among major radio-epidemiological databases, which have not been covered by AIR², several projects must be mentioned. This includes ongoing international analyses such as the Poolded Uranium Miners Analysis (PUMA), international Pooled Analysis of Uranium Workers (iPAUWthe United States Based Million Person Study, the EURATOM-Funded HARMONIC project). The Fukushima health management survey is also a study that would deserve additional coverage in the future. Studies on natural background radiation have not been included (although some authors have been contacted), as well as other studies covering different situations of environmental exposure (e.g. other radiation fallout studies, residents of radiocontaminated buildings in Taiwan). Last, many cohorts of medical exposure (including medical workers) have not been covered, notably studies of U.S. Radiologic Technologists Study in the United States and South Korea. A very large study of childhood CT scans exists in Australia. Several studies of radiotherapy patients in Europe (e.g. childhood cancer survivors studies grouped in the PanCareSurFup project covering 11 European countries), but also in North America (childhood Cancer Survivors studies in the US and Canada). Many studies of adults receiving radiotherapies for various conditions exist worldwide and have led to joint analyses or meta-analyses [23]. A wealth of other finalized and ongoing cohort studies related to different medical exposure exist. Properly reviewing all of them would require major collective efforts on a global scale.

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Chapter 3: Analytical platforms, Models & Tools

The nature and complexity of the societal challenges related to low-dose research require an international approach to answer the open questions in the radiation community. For this purpose, it is essential to have access to best platforms with cutting-edge technologies in order to achieve not only scientific excellence but also public health impact. Such technologies, but also models and tools to optimise the data analysis, increase the value of analytical platforms. This web handbook introduces some European platforms together with suitable models and tools as described in the next sessions.

(a) Analytical platforms

Research infrastructures, including analytical platforms, are at the core of the knowledge triangle of research, education and innovation and therefore play a vital role in the advancement of science, knowledge and technology. Analytical platforms play a key role in the construction of an efficient research and innovation environment and are one of the most efficient tools to facilitate European cooperation in radiation research.

In the low-dose research, analytical platforms are often designed to address questions related to systems biology studies with the goal to understand the mechanisms underlying radiation response. Analytical platforms described in this handbook are using different technologies and tools to answer challenging biological questions. This will allow the implementation of systems-based analyses that often generate large data sets [1]. These, in their turn, require resources for safe storage and management of information in the long term.

Several criteria need to be considered regarding such infrastructures. Firstly, performance is an important aspect for analytical platforms. The platform should have high score performance with constant quality controls included. In addition, detailed operating procedures should exist since they help the user to perform the work correctly, naturally with the help of the local user.

Secondly, the platform should be easily accessible for guest scientists to perform their analysis. Alternatively, the platform should provide a core-service type analysis. The security of access and the reliability of the experimental processes should be well managed and monitored all times. The user should be able to give feedback, both positive and negative, as suggestions how to improve a platform are often very useful. All collected data should be well documented and well governed *via* storage in secure open-access databases such as the STORE DB [1].

Strong investment in research and innovation is needed to address pressing societal challenges in radiation protection. Analytical platforms play an important role in addressing these challenges. However, it is essential to enhance collaboration between the different fields of radiation research in order to optimise the use of scarce resources for increasingly expensive facilities, in order to overcome the problems arising from fragmented funding in research infrastructures across Europe.

(b) Models & Tools

The category 'Models & Tools' encompasses a wide range of mathematical, statistical, biological (*in vitro*, *ex vivo* and *in vivo*), biochemical and physical models and tools, created and maintained by partners across the CONCERT consortium and wider collaborators, to support radiation protection research. As is clear from the CONCERT joint roadmap and related strategic research agendas of the radiation protection platforms [2, 3], models and the tools that support their use are essential to maintain innovative scientific research and development across the different platforms and projects in the field of radiation protection. For example, in the field of biological dosimetry and biomarker research (RENEB Analytical Platform) [4], ISO standard methodologies exist for translation of biological and biochemical observations into estimates of dose to support both emergency response (NERIS platform) [5] and medical management (EURAMED) [6] of individuals. Wider use of these techniques for molecular epidemiology, for example in the MELODI platform [7], is supported by provision of user-friendly tools such as Dose Estimate, NETA and CABAS. Continuing with the emergency response theme, the Severe Nuclear Accident Program (SNAP) tool provides a means to identify unknown sources of radiation, indicated by elevation in normally measured levels. The Multi Criteria Decision Analysis (MCDA) tool gives guidance to decision makers regarding selection of concerted emergency response strategies. For non-human populations (ALLIANCE platform) [8], the Environmental Risk Assessment tool (ERICA) supports environmental risk

assessment and the Biological Radiation Effects for Non-human Dose Assessment (BRENDA) model facilitates estimation of the non-stochastic effects of radiation on repairable radiation damage, reproductive ability and mortality.

In the field of physical modelling of radiation effects, several bespoke radiation transport codes have been created and further models which attempt to provide accurate representations of the biological and biochemical consequences of exposure are now in existence. Examples include the now relatively well established GEANT4-DNA, BIophysical ANalysis of Cell death and chromosome Aberrations (BIANCA) and COmputation Of Local Electron Release (COOLER) tools. Extending computational support to the medical protection research field (EURAMED platform), the OEDIPE tool, for example, supports personalised dosimetry in nuclear medicine.

The CONCERT project and the joint SRAs clearly indicate the need for interdisciplinary research to address the key research lines. As the radiation research community continues to grow and flourish, it is likely that its members will need to work more and more across disciplinary boundaries. The utility of such user-friendly models and tools in this context is clear, as it is in the context of emergency response when tools to support fast and effective decision-making will be invaluable.

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In situ analytical techniques applied in the field

In the field of radioecology and radiological protection, detailed information on the physico-chemical forms (speciation) of radionuclide, transformation processes changing the radionuclide speciation over time, and associated kinetics is essential. Radionuclides can be present in different physico-chemical forms in waters and in soils/sediments and the specie distribution of radionuclides will influence the ecosystem transfer, biological uptake and effects. Thus, it is essential to obtain information of the physical-chemical form of the radionuclides in the field.

Although a series of fractionation and speciation techniques are available [1] and are usually applied in laboratories, results could be influenced by the storage conditions. During storage of for instance waters, charged cations can adsorb to container walls, changes in pH and redox conditions due to the presence of microorganisms (CO_2 production) could induce hydrolysis, complexation, and chelation that may change radionuclide species. During storage of sediments, changes in redox conditions would influence binding mechanisms and thereby remobilization of radionuclide species. Thus, fractionation techniques should be applied in the field.

To separate radionuclide species (particles, aerosols) transported by air, air filter device including cascade impactors are frequently applied in the field. Based on cascade impactors, particles of different aerodynamic diameters can be collected simultaneously. Then, air fractioned samples can be subjected to various laboratory techniques (e.g. γ-spectrometry, µ-XRF), and autoradiography of air filters can be an effective means to extract individual particles for further analysis.

To collect radionuclides species including particles in waters, *in situ* fractionation techniques such as filtration (0.45, 0.2, 0.1 µm), tangential cross flow or ultrafiltration using nm to µm cut-off range membranes are frequently applied. Combining size fractionation techniques such as filtration and hollow fibre ultrafiltration with charge fractionation techniques such as cation chromatography, most useful information on the distribution of specie categories is attained, such as low molecular mass (LMM) charged or neutral species, colloids and particulate material [2].

To identify hot spots in soils, *in situ* portable devices such as GM counters, NaI(Tl), HPGE scintillators, high-resolution HPGe detector or portable XRF detectors are utilized for screening purposes. Again, autoradiography can be used to locate the position of hot spots. Then, radioactive particles can be characterized with respect to properties being essential for transfer and biological uptake (e.g. size, crystalline structure, morphology, oxidation states) using advanced metrology (e.g. electron microscopy, SIMS, synchrotron x-ray microscopic techniques). To obtain information on potential mobility of radionuclide species in soils or sediments, sequential extractions or leaching experiments should take place at site or shortly after sampling. Following the steps in a sequential extraction procedure, information on radionuclide species being reversible or irreversible associated to soil/sediment components is attained [3]. Then, further analysis of extracted fractions can be performed in laboratory.

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Chapter 4: Protocols issued from harmonization procedures

Harmonization procedures within RENEB (European Network of biological dosimetry and retrospective physical dosimetry)

Harmonization is an important process to pool existing knowledge and capacities. In the field of biodosimetry and retrospective physical dosimetry, this procedure was successfully carried out in the frame of establishing the RENEB network. RENEB has been created to strengthen the emergency preparedness and response capabilities in Europe in case of a large-scale nuclear accident or radiological emergency [1].

In both contexts, biological and retrospective physical dosimetry are essential tools to estimate the actual absorbed dose, not being influenced by temporal or individual variations in blood counts or confounding factors such as chemical agents or psychogenic reactions. Based on the results of biological and personalised physical dose estimation, individuals requiring extensive medical care due to severe radiation symptoms can be distinguished from individuals who show similar symptoms without receiving high radiation doses.

An essential element of such an emergency network is its operational basis. Within RENEB, seven biodosimetric and physical assays were tested and harmonized, five using human peripheral blood lymphocytes (PBL) and two using smartphone-based dosimetry.

In order to establish the operational basis of the network, two practical intercomparisons, one being on the global level, and an accident simulation exercise were performed. The results confirmed a good and homogeneous performance of the RENEB laboratories and an efficient shipment of samples within the EU.

Further harmonization activities in the frame of RENEB were set up to improve the performance of the partners. Here, various training activities, including practical training exchanges, were applied. Special emphasis was put on Quality Assurance (QA) and Quality Management (QM) of the network. Several seminars on quality metrology, statistics, and QA&QM were held. Furthermore, a QA&QM manual for RENEB was developed and a long-term training programme established. An accident simulation exercise with a focus on QA was performed to test and improve the link between national authorities and reference laboratories. A concept to integrate new members was established and applied for candidates. Informal contacts with European training structures and programmes with a strong impact in this field were installed [2].

Protocols about the use of STORE

The STORE database was developed under European Commission funding (2009 – 2012) to propagate the idea of public data sharing and reuse in radiation biology. It was sustained and further developed with the help of small but successive grants and was opened to public use in 2014. The STORE database provides a platform for different types of data, ranging from epidemiological data to cytogenetics, various “omics”, computer codes, and documents. File structures in STORE are project-based forming an envelope for datasets and individual data items in a nested fashion. This enables the clustering of different types of data associated with a particular project to form a coherent set of elements. Yet, each file can be searched and accessed separately, offering clear advantages if compared to commercial data repositories that are often centred on the data entry itself.

Since STORE provides digital object identifiers (DOIs) and accession IDs for all data, large projects are more and more using STORE to coordinate and archive data to be linked to reports and publications. The database is physically located at the Federal Office for Radiation Protection (BfS) that guarantees the full security of a German Federal data service. The access to STORE is provided via ORCID user IDs through an intuitive web interface and is free of charge. A live storage of data is guaranteed for a period of seven years after the most recent access. If data are not accessed for longer than this period they will be taken offline and stored in a ‘cold storage’ or archived to permanent and less expensive media [3]. STORE is available on http://www.storedb.org. More information about STORE can be found in Schofield et al. [4].

Recommendations about archive materials

Medicine has used radiation therapy as a treatment for cancer for more than 100 years, almost since the discovery of x-rays in 1895 by Wilhelm Röntgen. Almost equally as long, pathologists worldwide have used formalin-fixed paraffin-

embedded (FFPE) tissues due to their outstanding format for histological analysis and long-term storage. Many clinical tissue archives, with the attached information on patient data such as diagnosis and outcome, represent an important source of information on radiation response in cancer and normal tissues [5].

Large archives with FFPE material containing irradiated tissue exist not only in the clinics. Collecting biological material was at its peak between 1952 and 1992 when more than 200 large-scale experiments were conducted on non-human animals, mainly mice and beagles, in the USA, Europe and Japan [4]. Although most of these experiments used high radiation doses, low dose exposures were often included to give information about the shape of the dose-response curve. In addition, the number of animals in the low-dose groups was also high, increasing the significance of the findings.

Clinical and radiobiological tissue banks provide retrospective information, not only about the nature of radiation-induced disease, but also about the molecular pathways and cellular processes leading to such end-points. The "omics" technologies such as genomics, transcriptomics, metabolomics, and proteomics are part of the arsenal of experimental tools suitable in identifying and quantifying the causes, triggers and promoters of harmful environmental and occupational stressors including ionizing radiation, leading to a disease [6, 7]. FFPE tissue has been considered even as an alternative to fresh/frozen tissue in the discovery of disease biomarkers [5]. Principally, the rapid expansion in technology-driven analytical methods could offer great rewards also to a radiation biologist intending to use FFPE material. However, the harsh and irreversible fixation and the long storage times make retrospective biological studies on archival material a difficult task. In many cases, the tissue archives represent the only source of biomaterial available. Consequently, experiments using FFPE tissue have to be carefully designed to avoid unnecessary material loss or damage. For all these reasons, standardized methods how to best use archival samples are necessary.

One of the goals of EURATOM FP7 project "Sustaining access to Tissues and data from Radiobiological Experiments" (STORE) (2009 - 2012) was to establish Standard Operating Procedures (SOPs) to test the quality of archived samples and remove limitations in the quantification of DNA, RNA, and protein content by developing new analytical methods. This was particularly successful in the case of proteins. A new method for protein extraction [8] and the application of label-free proteomics [9] enabled a good identification and quantification of the irradiated cell or tissue FFPE proteome. Furthermore, the development of a rapid lysis method to evaluate the quality of the DNA and RNA content in the FFPE material [10] has been used and cited since its publication in more than 70 original articles.
The SOPs can be found in: https://www.storedb.org/store_v3/documents.jsp
The development of new methods using FFPE material has not ceased with the end of the STORE project. Their application in radiation biology depends largely on the willingness of the funding organisations for radiation research to support proposals using archival material.

Development of Youtube tutorials focusing on the main biodosimetry techniques

WP6 worked towards the harmonization of practices and protocols. More precisely, in the frame of *Subtask 6.2.4 Harmonization and exercises* (Lead: CEA) and *Subtask 6.3.2 Developing training* (Lead: UNIPV) we developed a series of Youtube tutorial videos focusing on the main techniques used in biodosimetry.

To begin with this feasibility exercise, we performed a thorough online research to evaluate whether online sources and material covering topics of interest to the Radiation Protection Research community exist and to which extend. An analysis of the most popular MOOC platforms such as EdX, Coursera and Udavity revealed that there are currently no courses available on cytogenetics and biodosimetry, while courses covering other topics relevant to Radiation Protection Research are scarce. By far, the most important source of online educational material was Youtube and the Video journal Jove. Nevertheless, the few videos describing how to perform the main biodosimetry techniques in the laboratory were of low image and/or sound quality and failed to provide the viewer with sufficient information and experimental details. Thus, there was an identified lack of digital E&T tools.

Our efforts focused on creating 5 protocol videos, showing step by step the cytogenetics techniques and aiming to contribute to the harmonization of practices. The videos have been uploaded and hosted in the Youtube Channel "CEA Sciences", which counts more than 16K subscribers, in order to reach out to the maximum number of people. Below you can find the list of the techniques and the respective links to each video:

1) The Dicentric Chromosome Assay (https://www.youtube.com/watch?v=ZG5ssFNI3Jc&t=620s)
2) The Cytokinesis Block Micronucleus Assay (https://www.youtube.com/watch?v=gc5uyTyHTrU&t=124s)
3) The Premature Chromosome Condensation Assay (https://www.youtube.com/watch?v=lECSDGTxOp0&t=1419s)
4) The Telomere and Centromere FISH staining (https://www.youtube.com/watch?v=RqI1ulPWD_E&t=187s)
5) The multi FISH staining (https://www.youtube.com/watch?v=99Cv7GjHxVs)

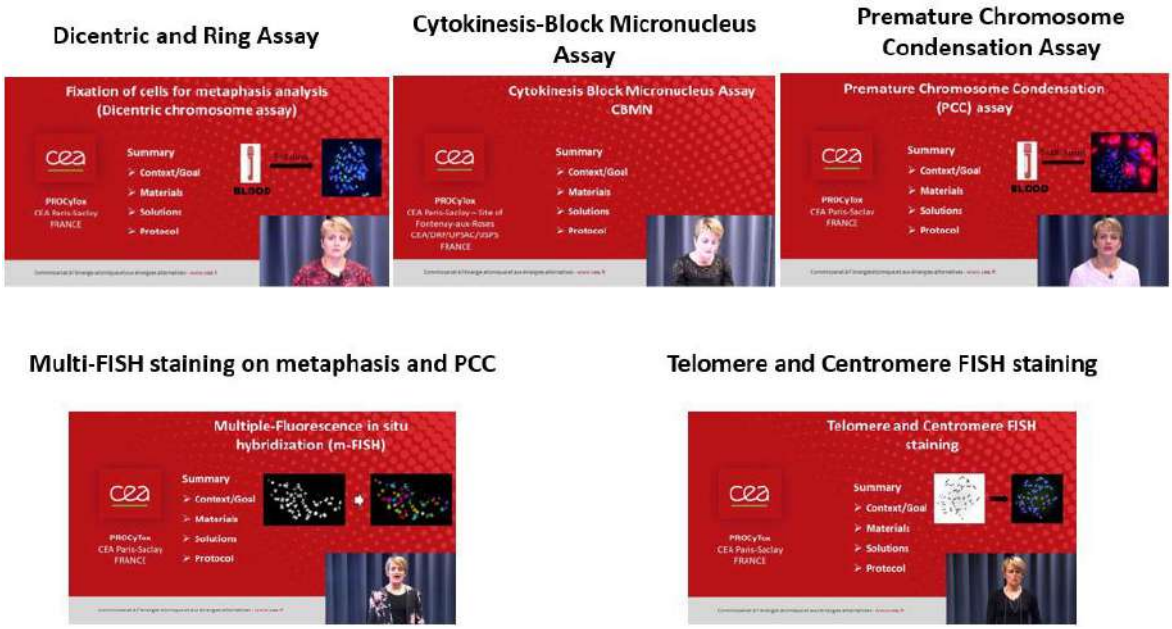

Figure 1: The 5 cytogenetics tutorial videos developed in the frame of WP6

The average duration of the videos is 25 minutes. Each video comprises an introduction focusing on the theory behind each assay and explaining the context and goal of the video, the list of materials and solutions required for performing each assay, a detailed presentation of the experimental steps and a Q&A session.

Figure 2: The structure of each tutorial video comprising 4 main parts: an introduction, a list of materials, the experimental steps, a session of Q&A

This feasibility exercise has been presented in the European Radiation Protection Week 2019 in Stockholm (https://erpw2019.eu/) with an oral presentation in the session Education & Training and a poster. In addition to that, a "The floor to…" article has been published in AIR^2 special issue n°9 and a publication on the same topic is under preparation.

References Chapter 4

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Conclusions and perspectives

In this deliverable, 120 infrastructures, published till September 2019 in the 40 Issues of AIR² are presented. We have added also 8 infrastructures published in 2 Special Issues presented in the "Add-on" section. This web handbook consists of 3 main chapters, representing the 3 categories that AIR² readers are already familiar with: "Exposure platforms", "Databases, Sample banks, Cohorts", "Analytical platforms, Models & Tools". Each chapter has been divided into subcategories aiming to facilitate researchers and students in the field of Radiation Protection research finding information about potential infrastructures they need. First level of information with detailed technical characteristics, access conditions and a contact are provided about "well known" but also for "newly-developed" infrastructures. They have been described going beyond CONCERT partners and even including non-EURATOM countries in order to more accurately draw the radiation protection infrastructure landscape.

Europe has many high quality infrastructures to support Radiation Protection research. It will nevertheless be important to identify gaps and remain responsive to new requirements that may emerge with scientific and technological developments. Some categories of infrastructures are quite straightforward, while others, such as "Databases, Sample Banks and Cohorts", are more complex. Exposure platforms are the cornerstone of most radiation protection research activities, indeed we feature 45 of them in comparison to 35 "Databases, Sample banks, Cohorts" and 40 "Analytical platforms, Models & Tools". Some less visible infrastructures are also the most fragile. Frequently created during a European project to answer a particular need, they fall dormant afterwards through lack of sustainable funding, when they could have been so useful for future research if kept active and updated. AIR² focused its efforts in keeping them under the spotlight. Similarly, efforts will be focused to enlarge the scope to other subcategories such as, for example, infrastructures for image-guided small animal radiotherapy, microbeams, internal contamination facilities, observatory sites, sample banks and so on.

Most of the infrastructures needed for Radiation Protection research exist across Europe (and sometimes outside). CONCERT promotes the visibility of those infrastructures and recommends their use. One of the roles of CONCERT has been to ensure the availability of and facilitate access to operational "state-of-the-art" research infrastructures required to support the research efforts of Radiation Protection researchers. The priority is promote the use of mature infrastructures and avoid unnecessary duplication. The open approach of CONCERT involves the use of infrastructures, which fulfil recommended criteria. They are integrated on the voluntary basis into a searchable available database AIR²D² (http://www.concert-infrastructures.eu/home) that can be updated to include new candidates. At the time being, the best way to achieve the sustainability of these infrastructures is to use them for research projects. The web-handbook answers also to enforce their visibility and increase their funding potential through European projects. The web-handbook may be seen as the funding preliminary act of a dedicated virtual open network to support Radiation Protection research.

The web-handbook is based on the 40 classic issues of AIR², together with additional research. It is a result of "ongoing" work and we can easily imagine a possible future with revised and extended version because infrastructures like other research labs disappear and sometimes new ones are created.

Future extensions are possible: various hyperlinks with the future extended AIR²D² database and more direct actualized information issued directly from owners and why not, directly other links using tools already available through Internet. It is sure that it could become a continuous integrative tool for researchers to find their suitable platform but also for reviewers to evaluate and control the quality of this type of support/partners for European projects financially supported by the EC. It could become a strong recommendation to obtain the highest value in the evaluation of the scientific excellence, if not a requirement.

The web-handbook is a great tool to analyse the actual landscape and open-mindedness of infrastructures. This is a key point, which by this construction shows inherently its strengths and weaknesses. It is the first time that they accept to be together without a competitive spirit. Each owner considers only that this visibility increases its chances of continuation. Nevertheless, it also shows that they are not organized; they do not constitute a network and are more competitors than partners. Today, the competition is focused on the visibility of their specificity.

The help of the entire Radiation Protection Research community is required to cover all the radiation protection related present and future topics of research: low dose, radioecology, dosimetry, emergency situations, medical use, social sciences, etc….

Even if the present status of the web-handbook includes 120 infrastructures, at the time being nobody knows which would exactly be the ideal closed system with the “TOP 100” in each category. Surely, these 120 collected infrastructures are among the top listed ones, however it is not an exhaustive description of the entire landscape of the potentially available infrastructures in Europe. Shortly, this is not a “closed” web-handbook and we will hopefully open it and revise it on a continuous basis in the future.

Cross Tables

Chapter 1: Exposure platforms		
Subcategories	**Infrastructure**	**Other subcategories**
(a) Low doses and low dose rates	FIGARO	(d)
	PULEX-Cosmic Silence	(c)
	Silesian Centre for Environmental Radioactivity (SCRS-GIG)	(c) (d)
	LIBIS	
	Microtron Laboratory	
	Low dose rate facility at Stockholm University	
	MICADO'LAB Experimental Platform	
	LERF	
	AMBIC	
	The Calliope facility	
(b) Microbeams	SNAKE	
	PTB-Microbeam, ion and neutron fields	
	The MIRCOM microbeam	
	AIFIRA	
(c) Particular radiation qualities: ions, neutrons, alpha…	Radon Exposure Chamber	(a) (d)
	Biological Irradiation Facility (BIO)	(a)
	CIRIL	
	Mixed alpha and X-ray exposure facility	
	Alpha particles irradiator	
	Changing dose rate exposure facility	
	Proton IRRADiation facility (IRRAD)	(f)
	CERF	
	TIFPA	
	HIT	
	The AGOR Facility at KVI-CART	
	FAIR	
	Research Neutron Source Heinz Maier-Leibnitz (FRM II)	
	NASA Space Radiation Laboratory (NSRL)	
(d) Internal contamination	B3, Animal Contamination Facility	(c)
	Facility radionuclides availability, transfer and migration	
	Nanoparticle Inhalation Facility	
	PARISII	

(e) Observatory sites	The Chernobyl Exclusion Zone Forest observatory site in Yamakiya Belgian NORM Observatory Site IRSE Experimental Farm, Kazakhstan Phosphogypsum stack at Barreiro, Portugal ZATU (Zone Atelier Territoire Uranifère), France	
(f) Metrology exposure platforms	Laboratory for retrospective Radon and Thoron dosimetry Calibration Laboratory at KIT MELAF Radiation Metrology Laboratory (DOS) Laboratory for Dosimetry Standards (NDS) CALibration LABoratory(CALLAB) Radon Calibration Laboratory of BfS Calibration and Dosimetry Laboratory (INTE-UPC) The Nuclear Metrology Group (NMG) UNIPI neutron irradiation facility Laboratory for Nuclear Calibrations at SCK•CEN CIEMAT External Dosimetry Service and Retrospective Luminescence Dosimetry Lab	(c) (c) (c)

Table 8: Exposure Platforms cross table with tags for each infrastructure

Chapter 2 : Databases, Sample banks, Cohorts		
Subcategories	**Infrastructure**	**Other subcategories**
(a) Databases	FREDERICA STORE Wildlife Transfer Database RES^{3}T JANUS Animal Radiobiology Archive MARiS – MARine Information System The BRIDE platform Database of Mayak workers' families NASA's LSAH and LSDA repositories The "hematopoietic system" database for Mayak nuclear workers	 (b) (b)
(b) Sample banks	Biobank of Eastern Finland Chernobyl Tissue Bank Belgian Soil Collection The Bank of Biological Materials of SBRC Russian Human Radiobiological Tissue Repository (RHRTR)	

(c) Cohorts	The Wismut Cohort and Biobank	(b)
	French Haemangioma Cohort and Biobank	(b)
	3-Generation exposure study	(b)
	Portuguese Tinea Capitis Cohort	(b)
	French longitudinal study of children (Elfe)	(b)
	INWORKS Cohort	
	EPI-CT scan cohort	
	Chernobyl clean-up workers from Latvia	
	ESTCHERN Cohort	(b)
	German airline crew cohort	
	The Techa River Cohort (TRC)	(b)
	Greek interventional cardiologists cohort	
	The German Thorotrast Cohort Study	
	Mayak PA worker cohort (MWC)	(b)
	The TRACY cohort	
	The ISIBELa cohort	(b)
	The ISE cohort	(b)
	CONSTANCES	(b)
	IMMO-LDRT01 cohort	(b)
	The BACCARAT study	(b)
	Life Span Study (LSS)	
	REQUITE	(b)

Table 9: Databases, Sample banks, Cohorts cross table with tags for each infrastructure

Chapter 3 : Analytical platforms, Models & Tools	
Subcategories	**Infrastructure**
(a) Analytical platforms	RENEB
	The Genomic Medicine and Bioinformatics Core Facility
	MetaboHUB
	ProFI
	Radiobiology and immunology platform (CTU-FBME)
	France Génomique
	The SCK•CEN Genomics platform
	CATI
	HZDR–Radioanalytical Laboratories
	Advanced Technologies Network (ATeN) Center
	BfS In Vivo Measurement Facilities
	ECORITME

	Consolidated Radioisotope Facility (CORiF) Centre for Omic Sciences (COS) The iGE3 Genomics Platform VIB Proteomics Core MARS beamline at Synchrotron SOLEIL CIEMAT Whole Body Counter (WBC) DSA Environmental Laboratory Radiochemical and Radioactive Analysis Laboratory (INTE-UPC) CIEMAT In Vitro Internal Dosimetry Laboratories LRM TU Dublin Analytical Platform NASA Genelab
(b) Models & Tools	Dose Estimate, CABAS and NETA LDRadStatsNet ERICA Tool CROM-8 The Analytical Platform of the PREPARE project Symbiose INFRAFRONTIER The CERES Platform The Severe Nuclear Accident Program (SNAP) The BIANCA code OEDIPE Geant4-DNA D-DAT COOLER BRENDA The EFFTRAN code The MCDA Tool

Table 10: Analytical platforms, Models & Tools cross table with tags for each infrastructure

Infrastructure	Exposure platforms						Databases, Sample banks, Cohorts			Analytical platforms, Models & Tools	
	Low doses and low dose rates	Microbeams	Particular radiation qualities: ions,	Internal contamination	Observatory sites	Metrology exposure platforms	Databases	Sample banks	Cohorts	Analytical platforms	Models & Tools
FIGARO	■			■							
PULEX-Cosmic Silence	■		■								
Silesian Centre for Environmental Radioactivity (SCRS-GIG)	■		■	■							
LIBIS	■										
Microtron Laboratory	■										
Low dose rate facility at Stockholm University	■										
MICADO'LAB Experimental Platform	■										
LERF	■										
AMBIC	■										
The Calliope facility	■										
SNAKE		■									
PTB-Microbeam, ion and neutron fields		■									
The MIRCOM microbeam		■									
AIFIRA		■									
Radon Exposure Chamber	■		■	■							
Biological Irradiation Facility (BIO)	■		■								
CIRIL			■								
Mixed alpha and X-ray exposure facility			■								
Alpha particles irradiator			■								
Changing dose rate exposure facility			■								
Proton IRRADiation facility (IRRAD)			■			■					
CERF			■								
TIFPA			■								
HIT			■								
The AGOR Facility at KVI-CART			■								
FAIR			■								
Research Neutron Source Heinz Maier-Leibnitz (FRM II)			■								
NASA Space radiation Laboratory (NSRL)			■								
B3, Animal Contamination Facility			■	■							
Facility radionuclides availability, transfer and migration				■							
Nanoparticle Inhalation Facility				■							
PARISII				■							

The Chernobyl Exclusion Zone											
Forest observatory site in Yamakiya											
Belgian NORM Observatory Site											
IRSE Experimental Farm, Kazakhstan											
Phosphogypsum stack at Barreiro, Portugal											
ZATU (Zone Atelier Territoire Uranifère), France											
Laboratory for retrospective Radon and Thoron dosimetry											
Calibration Laboratory at KIT											
MELAF											
Radiation Metrology Laboratory (DOS)											
Laboratory for Dosimetry Standards (NDS)											
CALibration LABoratory(CALLAB)											
Radon Calibration Laboratory of BfS											
Calibration and Dosimetry Laboratory (INTE-UPC)											
The Nuclear Metrology Group (NMG)											
UNIPI neutron irradiation facility											
Laboratory for Nuclear Calibrations at SCK•CEN											
CIEMAT External Dosimetry Service and Retrospective Luminescence Dosimetry Lab											

Table 11: Summary table for the category Exposure Platforms

Infrastructure	Exposure platforms						Databases, Sample banks, Cohorts			Analytical platforms, Models & Tools	
	Low doses and low dose rates	Microbeams	Particular radiation qualities: ions,	Internal contamination	Observatory sites	Metrology exposure platforms	Databases	Sample banks	Cohorts	Analytical platforms	Models & Tools
FREDERICA											
STORE											
RES^{3}T											
Wildlife Transfer Database											
JANUS Animal Radiobiology Archive											
MARiS – MARine Information System											
The BRIDE platform											
Database of Mayak workers' families											
NASA's LSAH and LSDA repositories											
The "hematopoietic system" database for Mayak nuclear workers											

Biobank of Eastern Finland											
Chernobyl Tissue Bank											
Belgian Soil Collection											
The Bank of Biological Materials of SBRC											
Russian Human Radiobiological Tissue Repository (RHRTR)											
The Wismut Cohort and Biobank											
French Haemangioma Cohort and Biobank											
3-Generation exposure study											
Portuguese Tinea Capitis Cohort											
French longitudinal study of children (Elfe)											
INWORKS Cohort											
EPI-CT scan cohort											
Chernobyl clean-up workers from Latvia											
ESTCHERN Cohort											
German airline crew cohort											
The Techa River Cohort (TRC)											
Greek interventional cardiologists cohort											
The German Thorotrast Cohort Study											
Mayak PA worker cohort (MWC)											
The TRACY cohort											
The ISIBELa cohort											
The ISE cohort											
CONSTANCES											
IMMO-LDRT01 cohort											
The BACCARAT study											
Life Span Study (LSS)											
REQUITE											

Table 12: Summary table for the category Databases, Sample banks, Cohorts

Infrastructure	Exposure platforms						Databases, Sample banks Cohorts			Analytical platforms Models & Tools	
	Low doses and low dose rates	Microbeams	Particular radiation qualities: ions,	Internal contamination	Observatory sites	Metrology exposure platforms	Databases	Sample banks	Cohorts	Analytical platforms	Models & Tools
RENEB											
The Genomic Medicine and Bioinformatics Core Facility											
MetaboHUB											
ProFI											

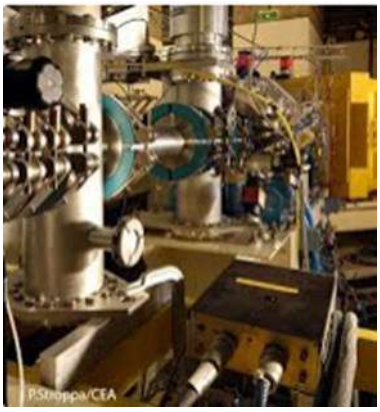
Radiobiology and immunology platform (CTU-FBME)											
France Génomique											
The SCK•CEN Genomics platform											
CATI											
HZDR–Radioanalytical Laboratories											
Advanced Technologies Network (ATeN) Center											
BfS In Vivo Measurement Facilities											
ECORITME											
Consolidated Radioisotope Facility (CORiF)											
Centre for Omic Sciences (COS)											
The iGE3 Genomics Platform											
VIB Proteomics Core											
MARS beamline at Synchrotron SOLEIL											
CIEMAT Whole Body Counter (WBC)											
DSA Environmental Laboratory											
Radiochemical and Radioactive Analysis Laboratory (INTE-UPC)											
CIEMAT In Vitro Internal Dosimetry Laboratories											
LRM											
TU Dublin Analytical Platform											
NASA Genelab											
Dose Estimate, CABAS and NETA											
LDRadStatsNet											
ERICA Tool											
The Analytical Platform of the PREPARE project											
CROM-8											
Symbiose											
INFRAFRONTIER											
The CERES Platform											
The Severe Nuclear Accident Program (SNAP)											
The BIANCA code											
OEDIPE											
Geant4-DNA											
D-DAT											
COOLER											
BRENDA											
The EFFTRAN code											
The MCDA Tool											

Table 13: Summary table for the category Analytical platforms, Models & Tools

Index (alphabetical order)

Laboratory for Nuclear Calibrations at SCK•CEN – 1f
Laboratory for retrospective Radon & Thoron dosimetry – 1f, 1c
LDRadStatsNet – 3b
LERF – 1a
LIBIS – 1a
Life Span Study (LSS) – 2c
Low dose rate facility at Stockholm University – 1a
LRM – 3a
MARiS – MARine Information System – 2a
MARS beamline at Synchrotron SOLEIL -3b
Mayak PA worker cohort (MWC) – 2b, 2c
MELAF – 1f, 1c
METABOHUB – 3a
MICADO'LAB Experimental Platform – 1a
Microtron laboratory – 1a
Mixed alpha and X-ray exposure facility – 1c
Nanoparticle Inhalation Facility – 1d
NASA Genelab – 3a
NASA's LSAH and LSDA repositories – 2a, 2b
NASA Space Radiation Laboratory (NSRL) – 1c
OEDIPE – 3b
PARISII – 1d
Phosphogypsum stack at Barreiro, Portugal - 1e
Portuguese Tinea Capitis Cohort – 2c, 2b
ProFI – 3a
Proton IRRADiation Facility (IRRAD) – 1c, 1f
PTB-Microbeam, ion and neutron fields – 1b
PULEX Cosmic Silence – 1a, 1c
Radiation Metrology Laboratory – 1f
Radiobiology and immunology platform (CTU-FBME) – 3a
Radiochemical and Radioactive Analysis Laboratory (INTE-UPC) – 3a
Radon Calibration Laboratory of BfS -1f
Radon exposure chamber – 1c, 1a, 1d
RENEB – 3a
RES$_3$T – 2a
Research Neutron Source Heinz Maier-Leibnitz (FRM II) – 1c
REQUITE – 2b, 2c
Russian Human Radiobiological Tissue Repository (RHRTR) – 3b
Silesian Centre for Environmental Radioactivity (SCRS-GIG) – 1a, 1c, 1d
SNAKE – 1b
STORE – 2a
Symbiose – 3b
The AGOR Facility at KVI-CART – 1c
The Analytical Platform of the PREPARE project – 3b
The BACCARAT study – 2b, 2c
The Bank of Biological Materials of SBRC – 2b
The BIANCA Code – 3b
The BRIDE platform – 2a
The Calliope facility – 1a
The CERES Platform – 3b
The EFFTRAN code – 3b
The Chernobyl Exclusion Zone – 1e
The Genomic Medicine and Bioinformatics Core Facility – 3a
The German Thorotrast Cohort Study – 2c
The "hematopoietic system" database for Mayak nuclear workers – 2a, 2b
The iGE3 Genomics Platform – 3a
The ISE cohort – 2b, 2c
The ISIBELa cohort – 2b, 2c

The MCDA Tool – 3b
The MIRCOM microbeam – 1b
The Nuclear Metrology Group (NMG) – 1f
The SCK●CEN Genomics Platform – 3a
The Severe Nuclear Accident Program (SNAP) – 3b
The Techa River Cohort (TRC) – 2c, 2b
The TRACY cohort – 2c
The Wismut Cohort and Biobank – 2c, 2b
TIFPA – 1c
UNIPI neutron irradiation facility – 1f, 1c
VIB Proteomics Core – 3a
Wildlife Transfer Database – 2a
ZATU (Zone Atelier Territoire Uranifère), France – 1e



Exposure platforms

Databases, Sample banks, Cohorts

Analytical platforms, Models, &Tools

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The numbers speak for themselves: 40 issues, 120 infrastructures, more than 20 countries and 50 institutes represented and 1000 monthly readers of AIR^2! Thank you all!

This work has also resulted in 2 additional Special Issues dedicated to infrastructures and 11 Special Issues focused on CONCERT projects or ongoing European projects related to the radiation protection field.

Finally, special thanks are also due to all the indirect contributors to AIR² and AIR²D², technicians and researchers working to maintain and expand the quality and potential of infrastructures and to make them available to the radiation protection community.

Contents

Introduction

CONCERT, the European Joint Programme for the Integration of Radiation Protection Research, is operating as an umbrella structure based on the strategic research agendas already prepared in the fields of low dose risk research (MELODI), radioecology (ALLIANCE), nuclear emergency preparedness (NERIS), dosimetry (EURADOS), medical radiation protection (EURAMED) and finally of the newly formed European platform for Social Sciences and Humanities related to ionizing radiation (SHARE). CONCERT aims at attracting and pooling national research efforts with European ones in order to make better use of public R&D resources and to tackle common European challenges in Radiation Protection more effectively by joint research efforts in key areas.

Coming to CONCERT WP6- Access to Infrastructures, its major focus is to increase the visibility of high quality infrastructures available to perform cutting-edge research in any of the disciplines related to Radiation Protection, and to facilitate access to these facilities for researchers and students in the field. The term "infrastructures" comprises so-called large infrastructures such as exposure platforms, including those for animal and plant experiments (both laboratory and field facilities), epidemiological cohorts, sample banks, databases, analytical platforms such as biological dosimetry facilities and 'omics platforms and e-infrastructures as well as models and tools. The necessity to focus on infrastructures in the Radiation Protection field has been highlighted by the HLEG (High Level Expert Group) in 2009. Since then, large EURATOM projects (e.g. DoReMi, STAR, OPERRA…) have included specific WPs and tasks dedicated to infrastructures. Surveys performed in former projects have revealed that the prevailing opinion is that most necessary infrastructures are already available although, not at the bench of each user. Indeed, besides the funding of experiments, the access to state-of-the-art infrastructures is a major bottleneck. Therefore, CONCERT WP6 started listing the infrastructures and provided a description of recommended criteria, both common ones (general information about the facility, its owner and the access rules) and technical ones, tailor-made for each infrastructure category. In order to best utilize existing resources, emphasis was put on promoting the visibility, using "mature" infrastructures to avoid unnecessary costs and duplication and aiming at sustainability.

To this end, two main tools have been developed by the WP6: the database **AIR²D²** (**A**ccess to **I**nfrastructures for **R**adiation protection **R**esearch **D**ocumented **D**atabase) and CONCERT's monthly bulletin (10 issues/year), **AIR²** (**A**ccess to **I**nfrastructures for **R**adiation protection **R**esearch). Since October 2015, AIR² serves for the dissemination of the information available on infrastructures related to Radiation Protection research and has now reached its 40th Issue with 120 infrastructures. The bulletins and the database are housed on the CONCERT website:
https://www.concert-h2020.eu/en/Concert_info/Access_Infrastructures.

AIR² consists of 5 pages: The 1st page includes the editorial of the WP6 leader (Dr Laure Sabatier, CEA) and the section "The floor to …", in which leaders of the CONCERT WPs, presidents of the European platforms MELODI, EURADOS, ALLIANCE, NERIS, EURAMED, CONCERT grantees, POMs and national contact points related to infrastructures are invited to highlight their work through the infrastructure binocular. The next three pages are dedicated to presenting infrastructures: one infrastructure from the category "Exposure platforms" (page 2), one from the category "Databases, Sample banks, Cohorts" (page 3), and one from the category "Analytical platforms, Models & Tools" (page 4). These three pages are structured in the same way, i.e. with a text featuring the infrastructure, written by its owner, two spaces for images/photographs/schemes, a photo of the author, two key references of work involving the infrastructure, and an ID card which provides key information of the infrastructure at a glance. Finally, page 5 resumes the list of infrastructures published to date, those to be featured in the next issue and a list of CONCERT courses and future events related to Radiation Protection E&T and research, together with their respective hyperlinks. It was decided to use the colours of the CONCERT logo for the bulletin, with one colour per page: "Exposure platforms"= **green**, "Databases, Sample banks, Cohorts"= **orange**, "Analytical platforms, Models & Tools"= **yellow**.

The third tool developed as instrument of visibility to facilitate the future set-up of projects in the radiation protection field is the present web-handbook. It is issued directly from the efforts made to create and to sustain AIR² and AIR²D². All the pages featuring infrastructures (pages 2, 3 and 4 of the AIR² bulletin) are assembled;

differently listing all the published infrastructures. This web-handbook includes 120 infrastructures of the 3 aforementioned categories, each of which is divided into new subcategories, e.g. Exposure Platforms are subdivided into (a) Low dose and low dose-rates, (b) Microbeams, (c) Particular radiation qualities: ions, neutrons, alpha…, (d) Internal contamination, (e) Observatory sites and (f) Metrology exposure platforms; the category "Databases, Sample banks, Cohorts" is divided into "Databases", "Sample banks" and "Cohorts" and similarly the category "Analytical platforms, Models & Tools" into "Analytical platforms" and "Models & Tools". To enrich the web-handbook, each category and subcategory has been introduced by a dedicated short text to describe the current landscape under visibility. Included in the Chapter 3, a special focus part entitled "In situ analytical techniques applied in the field" has been added.

Besides this introduction, this document comprises also a short chapter entitled "The CONCERT's Infrastructure Web-handbook", where the principal parts extracted from the web-handbook are shown: definitions, a categories and subcategories table, the three cross tables corresponding to the three categories "Exposure platforms", "Databases, Sample banks, Cohorts" and "Analytical platforms, Models & Tools" including the 11 subcategories with a first classification of the 120 infrastructures published till September 2019 also shown in the 40 issues of AIR².

A new Chapter 4 entitled "Protocols issued from harmonization procedures" has been added describing various efforts that have been made to diffuse protocols mainly focusing on biodosimetry techniques. Protocols have also been developed concerning STORE and data archiving from CONCERT's projects and from older results issued from previous radiation protection research activities.

The "Conclusions and perspectives" section of this deliverable considers the actual landscape and compares all these highlighted infrastructures to others legitimate that could and/or should be introduced. It analyses also its strengths and weaknesses, possible improvements and potential developments.

Finally, a connected (with hyperlinks) pdf file constitutes the final version of all infrastructures for the web-handbook and is provided in the annex.

This version of the web-handbook comprises:

- How to use this web-handbook
- Definitions
- A table of categories and subcategories
- Three cross tables corresponding to each chapter with hyperlinks and containing labels/tags for each infrastructure
- An index

How to use this web-handbook

The present web-handbook consists of the following parts:

- Detailed **"Definitions"**, explaining which infrastructures correspond to each category and subcategory. Namely, the terms *Exposure platform*, *Low dose and low dose rates*, *Microbeam*, *Internal contamination facility*, *Observatory site*, *Metrology exposure platforms*, *Databases*, *Sample Banks*, *Cohorts*, *Analytical platform* and *Models & Tools* are clearly defined.

- 1 **blue context table** providing an overview of the chapters to follow. Hyperlinks to all the main chapters and subchapters are provided in order to facilitate the reading.

- 1 **green content table** for the 1st Chapter, Exposure platforms, including the subcategories of (a) Low doses and low dose rates, (b) Microbeams, (c) Particular radiation qualities: ions, neutrons, alpha…, (d) Internal contamination, (e) Observatory sites and (f) Metrology exposure platforms. All the 45 infrastructures presented until September 2019 in the 40 issues of AIR^2 are attributed to their corresponding subcategories and hyperlinks that redirect the reader to the respective article are provided.

- 1 **orange content table** for the 2nd Chapter, Databases, Sample banks, Cohorts, including the subcategories of (a) Databases, (b) Sample banks, (c) Cohorts. All the 35 infrastructures presented until September 2019 in the 40 issues of AIR^2 are attributed to their corresponding subcategories and hyperlinks that redirect the reader to the respective article are provided.

- 1 **yellow content table** for the 3rd Chapter, Analytical platforms, Models & Tools including the subcategories of (a) Analytical platforms (b) Models & Tools. All the 40 infrastructures presented until September 2019 in the 40 issues of AIR^2 are attributed to their corresponding subcategories and hyperlinks that redirect the reader to the respective article are provided.

- The 3 main Chapters: **1. Exposure platforms**, **2. Databases, Sample banks, Cohorts** and **3. Analytical platforms, Models & Tools** in the form of AIR^2 individual articles. The infrastructures are presented in respect to the order of appearance of the main subcategory that they belong (see the 3 content tables).

In order to facilitate the navigation of the reader and provide more information, hyperlinks are provided throughout the web-handbook. Just click the underlined words! Enjoy reading.

Definitions

Exposure platform:
A facility where organisms, samples or instruments may be irradiated under controlled conditions in which dosimetric characteristics are well defined and measured under a quality control system. The traceability is guaranteed by a continuous chain of calibrations to the highest references in ionizing radiations, built through the International System of Units (SI) (see also BIPM website).

Low dose and low dose rates:
An ionising radiation dose of <100 mGy and a dose rate of <0.1 mGy/min averaged over 1 h (corresponding to 6 mGy/h) (UNSCEAR 2012).

Microbeam:
A small collimated beam, with micrometre or sub-micrometre dimensions. Together with integrated imaging techniques, they allow precisely localized radiation damages.

Internal contamination facility:
Facility where animals (or plants) are exposed to radiation *via* ingestion, inhalation or by wounds. Organisms are kept under controlled conditions.

Observatory site:
Natural site contaminated by radionuclides (NORM: Naturally Occurring Radioactive Materials or anthropogenic) *via* industrial activities or accidental releases.

Metrology exposure platforms:
Metrology is defined by the International Bureau of Weights and Measures (BIPM) as "the science of measurement, embracing both experimental and theoretical determinations at any level of uncertainty in any field of science and technology". They are facilities dedicated to well define and quantified radiation beams or radioactive sources to irradiate, to test and/or calibrate measurement devices aiming to ensure that the produced results and their uncertainties during research projects are confident, reliable, and traceable to SI system.

Databases:
Organised collections of data.

Sample Banks:
Collection of biological samples (e.g. humans, animals, or plant samples…) and inert samples (soils, water, …)with a relation to radiation topics (e.g. nuclear workers, irradiation during childhood with low doses, irradiation during a radiological accident…) and generally associated/connected to databases.

Cohorts:
Grouping of information and/or data about one particular population in radiation research areas (e.g. nuclear workers, irradiation during childhood with low doses, irradiation during a radiological accident…). Generally applied for epidemiological and or health studies can be linked to a sample bank.

Analytical platform:
Depending on the endpoints, dedicated analytical platform should be selected to investigate irradiated or potentially irradiated samples in order to define the received dose or to study biological alteration in the sample due to the irradiation (e.g. expression of proteins or genes, post-translational modification of proteins, activation/inactivation of regulatory and other biological pathways, DNA damage and repair ‘omics platforms).

Models & Tools:
Predictive or analytical software or processes, as well as biological model (such as animal or plant model).

CHAPTER 1
Exposure platforms

Chapter 1: Exposure platforms

Exposure platforms are facilities where organisms, samples or instruments can be exposed to ionizing radiation under controlled conditions with well-characterized dosimetry and traceability. They include laboratory facilities that are capable of carrying out *in vivo* exposure of animals and plants or *in vitro* exposures of tissues, organs or cells, as well as field facilities and observatories. Based on criteria developed within CONCERT WP6 (Deliverable 6.2), a list of infrastructures has been created to provide a database of facilities mainly located in Europe. Recognizing that facilities have a range of applications and can utilize different exposure scenarios, varying in field, beam size, radiation quality and exposure route (external and internal), the exposure platforms have been divided into different categories, covering:
Low doses and low dose rates - facilities with ionizing radiation dose of <100 mGy and dose rates of <0.1 mGy/min averaged over 1 hour (UNSCEAR 2012);
Microbeams – facilities with small collimated beams of micrometre or sub-micrometre dimensions.
Particular radiation qualities – an overview of the facilities that allow exposure to radiation of different qualities;
Internal contamination - facilities where animals or plants are exposed to radiation *via* ingestion, inhalation or by wounds;
Observatory sites - natural sites contaminated by radionuclides (NORM or anthropogenic) *via* industrial activities or accidental releases and;
Metrology exposures - facilities dedicated to well-quantified radiation beams or radioactive sources to test and/or calibrate measurement devices.

Each subcategory is described shortly in the following subchapters, which give an overview and short description of platforms described in AIR^2, either as a table or a list of relevant platforms.

(a) Low doses and low dose rates

Low dose and low dose rate facilities allow the irradiation of a range of samples from cells to whole organisms, primarily to external gamma irradiation [1]. Table 1 lists the major features of facilities described in AIR^2 issues. The list (in order of increasing dose rate) is not exhaustive, and other gamma irradiation facilities can be found in AIR^2D^2. Most of the listed facilities use a ^{137}Cs source, and are focusing on external gamma irradiation, while in some cases, other radiation types besides photons are available at the same location. For larger facilities, simultaneous irradiation to controls and a range of doses can be attained by exposing samples at different distances to the source, while other facilities use shielding of the source to vary dose ranges.

The available facilities cover a wide dose range for low dose rate scenarios, including underground facilities that can achieve very low experimental dose rates through natural radiation shielding. This makes it possible to carry out systematic investigations and comparisons of doses and dose rates, covering sub-background, background and enhanced doses. With respect to the below underground facilities, in addition to the Gran Sasso National Laboratory (LNGS) in Italy there are several other low level labs in the world presently involved in biological studies [2].

Facility (AIR^2 issue)	Location	Radiation source	Dose rate (mGy/h)	Biological samples
PULEX-COSMIC SILENCE ***(Issue 3, December 2015)*** *Facility located inside a tunnel with 1400 m rock overburden: negligible contribution by directly ionising cosmic rays and neutrons*	LNGS-INFN Assergi, Italy	Environmental radiation (mostly γ-rays) *(muon and neutron fluxes of $3*10^{-8}$ & $3.78*10^{-6}$ respectively)*	~ $2*10^{-5}$ ~ 0.5 $*10^{-5}$ *(with Fe shielding)*	Cells and small animals (*e.g. Drosophila melanogaster*)
LIBIS ***(Issue 11, October 2016)***	ISS Rome, Italy	Cs-137	$2*10^{-3}$ – $2*10^{1}$	Cells and small animals (*e.g. Drosophila melanogaster*)
MICADO'LAB ***(Issue 19, July 2017)***	IRSN Saint Paul Lez Durance, France	Cs-137	$5*10^{-3}$ - 10^{2}	Model organisms in ecotoxicology (nematode, daphnid, zebrafish, plants)
AMBIC ***(Issue 39, July 2017)***	IES Rokkasho, Aomori Japan	Cs-137	$4.2*10^{-2}$ & $8.33*10^{-1}$ 8.33 & 16.67 $4.56*10^{4}$	Rodents (mice & rats) and cells
FIGARO ***(Issue 1, October 2015)***	CERAD, NMBU Norway	Co-60	$4*10^{-1}$ - $3*10^{3}$	Cells and small animals (small rodent, fish, amphibians, invertebrates) plants, GMO*
LOW DOSE RATE FACILITY ***(Issue 16, April 2016)***	Stockholm University, Sweden	Cs-137	1 - 50 (cells) 1 - 70 (mice) *(with lead shielding)*	Cells and small animals *(4 cages, 5 mice/cage)*
SCRS-GIG ***(Issue 9, July 2016)***	Główny Instytut Górnictwa Katowice, Poland	Photons (Cs-137; X-rays) *Neutrons (Am-Be) Beta (Sr-90) Radon*	γ-rays (collimated) $1*10^{-3}$ - $1.87*10^{2}$ γ-rays (panoramic) $1.5*10^{-1}$ - 1.7 X-rays (collimated) up to $4*10^{4}$ *Neutrons (panoramic)* $3*10^{-2}$ *Beta (collimated) 50* - $3*10^{3}$ *Radon in air up to 10 kBq/m^3*	Easily adaptable to expose living organisms (cell culture and small animals, plants) to different radiation types
MICROTRON LAB ***(Issue 12, November 2016)***	Nuclear Physics Institute of the CAS Reź, Czech Rep	Electron and gamma beam, *Neutrons*	$6*10^{2}$ - $6*10^{8}$	Cells and small animals (fish, rodents etc) plants …

*GMO: Genetically modified organisms.

Table 1: List of the low dose and low dose rate facilities (in order of increasing dose rate)

(b) Microbeams

Microbeams are valuable instruments for the exploration of radiobiological response mechanisms. The strength of microbeams lies in their ability to deliver precise doses of radiation at a cellular and subcellular scale with an accuracy of one or a few micrometres. Together with integrated imaging techniques, they can enable assessment of localized radiation damages. These abilities have led to the development of a range of microbeam facilities around the world allowing the delivery of precisely defined beams of charged particles, X-rays, or electrons.

An overview of the facilities currently in operation, dedicated to biology or shared with analytical experiments, is presented in table 3 below.

Facility	Location	Particle	Energy range
RARAF (Columbia University)	New York	protons, alpha	1–5 MeV
SPICE (NIRS)	Chiba	Protons	3.4 MeV
Ion Beam Centre (University of Surrey)	Guildford	protons, alpha up to Ca	1–12 MeV
IMP	Fudan	protons, alpha	6 MeV
PTB	Braunschweig	protons, alpha	2–20 MeV
RIKEN	Wako	protons, alpha	3–4 MeV
SNAKE	Munich	protons, alpha, Li, O, Si, Cl, I	4–28 MeV 1–10.5 MeV/u
GSI	Darmstadt	protons, alpha, C to U	1.4–11.4 MeV/u
JAERI	Takasaki	A, C, Ne, Ar	12.5–17.5 MeV/u
LIPSION (University of Leipzig)	Leipzig	H, He	2.25 MeV
Microbeam (PNNL)	Richland	Electrons	Variable energy
MIRCOM	Cadarache	protons, alpha up to C	Up to 8-12 MeV

Table 2: Microbeam facilities currently in operation (updated from [3])

(c) Particular radiation qualities: ions, neutrons, alpha,…

The health risks of radiation exposure depend not only on absorbed dose, but also on radiation quality. For radiation protection purposes, radiation weighting factors are applied to account for the effects of radiation quality which is strongly related to the spatial pattern of energy deposition at the subcellular scale [3]. The existence of radiation weighting factors implies that there is a strong evidence base showing the different biological and health consequences due to different radiation qualities. However, there is a lack of mechanistic understanding of how radiation qualities affect risk, while the exact values of radiation weighting factors are also debated.

The inhomogeneous spatial pattern of energy deposition is a real feature of many environmental, medical and occupational exposures. In addition, it is gaining further importance because of the more wide-spread availability of external beam hadron therapy, the perspective of longer duration space travel (as well as space tourism) in the future, and the increasing clinical use of radionuclides [4].

Much of the information on the effects of radiation quality is obtained from studies on internal exposures, which adds an additional complexity to understanding the effects of radiation quality. In many cases, internal exposures feature three main differences compared to, for example, the radiation field that A-bomb survivors were exposed to. Besides the differences in radiation quality, dose rate and intra-organ distribution, the super-cellular distribution of energy deposition can also be very different, making it difficult to separate health effects of radiation quality from the effects of dose rate and from the effects of inhomogeneous distribution of radionuclides. Although it is possible to test the effects of radiation quality alone at the single cell level, it provides very little information on how radiation quality modulates radiation risk. On the other hand (and at the other

end of biological organization), exposure of multicellular organisms is more useful for risk assessment, but in most cases it also involves effect modifying factors other than radiation quality.

The infrastructures listed in the webhandbook under the title ”Particular radiation qualities” include photon, neutron (BIO, FRM II), light (AGOR, alpha particles irradiator, IRRAD, FAIR, HIT, TIFPA), and heavy ion (CIRIL, FAIR) sources as well as exposure to different radionuclides (Radon Exposure Chamber, GSI). Exposures to mixed fields (CERF, Mixed alpha and X-ray exposure facility) and changing dose rate (Changing dose rate exposure facility) are also available. While PULEX Cosmic-Silence (photons, cosmic rays, neutrons), SCRS-GIG (alpha-, beta-, gamma-, radon), and B3 (actinides) are listed in other chapters of the web-handbook, they are also suitable to study the effects of radiation quality. Many of these infrastructures are available for both cell culture and small animal studies. However, some others are mainly used for dosimetry purposes (CERF, FRM II, IRRAD) along with those listed under the Metrology exposure platforms (Laboratory for retrospective radon and thoron dosimetry, MELAF). The detailed description of these infrastructures can be found at the hyperlinks.

Given the challenges described above and in the Second joint roadmap for radiation protection research (CONCERT D3.7) (Challenge A and B in particular, [5]) the understanding of the effects of radiation quality requires the maintenance of a large network of research infrastructures, and strong collaboration between research groups within and outside Europe.

(d) Internal contamination

Seven facilities are registered as potential laboratories, which can manage internal contamination mainly for small animals (rodents) but also cells and plants, showing that this capability is now relatively rare. The objectives are to study the consequences of a chronic exposure to low activity concentrations of radionuclides issued for example from nuclear activities or accidents, and from the environment (Rn, NORM). The classic way of incorporation of radionuclides is through ingestion or inhalation. Associated with the internal contamination facilities, generally supporting labs are available: radiochemistry, cell culture, dissection… and of course instrumentation to measure radioactivity.

To evaluate the consequences of those uptakes/intakes of radionuclides, the chronic exposure should be quantified as doses. To obtain that information, it is the role and interest of the internal dosimetry. So, this particular link could be highlighted here with three analytical platforms also registered in this web-handbook and given in Table 3.

Internal dosimetry consists in the assessment of internal exposures by interpreting the monitoring data of incorporated radionuclides in terms of intake (Bq) and committed effective dose E(50) (mSv). Measurements of the content of internal X-ray and gamma emitters retained in the body can be obtained by *in vivo* monitoring in body-counters (activity (Bq) in total body or in an organ is obtained) and by *in vitro* bioassay measurements of excreted radionuclides in biological samples (typically activity concentrations Bqd^{-1}, BqL in urine or in faeces are obtained). The activity that is incorporated by an exposed person can also be estimated from the results of air samplers (activity concentration (Bq/m^3) in the environment) e.g. in a workplace.

The assessment of E(50) from measurement results is carried out by applying the correct and current ICRP retention and excretion models and dose coefficients, depending on the intake scenario and exposure conditions. Software tools are available for such dose assessments, developed by reference institutions in Europe e.g. PHE-UK (IMBA, Taurus), IRSN-France (MIODOSE), RPI-Ukraine (IMIE), and from outside Europe (e.g. AIDE software by Los Alamos Nat. Lab. in US, MONDAL-MONDES by NIRS in Japan). ICRP is in the process of updating biokinetic models and dose coefficients through the OIR (Occupation Intakes of Radionuclides) series of reports (Parts I-IV already available, Part V in process) in agreement with ICRP Publication 103. An electronic Annex is provided (and updated) through ICRP website as “Data Viewer” that allows the access of all the OIR relevant data needed for dose evaluations, for most common radionuclides at risk to be incorporated by workers in a workplace.

Facility (AIR² issue) Analytical Platforms Models and Tools	Location	Radiation source	Dose	Biological samples
CIEMAT Whole Body Counter Internal Dosimetry (Issue 33, December 2018)	Madrid Spain	Gamma emitters inside the body: In total body (e.g. ^{137}Cs, ^{60}Co,…) In thyroid (radioiodine e.g. ^{131}I, ^{125}I) In lungs (Actinides e.g. ^{235}U, ^{241}Am)	Measurement of activity content (Bq) of radionuclide in total body or in specific organs (interpretation of monitoring data in terms of committed effective dose E(50)	Exposed workers Exposed population
CIEMAT In vitro Internal Dosimetry Laboratories ***(Issue 38, June 2019)***	Madrid Spain	Alpha emitters in excreta samples (urine and faeces), typically U, Am, Pu Beta emitters in urine, typically ^{3}H and ^{90}Sr	Measurement of activity concentration (Bq.d^{-1}, Bq L^{-1}) in excreta samples (urine and faeces) (interpretation of monitoring data in term of committed effective dse E(50)	Exposed workers Exposed population
ŒDIPE – Nuclear Medicine ***(Issue 26, April 2018)*** https://www.irsn.fr/EN/Research/Scientific-tools/Computer-codes/Pages/OEDIPE-Personalised-dosimetric-evaluation-tool-3443.aspx	IRSN, Fontenay -aux- Roses France	Radiopharmaceuticals for diagnosis and therapy (e.g. using ^{131}I, ^{90}Y, ^{177}Lu, ^{223}Ra,…)	Dose assessment in nuclear medicine: Absorbed dose and biologically effective dose considerations	Nuclear medicine patients

Table 3: Three analytical platforms doing internal dosimetry

Recently, the European Commission has published the RP188 Report (Radiation Protection series) in which technical recommendations are given for monitoring individuals with occupational intakes of radionuclides. This internal dosimetry reference document in Europe was developed by EURADOS Working Group 7 members as a outcome of the TECHREC Project supported by EC-DGENER.
Another aspect of internal dosimetry is the patient exposure in a nuclear medicine frame, by using radiopharmaceuticals for diagnosis and therapy. An important tool for such dose assessments (OEDIPE code) is presented in the table above, developed by IRSN (France) for absorbed dose evaluation and biologically effective dose considerations.

(e) Observatory sites

The Observatory sites are radioactively (and chemically) contaminated field sites, first presented in a OECD/NEA report [6], which represent a powerful tool to integrate research activities done in different disciplines of radiation protection (radioecology, radiation biology, environmental toxicology, ecotoxicology and ecology, among others), through common studies, shared data, etc.

Presently four sites have been selected as radioecological Observatory sites by ALLIANCE, three of which have been published in the AIR² bulletin:

- Chernobyl Exclusion Zone, Ukraine (Issue 17, May 2017)
- Forest observatory site in Yamakiya, Japan (Issue 26, April 2018)
- Belgian NORM Observatory Site (Issue 27, May 2018)
- Upper Silesian coal basin, Poland (https://radioecology-exchange.org/content/upper-silesian-coal-basin).

Table 5 summarizes the major features of the three observatory sites selected by ALLIANCE published in the AIR^2 bulletin (including a link where more information can be obtained).

The Chernobyl Exclusion Zone and the Forest in Yamakiya observatory sites offer a radiation contamination gradient, in which relevant amounts of non-radioactive pollutants are almost absent.
The Belgian NORM Site and the Upper Silesian coal basin observatory sites offer a mixed radioactively-chemically contaminant situation, in which naturally occurring radionuclides (i.e. U-238 and/or Th-228, and their decay products Ra-226, Rn-222, Pb-210 and Po-210) and heavy metals (i.e. As, Cd, Pb, Zn, etc.) are present.
Observatory sites offer a unique opportunity for E&T activities. The ALLIANCE has organised in the past field courses in The Chernobyl Exclusion Zone and in the Upper Silesian coal basin (Poland).

Feature	Chernobyl Exclusion Zone	Forest in Yamakiya	Belgian NORM Site
Type of ecosystem contaminated	Terrestrial and freshwater (and urban)	Terrestrial semi-natural forest	Terrestrial - forest
Compartment of environment contaminated	All sample types	Soil, water, sediments, plants, animals	Soil, sludge, vegetation
Contamination source	Mainly: Cs-137, Sr-90, Am-241, Pu-isotopes, U-isotopes, I-129, C-14, Tc-99 (also as 'hot particles')	Radiocaesium (major source of contamination) Pu, Sr-90 are also present	Naturally occurring radionuclides present in the sludge: U-238,Ra-226, Pb-210 and Po-210
Radioactivity or dosimetric characteristics	Activity concentrations and dose rates	NA	Activity concentrations and dose rates
Total contaminated area	➢ 4,700 km^2	953 km^2 (>20 mSv·y^{-1})	Approximately 0.07 Km^2
Species exposed/ present in the site	400 species of vertebrates including: 73 mammals, 251 birds, 7 reptilians, 11 amphibians, 67 ichthyoids	Animals: earthworm, frog, newt, mouse, wild boar, etc. Plants: Japanese cedar, pine and broad-leaf trees, fern, bamboo, sasa plant	Trees, shrubs, herbs, grasses, insects, etc.
Presence of an associated contamination	No significant evidence for this	N.A.	Co-contaminants such as As, Cd, Cr, Pb and Zn
Supporting lab	Basic laboratory facilities are available in the Chernobyl Exclusion Zone	Institute of Environmental Radioactivity (IER) of Fukushima University supports sampling, pretreatment and analyses	No laboratory infrastructure available on site. SCK•CEN laboratories can be made available (subject to agreement)
Access	Require permission - achieved through a local collaborator	Permission from IER is required	Permission via SCK•CEN is required
Link	https://radioecology-exchange.org/content/chernobyl-exclusion-zone	https://radioecology-exchange.org/content/fukushima-radioecological-observatory-yamakiya	https://radioecology-exchange.org/content/belgian-norm-site

Table 4: Summary of the major features of the three Observatory sites selected by ALLIANCE published in the AIR^2 bulletin

In addition, three other contaminated sites, which could be used as observatory sites, have been published in the AIR^2 bulletin:

- IRSE Experimental Farm (Issue 35, March 2019), sited in the Semipalatinsk Test Site in Kazakhstan. Is a territory of 18,500 km^2 of steppe semi-desert environment contaminated with radionuclides (cesium, strontium, transuranium elements, tritium, among others) and heavy metals (http://irse.nnc.kz/).
- Phosphogypsum stack at Barreiro, Portugal (Issue 36, April 2019), is a territory of around 55,000 m^2 of phosphogypsum stack, contaminated with natural radionuclides (Ra-226 and Pb-210), heavy metals and rare earth elements (http://www.baiadotejo.pt/en/park/barreiro).
- ZATU (Zone Atelier Territoire Uranifère) in France (Special Issue 10, April 2020), is a watershed area of around 5 km^2, contaminated with natural radionuclides (U, Ra, Rn, Po) and heavy metals (As, Pb, …) (https://zatu.org/).

(f) Metrology exposure platforms

Metrology exposure platforms are facilities dedicated to well defined and quantified radiation beams or radioactive sources to irradiate, to test and/or calibrate measurement devices and rarely cells. These aim to ensure that the produced results and their uncertainties during research projects are confident, reliable, and traceable to SI systems. A summary of the facilities listed within the AIR[2] bulletins is provided in Table 5, which is a very weak sample among a large potential of laboratories in each European country (i.e SDOS, IRSN France – LNHB, CEA, France - , PTB, Germany – METAS, Switzerland – BEV, Austria – ENEA, Italy, CIEMAT, Spain….). As the highest level of accuracy for dosimetry measurements is associated with the best uncertainties, they give a high quality services and a guarantee through their accreditation ISO 17025. They are the most often related to EURADOS activities and connected together through the EURAMET association (network). Harmonization of protocols and methods and intercomparisons are for them essential activities to maintain the consistency of dosimetric quantities through Europe.

Name	**Location**	**Irradiation type**	**Dose rate**
Laboratory for retrospective Radon and Thoron dosimetry	Sofia University, Bulgaria	Alpha particles	^{222}Rn: 1-2000 kBq/m^3 ^{220}Rn: 2-1800 kBq/m^3
Radon Calibration Laboratory	BfS, Germany	Alpha particles	^{222}Rn: 0.5 - 100 kBq/m^3
MELAF	PTB, Germany	γ rays Electrons	0.01- 100 mGy/h
Laboratory for Dosimetry Standards (NDS)	JSI, Slovenia	γ rays X-rays	0-0.1 Gy/min
Calibration & Dosimetry Laboratory (INTE-UPC)	Polytechnic University of Catalonia, Spain	Photons γ X-rays Beta particles	γ: 1 µGy/h- 54 mGy/h X-rays: 0.1 mGy/h -10 Gy/h β: 4 mGy - 0.5 Gy/h
Radiation Metrology Laboratory (DOS)	STUK, Finland	γ rays X-rays Beta particles Neutrons	700 nGy/h - 40µGy/h
Calibration Laboratory (CALLAB)	CERN, Switzerland	γ rays X-rays Beta particles Neutrons Mixed field γ+n	0.36 - 360 µGy/h
Calibration Laboratory at KIT	KIT, Germany	γ rays Electrons Neutrons	2 µGy/h - 80 mGy/h
The Nuclear Metrology Group (NMG)	NPL, United Kingdom	Mixed field γ+n γ rays	1 µGy/h - mGy/h
Neutron irradiation facility (UNIPI-AmBe)	Pisa University, Italy	γ rays Neutrons	γ: 0.53 mSv/h n: 9.4 µSv/h
Laboratory for nuclear Calibration (LNK)	SCK•CEN, Belgium	γ rays X-rays Beta particles Neutrons	Few mSv

Table 5: The eleven metrology exposure platforms listed within AIR² issues

This proposed classification depending the irradiation type shows that two platforms are dedicated to Rn metrology, however the labs have generally a large offer of possibilities with beams and radioactive sources. Just on the front line (behind National Metrology Institutes, NMI, that establish standards) for the diffusion of the

best dosimetric quantities through calibrations. They are essential for all dosimetric measurements systems and for all exposure platforms to guarantee that all experiences and results could be comparable and compatible. Regarding the existing chain of NMI in ionizing radiation through Europe and their calibration labs, this sample of 11 platforms is very small and this first inventory is far from a complete overview of the existing potential. It is probably a sign that the best physical dosimetry is not well connected to numerous applications in the radiation protection research multidisciplinary field.

References Chapter 1

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[6] OECD/NEA. Scientific Issues and Emerging Challenges for Radiological Protection. Report of the Expert Group on the Implications of Radiological Protection Science. 2007. NEA No. 6167; OECD Publishing; 2 rue André-Pascal, 75775 Paris.

Chapter 1: Exposure platforms		
Subcategories	**Infrastructure**	**Other categories**
(a) Low doses and low dose rates	FIGARO	(d)
	PULEX-Cosmic Silence	(c)
	Silesian Centre for Environmental Radioactivity (SCRS-GIG)	(c) (d)
	LIBIS	
	Microtron Laboratory	
	Low dose rate facility at Stockholm University	
	MICADO'LAB Experimental Platform	
	LERF	
	AMBIC	
Add-on section	The Calliope facility	
(b) Microbeams	SNAKE	
	PTB-Microbeam, ion and neutron fields	
	The MIRCOM microbeam	
Add-on section	AIFIRA	
(c) Particular radiation qualities: ions, neutrons, alpha…	Radon Exposure Chamber	(a) (d)
	Biological Irradiation Facility (BIO)	(a)
	CIRIL	
	Mixed alpha and X-ray exposure facility	
	Alpha particles irradiator	
	Changing dose rate exposure facility	
	Proton IRRADiation facility (IRRAD)	(f)
	CERF	
	TIFPA	
	HIT	
	The AGOR Facility at KVI-CART	
	FAIR	
	Research Neutron Source Heinz Maier-Leibnitz (FRM II)	
Add-on section	NASA Space Radiation Laboratory (NSRL)	
(d) Internal contamination	B3, Animal Contamination Facility	(c)
	Facility radionuclides availability, transfer and migration	
	Nanoparticle Inhalation Facility	
	PARISII	
(e) Observatory sites	The Chernobyl Exclusion Zone	

Add-on section	Forest observatory site in Yamakiya Belgian NORM Observatory Site IRSE Experimental Farm Phosphogypsum stack at Barreiro, Portugal ZATU (Zone Atelier Territoire Uranifère), France	
(f) Metrology exposure platforms Add-on section	Laboratory for retrospective Radon and Thoron dosimetry Calibration Laboratory at KIT MELAF Radiation Metrology Laboratory (DOS) Laboratory for Dosimetry Standards (NDS) CALibration LABoratory(CALLAB) Radon Calibration Laboratory of BfS Calibration and Dosimetry Laboratory (INTE-UPC) The Nuclear Metrology Group (NMG) UNIPI neutron irradiation facility Laboratory for Nuclear Calibrations at SCK•CEN CIEMAT External Dosimetry Service and Retrospective Luminescence Dosimetry Lab	(c) (c) (c)

Table 6: Exposure Platforms cross table with tags for each infrastructure

CHAPTER 1 Exposure platforms

a) Low doses and low dose rates

Exposure platforms

FIGARO

Low Dose Irradiation Facility at the Centre for Environmental Radioactivity

The Norwegian University of Life Sciences (NMBU) has had a gamma irradiation facility on campus since 1952. In 2003 a facility for low-dose exposure ecotoxicological experiments was opened and used for a variety of chronic and sub-chronic exposure studies (e.g., fish, mussels, earthworms, plants). With the support of DoReMi, the facility underwent extensive upgrades in 2012 in order to meet the requirements for small rodent chronic exposure experiments. The present facility, FIGARO, at the Centre of Environmental Radioactivity (CERAD), is equipped with a climate control system (temperature, light, humidity), and is fully approved as an animal research facility, including the use of GMO rodent and other plant and animal models.

Photo: H. Sparre/NMBU

Ole Christian Lind

The capacity for small rodent irradiation depends on the dose rate and the animal cage system. FIGARO has access to both ScanClime and Innovive racks. As an example, irradiation of up to 150 mice can be carried out at 2 mGy/hr with an additional 80-160 controls, and larger numbers can be accommodated at lower dose rates. DoReMi has supported collaborative projects involving long-term irradiation of mice (up to 3 months). These projects involved the successful transport, irradiation and return of more than 1000 mice to respectively Germany and the UK.

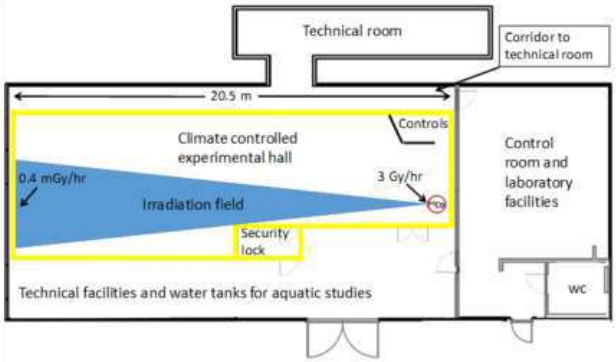

Photo: Gisle/Bjørnebye

The NMBU FIGARO gamma irradiation facility. Left: The ^{60}Co source installation located at the front of the experimental hall. Right: Outline of the facility. The ^{60}Co irradiation source (red circle) is at the front end of a climate controlled experimental hall (shown in yellow).

FIGARO is primarily designed as an external gamma irradiation facility, although it is also authorised for radionuclide internal exposure (including alpha emitters), as well as other chemical stressors (e.g., metals, organics, nanoparticles) and UV exposure. The irradiation source is 12 Ci Co-60 which provides a continuous dose rate field from 3 Gy/hr (at source) down to 400 µGy/hr (when maximally loaded) and allows simultaneous, chronic exposure of samples over the whole dose -rate field. Temperature and pH controlled flow-through systems are available for aquatic organism exposures. The climate control specifications for the experimental hall are: Temperature: 4 - 37°C (+/- 1°C) Light: ca. 50 - 300 lux with automatic dimmer (10 min) Humidity: 45 - 65% (ScanClime) Ventilation: 300 m^3/h.

CERAD continues to carry out a number of studies using other organisms, focusing on both mechanistic and ecotoxicological investigations. In addition to mice, 2014-2019 saw experiments on zebrafish, nematodes (*C. elegans*), salmon, algae, daphnia, earthworms, various plant species (*Lemna minor*, Norway spruce, Scots pine, *Arabidopsis thaliana*) and multi-species cosm-exposure.

CERAD/FIGARO is open for collaboration, and we welcome suggestions for projects with CONCERT partners.

Photo: NMBU

Irradiation of zebrafish at the NMBU FIGARO gamma irradiation facility.

The NMBU FIGARO low dose irradiation facility, Lind O. C., Oughton D. H., Salbu B. (2019), Int J Radiat Biol, 95 (1), 76–81

A framework for exposure characterization and gamma dosimetry at the NMBU FIGARO irradiation facility, Hansen E. L., Lind O. C., Oughton D. H., Salbu B. (2019), Int J Radiat Biol, 95 (1), 82-89

ID Card:

Exposure type:
External (internal possible), multiple stressors

Source:
Co-60

Dose rate:
3 Gy - 400 uGy/hr

Irradiation type:
Gamma

Irradiated organism type:
Cell cultures, animals (small rodents, fish, amphibians, invertebrates), plants. Multi-species microcosms. Approved for GMO organisms.

Address:
Centre For Environmental Radioactivity (CERAD), Norwegian University of Life Sciences, PO Box 5003, 1432 Aas, Norway

Access:
Joint research collaborations only, ongoing applications

Supporting lab:
Molecular and biochemistry analysis or sampling for biobanking, histology and microscopy analysis, plant cell culture, dissection.

Internet link:
www.nmbu.no/cerad

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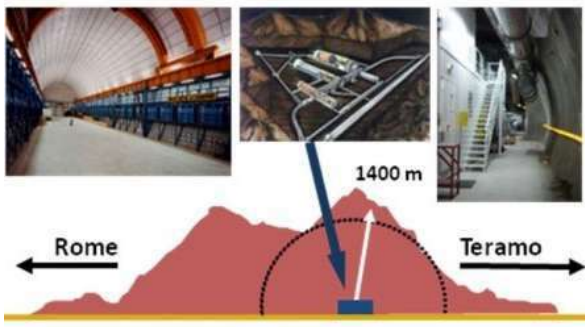
Related to:
ALLIANCE/MELODI

PULEX-COSMIC SILENCE

Extremely low radiation background facilities at INFN-LNGS

The Gran Sasso National Laboratory (LNGS) in Italy is one of the four national laboratories of the INFN (National Institute for Nuclear Physics). It is the largest underground laboratory in the world devoted to neutrino and astroparticle physics. Located between L'Aquila and Teramo, approx 120 km from Rome, the underground structures are situated on one side of the 10 km long highway tunnel which crosses the Gran Sasso massif. The underground complex consists of three huge experimental halls and bypass tunnels. The halls are equipped with all technical and safety equipment and plants necessary for the experimental activities and to ensure proper working conditions for the people involved.



Picture: modified from Eur. Phys. J. Plus (2012) 127: 37

The INFN-LNGS underground laboratory

The PULEX cell culture facility is located in one of the bypass tunnels. The facility was set up to perform in vitro experiments in extremely low radiation background in the context of a close collaboration between INFN, Istituto Superiore di Sanità (ISS) and Centro Fermi. In this environment, the natural coverage of 1400 m thick rock provides a reduction factor of one million in the cosmic ray flux, and the neutron flux is a thousand times less than on the surface. In the PULEX facility, the Radon concentration is kept at a very low level by an efficient ventilation system that pumps air from the outside. Moreover, the cell culture laboratory hosts two CO2 incubators, one of which is shielded with 5 cm of Fe to further reduce the gamma component of the radiation spectrum.

Since the pioneering work on yeasts carried out by Satta and co-workers in the late 90's, several experiments have been performed using rodent and human cell cultures grown in parallel in the PULEX facility and in external laboratories, with the aim of investigating if modulation of the radiation environment can modify the biochemistry of biological systems and their response to genotoxic agents. Interestingly, the overall results obtained using different in vitro models have shown that cells cultured in a strongly reduced radiation environment are less tolerant to radiation-induced DNA damage and less efficient in scavenging reactive oxygen species than cells grown in the external reference environments.

Photo: ISS/M. Sabatini

Antonella Tabocchini

At present, an animal house facility is under construction next to the PULEX cell culture laboratory. This new facility, named COSMIC SILENCE, will be provided with temperature and light control systems, as well as an independent ventilation system. Once it is ready, the first planned experiments will be done with Drosophila melanogaster. In the future, after authorization, it will be possible to perform experiments with mice. To this end, the facility has been designed to host a 60-cage mouse rack.

On a smaller scale, the PULEX-COSMIC SILENCE facilities nicely complement the FIGARO facility allowing radiobiological investigation in a radiation environment below the average background level. The PULEX facilities are open to collaboration, including use of other organisms, and any suggestions for projects with CONCERT partners are very welcome.

Inside and outside the PULEX cell culture facility underground the LNGS

Photo:ISS/M.A. Tabocchini

ID Card:

Exposure type:
External (extremely low radiation background)

Source:
Environmental radiation with negligible contribution by directly ionizing cosmic rays and neutrons

Dose rate:
~ 5 nGy/h (with Fe shielding)
~ 20 nGy/h (w/o shielding)

Irradiation type:
gamma (cosmic & terrestrial), alpha (radon)

Irradiated organism type:
Presently cells and small animals, e.g. insects, worms. Mice in the future, after authorization.

Address:
Laboratori Nazionali del Gran Sasso
Via G. Acitelli, 22
67100 Assergi L'Aquila, Italy

Access:
Joint research collaboration and scientific committee approval

Supporting lab:
external cell culture lab, (bio) chemistry lab

Internet link:
https://www.lngs.infn.it/en

Contact:
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Marco Balata: marco.balata@lngs.infn.it +39 0862437292

Related to:
MELODI, ALLIANCE

LOW-RADIATION ENVIRONMENT AFFECTS THE DEVELOPMENT OF PROTECTION MECHANISMS IN V79 CELLS. Fratini et al., 2015. Radiat Environ Biophys 54 (2):183-194

FRUIT FLIES PROVIDE NEW INSIGHTS IN LOW-RADIATION BACKGROUND BIOLOGY AT THE INFN UNDERGROUND GRAN SASSO NATIONAL LABORATORY (LNGS). Morciano et al., 2018. Radiat Res 190 (3):217–225

Silesian Centre for Environmental Radioactivity (SCRS-GIG)

A multipurpose irradiation facility for all types of radiation

Radiation research at the Central Mining Institute (GIG) began in the early 1970s with the discovery of enhanced natural radioactivity in coal mines. The rapid development of scientific and technical capabilities and the wider understanding of radiation protection which followed, led to the creation of the Silesian Centre for Environmental Radioactivity (SCRS-GIG); the facility moved to new premises in 2012. Furthermore, the experience gathered in complex NORM investigation allowed the SCRS-GIG team to assist the emerging Polish nuclear industry to solve problems related to environmental radioactivity.

Photo: S. Jarosławska-Sobór/GIG

Optical calibration bench for controlled exposure to gamma and X radiation using IM6/M-2 irradiator (Cs-137: source activity: 100 Ci, 1 Ci and 10 mCi) and/or XCS-320-ST/X-RAY CAL Vacuum tube (320kV)

In order to maintain the provision of high quality radiation monitoring, a complex system of irradiation facilities has been developed. A radon chamber of 17 m^3, allowing control of climatic parameters, is used for exposure to alpha radiation in the atmosphere with controlled radon concentration. As radon progeny-forming aerosols are crucial in this case, it is possible to generate and measure polydisperse/monodisperse aerosols in the air, in the size range of nm to µm, using instrumentation from TSI (USA).

Using a Gamma irradiator IM6/M-2 with Cs-137 sources (air kerma rate varies from 1.5 µGy/h to 187 mGy/h) or with an X-Ray machine of the type XCS-320-ST/X-RAY CAL (320 kV), equipped with a set of filters in order to modify the X-Ray beam according to ISO rules an object can be irradiated at different distances, ranging from 300 to 4000 mm, changeable every 1 mm. Maximal air kerma rate is ca. 40 Gy/h.

Photo: A. Jastrząb-Neigbor

Malgorzata Wysocka

Besides exposure to a straight radiation beam, two stands are used for panoramic irradiation at given distances (1m, 0.7m and 0.3m) using an IN1/P neutron irradiator with Am-241/Be source, 1 Ci activity (flux density: $6.6x10^{-5}$ $Nxs^{-1}xBq^{-1}$ for neutron energy 0.025 eV - 12 MeV; dose rate at a distance of 1m: ca. 30 uSv/h) or with an IM1/P gamma irradiator with a Cs-137 0.05 Ci source (available air kerma rate: 150 - 1700 µGy/h). As high penetrating radiation is not the only source of risk, an installation with an IB1/P beta irradiator (Sr-90, 0.05 Ci) is also in use. The radiation beam is collimated and the distance can be changed up to 1m from the source. The dose rate varies from 50 to 3100 mSv/h.

All these installations are located in an air-conditioned, shielded room in the underground part of SCRS-GIG's new headquarters, and are currently used for calibration of a wide variety of radiometric devices under different ambient conditions.

As all these activities need to be coupled with relevant measurement possibilities, a wide variety of radon and radon progeny, and dose and exposure measurement techniques has been developed and implemented. Additional support is provided by a well equiped low-background, high resolution gamma spectrometry laboratory, an alpha spectrometry laboratory or LSC laboratory with two QUANTULUS counters.

All the installations can be easily adapted, upon request, to expose living organisms to different kinds of radiation.

Radon chamber (17m^3)

Photo: B. Michalik/GIG

ID Card:

Exposure type:
Internal (inhalation), external

Sources:
Radon & radon progeny, X-ray tube, Cs-137, Am-241/Be, Sr-90

Dose rate:
Gamma (collimated beam): 0.001 – 187 mGy/h
Gamma (panoramic): 150 - 1700 µGy/h
X-ray (collimated beam): up to 40 Gy/h
Neutron (panoramic): ca 30 uSv/h
Beta (collimated beam): 50-3000 mSv/h
Radon: activity concentration in air up to ca 10 kBq/m^3

Irradiation type:
Alpha - ambient atmosphere (3D), Gamma - beam & panoramic, Neutron - panoramic, Beta- beam

Irradiated organism type:
Possible, not exposed yet : Cell cultures, animals (small rodent size), vegetation (pot size).

Address:
Główny Instytut Górnictwa
PLac Gwarków 1, 40-166 Katowice, POLAND

Access:
selection committee (bilateral/ multilateral collaboration, access frequency limited

Supporting lab:
alpha, gamma spectrometry, LSC, TLD dosimetry, X-ray & gamma secondary reference standards

Internet link:
www.radiometria.gig.eu

Contact:
M. Wysocka, +48 32 2592014, mwysocka@gig.eu
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Related to:
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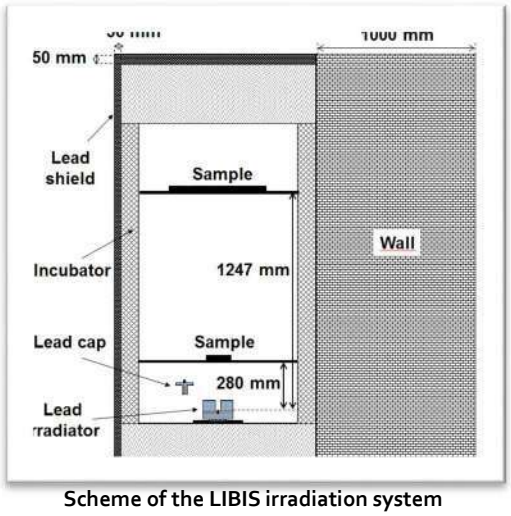
MEASUREMENTS OF LOW DOSES WITH PANASONIC DOSIMETERS. ALGORITHM AND TESTS. Skubacz K., 2015. Radiat. Meas. 75. 9-14.
APPLICATION OF THE BOHM CHAMBER FOR REFERENCE BETA DOSE MEASUREMENTS AND THE CALIBRATION OF PERSONAL DOSIMETERS. Skubacz K. 2016. Nukleonika (MS 2/15).61(1), 61-67, DOI: 10.1515/nuka-2016-0001

LIBIS

Low dose rate gamma irradiation facility for cell cultures

The Italian National Institute of Health (Istituto Superiore di Sanità, ISS) has a long- standing tradition in radiation research, dating back to the days of its foundation in the 1930's. In 1993, ISS acquired a Gammacell® 40 Exactor (Nordion International Inc.) for acute irradiation of biological samples, with gamma rays from a Cs-137 source, at a dose rate of about 1 Gy/min.

The support of DoReMi made it possible to build a facility for low dose rate and chronic gamma irradiation of cell cultures: LIBIS (**L**ow dose/dose rate gamma **I**rradiation facility for in vitro **BI**ological **S**ystems). This recently completed facility, designed and built at ISS, was explicitly conceived to accommodate a very wide range of low dose rates. It allows samples to be irradiated with Cs-137 gamma rays, from 20 mGy/h down to 2 mGy/h, and the rate can be varied in a practically continuous way within this range. The irradiations are performed inside a CO_2 cell culture incubator, allowing the physiological conditions to be maintained even in experiments lasting many weeks. The incubator is shielded by lead shields (on two sides and on the top) and by very thick brick walls (on the other two sides).



Drawer: Institute: G. Esposito/ISS

Scheme of the LIBIS irradiation system

The main components of the facility are its three lead irradiators, each of which houses a Cs-137 source; the activities of the three sources are in the ratio 1:20:500, with the activity of the strongest source being about 18 GBq. To conduct an experiment, one of the irradiators is placed at the bottom of the incubator, and the sample can be placed at a distance from the source varying from 28 cm to about 125 cm (see illustration). All experiments are performed in completely safe operating conditions, in line with radiation protection criteria. The facility has been designed to ensure that the irradiation areas for samples placed at various distances will provide a high dose rate uniformity over the sample. It is also possible to irradiate several samples at the same time with different dose rates. Accurate measurements can be performed before and during an experiment to ensure precise dosimetry.

Photo: B. Caccia/ISS

Alessandro Campa

Given the dose rates involved, the LIBIS facility allows the biological effects on cell cultures to be studied under low and very low dose rate low LET radiation. The facility offers added value through its ability to enable comparisons to be made with the effects of acute irradiations, using the Gammacell® 40, which is housed in the same room of LIBIS, and with the effects of low dose rate high LET irradiation, using the alpha irradiator available within the same department. Thus, the relevance of radiation quality in low dose rate exposures can be studied.

LIBIS is open to collaboration with all interested research groups. Suggestions and proposals for projects are most welcome. Access to the infrastructure for joint research collaboration is free of charge under written agreement. The department also offers access to cell culture, biochemistry and molecular biology laboratories.

Photo: G. Esposito/ISS

The LIBIS facility: the lead shields surrounding the incubator

ID Card:

Exposure type:
External

Source:
Cs-137

Dose rate:
2 µGy/h - 20 mGy/h

Irradiation type:
Gamma

Irradiated organism type:
Cells

Address:
Istituto Superiore di Sanità
Viale Regina Elena, 299
00161 Roma, Italy

Access:
Joint research collaboration

Supporting lab:
Cell culture, biochemistry and molecular biology labs

Internet link:
Under construction

Contact:
Alessandro Campa
campa@iss.infn.it
+39-0649902624

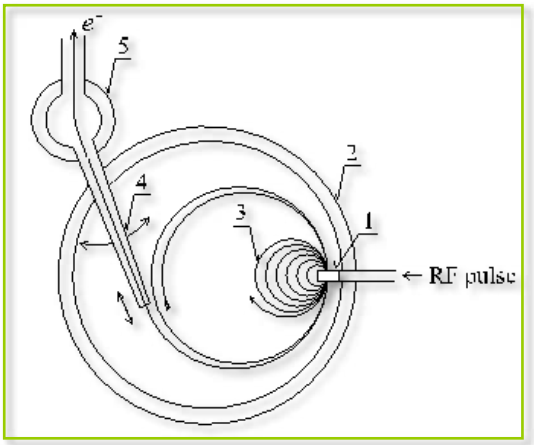
Related to:
DOREMI, MELODI, EURADOS

FACILITY FOR GAMMA IRRADIATIONS OF CULTURED CELLS AT LOW DOSE RATES: DESIGN, PHYSICAL CHARACTERISTICS AND FUNCTIONING. G. Esposito, et al. Applied Radiation and Isotopes, 115, 227-234 .

Microtron Laboratory

Microtron for biomedical, environmental and PAA procedures

The MT 25 Microtron in Prague is a cyclic electron accelerator with a Kapitza type resonator. The particles are accelerated by an RF electric field of constant frequency in a constant uniform magnetic field. In the vacuum chamber, the electrons follow circular paths with a common tangent point. The accelerating cavity, which is excited by the RF field, is located at this point. The Microtron MT 25 serves as a source of relativistic electrons (primary electron beam), secondary photon beams (bremsstrahlung) and neutrons from nuclear reactions.



The microtron scheme

Examples of accelerator applications:

Radiation resistance testing and studies in well controlled and monitored conditions are possible for electron and photon beams and for neutrons. Photon beams are frequently used for photon activation analysis of geological, biological, environmental and other samples. This method allows non-destructive determination of a large number of elements. The laboratory is equipped with a coaxial HPGe detector and multichannel analyser. The microtron laboratory was recently installed with a fully automatic pneumatic post for fast transport of samples between irradiation positions and a HPGe detector. This system expands the possibilities of photon activation analysis, as it enables determination of samples with short half-life. Some photo-nuclear reactions can produce a number of radionuclides. For example, it is possible to install a pilot apparatus for ^{123}I production. ^{124}Xe is irradiated under pressure; this radioisotope is generated for radiopharmaceutical production in an external workplace. The single workstation is equipped with a contrivance for the generation of highly homogeneous gamma and electron fields which determine with exactitude the values of dose rate (gamma fields – max. 10 Gy/min, electron fields – several hundred Gy/min, field size is 10x10cm^2). The calibrated ionisation chambers for gamma and electrons are made available (with relevant measure lines and a precision calibrated electrometer). The microtron laboratory is equipped with accurate, integral, electron current measurement from 10^9 to 10^{16} electrons/cm^2 for nuclear physics purposes.

Photo: Chvatil/NPI

David Chvatil

Radiation colouring of plastic materials, glasses and crystals produced by bremsstrahlung, and the modifications of their optical, electrical and mechanical attributes can be studied and tested. Both electron and photon beams are suitable for sterilisation. In the case of the electron beam, the sterilisation dose is reached within a few minutes (depending on the sample size). The beams with energy of up to 10 MeV are used for irradiation of biological, food and similar sample types. Crosslinking improves some properties of the polymers. Irradiation creates free radicals which will often produce various chemical reactions. The free radicals can recombine forming crosslinks. Radiation crosslinking can be performed using electron or photon beams. Electron beams are also used to produce the NV centres in nanodiamonds.

Vacuum chamber of the accelerator

Photo: Chvatil/NPI

ID Card:

Exposure type:
External

Source:
Electron accelerator Microtron MT25

Dose rate:
0.01 Gy – 10 kGy / min

Irradiation type:
Electron and gamma beam, neutron

Irradiated organism type:
Cells, animals (fish, rodents etc.) vegetal…

Address:
Nuclear Physics Institute of the CAS, p.r.i., Řež 130, 25068 Řež, Czech Republic

Access:
Free

Supporting lab:
SPF animal facility for experiments and breeding of small rodents, cell culture and immunology laboratory, microscopy

Internet link:
http://accs.ujf.cas.cz/mt25

Contact:
Anna Fiserova
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+420 724127666
David Chvatil,
chvatil@ujf.cas.cz,
+420 222323657

Related to:
MELODI, ALLIANCE

A MATHEMATICAL MODEL OF THE MT 25 MICROTRON. *Journal of Instrumentation*. (2011),Krist, P. et al: T10005/1-T10005/13. ISSN 1748-0221
INNOVATIONS AT THE MT 25 MICROTRON AIMED AT APPLICATIONS IN PHOTON ACTIVATION ANALYSIS. *Journal of Radioanalytical and Nuclear Chemistry*. (2015), Krist, P. - et al s. 183-188. ISSN 0236-5731

Exposure platforms

Low dose rate facility at Stockholm University

Low dose rate exposure facilities for cells and animals

Stockholm University was founded in 1878. Today, it has 70,000 students, 1,800 doctoral students and a staff of 5,000 who are active within science, the humanities, social sciences and law. The first Chair of Radiobiology was appointed in 1962, at a time when the work focused on genetics and plant breeding. In 1972, Radiation Biology moved to the Wallenberg Laboratory at the new campus in Frescati, and in 1985 to the Arrhenius Science Laboratories.

In the 1970's, low dose radiation facilities were constructed for field experiments, mainly for plant genetics and genotoxicology. At that time there was already a strong focus on DNA damage, and several new methods were invented to measure DNA strandbreaks as well as chromosomal damage in plants and eukaryotic cells.

In the last two decades, the interest of the research groups has gradually moved towards risk estimates of low doses and dose rates, and to exploration of new technologies such as omics to study the cellular responses to doses in the mGy range. Thus new radiation exposure facilities were needed in the department and, with the help of skilled technicians and an excellent workshop, several new facilities were constructed, as described below.

At present two radiation facilities with caesium sources are available for chronic exposure of cells in culture, with dose rates ranging from 1 mGy/h up to 50 mGy/h, and dose rate can be decreased by lead shielding to a few µGy/h (picture 1) [1, 2].

A new radiation facility for animal exposure was constructed in 2015 and is equipped with a caesium source. This facility is constructed for exposure of mice to low doses and low dose rates. The dose rates range from 1 mGy/h up to 70 mGy/h and dose rate can be decreased by lead shielding to a few µGy/h. Mice can be exposed chronically and exposure time should not exceed 4 weeks. The animals are hosted in standard cages with space for up to 5 mice per cage. The facility can accommodate four cages placed one on top of the other, providing a gradient of dose rates (picture 2). After exposure, the mice can be kept in the animal facility for extended periods depending on the choice of endpoints.

Photo: Siamak Haghdoost (SU)

Siamak Haghdoost

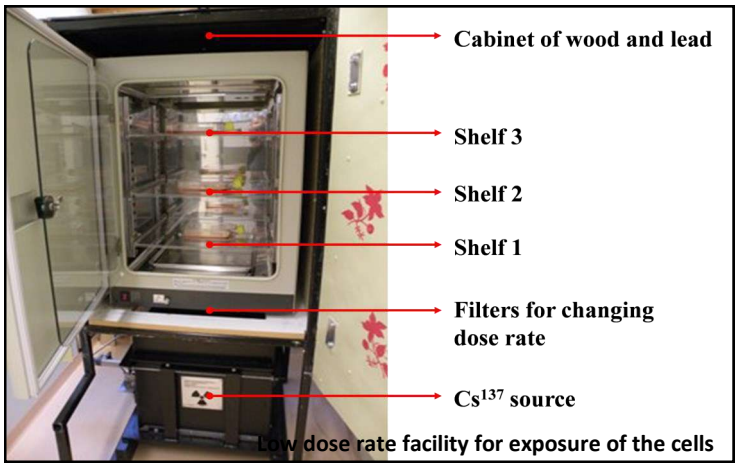

Photo: Siamak Haghdoost (SU)

Low dose rate facility for exposure of the cells

The construction has been approved by the Swedish Radiation Safety Authority (SSM) and complies with the ethical rules for animal experiments. The primary objective is to provide scientists in the field of radiation protection research with access to a low dose and dose rate exposure facility for short term exposure of mice.

The animal exposure facility is located in the Stockholm University animal facility, and includes animal care, animal exposure and post irradiation handling, for example, preparation of organs/samples at different times post irradiation. This radiation facility is primarily constructed for the study of biomarkers in response to low doses and dose rates and for studies of the mechanisms behind cellular/organ responses. It may also be used for pilot studies where only a small number of animals are needed.

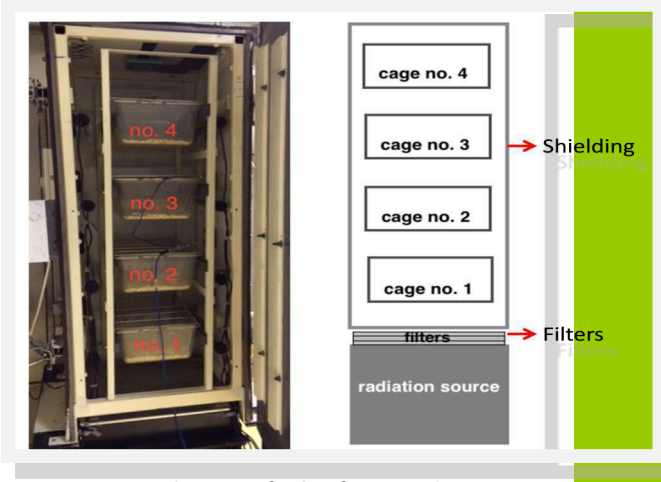

Photo: Siamak Haghdoost (SU)

Low dose rate facility for animal exposure

Stockholm University

ID Card:

Exposure type:
Low dose rates external gamma radiation

Source:
Cesium 137

Dose rates

Cell culture facility:
From 1 to 50 mGy/h with lead shielding

Animal facility:
From 1 up to 70 mGy/h with lead shielding
Housing capacity: 4 cages and 5 mice per cage

Preferred type of organism for irradiation:
Mouse

Exposure time:
Up to 4 weeks

Address:
Centre for Radiation Protection Research
Department of Molecular Bioscience, Wenner-Gren Institute
Stockholm University
10691 Stockholm
Sweden

Access:
Joint research collaboration and upon ethical approval by the ethical committee

Contact:
Siamak Haghdoost
siamak.haghdoost@su.se
tel:+46(0)8164064
Andrzej Wojcik
Andrzej.Wojcik@su.se
tel:+46(0)8161217

Related to:
MELODI, EURADOS

THE NUCLEOTIDE POOL, ATARGET FOR LOW-DOSE GAMMA-RAY-INDUCED OXIDATIVE STRESS,T. Sangsuwan, S. Haghdoost, Radiation Research, 170 (2008), 776-783
QUANTITATIVE PROTEOMIC ANALYSIS REVEALS INDUCTION OF PREMATURE SENESCENCE IN HUMAN UMBILICAL VEIN ENDOTHELIAL CELLS EXPOSED TO CHRONIC LOW-DOSE RATE GAMMA RADIATION. Yentrapalli, O. Azimzadeh, Z. Barjaktarovic, H. Sarioglu, A. Wojcik, M. Harms-Ringdahl, M.J. Atkinson, S. Haghdoost, S. Tapio, Proteomics, 13 (2013) 1096-1107

MICADO'LAB Experimental Platform

Effects on ecosystems of chronic exposure to gamma radiation

On 22 May 2017, the French Institute for Radiological Protection and Nuclear Safety (IRSN) inaugurated its new irradiation platform. MICADO'Lab (Moyen d'Irradiation Chronique pour l'Acquisition de relations DOse effet en Laboratoire) is an external gamma irradiation platform designed to study the effects on ecosystems of chronic exposure to ionising radiation.

MICADO'Lab is designed to cover the reference values for the ecosystem's protection and the band of dose rates (see graph) that could potentially result in deleterious effects in individuals from the different types of Reference Animals and Plants (Derived Consideration Reference Levels, DCRLs). The MICADO'Lab platform, set up on the Cadarache site (Bouches du Rhône, France), consists of an air-conditioned irradiation hall measuring 4 m in width, 35 m in length and 5 m in height, which is able to accommodate experimental equipment for the exposure of different biological models (cell cultures, plants and animals). Four ^{137}Cs sources are used to irradiate the organisms at dose rates ranging from 5 µGy/h to 100 mGy/h. The irradiation period of between a few hours and several weeks means that chronic exposure of one or more generations can be carried out.

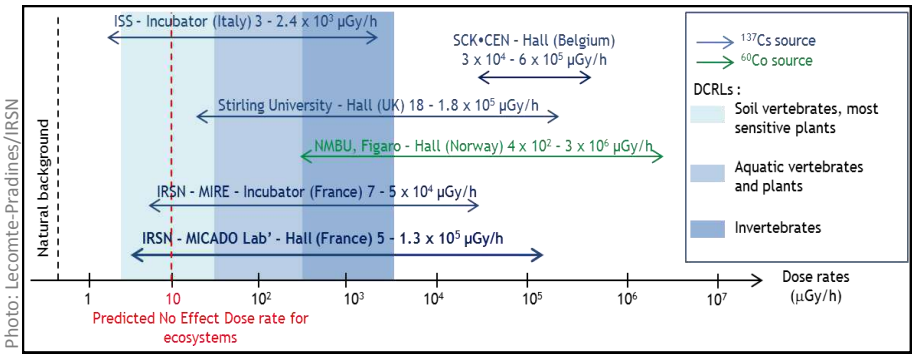

Photo: Lecomte-Pradines/IRSN

Comparison of MICADO'Lab and other European facilities
(reference value for ecosystem protection and DCRLs are indicated)

MICADO'Lab is open for scientific collaboration, especially on research conducted within the framework of European projects. This irradiation platform offers unique exposure conditions that complement the conditions offered by other European facilities, particularly in terms of the radiation energy and the range of dose rates that can be applied.

The research for which the facility is being used aims to:

- understand the mechanistic links between the effects observed at different biological levels (from molecules to individuals), in particular to identify early markers of toxicity (biomarkers),
- characterise and compare the radiosensitivity of species,
- evaluate the transgenerational effects (heritability, reversibility, adaptation),
- characterise the effects on the structure and function of ecosystems.

These studies are conducted on model organisms that are widely used in ecotoxicology (e.g. the zebrafish *Danio rerio*, the nematode *Caenorhabditis elegans* and the daphnid *Daphnia magna*) distinguished by their life cycle and radiosensitivity (see additional graph 1). Breeding facilities are available for such vertebrate and invertebrate species. Growth-chambers are also available for the research on plants and experiments with contaminated soils.

Photo: C. Adam-Guillermin/IRSN

Dr Christelle Adam

MICADO'Lab is part of a wider IRSN platform dedicated to the ECOtoxicology of Ionising Radiation & Trace Metals (ECORITME), allowed to host experiments using a wide spectrum of radionuclides. The effects of ionising radiations are measured experimentally from molecular level to individual level. Establishing the links between the different biological levels relies on the use of modelling tools (see analytical platform ECORITME page 4). The platform offers:

- analytical support consisting of physiology, cellular and molecular biology, biochemistry, microscopy and dosimetry laboratories, which are essential for characterizing radiation-induced effects at different biological levels;
- modeling support for performing and improving predictive ecological risk assessments for chronic exposure to low doses of ionising radiation and/or metals, in isolation or in mixtures (speciation-bioavailability relationships, dose-effects relationships, mixture exposure and effects models, PBPK models, individual to population extrapolation, ecological risk).

MICADO'Lab control room and view of the irradiation hall

Photo: Francesco Acerbis/IRSN

Gagnaire B et al. (2015) External gamma irradiation-induced effects in early-life stages of Danio rerio. Aquat Toxicol 169:69
Parisot F et al (2015) DNA alterations and effects on growth and reproduction in Daphnia magna during chronic exposure to gamma radiation over three successive generations. Aquat Toxicol 163: 27-36

IRSN
INSTITUT DE RADIOPROTECTION ET DE SÛRETÉ NUCLÉAIRE

ID Card:

Exposure type: External

Source: ^{137}Cs (4x111 GBq)

Dose rate: 5 µGy/h to 100 mGy/h

Irradiation type: gamma

Irradiated organism type: model organisms in ecotoxicology (nematode, daphnid, zebrafish, plants…)

Address:
IRSN/PRP-ENV/SERIS
Bât. 159 – Cadarache, B.P. 3
13115 Saint Paul Lez Durance
France

Access: Joint research collaborations only

Supporting lab: cellular biology laboratory, breeding facilities, analysis platform (physiology, cellular and molecular biology, biochemistry, microscopy), dosimetry

Internet link:
http://www.irsn.fr/FR/Larecherche/outils-scientifiques/installations-moyens-experimentaux/Micado-Lab/

Contact: micado-lab@irsn.fr

Related to: ALLIANCE, MELODI

Exposure platforms

LERF

Low-Dose Radiation Effects Research Facility at IES

The Institute for Environmental Sciences (IES) was established in Rokkasho in Aomori, Japan in 1990 to evaluate the safety and effects of radiation and radionuclides in humans and on the environment in response to public concern over the creation of the Spent Nuclear Fuel Reprocessing Plant.

Photo: IES

One of the mouse irradiation rooms in the SPF Facility

The LERF or Low-dose radiation Effects Research Facility, a specific pathogen-free (SPF) mouse facility, was first opened in March 1996 and later underwent a complete renovation in 2014 including replacement of the radiation sources. The facility is environmentally controlled and is maintained at 23±2°C with 50±10% humidity, + 6mm Aq atmospheric pressure with a 12 hour light/dark cycle, and is supplied with filtered air at a rate of 12-13 room volumes/h.

Designed as an external gamma irradiation facility for chronic or long-term exposures, it has 3 irradiation rooms equipped with sealed Cesium 137 as gamma ray sources: 74 (20 mGy/d), 3.7 (1 mGy/d) and 0.185 GBq (0.05 mGy/d, world's lowest dose rate). These dose rates were selected in an attempt to simulate the chronic low dose rate exposure conditions of nuclear power plant workers for the entire duration of their career.

Mice are exposed to radiation continuously for 22 h/day, from 12:00 to 10:00 h the following day. The remaining 2 hours from 10:00 to 12:00 h are used to conduct animal husbandry procedures (change cages, supply food and water) and monitor the health of the mice. The radiation source is located in the centre of the room and the mouse cages are placed on shelves arranged around it. Each irradiation room has a maximum capacity of 300 mice each, i.e. a total of 900 mice can be irradiated simultaneously. The LERF also has 4 animal rooms that can house a total of 3,200 mice at any one time, with total capacity at LERF for a little over 4,000 mice.

Photo: IES

Dr Ignacia Tanaka

A life span study consisting of 4,000 mice was conducted in this facility as well a serial sacrifice study on tumour latency and progression. Aside from collaborative work with local institutions and universities in Japan, two collaborations have been successfully completed with (1) ENEA using Ptch1+/- mice (DoReMi) and with (2) both HMGU and ENEA using ApoE-/- mice (PROCARDIO). These projects involved conversion of conventional mice to SPF, their transport from Europe to Japan, long-term low dose-rate irradiation, necropsy and tissue sample collection, as well as shipment of samples back to Europe for analyses.

The IES continues to carry out studies on chronic irradiation exposure at the LERF using various strains of inbred and genetically engineered mice under various conditions, focusing on late biological effects such as life span, neoplastic incidence and non-neoplastic disease, and on transgeneration and in utero exposure effects, as well as mechanistic studies. Selected biological samples from various experiments are stored and are available upon request to joint collaborators.

IES is open to new joint scientific collaborations.

Photo: IES-LERF

Low-dose radiation Effects Research Facility (LERF)

No lengthening of life span in mice continuously exposed to gamma rays at very low dose rates, Tanaka S., Tanaka I. B., Sasagawa S., Ichinohe K., Takabatake T., Matsushita S., Matsumoto T., Otsu H., Sato F. (2003), Radiat Res, 160 (3), 376-379

Cause of death and neoplasia in mice continuously exposed to very low dose rates of gamma rays, Tanaka I. B., Tanaka S., Ichinohe K., Matsushita S., Matsumoto T., Otsu H., Oghiso Y., Sato F. (2007), Radiat Res, 167 (4), 417-437

ID Card:

Exposure type:
External

Source:
Cesium 137

Dose rate:
0.05 , 1.0 and 20 mGy/day

Irradiation type:
Gamma

Irradiated organism type:
Rodents (mainly mice)

Address:
Institute for Environmental Sciences (IES)
1-7 Ienomae, Obuchi,
Rokkasho, Aomori 039-3212
Japan

Access:
Joint collaboration only

Supporting lab:
SPF Animal Facility, Microbiology and Pathology Laboratories

Internet link:
http://www.ies.or.jp/index_e.html

Contact:
Ignacia Tanaka
tanakaib@ies.or.jp
+81 175 71 1970

kanken@ies.or.jp
+81 175 71 1200

Exposure platforms

AMBIC

Advanced Molecular Bio-Sciences Research Center at the IES

In October 2004, the Institute for Environmental Sciences (IES) opened its second specific pathogen-free (SPF) animal irradiation facility, AMBIC. A third animal facility, located in the annex, is also equipped with a radiation source. It is a conventional housing facility and was completed in March 2008.

Photo: IES

Dr Ignacia Tanaka

The SPF animal rooms have a maximum capacity of 6,000 mice, whereas the conventional animal rooms have a maximum capacity of approximately 2,400 mice + 560 genetically modified mice.

Photo: IES-AMBIC

Left to right: (top) irradiation room in the SPF Facility; Gammacell irradiator, SPF and conventional facilities; (bottom) Gamma simulator; and the variable dose-rate irradiation

The AMBIC facilities are supported by several laboratories dedicated to microbiology (quarantine and SPF monitoring), genetic engineering, cellular and molecular biology, genome analysis (FACS, FISH, PCR), embryo transfer and engineering, and pathology (necropsy, histopathology, etc.).

In addition to life span studies and neoplasm incidence after long-term low-dose rate exposure, studies on tumor transplantability, changes in chromosome structure and gene mutations, changes in mRNA and protein levels, transgenerational effects, and *in utero* exposure are in progress.

As with the Low-dose radiation Effects Research Facility (LERF), AMBIC is also designed as an external gamma-radiation exposure facility with Cesium 137 sources. Its SPF facility is equipped with two irradiation rooms for chronic exposure of mice (600 mice/room max.) with two sources in each room (1480, 740, 74 and 3.76 GBq).

The SPF and conventional facilities are also equipped with Gammacell irradiators (66.6 TBq) and a Gamma simulator (1110, 110, 11 GBq) for higher dose rates and shorter exposure times of mice and cell cultures, is also installed in the SPF facility. In the conventional facility of the annex, the variable dose-rate irradiation room (max. capacity = 200 mice) is equipped with 7.4-TBq and 740-GBq Cesium 137 sources. Irradiation exposure conditions and environmental conditions are identical to those of the LERF.

Studies on the effects of environmental enrichment (e.g. igloos) and behavioral analyses are also underway in the conventional facilities. Selected biological samples from various experiments are stored and available upon request to joint collaborators.

Collaborations with other institutions include ongoing studies on alterations in mRNA and protein levels and radioprotectors.

The IES is open to new joint scientific collaborations.

Photo: IES-AMBIC

Advanced Molecular Bio-Sciences Research Center (AMBIC)

ID Card:

Exposure type:
External

Source:
Cesium 137

Dose rate:
1 and 20 mGy/day, 200 and 400 mGy/day, 0.76 Gy/min

Irradiation type:
Gamma

Irradiated organism type:
Rodents (mice and rats), cells

Address:
Institute for Environmental Sciences (IES)
2-121 Hacchazawa, Takahoko, Rokkasho, Aomori 039-3213 Japan

Access:
Joint collaborations only

Supporting lab:
SPF and Conventional Animal Facility, Microbiology, Radioisotope, Genetic Engineering, Cell and Molecular Biology, Embryo Engineering, Genome Analysis and Pathology Laboratories

Internet link:
http://www.ies.or.jp/index_e.html

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+81-175-71-1200

Pathology of serially sacrificed female B6C3F1 mice continuously exposed to very low-dose-rate gamma rays, Tanaka I. B., Komura J., Tanaka S. (2017), Radiat Res, 187 (3), 346-360

Experimental studies on the biological effects of chronic low dose-rate radiation exposure in mice: overview of the studies at the Institute for Environmental Sciences, Tanaka I. B., Tanaka S., Kohda A., Takai D., Nakamura S., Ono T., Tanaka K., Komura J. I. (2018), Int J Radiat Biol, 94 (5), 423-433

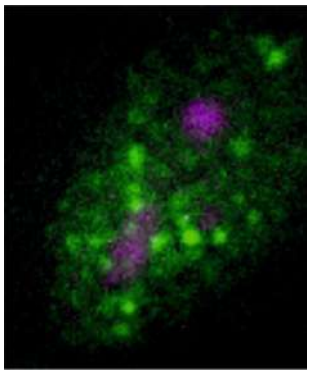
CHAPTER 1
Exposure platforms

b) Microbeams

SNAKE

Munich Ion Microbeam Irradiation Facility

The ion microprobe SNAKE (Superconducting Nanoprobe for Applied nuclear (German: Kern) physics Experiments) is installed at the 14 MV Tandem Accelerator in Garching near Munich and can be used for material analysis as well as for radiation biology research. The sub-micrometer beam size allows the targeted irradiation of single defined cells but also of more complex samples with single or counted ions, making it a suitable tool for low and high dose research. SNAKE provides protons and heavier ions with a wide energy range and thus LET range (2-2000 keV/µm), as follows:



Photo, C. Siebenwirth/UnibwM

Targeted irradiation (green cross) of a nucleolus (purple) in a cell nucleus

- protons: 4 – 28 MeV
- d, He, B, C, O: 2 – 10 MeV/nucl
- heavier ions: 0.2 – 4 MeV/nucl

By scanning the ion microbeam to irradiate one spot after another with a predefined pattern without targeting, it is possible to irradiate several cm² of cell cultures, tissues and small animals. The maximum ion range is obtained with protons, allowing irradiation of samples of up to 5 mm thick, such as 3D tissues, mouse ears or tumours. The heavier ions are more suitable for the exposure of single cell layers due to their lower range.

The live cell imaging setup with temperature control was designed for the irradiation of living cells with online monitoring. It can be used for targeted irradiation of single cells or even cellular substructures like mitochondria or nucleoli with a targeting accuracy <2 µm. Furthermore, it enables kinetic and dynamic studies of cell reactions, such as the (sequential) recruitment of several repair factors after DNA double-strand break induction.

Photo: UnibwM

Guenther Dollinger

At SNAKE, LET dependent studies using low and high LET particles can be used for intercomparison studies, in particular to investigate various endpoints of cell reactions after irradiation, especially at low doses.

Using the chopper-buncher system installed at the tandem accelerator, it is possible to form a short pulsed proton beam of about 1 ns duration at the target station of SNAKE. Using the focusing system of SNAKE, up to 20 Gy can be delivered in a single proton pulse to a beam spot of about 100 µm. This can be used to investigate ultra-high dose rate effects when irradiating from low to high doses.

The Facility offers access to the SNAKE microbeam, including all possible irradiation modes as described above, to potential users. Especially low-dose effects, also in the framework of bystander research, can be studied. In addition, for radiobiological experiments at SNAKE, access is provided to the biolab, including the cell cultures that have been developed, cell containers and irradiation and/or biological protocols. The user support staff are experienced in developing new irradiation as well as biological protocols as required, and in implementing and performing these protocols in collaboration with the external users.

SNAKE irradiation facility

Photo: T. Naeser/MAP

ID Card:

Exposure type:
External

Source:
14 MV Tandem Accelerator

Dose rate:
Single ion irradiation up to 10^9 Gy/s

Irradiation type:
Ions (protons, Li, C, …)
LET: 2-2000 keV/µm
Range < 5mm
Horizontal beam
Microbeam < 1 µm
Targeting accuracy < 2 µm

Irradiated organism type:
Cells, tissue, small animals

Address:
Maier-Leibnitz-Laboratorium (MLL),
85748 Garching, Germany

Access:
Joint research collaborations only, 3-6 beam times/yr

Supporting lab:
Cell culture

Internet link:
https://www.unibw.de/lrt2/forschung/snake

Contact:
Günther Dollinger,
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Related to:
MELODI, EURADOS, ALLIANCE

MICROIRRADIATION OF CELLS WITH ENERGETIC HEAVY IONS. Hauptner et al. 2004, Radiat Environ Biophys 42:237-245
LIVE CELL IMAGING AT THE MUNICH ION MICROBEAM SNAKE – A STATUS REPORT. Drexler et al. 2015, Radiat Oncol. 18;10:42

PTB-Microbeam, ion and neutron fields

High- and low-LET Microbeam irradiations

The PTB accelerator facility (PIAF) for ion and neutron research and the charged-particle microbeam are established user facilities which have been used for a variety of international projects and European framework programmes. The microbeam facility has been in routine operation for more than 15 years and irradiations of various cell types have been carried out for a variety of collaborative projects with outside groups. In particular, the PTB-microbeam has been part of the INTERSTANDER project for the investigation of bystander effects and the BioQuaRT project.

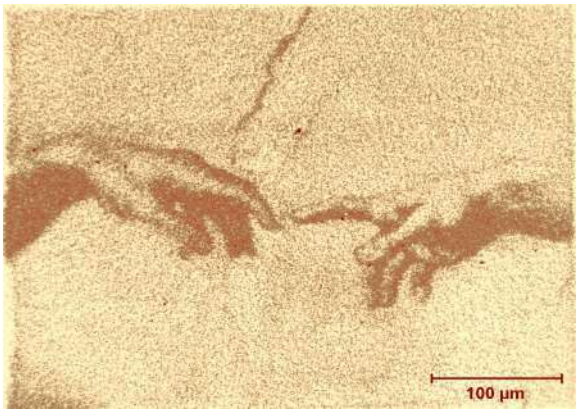

Photo: F. Langner/PTB

80 000 α-particles on a CR39 track etch detector

The microbeam provides high-LET α-particles and low-LET protons with energies of (2 to 20) MeV. This range of ions and energies allows the selection of radiation qualities with LET values between (3 to 200) keV/µm, which covers almost entirely the range from diagnostic X-rays to naturally occurring α-radiation. With the charged-particle microbeam, substructures (cell nucleus or cytoplasm) of individual cells can be targeted with a spatial resolution of about 2 µm, and irradiated with a single particle or with precisely counted multiple particles.

For the study of bystander effects, it is possible either to target selected cells or a fraction of cells in a dish and study the radiation response in directly irradiated and bystander cells. Presently, up to 50,000 cells per hour can be automatically processed including all experimental steps (imaging, cell recognition, position analysis and irradiation). The use of reference markers allows revisiting of each cell in a dish for later analysis of radiation response using a variety of endpoints. Live-cell imaging of GFP- or RFP-tagged reporter genes has been established at PTB and is available.

In addition to microbeam irradiations, broadbeam irradiations with protons or α-particles and irradiations in neutron fields with energies in the range (0.1 to 15) MeV can also be made available.

Photo: PTB

Dr Ulrich Giesen

An S1 laboratory for cell culture and microbiological preparations is available in close proximity to the microbeam facility. The local research team will carry out all the procedures at the microbeam and will support the external partners as much as possible. Access to the biology laboratory well ahead of the scheduled microbeam time can be provided for initial preparations and developments, studies of backgrounds (γ-H2AX, etc) and controls, as well as tests using an α-source. There is a guest house on site and a hotel located close to PTB.

In summary, the experimental conditions are perfectly suited to external research groups studying in detail biological effects at the level of individual cells (or co-cultures) and tissues with single particles, low doses or inhomogeneous dose distributions.

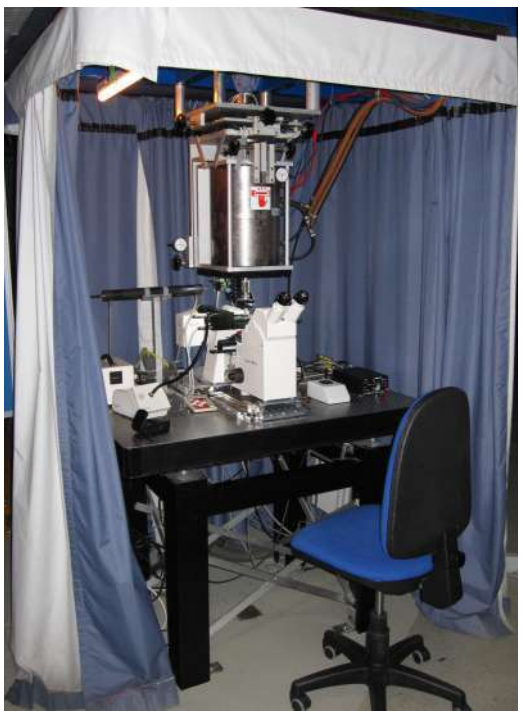

Photo: U. Giesen/PTB

Microbeam cell irradiation station

The PTB single ion microbeam for irradiation of living cells, Greif K. D., Brede H. J., Frankenberg D., Giesen U. (2004), Nucl Instrum Meth B, 217 (3), 505-512

53BP1 and MDC1 foci formation in HT-1080 cells for low- and high-LET microbeam irradiations, Mosconi M., Giesen U., Langner F., Mielke C., Dalla Rosa I., Dirks W. G. (2011), Radiat Environ Biophys, 50 (3), 345-352

ID Card:

Exposure type:
External

Source:
3 MV Tandem Accelerator
Compact Cyclotron

Dose rate:
Single ion irradiation
up to about 100 Gy/s

Irradiation type:
Proton- and alpha-microbeam from top
proton and alpha broadbeam
neutrons

Irradiated organism type:
Cells, tissue

Address:
Physikalisch-Technische Bundesanstalt (PTB)
Bundesallee 100
D-38116 Braunschweig
Germany

Access:
Joint research collaborations, up to 10 weeks per year

Supporting lab:
Cell culture lab, detector electronics lab

Internet link:
www.ptb.de/cms/en/ptb/fachabteilungen/abt6/fb-65/654-biological-radiation-effects.html

Contact:
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Involved in:
INTERSTANDER
BioQuaRT

Related to:
EURADOS
MELODI

The MIRCOM microbeam

Targeted ion irradiation of living biological samples

IRSN conducts research and development to better identify and to prevent side effects from the use of ionizing radiation for therapeutic purposes. To complete its experimental facilities dedicated to this research, IRSN has set up a platform named MIRCOM (Ion microbeam for the radiobiology of intra- and intercellular communications) enabling it to produce and use an ion microbeam.

Photo: F. Vianna-Legros/IRSN

Dr F. Vianna-Legros

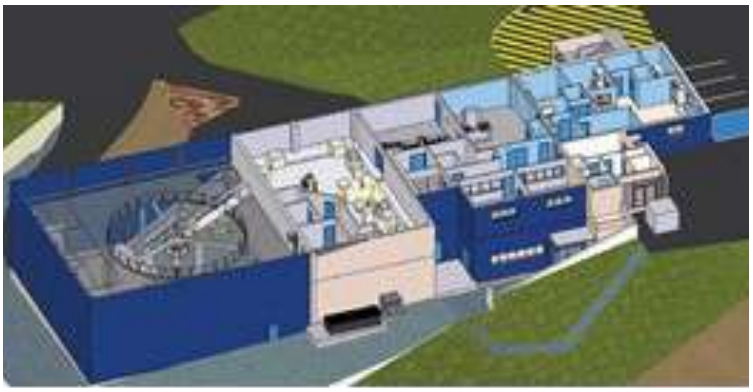


Photo: IRSN

The MIRCOM building (700 m²) houses the microbeam line and a biology laboratory.

The main purpose of the MIRCOM platform is to study radiation-induced damage not only at DNA level but also at the level of intra- and intercellular communications. Its microbeam is capable of targeting cellular and subcellular elements to the nearest micrometer in order to irradiate them with a defined number of ions of a given energy.

The effects of this irradiation can then be directly observed by time-lapse imaging. The experimental irradiation conditions produced by MIRCOM are similar to those encountered in the medical field, especially with new radiotherapy techniques, but also in fields involving exposure to high energy radiation (particle accelerators, cosmic radiation, lasers, etc.) or α-emitting radioelements.

These specific characteristics mean that MIRCOM can also be used to explore specific problems associated with exposure to both low doses and high doses.

The MIRCOM platform is integrated in the AMANDE facility, which is France's national reference for neutron metrology in monoenergetic fields since 2005. This enables MIRCOM to use AMANDE's 2 MV Tandetron™ accelerator, which produces proton and deuteron beams in the 100 keV to 4 MeV range. Two new sources complete the facility, enabling the production of ions ranging from alpha particles (up to 6 MeV) to oxygen ions (up to 10 MeV). All these particles can be used to reproduce a wide range of situations involving the irradiation of cells and their constituents (exposure to the secondary particles generated when neutrons interact, to high energy radiation with biological media, to alpha-emitting radionuclides, etc.).

The platform also has a biology laboratory equipped with two cell culture rooms for preparing biological samples. All these features give the MIRCOM platform its unique characteristics.

MIRCOM was developed jointly within a collaboration between IRSN and the Centre for Nuclear Research at Bordeaux-Gradignan (CENBG), an establishment run by CNRS/IN2P3 and the University of Bordeaux. MIRCOM is open to research teams from the national and international scientific community, in the context of radiation protection research programmes.

ID Card:

Exposure type:
Horizontal ion microbeam (protons, alpha particles, B, C, O, ...)

Source:
2 MV Tandem accelerator

Dose rate:
From single ion irradiation to a few thousand ions per second

Irradiation type:
Targeted micro-irradiation

Irradiated organism type:
Cells, small multicellular organisms

Address:
IRSN/PSE-SANTE/SDOS/LMDN
B.P. 3
13115 Saint-Paul-Lez-Durance
France

Access:
Open to collaboration, selection committee

Supporting lab:
Cell culture labs, Biochemistry lab

Internet link:
https://www.irsn.fr/EN/Research/Scientific-tools/experimental-facilities-means/

Contact:
François Vianna-Legros
LMDN@irsn.fr
+33 4 42 19 96 54

Related to:
EURADOS
MELODI

Photo: F. Acerbis/IRSN

Panoramic view of the microbeam line

As the commissioning of this facility has started at the end of 2018, there is no article of reference available yet. The first publication about the performance of the microbeam is scheduled at the end of 2019.

CHAPTER 1 Exposure platforms

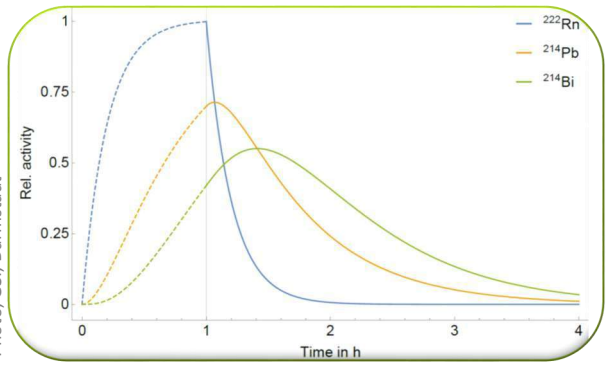
c) Particular radiation qualities: ions, neutrons, alpha...

Radon Exposure Chamber

Investigating anti-inflammatory effects of ionizing radiation

Radon is used in the treatment of chronic inflammatory diseases such as rheumatoid arthritis or ankylosing spondylitis. Patients are subjected to radon baths or inhalation therapies in radon galleries. Within the GREWIS project, eight scientific groups at GSI, TU Darmstadt and the Universities of Frankfurt and Erlangen are currently investigating the underlying physical and biochemical mechanisms and the genetic effects potentially linked to low dose radon exposure.

At GSI, a radon chamber was constructed to mimick stable radon gallery conditions and up to 15 times higher radon concentrations. The complete chamber is positioned in a radiologically controlled area. In adjacent biological laboratories, experiments can be performed with cell cultures and small animals such as mice. The exposure chamber has a volume of 50 litres allowing the exposure of up to 15 mice or 24 petri dishes (diameter: 5.5 cm). During experiments, the samples are exposed to radon-222 and its short lived daughters. The gas accumulates in a radium-226 source and is flushed into the experiment chamber. By varying the accumulation time, it is possible to adjust the radon concentration. The dose depends on the activity-concentration and the exposure time and is usually in the µGy range. During the experiments, the system operates as a closed circuit. Before removing the samples from the chamber, it is flushed with air to dilute and wash out the radon, which is collected in an activated coal filter.



Photo, GSI, Darmstadt

Relative activity of the primary Rn-222 and the daughter nuclei Pb-214 and Bi-214 over time taking radioactive decay and diffusion into account

The chamber is mounted in a heated water bath with an integrated thermostat, which enables the temperature to be controlled with high accuracy and stability. In addition, the relative humidity is controlled using a carrier gas mixed with vaporized sterile water to avoid biological contamination. For cell culture experiments, additional CO_2 regulation can be used which is deactivated for animal experiments. A summary of the different parameters and their limiting values is illustrated in the table below.

Photo: G. Otto/GSI, Darmstadt

A. Maier, G. Kraft, C. Fournier

After an intense test phase, the radon chamber was used to expose mice in therapy-like conditions, and biological tissue up to the highest possible concentration. In the mice experiments, the local exposure of radon was detected using a marker for DNA damage (double strand breaks) in various tissues. Tissue samples such as fat, bone and tendon from commercially available pork meat were used for the first measurements. These revealed that primary radon diffuses out of the tissue within a few minutes after exposure and that the residual radioactivity originates from the daughter nuclei. The amount of the primary radon in the tissue sample could be calculated from the measurement of the gamma activity of lead and bismuth using a sensitive intrinsic Ge detector. A new mobile detector system has been established that will enable in situ measurements to be performed at the radon therapy locations.

Parameter	Range
Activity concentration	0-620 kBq/m³
Temperature	20-37°C
Relative humidity	0-100%
CO_2-concentration	0-20% (only during cell experiments)

Radon exposure chamber

Photo: E. Thoennes/GSI, Darmstadt

ID Card:

Exposure type:
External (cell culture)
External/Internal (mice)

Source:
Radon-222

Dose rate:
To be determined according to the radon activity concentration, the biological half-life and the duration of the exposure

Irradiation type:
Alpha (5.5 MeV, 6.0 MeV, 7.7 MeV)

Irradiated organism type:
Cells, animals (e.g. mice)

Address:
GSI Helmholtzcenter for Heavy Ion Research, Planckstraße 1, 64291 Darmstadt, Germany

Access:
Registration for cell experiments; animal experiments need to be licensed by local authorities

Supporting lab:
Biochemistry lab, cell culture lab, microscopy, FACS

Internet link:
www.gsi.de/en/work/research/biophysics.htm

Contact:
Claudia Fournier, c.fournier@gsi.de, +49 6159 71 2106
Andreas Maier, a.maier@gsi.de, +49 6159 71 2585

Related to:
MELODI, EURADOS, ALLIANCE

EXPERIMENTAL SETUP FOR RADON EXPOSURE AND FIRST DIFFUSION STUDIES USING GAMMA SPECTROSCOPY. A. Maier et al., Nucl. Instr. Meth. Phys. B 2015, 326: 187-193

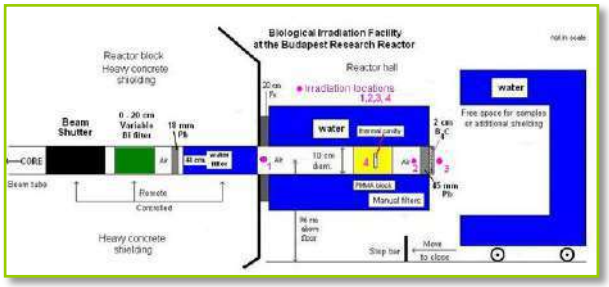
RADON EXPOSURE SETUP FOR CELLS AND SMALL ANIMALS. A. Maier et al. GSI Scientific Report 2013, p. 247

BIOLOGICAL IRRADIATION FACILITY (BIO)

Providing a reliable platform for biological irradiation studies

The Biological Irradiation Facility operates within the Budapest Neutron Centre (BNC) to provide a reliable platform for biological irradiation studies. The physical properties of the facility are described below.

The channel lock consists of 3 segments made of steel and heavy concrete and turnable around an eccentric axis to open and close the channel. There is a remotely controlled internal filter holder, at a distance of 262 cm from the core, which has six windows with the following characteristics: four Bi disks of 5, 10, 15 and 20 cm, one Pb disk of 20 cm thickness, and the 6th window is an open hole. At the orifice of the beam tube, two cylindrical tanks constructed from alumina serve respectively as a water shutter and as its emergency water storage. The water can be pumped up from and released into a larger buffer tank located outside the reactor shielding block using pressurised air. The construction materials inside the beam tube work as internal, non-removable filters with total thickness of 18 mm Pb and 15 mm Al.



Source: www.bnc.hu

Figure 1: Schematic view of the Biological Irradiation Facility

The irradiation cavity is situated outside the shielding block of the reactor at a distance of 1400 mm, thus its surface-to-reactor core distance is 3100 mm including the exchangeable core window (65 mm), made either of beryllium (serving as the fast neutron reflector also) or aluminium. The use of the aluminium window results in a hard neutron spectrum. Between the shielding surface of the reactor and the cavity, there is a borated water shielded collimator with a useful diameter of 10 cm. It is possible to use this collimator as a holder for external filters of about 800 mm length. At present, filters made of plexiglass, polyethylene, iron, aluminium and lead are available to decrease the gamma and neutron intensity or to modify the neutron spectrum and the neutron-to-gamma ratio. There are two changeable filter disks of boron-carbide which work as thermal and epithermal absorbers. The collimator is movable on a rail. The samples to be irradiated can be rotated to achieve a uniform, homogeneous irradiation. Cadmium or boron-carbide filters are used, if required, for decreasing the thermal neutron contribution.

Balázs Zábori

Three levels of the dosimetry system were developed: real time, active beam monitors; passive activation, track-etched and TL detectors, and computer codes for spectrum and dose calculations. Each exposure is individually planned and continuously monitored during the procedure. Some typical dose and flux values are presented in Table 1 and a schematic view of the system is presented in Figure 1.

The irradiation facility is suitable for studying the effects of the neutron and gamma radiation and high dose rate on seeds, cells, electronic devices, etc.

Quantity	Energy range	Min	Max
Neutron dose rate (mGy/s)	E > 0.5 eV	0.023	14
Gamma dose rate (μGy/s)	-	1.5	2570
Fast neutron flux ($cm^{-2}s^{-1}$)	E > 100 keV	2×10E+6	2×10E+9
Intermediate neutron flux ($cm^{-2}s^{-1}$)	100 keV > E > 0.5 eV	8×10E+3	2×10E+6
Thermal neutron flux ($cm^{-2}s^{-1}$)	E < 0.5 eV	5×10E+4	3×10E+8

Table 1:Presently existing minimum and maximum dose and flux values.

The hall of the research reactor

Source: www.bnc.hu

BNC Budapest Neutron Centre

ID Card:

Exposure type:
External

Source:
Research reactor

Neutron dose rate:
0.023 – 14 mGy/s

Gamma dose rate:
1.5 – 2570 μGy/s

Irradiation type:
Neutron, gamma

Possible targets:
Seeds, cells, small animals, electronic devices etc.

Address:
H-1121, Budapest, Konkoly-Thege M. út 29-33.
Hungary

Access:
Joint ongoing research collaboration or made available with charge for access costs

Supporting lab:
Radiation protection laboratories, cell culture lab in the near future

Internet link:
http://www.bnc.hu/?q=node/8

Contact:
Balázs Zábori,
zabori.balazs@energia.mta.hu

Related to:
ALLIANCE, EURADOS, MELODI

REALISTIC NEUTRON SPECTRA FOR RADIATION PROTECTION AND OTHER APPLICATIONS AT AERI, BUDAPEST. Pálfalvi J.K., et al. 2002. Nucl. Instrum. Methods A 476, 452-456.
RADIATION DAMAGE IN VIDEO DIAGNOSTIC DEVICES FOR WENDELSTEIN 7-X. Náfrádi, et al. 2008. 4 p. (Europhysics conference abstracts; Vol 32D P 5.079.)

Exposure platforms

CIRIL

Centre for Interdisciplinary Research with Heavy Ions

The heavy ions accelerated at the GANIL facility (Caen, France) interest not only nuclear, atomic or solid state physics but are also a valuable tool for various studies in radiobiology. The GANIL accelerator can provide various beams, from carbon to uranium, at maximum energies ranging from 95 MeV/A for light ions down to 24 MeV/A for uranium. GANIL cyclotrons supply a wide range of energy, which can be extended further by beam degraders. For the last 20 years, the CIMAP laboratory has managed the CIRIL platform lab user facility for Interdisciplinary research at GANIL, which was reinforced 15 years ago by the radiation-biology laboratory LARIA. The biology platform operated by LARIA includes a comprehensive tissue culture room, a molecular biology laboratory and a proteomics laboratory, allowing hosted teams to perform various canonical assays in the radiation biology field. Furthermore, the platform can be adapted for special requirements. The automatic biological sample holder designed at CIMAP can be used with 12.5 and 25 cm^2 flasks, tubes (0.5 ; 1.5 ; 2 and 15 ml), lab-tek™ chamber slide, 8 cm^2 culture dishes and 96-well plates (36 wells irradiated). Fields of interest for platform users are either radiation protection of space travelers (healthy tissues) or cancer treatment (tumours and surrounding healthy tissues). The CIRIL staff consists of the scientific coordinators, the technical coordinators of the four beam lines devoted to interdisciplinary research, the CIMAP technical staff, the physicists of AMA and MADIR, and the radiation-biologists of the LARIA groups who serve as local contacts or beamline scientists for external users.

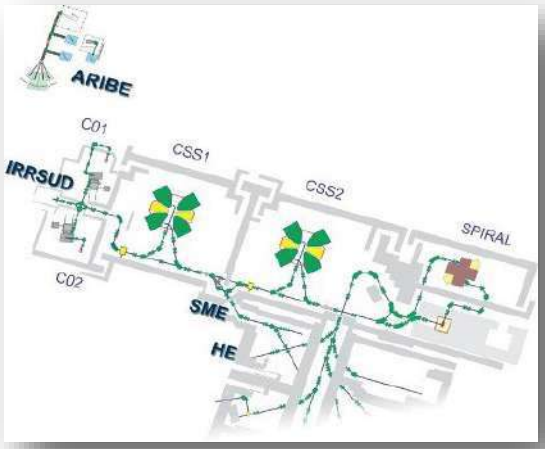


Photo: GANIL

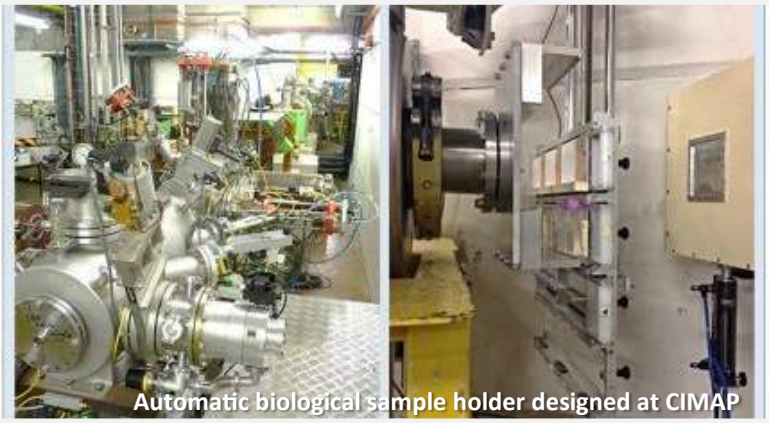
The 4 beamlines for the interdisciplinary researches corresponding to 4 exits at different locations on the ion accelator. ARIBE is located outside the GANIL INB, whereas IRRSUD, SME and HE are inside the INB on the GANIL facility.

Photo: F. Chevalier, LARIA-IRCM

F. Durantel - Y. Saintigny

Most biology ion exposures are currently performed in the D1 experimental area through the high energy (HE) beam line IRABAT and soon through the medium energy (SME) beam line IRASME. Thanks to the CIMAP expertise in ion irradiation, specific on-line instrumentation has been developed, such as the multi-sample irradiation holder (remotely controlled), beam control software and low dose on-line dosimetry. Most importantly, for each experiment, a team of physicists participates in the beam tuning and dosimetry. This activity has been the initial step to larger local projects linked to the development of hadron-therapy in France (Archade). Most irradiation for biological experiments is done at low dose/fluence (<10 Gy, 10^5-10^7 particles/cm^2). Moreover, studies are focused on ion distribution in adherent cells or 3D models. Providing accurate dosimetry is thus a crucial point for these kinds of experiments.

All the interdisciplinary experiments performed at GANIL have to be evaluated by an international and independent scientific committee (iPAC), even those proposed by CIMAP researchers. Each year, more than 25 UT (25 x 8 hours) of beam time are allocated to the radiation-biology programme by iPAC.



Automatic biological sample holder designed at CIMAP

Photo: F. Chevalier, LARIA-IRCM

ID Card:

Exposure type:
External exposition

Source:
Cyclotrons

Dose rate:
0.5 to 5 Gy/min

Irradiation type:
Accelerated ions beam (^{12}C to ^{206}Pb). Horizontal

Irradiated organism type:
Cells (2D and 3D models)

Address:
GANIL – CIMAP, Bd Henri Becquerel, 14070 Caen, France

Access:
Selection committee (iPAC)

Supporting lab:
Radiation biology platform with cell culture lab, biomolecular and biochemistry lab.

Internet link:
http://cimap.ensicaen.fr/spip.php?rubrique138

Contact:
Florent Durantel, durantel@ganil.fr; ciril@ganil.fr

Yannick Saintigny, saintigny@ganil.fr

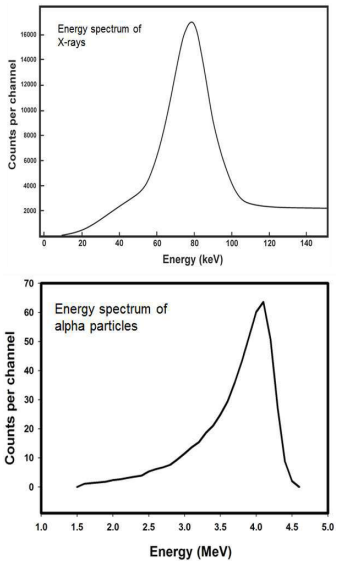
Related to:
MELODI, ALLIANCE, EURADOS

DOSIMETRY FOR RADIOBIOLOGY EXPERIMENTS AT GANIL. Durantel et al. NIM A. 2016.
ACTIVATION OF THE NUCLEAR FACTOR KB PATHWAY BY HEAVY ION BEAMS OF DIFFERENT LINEAR ENERGY TRANSFER. Hellweg et al. Int. J. Radiat. Biol., vol. 87, no. 9, pp. 954–963, Sep. 2011.

Mixed alpha and X-ray exposure facility

Simultaneous exposure of cells to high and low LET radiation

People are often simultaneously exposed to a mixed field of low and high linear energy transfer (LET) radiation. The most common scenario occurs in areas with high natural background radiation, where both the levels of gamma radiation and indoor radon are elevated. Another situation occurs during aeroplane and space flights where cosmic high LET radiation interacts with shielding material to produce gamma radiation. Finally, radiotherapy patients treated with intensity-modulated radiation therapy, fast neutron therapy and boron neutron capture therapy are exposed to mixed beams of neutrons and photons.



An important question related to the health effects of exposure to mixed beams is whether the risk can be calculated by simply adding the effects of the low and high LET dose components or whether the different radiations act in a synergistic manner. The available experimental data do not allow a definite conclusion to be drawn. Indeed, both additivity and synergism have been reported. The reason for this discrepancy is not understood but one factor could be that cells are exposed sequentially, rather than simultaneously, to the two types of radiation. Simultaneous irradiation is the desirable scenario but requires a dedicated irradiation facility. At Stockholm University, a facility has been constructed where cells can be simultaneously exposed to 241Am alpha particles and X-rays at 37 °C.

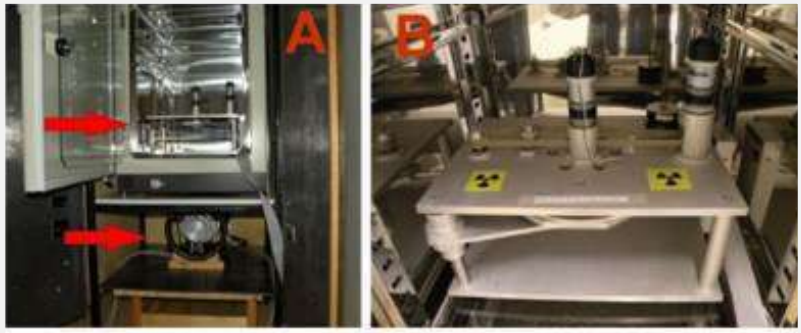
Photo: A. Wojcik/SU

Andrzej Wojcik

The facility consists of an alpha irradiator, custom-constructed in the Institute of Nuclear Chemistry and Technology, Warsaw, Poland, an X-ray tube (YXLON SMART 200, Yxlon International, Hamburg, Germany) and a 164 l cell incubator. The alpha irradiator is positioned inside and the X-ray tube under the incubator. The whole setup is placed in a lead container so that it can be safely operated in a laboratory room.

The source of alpha radiation is 241Am (Eckert and Ziegler, Berlin, Germany) with a total activity of 50 MBq. The source is attached to a steel disc that in turn is glued to a circular turn-table, with the active side (ca 15 cm in diameter) facing downwards. Below the source is an aluminium shelf on which cells on polyamide discs can be positioned for exposure and covered by a Mylar foil. The shelf can be moved vertically by a remote-controlled step-engine. The X-ray tube is operated at 190 kV, 4.0 mA without any additional filtering.

The facility works as intended, allowing exposure of cells to alpha particles, X-rays and a combination of both in a temperature-controlled environment. It allows to further characterise the response of cells, both adherent and in suspension, to mixed beams of high and low LET, thus providing the opportunity to generate much needed data on the effect of mixed beams of ionizing radiation.



A: Incubator with the alpha irradiator (top arrow) and the X-ray tube underneath (bottom arrow). B: Close-up picture of the alpha irradiator

Photo: A. Wojcik/SU

ID Card:

Exposure type:
External

Source:
Am-241, X-ray machine

Dose rate:
Alpha: 0.26 Gy per minute
X-rays: 0.06 Gy per minute

Irradiation type:
Alphas and photons, vertical beams

Irradiated organism type:
Adherent cells

Address:
Stockholm university

Access:
Free, decision by source owner

Supporting lab:
Biomolecular and cell culture lab

Contact:
Andrzej Wojcik
andrzej.wojcik@su.se
tel: 0046762122744

Related to:
MELODI, EURADOS

CHARACTERISATION OF A SETUP FOR MIXED BEAM EXPOSURES OF CELLS TO 241AM ALPHA PARTICLES AND X-RAYS. Staaf E, et al. Radiat Prot Dosimetry. 2012 Sep;151(3):570-9.

COMPLEX ABERRATIONS IN LYMPHOCYTES EXPOSED TO MIXED BEAMS OF 241AM ALPHA PARTICLES AND X-RAYS. Staaf E, et al. Mutation Research 756: 95-100, 2013.

Alpha particles irradiator

Irradiator for studies with cultured cells at low dose rate

The alpha-particle irradiator was designed and constructed at the Istituto Superiore di Sanità (ISS) in Rome, for the exposure of cultured cells in physiological conditions, to dose rates ranging from a hundred of microGy/h to few tens of Gy/h. It consists of a stainless steel cylindrical chamber, 240 mm in diameter and 197 mm high, that can be equipped alternatively with Cm-244 or Am-241 sources of different activities. The bottom and top of the cylinder are closed by flanges of the same stainless steel. The chamber, flushed with helium gas at a pressure kept slightly above the external pressure, is inserted into a cell culture incubator where temperature and CO2 concentration are strictly controlled. The top flange has a hole where a specially designed petri dish 56 mm in diameter, with a thin Mylar^{R} bottom, can be inserted to irradiate the cells growing as a monolayer on the Mylar^{R} foil. The residual range of alpha particles at the cell entrance is enough to irradiate the cells in a nearly track-segment mode.

Spectrometric and dosimetric characterisation of the irradiator was carried out by means of an ion-implanted silicon charged-particle detector, CR39 detectors, and Monte Carlo simulations. For both sources, the uniformity of the alpha particles dose on the sample was better than ±7 %; this uniformity is obtained by an appropriate compromise between the source-to-sample distance and the sample area. The values of the LET incident on the cell sample can be varied in the range (90 – 130) keV/micron approximately. The dose rate can be varied by changing the source-to sample distance or by placing a collimator in proximity of the source.

The facility is especially suitable for bystander experiments. Adaptors have been designed in order to reproduce the geometry of commercial cell culture companion plates. A co-culture system can be used to investigate effects induced by factors released into the culture medium from directly targeted cells on cells, growing on inserts, placed at a distance that is well beyond the range of the alpha particles. Partial irradiation of the sample can also be performed by shielding part of the irradiation dishes. For both the Cm-244 and Am-241 sources, the photon dose to directly irradiated and bystander cells is negligible.

This alpha irradiator facility represents a useful resource to study a variety of biological effects induced by low dose rate alpha particles. These studies can provide data of interest for radiation protection and therapy due to the role of alpha particles in background radiation exposure (which is largely due to inhalation of radon and its progeny) and in nuclear medicine therapies with alpha emitters. The facility is open for collaboration, and any suggestions for projects with CONCERT partners are very welcome.

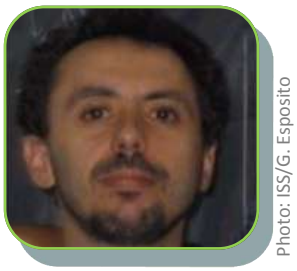


Photo: ISS/G. Esposito

Dr Giuseppe Esposito

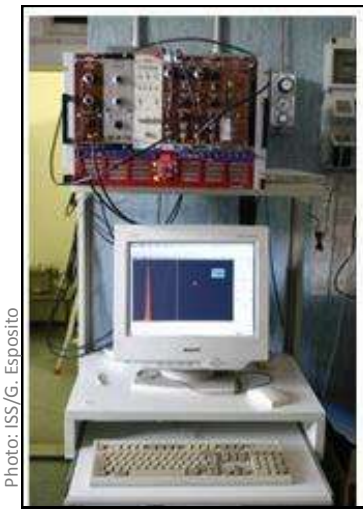
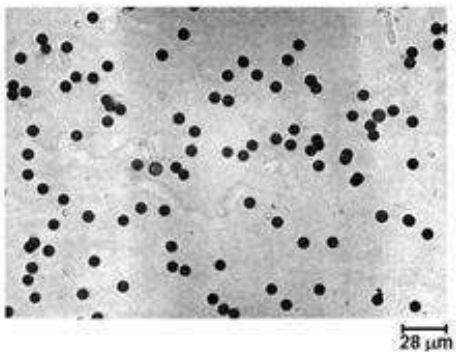


Photo: ISS/G. Esposito

← **Electronic chain implemented by (NIM)-modules for the energy spectrum measurement**



↑ **Etched tracks in a CR39 detector**

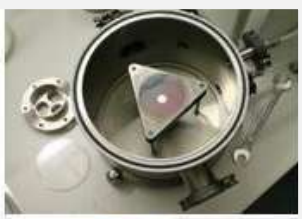


Photo: ISS/G. Esposito

Alpha particles irradiator at the Istituto Superiore di Sanità

Esposito G. et al., 2006, A ^{244}Cm Irradiator for protracted exposure of culture mammalian cells with alpha particles, Health Physics, 90, p66-73

Esposito G. et al., 2009, An alpha particle irradiator for biological research and its implementation for bystander effect studies, Radiation Research, 172, p632-642

ID Card:

Exposure type:
External

Source:
Am 241 or Cm 244

Dose rate:
~130 µGy/h to 20 Gy/h

Irradiation type:
Alpha particles

Irradiated organism type:
Cells

Address:
Istituto Superiore di Sanità
Viale Regina Elena, 299
00161 Roma, Italy

Access:
joint research collaboration

Supporting lab:
Cell culture, biochemistry and molecular biology labs

Internet link:
Under construction

Contact:
Giuseppe Esposito,
giuseppe.esposito@iss.infn.it
+39 0649902006
Maria Antonella Tabocchini,
antonella.tabocchini@iss.it
+39 0649903020

Related to:
MELODI, EURADOS

Changing dose rate exposure facility

Exposure of cells to continuously changing photon dose rate

Exposure scenarios where the dose rate is continually changing are very common. A good example is aircraft flight where the dose rate of cosmic radiation can change 16-fold during take-off and landing. Moreover, there are many accidental exposure scenarios where either the sources or the exposed subjects are in motion with respect to one another. Despite the fact that many exposures involve changing dose rates, the vast majority of research studying the effects of ionising radiation is performed exposing samples at constant dose rates. It is possible that the technical limits of the irradiation equipment used may prevent other types of exposure scenarios. However, effects from such exposures may be highly relevant for the assessment of radiation risk. Thus, it is surprising that research on the biological effects of changing dose rates has, until recently, been neglected.

Photo: Andrzej Wojcik (SU)

The facility inside an incubator

The presistaltic pump is not visible. The X-ray tube is positioned below the incubator and the whole setup is enclosed in a lead cabinet for safe use

To study the effects of changing dose rates, we have constructed a facility where three samples can be simultaneously irradiated with X-rays either at an increasing, a decreasing, or a constant dose rate. The facility fits inside a 37°C incubator that can be positioned above an X-ray tube or a gamma source. Cells in tubes, flasks or Petri dishes can be simultaneously exposed to an increasing, a decreasing and a constant dose rate in the range of 2.2 to 37 mGy per minute.

The facility is composed of three identical Plexiglas tanks, separated by 4 mm lead plates to absorb scattered radiation. Tanks 1 and 2 are interconnected by a silicone tube via a peristaltic pump. Cell samples can be positioned on top of the tanks. The facility fits inside a 164 l cell incubator modified so that there are no wires or electronic components in its bottom plate. An X-ray tube is placed under the incubator and the distance from the X-ray source to the bottom of the facility is ~ 30 cm. The beam angle, as given by the manufacturer, is 40º x 55º.

Photo: Andrzej Wojcik (SU)

Andrzej Wojcik

During exposure, the pump transfers the shielding medium, an aqueous solution of barium chloride, from one tank (increasing dose-rate, IDR) into the other (decreasing dose-rate, DDR), resulting in an exponential, 14-fold dose-rate change during the exposure. Tank 3 (average dose-rate, ADR) contains a volume of barium chloride resulting in the same dose-rate on top of the tank as the average dose-rate on top of tanks 1 and 2. The exposure is monitored with an ionisation chamber positioned on the tank that is acting as the IDR tank, and terminated when the starting conditions have been reversed on top of tanks 1 and 2. Consequently, the same total dose will have been delivered on top of all three tanks when the exposure is terminated.

The facility makes it possible to characterise the cellular response to changing dose rates. The design and low building cost of the device permit users to customise and build a device to suit their particular needs, encouraging other research groups to contribute to the understanding of the effects of changing dose rates.

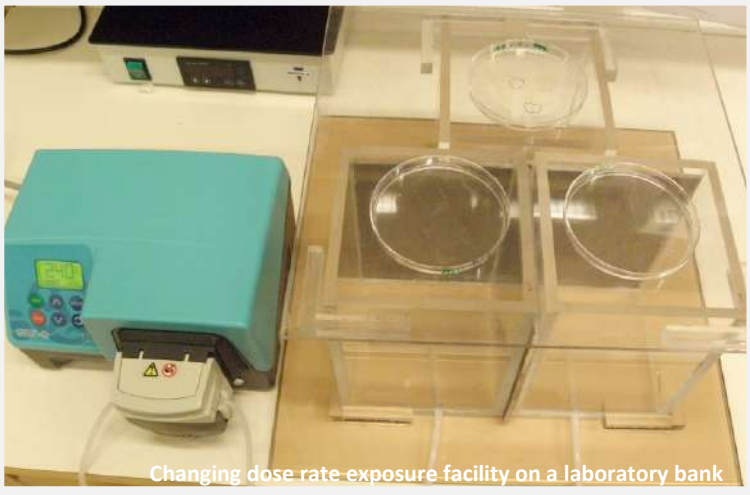


Photo: Andrzej Wojcik (SU)

Changing dose rate exposure facility on a laboratory bank

Petri dishes are placed on top of tanks between which a barium chloride solution is pumbed with the help of a peristaltic pump (green). A third tank (visible behind the two front tanks) is permanently filled with a volume of barium chloride that yields the average dose rate. Consequently, cells on all three tanks receive the same dose

A NEW DEVICE TO EXPOSE CELLS TO CHANGING DOSE RATES OF IONISING RADIATION, Brehwens K et al. Radiation Protection Dosimetry, 148 (2003), 366-371

MICRONUCLEUS FREQUENCIES AND CLONOGENIC CELL SURVIVAL IN TK6 CELLS EXPOSED TO CHANGING DOSE RATES UNDER CONTROLLED TEMPERATURE CONDITIONS, Brehwens K et al. International Journal of Radiation Biology, 90 (2014), 241-247

Stockholm University

ID Card:

Exposure type:
External

Source:
Xray machine

Dose rate:
2.2 to 37 mGy per minute

Irradiation type:
photons, vertical beam

Irradiated organism type:
Cells in culture

Address:
Stockholm University

Access:
free, decision by source owner

Supporting lab:
Biomolecular and cell culture lab

Internet link:

Contact:
Andrzej Wojcik
Andrzej.wojcick@su.se
tel:+46(0)8161217

Related to:
MELODI, EURADOS, RENEB

Proton IRRADiation facility (IRRAD)

A 24 GeV/c p^+ beam for the qualification of HEP components

The proton **IRRAD**iation Facility (IRRAD), located in the East Area of the Proton Synchrotron (PS) accelerator at CERN, is mainly used to qualify components for High Energy Physics experiments. This includes both low-Z samples such as thin silicon devices and particle-detector test structures, and high-Z samples such as the dense materials used in the construction of calorimeter devices. Moreover, at IRRAD it is also possible to perform tests on electronic components/systems, radiation monitoring devices and dosimeters in passive mode with reduced power requirements, and with an active readout.

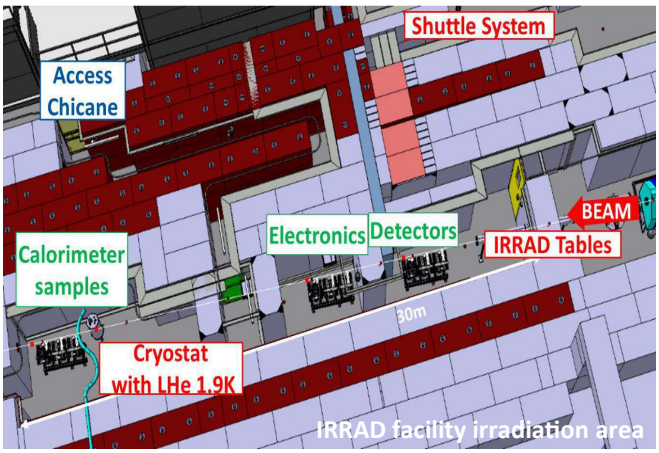


Photo: IRRAD team/CERN

The PS accelerator supplies IRRAD with a 24 GeV/c proton beam of variable size ranging from 12×12 mm^2 to 20×20 mm^2 in spills of ~400 ms duration, every 10 s on average. Other beam sizes are available to users upon request. IRRAD is equipped with remotely controlled tables to precisely position the samples in the proton beam. The volume available for irradiation may reach up to 20×20×50 cm^3. In addition, a remotely controlled conveyer (*IRRAD1 shuttle*) is available for the irradiation of small and passive samples, with maximum overall dimensions of 5×5×15 cm^3; this shuttle can be moved from the outside area to the irradiation position without the need to stop the beam and disable human access inside the area.

The IRRAD1 shuttle travels across the radiation shielding blocks for a distance of ~10 m through a conduit of 400×400 mm^2, designed to minimise direct radiation streaming. For both types of systems, dedicated user interfaces allow users to remotely control them in an easy and user-friendly manner, and to monitor the sample positions and the environmental conditions of IRRAD in real time. All this information is displayed on dedicated webpages accessible to the users.

Furthermore, at IRRAD it is also possible to perform irradiations at low temperature (down to -25°C). Two cooling systems located outside the irradiation area provide chilled fluid to the specially designed cold boxes positioned on two IRRAD tables. In addition, a cryostat filled with liquid Helium (LHe) allows special irradiations to be performed with samples exposed at cryogenic temperatures down to 1.9 K.

Photo: CERN EP/EN department

IRRAD facility team

With regard to dosimetry, pure Aluminum foils are used to measure the total proton fluence delivered to a sample with a precision of ±7%. This is achieved by performing γ-spectrometry measurements of the irradiated foil samples to evaluate the ^{24}Na and ^{22}Na activities. Other types of dosimetric technologies are also available at IRRAD (Alanine, RPLs, GaF films, etc.) depending on user requirements.

To guarantee precise beam steering along the beamline, a dedicated instrument, the Beam Profile Monitor, is used. This provides a real time image of the Gaussian beam profile in a webpage display. The same type of detector is used to align the IRRAD tables with regard to the beam trajectory and to provide users with detailed information on the beam delivered to their samples.

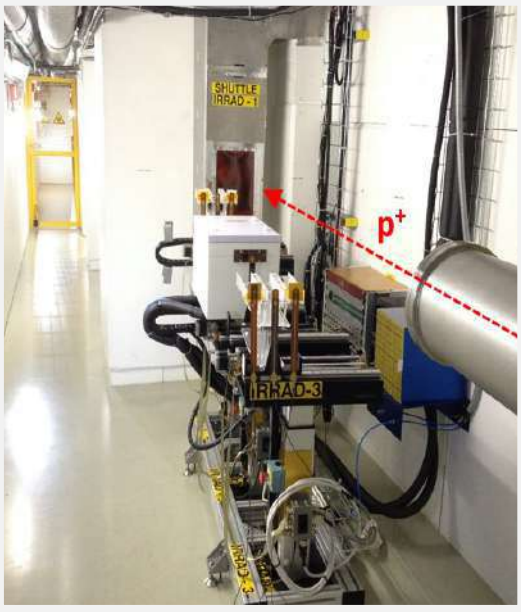


Photo: IRRAD team/CERN

IRRAD tables (foreground). IRRAD1 shuttle conduit (background).

IRRAD: The New 24GeV/c Proton Irradiation Facility at CERN, Gkotse B., Glaser M., Moll M., Ravotti F. (2015), In Proc. AccApp'15 , Washington, DC, 182-187

The Beam Profile Monitoring System for the IRRAD Proton Facility at the CERN PS East Area, Gkotse B., Glaser M., Matli E., Ravotti F., Gan K. K., Kagan H., Smith S., Warner J. (2015), In Proc. AccApp'15, Washington, DC, 479-484

ID Card:

Exposure type:
External

Source:
CERN Proton Synchrotron Accelerator

Dose rate:
~5×10^{11} p/spill
(~5×10^{15} p/cm^2/week corresponding to ~ 1.5 MGy/week in Si on 10×10 mm^2)

Irradiation type:
Proton

Irradiated organism type:
N/A

Address:
CERN
CH-1211
Geneva 23
Switzerland

Access:
Prior agreement/research collaboration services

Supporting lab:
N/A

Internet link:
https://ps-irrad.web.cern.ch

Contact:
Federico Ravotti
+41 22 76 74280
irrad.ps@cern.ch
Federico.Ravotti@cern.ch

Related to:
AIDA-2020
EURADOS

CERF

The CERN-EU high-energy Reference Field facility

Neutron calibrations and instrumentation tests often need to be performed at neutron energies or spectra very different from those generated by radioactive sources. The CERN-EU high-energy Reference Field (CERF) facility is a workplace field, unique in its kind, which reproduces the mixed radiation field encountered in the vicinity of high-energy particle accelerators and at commercial flight altitudes. Located in the North Experimental Area of CERN, CERF is served by a secondary beam from the Super Proton Synchrotron (SPS), which consists of a 120 GeV/c positively charged hadron beam (about 2/3 pions and 1/3 protons), impinging on a copper target 50 cm thick.

Photo: CERF

Dr Marco Silari

the target, ambient dose equivalent rates can be obtained from approximately 5 µSv/h (30 nSv per spill) to 250 µSv/h (1.5 µSv per spill) on the concrete roof, and from 18 µSv/h (100 nSv per spill) to 360 µSv/h (2 µSv per spill) on the iron roof. The uncertainty on the reference values of ambient dose equivalent rate is about 15%.

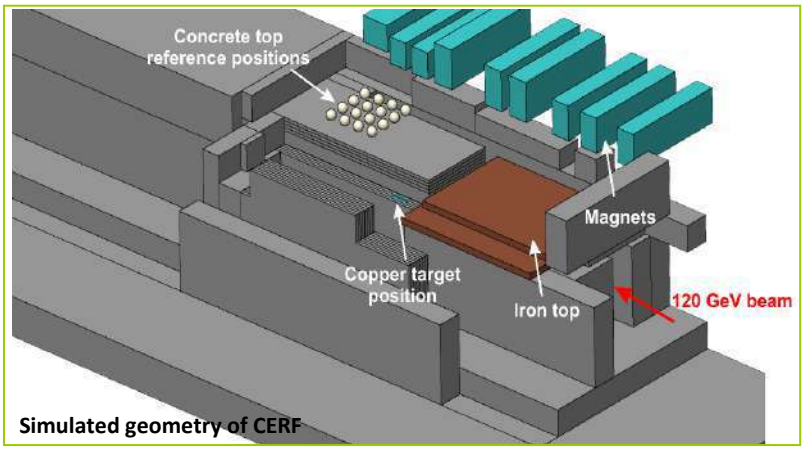


Photo: CERF

Simulated geometry of CERF

The target can be placed below either an 80 cm thick concrete roof shield or a 40 cm thick iron roof shield (see figure above). Sixteen reference exposure locations (50 x 50 cm^2 each) are provided on the top of the two roofs. Eight additional exposure locations are available outside an 80 cm thick lateral concrete shield.

CERF is primarily a simulated workplace field for testing radiation protection instrumentation (active monitors and passive dosimeters) used at high-energy accelerators and/or for aircrew dosimetry. In addition, the Linear Energy Transfer (LET) distribution of dose equivalent makes CERF a suitable facility for space dosimetry.

Other applications of the CERF radiation field are: radiobiology studies; spallation cross section measurements (in the hadron beam); investigation of activation of accelerator materials (by exposing them next to the target); intercomparison of individual dosimeters; benchmarking Monte Carlo codes against experimental data. For a more exhaustive list of possible applications, see the references cited below.

The beam is delivered to CERF with a typical intensity in the range 10^6 to 10^8 particles per SPS beam extraction (spill), with two to three beam extractions of about 5 s duration over an SPS cycle (the duration of which varies in the range 30-45 s). The beam monitoring, on which the normalisation of all measurements relies, is provided by an air-filled, parallel-plate, transmission-type ionisation chamber (IC), calibrated with the multi-foil activation technique. Typical values of ambient dose equivalent rates are 0.2-0.3 nSv per IC-count on the concrete roof and 1-1.5 nSv per IC-count on the iron roof. By assuming an average of three spills per minute and adjusting the beam intensity on

Photo: CERF

Typical set-up of radiation detectors and dosimeters exposed on the concrete roof.

The CERN-EU high-energy Reference Field (CERF) facility: applications and latest developments, Silari M., Pozzi F. (2017), Eur. Phys. J. Web of Conf., 153, 03001

The CERN-EU high-energy Reference Field (CERF) facility for dosimetry at commercial flight altitudes and in space, Mitaroff A., Silari M. (2002), Radiat. Prot. Dosimetry, 102 (1), 7-22

ID Card:

Exposure type:
External

Source:
120 GeV/c proton and pion beam
Simulated workplace mixed radiation field

Dose rate:
5 µSv/h to 250 µSv/h (concrete roof)
18 µSv/h to 360 µSv/h (iron roof)

Irradiation type:
Neutron, proton, pion, gamma

Irradiated organism type:
None

Address:
CERN
1211 Geneva 23
Switzerland

Access:
One or two beam periods of one week per year, subject to acceptance by the facility manager

Supporting lab:
Radiation calibration laboratory

Internet link:
http://cerf-dev.web.cern.ch/

Contact:
Dr Marco Silari
Marco.Silari@cern.ch

Related to:
EURADOS

Exposure platforms

TIFPA

Trento Institute for Fundamental Physics and Applications

The TIFPA (Trento Institute for Fundamental Physics and Applications) proton irradiation facility is embedded in the Trento Proton Therapy Centre, Italy, which started clinical operations in October 2014 and has already treated more than 300 patients.

Photo: TIFPA

Photo showing the two sub-branches of the Trento proton irradiation facility, namely the 0° line (left) and 30° line (right)

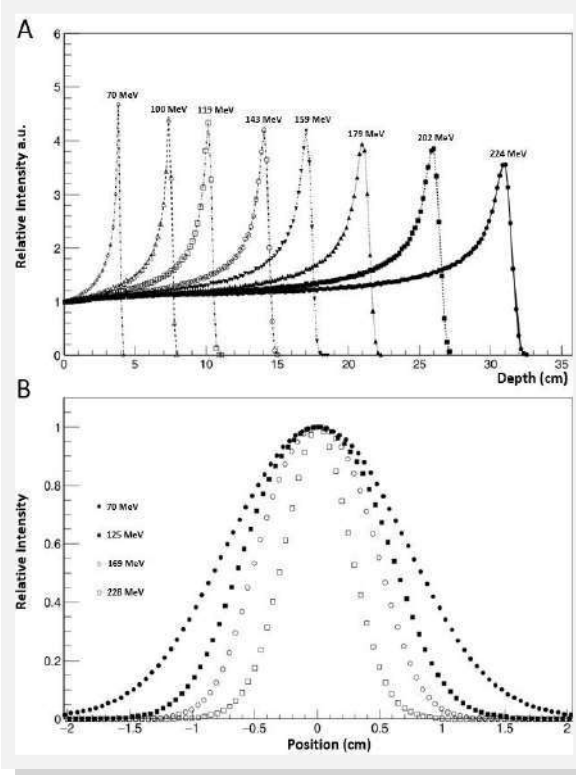
The TIFPA facility comprises an experimental area dedicated to a large spectrum of scientific applications including medical physics, detector testing, radiation hardness measurements, space research and radiobiology. Following an institutional agreement with APSS, the beam is available in the experimental room outside of clinical operation hours. Research activities are managed and supervised by TIFPA, which is part of the Italian National Institute for Nuclear Physics (INFN). Access to the research beam line is open to external users in the context of scientific collaborations or industrial applications, subject to acceptance by the Programme Advisory Committee.

Proton beam production and transport at the Trento facility are under the responsibility of the company IBA (Ion Beam Applications, Louvain-La-Neuve, Belgium), which produced and installed the related infrastructure. The cyclotron (IBA Proteus 235) accelerates the beam to a maximum energy of 228 MeV. Shortly after the cyclotron exit, an energy selection system allows fine selection of the desired energy in a range down to 70 MeV. Two branches of the main line transport the beam to the gantries, while a third branch connects it to the experimental room. Different beam intensities can be requested at the exit of the cyclotron, ranging from 1 to 320 nA. Transport efficiency depends on the energy and ranges from 0.1 to 10%. Interestingly, in addition to the above conventional intensities, it is possible to deliver low beam intensities (i.e. fluxes in the order of 10^1-10^5 particles/s) needed for a broad spectrum of basic physics experiments by operating the accelerator in "dark current" mode.

The experimental area consists of two different spaces: a multifunctional preparation room and an irradiation cave where the beam line is split into two sub-branches, referred to respectively as the "Biology" and "Physics" beam lines. A fixed pencil beam is available at the Physics line with same energy range as the clinical beams (70 to 228 MeV), with spot size ranging from about 1 to 3 cm in diameter (Gaussian FWHM). In contrast, a double-ring passive scattering system is installed at the Biology line, which is used for *in vitro* radiobiology experiments. This allows a 90% dose homogeneity to be obtained over an extended area (6-8 cm in diameter), with an adjustable dose rate of up to about 2 Gy/min. Lasers are available for target alignment at 1.25 m from the exit window, defined as "isocenter" in analogy to the treatment rooms. Tables with adjustable heights are used for target positioning. In the first few years of activity, over 30 experiments have been performed for different Italian and European partners, ranging from basic physics to space protection and radiobiology.

Photo: TIFPA

E. Scifoni F. Tommasino



Summary of the properties of the proton beam in air at the 30° beam line. Bragg curves (A) and Spot profiles (B) at representative energies (Tommasino et al. 2017)

Proton beam characterization in the experimental room of the Trento Proton Therapy facility, Tommasino F., Rovituso M., Fabiano S., Piffer S., Manea C., Lorentini S., Lanzone S., Wang Z., Pasini M., Burger W. J., La Tessa C., Scifoni E. et al. (2017), Nucl. Instrum. Methods Phys. Res., 869, 15-20

Study for a passive scattering line dedicated to radiobiology experiments at the Trento Proton Therapy Center, Tommasino F. et al. submitted to Radiat. Prot. Dosim.– Proceedings MICROS 2017

ID Card:

Exposure type:
External Radiation

Source:
Cyclotron, Accelerated Protons (70 -225 MeV)

Dose rate:
0.1-2 Gy/min

Irradiation type:
Horizontal proton beam

Irradiated organism type:
Cell cultures – Application in progress for small animals

Address:
via Al Desert 14
38123 Trento
Italy

Access:
Programme Advisory Committee (PAC):
http://www.tifpa.infn.it/sc-init/med-tech/p-beam-research/

Access fee applies

Supporting lab:
Cell culture lab. Possible access to other biological laboratories at the University of Trento

Internet link:
http://www.tifpa.infn.it/sc-init/med-tech/p-beam-research/

Contact:
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Francesco.tommasino@unitn.it
+3904611953116

Dr Emanuele Scifoni
Emanuele.scifoni@tifpa.infn.it
+390461283933

Involved in:
MoVe IT
FOOT
ESA Core ground-based facility

Related to:
MELODI, EURADOS

Exposure platforms

HIT

Platform for experiments with scanned ion beams

The Heidelberg Ion-Beam Therapy Centre (HIT for short) is part of the University Hospital of Heidelberg in Germany, and is strategically located at only 45 minutes from Frankfurt airport. It serves to provide tumour therapy with light ions. Approximately 750 patients per year are treated with proton and carbon ion beams, and it is planned to introduce helium treatments in the near future. The Centre also has extensive experience in treating children and adolescents.

Photo: HIT

Prof. T. Haberer
&
Prof. J. Debus

The beam application system is based on the technology of intensity-modulated raster scanning which allows maximal flexibility for the 3D distribution of radiation dose. In terms of measurements, several trigger signals are available as well as an online oscillograph for beam position, focus, intensity and many other parameters.

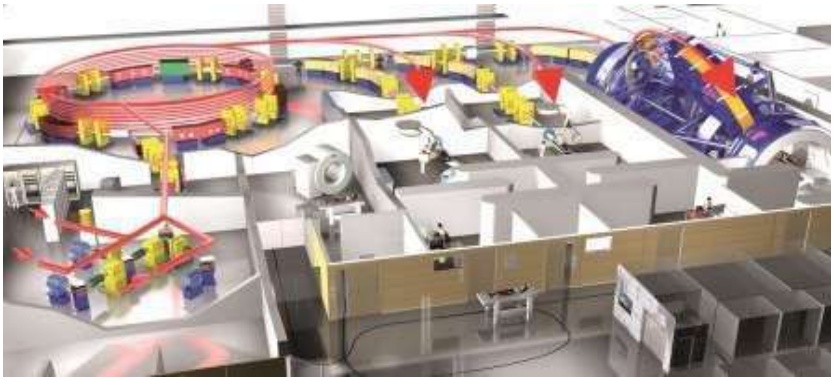


Photo: HIT

Schematic view of the therapy system. The experimental room is not visible but is located in the upper right corner of the diagramme.

Biological experiments can be performed in the experimental room (classified as an S1 lab) and are frequently done with cells, mice and rats. Labs are also available on-site, and access is subject to prior agreement. Local support personnel (physicists, radiobiologists, etc.) can also be provided.

Treatments take place in three dedicated treatment rooms, two of which have a horizontal beamline (fixed beam rooms) and the third is equipped with the world's first ion beam gantry, which allows treatment from every direction. In addition to the three treatment rooms, HIT has an experimental room with a technically identical beamline and beam-monitoring system. This room is typically available for conducting experiments during the night (23:00 – 05:00) and at weekends.

The cost of beam time is approximately €1300 per hour. Applications for beam time are evaluated by HIT and should be sent to Proposal.HIT@med.uni-heidelberg.de.

Before submitting an application, an informal contact would be helpful for both sides (see ID Card for local contact points).

Acceleration is done with a synchrotron; beam extraction is slow and therefore a continuous beam can be extracted for 5 s per ring filling. Approximately 420 full cycles per hour are available. ^{1}H, ^{4}He, ^{12}C and ^{16}O are provided in 255 energy levels corresponding to a penetration depth in water of 20-300 mm. Several intensities are preconfigured for each ion species with maximum values appropriate for a dose of 1 Gy/l/min; lower intensities can be provided upon request. Beam shape is Gaussian pencil beam with typical FWHM of 4-30 mm.

Photo: HIT

Beam exit with scanning nozzle in the experimental room

ID Card:

Exposure type:
Intensity Modulated Scanned Pencil Beam

Source:
Synchrotron

Dose rate:
Adjustable, customised, typically up to 10^{9} particles/s or 1 Gy/l/min

Irradiation type:
^{1}H, ^{4}He, ^{12}C, ^{16}O

Irradiated organism type:
Cells
Mice, rats, etc. subject to prior discussion

Address:
Im Neuenheimer Feld 450
69120 Heidelberg
Germany

Access:
Selection Committee (HIT)

Supporting lab:
Technical support on site.
Bio labs on site, availability to be discussed in advance.

Internet link:
www.hit-centrum.de

Contact:
Prof. Thomas Haberer
Thomas.Haberer@med.uni-heidelberg.de

Applications to:
Proposal.HIT@med.uni-heidelberg.de

Involved in:
CORA IBER (ESA)

Related to:
EURAMED

The Heidelberg Ion Therapy Center, Haberer Th., Debus J., Eickhoff H., Jäkel O., Schulz-Ertner D., Weber U. (2004), Radiother Oncol, 73 (Suppl. 2), S186-S190

Particle therapy at the Heidelberg Ion Therapy Center (HIT), Combs S. E., Jäkel O., Haberer Th., Debus J. (2010), Radiother Oncol, 95 (1), 41-44

The AGOR Facility at KVI-CART

Cell and Animal Irradiation

The AGOR cyclotron facility, located within the KVI-Centre for Advanced Radiation Technologies (KVI-CART), is part of the University of Groningen (the Netherlands). AGOR (Accélérateur Groningen-ORsay) is a superconducting K=600 MeV cyclotron used for the acceleration of both light and heavy ions, and is the result of a collaboration between KVI-CART and the IPN, Orsay, France.

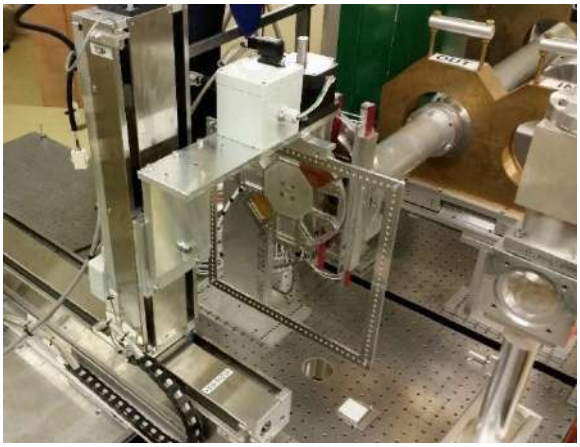


Photo: H. Kiewiet/KVI-CART

AGOR's in-air irradiation beamline

The cyclotron has just celebrated 20 years of successful operations, including the performance of numerous animal irradiations with proton beams and of cell cultures with proton, helium, carbon and oxygen beams at various energies. A high-precision and efficient ion irradiation facility for radiobiology has been developed to study DNA damage and gene expression after ion irradiation.

This system uses a double scatter foil to generate a 70 mm field size for ≤190 MeV protons (uniformity of ±1.5%) and a dose rate of up to 50 Gy/min. Carbon ions are also provided, using a single scatter foil at ≤90 MeV/u (uniformity of ±1.5%) and dose rates of 2-5 Gy/min for cell cultures, and up to 50 Gy/min for DNA damage studies. In all cases, a spread-out Bragg peak (SOBP) is formed with a modulator wheel (SOBPs of 1.3 mm and 3 mm have been provided for carbon ions). Neutron irradiations at dose rates of up to 100 mGy/min can be performed under near clinical conditions by stopping a proton of the required energy in water.

Since April 2018, a scanned pencil beam is available. Depending on the ion and energy chosen, and the required uniformity, the field size can be up to 10 x 10 cm^2 (protons). Uniform scanning with a frequency up to 200 Hz has already been implemented, and spot scanning is under development. Future development plans include image-guided animal irradiations (for which a large funding request is under evaluation) and flash (ultra-high dose rate) and mini-beam irradiations. The feasibility of higher dose rate neutron irradiations is currently under study.

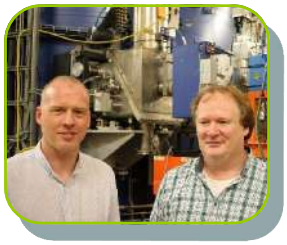


Photo: H. Kiewiet/KVI-CART

Dr B. N. Jones
&
Dr M. J. van Goethem

The AGOR facility is a user facility for the international scientific community. Beamtime can be obtained by submitting a proposal for evaluation by the AGOR Programme Advisory Committee (PAC). Proposal submission deadlines are 1 March and 1 October. In the context of Transnational Access within the EU/Horizon2020 Integrating Activities action, KVI-CART provides access support (travel and subsistence) under the Integrating Activities ENSAR2 and INSPIRE (see: https://www.rug.nl/kvi-cart/research/facilities/agor/).

AGOR has also been recognised by the ESA (European Space Agency) as a ground based facility for its research programme on the biological effects of space radiation (https://www.esa.int/Our_Activities/Human_Spaceflight/Research/Research_Announcements).

Access for commercial use is available to users from industry, businesses and the public sector with no need to submit a scientific proposal.

Photo: P. Tahl/KVI-CART

AGOR Cyclotron

Development of a facility for high-precision irradiation of cells with carbon ions, van Goethem M. J., Niemantsverdriet M., Brandenburg S., Langendijk J. A., Coppes R. P., van Luijk P. (2011), Med Phys, 38 (1), 256-263

Sparing the region of the salivary gland containing stem cells preserves saliva production after radiotherapy for head and neck cancer, van Luijk P., Pringle S., Deasy J. O., Moiseenko V. V., Faber H., Hovan A., Baanstra M., van der Laan H. P., Kierkels R. G. et al. (2015), Sci Transl Med, 305 (7), 305ra147

university of groningen

ID Card:

Exposure type:
Scanned pencil and scattered beam

Source:
Cyclotron

Dose rate:
Adjustable, protons with typical dose rates of up to 50 Gy/min

Carbon ions at ≤90 MeV/u with typical dose rates of up to 50 Gy/min

Flux: max 10^9 protons per cm^2 per second, 10^6 heavy ions per cm^2 per second

Irradiation type:
Proton beam of up to 190 MeV, He to O up to 90 MeV/amu

Irradiated organism type:
Cells, animals (rats using protons, 10 x 10 cm^2 field and max range 15 cm water equivalent)

Address:
AGOR irradiation liaison KVI-CART,
Zernikelaan 25
9747 AA GRONINGEN
The Netherlands

Access:
EU support available for travel and subsistence costs (PAC approved)

Technical support available

Supporting lab:
Limited microbiology facilities on site, support from UMCG radiobiology group can be arranged.

Internet link:
https://www.rug.nl/kvi-cart/

Contact:
AGOR irradiation liaison (KVI-CART)

Dr M. J. van Goethem
irradiations@kvi.nl

Involved in:
ESA-CORA-GBF
ENSAR2
INSPIRE, both within the EU H2020 programme

Related to:
EURADOS

Exposure platforms

FAIR

FAIR phase-0 at GSI in Darmstadt, Germany started in 2019

The Facility for Antiprotons and Ion Research (FAIR) is the most ambitious infrastructure for nuclear physics under construction worldwide. FAIR is based at GSI, the Helmholtz Research Institute in Darmstadt (Germany), well known for the discovery of six new heavy elements in the periodic table (107<Z<112) and for having started cancer therapy with high-energy carbon ions in Europe (1997-2007).

Photo: Brinner/GSI

Dr Marco Durante

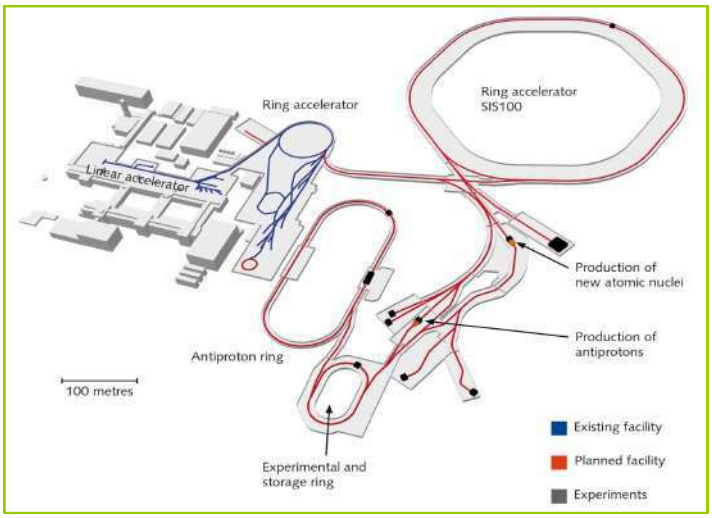


Photo: GSI/FAIR

The current GSI complex and design of the future FAIR complex

GSI operates the SIS18 synchrotron (18 Tm rigidity), an impressive heavy-ion facility that can accelerate ions from H to U up to energies of approximately 1 GeV/n. The new FAIR synchrotron, SIS100 (100 Tm rigidity), will be characterized by higher energies (up to 10 GeV/n) and 100-1000-fold higher beam intensities. This unique facility provides new exciting opportunities in nuclear physics in the four main experiments in nuclear astrophysics (NuSTAR), compressed baryonic matter (CBM), antiproton annihilation (PANDA), and applied physics (APPA, including atomic and plasma physics, materials research, and biophysics).

The biomedical program is highly diverse and run by the GSI Biophysics Department, directed by Marco Durante, Professor of Physics at the Technische Universität Darmstadt. A large, international biophysics collaboration met in May at GSI to discuss the biomedical applications of FAIR (https://indico.gsi.de/event/7796/). This collaboration will exploit both characteristics of the new FAIR facility.

The higher energy is especially useful for space radiation research, because FAIR will be able to simulate the full spectrum of galactic cosmic radiation. It can also be useful for biomedical studies, especially particle radiography. The high intensity has far-reaching applications in cancer therapy, e.g. for ultra-fast beam delivery (FLASH radiotherapy), minibeam therapy (using grids), acceleration of radioactive ion beams (especially positron-emitting nuclides, which can be visualized online by PET), and the production of heavy radioisotopes for targeted alpha-particle therapy.

The construction of SIS100 will be completed in 2025, but FAIR phase-0 already started in 2019 at SIS18, with the increased beam current necessary for FAIR. Approximately 20 radiobiology experiments have been implemented, using either C-ions (for pre-clinical therapy research) or Fe-ions (for space radiation protection; supported by the ESA within the IBER program). FAIR-phase-0 is now accepting applications *via* the GSI Program Advisory Committee (for therapy or radiation protection studies) and the ESA for space radiation research.

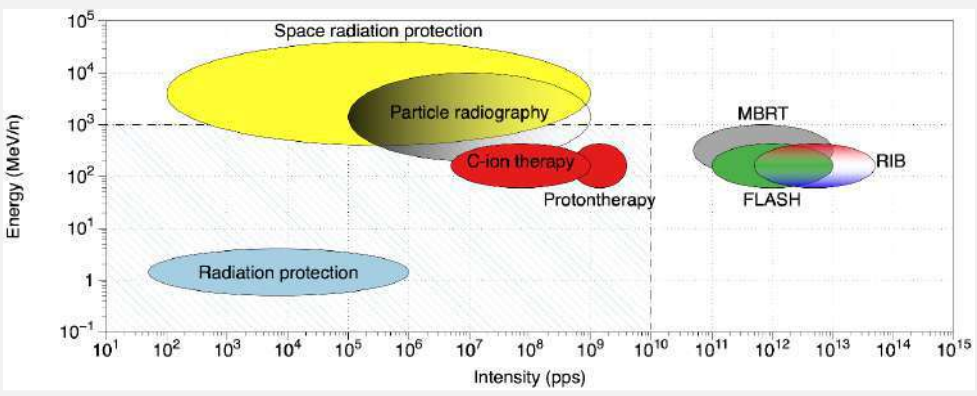


Photo: M. Durante /GSI

Radiation research at the accelerators. The energy (in MeV/n) and intensity (in particles per second) define the phase space in which different applications can be performed. The shaded region includes energy values and intensities covered by the present accelerators, whereas the other regions will be covered by FAIR. MBRT, minibeam radiotherapy; RIB, radioactive ion beams; FLASH, high dose-rate radiotherapy.

All the fun of the FAIR: fundamental physics at the facility for antiproton and ion research, Durante M., Indelicato P., Jonson B., Koch V., Langanke K., Meißner Ulf-G., Nappi E., Nilsson T., Stöhlker Th., Widmann E., Wiescher M. (2019), Phys Scr, 94 (3), DOI: 10.1088/1402-4896/aaf93f

Applied nuclear physics at the new high-energy particle accelerator facilities, Durante M., Golubev A., Park W. Y., Trautmann C. (2019), Phys Rep, 800, 1-37

ID Card:

Exposure type:
External

Source:
Accelerator

Dose rate:
0.01-1000 Gy/min

Irradiation type:
All ions from H to U

Irradiated organism type:
Cells, Tissues, Animals, Plants

Address:
GSI Helmholtzzentrum für Schwerionenforschung
Biophysics Department
Planckstraße 1
64291 Darmstadt - Germany

Access:
Free after scientific evaluation by a program advisory committee. Space-related projects are evaluated by ESA.

Supporting lab:
Cell/molecular biology/animal facility/electronics/workshop

Internet link:
www.gsi.de/biophysik

Contact:
Marco Durante
M.Durante@gsi.de
+49 6159 71 2009

Related to:
ESA

Exposure platforms

Research Neutron Source Heinz Maier-Leibnitz (FRM II) Technical University of Munich

Irradiation facility for radioisotopes: e.g. Lutetium-177

The Heinz Maier-Leibnitz (FRM II) research neutron source is one of the most powerful and advanced neutron sources in the world. It uses the nuclear fission of uranium to produce more than 1 E14 free neutrons per square centimetre per second, which are used for research, industry, and medicine. The thermal power amounts to 20 MW.

As a neutron source, the FRM II is used for the solution of fundamental questions and, notably for applied science. In addition, approximately 30% of the usable neutron flux is reserved for joint projects with industry. The facilities offer a range of activities from materials analysis by neutron scattering (non-destructive testing, analysis using neutrons), which is possible at the 30 different beam tube instruments, to the generation of stable and radioactive isotopes and the treatment of tumors by irradiation. As a result, neutrons of the FRM II are used by the automotive, semiconductor, and aerospace industries, as well as for mechanical engineering, chemistry, medical technology, environmental, energy, geology, archaeology, and art history studies.

The FRM II is equipped with a series of irradiation facilities which cover a wide range of applications:

- Pneumatic Rabbit Irradiation System (RPA)
- Capsule Irradiation System (KBA)
- Mechanical Irradiation System
- Silicon Doping Facility
- Irradiation Position in the Control Rod
- Irradiation with fast neutrons at the MEDAPP and NECTAR instruments
- Irradiation with cold neutrons at the PGAA instrument

Lutetium-177 for therapy

Photo: Schürmann/TUM

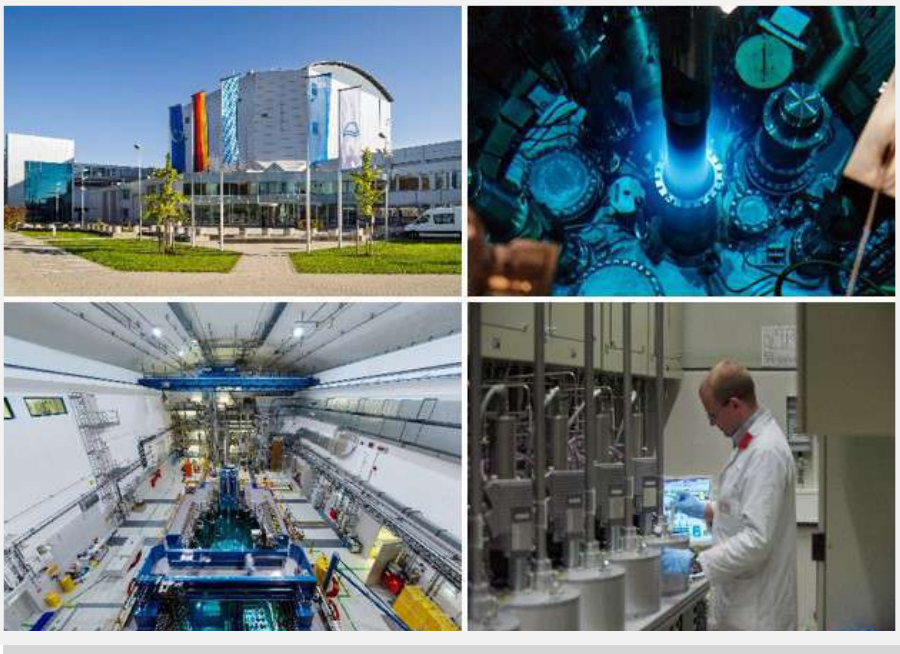
Florian Jeschke

For several years, Lu-177 has been used for the treatment of neuroendocrine tumours and/or metastases, such as those that occur in the pancreas. Lu-177 is, in this case, coupled to a protein molecule, a so-called “ferry”, and thus moves directly into the tumour. Lu-177 is a beta emitter (an electron is emitted) with a very low range of approximately 2 mm, which means that healthy tissue remains virtually undamaged.

At the FRM II, Lu-177 is produced from the irradiation of Ytterbium-176 (Yb-176) through the very short-lived nuclide Yb-177, which quickly decays to Lu-177. This process guarantees the production of pure Lu-177 (free of Lu-176), which can then be used without a carrier. This means there is less radioactive waste for clinics and the preparation can be used for a longer period, since it still contains a sufficient amount of therapeutically active Lu-177, even after 7 to 10 days.

This technically very complex method was developed by Radiochemistry Munich RCM, which is also a scientific institute based at the TUM and is currently commercially utilized by ITM Isotopen Technologien München AG on the site of the FRM II.

Photo: TUM



The Research Neutron Source Heinz Maier-Leibnitz (FRM II) facilities

Production of ^{177}Lu at the new research reactor FRM-II: Irradiation yield of ^{176}Lu(n,γ)^{177}Lu, Dvorakova Z., Henkelmann R., Lin X., Türler A., Gerstenberg H. (2008), Appl Radiat Isot, 66 (2), 147-151

Separation of carrier-free lutetium-177 from neutron irradiated natural ytterbium target, Balasubramanian P. S. (1994), J Radioanal Nucl Chem, 185 (2), 305 -310

ID Card:

Exposure type:
External irradiation with neutrons

Source:
Research Neutron Source Heinz Maier-Leibnitz (FRM II) Technical University of Munich (TUM)

Dose rate:
Thermal neutrons: up to 1.1 x 10^{14} $cm^{-2}s^{-1}$

Irradiation type:
Neutron (neutron flux)

Irradiated organism type:
Organic and inorganic substances

Address:
Lichtenbergstr. 1
85748 Garching, Germany

Access:
Fee-based

Supporting lab:
Radiochemistry Munich RCM and ITM Isotopen Technologien München AG

Internet link:
A video depicts the complex production of Lu-177

www.mlz-garching.de

www.frm2.tum.de

Contact:
Florian Jeschke
Florian.Jeschke@frm2.tum.de
+49 89 289-14739

Related to:
EURADOS

CHAPTER 1 Exposure platforms

d) Internal contamination

B3, Animal Contamination Facility

Actinide behavior following lung or wound contamination

The RadioToxicology Laboratory (LRT) was created in 1961. Since then, numerous experiments have been carried out using a variety of radionuclides. The main focus of activity is on actinides.

The LRT houses a radiologically-controlled zone with a dedicated animal house facility where inhalation and other methods of internal contamination using alpha emitter actinides

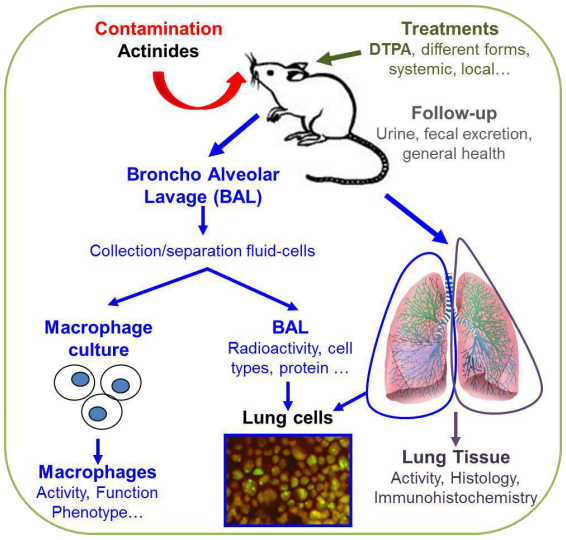


Diagram: CEA/N. Griffiths

Road map for studies after inhalation of actinides

(Plutonium Pu, Americium Am, MOX: Mixed OXide of Uranium U, Pu) are performed. The use of actinides is tightly controlled and requires effective confinement during experimental procedures. The inhalation system to expose animals is within a modified glove box. During inhalation, the animals are conscious and restrained in cardboard tubes with a perforated cover at the head end to allow breathing. This type of exposure is termed "nose-only", and up to 30 rats can be exposed at any one time.

The aerosols created for contamination may be collected and characterized in terms of particle size (cascade impactor). This experimental technique allows simulation of a realistic contamination scenario involving radioactive elements, most likely in an insoluble form, which could be released into the atmosphere (see example of a road map for an actinide inhalation study in figure).

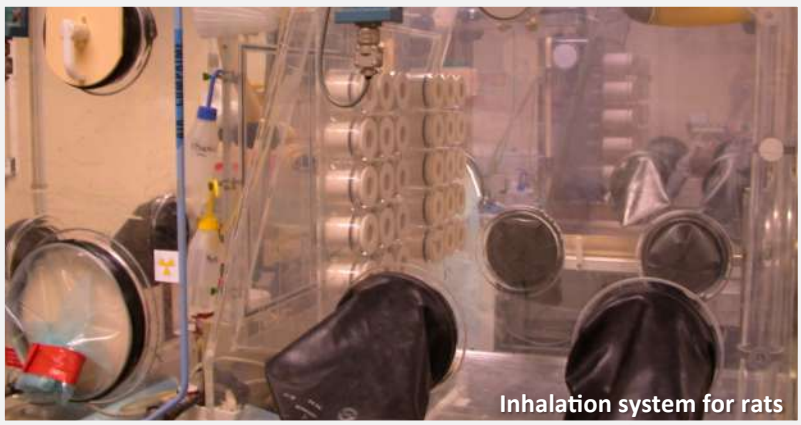
In addition to inhalation studies and lung pathologies with MOX, Pu or Neptunium, the following subjects have been addressed: Pu-induced osteosarcomas, development of a wound model for actinide contamination and evaluation of different decorporation regimens. Tissue samples, mainly paraffin embedded and collected over the decades, have recently been classified, and form the basis of the in-house "Experimental Radiotoxicology Biobank". This bioresource incorporates different tissues, contaminants and routes of contamination.

Photo: P Herpin

Nina Griffiths

LRT also carries out *in vitro* experiments to improve the estimation of dose distribution in human lung epithelial cell monolayers after contamination with alpha emitting radionuclides. Numerical models of cell monolayers can be derived from confocal images. γH2AX foci are markers of radiation-induced DNA damage. This work aims to facilitate assessment of the heterogeneity of dose distribution from alpha particle emitters in cells.

Lastly, LRT performs research *in silico* and is currently developing a unique numerical toolkit to facilitate storage and analysis of the numerous experimental data acquired in the laboratory under various conditions. This toolkit is designed to contribute to a better understanding of actinide biokinetics with particular emphasis on contamination conditions such as the route of intake or the physicochemical form.



Inhalation system for rats

Photo: CEA/DAM/CADAM

ID Card:

Exposure type:
Internal contamination

Source:
Actinides

Dose rate:
To be determined as a function of the radionuclide, radioactive and biological half-life, the administered activity, the duration of the experiment and the potential use of decorporation/ decontamination procedures.

Irradiation type:
Alpha (5000 keV)

Irradiated organism type:
rats, cells

Address:
CEA of Bruyères-le-Châtel,
Domaine du Grand Rué,
BP12 Bruyères-le-Châtel,
91297 ARPAJON cedex , France.

Access:
Use of the facility requires specific authorization for people and projects in addition to authorization for animal experiments

Supporting lab:
Radiochemistry, biochemistry, cell culture, microscopy

Internet link:
http://ircm.cea.fr/dsv/ircm/Pages/Equipes/LRT.aspx

Contacts:
Jaime Angulo-Mora: jaime.angulo-mora@cea.fr
+33 (0)1 69 26 56 01
Nina Griffiths:
nina.griffiths@cea.fr
+33 (0)1 69 26 57 12

Related to:
EURADOS, MELODI, STORE

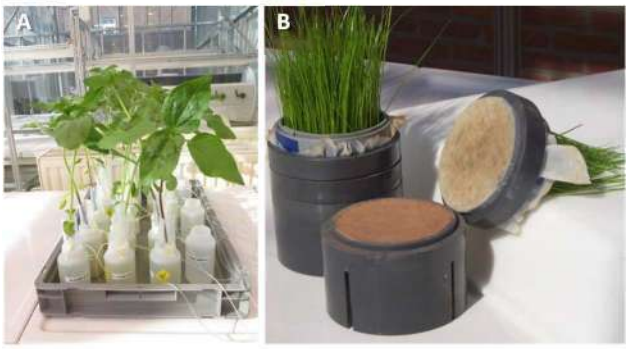
PREFERENTIAL DECORPORATION OF AMERICIUM BY PULMONARY ADMINISTRATION OF DTPA DRY POWDER AFTER INHALATION OF AGED PUO(2) CONTAINING AMERICIUM IN RATS. O. Grémy et al., Radiat Res. 2010; 174(5):637-44.
INTERNAL CONTAMINATION BY ACTINIDES AFTER WOUNDING: A ROBUST RODENT MODEL FOR ASSESSMENT OF LOCAL AND DISTANT ACTINIDE RETENTION. NM. Griffiths et al., Health Phys. 2012; 103(2):187-94.

Exposure platforms

Facility radionuclides availability, transfer and migration

Understanding the behaviour of radionuclides in the biosphere

At the Biosphere Impact Studies group (BIS) of the Belgian Nuclear Research Centre (SCK•CEN), mechanisms and processes are studied to better understand and predict radionuclide behaviour in the terrestrial, freshwater and marine environment by using dedicated laboratory set-ups, greenhouse experiments and field studies, as well as developing modelling tools calibrated and validated with the data sets thus developed. To perform this research, an infrastructure is available for conducting lab experiments to study radionuclide availability, transfer and migration in the environment.



Photos: SCK•CEN

Fytoremediation experiment with sunflower (A) - Rhizoplan system (B)

The facility is located in a controlled area, making it possible to work with open radioactive sources. A large range of radionuclides can be used, e.g. ^{134}Cs, ^{137}Cs, ^{60}Co, ^{90}Sr, ^{238}U, ^{232}Th, ^{241}Am. The permitted activities are dependent on the dose rate, shielding possibilities, radioactive waste limits, etc., and need to be discussed and approved by the physical control unit of SCK•CEN before starting the experiments.

The facility offers the possibility to contaminate soil, sediment and water and simulate atmospheric deposition. Plants (and other organisms) can be grown on/in these contaminated substrates to study their uptake of radionuclides (figure A). Many plant species have already been used in the labs, e.g. ryegrass, sunflower, clover, maize, pine trees and rice, plus other organisms such as mycorrhizas.

Specific experimental set-ups have been developed at BIS, for example:

- In order to screen the radionuclide uptake potential of plants for a large array of soils, a rhizoplan system was developed in which only a small amount of soil is used, and the roots, shoots and soil can be harvested separately (figure B).
- To be able to differentiate between root uptake and stem uptake of radiocaesium by rice, a hydroponic system was developed in which rice stems are in contact with ^{134}Cs while rice roots are in contact with ^{137}Cs (figure C).

Photo: Patrick Liebens

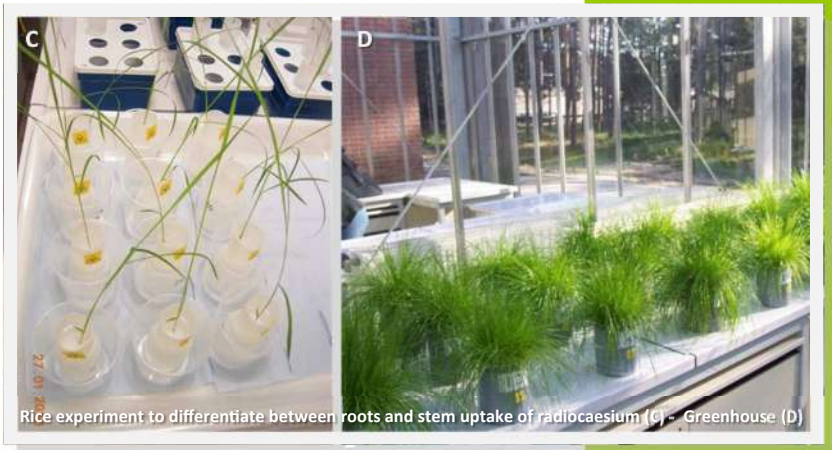
Nathalie Vanhoudt

The facility is equipped with a greenhouse consisting of four compartments (each 20 m²) in which the environmental conditions can be separately regulated with heaters, screens, natural ventilation and lights (figure D). To ensure more controlled environmental conditions, two large climate chambers (8 m² and 3 m²) are available in which the temperature and light conditions can be programmed and controlled. Also, one fully controlled climate chamber of 1 m² is available if, in addition to light and temperature, humidity also needs to be regulated.

In addition to the indoor lab experiments, lysimeters are available with different soil types to perform outdoor experiments.

The facility is supported by fully equipped labs for soil sampling and characterisation, element analyses (ICP-MS, IC, etc.) and radioactivity measurements (low level alpha, beta, gamma). In addition, a collection of Belgian, Japanese and European soils is available.

The facility is open for collaboration, and proposals for projects with CONCERT partners are welcome.



Rice experiment to differentiate between roots and stem uptake of radiocaesium (C) - Greenhouse (D)

Photo: SCK•CEN

SCK•CEN
STUDIECENTRUM VOOR KERNENERGIE
CENTRE D'ETUDE DE L'ENERGIE NUCLEAIRE

ID Card:

Exposure type:
Internal exposure (through uptake of radionuclides from contaminated soil/sediment/water)

Source:
Large range of radionuclides (^{134}Cs, ^{137}Cs, ^{238}U, ^{232}Th, ^{90}Sr, etc.)

Dose rate:
Radionuclide-dependent (according to radiation type, shielding possibilities, radioactive waste limits, etc.)

Irradiation type:
Alpha, beta, gamma

Irradiated organism type:
Exposure of plants and mycorrhiza via contaminated soil, sediment or water

Address:
Belgian Nuclear Research Centre (SCK•CEN), Boeretang 200, 2400 Mol, Belgium

Access:
Joint research collaboration and subject to internal approval

Supporting lab:
Labs for soil characterisation and (radio) analytical chemistry

Contact:
Nathalie Vanhoudt, nathalie.vanhoudt@sckcen.be, +32 14 33 21 12

Related to:
ALLIANCE

CAN WE PREDICT URANIUM BIOAVAILABILITY BASED ON SOIL PARAMETERS? PART 1: EFFECT OF SOIL PARAMETERS ON SOIL SOLUTION URANIUM CONCENTRATION. H. Vandenhove et al., Environ. Pollut. 2007; 145(2):587-95.

PREDICTING RADIOCAESIUM SORPTION CHARACTERISTICS WITH SOIL CHEMICAL PROPERTIES FOR JAPANESE SOILS. S. Uematsu et al., Sci.Total Environ. 2015; 524-525:148-56.

Nanoparticle Inhalation Facility

PHE Centre for Radiation, Chemical and Environmental Hazards

The Centre for Radiation, Chemical and Environmental Hazards (CRCE) has had an inhalation exposure facility for many decades. The facility was originally developed to undertake inhalation studies using aerosols of relevance to the nuclear industry. In 2008 the facility was extensively re-furbished to enable it to undertake studies to explore the toxicity of inhaled nanomaterials.

Photo: PHE

Rachel Smith

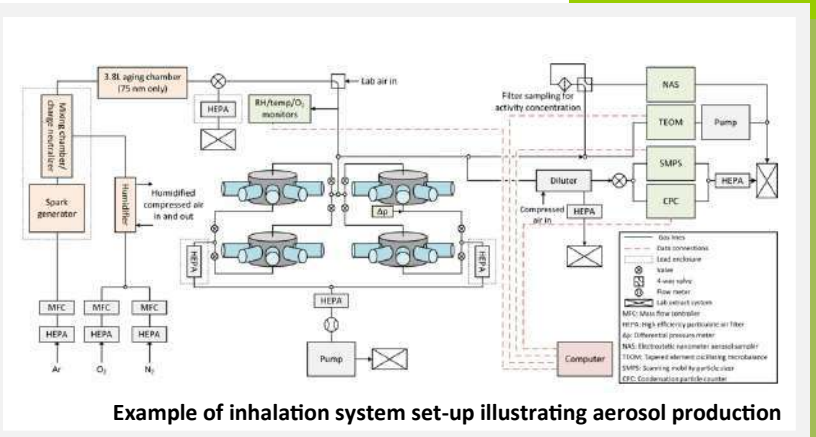
The facility is flexible and has a range of aerosol production, delivery and characterisation options. Aerosols can be generated from carbon or metallic electrodes using a spark generator, and carbon nanotube aerosols can be produced using a 'NIOSH style' acoustic aerosol generator. Aerosols can be generated from materials in dispersions using various atomisers and nebulisers. Aerosols can be delivered to a range of small rodents, both nose-only and whole-body, and to cell cultures using a CultexTM system. We have an extensive range of aerosol characterisation equipment to cover aerosols from nano to micron sized. On-line equipment to measure aerosol particle size distributions includes: TSI Aerodynamic Particle Sizer (APS), TSI Scanning Mobility Particle Sizer (SMPS) with standard and nano-DMA, and nano-MOUDI cascade impactor. Aerosol mass concentrations are measured using filter based gravimetric methods and on-line using a Tapered Element Oscillating Microbalance (TEOM). Aerosol particles can also be sampled onto EM grids using a number of options including an electrostatic precipitator, for post-exposure analysis. The temperature, humidity and oxygen content of the aerosol delievered is also monitored continuously during exposures.

Photo: PHE

Nose-only aerosol delivery system

The facility currently focuses primarily on inhalation toxicity studies using non-radioactive nano-sized aerosols, however, it is possible to use radioactive aerosols in the facility. For example, a recent study to explore the deposition, clearance and translocation of nano-sized aerosol particles following inhalation was performed using nano-sized iridium-192 aerosol particles produced using an iridium-192 electrode in one of the aerosol spark generators. This study made use of radioactive counting and analysis equipment from the significant range available at CRCE.

CRCE is open for collaboration and welcomes suggestions for projects with partners.



Example of inhalation system set-up illustrating aerosol production

Photo: PHE

ID Card:

Exposure type:
Internal, Inhalation

Source:
Various options

Dose rate:
Variable

Irradiation type:
All

Irradiated organism type:
Cells, small rodents

Address:
Centre for Radiation, Chemical and Environmental Hazards
Harwell Science Campus,
Didcot,
Oxfordshire OX11 0RQ
UK

Access:
Joint research collaborations

Supporting lab:
Radioactive counting, radiochemical analysis, cell culture, dissection

Internet link:
NA

Contact:
Rachel Smith,
Rachel.Smith@phe.gov.uk
+44 (0)1235 825191

Related to:

SIZE DEPENDENT DEPOSITION OF INHALED NANOPARTICLES IN THE RAT RESPIRATORY TRACT USING A NEW NOSE-ONLY EXPOSURE SYSTEM. Buckley A, et al. (2016). J Aerosol Science and Technology

PARISII

Internal contamination facility for rodents

The international scientific community, and particularly scientists in the field of radiation protection in Europe, are confronted with the effects of chronic exposure to low concentrations of radionuclides, a problem highlighted by the consequences of the accident at the Fukushima nuclear power plant. To tackle this problem requires implementation of *in vivo* experimental studies based on the effects of long term exposure of rodents (rats and mice), complemented by *in vitro* studies. This type of research programme requires an authorized animal facility for rodents (rats, mice) contaminated by radionuclides, and radiotoxicology laboratories for the exploitation of biological material. This is the aim of PARISII, an experimental platform unique in Europe and operational since September 2017.

Rodents can be exposed either by ingestion or inhalation in order to study the effects of internal contamination, notably by different radionuclides such as radioactive uranium, cesium and strontium, over the short, medium and long term (up to 24 months). Exposure to some radiopharmaceuticals is also possible. This platform is suitable for conducting research projects on environmental, occupational and accidental situations complementary to epidemiological studies.

PARISII includes a fully-equipped experimental platform with 850 m^2 dedicated to *in vivo* experiments and 600 m^2 to associated laboratories:

- Eight rooms for housing rats (1300) and mice (1500) in racks with ventilated cages, and auxiliary rooms (laundry, storage).
- A behavioural studies laboratory with different tests (open-field test, elevated-plus maze, water-maze, forced swim test, rotarod test…).
- An inhalation platform using nose-only inhalation chambers, including one for polydispersed micronic aerosols and another for nanosized aerosols.
- Several laboratories dedicated to surgery, biochemistry, radiochemistry, molecular biology, microscopy, histology and electrophysiology.
- Two cell culture rooms (L2).

Photo: IRSN

Dr Laurence Roy

- Beta and gamma counters are available to monitor exposure and incorporation of radionuclides in the animals following euthanasia. A zooradiameter also allows beta and gamma measurements to be performed on live animals. Another group of laboratories is dedicated to the preparation of biological samples (calcination and mineralization) for subsequent analysis by ICP-MS.

PARISII is open to national and international scientific collaboration with both academia and the private sector. These collaborations are supported by IRSN's multidisciplinary research teams, which include toxicologists, radiobiologists, chemists, veterinarians, and physiology and animal experiment technicians. Special attention is given to the housing and care of the animals to ensure their well-being, in line with animal ethics guidelines and regulations.

Photo: F. Acerbis/IRSN

Clockwise from top left: (1) Ratroom, (2) Inhalation glove box for micro and nanoparticles exposure, (3) Procedure room (surgery, dosing and sampling, euthanasia…), (4) Behavioural laboratory, with Morris Water Maze apparatus, (5) Mouse room

Assessment of the central effects of natural uranium *via* behavioural performances and the cerebrospinal fluid metabolome, Lestaevel P., Grison S., Favé G., Elie C., Dhieux B., Martin J. C., Tack K., Souidi M. (2016), Neural Plast, 2016, 9740353

DNA damage induced by Strontium-90 exposure at low concentrations in mesenchymal stromal cells: the functional consequences, Musilli S., Nicolas N., El Ali Z., Orellana-Moreno P., Grand C., Tack K., Kerdine-Römer S., Bertho J. M. (2017), Sci Rep, 7, 41580

ID Card:

Exposure type:
Internal contamination

Sources:
U, Sr, Cs, Pb, C, Co,
H Radiopharmaceuticals

Dose rate:
According to each radionuclide and within administrative authorization

Irradiation type:
Alpha, beta, gamma

Irradiated organism type:
Cells, animals (rodents)

Address:
IRSN
31 avenue de la Division Leclerc
92262 Fontenay-aux-Roses Cedex,
France

Access:
Open to collaboration

Supporting lab:
SPF animal facility, Inhalation chambers, Biomolecular lab, Biochemistry lab, Cell culture lab, Imaging, Behaviour platform

Internet link:
https://www.irsn.fr/EN/Research/Scientific-tools/experimental-facilities-means/

Contact:
Laurence Roy
parisii@irsn.fr
+33 1 58 35 72 52

Related to:
EURADOS
MELODI

CHAPTER 1 Exposure platforms

e) Observatory sites

THE CHERNOBYL EXCLUSION ZONE

A radioecological observatory
A focus for joint, long-term, radioecological research

Radioecological Observatories are radioactively (and chemically) contaminated field sites that will provide a focus for joint, long-term, radioecological research. The Chernobyl Exclusion Zone (CEZ) Observatory is one of four proposed by the EC funded STAR and COMET projects.

Site overview

The Chernobyl Exclusion Zone contains the most radioactively contaminated sites in the world. The area is highly heterogeneously contaminated by a number of radionuclides including ^{137}Cs, ^{90}Sr, ^{241}Am and Pu-isotopes. The Ukrainian area of the CEZ (approximately 2600 km^2) contains forests, abandoned farmlands, wetlands, flowing and standing waters, deserted villages and urban areas. The Belarusian CEZ (approximately 2160 km^2) consists mainly of forests, swamps, marshes and peat-bogs.

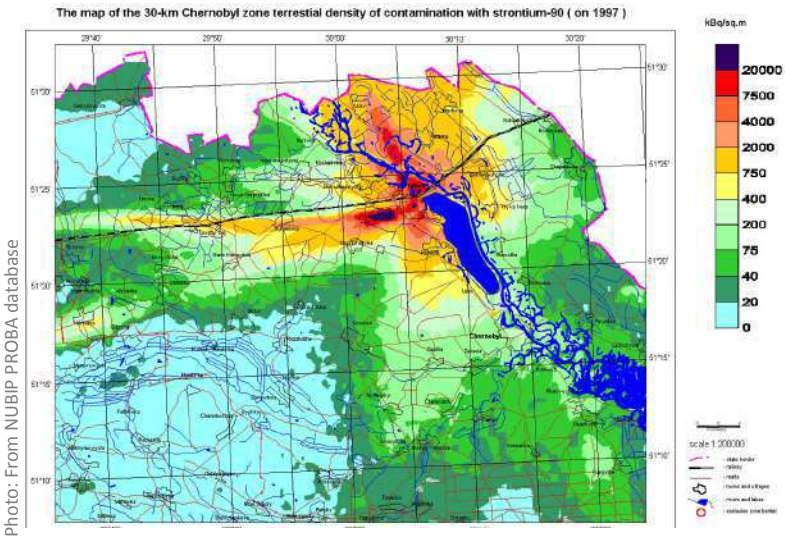


Photo: From NUBIP PROBA database

Sr-90 in the Ukrainian CEZ

(http://www.radioecology-exchange.org/content/nubip)

The site is species rich with >400 species of vertebrates, including 67 ichthyoids, 11 amphibians, 7 reptilians, 251 birds and 73 mammals; many are Red Book species. The climate is temperate-continental with the growing period beginning around mid-April and ending in late October.

Why is the CEZ a Radioecological Observatory?

The CEZ has many features making it an important radioecological site:

- Contamination levels are such that the behaviour/transfer/mobility of a number of radionuclides can be studied (^{137}Cs, ^{90}Sr, ^{241}Am, Pu-isotopes, U-isotopes, ^{129}I, ^{14}C and ^{99}Tc)
- The presence of 'hot particles' means that their behaviour in the environment can be studied
- Dose rates remain sufficiently high that we may expect to observe effects on wildlife in some areas
- Published results on radiation effects from the CEZ are contentious with a lack of agreement on interpretation amongst scientists (see http://dx.doi.org/10.1002/ieam.238)

Photo: N Bersford/CEH

Pr Nick Beresford

- A wide range of species and habitats are present.

ALLIANCE activities in the CEZ

COMET partners have collaborated to conducted studies on radionuclide transfer to wildlife and agricultural products, and also radiation effects to a range of wildlife species (frogs, earthworms and plants). Datasets from the CEZ presenting spatial data on radionuclide deposition, soil properties, land use and radionuclide activity concentrations in wildlife are currently being prepared for submission to openly accessible data centres. COMET also ran a field studies course for international students in the CEZ.

On-going and future ALLIANCE activities include: jointly supervised PhD on radiation effects in birds and collaboration in RED FIRE, a study looking at the effects of radiation on the Red Forest as it recovers from a largescale fire in the summer of 2016.

Photo: Nick Bersford/NERC-CEH

ID Card:

Type of ecosystem contaminated:
Terrestrial and freshwater (and urban)

Compartment of environment contaminated:
All sample types

Contamination source:
Radionuclides released by the Chernobyl accident (including Cs-137, Sr-90, Am-241, Pu-isotopes, U-isotopes, I-129, C-14, Tc-99) including in the form of 'hot particles'

Radioactivity or dosimetric characteristics:
Activity concentrations and dose rates

Total contaminated area:
>4700 km^2

Species exposed/present in the site:
Area is species rich, e.g. 400 species of vertebrate animals, including: 67 ichthyoids, 11 amphibians, 7 reptilians, 251 birds and 73 mammals

Authorized related data/samples:
http://www.radioecology-exchange.org/content/chernobyl-exclusion-zone

Presence of an associated contamination:
No significant evidence for this

Supporting lab:
Basic laboratory facility are available in the Chernobyl Exclusion Zone

Access:
Require permission - achieved through a local collaborator. Work will require pre-planning to ensure permissions etc. are in place

Internet link:
http://www.radioecology-exchange.org/content/chernobyl-exclusion-zone

Other links
http://www.radioecology-exchange.org/content/radioecological-observatories)
http://www.ceh.ac.uk/news-and-media/blogs/understanding-ecological-impact-major-fire-chernobyl-red-forest)
https://resy5.iket.kit.edu/CONFIDENCE/

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Related to:
ALLIANCE

CHERNOBYL CATASTROPHE AND CONSEQUENCES, Smith J. T. , Beresford, N.A. (2005) Springer Praxis Books, Praxis Publishing Ltd, Chichester, UK, ISBN: 9783540238669, https://link.springer.com/book/10.1007%2F3-540-28079-0

THIRTY YEARS AFTER THE CHERNOBYL ACCIDENT: WHAT DO WE KNOW ABOUT THE EFFECTS OF RADIATION ON THE ENVIRONMENT?, Barnett C., Welch S,. (2016) COMET Workshop report, http://bit.ly/2p2BPVH

Forest observatory site in Yamakiya

Fukushima observatory sites contaminated by radiocaesium

Fukushima University has established forest observatory sites in Yamakiya, Tsushima and Okuma (Fukushima). The Yamakiya forest observatory site (37º35'20.5"N, 140º42'37.1"E) is located 35 km north-west of the TEPCO* Fukushima Daiichi Nuclear Power Station and has been operational since it was established in 2014.

Photo: H. Tsukada/IER

Forest observatory site in Yamakiya, Fukushima

The site is a cedar-dominant community of approximately 7 ha, with an elevation difference of approximately 100 m. Average temperature is 12.7°C (-9.3-37.1°C) and annual precipitation is 1220 mm ·y^{-1}.

The major soil type is Andosols and it supports a planted Japanese Sugi cedar stand. The ^{137}Cs inventory is 670 ± 400 kBq·m^{-2} (n=6) and ^{137}Cs activity concentration in surface soil (humus + depth of 0-10 cm) is 19 ± 8.3 Bq·g^{-1}. The distributions of ^{137}Cs in exchangeable, bound-to-organic matter and residual fractions in the 0-5 cm soil layer collected in 2015 were 5%, 4% and 91% respectively, with most of the ^{137}Cs in the strongly bound fraction.

No other contamination by heavy metals was observed in the area. Aggregated Transfer Factor (TF) for ^{137}Cs, defined as the concentration of ^{137}Cs in animals (Bq·kg^{-1} FW) divided by soil ^{137}Cs levels (Bq·m^{-2}), has been determined. Tags in earthworm, frog, newt, bee, mouse and boar were 0.0022, 0.0014, 0.00049, 0.00016, 0.012 and 0.0019 respectively.

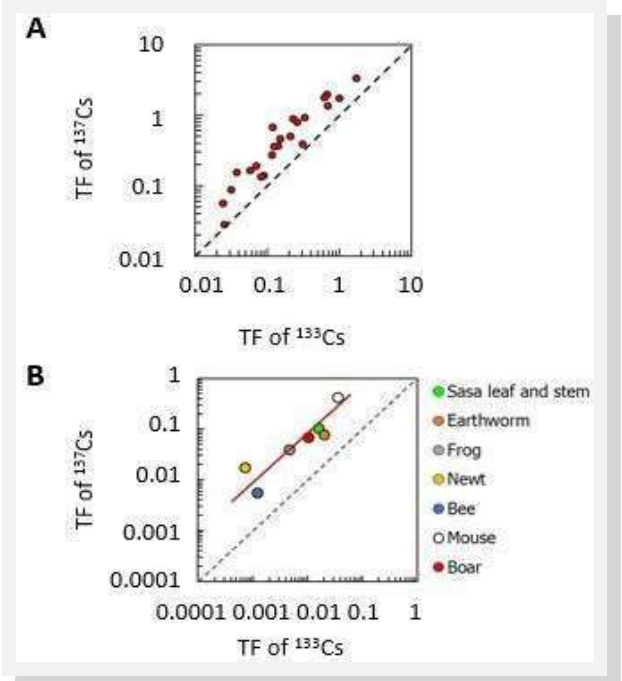
The mean ^{137}Cs radioactivity concentration in the Montane brown frog collected at the Yamakiya observatory site in 2016 was 1.12 ± 0.81 (n=20) Bq·g^{-1} FW. The range of radioactivity concentration (0.08 - 3.2 Bq·g^{-1} FW) was two orders of magnitude, even in the limited area. The external radiation dose in the frog from radiocaesium ($^{134+137}$Cs) calculated using the ERICA tool was 4.2 µGy·h^{-1}. The internal radiation dose in the frog was 0.2 µGy·h^{-1}, which was 5% of the external dose.

Photo: H. Tsukada/IER

Dr Hirofumi Tsukada

Previously reported TF from substrate to mushroom of ^{137}Cs is well correlated with that of stable ^{133}Cs. This suggests that the transfer of ^{133}Cs from substrate to mushroom is utilised as a natural analogue of radiocaesium. The transfer factors, defined as the concentration of ^{137}Cs in plant and animals divided by that in surface soil, were well correlated with the transfer factor of ^{133}Cs. This indicates that the behaviour of ^{133}Cs can be regarded as a useful analogue for predicting long-term changes of radiocaesium in the forest environment.

*Tokyo Electric Power Company



A) Comparsion of transfer factor of stable ^{133}Cs and ^{137}Cs in mushroom in 1992.

B) Comparsion of transfer factor of stable ^{133}Cs and ^{137}Cs in plants and animals collected in Yamakiya, Fukushima.

Radiocesium distribution and fluxes in the typical *Cryptomeria japonica* forest at the late stage after the accident at Fukushima Dai-Ichi Nuclear Power Plant, Yoschenko V., Takase T., Konoplev A., Nanba K., Onda Y., Kivva S., Zheleznyak M., Sato N., Keitoku K. (2017), J Environ Radioact, 166, 45-55

Transfer of radiocaesium and stable caesium from substrata to mushrooms in a pine forest in Rokkasho-mura, Aomori, Japan, Tsukada H., Shibata H., Sugiyama H. (1998), J Environ Radioact, 39, 149-160

ID Card:

Type of ecosystem contaminated:
Semi-natural forest environment

Compartment of environment contaminated:
Soil, water, sediments, plants, animals

Contamination source:
Radiocaesium, radioiodine and other radionuclides from TEPCO's FDNPS accident

Radioactivity or dosimetric characteristics:
Radiocaesium is the major source of contamination, and Pu, ^{90}Sr et al. are also deposited in the surrounding areas of the FDNPS

Total contaminated area:
953 km^2 (>20 mSv·y^{-1}, 7% of Fukushima Prefecture)

Species exposed/present in the site:
Japanese cedar, pine and broad-leaf trees, bamboo, fern, sasa plant, earthworm, frog, newt, mouse, wild boar, etc.

Authorized related data/ samples:
COMET report, publications

Supporting lab:
Institute of Environmental Radioactivity (IER) at Fukushima University supports sampling, pretreatment and analyses

Access:
Permission from IER is required

Address:
Yamakiya, Kawamata, Fukushima Prefecture

Contact:
Pr. Dr Hirofumi Tsukada
hirot@ipc.fukushima-u.ac.jp
+81 24 503 3013

Related to:
ALLIANCE

Belgian NORM Observatory Site

Opportunities for joint, long-term radioecological research

To ensure joint, long-term radioecological research, four observatory sites have been proposed by the EU-projects STAR and COMET. Among these is the Belgian NORM observatory site, a calcium difluoride sludge heap from the phosphate industry, partly covered with vegetation such as trees, grasses and shrubs. Levels of ^{226}Ra contamination of between 2000 and 6000 Bq kg^{-1} can be found in the soil and sludge in combination with contaminants such as As, Cd, Cr, Pb and Zn. Although remediation measures are planned, approximately 7 ha of the site are available for the next 10 to 15 years to perform long-term radioecological research in a NORM-contaminated terrestrial ecosystem.

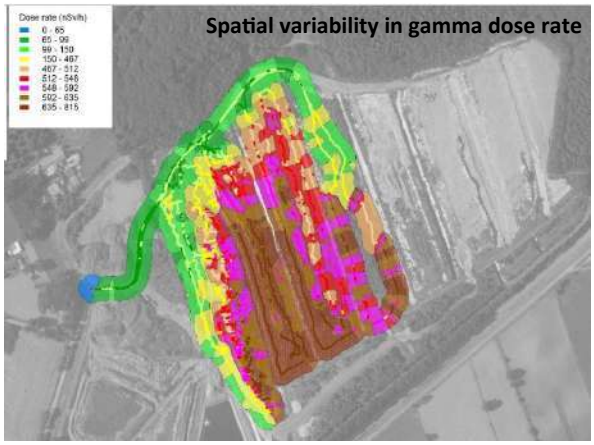


Photo: SCK•CEN

Since the site is private domain, by agreement with the site owner, permission to access and work there has to be obtained *via* SCK•CEN (nathalie.vanhoudt@sckcen.be) and is subject to signature of a working agreement.

In the COMET project, a working group has been created for the site in order to define common goals and establish joint research actions. Several research institutes have shown an interest, and common research activities have begun.

For example, a monitoring campaign was carried out to map the gamma dose rate at the site. Subsequently, the spatial variability in contaminant concentrations was evaluated by radiological and chemical characterisation of 9 superficial soil samples. Additionally, a sampling campaign was undertaken to determine the radionuclide distribution between soil (at different depths), tree roots, needles, bark, grasses, moss, etc. A leaching experiment was performed for U- and Th-isotopes and ^{210}Po to evaluate the mobility of radionuclides in the soil. Further investigations will deepen the knowledge of the processes that determine radionuclide mobility and bioavailability in soil and sludge.

Future plans for collaborative studies at this site include:

Photo: Patrick Liebens

Dr Nathalie Vanhoudt

- Understanding and modelling the long-term influence of vegetation on radionuclide dispersion in forest ecosystems. As part of the TERRITORIES project (EU-CONCERT funded project), a pine forest plot is being instrumented at the site, with equipment to follow the cycling of naturally occurring radionuclides and other elements in the trees, integrated with monitoring of the energy and water cycles. It is also planned to monitor the radionuclide content in seasonal samples of soil, sludge, tree roots, bark, wood, branches, tree needles and litterfall.
- Additional sampling campaigns will be set up to further characterise the site in order to gain more in-depth knowledge of the processes that determine radionuclide mobility and bioavailability in soil and sludge, and to compare radionuclide behaviour at different NORM sites.
- The resulting site-specific data will be used to improve and/or validate radiological models and to assess their transferability to different environments.
- The data and knowledge gathered will be shared between the partners to ensure efficiency, continuity and sustainability in radioecological research.

Photo: Nathalie Vanhoudt/SCK•CEN

ID Card:

Type of ecosystem contaminated:
Terrestrial - forest

Compartment of environment contaminated:
Soil, sludge, vegetation

Contamination source:
Naturally occurring radionuclides present in the sludge (including ^{238}U, ^{226}Ra, ^{210}Pb and ^{210}Po)

Radioactivity or dosimetric characteristics:
Activity concentrations: e.g. 4-6 Bq g^{-1} ^{238}U and 2-6 Bq g^{-1} ^{226}Ra
Dose rates: up to 800 nSv h^{-1}

Total contaminated area:
Approximately 7 ha

Species exposed/present in the site:
Trees, shrubs, herbs, grasses, insects, etc.

Presence of an associated contamination:
Co-contaminants such as As, Cd, Cr, Pb and Zn

Supporting lab:
No laboratory infrastructure available on site. Subject to agreement, SCK•CEN laboratories can be made available

Access:
Permission to access and work at the site has to be obtained *via* SCK•CEN (nathalie.vanhoudt@sckcen.be) and is subject to signature of a working agreement

Internet link:
http://www.radioecology-exchange.org/content/belgian-norm-site

Contact:
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+32 14 33 21 12

Related to:
ALLIANCE
NERIS

Concentrations and distributions of Al, Ca, Cl, K, Mg and Mn in a Scots pine forest in Belgium, Gielen S., Vives i Batlle J., Vincke C., Van Hees M., Vandenhove H. (2016), Ecological Modelling 324, 1-10
Modelling water and ^{36}Cl cycling in a Belgian pine forest, Vives i Batlle J., Vandenhove H., Gielen S. (2014), 3rd Int. Conf. Radioecol. & Env. Radioact. (ICRER), Paper OP-035

IRSE Experimental Farm

Investigation of radionuclide transfer to plants and animals

Unauthorised agricultural activities on the Semipalatinsk Test Site (STS) have been carried out by the local population following the formal closure of the test site in the 1990s. Today, there are about a hundred pastoral farms at the STS, mainly focused on horse, cattle and sheep-breeding, and on forage production.

Since 2007, the Institute of Radiation Safety and Ecology (NNC RK - IRSE) has been running diverse natural experiments to investigate the parameters of radionuclide transfer from soil into agricultural products, in order to assess the opportunities for future agricultural use of the STS territory (18,500km^2). These investigations are conducted on a purpose-built experimental farm located in one of the highly contaminated areas of the test site ("Experimental Field"). High activities of the radionuclides ^{3}H, ^{137}Cs, ^{90}Sr, $^{239+240}$Pu and ^{241}Am in the soil are found within the limits of the testing sites, such as "Experimental field", "Degelen", "4A" and other areas (see Figure).

The natural experiments are performed during the summer months. These involve farming and investigation of livestock and birds typical to the region (large and small cattle, horses, pigs, wild boars, hens, broilers), as well as agricultural crops and vegetation (gramineae, fruits, coleworts, roots, tuberiforms, berries – 21 species in total). Different groups of animals and birds were fed with contaminated forage, soil and water; in some of the experiments, the animals were given ware containing a solution of known amounts of radionuclides.

The forage and soil were prepared at diverse contaminated testing sites within the STS with different radionuclide contamination characteristics (places used for surface nuclear tests, tests of combatant radioactive substances, areas of radioactive waterways). Investigated crops and vegetation were sown or planted out at the experimental farm where high concentrations of radionuclides in soil are observed.

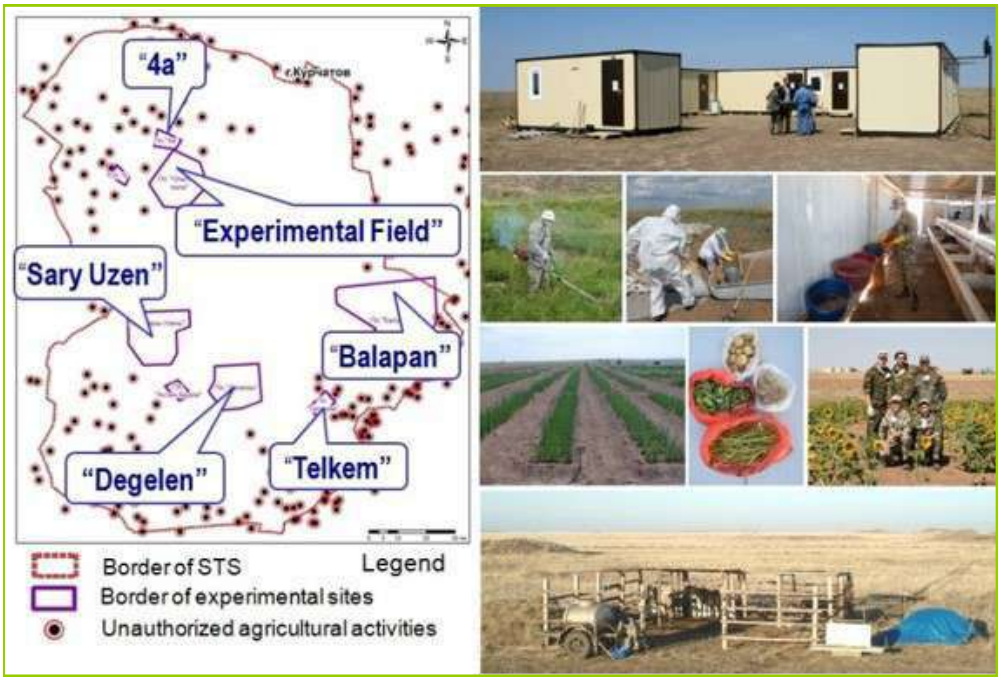
Photo: Z. Baigazinov/IRSE NNC RK

Dr Zhanat Baigazinov

For animals, the dynamics of accumulation and excretion of radionuclides into edible products along with the distribution of radionuclides in organs and animal tissues have been studied and transfer factors to edible products have been calculated (Tf and CR values). For crops, soil to plant transfer coefficients (Af values) have been determined.

Although high activities of the radionuclides ^{3}H, ^{137}Cs, ^{90}Sr, $^{239+240}$Pu and ^{241}Am in the soil are found within the testing sites of the STS, the investigations confirm that agricultural products can be safely produced even within some of these testing grounds (concentration in the products will be well below permissible levels). For animals, this is because of the relatively low migration of radionuclides in the system "soil – vegetation – livestock products". This fact is a peculiar feature of the STS contamination. Exception is the areas around the Shagan River and adjacent to water sources that come from the "Degelen" site, where increased concentrations of ^{3}H are possible in animal and crop products.

Photo: Z. Baigazinov/IRSE NNC RK



Unauthorised agricultural activities on the STS (left). The Experimental Farm (right).

ID Card:

Type of ecosystem contaminated:
Steppe, semi-desert environment

Compartment of environment contaminated:
Soil, water, sediment, plants, animals

Contamination source:
Different nuclear experiments, mostly atomic bombs

Radioactivity or dosimetric characteristics:
Radiocesium, radio strontium, transuranium elements, tritium and others can reach MBq

Total contaminated area:
STS territory is 18,500 km^2

Species exposed/present at the site:
Typical for Kazakhstan region: all types of flora and fauna (see text)

Authorised related data/ samples:
Collection of proceedings of IRSE, publications

Presence of an associated contamination:
Radionuclides, heavy metals

Supporting lab:
Institute of Radiation Safety and Ecology (NNC RK)

Address:
Krasnoarmayskaya 2, 071100, Kurchatov, Kazakhstan

Access:
Permission from Energy Control Committee is required

Internet link:
http://irse.nnc.kz/

Contact:
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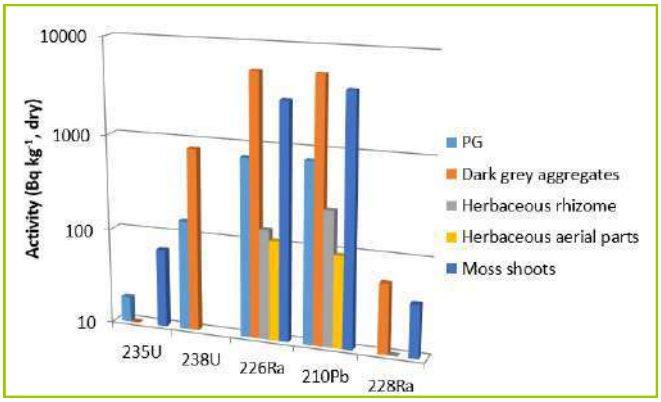
Related to:
ALLIANCE

Transfer of tritium into laying hen's meat and eggs at prolonged intake with atmospheric air, water and grass meal, Baigazinov Z. A., Lukashenko S. N., Karatayev S. S., Panitski A. V., Mamyrbayeva A. S., Baigazy S. A., Kozhakhanov T. Y., Subbotina L. F. (2017), J Environ Radioact, 178-179, 110–115
Accumulation of artificial radionuclides in agricultural plants in the area used for surface nuclear tests, Kozhakhanov T. E., Lukashenko S. N., Larionova N. V. (2014), J Environ Radioact, 137, 217-226

Phosphogypsum stack at Barreiro, Portugal

Radionuclides, metals and rare earths in phosphogypsum

The Portuguese phosphate industry began in the 1950's with a facility located in the city of Barreiro, on the south shore of the Tejo river estuary. For decades, the plant produced phosphoric acid and dumped tons of phosphogypsum (PG) in sludge ponds. The decanted PG was stockpiled in a selected area of the nearby shoreline. Initially the stack was approximately 1.1 x 10^6 m^3 but has expanded, now occupying an area of about 5.5 x 10^4 m^2. The surface of the stack is covered with patches of wild vegetation. As the land on which the landfill is located is in the private domain, permission to access it for field work campaigns has to be obtained directly from the owner, Baia do Tejo S.A.



Concentrations of natural radionuclides in whole PG and dark grey aggregates, aerial parts and rhizomes of herbaceous *Plantago coronopus* and shoots of moss *Bryum argenteum*.

A recent survey revealed the mineralogical and chemical aspects, and the magnitude of the concentrations of trace elements, rare earths and natural radionuclides in the raw materials, and the concentrations accumulated in the herbaceous plant, *Plantago coronopus*, and in the moss, *Bryum argenteum*.

Mineralogical analysis by X ray diffraction showed, in addition to gypsum, some small and variable amounts of brushite and bassanite as well as traces of quartz, feldspars and Ti oxides. The homogeneity of silt size particles was found to be disturbed by the presence of dark grey, white and layered grey aggregates of crystals. All aggregates were gypsum rich. In the dark grey aggregates, high amounts of bassanite and traces of Ti oxide were present; in the white aggregate, a significant amount of brushite was found; in the layered grey aggregates, bassanite was also detected.

Photo: J. Corisco/IST

Dr José A. Corisco

Neutron activation analysis revealed a wide heterogeneity among the concentrations of elements in the PG matrix, with the dark grey aggegates having the highest concentrations of Sc, Cr, Zn, Ga, Ba, REE, Ta, W, Th and U. The concentration ratio (CR) between the vegetation and the underlying PG showed two values above 1, 10 and 100 in herbaceous *P. coronopus*, namely, Co, W >1, Zn, Br >10 in rhizomes and Co, Zn, As, W >1 and Br >100 in aerial parts. CRs for all the elements analysed in the moss *B. argenteum* exceeded the unity, notably for rare earth elements, in clear contrast to findings observed for herbaceous plants.

Natural radioactivity analysis performed by gamma spectrometry revealed similar levels of ^{226}Ra (735±70 Bq kg^{-1}) and ^{210}Pb (776±95 Bq kg^{-1}) in the whole PG, notably in the dark grey aggregates within its matrix: 5385±473 Bq kg^{-1} ^{226}Ra and 5485±2302 Bq kg^{-1} ^{210}Pb respectively. The herbaceous plant *P. coronopus* and the moss *B. argenteum* showed significant concentrations of ^{226}Ra and ^{210}Pb, with *B. argenteum* exhibiting higher concentration levels than the underlyng PG in the root system: 2900±200 Bq kg^{-1} dry ^{226}Ra, 4000±660 Bq kg^{-1} dry ^{210}Pb.

Photo: J. Corisco/IST

A) Landscape on top of the PG stack; B) slope of PG stack on the estuarine shoreline; C) Sampling the upper 20 cm layer of the PG stack; D) Sampling the wild vegetation growing on the PG stack.

Natural radionuclides, rare earths and heavy metals transferred to the wild vegetation covering a Phosphogypsum Stockpile at Barreiro, Portugal, Corisco J. A., Mihalík J., Madruga M. J., Prudêncio M. I., Marques R., Santos M., Reis M. (2017), Water Air Soil Pollut, 228, 235

Distribution of natural radionuclides, rare earth elements, metals and metalloids in a Phosphogypsum Stockpile, Madruga M. J., Prudêncio M. I., Corisco J. A., Mihalik J., Marques R., Santos M., Reis M., Paiva I., Dias M. I. (2019), Int J Waste Resour, 9 (1), DOI: 10.4172/2252-5211.1000363

TÉCNICO LISBOA

ID Card:

Type of ecosystem contaminated:
Terrestrial

Compartment of environment contaminated:
Soil, sediments, etc.

Contamination source:
Phosphogypsum

Radioactivity or dosimetric characteristics:
Becquerel, Gray

Total contaminated area:
~5.5E+04 m^2(total area of the PG stack)

Species exposed/present at the site:
Herbaceous plants, moss on the PG stack

Presence of an associated contamination:
Natural radionuclides, heavy metals and rare earth elements

Address:
Barreiro, Portugal

Access:
No fences, permission from private owner is required for sampling

Internet link:
http://www.baiadotejo.pt/en/park/barreiro

Contact:
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(+351) 219 946 269

Related to:
ALLIANCE

CHAPTER 1 Exposure platforms

f) Metrology exposure platforms

Exposure platforms

Laboratory for retrospective Radon and Thoron dosimetry

Advancing retrospective radon and thoron dosimetry

The infrastructure for retrospective radon and thoron dosimetry at Sofia University in Bulgaria was completed in 2015 in the framework of the DoReMi project. Its main purpose is to provide low dose retrospective dosimetry for epidemiological studies in which radon/thoron is the primary risk agent or a confounder. However, it can be used for other types of research involving radon/thoron exposure, detector response studies, radon/thoron measurement in buildings and in the environment, etc.

The infrastructure comprises two basic units:
1) Radon (Rn-222) and Thoron (Rn-220) Exposure Facility (RTEF);
2) Laboratory for Electro-Chemical Etching of track-etch detectors (LECE). The emphasised method for retrospective measurements employs CDs/DVDs stored indoors as track-etch detectors.

Photo: D. Dimitrov, Sofia University

Dobromir Pressyanov

designed thermostat that can support programmable static or dynamic temperature regimes.

The RTEF is suitable for:
- Experiments at different (static or dynamic) reference radon and/or thoron concentrations for exposure times ranging from less than an hour to several months (e.g. for calibration of radon and thoron detectors, study of the detector's response and cross-talk between the radon and thoron signals in a mixed atmosphere, exposure of cell cultures, studies of radon sorption and desorption in biological substrates and other materials);
- Exposures under dynamic activity concentration and temperature reproducing the conditions in the real environment.

The LECE is oriented mostly to etching alpha tracks created by radon/thoron and their progeny in CDs/DVDs or other solid state nuclear track detectors. Various etching regimes at HV (effective) within 100 – 4000 V and a frequency of 6 kHz are possible. High precision is achieved by individual *a posteriori* calibration of each disk by additional exposure in the RTEF after the disk is collected. The infrastructure at Sofia University has sufficient capacity to manage the workload of large-scale epidemiological studies or other measurement campaigns

Photo,

The RTEF and the research team (from left: S. Georgiev, K. Mitev, I. Dimitrova, D. Pressyanov)

The RTEF is designed for exposures at a wide range of activity concentrations and temperatures. It has the unique capability to support not only static but also dynamic reference exposure conditions in which radon and thoron concentrations and/or the temperature follow pre-programmed time functions. Mixed as well as pure radon and thoron atmospheres can be created with programmable levels/ratios.The RTEF is illustrated in the diagramme and photo, and its capabilities are summarised in the ID card. The activity concentration in the system is controlled by setting the flow regime and the flow rate of air through the sources of radon and thoron. The pump flow rate is controlled by a computer with dedicated hardware and software. The reference activity of radon and thoron in the system is measured by calibrated monitors (AlphaGUARD or RAD7). The temperature inside the exposure vessel is maintained by a specifically

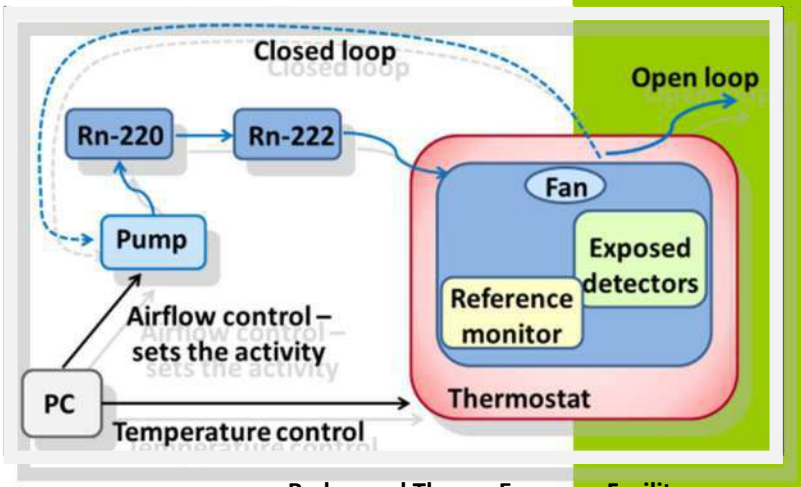


Photo: Faculty of Physics, Sofia University

Radon and Thoron Exposure Facility

ID Card:

Exposure type:
Exposure to staic or dynamic radon/thoron activity concentrations with time-dependent temperature regime

Source:
^{222}Rn and ^{220}Rn

Dose rate:
^{222}Rn: 1-2000 kBq/m^3
^{220}Rn:2-1800kBq/m^3

Temperature range:
-15°C to +60°C

Irradiation type:
alpha particles (5.5, 6.0,6.1,6.3,6.8,7.7,8.8 MeV)

Possible targets:
^{222}Rn and ^{220}Rn detectors cells

Address:
5 James Bourchier Blvd, Sofia 1164, Bulgaria

Access:
Available upon request and task specification

Supporting lab:
Laboratory of Dosimetry and Radiation Protection, Faculty of Physics, Sofia University "St Kliment Ohridski", Sofia, Bulgaria

Internet link:
http://doremi-noe.net/irradiation_facilities

Contact:
Dobromir Pressyanov
pressyan@phys.uni-sofia.bg
+359 2 8161 268

Related to: DOREMI

LABORATORY FACILITYTO CREATE REFERENCE RADON+THORONATMOSPHERE UNDER DYNAMIC EXPOSURE CONDITIONS D. Pressyanov, K. Mitev, S. Georgiev, I. Dimitrova, J. Kolev., J. Environ. Radioact., 166 (2017), 181-187

OPTIMIZATION OF ETCHING CONDITIONS OF CDs/DVDs USED AS DETECTORS FOR Rn 222 D.Pressyanov, K. Mitev, S. Georgiev, I. Dimitrova,. Radiat. Meas. 83 (2015), 36-40

CALIBRATION LABORATORY AT KIT

Accreditation for irradiations according to ISO 17025

The Irradiation Facility at Karlsruhe Institute of Technology provides photon, electron and neutron irrradiations in the dose range from 50 µGy up to 5 Gy. Dose rates vary from 2 µGy/h up to 80 mGy/h (air KERMA rate for photons). All doses can be converted to the appropriate operational quantities (e.g. Hp (3) or H*(10)) in Sieverts.

For photon irradiations, the facility uses 6 sources of Cs-137 at different activity levels ranging from 1E+7 Bq up to 1E+13 Bq, and two X -Ray tubes (soft X-rays with voltages up to 60 kV, hard X-rays up to 320 kV, currents up to 20 mA), in combination with different filters. The irradiation workbench, 8 metres in length, allows maximum field sizes of up to 100 cm x 100 cm (95% isodose). Mounting frames for different kinds of samples are available. Figure 1 shows the placement before irradiation of a 10 L ionisation chamber for low dose rate, located within the facility.

A Beta Secondary Standard (BSS2) with sources of Pm-147, Kr-85 and Sr-90/Y-90 (activities in the E+08 Bq range) is available for electron irradiation.

In 2009, the facilities for photon and electron irradiation were awarded an accreditation to the ISO/IEC 17025:2005 standard.

Neutron irradiations in air are performed using either a Cf-252 source (E+06 Bq, E=2.13 MeV, 11,3 neutrons/cm^2*s) or an Am-Be-Source (E+11 Bq, E=4.16 MeV, 225 neutrons/cm^2*s). The hall in which these irradiations are performed is constructed from wood materials to reduce backscatter. Application for accreditation of these irradiations is also planned in the near future.

Photo: Lukas Exner (KIT)

Lukas Exner

A solid state dosimetry laboratory using TLD and track-etch detectors is available, close to the facility. The irradiation facility was originally designed for the irradiation and calibration of active and passive dosemeters, but in addition has always been used for research and development. For example, both laboratories recently developed a dosemeter for monitoring doses to the eye lens in the appropriate quantity Hp(3). This new dosimeter has been used in a study on eye lens doses in the workplaces and took part in several intercomparison exercises.

Access to the facilities is available via research collaborations or service contracts for irradiations.

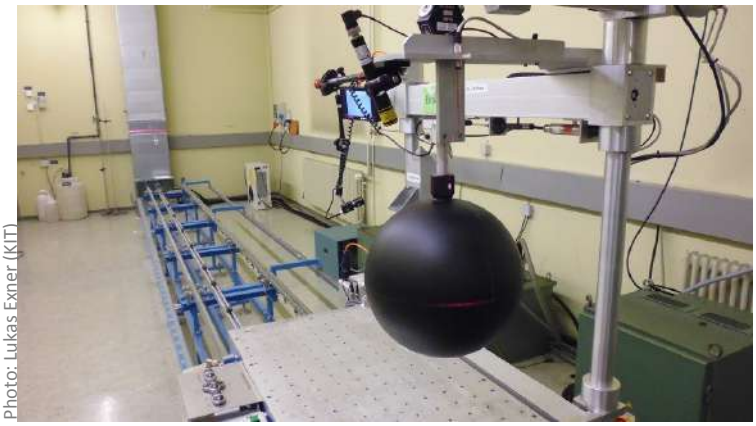


Photo: Lukas Exner (KIT)

The positioning of a 10L ionisation chamber for low dose rate before irradiation with photons. A moveable arm is used to move the chamber into the correct position, a Laser system is used to monitor the correct placement

Photo: Florian Arend (KIT)

A CAD-drawing of the photon irradiation set-up. The field generated by one of the ^{137}Cs sources is displayed. The X-Ray tubes with the different filter options mounted on the two wheels have been moved into the parking position

Behrens et al., 2016, Intercomparison of eye lens dosemeters, Radiation Protection Dosimetry (http://rpd.oxfordjournals.org/content/early/2016/03/22/rpd.ncw051.full, Radiat Prot Dosimetry (2016) doi: 10.1093/rpd/ncw051)

Burgkhardt B. et al., 2002, Experience in long-term neutron dose equivalent measurements using etched track detectors with (n, alpha) converters in moderator, Radiation Protection Dosimetry, 101, p579-584

ID Card:

Exposure type: *external*
Source:
Photons : Cs-137, X-Ray tubes
Electrons: Beta Secondary Standard BSS2
Neutrons: Cf-252, Am-Be
Dose rate:
2 µGy/h – 80 mGy/h (air Kerma)
Irradiation type:
Photons, Electrons, Neutrons
Irradiated organism type:
Samples and Measurement Devices

Address:
Karlsruhe Institute of Technology
Sicherheit und Umwelt
Kalibrierlabor
Hermann-von-Helmholtz-Platz 1,
76344 Eggenstein-Leopoldshafen

Access:
joint research collaborations, service contracts

Supporting lab:
solid state dosimetry laboratory

Internet link:
www.sum.kit.edu

Contact:
Lukas Exner
lukas.exner@kit.edu,
Phone: +49 721 608 26320
Christian Naber
christian.naber@kit.edu,
Phone: +49 721 608 22644

Related to:
MELODI, EURADOS

MELAF

Facility for high energy photon and electron radiation

The German National Metrology Institute (PTB-Physikalisch-Technische-Bundesanstalt) operates the Metrological Electron Accelerator Facility (MELAF) for service and research in the field of dosimetry for external beam radiotherapy. A custom-designed research electron linear accelerator (LINAC) and two commercially available medical LINACs, together with a Co-60 irradiation facility, offer excellent experimental conditions for investigations requiring high-energy photon and electron radiation. The PTB makes available its metrologically well-characterised radiation fields to external researchers from, for example, the field of radiobiology or medical radiation protection research.

Photo: A. Schüller/PTB

Dr Andreas Schüller

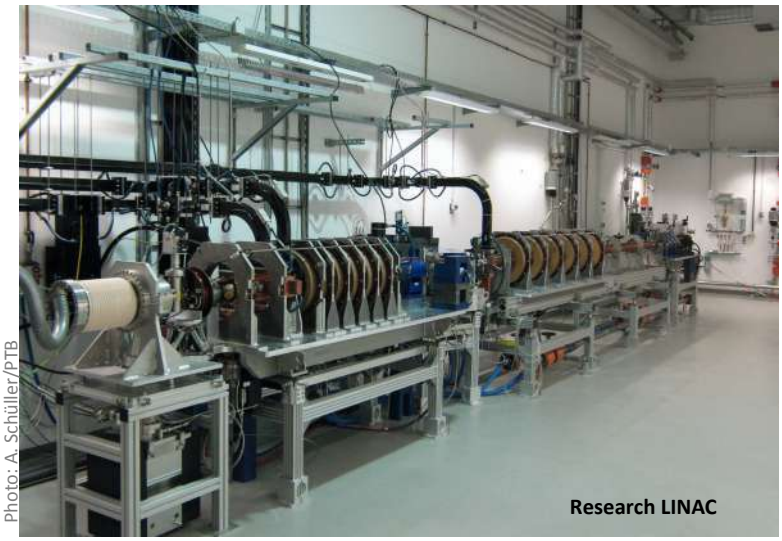


Photo: A. Schüller/PTB

Research LINAC

The MELAF is located in a dedicated building with four irradiation rooms. Two irradiation rooms are equipped with medical LINACs of the type *Elekta Precise Treatment System*. In total, 9 electron beam qualities (nominal energy 4 MeV to 22 MeV) and 6 photon beam qualities (nominal accelerating voltage 4 MV to 25 MV) can be generated. The LINACs provide a pulsed beam (6 Hz to 400 Hz, 3 µs pulse duration) and are equipped with a multileaf collimator which allows irregularly shaped fields of up to 40 cm x 40 cm at 1 m distance. Typical dose rates are 0.1 Gy/min to 5 Gy/min.

The research LINAC consists of a low-energy section (0.5 MeV to 10 MeV) and a high-energy section (6 MeV to 50 MeV). At both sections the electron beam can be deflected into the dedicated beam line in its respective irradiation room. The properties of the beam, e.g. the spectral electron fluence or the beam current, are measured as absolute values with small uncertainties. Thus, radiation effects can be studied as a function of these quantities. The research LINAC provides a pulsed beam (1 Hz to 100 Hz, 2.5 µs duration), and the energy can be varied continuously. At the end of each beam line, the electrons either pass through an exit window for electron irradiations or impinge on a bremsstrahlung target for the generation of high-energy photons. Dose rates are up to several Gy/s.

The MELAF is also equipped with an irradiation facility for Co-60 gamma radiation (129 TBq as at May 2017). It generates a radiation field with a field size of 10 cm x 10 cm at a distance of 1 m from the source. Typical dose rates range from 3 Gy/min to 0.03 Gy/min depending on distance from the source (0.5 m to 5 m).

Ionisation chambers with calibrations traceable to the PTB primary standards are available for dose measurements at the highest accuracy level. An alanine/ESR dosimetry system is available for the determination of the total dose in relatively small volumes (alanine probe: ø=4.8 mm, h=3 mm).

Furthermore, the PTB provides an S1 laboratory for cell culture and microbiological preparations with approval to work on genetically modified cells.

Access to the facility is available upon request. The PTB is willing to support external investigators, offering its expertise in the field of dosimetry and on all issues related to the MELAF.

One of the two medical LINACs

Photo: A. Schüller/PTB

ID Card:

Exposure type:
external

Source:
Electron linear accelerator
Co 60

Dose rate:
0.01 Gy/min –100 Gy/min

Irradiation type:
electron and photon beam (vertical and horizontal)
Gamma (horizontal)

Irradiated organism type:
Cell cultures, blood, insects, Plants, measurement devices

Address:
Physikalisch-Technische Bundes-anstalt (PTB), Bundesallee 100, 38116 Braunschweig, Germany

Access:
free, available upon request

Supporting lab:
for cell culture (S1) and microbio-logical preparations,
for reference dosimetry

Internet link:
www.ptb.de/MELAF

Contact:
Andreas Schüller
andreas.schueller@ptb.de
Tel.: +49 531 592-6209

Related to: EURADOS

K. Derikum, A Dedicated Irradiation Facility for Radiotherapy Dosimetry, IFMBE Proceedings (2009) p53-55

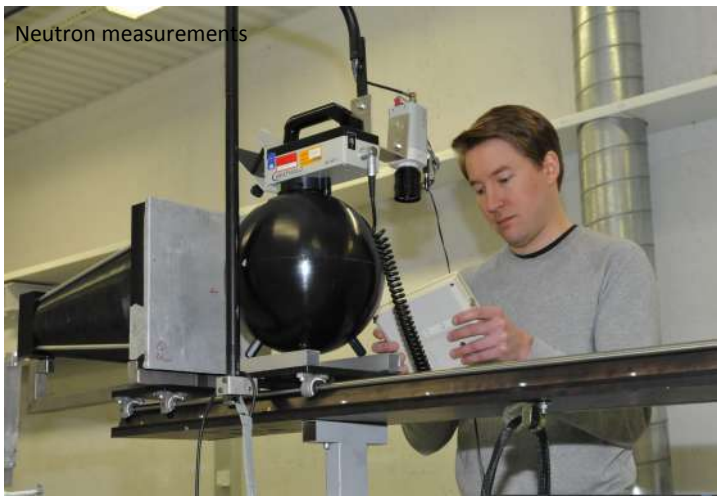
H. Zutz, **O. Hupe**, Ambient dose and dose rate measurements in the vicinity of Elekta Precise accelerators for radiation therapy, Radiation Protection Dosimetry (2014), 162, 4, p431-437

RADIATION METROLOGY LABORATORY

Facilities with wide range of radiation sources at STUK

The Finnish national standard for ionising radiation is maintained by the Radiation metrology laboratory (DOS) at the Radiation and Nuclear Safety Authority (STUK) in Helsinki. In addition, DOS provides a wide range of irradiation and calibration facilities.

The facilities at STUK include equipment for calibration, testing and irradiation of active and passive targets such as electronic components, with the following radiation qualities:



Neutron measurements

Photo: Teuvo Parviainen/STUK

- Gamma-ray sources: 4 x ^{137}Cs and 5 x ^{60}Co
- ^{241}Am photon source
- Two X-ray devices with voltage span from 10 kV to 320 kV
- Beta-active point sources (^{90}Sr, ^{85}Kr, ^{147}Pm)
- Neutron sources (AmBe, ^{252}Cf)
- Planar sources (^{90}Sr, ^{36}Cl, ^{60}Co, ^{14}C, ^{241}Am, ^{239}Pu, ^{137}Cs).

The air Kerma rate available is from 700 nGy/h to 40 Gy/h. In addition, a medical X-ray imaging facility with digital radiography is at hand. The calibration and irradiation premises include three separate irradiation halls for radiotherapy, radiation protection and X-ray calibrations and a common control room to operate irradiation instruments. Typically, either measurement devices or passive targets are irradiated. There is no facility available for maintenance of living biological materials.

Quality assurance and quality control at the national laboratory are maintained in accordance with the international Mutual Recognition Arrangement CIPM MRA (Comité International des Poids et Mesures). The quality systems of the laboratories recognised by the CIPM MRA arrangement meet the requirements of the ISO 17025 standard. The approval decision to join CIPM MRA is by self-declaration. In order to earn recognition by other laboratories, it is necessary to deliver annual reports to the EURAMET association and participate in regular intercomparison measurements and external audits.

Photo: Tosikuva Oy/Jarkko Översti

Dr Reetta Nylund

STUK is a member of the IAEA/WHO SSDL laboratory network and the European Association of National Metrology Institutes (EURAMET) and has contributed to a vast number of EURAMET- operated research projects in the field of dosimetry and metrology. The research conducted in the laboratory has generally been related to the use of radiation, such as in dosimetry, occupational and clinical radiation exposure, X-ray imaging and measuring methodologies. Several equipment manufacturers use the services of the laboratory as an integral part of their R&D process. In addition, STUK has agreements with Finnish universities for research cooperation involving the use of STUK's irradiation facilities. Access to the STUK facilities is by prior agreement either in the context of collaborative research projects or for irradiation and calibration services.

GBX200 ^{60}Co irradiation unit with a water phantom

Photo: Teuvo Parviainen/STUK

ID Card:

Exposure type:
External

Source:
see text

Dose rate:
700 nGy/h to 40 Gy/h

Irradiation type:
gamma, X-ray, alpha, beta, neutron

Irradiated organism type:
not available

Address:
Radiation and Nuclear Safety Authority (STUK)
Laippatie 4, 00880 Helsinki, Finland

Access:
Prior agreement/research collaboration service

Supporting lab:
No

Internet link:
www.stuk.fi

Contact:
Reetta Nylund
+358401520941
Reetta.nylund@stuk.fi

Related to:
EURADOS, MELODI, EURAMED

Hourdakis C.J., et al, (2016) Comparison of pencil-type ionization chamber calibration results and methods between dosimetry laboratories, Physica Medica,32(1):42-51.

Csete I., et al, (2010) Report on EUROMET.RI(I)-K1 and EUROMET.RI(I)-K4 (EUROMET project no. 813): Comparison of air kerma and absorbed dose to water measurements of ^{60}Co radiation beams for radiotherapy, Metrologia, Vol 47,Technical supplement 06012

Laboratory for Dosimetry Standards (NDS)

HQ metrological support for ionising radiation measurements

The Laboratory for Dosimetry Standards was established at Jozef Stefan Institute in 1992. In 2008 it was appointed by Metrology Institute of the Republic of Slovenia (MIRS) as Designated institute (DI) and holder of Slovenian national standard for ionising radiation (air kerma, Ka, and dose equivalent, H). NDS is accredited according to the ISO/IEC 17025:2005 standard by Slovenian Accreditation. With calibration of dose / dose rate meters and surface contamination monitors we provide dissemination of metrology traceability on national and international level. We are actively engaged in the work of Technical Committee for Ionising Radiation (TC-IR) at the international organisation EURAMET. In 2015 best Calibration and Measurement Capabilities (CMC) of the NDS were approved and reported by BIPM.

Photo: JSI

M.Sc. Matjaž Mihelič

For calibrations in gamma radiation beams, the NDS uses collimated photon beams produced with ^{137}Cs and ^{60}Co sources and a set of lead attenuators with attenuation range of 16.000 (^{137}Cs), installed in a revolver type homemade irradiator. Additional variation of the dose rates at the irradiated object can be achieved with distance changes in the range from 1 to 100. This is also true for ^{241}Am source which does not have attenuators. The shape of the field is 30 x 30 cm for ^{137}Cs and ^{60}Co sources and 30 cm in diameter for ^{241}Am source, all at 1 m distance. The shape of X-ray fields are circular 18 cm (N, RQR, RQA qualities) and 10 cm (RQR-M, RQA-M qualities) in diameter at 1 m distance. Dose rate can be varied in orders of magnitude with anode current and distance. The irradiated object is put into the central beam of selected source with the aid of several lasers. Relative shifts are made with remotely controlled 3 dimensional coordinate system.

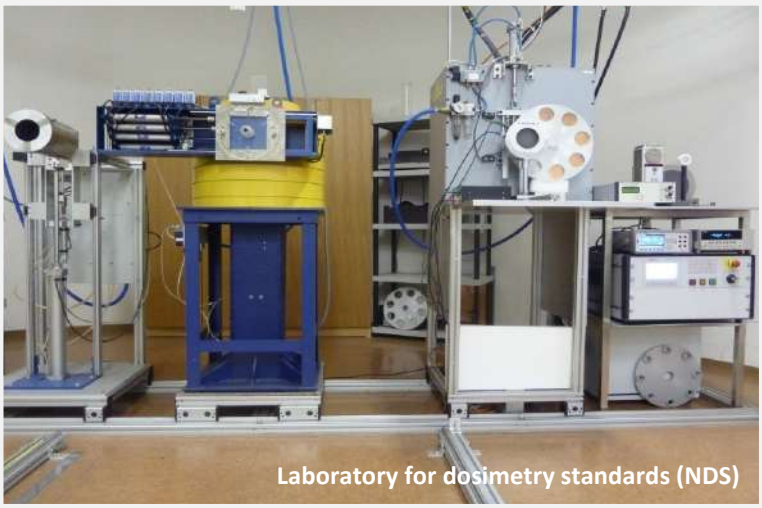
Photo: JSI

Dissemination of metrology traceability on national and international level; ionisation chambers from top to bottom: 1. LS-01 ensures the traceability for ^{137}Cs, ^{60}Co, ^{241}Am sources, and X-ray narrow spectra; 2. TW 34060 ensures traceability for RQR and RQA radiation qualities; 3. RC 06 M ensures traceability for RQR-M in RQA-M radiation qualities

Our lab can irradiate arbitrary samples within the above mentioned dimensions. The irradiation time is controlled by means of electronic timer. The ambient parameters are measured with traceable sensors of temperature, pressure and humidity.

Background irradiation is regularly measured and kept within narrow margins.

The reference quantity for the beam calibrations is the air kerma, determined with secondary standard ionization chambers traceable to the primary standards of the Hungarian Trade Licensing Office (MKEH) and International Atomic Energy Agency (IAEA, Austria).



Laboratory for dosimetry standards (NDS)

Photo: JSI

ID Card:

Exposure type: external

Sources: ^{60}Co, ^{137}Cs, ^{241}Am, X-ray: 10-160 keV (ISO 4037 narrow spectra N, IEC 61267 diagnostic spectra: RQR, RQA), X-ray: 2-60 keV (IEC 61267 mammographic spectra: RQR-M, RQA-M)

Irradiation type: Gamma, X-ray

Dose rate range: 0- 0.1 Gy.min^{-1}

Dose range: 0- 1 Gy

Energy, Energy range: 2- 1250 keV

Possible duration of exposure: 100 h

Dose rate modulation options: manual: 10^4

Space available to install the objects to be irradiated: 7 m

Main use of the facility: calibration, irradiation

Dosimetric quantity used: Air kerma, ambient dose equivalent H*(10), personal dose equivalent Hp(10), personal dose equivalent Hp(0,07), surface emission rate: α,β

Address:
Jozef Stefan Institute
Jamova cesta 39
1000 Ljubljana, Slovenia

Access: by prior arrangement with head of the laboratory

Internet link: http://ol.ijs.si/?module=1&lan=1&id=13&mid=7_11_13

Contacts:
Matjaž Mihelič
matjaz.mihelic@ijs.si
+38614773651
Benjamin Zorko
benjamin.zorko@ijs.si
+38614773416

Related to: MELODI, EURADOS

Calibration and measurement capabilities of NDS, confirmed with BIPM supplementary intercomparisons are published in BIPM KCDB database

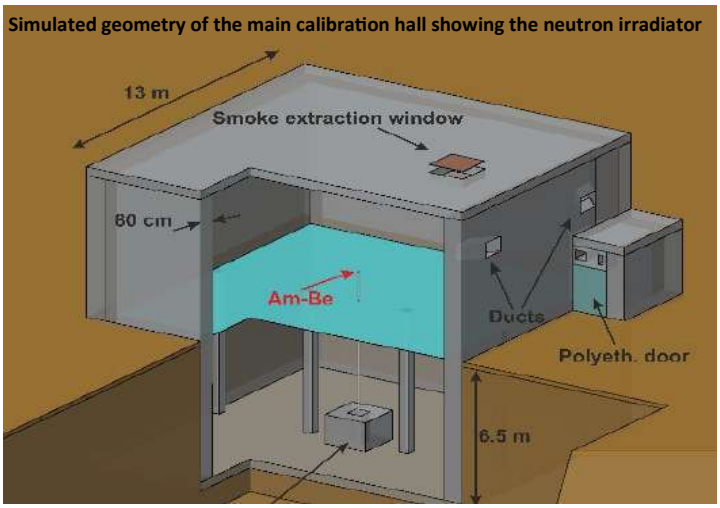
Štuhec, M., Zorko, B., Vekić, B., Miljanić, S., Basić, B., Ban, R. (2007) Harmonization of individual dosimetry quality control within metrology system of a small country, Radiation Protection Dosimetry, Vol. 125, 1-4, p117-120

CALibration LABoratory(CALLAB)

CERN Radiation Protection Calibration Facility

The CERN radiation protection CALibration LABoratory (CALLAB), in service since 2015, is a new state-of-the-art calibration facility designed according to the requirements of the ISO 17025 standard. Its design, safety and shielding calculations have been the subject of the Ph.D thesis of Dr F. Pozzi. CALLAB consists of two irradiation rooms (named CC60 and main calibration hall), office space, storage and control rooms.

The CC60 room houses a Co-60 source (nominal activity of 11.8 TBq in August 2014). For large systems of around 1 m^3, the Total Ionizing Dose (TID) delivered ranges from 1 to 10 kGy whereas for smaller samples it can reach up to 100 kGy within days or weeks depending on the position.



Simulated geometry of the main calibration hall showing the neutron irradiator

Photo: F. Pozzi/CERN

The CC60 room is expected to be upgraded with a 100 TBq Co-60 source for higher air kerma rate testing. Typical uncertainties on the air kerma values are around 5%.

The CC60 room is used for the qualification of the electronic components against TID effects. The irradiation room size permits coverage of the two windows of low air kerma rate (0.36 to 3.60 Gy/hr) and standard air kerma rate (36 to 360 Gy/hr) as defined by the European Space Agency (ESA) standard .

The main calibration hall is a 13x13x13 m^3 concrete vault, half of which is underground to take advantage from the natural shielding provided by the earth. It houses:

- four Am-Be sources, providing H*(10) rate between tens of nSv/h and 700 µSv/h;
- five Cs-137 sources and one Co-60 source providing H* (10) rate between tens of nSv/h and 200 mSv/h;
- two beta sources : 1.85 GBq of Sr-90 and 4 GBq of Kr-85;
- one X-ray generator with a peak voltage of 320 kV.

Photo: Pierre Carbonez/CERN

Pierre Carbonez

Typical uncertainties on the reference values are below 5%. All the irradiators and their calibration benches are remotely operated from the control room. Simultaneous neutron/photon irradiations are possible in a shared bench to investigate the response of detectors in mixed radiation fields. The layout of the calibration hall is specifically designed to minimise neutron scattering. CALLAB is currently undergoing the ISO 17025 accreditation process.

Every year, about 9000 semi-passive photon dosimeters (DIS-1), 1500 operational photon dosimeters (DMC 2000/3000), 800 portable radiation monitoring devices and ionisation chambers are calibrated at CALLAB. The laboratory is also used to test and evaluate prototype detectors and new commercial products. The investigation of Single Event Effects (SEEs) induced by neutrons is also possible by attaching the instrumentation to the holder of the Am-Be source.

Dr Pozzi installing a REM counter on the Neutron Calibration bench

Photo: Pierre Carbonez/CERN

ID Card:

Exposure type:
External

Source:
Am-Be (x 4) : 100 MBq – 888 GBq
Cs-137(x 5) : 300 MBq – 3 TBq
Co-60 (x 2) : 5 GBq and 10 TBq
Sr-90 : 1.85 GBq
Kr-85 : 4 GBq
X-ray generator 320 kV

Dose rate:
tens of nSv/h to Sv/h

Irradiation type:
gamma, neutron, beta, X-rays, mixed gamma + neutron

Irradiated organism type:
None

Address:
CERN
route de Meyrin
1211 Geneva 23
Switzerland

Access:
Subject to acceptance by the facility manager

Supporting lab:
CERN Dosimetry Service

Internet link:
https://hse.cern/content/rp/calibration-services

Contact:
Pierre Carbonez
Pierre.Carbonez@cern.ch

Related to:
EURADOS

CERN irradiation facilities, Pozzi F., Alia R.G., Brugger M., Carbonez P., Danzeca S., Gkotse B., Jaekel M. R., Ravotti F., Silari M., Tali M. (2017), Radiat. Prot. Dosimetry, doi: 10.1093/rpd/ncx187

New radiation protection calibration facility at CERN, Brugger M., Carbonez P., Pozzi F., Silari M., Tali M. (2014), Radiat. Prot. Dosimetry 161, 181-184

Radon Calibration Laboratory of BfS

Controlled Rn-222, Rn-220, climate and aerosol parameters

Radon measurements in the area of radiation protection and research should be reliable. In order to meet this objective, the Federal Office for Radiation Protection (BfS) operates a laboratory for exposure to Rn-222 (radon) and Rn-220 (thoron) and their progenies, under defined climate conditions. Its infrastructure is dedicated to calibration exposures of measurement instruments, testing of metrological properties (type test), development of measurement methods and further research in the field of radon metrology.

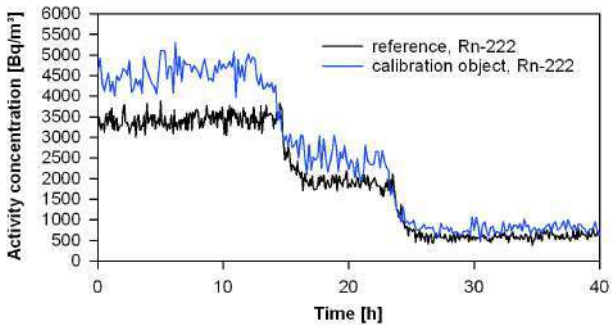


Photo: BfS

Rn-222 activity concentration within the chamber during exposure at different constant Rn-222 levels, measured by a calibration object and the laboratory's reference standards.

The measurands (Rn-222 and Rn-220) of activity concentration in air (CRn, CTn) and the potential alpha energy concentration of the short-lived Rn -222 progenies (PAEC), as well as the environmental parameters, are all traced back to national standards. The laboratory has been accredited since 1999 as a calibration laboratory for the measurands CRn and PAEC according to the norm EN ISO/IEC 17025. International comparisons of passive radon measuring instruments have been carried out since 2003. In addition to offering exposure and calibration services, the laboratory welcomes research collaborations with metrological or scientific institutions.

The radon atmospheres are generated either in several stainless steel containers with volumes of 0.4 m³, or in walk-in chambers with an inner volume of 11m³ and 30m³ (PAEC chamber). Rn-222 activity concentrations of between 50 Bq/m³ and 100 kBq/m³ are adjusted by injections of Rn-222 gas obtained from an Ra-226 source. To compensate for Rn-222 losses due to radioactive decay, the containers are permanently connected to Ra-226 flow-through sources via flow dividers or computer-controlled piston pumps. Atmospheres containing Rn-220 are created by a Th-228 source. The air inside the containers is continuously mixed by fans installed internally, which allow the activity concentrations to be kept sufficiently homogenous and constant in time during the exposures.

Photo: F. Schneider / BfS

Calibration laboratory group

The activity concentrations are continuously measured by scintillation cells and/or with a commercially available instrument. Temperature and humidity are monitored within all calibration containers; in the case of the walk-in chambers, temperature can be adjusted from -2°C to 40°C, and relative humidity from 10% to 90%. Ambient air pressure is also monitored.

The aerosol concentration, aerosol size distribution and air velocity all have a significant influence on the radon decay product atmosphere. Therefore, the PAEC chamber is equipped with:

- an aerosol generator to create aerosols with desired particle concentration (range 200-50,000 per cm³) and desired size distribution,
- a scanning mobility particle sizer spectrometer to measure the aerosol particle concentration and size distribution, and
- fans with adjustable tilt and power.

Thus, the equilibrium factor in the PAEC chamber can be adjusted between 0.1 and 0.9, and the unattached fraction of the radon progenies between 1% and 60%. The PAEC itself reaches values of between 0.3 and 640 µJ/m³. In addition, an air filter system and different alpha and gamma spectrometers are also available.

Laboratory with stainless-steel containers, measurement and dosing system

Photo: MD/ BfS

Bundesamt für Strahlenschutz

ID Card:

Exposure type:
External

Source:
^{222}Rn, ^{220}Rn and their short-living progenies

Dose rate:
^{222}Rn activity concentration
0.5 – 100 kBq/m³

PAEC 0.3 – 640 µJ/m³

Irradiation type:
Alpha radiation (5.3 MeV, 6.0 MeV, 6.8 MeV, 7.7 MeV, 8.8 MeV)

Irradiated organism type:
non-biological materials

Address:
Federal Office for Radiation Protection (BfS)
Koepenicker Allee 120-130,
10318 Berlin, Germany

Access:
Site access by prior appointment only

Internet link:
http://www.bfs.de/EN/topics/ion/service/radon-measurement/calibration-laboratory/calibration-laboratory_node.html

Contacts:
E. Foerster
Dr M. Dubslaff
cal-radon@bfs.de

Related to: MELODI, EURADOS

Performance tests for instruments measuring radon activity concentration, Beck T.R., Buchroeder H., Schmidt V. (2009), Applied Radiation and Isotopes 67 (5), 876-880

The measurement accuracy of passive radon instruments, Beck T.R., Foerster E., Buchroeder H., Schmidt V., Doering J. (2013), Radiation Protection Dosimetry, 158 (1), 59-6

Exposure platforms

Calibration and Dosimetry Laboratory (INTE-UPC)

Radiation Protection and Medical Radiation Physics

The Calibration and Dosimetry Laboratory (in Spanish, LCD) of the Institute of Energy Techniques (INTE) at the Polytechnic University of Catalonia (UPC) is a secondary standard metrology laboratory for ionising radiation, accredited by the Spanish accreditation body (ENAC). The LCD obtained its first formal recognition in 1987 with the award of the EN 45001 standard, followed in 2009 by the ISO/IEC 17025.

Photo: INTE-UPC

Dr Mercè Ginjaume

Photo: INTE-UPC

UPC Photon calibration facility

The main equipment of the Laboratory includes the following: a photon irradiator with six ^{137}Cs and one ^{60}Co sources; an HS320 Rich Seifert X-ray generator of high stability with a maximum high voltage of 320 kV; a MAMMOMAT Siemens low-energy X-ray generator with Mo anode to produce mammography qualities; an Amersham-Buchler BSS-1 beta secondary standard irradiator with two sources of ^{90}Sr, and several 10 cm x 10 cm alpha-beta sources designed for calibrating portable surface contamination monitors.

Measurement traceability for photon radiation is ensured through the calibration of several ionisation chambers to the National Metrology Institute of Germany (PTB) and through the calibration of the beta secondary standard to the National Institute of Standards in the United States (NIST).

The LCD offers a calibration service for users of ionising radiation, mainly in Spain. The most common services include: calibration of environmental and radiation protection instruments; surface contamination monitors; kVp meters and dosimeters for X-ray quality control, and the irradiation of personal dosimeters both passive and active. LCD also collaborates with the Spanish Nuclear Safety Council (CSN, Spanish regulator), to organise periodic intercomparisons of Spanish-approved personal dosimetry services.

As a university laboratory, LCD organises training sessions for graduate and post-graduate students on topics related to the field of radiation protection. LCD is part of the Biomedical Engineering Research Centre (CREB) of the UPC. The LCD team is currently participating in several national and international research projects and is also actively involved in several activities of the European Radiation Dosimetry Group (EURADOS).

The main research projects undertaken at LCD include the FP7 project ORAMED (2008 -2011), various projects financed by the CSN (e.g. *Development of Methodologies for Estimating the Dose to the Eye Lens in Interventional Radiology* (2012-2015)), and the Horizon 2020 project, MEDIRAD (2017-2021). The research activities of the Laboratory are linked to the INTE's Dosimetry and Medical Radiation Physics research programme. Further details regarding projects, publications and theses involving the facilities, are available via the website.

Low energy X-ray laboratory

Photo: INTE-UPC

UNIVERSITAT POLITÈCNICA DE CATALUNYA
BARCELONATECH
Institut de Tècniques Energètiques

ID Card:

Exposure type:
External

Source:
ISO 4037-1 Narrow X-Ray series, ^{137}Cs, ^{60}Co, IEC 61267 diagnostic (RQR) and mammography (RQR-M) radiation qualities, ISO 6980-1 ^{90}Sr-^{90}Y, wide area reference sources (^{90}Sr-^{90}Y, ^{60}Co, ^{14}C, ^{241}Am, ^{36}Cl)

Dose rate:
^{137}Cs (1 µGy/h - 54 mGy/h), ^{60}Co (11 µGy/h - 0.45 mGy/h), X-ray (narrow series) (0.1-200 mGy/h), X-ray (diagnostic) (0.1-10 Gy/h), ^{90}Sr-^{90}Y (4 mGy/h; 0.5 Gy/h)

Irradiation type:
gamma, X-ray, beta

Irradiated organism type:
None

Address:
Polytechnic University of Catalonia
Institute of Energy Technologies
Calibration and Dosimetry Laboratory
Diagonal, 647
08028 Barcelona (Spain)

Access:
Joint research collaborations, service contracts

Supporting lab:
Thermoluminescent Dosimetry Laboratory (TLD), Computer cluster

Internet link:
https://inte.upc.edu/en

Contact:
Mercè Ginjaume
+34 93 405 44 57
merce.ginjaume@upc.edu
+34 93 401 18 72
calibracion.laboratorio@upc.edu

Related to:
EURADOS, MELODI

First EURADOS intercomparison exercice of eye lens dosemeters for medical applications, Clairand I., Ginjaume M., Vanhavere F., Carinou E., Daures J., Denoziere M., Silva E.H., Roig M., Principi S., Van Rycheghem L. (2016), Radiat. Prot. Dosimetry 170 (1-4), 21-26

A practical approach to perform the isotropy test for extremity dosemeters, Gultresa J., Llansana J., Roig M., Ginjaume M. (2016), Radiat. Prot. Dosimetry 170 (1-4), 95-99

Exposure platforms

The Nuclear Metrology Group (NMG)

Neutron measurement and irradiation facility

NPL is the UK's National Measurement Institute and is a centre of excellence in developing and applying the highest quality measurement standards available. The Nuclear Metrology Group (NMG) represents one of NPL's many activities, and has world-class facilities for producing a wide range of well-characterised neutron fields. NMG can also determine the neutron output of radionuclide sources to high precision by measuring the activation of manganese in a manganese sulphate bath. These facilities are used for type testing and calibrating neutron-sensitive instruments, characterising neutron sources, and for research aimed at improving neutron standards and neutron measuring instruments. Much of the work is for radiation protection.

Photo: NPL

Dr Nigel Hawkes

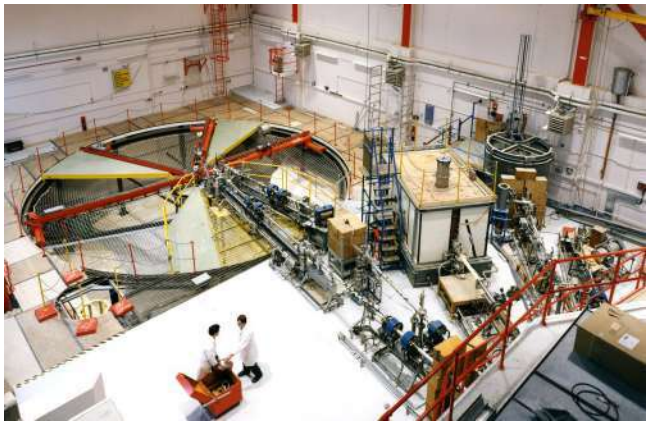


Photo: NPL

Main experimental area, measuring 18 x 18 x 26 m. From bottom right towards top left, the photo shows the accelerator beam lines, the thermal pile, and the low-scatter area.

In the main experimental area, protons or deuterons from a 3.5 MV Van de Graaff accelerator can be directed onto a suitable target to produce monoenergetic neutrons at energies from under 100 keV to 16.5 MeV (although not all energies within this range are available). The target is at the centre of a low-scatter area, at least 6 m away from the floor or any massive structures, in order to minimise room scatter. The neutron fluence is measured using carefully calibrated long counters.

To produce thermal neutrons, deuterons from the same accelerator are directed instead into the thermal pile, which consists essentially of two high-output neutron-producing targets inside a large graphite moderator. The highest fluence rates are available near the centre of the moderator via a 12 cm diameter access hole, while wider artefacts can be irradiated in a vertical thermal beam that emerges from the top of the pile.

The low-scatter area is also used for irradiations with radionuclide sources, of which the group has several of various types, including ^{241}Am/Be and ^{252}Cf. A D_2O-moderated ^{252}Cf field is also available. A pneumatic transfer system is used to bring the strongest of the sources from the shielded store to the irradiation position.

In addition to its irradiation facilities, the NMG has several neutron instruments, including Bonner sphere spectrometer sets and tissue equivalent proportional counters. These are used for neutron research, usually dosimetry-related, or for making off-site measurements at a customer's own premises. NMG also has considerable expertise in neutron-related calculations, including Monte Carlo modelling and the unfolding of neutron energy spectra from pulse height spectra. Currently the group is planning a new facility to produce an intense neutron field for radiation hardness testing.

Some examples of the type of work undertaken by the group are:

- Irradiating personal dose meters to precisely known doses for an intercomparison exercise;
- Contributing to the design of novel neutron instruments through Monte Carlo modelling and experimental measurements;
- Characterising the angular distribution of the output of a neutron source or generator, relative to its symmetry axis;
- Measuring neutron dose rates close to radiotherapy facilities.

Photo: NPL

The Manganese Bath facility for measuring the neutron output of radionuclide sources by the activation of manganese sulphate solution.

Progress in providing neutron standards at the UK National Physical Laboratory, Hawkes N. P., Bennett A., Cheema S. S., Horwood N. A., Jones L. N., Kolkowski P., Roberts N. J., Taylor G. C. and Thomas D. J. (2007), Nuclear Instruments and Methods in Physics Research Section A, 580, 183–185
Recent developments in radionuclide neutron source emission rate measurements at the National Physical Laboratory, Roberts N. J. and Jones L. N. (2010), Applied Radiation & Isotopes, 68, 626-630

NPL National Physical Laboratory

ID Card:

Exposure type:
External

Source:
Am/Be, Am/B, Am/F, Am/Li, ^{252}Cf, D_2O-moderated ^{252}Cf; ^{60}Co, ^{137}Cs;
Monoenergetic neutrons 70 keV to 16.5 MeV;
Thermal pile.
Measurement of neutron source emission rate via Mn bath.

Dose rate:
Depending on source and energy, 1 to several thousand µSv/h at 1 m
Thermal pile: max neutron fluence rate $3x10^7$ cm^{-2} s^{-1}.

Irradiation type:
Neutron with gamma present, gamma

Irradiated organism type:
None

Address:
National Physical Laboratory
Hampton Road
Teddington,
Middx. TW11 0LW
United Kingdom

Access:
See contacts below

Internet link:
http://www.npl.co.uk/science-technology/neutron-metrology/

Contact:
David Thomas
david.thomas@npl.co.uk

Nigel Hawkes
nigel.hawkes@npl.co.uk

neutron_enquiries@npl.co.uk

+44 20 8943 8637

Related to:
EURADOS

UNIPI neutron irradiation facility

Neutron irradiation room with AmBe and gamma sources

The University of Pisa's neutron irradiation facility (UNIPI-AmBe) has been in operation since 2010, and consists of an irradiation room for fast neutrons and gamma exposures designed to minimise neutron scattering. The facility, which is part of the Nuclear Measurement Laboratory of the University of Pisa, has been performing nuclear measurements for over 50 years.

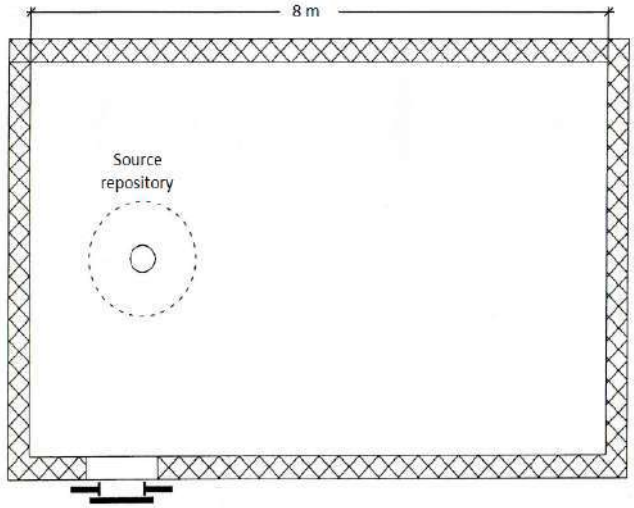


Photo: R. Ciolini/Pisa University

Top view of the neutron/gamma irradiation facility

It consists of an open space (5 m x 8 m x 2.5 m) with concrete walls, no windows and only one access door. Located in a 2 m deep ground repository, it houses two radionuclide AmBe neutron sources with a total nominal activity of 14.2 GBq, and a ^{60}Co source with a nominal activity of 1.1 GBq. The reference neutron dose rate H*(10) is 9.4 µSv/h at 1 m neutron source distance. Moreover, a ^{60}Co calibrated source (dose rate 0.53 mSv/h at 1 m free in air) is available in the source repository, to be used for personal gamma dosimetry calibration or together with neutron sources to investigate the response of the detectors to mixed radiation fields. A broad range of neutron and gamma dose rates can be obtained by varying the distance between the source and the irradiated device.

An air conditioning system maintains the room temperature at a constant value during the exposures. The radioactive sources are extracted from the storage box and positioned inside the room, at a specified distance from the device/detector to be irradiated. At the end of the irradiation, they are stored again in the repository. There are no particular restrictions on the items to be irradiated; only size limitations due to the dimensions of the room and the entrance door. The duration of each exposure is normally within an interval of 0–24 h, but longer time intervals are possible. The facility is protected by a controlled access security system. All irradiation procedures and instrument calibrations are performed according to the facility's ISO 9001 standard certification.

Photo: R. Ciolini/Pisa University

Dr Riccardo Ciolini

The UNIPI-AmBe facility includes ancillary equipment such as a Bonner sphere spectrometer system, 30 cm x 30 cm x 15 cm ISO phantoms, supports for objects to be irradiated, and Rem counters and gamma dose rate meters for environmental gamma/neutron monitoring. The facility is mainly used for nuclear measurement research, instrument calibration (dose/dose rate meters) and radiation protection measurements, but also performs teaching activities (Nuclear and Biomedical Engineering Master's degree courses). In addition to offering exposure and calibration services, the facility welcomes research collaborations with metrological or scientific institutions.

Photo: R. Ciolini/Pisa University

View of the irradiation room

ID Card:

Exposure type:
External

Source:
AmBe and ^{60}Co

Dose rate:
9.4 µSv/h at 1 m (neutron) and 0.53 mSv/h at 1 m (gamma)

Irradiation type:
Neutron, gamma

Irradiated organism type:
None

Address:
Bruno Guerrini Laboratory
Department of Civil and Industrial Engineering (DICI)
University of Pisa
Via di Torretta
I-56122 San Piero a Grado
Pisa, Italy

Access:
Subject to prior agreement with the management staff

Supporting lab:
Nuclear Measurement Laboratory
Department of Civil and Industrial Engineering (DICI)
University of Pisa
Largo Lucio Lazzarino 2
I-56126 Pisa, Italy

Internet link:
www.dici.unipi.it

Contact:
Riccardo Ciolini
+39 050 2218026
r.ciolini@ing.unipi.it

Related to:
EURADOS

Track size distributions in CR-39 neutron dosimeters treated with carbon dioxide, d'Errico F., de Vasconcelos D. A. A., Ciolini R., Hulber E. (2017), Radiation Measurements, 106, 607-611

Application of a Bonner sphere spectrometer for the determination of the angular neutron energy spectrum of an accelerator-based BNCT facility, Mirzajani N., Ciolini R., Di Fulvio A., Esposito J., d'Errico F. (2014), Applied Radiation & Isotopes, 88, 216-220

Laboratory for Nuclear Calibrations at SCK•CEN

Irradiations of a wide range of samples in ISO standard beams

The Laboratory for Nuclear Calibrations (LNK) at SCK•CEN performs calibrations of dosemeters from research centres, nuclear power plants, industry and hospital radiotherapy departments. The irradiations of different sample types represent a significant part of the activity. Samples used for research in radiobiology, radioecology or dosimetry are irradiated following the recommendations of specific ISO standards.

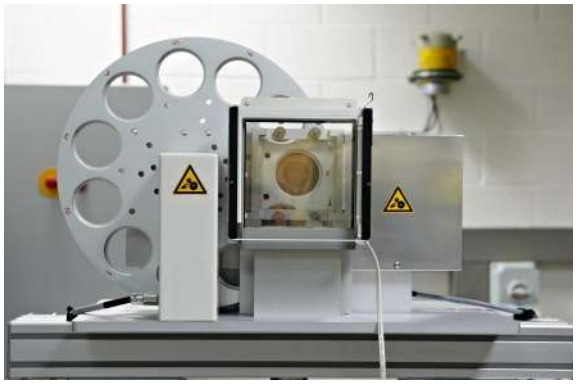


Photo: SCK•CEN

The 100 kV tube of the X-ray generator. A filter wheel with holes for 11 filters and a DAP ionisation chamber are visible downstream the focal point.

LNK was set up more than 30 years ago. It has been a member of the EURAMET network and a Designated metrology Institute (DI) since 2012, and is also a member of the Secondary Standard Dosimetry Laboratories (SSDL) network of the IAEA (International Atomic Energy Agency). In 2016, its first primary standard (for air kerma in Co -60 beam) was characterised and officially compared with the standard of the International Bureau of Weights and Measures (BIPM, Sevres, France). Most of the Calibrations and Measurement Capabilities (CMC) of LNK are covered by the scope of ISO 17025 accreditation.

LNK performs irradiations for a wide range of samples and dosimetry equipment with dose rates of up to a few Sv/h for photons and a few mSv/h for neutrons. The laboratory is specially designed for dosimetry irradiations and calibrations and follows the ISO 4037 (photons) and ISO 8529 (neutrons) recommendations. Encapsulated and small-size radioactive sources are used for the irradiations. Sample sizes of up to tens of cm can be fitted inside the beam while holders and electronic equipment can be kept outside the beam. A lot of space is available around the sources; the irradiation rooms are several metres wide. Irradiation times can vary from a few seconds to several days, or even weeks, depending on the availability of the irradiators and the needs of the customer.

Photo: SCK•CEN

Dr L. C. Mihailescu

Several irradiators are available with different types of collimation systems and beam directions:

- Cs-137 and Co-60 irradiators with horizontal and vertical beam and 20 degree angle collimators,
- Cs-137 and Co-60 irradiator in a panoramic 2π beam, very useful for simultaneous irradiation of many dosemeters or samples,
- Dual tube X-ray generator that covers the energy range from 10 keV up to 300 keV,
- Panoramic 2π neutron beam from Cf-252 and Am-Be sources,
- Co-60 irradiator with horizontal beam for radiotherapy dosimetry calibrations (IAEA TRS-398 protocol).

The X-ray system is intensively applied for irradiation of radiobiological samples using standard H-250 (high air kerma rate series) beam quality (ISO 4037). Photon spectroscopy is used to verify the energy spectra of the beam qualities used at LNK.

Access to the facility is possible with proper planning. Approximately 500 irradiation certificates and 200 calibration certificates are issued every year at LNK.

An ISO 17025 accredited irradiation facility is available at SCK•CEN for dosimetry, radiobiology or radioecology experiments. Additional support can be obtained through collaboration with other research groups at SCK•CEN.

Photo: SCK•CEN

Horizontal Cs-60 and Co-60 irradiator

ID Card:

Exposure type:
External

Source:
γ-rays: Cs-137, Co-60
X-rays: 10-300 kVp (ISO 4037 N-series, H-250 and IEC RQR-series)
β particles: Sr-90/Y-90,
neutrons: Cf-252, Am-Be

Dose rate:
Up to a few Sv/h for photons and a few mSv/h for neutrons

Irradiation type:
γ-rays, X-ray, β particles and neutrons

Irradiated organism type:
Any sample, flexibility for size

Address:
Laboratory for Nuclear Calibrations (LNK)
SCK•CEN
Boeretang 200
B-2400 Mol
Belgium

Access:
Free (no Scientific Committee)

Supporting lab:
Radiobiology and Radioecology research groups at SCK•CEN

Internet link:
www.sckcen.be

http://science.sckcen.be/en/Services/RDC/Dosimetry_calibrations

Contact:
Dr Liviu-Cristian Mihailescu

nuclearcalibrations@sckcen.be
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+32 1433 2389
+32 1433 2005

Involved in:
Secondary Standard Dosimetry Laboratories (SSDL) of IAEA

Related to:
EURAMET

Key comparison BIPM.RI(I)-K1 of the air-kerma standards of the SCK•CEN, Belgium and the BIPM in ^{60}Co gamma radiation, Kessler C., Burns D., Mihailescu L. C., Chiriotti S. (2017), Metrologia, 54, Tech Supl 06004

Photon energy (8–250 keV) response of optically stimulated luminescence: Implications for luminescence geochronology, Guérin G., Mihailescu L. C., Jain M. (2018), J Lumin, 204, 135-144

Chapter 2: Databases, Sample banks, Cohorts

Chapter 2: Databases, Sample banks, Cohorts

As part of the 40 regular issues of the AIR² bulletin, a total of 36 infrastructures listed in the "Databases, Sample banks, Cohorts" category have been covered. This includes 8 databases, 19 sample banks and 24 cohorts. Special issues of AIR² also covered additional databases, either already existing or being constructed. It must be outlined that a few "double counts" had to occur across subcategories, since some sample banks are attached to cohorts and these are sometimes - but not always - considered as separate infrastructures. As a result, some biobanks attached to cohorts were either presented in the same issue of AIR² as the source cohort, or not. In addition, whether some infrastructures had to fall into the "Sample banks" or the "Databases" category was not always a clear cut. Finally, one might also reasonably consider that a cohort is, first, a database - and might therefore fall into a more general "database" category. Actually, cohorts are simply specific types of databases, which have been treated separately because of their major role in human radiation protection research and of their specific requirements regarding individual data protection.

The other databases identified cover a broad spectrum of purposes and uses, from collections of pure environmental data (e.g. levels of radionuclides in the marine environment) and parameters (e.g. mineral-specific sorption data), to data on transfer of radionuclides to organisms and finally ionising radiation-induced effects in various non-human biota. Of course, STORE, a platform for resource sharing covering all kinds of radiation research, which enables users to locate data or bioresources, has been presented, as well as the FREDERICA database devoted to radioecology. Both databases were produced under EC funded projects. The availability of legacy datasets and biological materials resources still mainly depends on uncoordinated, often institutional, initiatives to curate and archive them, yet there are still few stable platforms for their preservation, sharing, and reuse [1]. This is why CONCERT Subtask 6.2 included efforts to maintain the STORE and FREDERICA databases.

Drs Maria Gomolka and Paul Schofield provided their expert views on the sample banks and databases covered by the AIR² bulletin, and described additional infrastructures that could not be covered whatever the reasons (see the introductions of the dedicated subchapters). Regarding cohorts and sample banks at least, it appears that the most well established radiobiology and radio-epidemiological datasets available in the European Union have been covered by AIR². Some major infrastructures located outside of the European Union have also been covered (e.g. in Japan, USA, Russia, Kazakhstan). This includes for instance the Life Span Study of Japanese Atomic Bomb survivors, the American JANUS and NASA radiobiological archives, the Mayak and Techa River cohorts and biobanks, and more.

In summary, although exhaustive coverage of existing infrastructures for radiation research worldwide in only 40 issues was of course impossible, the AIR² bulletin provided a very useful overview of major databases, sample banks and cohorts available for radiation protection research. This helped reaching the WP6 goal of increasing the visibility of these infrastructures and provided solid grounds for the continuation of this work, as part of MELODI and other European platforms for radiation research.

(a) Databases

Background

Radiobiology was one of the first disciplinary areas to start generating very large structured datasets in the biological sciences. From the 1940s onwards the collection of accidental and experimental exposure data globally has been a major undertaking, and its archiving and dissemination has been a significant challenge for a variety of reasons. More recently, the collection of epidemiological and environmental data, either routine monitoring or post-incident follow-up has added to the importance of data archiving and retrieval. In addition to these large-scale, and in some areas long-duration, experiments and monitoring and epidemiological exercises, the production of data from hypothesis-driven experimentation has accelerated enormously and the archiving, sharing and reuse of this data present particular challenges. Existing public repositories either do not cater for the high-resolution metadata needed for radiation biology or cannot accommodate coherent large datasets. The ongoing nature of data collection and curation also means that in contrast to the archiving and sharing of legacy datasets, sustainability of the infrastructure and user training are of critical importance. The reader is referred to a recent paper surveying the international landscape of radiation biology and epidemiology for a comprehensive temporal, geographical and thematic overview of the current state of play and Table 1 of this paper is a useful summary of the findings [1]. 23 major databases and data resources were described and many also have comprehensive entries in the AIR² infrastructures bulletin series. This section of the web handbook will therefore deal at summary level with the current strengths and challenges in the data landscape for radiation biology and epidemiology.

The issues of data archiving and reuse have been under considerable scrutiny in recent years, resulting in the formulation of the FAIR guidelines for Open Data [2]. Resulting from extensive consultation between funding agencies, journals and scientists, these guidelines have been adopted by many major funding agencies, the European Commission and formally by the countries of the OECD and G20 group of nations [3, 4]. Findability, Accessibility, Interoperability, and Reusability represent the four principles of Open data and are essential for effective data governance and management [5]. The advantages of data sharing are overwhelming, amongst which are improved reproducibility, accountability, and the added value, both scientific and financial, of reusing data for purposes for which it was not originally intended; aggregating with other datasets, or conducting novel analysis in the light of new methods or paradigms [6]. For the individual this also provides increased recognition and often collaborations or further developments of studies that they had not anticipated.

The problem of data availability has recently been raised by Beresford et al. [7] and reflects a common issue about the provision of summary data alone, or in some cases no primary data at all. Withholding of primary data not only slows the progress of science, for example withholding unique contamination datasets, but also makes intercomparison and aggregation of datasets impossible. This adds to the uncertainty about reliability of conclusions where it is impossible to replicate the analysis. Where this kind of problem impacts on regulatory activities and safety assessments, with potentially huge implications for humans and environmental safety, as well as major economic impacts, there is an additional imperative for the community to ensure that the highest standards are met.

The development of very large datasets in recent years has increased the willingness to share, though there are still some issues, common with other disciplines [8-10] that inhibit full and free sharing. These include protectionism, concerns that flaws in analysis might be revealed, lack of time, expertise or funding for preparation of data for upload, lack of appropriate sharing platforms, concerns over intellectual property protection, and loss of "ownership". These are common to many disciplines and, respondents in a recent survey of data sharing in a large European radiobiology project, CONCERT, the responses received broadly reflected these common findings [11].

Increasingly funding agencies, and specifically the European Commission, have adopted a policy of free and open data sharing. A comprehensive list of international data sharing requirements for funding agencies, journals and institutions is available on from the FAIR sharing project. The requirement for data management plans (DMPs) will become mandatory in the next EC Framework programme, however it is not yet clear what level of accessibility and discovery will be acceptable as Data sharing, nor have the monitoring and compliance process been articulated. The latter is extremely difficult and so far other funding agencies have taken a sampling and

audit approach rather than an explicit confirmation that sharing goals in the DMP have been met. The generation of machine actionable and dynamic DMPs might in the future be a way of checking assertions that data has been shared but as yet these approaches have not been implemented to our knowledge [12].

During the course of the project we found several examples where data was purportedly shared, and yet despite protracted efforts was unavailable. This was either because of unresponsiveness of contacts, change of personnel and lack of continuity, or most often institutional reorganisation and loss of funding. This underlines the importance of using strategic sustainable databases rather than providing data access through individual investigators and their home institutions. Secondly, we found problems with explicit policies on the lifetime of data sharing: how long should data be shared for, how long should it be retained, how should it be made available? In principle, these should be addressed by data management plans, but in the course of the STORE project we saw no data management plans which adequately dealt with these issues, and none which complied with the basic principles of a DMP as laid down by the UK DCC, accepted as being the gold standard under H2020. We were not made aware of any systematic mechanisms for the assessment of DMPs for H2020 or CONCERT internal funding calls.

We identify the following challenges:

- Provision of a sustainable database at scale structured to deal with the volume of data generated and appropriate for legacy data. Attention to detailed metadata is required in order for data to become truly discoverable, consistent with FAIR guidelines.
- Requirement for DMPs and their oversight
- Education and training in appropriate community norms and the technical aspects of data sharing
- Human subject data

These challenges are not unique to the radiation biology community, although in some cases the solutions maybe rather particular.

A sustainable platform for data sharing

The STORE database has begun to address some of the issues concerning a platform for sharing and archiving radiobiology, radioecology and epidemiology data. This is in principle sustained by the generous commitment of the BfS, but cannot at present undertake the expansion to scale required to be commensurate with requirements. STORE is complementary to existing large-scale repositories, for example those run by ELIXIR as core resources, but current implemented structures, themes and metadata standards in these databases do not sufficiently encompass Radiation biology to make discovery and sharing of data possible. The development of a formal ontology for radiation biology metadata is currently in progress in collaboration with the NASA Ames Laboratory in the USA.

Data Management Plans

Currently the Commission is advising DMPs for H2020, as discussed above, but these are not uniformly required by the major funding agencies and institutions across Europe and recognition of the importance of data science in support of the biological sciences is only slowly taking place, in a large part promoted by international membership of the ELIXIR bioinformatics network.

Education

Education in community norms for data management and that use of public data resources has emerged as a critical bottleneck for developing an international radiobiology commons. Targeting young scientists and early stage researchers is the most important area, but increasing awareness of FAIR issues amongst established investigators is also important if we are to change attitudes and compliance in the community. Along with this goes increasing awareness of data available, which might help in the design of execution of projects or even be the basis of new projects and at the moment this very positive aspect of data sharing is not widely leveraged.

Human subject data

Specific challenges exist for radiobiology and epidemiology research data concerning human subjects. While the collaborative and international sharing of data on human subjects has always been subject to appropriate legal and ethical constraints, the development of new international legal governance structures, particularly the European GDPR, and successful challenges to existing mechanisms for international data sharing, which potentially impact on the EU-US safe-haven concept for health data [13][1], have occurred at a time when new analytical techniques and international collaborations require large-scale data aggregation and integration to support the analysis of Big Data in the health sciences. The recent requirement for FAIR data archiving to facilitate sharing and reuse has intersected with acute regulatory concern about the reproducibility of epidemiological studies and transparency of drug trials [14, 15][2], leading to a complex set of ambiguities and contradictions in complying with these new obligations, particularly in Europe, made more difficult by investigators having to ensure compatibility with research ethics requirements concerning informed consent. While GDPR allows researchers to seek consent for participation in scientific studies within accepted ethical norms for the discipline, it is not yet clear whether, under some interpretations of GDPR requirements, this is sufficient for compliance, especially where consent is sought in broad terms.

Intrinsic to the aims of data sharing and reuse is the explicit intention that data be reanalysed and used in ways not foreseen when the data was collected. This is particularly the case where data is collected in the aftermath of a nuclear incident where the type of analysis to which that data might be subjected, or datasets with which it might be integrated or co-analysed, cannot be foreseen. In principle, this conflicts with GDPR provisions for specifying the defined processes for which the data is collected. Fortunately, the GDPR allows for a scientific research exemption, subject to Article 89(1) protections, which is designed to be broadly compatible with current ethico-legal frameworks for the conduct of scientific research. Article 9(2)(j) and Article 89 mean that researchers can retain patient health data long term, use data from one research project for others, and for legitimate areas of scientific research so long as they have appropriate ethical approval [16]. Recital 162 allows an exception for the statistical processing and processing for scientific reasons of personal data enabling the big data analytics and machine learning tools and facilitating data retention and reuse. It is not therefore expected that dataset archiving and reuse will be a problem for human subject data. However, the sharing of data for reanalysis and movement of data across national borders presents more complex potential problems.

A recent report from the European Parliament Panel for the Future of Science and Technology (STOA) has comprehensively addressed the impact of GDPR on the conduct of research on human subjects and personal data. The implementation of GDPR is as yet in its infancy and it is very hard as yet to assess the impact on either the feasibility of some types of research, or the administrative and financial overheads it might entail. Integration of GDPR into national legislative frameworks in Europe has already generated national heterogeneity as research exceptions and derogations may be introduced into national law by member states under Articles 89(2) and (3) of GDPR [17]. The impact of GDPR additionally potentially interacts with human rights legislation and the UN charter on human rights, which puts an obligation for the support of medical research on governments. Article 12 of the ICESCR requires states to “prevent, treat, and control epidemic, endemic, occupational, and other diseases to achieve the full realization of the highest attainable standard of physical and mental health”. This entails “fostering recognition of factors favouring positive health results, e.g., research”. In addition, there are complex interactions with intellectual property legislation discussed in [18] and [19], the consequences of which are yet to be worked through.

Strategies for dealing with these problems are being developed. For example the BBMRI ERIC is producing a unifying Code of Conduct for Health Research, which will address the interpretation and implementation of GDPR, and other strategies have been mooted such as blockchain-based data tracking and more recently

[1] Court of Justice of the European Union; Judgment in Case C-362/14 Maximillian Schrems v Data Protection Commissioner, 6 October 2015

[2] https://www.ema.europa.eu/en/documents/other/european-medicines-agency-policy-publication-clinical-data-medicinal-products-human-use_en.pdf

international database federation. The CINECA consortium has recently launched an infrastructure for the sharing of 1.4 million personal genomes, where data are geographically distributed but discoverable and/or accessible in a unified manner.

Radiation epidemiology datasets like those in other disciplines fall into the two main categories of exposure outcome estimation and clinical procedure or drug trials. More unusually several major occupational health datasets are proprietary and the impact of recent UK data subject legislation and GDPR is yet to be assessed on datasets where analysis is already published and data collection ongoing. With regard to epidemiology data discovery and access, the model currently adopted in STORE is that of describing the dataset metadata in as fine detail as possible and maintaining public contact details for the Data Controllers. In this way STORE hopes to support data reuse and reanalysis together with collaborative efforts without handling the data directly; at least until legal and ethical issues are resolved.

There remains a problem in addition to that of legal constraints on data sharing in the wide range of approaches and procedures adopted locally by clinical trial and epidemiological units, e.g. [20]. There is a clear need for community-wide homogenization and policy recommendations to ensure adherence to consistent best practice to ensure maximization of data sharing and exploitation. Hopefully, the BBMRI recommendations may go some way to developing a benchmark in this area.

In summary, we find that the implementation of FAIR sharing in the radiation science community lags behind other communities for cultural and practical reasons. Some of this practicality concerns adequate and sustainable provision of dedicated data platforms but also allocation to research projects of additional funding dedicated to data management. Training and education with a strong policy drive are also clearly important.

Issues with sharing human data are very similar to those in other epidemiology and clinical trial studies, but in the case of radiation epidemiology large datasets are often collected as part of ongoing monitoring with rather broad analytical intent and in most cases the intention is to store the data for extended period of time. These problems are likely to be resolved as the accepted implementations of GDPR in particular are agreed, but there is currently a risk that national divergence from GDPR through national derogations might generate more problems for sharing and integrating datasets. This needs to be addressed by policy-makers and investigators on a coordinated basis; especially where knowledge-based international regulatory activities are involved.

(b) Sample banks

Available Biobanks for Radiation Research

Biobanks are the cornerstone for any molecular epidemiological research in humans. What makes a biobank a real treasure chest is the combination of high quality biological material with high quality data concerning exposure assessment of the included individuals (not only radiation exposure), life style, health and medical data, as well as epidemiological data.

Biobanks for occupational and accidental radiation exposure

Extensive biobanks, in view of numbers and available information, exist from individuals exposed to radiation in the occupational context. Here first of all the nuclear workers from Russia. Here three Biobanks (Biobank of Mayak PA worker cohort, Russian Human Radiobiological Tissue Repository, Database of Mayak workers´ families) for Mayak workers (see Table 7 below) and also of their relatives are available harbouring several thousands of individuals with more or less quality of the available biosamples. But also, a huge biobank is available in Siberia (The Bank of Biological Materials of SBRC) and for uranium miners in Germany (German Uranium Miner Biobank). These biobanks are precious in respect to their composition – just a normal population cross section, in respect to the exposure assessment and the received dose (usually higher doses than from environmental exposure). The biobanks are especially suitable to follow up individual radiation susceptibility, especially to lung cancer, to investigate non-cancer induced radiation diseases, such as cardiac diseases and radiation specific fingerprints in tumour material. But also individuals exposed to accidental exposure such as the Chernobyl accident and the contamination in the Techa river (The Techa River Cohort Biobank). The Chernobyl Tissue Bank has already proven to be a highly valuable tool to investigate radiation marks in radiation induced thyroid tissue.

Biobanks for medical radiation exposure

Individuals exposed to medical radiation doses are also followed up for acute and late radiation effects after radiation therapy. Here a highly valuable biobank is the output from the REQUITE study, including more than 4,000 individuals mainly from Europe but also from the USA. If the biobank from the ISE cohort is included already in the REQUITE biobank was not stated. A small biobank BACCARAT study from just 114 patients exists also in France but with the advantage that only breast cancer patients are included that receive radiotherapy but no chemical treatment. Another prospective biobank is on the way to be set up from patients with chronic degenerative inflammatory joint diseases. This biobank (IMMO-LDRT01) may also be very precious to analyse effects on the immune system after low radiation dose exposure. Defined numbers of already included or envisaged individuals are not given.

Biobanks for childhood radiation exposure

Radiation side effects are of growing interest in individuals irradiated in their childhood. Here the ISIBELa biobank, the Portuguese Tinea Capitis Biobank and the French Hemangioma Biobank are available to follow up radiation induced effects. Biobanks for children receiving diagnostic radiation dose are on the way to be set up, but are not depicted in the bulletins.

Biobanks to analyse disease markers in population-based biobanks

Analyses of disease markers for adverse effects should best be investigated in huge population based biobanks existing now worldwide. The Biobank of Eastern Finland is highly remarkable since there are all essential health data available, but also the Biobank of the CONSTANCE cohort and the French longitudinal study of children (ELFE).

What is missing are huge already existing biobanks in Austria (Biobank Graz), Asia (Zhangjiang Biobank, Biobank Japan), UK (UK Biobank), Australia (Victoria Cancer Biobank), Canada (Canadian Partnership for Tomorrow Projects), the USA ("All of Us" biobank), FINNGEN Biobank, EuroBioBank network, Germany (German National Cohort Biobank) and Qatar Biobank to name the world largest biorepositories. These biobanks may also be useful in analysing e.g. radon associated risks.

Biobanks from non-human species

Two repositories do exist: the JANUS animal radiobiology archive which do contain material from large mouse and dog experimental studies and biospecimen from NASA´s sponsored life science experiments.

Biobank	Type of Samples	Size	Localization of Biobank	Cohort/Data	AIR² Bulletin
Wismut Biobank	Peripheral blood lymphocytes, blood DNA, blood RNA, plasma, PAXgene tubes, DNA and RNA from tumour and non-tumour FFPE lung tissue	442 high/low exposed workers >400 lung cancer cases of workers 81 children of workers	Munich, BfS, Germany	Wismut Cohort, partially also included in cohort, uranium workers blood samples were collected between 2008-2012; exposure stopped 1990	Issue 1 (October 2015)
French Hemangioma Biobank	Peripheral blood lymphocytes, DNA, cytogenetic slides from T- and B-cells	369 individuals	Paris, CEA, France	French Hemangioma Cohort (Hemangioma patients treated with radiotherapy in childhood, currently 42-75 years old	Issue 4 (February 2016)
Portuguese Tinea Capitis Cohort	Blood DNA (400 cases), oral mucosa cells, lymphocytes, plasma, serum, tumour and normal tissue DNA from thyroid and basal cell carcinoma From patients An age-matched non irradiated control group is also available	1,375 cases	Porto, Ipatimup/Cancer Biology, Portugal	Portuguese Tinea Capitis Cohort – Evaluation of lon term effects of childhood LDR exposure	Issue 7 (May 2016)
French longitudinal study of children (Elfe)	Maternal urine, blood, milk and hair at birth, cord blood and	For a subgroup (~400?)	https://www.elfe-france.fr/en/the-research/publications/academic-journals/	18,000 children involved in the cohort, children followed from birth to adulthood, Radon	Issue 8 (June 2016)

	meconium stools and hair from newborns, urine and stools from children			study included and medical irradiation	
JANUS Animal Radiobiology Archive	FFPE tissue from different animal species (mice, dogs) irradiation experiments		NASA and US Department of Energy http://janus.northwestern.edu/janus2/index.php Northwestern University, USA	Animal lifespan, diseases and time of death from animal studies between 1950-1990	Issue 11 (October 2016)
Biobank of Eastern Finland	FFPE tissue samples, Frozen tissue samples, plasma and serum, blood, DNA	250,000 samples from 100,000 individuals	https://ita-suomenbiopankki.fi/en/researchers/ North Savo Hospital District, the South Savo Social and Health Care Authority, Siun sote – the Joint Municipal Authority for North Karelia Social and Health services, the Eastern Savo Hospital District, and the University of Eastern Finland	Hospital integrated Biobank – each new patient is asked to donate biosamples	Issue 13 (Decembe er 2016)
Chernobyl Tissue Bank	Frozen tissue, DNA and RNA extracted from frozen tissue, blood samples, DNA from blood, serum, sections from FFPE tissue	4,500 cases	London, Coordinating Centre: CTB secretariat, Department of Surgery and Cancer, Imperial College, UK	Cases of thyroid cancer and adenoma from exposed Chernobyl fall out areas of Ukraine and Russia and also from non-exposed areas. Part of the samples are included in the Ukraine-American Cohort	Issue 14 (February 2017)
The Techa River Cohort Biobank	Cells, DNA, fixed slides	30,000 individuals in cohort, but how many biosamples is not clear	Chelyabinsk, Urals Research Center for Radiation Medicine, Russia	Techa River Cohort (Cohort study of general population exposed on the Techa River) – population exposed to radionuclide (^{99,90}Sr, ^{137}Cs release in water/river sediments	Issue 23 (Decembe r 2017)
The Bank of Biological Materials of SBRC	Blood, blood DNA, tissue samples (normal and tumor),	20,000 samples from 10,000 individuals	Seversk, Seversk Biophysical Research Center, Russia	Siverian Group of Chemical Enterprises (SGCE), the world´s largest nuclear industrial complex, residents of Seversk	Issue 26 (April 2018)

	ethanol/acidic acid cell suspension				
Biobank of Mayak PA worker cohort	Tumour and non-tumour tissue fixed in formalin and embedded in paraffin, blood components, DNA	22,000 (from 13% biological material available) ~ 2860 individuals?	Ozyorsk, Southern Urals Biophysics Institute, Russia	Mayak PA Worker Cohort	Issue 28 (June 2018)
Russian Human Radiobiological Tissue Repository (RHRTR)	Organs and tissues fixed in formalin and embedded and stored as paraffin blocks and histology slides	350,000 samples from 9,560 individuals	Ozyorsk, Southern Urals Biophysics institute, Russia	Mayak PA Worker Cohort	Issue 29 (July 2018)
ISIBELa, KIKme	Fibroblasts, Saliva	104 cases of secondary neoplasm; 377 cases no SPN; 137 sex and age matched controls	Mainz, University Mainz, Germany	The ISIBELLA Cohort (an interdisciplinary study on radiation induced second cancer) – childhood cancer 0-15 years of exposure	Issue 33 (Decembe r 2018)
The ISE cohort	DNA, RNA	476	Heidelberg, DKFZ, Germany	The ISE Cohort (Individual sensitivity to radiotherapy for breast cancer)	Issue 34 (February 2019)
NASA´s sponsored life sciences experiments	Various Biospecimen (human, animal, plant, bacteria)	7,000	https://lsda.jsc.nasa.gov/Biospecimen	NASA experiments	Special Issue 4, February 2019
Database of Mayak workers´ families	Tumour and non-tumour tissues (formalin-fixed, paraffin embedded tissue	11,030	Ozyorsk, Southern Urals Biophysics Institute, Russia	Mayak PA worker Cohort (Unclear which material is available for family members	Issue 35 (March 2019)

	blocks, histological slides), blood and its components?, DNA				
CONSTANCES	Blood, urine	200,000		CONSTANCES (population-based cohort in France from 2012-2019) 18-69 years	Issue 36 (April 2019)
IMMO-LDRT01 Cohort	Serum, Plasma, frozen PBMC	N?	Erlangen, Germany	IMMO-LDRT01 CORHORT (Cohort of locally low-dose irradiated patients with chronic degenerative, inflammatory joint diseases) prospective study in Erlangen	Issue 37 (May 2019)
BACCARAT	Plasma	114	Paris, IRSN, France PI: Dr. Sophie Jacob	The BACCARAT Study (Early cardiotoxicity after radiotherapy for breast cancer): only Radiotherapy patients without chemotherapy included, 2 years prospective study	Issue 38 (June 2019)
REQUITE	Blood DNA (N = 4,400), RNA (N= 1,837), PAXgene tubes (1,202)	4,438	Data and Biobank centralized in Manchester, UK	REQUITE (Mainly European, USA included): Radiotherapy Patients (lung cancer, prostate cancer, breast cancer	Issue 40 (Septemb er 2019)

Table 7: Overview of existing biobanks and cohorts

(c) Cohorts

Cohorts are essential infrastructures for human radiation protection research. Although many health effects of ionizing radiation exposure on human health (mostly on cancer) have been strongly established, it is still relevant to use a variety of cohorts in order to study the potential health effects of exposures occurring at ever decreasing doses, including cancer but also non-cancer outcomes. Linking these cohorts with biobanks is essential to determine biological pathways from radiation exposure to radiation-related diseases, in order to better communicate judgements on the causal nature of observed associations, improve predictions and possibly to identify biomarkers that would be useful for prevention and monitoring of radiation-related risks.

One of the reasons why so many cohorts are needed (beyond the obvious desirability to replicate and validate findings across study setting), is also to evaluate whether the various modalities of radiation exposure (e.g. particle types, internal versus external exposures, dose levels, dose rates) yield health effects that are compatible with hypotheses retained by the ICRP to define radiation protection standards, and evaluate whether any change is necessary. The various characteristics of study populations (children versus adults, men versus women, people with different genetic backgrounds or lifestyles) also justify the conduct of studies in cohorts contrasted on these characteristics in order to study radiosusceptiblity and radiosensitivity [21].

Essential criteria for quality and informativeness of cohorts have been reviewed by UNSCEAR [22]. This notably includes adequate dosimetry, information on potential confounding factors, absence of selection bias, sufficient follow-up and size in order to get enough statistical power for analysis.

The cohorts presented in the AIR² bulletins cover a variety of radiation exposure situations: medical, occupational, and environmental (including post-accidental) exposures. They cover external exposure at various doses and dose rates (from low dose to high doses delivered for radiotherapies) and internal exposure to a wide array of radionuclides. Various age at exposures have also been considered.

Most well-established radio-epidemiological cohorts available (at least in part) in Europe have been covered. This notably includes large international projects such as the EPI-CT cohort of CT scans or the INWORKS study of radiation workers. When such international studies have been covered, no further focus on national datasets included in these international analyses have been made. Some cohorts located outside of the European Union (e.g. in Japan, USA, Russia, Kazakhstan) have also been presented.

Among major radio-epidemiological databases, which have not been covered by AIR², several projects must be mentioned. This includes ongoing international analyses such as the Poolded Uranium Miners Analysis (PUMA), international Pooled Analysis of Uranium Workers (iPAUWthe United States Based Million Person Study, the EURATOM-Funded HARMONIC project). The Fukushima health management survey is also a study that would deserve additional coverage in the future. Studies on natural background radiation have not been included (although some authors have been contacted), as well as other studies covering different situations of environmental exposure (e.g. other radiation fallout studies, residents of radiocontaminated buildings in Taiwan). Last, many cohorts of medical exposure (including medical workers) have not been covered, notably studies of U.S. Radiologic Technologists Study in the United States and South Korea. A very large study of childhood CT scans exists in Australia. Several studies of radiotherapy patients in Europe (e.g. childhood cancer survivors studies grouped in the PanCareSurFup project covering 11 European countries), but also in North America (childhood Cancer Survivors studies in the US and Canada). Many studies of adults receiving radiotherapies for various conditions exist worldwide and have led to joint analyses or meta-analyses [23]. A wealth of other finalized and ongoing cohort studies related to different medical exposure exist. Properly reviewing all of them would require major collective efforts on a global scale.

References Chapter 2

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Chapter 2 : Databases, Sample banks, Cohorts		
Subcategories	**Infrastructure**	**Other categories**
(a) Databases	FREDERICA	
	STORE	
	Wildlife Transfer Database	
	RES³T	
	JANUS Animal Radiobiology Archive	
	MARiS – MARine Information System	
	The BRIDE platform	
	Database of Mayak workers' families	
Add-on section	NASA's LSAH and LSDA repositories	(b)
Add-on section	The "hematopoietic system" database for Mayak nuclear workers	(b)
(b) Sample banks	Biobank of Eastern Finland	
	Chernobyl Tissue Bank	
	Belgian Soil Collection	
	The Bank of Biological Materials of SBRC	
	Russian Human Radiobiological Tissue Repository (RHRTR)	
(c) Cohorts	The Wismut Cohort and Biobank	(b)
	French Haemangioma Cohort and Biobank	(b)
	3-Generation exposure study	(b)
	Portuguese Tinea Capitis Cohort	(b)
	French longitudinal study of children (Elfe)	(b)
	INWORKS Cohort	
	EPI-CT scan cohort	
	Chernobyl clean-up workers from Latvia	
	ESTCHERN Cohort	(b)
	German airline crew cohort	
	The Techa River Cohort (TRC)	(b)
	Greek interventional cardiologists cohort	
	The German Thorotrast Cohort Study	
	Mayak PA worker cohort (MWC)	(b)
	The TRACY cohort	
	The ISIBELa cohort	(b)
	The ISE cohort	(b)
	CONSTANCES	(b)
	IMMO-LDRT01 cohort	(b)
	The BACCARAT study	(b)

	Life Span Study (LSS) REQUITE	(b)

Table 8: Databases, Sample banks, Cohorts cross table with tags for each infrastructure

Chapter 2: Databases, Sample banks, Cohorts

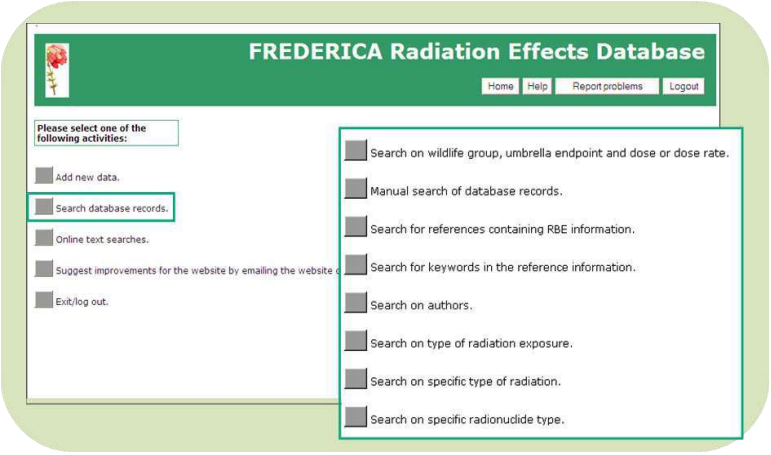
a) Databases

FREDERICA

A unique database on the effects of ionising radiation in non-human biota

Knowledge of ionising radiation-induced effects on diverse organisms is crucial to assess the radiological impact on the environment. The FREDERICA radiation effects database was developed to provide an online compilation of the known effects of ionising radiation on non-human species. The database was produced under the EC funded project ERICA (Environmental Risk from Ionising Contaminants: Assessment and Management) and is available online (see link in ID Card).

FREDERICA contains some 30,000 data entries from 1,231 references. The data entries correspond to pairs of points (exposure level, biological effect) along with information on the conditions in which these data were obtained (tested species, life stage, exposure regime, effect endpoint, etc.). The data are organised into wildlife groups (amphibians, aquatic invertebrates, aquatic plants, bacteria, birds, crustaceans, fish, fungi, insects, mammals, molluscs, mosses/lichens, reptiles, soil fauna, terrestrial plants and zooplankton). While the biological effects reported in the database are at an individual level, the endpoints considered include those relevant to possible responses at the population level (e.g. reproductive capacity, mortality, morbidity and mutations) [1].



Search capabilities of the FREDERICA database

Each reference in FREDERICA was reviewed for the information that is available to the reader in relation to dosimetry, experimental design and statistics. The information provided was scored to reflect the presence or absence of these key data. This provides a measure of the quality of the information in each reference so that if further work is needed (e.g. to refine risk assessment criteria) those papers which contain most, if not all, of the likely information can be easily found.

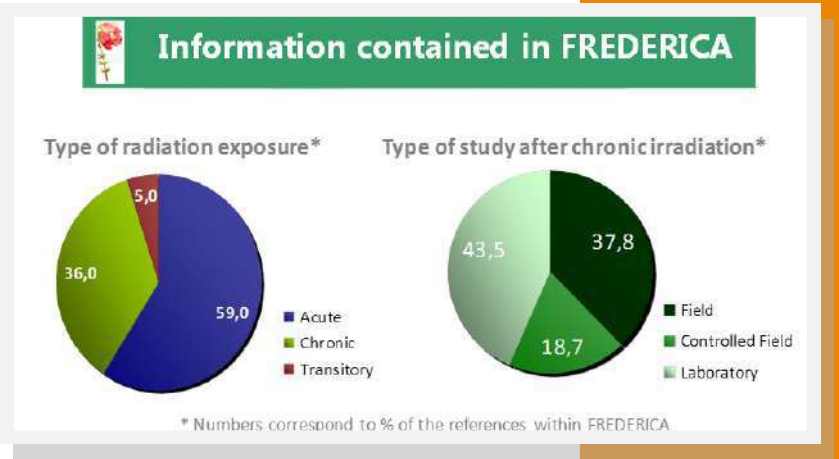
Almudena Real

Within the information compiled in FREDERICA, 64% of the data sets have been obtained after acute and transitory exposure to radiation (59 and 5%, respectively), whereas 36% of the data sets have been obtained after chronic irradiation. Chronic irradiation studies are considered to be more relevant to environmental radiological protection [2]. Considering chronic exposure data, fish, mammals and terrestrial plants are the wildlife groups most widely reported, representing 70.5% of the FREDERICA data for chronic irradiation. The information is scarce for bacteria, crustaceans, fungi, moss and lichen, and zooplankton, since only one or two references have been found for these groups. There is no information on the effects of chronic irradiation for amphibians, aquatic plants or reptiles [1].

FREDERICA offers several search capabilities (see Figure above), for which outputs can be exported as an Excel or text file.

The FREDERICA database has been used in many applications, such as:

- Helping define biological effect levels.
- Inclusion as part of the ICRP Reference Animals and Plants (RAPs) review.
- Inclusion as part of the UNSCEAR review on biological Endpoints.
- Integration into the ERICA Tool to perform environmental risk assessments.



FREDERICA Radiation Effects Database

ID Card:

Database topic:
Ionising radiation-induced effects

Information available type:
Exposure-biological effect, species, life stage, irradiation regime. Searchable

Data type:
Peer reviewed articles

Link with a biobank:
No

Exportable:
Yes

Species:
Non-human animals and plants

Internet link:
http://www.frederica-online.org/mainpage.asp

Access:
Free (user needs to register)

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+44 01786 467852

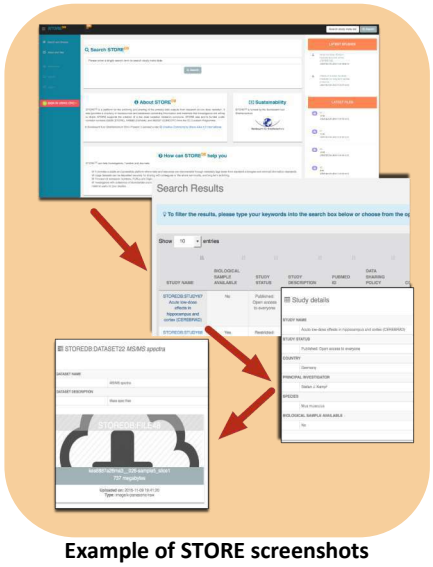
Related to: ALLIANCE

[1] THE DEVELOPMENT AND PURPOSE OF THE FREDERICA RADIATION EFFECTS DATABASE. D. Copplestone, et al. Journal of Environmental Radioactivity 99: 1456-1463 (2008).
[2] ISSUES AND PRACTICES IN THE USE OF EFFECTS DATA FROM FREDERICA IN THE ERICA INTEGRATED APPROACH. J. Garnier-Laplace, et al. Journal of Environmental Radioactivity 99: 1474–1483 (2008).

STORE

An infrastructure for sharing of data and resources

Sharing primary data to enable accountability, reproducibility and re-use has become a concern for the whole of the scientific community in recent years. Funding agencies and journals alike now insist that the products of publicly-funded science are made freely available. The European Commission has been in the forefront of open data policies, and the sharing of data and biomaterial from publicly-funded radiation protection related science will be required by Horizon 2020. Open data adds great value to the original investment and yields substantial scientific rewards [1].



Picture: P. Schofield/UCam

Example of STORE screenshots

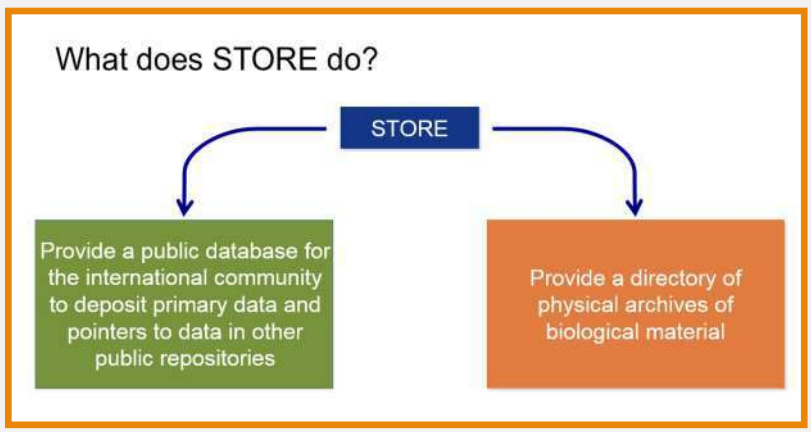
Based on experience from the ERA database [2], the STORE consortium created a platform to provide an infrastructure for the storage and dissemination of data from radiobiological research. When STORE became part of DoReMi, it was broadened to fit the needs of radiation epidemiology and it took on the additional role of acting as a directory of bioresources. With the start of CONCERT, it became clear that the needs of other platforms or consortia should also be considered, e.g. ALLIANCE and RENEB. CONCERT's Subtask 6.2.1 will develop STORE according to this new user need, and a contract between BfS and the University of Cambridge, the developer of STORE (UCam, Paul Schofield), has been signed within the framework of CONCERT.

STORE is a platform for resource sharing which enables users to locate data or bioresources, such as physical samples (tissue samples, FFPE blocks, slides, etc.), using structured metadata and standard vocabularies. Users, identified by their ORCID IDs, can upload primary data of any format, accession IDs for data in other databases, and details of physical samples. Data is assigned an accession number and will be given a DOI which will enable it to be cited in publications. Uploading is project-based and users retain control and ownership of their data. The BfS provides long term sustainability and data security so that users can be assured of longevity and security. Data may be stably archived for future use, cited in support of publications, or shared between collaborators. The database has additional applications for standardisation, validation, education and radiological emergency resilience.

Photo: R. Kanzliwius/BfS

Bernd Grosche

STORE is available at http://www.storedb.org. The resource is open and free to individual investigators, journals and funding agencies. It establishes the basis for long-term use and exchanges between scientists from different countries and from various fields; in addition, its flexibility and agility allows it to act as a sharing and archival infrastructure for the whole radioprotection research community. Links to other relevant databases have already been established (e.g. CTB, ERA, Janus) and further links will follow (e.g. FREDERICA). STORE will be federated with the European Commission's re3data initiative, Biosharing, and will be compliant with Nature Scientific Data's criteria for recognised repositories. Questions and suggestions are welcome at store@bfs.de.



Picture: P. Schofield/UCam, & B. Grosche/BfS

ID Card:

Database topic:
Primary data from low dose radiation studies, materials and bioresources.

Description:
STORE is a platform for the archiving and sharing of the primary data outputs from research on low dose radiation. In addition it provides a directory of bioresources and external databases containing relevant information and materials that investigators are willing to share.

Data ownership:
Ownership of Data remains with the originator, but the database is under the direction of BfS and UCam.

Data type:
Any kind of data, no format requirements

Access:
Free to deposit and recover data. Sign up via ORCID ID. Data can be selectively released by the originator or made totally open.

Exportable:
Data can be exported

Species:
Humans, animals, plants (to come)

Internet link:
http://rbstore.eu; http://storedb.org

Contact:
store@bfs.de
At BfS:
Bernd Grosche, bgrosche@bfs.de
Ulrike Kulka ,ukulka@bfs.de
Mandy Birschwilks, mbirschwilks@bfs.de
At UCam:
Paul Schofield ,pns12@cam.ac.uk
Michael Gruenberger (technical support), mg287@cam.ac.uk

Related to:
CONCERT, MELODI, ALLIANCE, RENEB

[1] **ARCHIVING LESSONS FROM RADIOBIOLOGY.** Schofield PN, Tapio S, Grosche B. Nature 2010; 468:634-634

[2] **THE EUROPEAN RADIOBIOLOGICAL ARCHIVES: ONLINE ACCESS TO DATA FROM RADIOBIOLOGICAL EXPERIMENTS.** Birschwilks M, et al. Radiat Res 2011; 175:526-531.

Wildlife Transfer Database

Database collating concentration ratios for wildlife

A key element of most systems for assessing the impact of radionuclides on the environment is a means to estimate the transfer of radionuclides to organisms. To facilitate this, an international wildlife transfer database (WTD) was developed

to provide an online (http://www.wildlifetransferdatabase.org/), searchable compilation of transfer parameters in the form of equilibrium-based whole-organism to media concentration ratios (CRwo-media). The database was subsequently used to produce IAEA (TRS-479) and ICRP (ICRP-114) publications and also to populate version 1.2 of the ERICA Tool (http://www.erica-tool.com/).

The original version of the WTD, as described by Copplestone et al. (2013) contained information from 523 references. There were more than 50,000 lines of data representing 86,979 CRwo-media values for 1438 species and 71 elements. Subsequently, about 17,000 additional CRwo-media values have been added to December 2013 (Brown et al., 2016). These new inputs include: data for representative species of the ICRPs Reference Animals and Plants from a UK forest; monitoring data from Finland and Japanese estuaries; Canadian wildlife data; Pu data from US weapons testing programme sites; data for wild plants and invertebrates from north western USA. The number of elements included, as of December 2013, had increased to 80.

Photo: R. Fawkes(University of Salford

Nick Beresford

Currently the database is being used to: develop the update of IAEA SRS-19; by the ICRP in the development of its environmental protection framework; and to develop novel transfer models by the TREE project (http://www.ceh.ac.uk/tree).

The wildlife transfer database is being maintained and is open for all interested parties to add appropriate data. Periodically updated summary tables are provided on the database website. A help file for completing the database is available from: https://wiki.ceh.ac.uk/x/-QHbBg. Anybody wanting to add large amounts of data should contact Nick Beresford or David Copplestone to discuss how this can be most efficiently done.

Sampling earthworms (http://www.ceh.ac.uk/tree)

Photo: C. Barnett/NERC-CEH

ID Card:

Database topic:
Radioecology

Information available type:
Wholebody radionuclide concentration ratios

Data type:
Database

Link with a biobank:
no

Exportable:
Summary tables only

Species:
All wildlife (plants and animals)

Internet link:
http://www.wildlifetransferdatabase.org/

Access:
Free – to add data and view/export summaries

Contact:
Nick Beresford
nab@ceh.ac.uk

David Copplestone
david.copplestone@stir.ac.uk

Related to:
ALLIANCE

AN INTERNATIONAL DATABASE OF RADIONUCLIDE CONCENTRATION RATIOS FOR WILDLIFE: DEVELOPMENT AND USES. Copplestone, D. et al. 2013. J. Environ. Radioact. 126, 288-298.

A NEW VERSION OF THE ERICA TOOL TO FACILITATE IMPACT ASSESSMENTS OF RADIOACTIVITY ON WILD PLANTS AND ANIMALS. Brown, J.E., et al. 2016. J. Environ. Radioact. 153, 141-148.

RES³T

Mineral-specific sorption data (for mechanistic models)

RES³T, the Rossendorf Expert System for Surface and Sorption Thermodynamics, is a digitised thermodynamic sorption database which is implemented as a relational database. It is mineral-specific and can therefore also be used for additive models of more complex solid phases such as rocks or soils. Its purpose is to support reactive transport modelling for contaminants through the geosphere and ecosphere. RES³T allows the parameterisation of mechanistic sorption models, offering added value in the form of explanations and scientific support for measured data, and increasing confidence levels especially for Kd values measured under complex site-specific conditions. Predictive uses can provide approximations for parameter spaces that are difficult or too time-consuming for experiments. Combined with sensitivity and uncertainty analyses, it can probe the influence of variability and uncertainties in geochemistry on Kd. It may also improve experimental set-up. In addition, it can provide scoping calculations and estimate the possible effect of "what-if" scenarios on Kd.

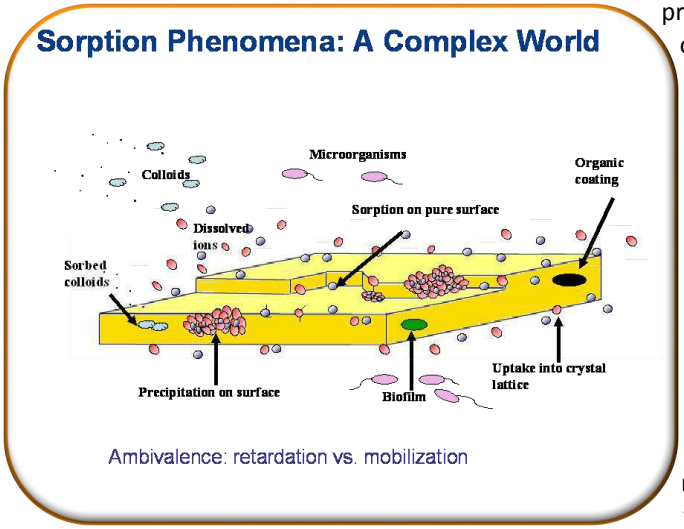


Photo: V. Brendler / HZDR

The universum of processes affecting the transport of contaminants through the ecosphere

An integrated user interface helps to access selected mineral and sorption data, to extract internally consistent data sets for sorption modelling, and to export them into formats suitable for other modelling software. Data records comprise mineral properties, specific surface area values, characteristics of surface binding sites and their protolysis, sorption ligand information and surface complexation reactions. The database contains originally published values only, i.e. for many surface reactions, different competing constants are provided (no recommended values), thus the user has to decide which values to actually use. The surface complexation models which are most extensively covered include the Constant Capacitance, the Diffuse Double Layer, the Triple Layer, the Non-electrostatic and the CD-MUSIC approaches. The two surface protolysis steps are supported. The selection of minerals via the RES³T interface allows comprehensive modelling of retardation in most of the relevant soil and rock types, thus delivering source terms for a broad variety of transfer coefficients. The focus for dissolved contaminants and ligands is currently set to radionuclide, heavy metals and arsenic, but in principle any dissolved moiety that is able to sorb onto surfaces can be included.

Photo: J. Grämer / HZDR

Vinzenz Brendler

An extensive bibliography is also included, providing links not only to the above-listed data items, but also to background information on surface complexation model theories, surface species evidence by independent spectroscopic and quantum chemical approaches, and sorption experiment techniques. Access to the database is free and requires no registration. However, the developers are grateful for any critical feedback to further improve functionality and extend the range of application areas.

This project was funded by the German Federal Ministry of Economics and Labour (BMWA) under contract No. PtWt+E 02E9471.

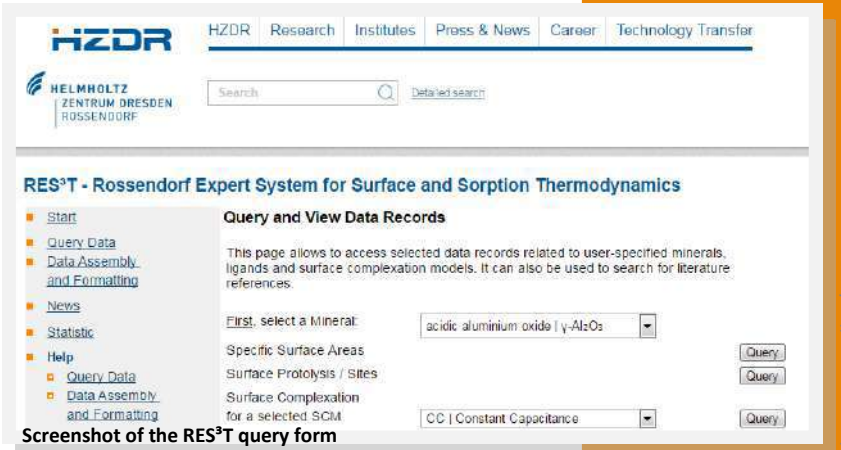


Photo: V. Brendler / HZDR

Screenshot of the RES³T query form

RES³T-ROSSENDORF EXPERT SYSTEM FOR SURFACE AND SORPTION THERMODYNAMICS. V. Brendler, et al. Journal of Contaminant Hydrology, 61 (2003), 281-291.
GUIDELINES FOR THERMODYNAMIC SORPTION MODELLING IN THE CONTEXT OF RADIOACTIVE WASTE DISPOSAL. Payne T.E., et al. Environmental Modelling & Software, 42 (2013), 143-156.

ID Card:

Database topic:
Geochemistry, Radioecology

Information available type:
Mineral-specific sorption data (for mechanistic models)

Data type:
Thermodynamic sorption data, mineral characteristics, bibliography

Link with a biobank:
Not available

Exportable:
ASCII, CSV, MS Excel

Species:
138 Ligands onto 135 minerals (as of April 2016)

Internet link:
www.hzdr.de/res3t

Access:
Free, but usage shall be cited

Contact:
Vinzenz Brendler
V.Brendler@hzdr.de
+49 351 260 2430

Related to:

JANUS Animal Radiobiology Archive

Irradiated animal data and tissue archive

Created by Dave Paunesku for the Woloschak Lab at Northwestern University and financed by NASA and the US Depatment of Energy, a collection of data and tissue samples from materials made at different US National Laboratories during animal studies done between 1950's and 1990's is accessible. The Janus experiments, carried out at Argonne National Laboratory from 1972 to 1989 and supported by grants from the US Department of Energy, investigated the effects of neutron and gamma radiation on mouse tissues primarily from B6CF1 mice.

photographer T. Paunesku

Pr Gayle Woloschak

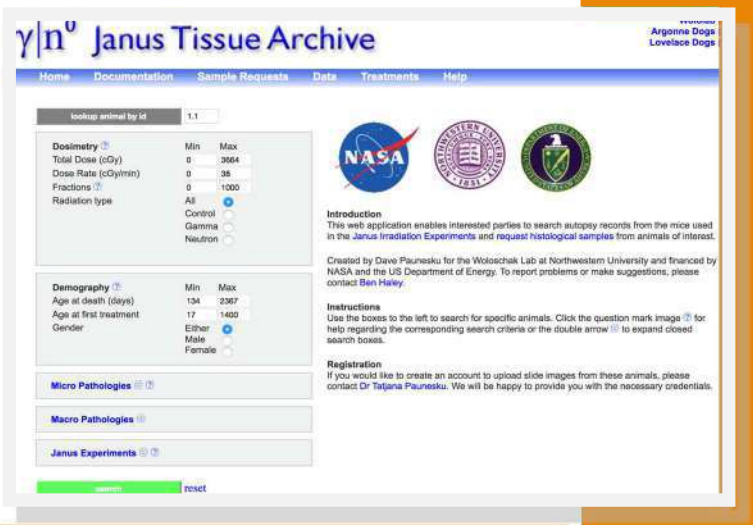
these animals is comprehensive, including details about irradiations (age of first exposure, dose, dose rate, delivery protocol etc.) as well as animals (gender, species, strain, age at first and final exposure, age at death, health status etc.). Much of the recent work was made public not only through publication but also through open source sharing.

Historic ANL photo

Janus irradiator configuration surrounded with animal cages

For example, both data [https://github.com/benjaminhaley/janus/blob/master/data/external5.rds] and scripts [https://github.com/benjaminhaley/janus/blob/master/scripts/exp/ddref.Rmd] used for work published in reference 1 are available on github. Therefore, materials available in Janus Animal Radiobiology Archive may also be used for training/educational purposes.

Data and paraffin embedded tissues from thousands of mice and dogs exposed to ionizing radiation are available for research. These materials were collected over several decades of DOE funded research. Studies using these materials and information include computational research (see e.g. reference 1) as well as use of tissues for PCRs, immunohistochemistry, X-ray fluorescence microscopy (e.g. reference 2) etc. All of these resources are available for collaborative research with CONCERT projects and may be of interest for several reasons: (a) archival materials include tissues from many thousands of animals exposed to low dose rates or low doses of radiation; (b) data about radiation exposures of



THE INCREASE IN ANIMAL MORTALITY RISK FOLLOWING EXPOSURETO SPARELY IONIZING RADIATION IS NOT LINEAR QUADRATIC WITH DOSE
Haley BM, Paunesku T, Grdina DJ, Woloschak GE. PLoS One. 2015 Dec 9;10(12)
PAST AND FUTURE WORK ON RADIOBIOLOGY MEGA-STUDIES: ACASE STUDY AT ARGONNE NATIONAL LABORATORY
Haley BM, Wang Q, Wanzer B, Vogt S, Finney L, Yang PL, Paunesku T, Woloschak G. Health Phys. 2011 Jun;100(6):613-21.

ID Card:

Database topic:
Radiobiology

Information available type:
Exposure dose, age of exposure, gender, species, dose rate, time of death, necropsy report (gross and micro pathology), searchable

Data type:
animal lifespan, diseases at time of death

Link with a biobank:
yes (paraffin tissues only)

Exportable:
yes

Species:
mice,dogs

Internet link:
http://janus.northwestern.edu/janus2/index.php

http://janus.northwestern.edu/janus2/dog_tissues/

http://janus.northwestern.edu/lovelace/

Access:
free

Contact:
Tatjana Paunesku
t.paunesku@gmail.com

Benjamin Haley
Benjami.haley@gmail.com

MARiS – MARine Information System

Measurements of radioactivity in the marine environment

On behalf of its Member States, the IAEA Environment Laboratories are responsible for the data curation and development of the Marine Information System (MARiS), an online database of levels of radionuclides in the marine environment. MARiS makes available data and information on radionuclides for scientists, policy-makers and interested members of the public to have a better understanding of radioactivity levels in the world's oceans.

Photo: V. Shi/Xiamen University

Paul J. Morris

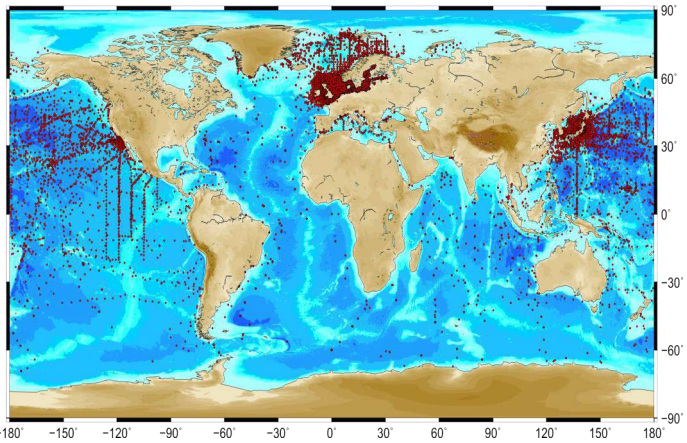


Photo: P. Morris/IAEA

The global distribution of measurements of radionuclides in seawater contained in MARiS

Seawater, sediments and biota in the ocean are naturally radioactive. In addition, the ocean contains a comparatively small amount of radioactivity resulting from anthropogenic activity (i.e. human-caused). The major sources of anthropogenic radionuclides include fallout from nuclear weapons testing, and both routine and accidental releases from nuclear facilities. These radionuclides end up in the marine environment through direct discharges, atmospheric deposition, or run-off from land. The majority of naturally-occurring radionuclides originate from the rocks and sediments that make up the Earth's crust and ocean floor, while others are produced by the interaction of cosmic rays with the higher atmosphere. Access to data on marine radioactivity is essential for understanding natural marine processes and humans' impact on the seas and oceans.

The MARiS database currently contains over 176,000 marine radioactivity data, representing more than 60 different radionuclides or radionuclide ratios in seawater, biota, seabed sediments, and suspended matter. Data contained in the MARiS database is extracted from a larger in-house database called GLOMARD, the Global Marine Radioactivity Database, which serves as the master database for data curation and validation prior to inclusion in MARiS. Marine radioactivity measurements have been collected, managed and curated at the Environment Laboratories in Monaco since the early 1990s. Data originates from published scientific papers, reports, and databases created within institutes or scientific programmes in Member States. Data included in MARiS has either already been published or has been submitted directly from a data provider with permission to include the data in MARiS. MARiS website users can search for data using various criteria, for example geographical region, type of sample, radionuclide, date or depth.

Data in MARiS can be used by Member States to assess distributions and trends of radionuclides; validate dispersion models, provide data constraints for radiological assessment models; and investigate marine processes (e.g. water-mass transport, carbon cycling, sedimentation rates), some of which influence pollution and climate. In addition to scientists and policy-makers, MARiS can be used by the public to access reliable information about radioactivity in the marine environment.

If you have data that you would like to contribute to MARiS you are invited to email the contact in the ID Card.

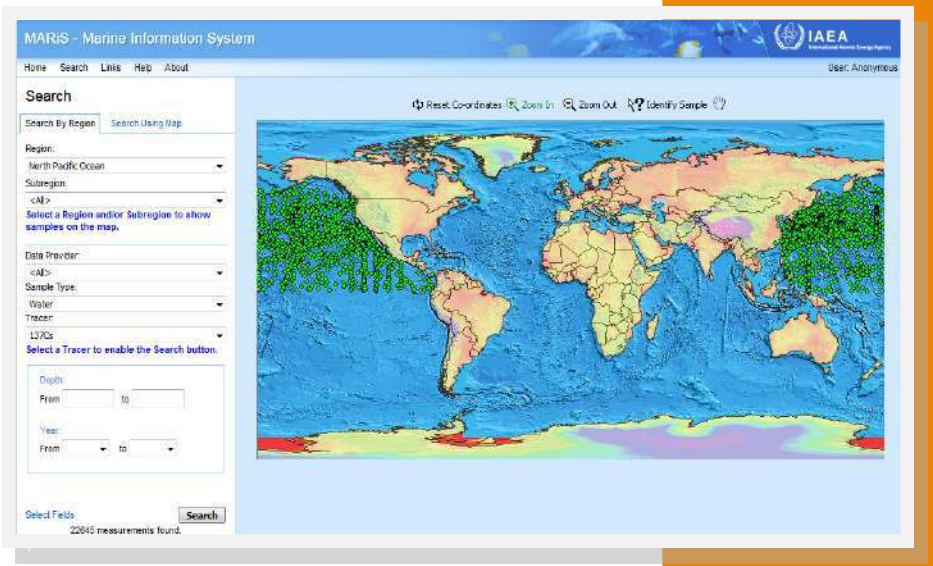


Photo: P. Morris/IAEA

Screenshot of the MARiS query form and auto-updating map when searching for measurements of, for example, Cs-137 in seawater in the North Pacific

ID Card:

Database topic:
Marine radioactivity

Information available type:
Measured activities of radionuclides in marine samples with associated metadata

Data type:
Reported values from publications, data reports, other databases, and direct submission from data-originators

Link with a biobank:
No

Exportable:
Preview table is exportable to a downloadable CSV file

Species:
Marine samples: seawater, sediment, biota, suspended matter

Internet link:
https://maris.iaea.org/

Access:
Open access with a request to acknowledge the source of the data

Contact:
MARIS.Contact-Point@iaea.org

Related to:
ALLIANCE

Global marine radioactivity database (GLOMARD), IAEA (2000), TECDOC-1146

MARiS homepage contains links to various presentations

The BRIDE platform

List of mouse genes affected by low-dose ionising radiation

BRIDE is a data integration platform which offers a lightweight approach for storage, analysis and distribution of relevant low-dose ionising radiation (LDIR) omics datasets at gene level and, through connections to other resources, it provides access to a wide range of additional information that can be explored by interested researchers.

Photo: BRIDE

List of tools by which the data can be accessed and/or linked to other domains (NCBI for sequence and other databases, Intact for protein interactions, Rbstore for StoreDB context, Allen Brain Atlas for relevant entries, MGI Phenotypes for phenotypic and other information and PC Viz for vizualisation).

It was developed as part of the FP7 project, CEREBRAD (Cognitive and Cerebrovascular Effects Induced by Low Dose Ionizing Radiation), the main aim of which was to identify the potential cognitive and cerebrovascular risks of radiation doses below 100mGy. In this project, experimental data were gathered from carefully crafted experiments using animal models exposed to radiation at different stages of brain development, with a range of doses and exposure times. The data were recorded in BRIDE, together with all other information available in the literature, extracted by curation of relevant articles. BRIDE currently lists 3174 instances of genes, mostly from the mouse (and some human genes), which exhibit responses induced by low dose radiation. All instances are connected via more than 50,000 links to other database entries, including genes, transcripts and transcriptomes, proteins and protein interactions, pathways, taxonomy, tissues and other relevant experimental information.

Photo: Personal archive

Dr Christos Ouzounis

These open access data are made available for reuse with the aim of supporting further research into the underlying molecular processes which represent stress responses to LDIR in the mammalian brain, and for the discovery of relevant cellular pathways.

All the results recorded in BRIDE are supported by carefully curated articles from the scientific literature as well as transcriptomics and proteomics data sets. BRIDE deploys a hybrid, distributed solution using both local storage and cloud technology. For the more technically oriented, the BRIDE platform is a browser client, 3-tier system, with the application running on the end-user's web browser, while the database and server components run on a database server; the tiers of BRIDE communicate through standard interfaces. Thus, the internals (including data storage and updates) can change without affecting the platform architecture.

BRIDE acts as a knowledge broker platform for LDIR researchers, to boost research on the systems biology aspects of the LDIR response in the mammalian brain. The data captured by a range of experiments in genomics, transcriptomics and proteomics are expected to grow, both in number and depth, with additional funding and support.

The data collection stored in BRIDE is available at: <bride.azurewebsites.net>.

PMID	GENE NAME	UNIPROT	TISSUE	DOSIMETRY	TIME	ORGANISM
25329592	Abr	H3BJY3	Brain	0.5 Gy	24h	Mouse
25329592	Abr	H3BJY3	Brain	1 Gy	24h	Mouse
25329592	Abr	H3BJY3	Brain	1 Gy	24h	Mouse
25329592	Acaa2	Q8BWT1	Brain	0.1 Gy	24h	Mouse
26420666	Acat1	Q8QZT1	Brain	2 Gy	24w	Mouse
26420666	Acat2	Q8CAY6	Brain	2 Gy	5w	Mouse
26420666	Acat2	Q8CAY6	Brain	2 Gy	24w	Mouse
26420666	Acot7	Q91V12	Brain	2 Gy	24w	Mouse
26578848	Acp1	Q9D358	Brain	0.1 Gy	6m	Mouse
25329592	Acsbg1	Q99PU5	Brain	1 Gy	24h	Mouse

Sample of the list of genes stored in BRIDE. PMID is the PubMed identifier of the corresponding article, Gene Name is the name of the corresponding gene, UniProt lists the UniProt identifier of the corresponding protein, Tissue reflects the relevant tissue where the gene response was detected, Dosimetry lists the dose in Gray units (Gy), Time lists the time of exposure in the experiment and Organism records the species (in this case, mouse).

CERTH
CENTRE FOR RESEARCH & TECHNOLOGY HELLAS

ID Card:

Database topic:
Systems Radiobiology, LDIR effects on the mammalian brain, list of 3174 affected genes

Information available type:
Gene name, Database identifier, Tissue type, Dosimetry (dose), Exposure (time), searchable

Data type:
Tabular format, various identifiers (over 55000 links to other resources), tissue, dose, time (brain-specific)

Links with other databases:
NCBI identifier (gene/protein), IntAct identifier (known binary interactions), Rbstore (StoreDB) context (inexact match), Allen Brain Atlas context (inexact match), MGI phenotypes, PCViz (visualisation of interactions, user-selected)

Exportable:
Interactive only, not exportable (yet)

Species:
Mostly mouse (some human)

Internet link:
http://bride.azurewebsites.net

Access:
Free

Contact:
Christos Ouzounis
ouzounis@certh.gr
+30 23 10 49 84 73

Involved in:
CEREBRAD

Related to:
MELODI

Brain Radiation Information Data Exchange (BRIDE): integration of experimental data from low-dose ionising radiation research for pathway discovery, Karapiperis C., Kempf S. J., Quintens R., Azimzadeh O., Vidal V. L., Pazzaglia S., Bazyka D., Mastroberardino P. G. et al. (2016), BMC Bioinformatics, 17 (1), 212
Neonatal irradiation leads to persistent proteome alterations involved in synaptic plasticity in the mouse hippocampus and cortex, Kempf S. J., Sepe S., von Toerne C., Janik D., Neff F., Hauck S. M., Atkinson M. J., Mastroberardino P. G., Tapio S. (2015), J Proteome Res, 14 (11), 4674–4686

Database of Mayak workers' families

Studying risks of adverse health effects in offspring of exposed parents

The MWF database contains data from a cohort of employees of the first Russian nuclear enterprise, the Mayak Production Association (PA), which comprises 22,377 individuals (including 25% female workers). The advantages of the cohort include its large size, long follow-up period (70 years), individually measured doses from a wide range of external and internal radiation, sex/age/ethnicity heterogeneity as well as varying initial health status of the workers, complete information on health effects and vital status, availability of data on non-radiation risk factors and stored biological specimens collected from cohort members. Studies conducted on this cohort of Russian nuclear workers provide strong evidence for association of incidence and mortality from leukemia, solid cancers, circulatory disease, chronic obstructive pulmonary disease and cataracts with chronic occupational low dose rate radiation exposure.

Annual health examinations of the Mayak PA personnel included routine questioning of workers from the study cohort with regard to their family members and non-radiation factors such as lifestyle, socioeconomic status, etc., using standardised questionnaires. The data from these questionnaires was used to create a database for the Mayak workers' families and offspring. The figure illustrates the roadmap used to build the database.

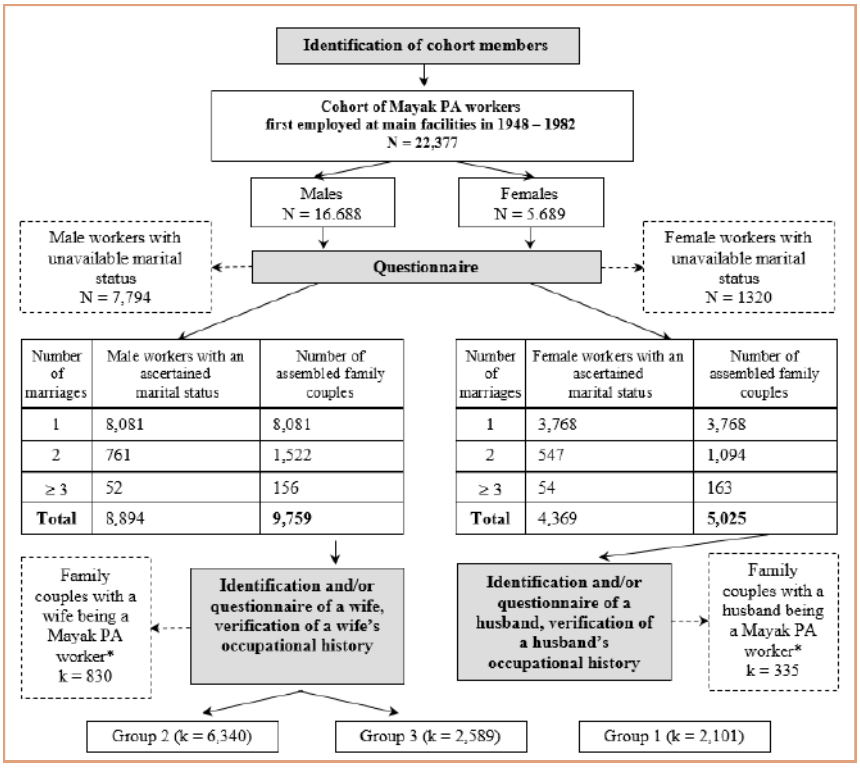
To date, complete information has been collected for 11,030 families from the Mayak PA worker cohort. This includes 6,340 families where only the father was occupationally exposed to radiation, 2,101 families where only the mother was occupationally exposed to radiation and 2,589 families where both spouses were exposed. The range of preconception absorbed gonadal doses is very wide: min 0.01 Gy, max 5.66 Gy, median 0.12 Gy. The mean cumulative preconception gonadal doses from external gamma-rays are 0.37 ± 0.61 Gy for fathers and 0.35 ± 0.50 Gy for mothers.

Photo: SUBI

Dr Tamara V. Azizova

As of 31 December 2018, a total of 16,585 offspring have been identified in these families. The database contains medical data for each family member for the entire follow-up period, data on parental reproductive health and non-radiation factors (smoking, alcohol, body mass index, hypertension, other) as well as individually measured annual (and for 10% of the cohort monthly) doses from preconceptional radiation, stored biological specimens collected from approximately 1,500 family triads, and sufficient statistical power. These resources provide the opportunity to study the risks of adverse health effects in offspring of exposed parents and to investigate the mechanisms of these alterations, including non-targeted and transgenerational effects.

Photo: SUBI



Database roadmap for Mayak workers' families and offspring

Notes: Asterisk (*) denotes that the husband or wife was a worker at the Mayak auxiliary facility or at the main facilities, first employed after 1982 (occupational histories and radiation doses have been clarified and updated), N is the number of workers, k is the number of families: group 1 includes families where only the wife was a Mayak worker, group 2 includes families where only the husband was a Mayak worker, and group 3 includes families where both spouses were employed at the Mayak PA.

ID Card:

Cohort type:
Individual data on families of Mayak PA workers occupationally exposed to external gamma- and internal alpha-radiation at wide dose ranges over prolonged periods.

Age:
- Age at exposure (first employment): 15 – 65 years
- Mean age at end of follow-up: 66 years
- Mean duration of follow-up: 42 years; 939,811 person-years

Biobank available:
Yes

Sample type:
Tumour and non-tumour tissues (formalin-fixed, paraffin-embedded tissues blocks, histology slides), peripheral blood and its components, DNA

Sample storage conditions:
18 - 20°C, -20°C, -80°C, liquid nitrogen

Access:
MWF database is owned by SUBI. Access to anonymous data is limited and is subject to approval by the SUBI Institutional Review Board.

Contact:
Dr Tamara V. Azizova
azizova@subi.su
+7-35130-29395

Address:
Southern Urals Biophysics Institute
Ozyorskoe shosse 19
456780 Ozyorsk
Chelyabinsk region

Related to:
MELODI

Analysis of genome instability in offspring of Mayak workers' families: Minisatellite CEB, Rusinova G. G., Glazkova I. V., Azizova T. V., Osovets S. V., Vyazovskaya N. S. (2014), Russ J Genet, 50 (11), 1200 – 1207
[**DNA bank of exposed Mayak workers and their families**], Rusinova G. G., Glazkova I. V., Azizova T. V. (2010), Medicine of extreme situations, 31 (1), 93–100

Chapter 2: Databases, Sample banks, Cohorts

b) Sample banks

BIOBANK OF EASTERN FINLAND

Potential for development of personalised medicine

The Biobank of Eastern Finland was established by the Hospital Districts of Eastern Finland and the University of Eastern Finland in 2015, in Kuopio. It is a hospital-integrated biobank with a catchment area population of over 800,000. The biobank aims at collecting samples from each new consenting patient entering a hospital in Eastern Finland ("Capture all newcomers" principle).

Existing pathology archives contain 250,000 samples from 100,000 persons. Population based diagnostic samples are connected with clinically relevant information from hospital records, including demographics, treatment, long-term follow-up and genomic data, if available. The advanced Finnish Biobank Act enables the donors to be re-contacted for collection of additional information. Digitalisation of FFPE-tumour material as well as tissue microarrays are ongoing. To ensure high quality samples and data, the Biobank of Eastern Finland implements the OECD Quality Guidelines.

Photo: Alias, Markus Aspergen

Digital pathology service

The population in Eastern Finland is highly homogenous due to the founder effect, geographic and historical barriers and low migration. The combination of the biobank sample material and related genomic and clinical information creates a valuable framework for research towards innovations in personalised medicine.

The specific benefits for Finnish biobank research include the availability of individual social security numbers, old church records dating back to the 17th century used to track people, national health care registries and hospital electronic health records. The data is continually integrated to provide tools for clients with innovative research initiatives. Special emphasis is set on the acceptance and support of the public for the biobank's goals and functions; the Finns, in general, are willing to provide personal information for medical research, which ensures a representative sample of the population.

Sisko Salomaa

Arto Mannermaa

Photo: UEF

The Finnish Biobank Act came into force in September 2013. The purpose of this new act is to promote medical research and innovation and also to protect donor rights and privacy. The key aspects of the legislation are broad consent for upcoming research and the enabling of secondary use of stored samples and related data.

The biobank can assign samples and related data for the sole purpose of high-level health sciences research and product development. Scientists who are planning a research project and would like to use the biobank's materials are invited to contact the biobank for further information for their research design.

The Biobank of Eastern Finland collaborates with the University of Eastern Finland (Department of Environmental and Biological Sciences) in the OPERRA project. The aim is to set up guidance and procedures for the biobanking of samples from patients exposed to medical radiation, and to provide high quality dosimetric information.

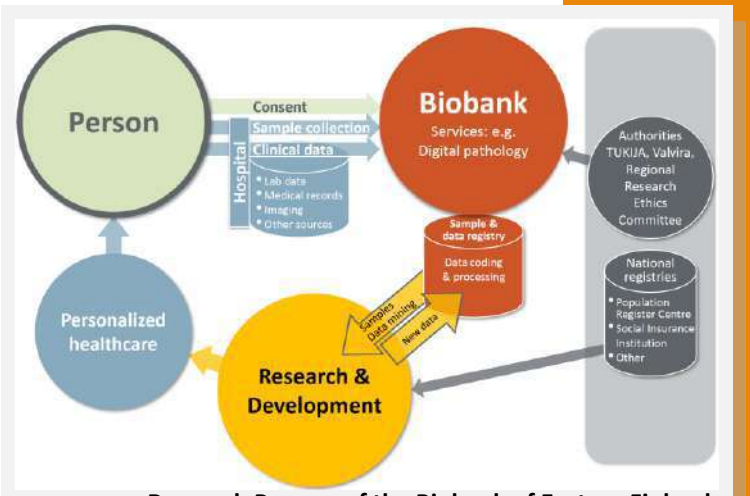


Photo: UEF

Research Process of the Biobank of Eastern Finland

ID Card:

Sample bank topic:
Clinical Biobank

Type of samples:
Human tissue samples and related clinical data from a population isolate in Eastern Finland

Sample type:
Blood, Serum, Plasma, Tissue (FFPE/frozen), DNA

Sample storage condition:
FFPE at room temperature; tissue samples, plasma and serum at liquid nitrogen vapor phase

Condition of use:
For medical research and R&D purposes

Access:
Researchers interested in the biobank material should contact biobank and send a proposal to biobank SAB

Internet link:
www.easternfinlandbiobank.fi

Contact:
Arto Mannermaa
Arto.mannermaa@uef.fi

Related to:
BBMRI,UEF, KUH

MELODI, EURADOS, EURAMED

CHERNOBYL TISSUE BANK

Providing quality assured and annotated human biosamples

The Chernobyl Tissue Bank (CTB) was established in 1998 to collect, store and distribute biological samples from patients born on or after 26th April 1967, and resident in the regions of Ukraine and Russia contaminated by fallout from the Chernobyl accident and who developed thyroid cancer. The project is supported financially by the National Cancer Institute of the USA and the Sasakawa Memorial Foundation of Japan, and has the political support of the Governments of Ukraine and Russia. Patients attending thyroid clinics in the Institute of Endocrinology in Kiev, Ukraine and the Medical Radiological Research Centre in Obninsk, Russia are asked to consent to the use of samples left over from their operation for suspected thyroid cancer for research. The study cohort includes any patient with a pre-operative diagnosis of suspected thyroid cancer, who was resident in the most heavily contaminated regions of Ukraine and Russia at the time of the accident and aged under 19 at the time of the accident (i.e. born on or after 26th April 1967).

Photo: Imperial College

Pr Gerry Thomas

Photo, A Galpine, Imperial College, London

CTB laboratory in IEM, Kiev, Ukraine

The current collection comprises 4500 cases of thyroid cancer and adenoma. 3094 of the 4500 cases are from the exposed areas of Ukraine and Russia, whereas 1406 cases come from the unexposed areas of Ukraine and Russia. There are also 758 post Chernobyl cases (born after 1st December 1986) from Ukraine and Russia: 475 cases are from the exposed areas and a further 283 are from unexposed areas. A thyroid dose is estimated for each case once the pathology consensus diagnosis is agreed. The collection includes samples from the Ukraine-American cohort.

A sample of blood for extraction of DNA, serum and samples of both frozen (where the tumour is large enough) and formalin fixed paraffin embedded (FFPE) tumour and normal thyroid tissue are provided by each patient. The pathology of every case submitted to the CTB is reviewed by an international panel of pathologists. Molecular biology quality assurance (QA) is carried out on each sample prior to release to researchers. In order to maximise the use of the resource, nucleic acids are extracted from the same frozen tissue block, aliquotted and are distributed to multiple researchers. Individual sections from FFPE blocks from individual cases are also issued to multiple researchers. Researchers apply for material through an online portal (https://cisbic.bioinformatics.ic.ac.uk/ctb/html_ctb_public/). Applications are reviewed by an independent external review panel, thus ensuring that the material is used appropriately in first class scientific research. Researchers agree to provide data from their studies back to the project in order that these can be integrated into future studies. So far, 2828 aliquots of RNA and 2377 aliquots of DNA extracted from tissue, 428 aliquots of DNA from blood, 375 vials of whole blood, 9107 sections from FFPE blocks, and 1137 tissue blocks have been released to researchers in 11 different countries for 39 separate projects.

Thomas GA, Unger K, Krznaric, K, Galpine A, Bethel JA, Tomlinson C, Woodbridge M, Butcher S (2012) The Chernobyl Tissue Bank — A Repository for Biomaterial and Data Used in Integrative and Systems Biology Modeling the Human Response to Radiation, Genes 3(2), 278-290

Thomas GA (2012) The Chernobyl Tissue Bank: integrating research on radiation-induced thyroid Cancer. J Radiol Prot;32:N77-80

ID Card:

Organism type of sample:
Human

Storage condition:
Depends on type of sample
See website for details

Sample type:
Frozen tissue, DNA and RNA extracted from frozen tissue, blodd samples, DNA extracted from blodd, serum, sections from FFPE tissue

Condition of use:
Available to any bona fide researchers in any country

Address:
Coordinating Centre: CTB secretariat, Department of Surgery and Cancer, Imperial College London, Room 11L04, Charing Cross Hospital, Fulham Palace Road, London W68RF

Internet link:
www.chernobyltissuebank.com

Access:
Application via CTB portal (see website for details), all applications considered by an External Review Panel.
Reviewed via email
No deadlines for application.
full details on website

Contact:
Pr GA Thomas
Gerry.thomas@imperial.ac.uk

BELGIAN SOIL COLLECTION

Uncontaminated Belgian soils to use in experiments

A collection of 20 uncontaminated Belgian soils (figure 1) is available at the Biosphere Impact Studies group of the Belgian Nuclear Research Centre (SCK•CEN). These soils can be contaminated with specific radionuclides (e.g. ^{137}Cs, ^{238}U, ^{232}Th, etc.) and used in dedicated lab experiments to study mechanisms and processes to improve the understanding of radionuclide behaviour in the terrestrial environment.

Photo: SCK•CEN

Dr Nathalie Vanhoudt

distribution coefficients to be calculated and relationships with soil characteristics to be evaluated. In addition, in order to evaluate radionuclide uptake by plants and to calculate transfer factors, soil-to-plant transfer studies were performed using several plant species such as ryegrass, clover, maize, etc. (figure 2). Furthermore, some of these soils were used to compare sequential extraction procedures for uranium fractionation in soil.

As highlighted in the September 2016 issue of AIR², SCK•CEN makes available facilities in which these soils can be used for the study of radionuclide availability, transfer and migration.

Photo: SCK•CEN

Figure1: Visible differences in colour as present in the Belgian soil collection

The soils were gathered from 20 locations spread over different geological parts of Belgium with the majority coming from Flanders. After removing the vegetation root mat, the soils were collected by sampling the upper 10 cm soil layer. The soils were air-dried, sieved (2 mm) and several soil characteristics were analysed such as texture, total organic matter (OM), cation exchange capacity (CEC), CaCO3, bulk density and field capacity.

In the past, subsamples of these soils were contaminated with ^{238}U, ^{226}Ra, ^{232}Th and ^{99}Tc to evaluate the possibility of linking the mobility and bioavailability of these radionuclides with soil characteristics. Following an incubation period of several weeks, soil characteristics such as pH, exchangeable cations, available P, amorphous Fe, etc., were analysed. Subsequent analysis of the radionuclide concentrations in the extracted soil solutions allowed solid-liquid

The facilities are supported by laboratories which are fully-equipped for soil-sampling and characterisation, element analysis and radioactivity measurements.

Photo: SCK•CEN

Figure 2: Plant uptake experiments in the greenhouse using contaminated soil

Vandenhove H., Van Hees M., Wouters K., Wannijn J., (2007), Can we predict uranium bioavailability based on soil parameters? Part 1: Effect of soil parameters on soil solution uranium concentration, Environmental Pollution, 145, p587-595

Vandenhove H., Van Hees M., (2007), Predicting radium availability and uptake from soil properties,. Chemosphere, 69, p664-674

ID Card:

Organism type of Sample:
Belgian Soil Collection

Storage Conditions:
Room temperature
Dry conditions

Sample type:
Uncontaminated soil
Upper 10 cm soil layer

Access Conditions:
Joint research collaboration
Subject to internal approval

Internet link:
No

Address:
Belgian Nuclear Research Centre (SCK•CEN)
Boeretang 200
2400 Mol, Belgium

Contact:
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Related to: ALLIANCE

The Bank of Biological Materials of SBRC

A 20,000 sample collection of individuals exposed to long term ionising radiation at various doses

The Bank of Biological Materials (BBM) was created in Seversk (Russia) in 2002 by the Seversk Biophysical Research Center of the Russian Federal Medical and Biological Agency (SBRC). The aim of the BBM is to collect samples from employees of the Siberian Group of Chemical Enterprises (SGCE), the world's largest nuclear industrial complex, and from the residents of Seversk, an industrial town located in immediate proximity to the SGCE.

Photo: SBRC

Low-temperature refrigerators "Sanyo MDF-U32V" for deep freezing and storage of biological samples

The BBM collection is subdivided into four categories: 1) Healthy employees of SGCE, 2) Healthy Seversk residents, 3) Patients with malignant tumours (MT) (SGCE employees and Seversk residents), and 4) Patients with acute myocardial infarctions (AMI) (SGCE employees and Seversk residents).

The collection currently comprises 20,000 samples from more than 10,000 donors. Sample types include whole blood, blood DNA, tissue samples (normal and tumour tissue) and cytogenetic suspensions. These four categories contain the following bioresources:

1) "Healthy employees of SGCE" category includes biological materials from 1,678 donors (1,139 men and 539 women) with no previous diagnosis of MT or AMI (Table 1). 197 employees of the SGCE have had no previous exposure to ionising radiation, 742 employees have been exposed only to external γ-radiation and 739 employees have been exposed to combined (external and internal) irradiation.

2) "Healthy Seversk residents" category contains biological materials from individuals with no previous diagnosis of MT or AMI, and no previous exposure to ionising irradiation. As of 2018, this category contains biomaterial from 1,734 donors (258 men and 1,476 women).

Photo: SBRC

Dr Ravil Takhauov

3) "MT patients" category contains whole blood samples from 982 MT patients (473 men and 509 women) of which 501 patients (319 men and 182 women) were employees of the SGCE and 481 (154 men and 327 women) were residents of Seversk who had never worked at the SGCE (Table 2). The "MT patients" category also includes tumour and normal tissue samples in FFPE blocks collected from 2,331 patients.

4) "AMI patients" category contains biological samples from 573 patients with AMI (394 men and 179 women). Out of a total of 573 patients, 386 (307 men and 79 women) were employees of the SGCE and 187 (87 men and 100 women) were residents of Seversk (Table 2).

A database (Unified Electronic Database or UED) was set up at SGCE in 2014 to provide information on donors and their biological material. This database contains information such as sex, age, donor's life status, presence/absence of radiation exposure, irradiation dose and diagnosis.

Together the BBM and UED constitute a unique resource of human biological materials and data for conducting studies on the molecular basis of individual radiosensitivity, and on the genetic mechanisms involved in the pathogenesis of common diseases following long-term exposure to low-dose ionising radiation, as well as other research studies involving radiation and medical genetics.

Table 1. Structure of the BBM category "Healthy employees of SGCE"

Healthy employees of SGCE	Unexposed to irradiation	External irradiation	Combined irradiation
Number	197	742	739
Average age (M±SE), years	59.73±1.07	56.20±0.40	55.36±0.41
Average duration of work (M±SE), years	29.93±1.58	28.75±0.66	27.09±0.76
External dose (M±SE), mSv	–	117.49±7.23	69.29±4.26

Table 2. Structure of the BBM categories "MT patients" and "AMI patients"

Parameter	Seversk residents	Employees of SGCE		
		Unexposed to irradiation	External irradiation	Combined irradiation
"MT patients"				
Number	481	254	147	100
Average age (M±SE), years	61.43±0.60	64.48±0.66	64.41±0.67	64.91±0.85
Average duration of work (M±SE), years	–	29.00±2.33	34.70±2.32	35.31±2.28
External dose (M±SE), mSv	–	–	169.67±18.63	113.46±14.04
"AMI patients"				
Number	187	147	125	114
Average age (M±SE), years	69.30±1.61	61.61±0.89	64.74±0.89	65.16±1.05
Average duration of work (M±SE), years	–	35.07±1.28	38.05±1.08	38.70±1.01
External dose (M±SE), mSv	–	–	135.02±19.73	120.22±14.86

The bank of biological samples representing individuals exposed to long-term ionizing radiation at various doses, Takhauov R. M., Karpov A. B., Albach E. N., Khalyuzova M. V., Freidin M. B., Litviakov N. V. et al. (2015), Biopreservation and Biobanking, 13 (2), 72–78

Different patterns of allelic imbalance in sporadic tumors and tumors associated with long-term exposure to gamma-radiation, Litviakov N. V., Freidin M.B., Sazonov A. E., Khalyuzova M. V., Buldakov M. A. et al. (2015), Mutation Research/Genetic Toxicology and Environmental Mutagenesis, 794, 8–16

ID Card:

Sample bank:
Collection of 20,000 biological samples (blood, tissue, blood DNA, cytogenetic suspensions) from more than 10,000 donors. Donors comprise: 1,734 Seversk residents, 1,678 healthy SGCE employees, 982 patients with cancer at different sites (Seversk residents and SGCE employees) and 573 patients with acute myocardial infarction (Seversk residents and SGCE employees).

Organism type of sample:
Human blood, total DNA, tissue samples

Storage condition:
–20°C, –80°C

Address:
Seversk Biophysical Research Center (SBRC)
87, Kommunistichesky avenue, Seversk, Tomsk Region, 636070, Russia

Access:
The database is owned by SBRC. Access to coded (anonymised) data is subject to permission from SBRC's Commission of Experts.

Internet link:
www.sbrc.ru

Contact:
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Related to:
EURADOS, MELODI, EURAMED

Russian Human Radiobiological Tissue Repository (RHRTR)

A unique resource for studies of radiation-exposed workers

A cohort of workers from the Russian atomic industry facility, the Mayak Production Association (PA), located in the Southern Urals close to the city of Ozyorsk, constitutes a unique research resource. The advantages of this cohort include its large size, extensive follow-up period (70 years), individual measured doses from a wide-range of external and internal radiation exposures, sex/age/ethnicity/initial health status heterogeneity, complete data on health effects and vital status, and available information on non-radiation risk factors. One of the main advantages of this cohort is the availability of biological samples from 25% of the cohort members.

Photo: SUBI

Dr Tamara V. Azizova

Photo: SUBI

Preparation of biological samples for analyses in the laboratory of SUBI clinical department

A collection of biological samples (organs and tissues fixed in formalin and embedded and stored as paraffin blocks and histology slides) was initiated in 1970. The Human Radiobiological Tissue Repository (abbreviation RHRTR) has been significantly extended since 1998 thanks to a Russian-US research collaboration.

Currently, the Repository of the Southern Urals Biophysics Institute (SUBI) stores about 350,000 biological specimens from 9,560 donors (3,460 samples from males and 6,100 samples from females) who were Mayak PA workers and residents of Ozyorsk located close to the nuclear facility. The Table on the right presents the types of biological material and storage conditions.

Each biospecimen is labelled with a barcode which provides a unique identification number, linking the sample to information about the donor, the sample type, date of collection, storage location and conditions, etc.

Importantly, the complete demographic information and medical data collected throughout the entire follow-up period is available for each donor, as well as data on occupational history, individual measured annual doses from external and internal radiation provided for 18 organs and tissues, and data on non-radiation risk factors such as smoking, alcohol consumption, height, weight, etc. These data are contained in the "Clinic" medical and dosimetry database. Notably, all techniques employed for collection, extraction, preparation and storage of biological specimens are based on, and comply with, standard operating protocols for certified laboratories.

The "Clinic" medical and dosimetry database and the Repository of biological specimens from the Mayak PA worker cohort constitute a unique resource for potential research which aims to investigate the biological mechanisms of radiation-induced cancer and non-cancer outcomes, to study individual radiosensitivity, and to identity biological markers of radiation exposure, etc., in individuals exposed to low-dose ionising radiation over prolonged periods.

Biosample type	Registrants		Storage conditions
	Mayak PA workers	Non-Mayak PA workers	
Tumour and non-tumour tissues	1,015	480	-80°C; formalin; paraffin-embedded blocks; histology slides
Peripheral blood and its components (whole blood, plasma, serum, leukocytes, lymphocytes, erythrocytes)	7,194	709	-80°C
DNA	6,426	482	-80°C
Other tissues (buccal epithelial cells, suspension and supernatant of induced sputum)	1,575	111	-80°C

Types of biological specimens stored in the SUBI Repository

ID Card:

Organism type of sample:
Humans (radiation workers, population of a city located close to a nuclear production facility)

Storage conditions:
18 - 20°C, -20°C, -80°C, liquid nitrogen

Sample type:
Tumour and non-tumour tissues (formalin-fixed, paraffin-embedded tissue blocks, histology slides), peripheral blood and its components, DNA

Condition of use:
In accordance with standardised protocols

Address:
Southern Urals Biophysics Institute
Ozyorskoe shosse 19
456780 Ozyorsk
Chelyabinsk region, Russia

Access:
Samples are available on request and following approval of their use for scientific research purposes. Sample transfer is regulated by special customs approval for biological specimen transfer.

Internet link:
http://rhtr.subi.su

Contact:
Dr Tamara V. Azizova
azizova@subi.su
+7 35130 29395

Involved in:
- "Epidemiological Studies of Exposed Southern Urals Populations" (SOLO, FP7)
- "Combining epidemiology and radiobiology to assess cancer risks in the breast, lung, thyroid and digestive tract after exposures to ionizing radiation with total doses in the order of 100 mSv or below" (EpiRadBio, FP7)
- "Cardiovascular Risk from Exposure to Low-dose and Low-dose-rate Ionizing Radiation" (PROCARDIO, FP7)

Related to:
MELODI

The Russian Human Radiobiological Tissue Repository: a unique resource for studies of Plutonium-exposed workers, Loffredo C., Goerlitz D., Sokolova S., Leondaridis L., Zakharova M., Revina V., Kirillova E. (2017), Radiat Prot Dosim, 173 (1-3), 10–15
A dose-dependent perturbation in cardiac energy metabolism is linked to radiation-induced ischemic heart disease in Mayak nuclear workers, Azimzadeh O., Azizova T., Merl-Pham J., Subramanian V., Bakshi M. V., Moseeva M., Zubkova O., Hauck S. M., Anastasov N. et al. (2017), Oncotarget, 8 (6), 9067–9078

Chapter 2: Databases, Sample banks, Cohorts

c) Cohorts

The Wismut Cohort and Biobank

A cohort of nearly 60,000 uranium miners with extensive exposure data

The German uranium miner cohort offers a unique basis for the assessment of health effects associated with inhalation of radon and its progeny and uranium dust, but also effects associated with exposure to low dose external gamma radiation. The cohort includes 58,982 male workers employed between 1946 and 1989 at the East German uranium mining company "Wismut" [1]. Individual information on exposure to radon, long-lived radionuclides and external gamma radiation is available for all cohort members. In addition, absorbed doses to various organs have been calculated with support from the European Commission (Alpha-risk project).

Cumulative exposure to	Mean	Median	Max
Radon progeny [WLM]	280	33	3224
External gamma radiation [mSv]	47	16	909
Long-lived radionuclides [kBqh/m³]	4.1	1.0	132.2

Distribution of radiation exposures among exposed miners (n=50,700)

Strengths of the cohort are the large size, long follow-up period (mean 37 years), large number of total deaths (25,438), wide range of radiation exposures, and availability of information on silica, fine dust and arsenic dust; some information is also available for smoking. Individual data from the cohort are accessible to the scientific community (http://www.bfs.de/EN/bfs/science-research/projects/wismut/wismut-cohort-proposals.html). These data allow investigation of the exposure-response relationship for cancer and non-cancer mortality, different radiation qualities (alpha-radiation, gamma radiation) and low dose or dose rate range. A European pooling of the uranium miner cohort studies (Czech, French and German miners) was performed in the EU alpha-risk project and a worldwide pooling of uranium miner cohorts from Canada, the United States and Europe is currently in preparation.

In addition to the cohort data, a biobank at the BfS contains biological samples from former Wismut employees, which overlap to some extent with the cohort. The biobank consists of three sets of biomaterial:

Michaela Kreuzer

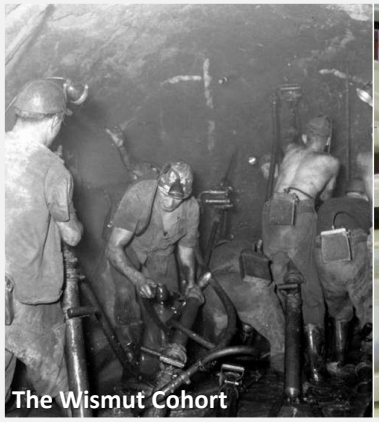
1) Biomaterial collected from 2009–2012 from miners alive at that time (n=442);
2) Biomaterial from miners who died from lung cancer (biomaterial obtained from the pathological archive) (n=400);
3) Biomaterial from children whose fathers died from lung cancer before the age of 50 (n=81).
The biomaterial (lymphocytes, plasma, DNA, RNA, fixed lymphocytes) from the first and third sets was obtained from blood and is of high quality [2], and is stored at -20°C, -80°C or in liquid nitrogen depending on the material. DNA and RNA for the second set are obtained from formalin-fixed paraffin-embedded tumour and normal lung tissue of lower quality.

For the miners whose material is in the biobank, the same exposure data are available as for the Wismut cohort. Additionally, information on smoking is partly available as are epidemiological and medical data and data for the material from the pathological archive tumour subtype.

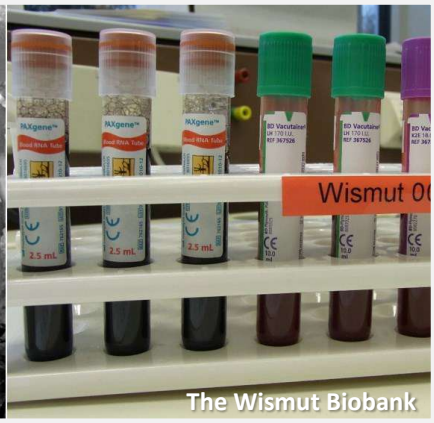
The biobank has already been used:

- To investigate leukemia specific markers
- To detect chronic radiation exposure using miRNA expression and whole genome expression arrays as well as mFISH analysis

Access to the Wismut biobank is restricted to approved proposals. Experimental data will be archived via STORE.



The Wismut Cohort



The Wismut Biobank

Photo left to right: Wismut GmbH, BfS/S. Hornhardt

Bundesamt für Strahlenschutz

ID Card:

Data base topic:
Male Uranium miners

Data owner:
BfS

Description:
Cohort study with individual data on exposure to radon, external gamma radiation and long-lived radionuclides

Biobank available:
GUMB - The German Uranium Miners Biobank

Sample type:
Blood: DNA, RNA, lymphocytes (cultured as well as fixed), plasma
Tumour tissue: DNA, RNA
Normal tissue: DNA, RNA

Sample storage condition:
-80°C (DNA, RNA, plasma) or liquid nitrogen (lymphocytes/plasma)

Access:
External scientists interested in the cohort data or biobank material may send a proposal to the BfS

Contact:
For cohort data:
Michaela Kreuzer:
mkreuzer@bfs.de,
+49 30 18333 2250

For biobank material:
Maria Gomolka:
mgomolka@bfs.de
+49 30 18333 2211

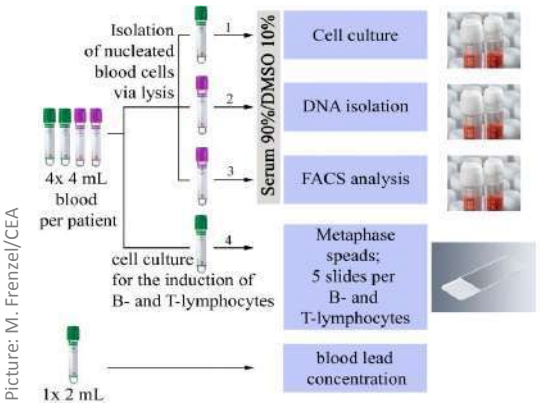
Related to:
Research: MELODI, EURADOS

[1] **COHORT PROFILE: THE GERMAN URANIUM MINERS COHORT STUDY (WISMUT COHORT), 1946 – 2003.** M. Kreuzer, et al. Int J Epidemiol 2010; 39:980-7.
[2] **ASSESSMENT OF mRNA AND microRNA STABILIZATION IN PERIPHERAL HUMAN BLOOD FOR MULTICENTER STUDIES AND BIOBANKS.** DG. Weber, et al. Biomark Insights. 2010;5:95-102.

French Haemangioma Cohort and Biobank

Cohort for low-dose study long-term after radiation therapy

The risk of exposure to low doses of ionising radiation below 100 mSv is still controversial and highly discussed since especially its effect on the appearance of long-term pathologies might be larger than assumed. There is evidence that exposure to low doses increases for example the cancer risk but this effect is less pronounced and concurs with other confounding factors such as smoking. Actually, most model calculations are based on in vitro experiments.



Picture: M. Frenzel/CEA

Scheme of the FHC blood biobank

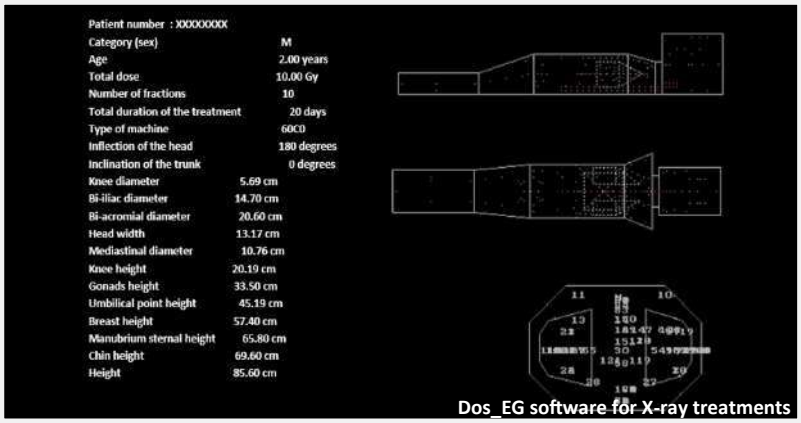
In France, children presenting with a skin haemangioma during early childhood were treated with radiotherapy from 1940-1973. Epidemiological analyses of this cohort have demonstrated a 3-fold higher risk of developing cancer (especially skin, breast and thyroid cancer). The French haemangioma cohort (FHC) is exceptional as it fulfils all necessary characteristics for low dose studies. It allows joint epidemiological and biological analyses to be performed for direct radiation risk assessment and the study of radiation-induced pathologies, due to accurate dosimetry calculations (i.e. the dose received at all major organs, taking into account the size of the baby/child during treatment) thanks to access to radiotherapy medical records. The FHC is very homogeneous, representing a normal healthy population characterised only by a haemangioma. It contains not only patients who received radiotherapy from different sources (^{226}Ra, X-rays, ^{32}P, ^{90}Y or ^{90}Sr) but also untreated individuals or those who received cryotherapy and serve as internal controls. A long-term post-irradiation follow-up exists.

A biobank for the FHC blood samples was set up through collaborations between INSERM (U1018, Florent de Vathaire) and the CEA (Radiation and Oncology Laboratory, Laure Sabatier) during the EU project, EpiRadBio. Only donors who received radiotherapy before the age of 3 years were selected, together with respective non-exposed controls. This biobank contains cytogenetic slides of metaphase spreads for T- and B-lymphocytes as well as isolated nucleated blood cells frozen in liquid nitrogen under conditions (10% DMSO in serum) to allow future cell culture experiments and DNA and FACS analyses to be undertaken. Supplementary information on confounding factors is available for every donor thanks to a questionnaire. This includes body weight and size, type of work, smoking and consumption of alcohol, (for women) number of pregnancies, appearance of cancer/benign tumour, radiological procedures during lifetime, chronic diseases, phototype and skin type. Additionally, the blood lead concentration at the time of blood donation has been determined. All this information is essential to distinguish the effect of radiation treatment from that of other factors which might influence cancer development.

Photo: Hartmuth Schröder

Monika Frenzel

The FHC allows in vivo studies and the identification of biomarkers to develop efficient models for long-term risk estimation for pathologies induced by low doses of ionising radiation, even a long time after exposure.



Dos_EG software for X-ray treatments

Picture: F. De Vathaire/INSERM

ID Card:

Cohort type:
French haemangioma cohort (humans, French citizens), 8335 subjects (5744 treated with radiotherapy), Brachytherapy (^{226}Ra, ^{32}P, ^{90}Y, ^{90}Sr) and X-ray (local treatment for skin haemangioma)

Age:
- at exposure: Starting from early childhood, mostly treated before the age of 15 years (7800 subjects, of whom 5473 received radiotherapy)
- currently: 42-75 years old

Biobank available:
Yes, 369 subjects (231 women, 138 men) of whom 70 non-exposed and 299 exposed subjects (under the age of 3 years; 261 donors <100 mSv, 38 donors 100 mSv; mean bone marrow dose)

Sample type:
Frozen nucleated blood cells (for cell culture, DNA/FACS analysis), cytogenetic slides with metaphase spreads of T- and B-lymphocytes

Sample storage conditions:
-20°C, liquid nitrogen

Conditions of use:
External use possible (via a selection committee)

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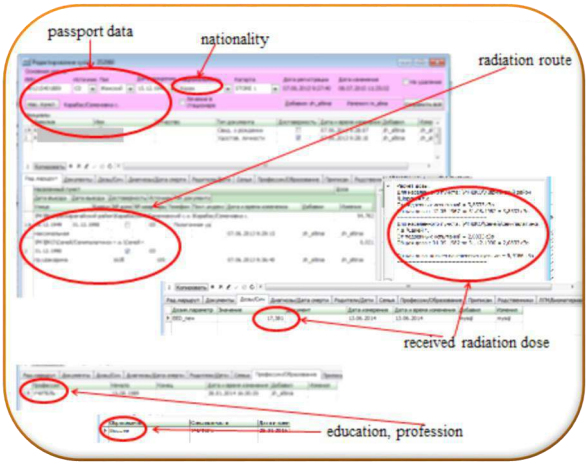
Related to:
MELODI, EURADOS, CARPEM

RADIOTHERAPY AS A RISK FACTOR FOR MALIGNANT MELANOMA FOLLOWING CHILDHOOD SKIN HEMANGIOMA. Haddy N et al. Melanoma Res. 2012, 1, 77-85.
ASSESSING CANCER RISKS OF LOW-DOSE RADIATION. Mullenders L. et al. Nature Reviews Cancer. 2009, 9, 596-604.

3-Generation exposure study

Data and biomaterial for studying transgenerational effects

The Semipalatinsk nuclear test site (STS) is located approximately 150 km west of the city of Semipalatinsk (now called Semey), and was a major site for nuclear weapons-testing by the former Soviet Union. It was here that the Soviet Union conducted their first nuclear test on 29 August 1949. Later, 465 nuclear explosions were carried out between 1949 and 1989, including 118 atmospheric events (88 air events and 30 surface events) from 1949-1962. The last event was conducted at the STS on 19 October 1989. The total yield of atmospheric events conducted at STS is reported to be 6.58 megatons of TNT equivalent, which corresponds to approximately 66% of the total estimated Soviet bomb yield.



Photo, Research Institute for Radiation Medicine and Ecology Semey, Kazakhstan State Scientific Automated Medical Register

Infrastructure of the State Scientific Automated Medical Register

The 118 atmospheric events conducted between 1949 and 1962 were the primary source of radioactive contamination of the environment and of the radiation exposure to the public. The most damaging tests, in terms of exposure, were those conducted on 29 August 1949, 24 September 1951, 12 August and 24 August 1956 [1].

The Research Institute for Radiation Medicine and Ecology in Semey, Kazakhstan, runs a registry of the population living around STS. It is the successor of the 1957-founded medical institution Dispensary No. 4 of the USSR Ministry of Health whose activities included studies on the health effects of radiation exposure to those residing adjacent to the STS.

Today, the Institute does follow-ups of those affected by nuclear bomb testing and their offspring. An important tool for this task is the State Scientific Automated Medical Register, which allows long-term individual follow-up and the study of radiation-related effects using incidence and mortality data. As of November 2015, the Register held information on 316,640 subjects (209,030 alive; 107,610 deceased) [2].

Photo: salon Saur

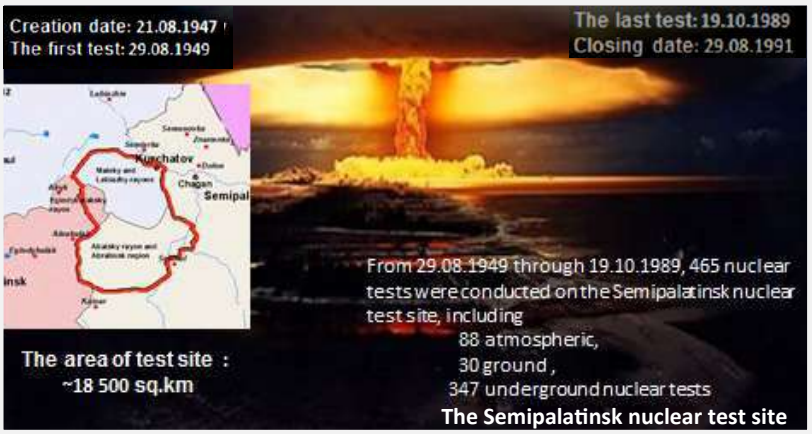
Kazbek Apsalikov

In 2014, the Institute started collecting information on 8,400 persons from the Register, setting up the basis for a three-generation study. The following data are abstracted:

a) registration data: individual's ID, sex, nationality, date and place of birth; b) medical information (where applicable): diagnoses names and dates, congenital malformations, cause of death; c) dosimetry data: radiation route, radiation dose (based on doses assigned by Kazakh legislation, which can differ from the doses estimated by other methods); d) information on lifestyle factors: smoking, alcohol; availability of biological samples: blood, DNA, tumour and normal tissues.

This information is included in the STORE database (AIR², #3). Of the 8,400 individuals registered, 2,380 were affected by the test, 2,937 belong to the F1 generation and 3,083 to the F2 generation. Overall, the following information is available: 11,327 medical diagnosis for incident cases, 1,199 causes of death, 1,937 smoking information, 2,982 drinking information, 215 blood samples, 79 DNA, 14 cancer and 14 healthy tissue samples, and for 145 information on chromosomal aberrations.

The database for the three-generation study can be extended.



The Semipalatinsk nuclear test site

Photo: Research Institute for Radiation Medicine and Ecology Semey, Kazakhstan

ID Card:

Database topic:
Epidemiology

Information available type:
Vital status, incidence data, congenital malformation, partly biosamples, radiation dose

Data type:
Cohort

Link with a biobank:
Yes

Exportable:
Yes (MS Excel)

Species:
Human

Access:
Information through STORE, access after agreement

Contact:
Prof. Kazbek N. Apsalikov, Director of the Scientific Research Institute of Radiation Medicine and Ecology
k.n.apsalikov@mail.ru

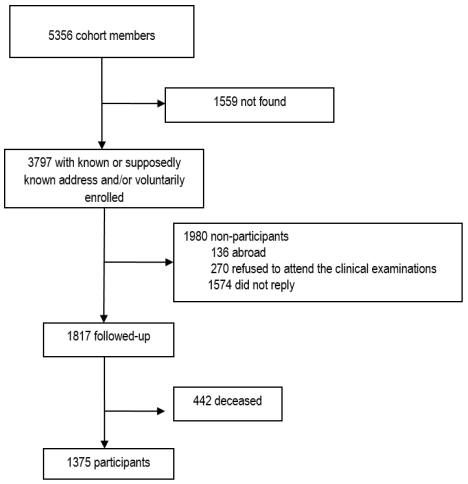
Related to:
MELODI

[1] **THE LEGACIES OF SOVIET NUCLEAR TESTING IN KAZAKHSTAN: FALLOUT, PUBLIC HEALTH AND SOCIETAL ISSUES. SOCIAL AND ETHICAL ASPECTS OF RADIATION RISK MANAGEMENT.** Bauer, et al (2013). Elsevier Science, 239-258.
[2] Statistical Report "**ANALYSIS OF THE CURRENT STATUS OF THE STATE SCIENTIFIC AUTOMATED MEDICAL REGISTER OF THE POPULATION AFFECTED BY THE SEMIPALATINSK TEST SITE.**" 2015. Research Institute of Radiation Medicine and Ecology, Semey.

Portuguese Tinea Capitis Cohort

Evaluation of long term effects of childhood LDR exposure

Before the introduction of Griseofulvin in 1959, the best approach to treat tinea capitis infection was X-ray scalp epilation combined with topical antimycotic ointments. The irradiation procedure used was the five point Keinbock–Adamson technique which consisted of applying a radiation dose of 5-6Gy to the scalp. Doses at other organs, such as thyroid and carotids, were in the low dose range.



Flowchart depicting participants and non-participants from the cohort

The original registry comprised 5356 cases, irradiated in the former DCHSP (North of Portugal), for which information is available on the dose applied, age at irradiation and treatment date (between 1950 and 1962) [1,2]. From this original registry, 1375 individuals were clinically observed from 2006-2011 – see flowchart above (Figure).

Clinical observation was directed mainly to the head and neck regions, and a summarized clinical history was obtained; for 70% of the individuals, a thyroid scan report was obtained. Blood and oral mucosa cells were collected, and DNA was extracted from total blood. For 400 of the 1375 cases, blood lymphocytes were also collected. DNA was extracted from formalin-fixed paraffin-embedded thyroid tumours and basal cell carcinomas, and also from adjacent normal tissue.

Since September 2012, these individuals have been observed a second time, in the context of carotid atherosclerotic disease, and a non-irradiated control group, mainly composed of the spouses (90%), is also being constituted. A total of 398 irradiated and 253 non-irradiated individuals have been observed. The following tests are performed: 1) Clinical examination directed to cardiovascular disease (including anthropomorphic data, blood pressure measurements, smoking load information); 2) B-mode ultrasound imaging of carotid arteries for carotid plaques assessment, intima media thickness and stenosis evaluation; 3) Several biochemical measurements (including homocysteine, hsCRP, lipoprotein A). Blood is collected for: 1) DNA extraction; 2) Lymphocyte isolation; 3) Plasma storage.

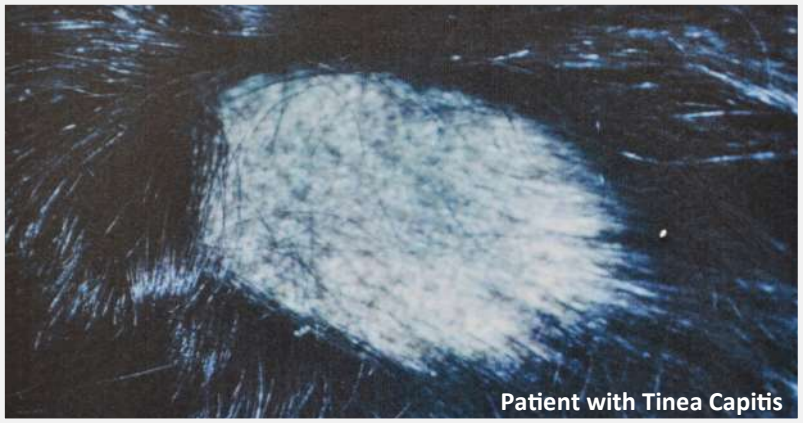
Photo: M. Gomes

Paula Boaventura

The strengths of this cohort are the long latency period between radiation exposure and evaluation of late effects (40 to 60 years), radiation exposure in childhood when individuals are more radiosensitive, information on the doses applied, and availability of biological samples for a considerable number of individuals from the original cohort. For about 400 individuals in the cohort, detailed information on their health status has been obtained (e.g. diabetes, hypertension, metabolic syndrome, presence/absence of carotid plaques), as well as DNA from two clinical observations. As an age-matched non-irradiated control group has also been collected, case control studies can be performed allowing the establishment of subgroups according to health status and radiation exposure.

The cohort and biobank have already been used for the study of genetic alterations in thyroid tumours and basal cell carcinomas, and to evaluate head and neck tumour prevalence.

Access to the cohort is restricted to approved proposals.



Patient with Tinea Capitis

Photo: Prof. Aureliano da Fonseca

1. **HEAD AND NECK LESIONS IN A COHORT IRRADIATED IN CHILDHOOD FOR TINEA CAPITIS TREATMENT.** Boaventura P, et al. Lancet Infect Dis. 2011;11(3):163-4.
2. **THYROID AND PARATHYROID TUMOURS IN PATIENTS SUBMITTED TO X-RAY SCALP EPILATION DURING THE TINEA CAPITIS ERADICATION CAMPAIGN IN THE NORTH OF PORTUGAL (1950-1963).** Boaventura P, et al. Virchows Arch. 2014;465(4):445-52.

ID Card:

Cohort type:
Tinea capitis, former scalp-irradiated patients: 1375 individuals. Scalp-irradiated according to the five point Keinbock–Adamson technique (325-400R in each point).

Age:
- at exposure: 7.2±3.0 (1-23)
- at moment of first clinical observation: 58.6±4.5 (47-75)

Sample type:
Total blood DNA, oral mucosa cells, lymphocytes, plasma, serum, tumour and normal tissue DNA (thyroid and basal cell carcinoma), stored at -20°C

Sample storage conditions:
Blood DNA stored a 4°C; oral mucosa cells stored at -80°C; lymphocytes stored at -80°C; tumour tissue DNA stored at -20°C; plasma and serum stored at -80°C

Conditions of use:
External researchers interested in the cohort data or biobank material should send a proposal to Ipatimup/Cancer Biology

Contact:
Paula Boaventura
mboaventura@ipatimup.pt;
R. Júlio Amaral de Carvalho, 45, 4200-135 Porto, Portugal

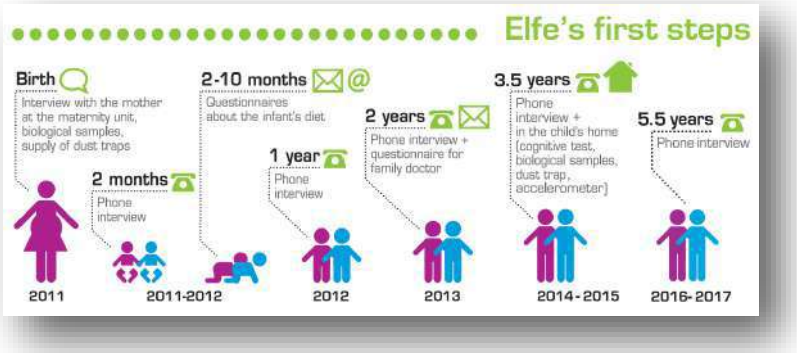
Related to:
MELODI

French longitudinal study of children (Elfe)

18,000 children followed from birth to adulthood

The conditions in which children live and grow are changing fast. Research is therefore needed to find out more about how children's environment in their early years affects their development, their health and even their socialisation. A cohort follow-up study is the best means of closely monitoring children's trajectories. This involves recruiting a large sample of children and tracking them throughout their development.

It was for precisely this reason that Elfe was set up, taking into account questions submitted by 15 themed groups representing more than 150 researchers, as well as concerns expressed by various public bodies. Launched in metropolitan France in April 2011, this resolutely multidisciplinary study recruited more than 18,000 children born that year.



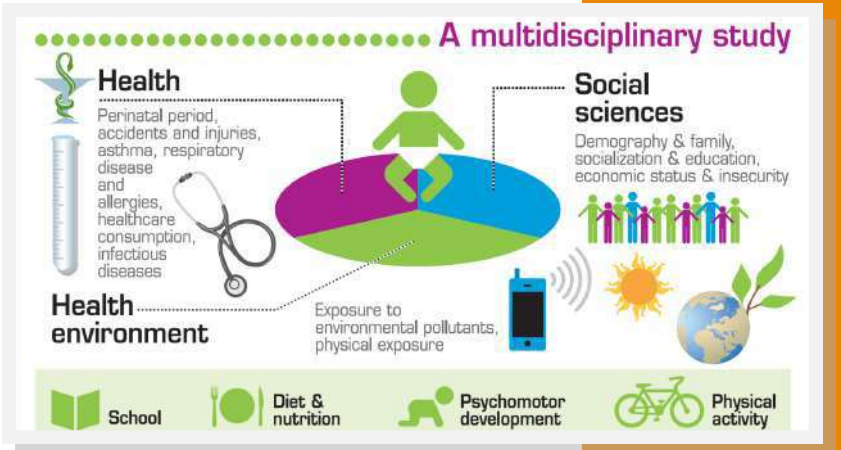
The bulk of the data has so far been collected via surveys of the children's parents (telephone interviews at the 2-month, 1-year, 2-year and 3.5-year milestones or postal/Internet questionnaires). The children were directly studied for the first time when they reached the age of 3.5 years, on the occasion of a home visit during the 2014-2015 wave.

Alongside the cohort, we have set up a biobank containing samples from a subgroup of Elfe families. These were collected in the maternity units where the children were born (mother's urine, venous blood, hair and breast milk, cord blood, newborn's meconium/stool), and again during the survey at 3.5 years (child's hair, urine and stool).

The research carried out by the Elfe teams can be placed under three main headings: health, social sciences and the environment. In the latter, the emphasis is on measuring exposure to various chemical substances or physical agents and studying their impact on children's health and development. Regarding physical agents, for example, the radon study undertaken by a team from the French Institute for Public Health Surveillance (InVS) seeks to identify variations in childhood exposure to radon in the home. A further aim is to assess the public health risks for the dose levels that are observed, and revisit current hypotheses on the dose-response relationship. The medical radiation study, meanwhile, led by researchers from the French Institute for Radiological Protection and Nuclear Safety (IRSN), is intended to provide a detailed and exhaustive picture of children's exposure to diagnostic medical imaging with or without ionizing radiation (IR). It will then be possible to establish dosimetric estimates of IR exposure, based on standardised measurements or literature findings. A second objective will be to join international consortiums collecting the same sort of data, in order to assess the risk of cancer and other pathologies potentially associated with this exposure.

Marie-Aline Charles

Since 2013, Elfe data have been available to researchers actively involved in the study - mainly in the design of its questionnaires, and a year ago, access was extended to the whole of the scientific community, under certain conditions.



ID Card:

Cohort type:
18,000 French children born in 2011

Age:
Birth to adulthood

Biobank available:
Yes

Sample type:
Maternal urine, blood, milk and hair at birth
Cord blood and meconium/ stools of newborns + hair, urine and stools of children aged 3,5 years

Sample storage conditions:
Hairs : room temperature
Urine, milk, stools : - 80°C
Products derived from blood (total blood, serum, plasma) : liquid nitrogen

Conditions of use:
External use possible subject to conditions

Access:
Access to data and/or biological samples subject to conditions

Internet link:
http://www.elfe-france.fr/
https://pandora.vjf.inserm.fr/public/

Contact:
marie-aline.charles@inserm.fr

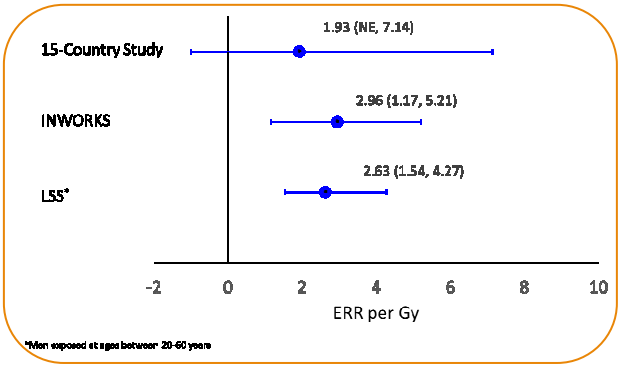
Related to:
MELODI

CONSTRUCTING A COHORT: EXPERIENCE WITH THE FRENCH ELFE PROJECT. Pirus C. et al. Population 2010, 65(4), 637-670.
QPCR STANDARD OPERATING PROCEDURE FOR MEASURING MICROORGANISMS IN DWELLINGS IN THE ELFE STUDY. Scherer E, et al. Sc Tot Environ 2014; 466-467:716-24.

INWORKS Cohort

Multinational cohort study of nuclear workers

The International Nuclear Workers Study (INWORKS) is a collaborative study of cancer risk among radiation workers in the nuclear industry. It is built upon the previous '15-Country Study' using the same core protocol and takes advantage of updated follow-up and exposure data from the three most informative cohorts involved in that study. The INWORKS study comprises 308,297 workers employed by the Atomic Energy Commission (CEA), AREVA Nuclear Cycle and the National Electricity Company (EDF) in France; the Departments of Energy and Defense in the USA; and, in the UK, by nuclear industry employers included in the National Registry for Radiation Workers (NRRW).



Comparison of INWORKS leukaemia findings with other studies

Workers from the nuclear industry represent a unique population in which to study the health effects of ionising radiation; they are mostly exposed to radiation at low levels over the course of their working life. Moreover, all workers included in INWORKS have records that provide individual quantitative radiation dose estimates. Workers in INWORKS were mainly exposed to external radiation, usually gamma-rays, and doses were measured regularly with personal dosimeters. For all participating cohorts, records of individual recorded doses have been kept since the very beginning of the industry in the 1940's. Recorded external penetrating radiation dose estimates are converted to absorbed organ doses expressed in gray (Gy) using the appropriate conversion factor. The mean individual cumulative colon and red bone marrow dose estimates over the period from 1945 to 2005 were 21mGy and 16mGy, respectively.

Over a mean follow-up duration of 27 years, the total number of observed deaths was 66,632, including 17,957 deaths due to solid cancers, 1,791 deaths due to haematological cancers and 27,848 deaths due to cardiovascular diseases.

Photo: R. Dray/IARC

Ausrele Kesminiene

INWORKS demonstrated a significant association between cumulative red bone marrow dose and the risk of all leukaemias, excluding chronic lymphocytic leukaemia (CLL) (n=531 deaths), with an Excess Relative Risk (ERR) of 2.96 per Gy, 90% Confidence Interval (CI)= [1.17 ; 5.21], and between cumulative colon dose and the risk of solid cancers, with an ERR of 0.47 per Gy, 90% CI = [0.18 ; 0.79]. Estimated dose-risk relationships are very close to those derived from the cohort of Japanese A-bomb survivors. Sensitivity analyses demonstrated the stability of the observed relationships. When restricting to low doses (below 100 mGy for solid cancer and below 300 mGy for non-CLL leukaemia), the dose-risk relationships demonstrated reduced precision; the estimated ERR per Gy were not significantly different from zero, but remained consistent with those obtained over the whole dose range.

INWORKS has assembled some of the strongest evidence to strengthen the scientific basis for the protection of adults from low dose, low dose rate exposures to ionising radiation.

Photo: R. Dray/IARC

International Agency for Research on Cancer
World Health Organization

ID Card:

Database type:
Individual data on humans exposed to protracted low-doses of ionising radiation

Cohort type:
International cohort comprising 308,297 workers from the nuclear industry in France, the UK and USA

Age/follow-up:
- age at exposure: from 20 to 60 years
- mean age at end of current follow-up: 58 years
- mean duration of follow-up: 27 years, total of 8.2 million person-years

Data available:
Vital status, causes of death for cancer and non- cancer diseases, individual organ doses due to external radiation, socio-economic status

Biobank available:
No

Access:
The data are maintained at IARC for an agreed period of time; for ethical reasons and due to agreements with data contributors, it is not possible to send the data outside of IARC.

Internet link:
http://www.iarc.fr/

Contact:
Ausrele Kesminiene, International Agency for Research on Cancer (IARC), Lyon, France
kesminienea@iarc.fr

Related to:
MELODI, CARPEM

IONISING RADIATION AND RISK OF DEATH FROM LEUKAEMIA AND LYMPHOMA IN RADIATION-MONITORED WORKERS (INWORKS): AN INTERNATIONAL COHORT STUDY. Leuraud K et al. Lancet Haematol 2015;2:e276-81
RISK OF CANCER FROM OCCUPATIONAL EXPOSURE TO IONISING RADIATION: RETROSPECTIVE COHORT STUDY OF WORKERS IN FRANCE, THE UNITED KINGDOM, AND THE UNITED STATES (INWORKS). Richardson DB et al. BMJ 2015;351:h5359

EPI-CT scan cohort

A multinational cohort of children who have undergone a computed tomography

EPI-CT is designed as a multinational cohort study of children and young adults who have undergone at least one computed tomography (CT) scan before the age of 22 years. It comprises three main parts: 1) an epidemiological cohort study assessing cancer effects of radiation exposure from CT; 2) a dosimetry system to evaluate individual doses and related uncertainty, and supporting dose reduction and optimisation strategies; 3) a pilot study to evaluate the feasibility of applying different biomarkers of hypersensitivity in young patients exposed to low doses from CT.

Photo: IARC

Dr Ausrele Kesminiene

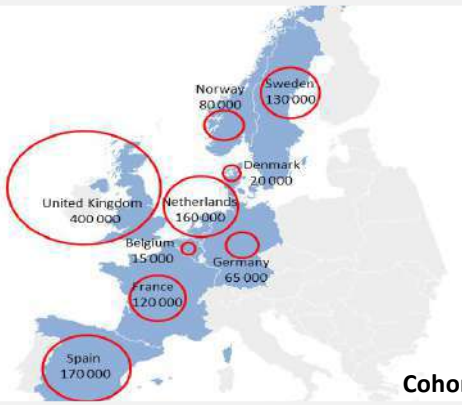
The study is built upon and has expanded existing cohorts in France, Germany and the UK, and has led to the setting up of similar cohorts in Belgium, Denmark, the Netherlands, Norway, Spain and Sweden, based on a common protocol. Coordinated by the International Agency for Research on Cancer (IARC), the study has recruited over 1,000,000 patients.

National cohorts have been assembled retrospectively and prospectively from radiology department records. Cohort members have been followed passively through linkage with cancer, mortality and other registries (including hospital discharge databases), to determine the cancer incidence and vital status of study participants.

Dosimetric data for the distant past is extremely limited, and only sparse information could be obtained for dose reconstruction. For recent years, detailed dosimetric data has been extracted from the Picture Archiving Communication System (PACS) with the use of dedicated PerMoS software. NCI-CT software, which uses Monte-Carlo (MC) simulation methods, is used to calculate organ doses for the ICRP reference phantoms. Dose reconstruction strategy, including uncertainty analysis, is based on a two-dimensional MC (2DMC) simulation approach, which provides alternative realisations of sets of doses for each organ of interest resulting from more than 2,000,000 CT examinations. The impact of various sources of bias on estimates of cancer risk is being characterised in countries where this information is available. Simulation studies are being conducted to investigate the impact of bias on the risk estimates from the entire study.

The biological pilot study has demonstrated that chromosomal aberration and DNA double-strand break induction rates were higher following CT irradiation of blood samples from newborns and young children compared to adults; these differences were also visible in the γ-H2AX-foci assay. *In vitro* assessment of the γ-H2AX-foci assay demonstrated that it is technically feasible to apply this assay in a multicentre prospective CT study.

As the largest and the most statistically powerful study of paediatric CT scans undertaken to date, the EPI-CT study provides direct epidemiological evidence on the potential cancer risk from exposure to low doses of ionising radiation, and may help to limit the radiation dose delivered to children.



Cohort repartition

EPI-CT

ID Card:

Database type:
Individual data on humans exposed to protracted low-doses of ionising radiation

Cohort type:
International cohort comprising 1,163,571 patients from BE, DK, FR, DE, NL, NO, ES, SE and GB, who have undergone CT examination.

Age/follow-up:
- age at exposure: from 0 to 22 years
- mean age at the first examination: 10 years,
-mean age at the end of current follow-up: 20 years
- follow-up period varies by country and ranges from 1973 to 2015

Data available:
-Individual organ doses due to external X-ray irradiation, including uncertainty analysis;
- cancer incidence;
-vital status (except in Germany and partially in FR;
-socioeconomic status available in BE, FR, NL, ES and GB
-cancer predisposing syndromes available in FR, NL and NO.

Link with a biobank:
no

Internet link:
http://epi-ct.iarc.fr/

Access:
The data are maintained by each individual country; national principal investigators should be contacted.

Contact:
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kesminienea@iarc.fr

Related to:
MELODI, EURAMED

ASSESSING ORGAN DOSES FROM PAEDIATRIC CT SCANS – A NOVEL APPROACH FOR AN EPIDEMIOLOGY STUDY (THE EPI-CT STUDY)
Thierry-Chef I, Dabin J, Friberg EG, Hermen J, Istad TS, Jahnen A, Krille L, Lee C, Maccia C, Nordenskjöld A, Olerud HM, Rani K, Rehel JL, Simon SL, Struelens L, Kesminiene A. Int J Environ Res Public Health. 2013 Feb 18;10(2):717-28

EPI-CT: DESIGN, CHALLENGES AND EPIDEMIOLOGICAL METHODS OF AN INTERNATIONAL STUDY ON CANCER RISK AFTER PAEDIATRIC CT
Bosch de Basea M, Pearce M S, Kesminiene A, Bernier MO, Dabin J, Engels H, Hauptmann M, Krille L, Meulepas JM, Struelens L, Baatout S, Kaijser M, Maccia C, Jahnen A, Thierry-Chef I, Blettner M, Johansen C, Kjaerheim K, Nordenskjöld A, Olerud H, Salotti J A, Andersen T V, Vrijheid M, Cardis E. Radiol Prot 2015 Jul 30; 35(3):611-628

LATVIAN STATE REGISTER OF PERSONS EXPOSED TO RADIATION DUE TO THE CHERNOBYL NUCLEAR POWER PLANT ACCIDENT

Cohort of Chernobyl accident clean-up workers from Latvia

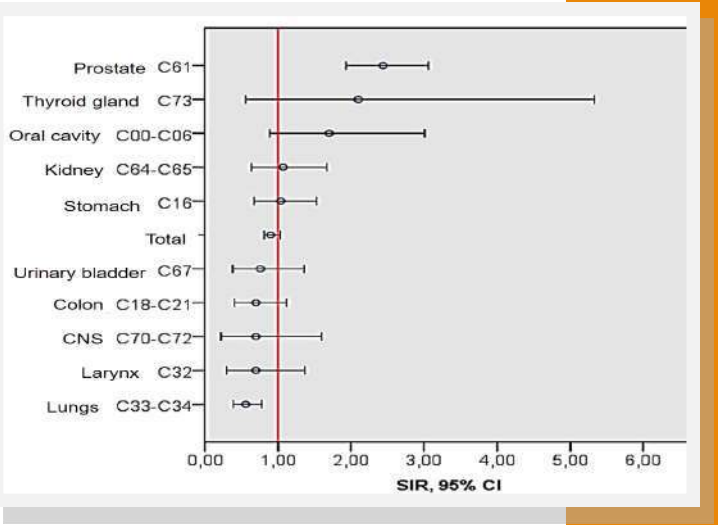
More than 6,000 Latvian inhabitants were among the Soviet people sent to Chernobyl to clean up the site of the nuclear power plant (CNPP) following the accident in 1986. At that time, most were healthy young males (military personnel and civilians of reproductive age). They stayed in Chernobyl for 1-6 months between 1986 and 1991, performing decontamination, transportation and construction tasks. During their stay, they were exposed to external radiation and radionuclides which were deposited into their bodies. Among the non-radiation factors, the most significant were the psycho-emotional stress, the physical overload and the effects of heavy metals and other chemicals. Contrary to Ukraine, Belarus and Russia, the territory of Latvia showed no significant increase in background radiation after the CNPP accident, thus since their return from Chernobyl, the clean-up workers have been living in an area relatively non-contaminated by radiation. Information on the health status of the CNPP accident clean-up workers has been gathered regularly in Latvia from 1987 to the present day, i.e. for about 30 years. Since 1994, this information has been recorded in the Latvian State Register of Persons Exposed to Radiation due to the CNPP Accident. On 1st January 2016, the register contained data from 5,043 persons registered as clean-up workers (who were within the 30 km zone of the CNPP), 1,795 persons who suffered effects of the accident, including 153 persons evacuated from Chernobyl and 1,642 children of clean-up workers born after the accident. The CNPP clean-up workers received regular medical follow-up throughout this time period at a single medical centre. This provided the opportunity to gather information on their health status from a single source. The data base contains individual data on regular medical check-ups and changes in health, as well as data on the cause of death, work tasks performed in Chernobyl and documented exposure doses (evaluable for 57% of clean-up workers). Mean exposure was estimated at about 130 mSv (min 0.1 mSv, max 500 mSv) but doses recorded in the "Military Passport" may not always be accurate. The register is maintained by specialists from the Centre of Occupational and Radiation Medicine (Pauls Stradins Clinical University Hospital). The research is carried out in collaboration with scientists from the Institute of Occupational Safety and Environmental Health (Riga Stradins University). Latvian scientists have conducted many studies based on the information collected, including studies in collaboration with scientists from other countries. Clinical observations and physiological, immunological and epidemiological studies of the Latvian CNPP workers cohort show that these individuals have a higher incidence of wide-ranging disease than the non-exposed general Latvian population. These findings create a need for further research to determine the reasons and mechanisms for the progression of health disorders in this cohort.

Photo: J Reste/RSU IOSEH

Monument in Riga dedicated to the victims of Chernobyl accident (annual memorial event on April 26th)

Photo: J Reste/RSU IOSEH

Dr Jelena Reste



Comparison of oncologic morbidity between CNPP workers and general Latvian male population

ID Card:

Database type:
Individual data on humans exposed to low-doses of ionizing radiation in nuclear power plant accident clean-up works

Cohort type:
6000 males, who were protractedly exposed to ionizing radiation during recovery works in Chernobyl in 1986-1991 (external irradiation and internal deposition of long-living radionuclides)

Age/follow-up:
- age at exposure: 32±7 years
- current age: 61±7 years
mean duration of follow-up: 29 years
follow-up period: from 1986 till now

Biobank available:
no, but feasible on demand

Data available:
individual data on working tasks performed in Chernobyl, health condition in dynamics during follow-up period, results of regular medical check-ups, causes of death for cancer and non-cancer diseases

Access:
Joint research collaboration. The data are maintained by Latvian State Register; the permission for use should be received; the processing of data may be done without personal sensitive information only; it is not possible to send the database outside

Internet link:
http://www.rsu.lv/eng/science-and-research/research-organisation/structure/institutes-and-laboratories/institute-for-occupational-safety-and-environmental-health

Contact:
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jelena.reste@rsu.lv

Related to:
MELODI

INVESTIGATIONS ON HEALTH CONDITIONS OF CHERNOBYL NUCLEAR POWER PLANT ACCIDENT RECOVERY WORKERS FROM LATVIA IN LATE PERIOD AFTER DISASTER. Reste J. et al (2016), Proc Latv Acad Sci B Nat Exact Appl Science,70(5), 257-265

CLINICAL ASPECTS OF THE HEALTH DISTURBANCES IN CHERNOBYL NUCLEAR POWER PLANT ACCIDENT CLEAN-UP WORKERS 5LIQUIDATOR FROM LATVIA, Eglite M. et al, Inflammopharmacology (2009), 163–169

ESTCHERN COHORT

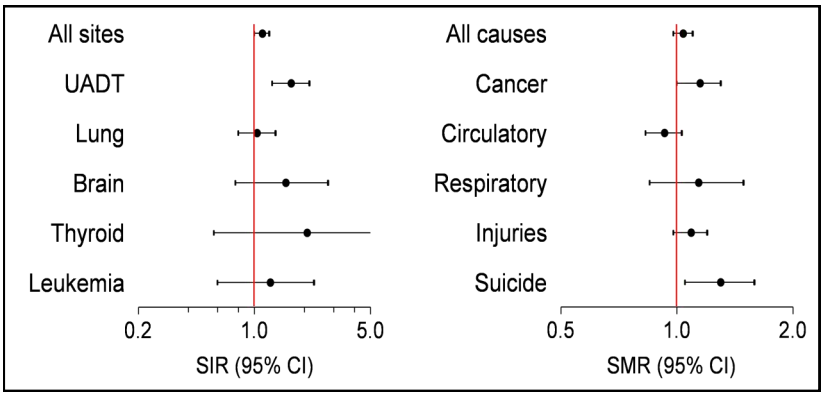
Cohort Study of Chernobyl clean-up workers from Estonia

The Estonian cohort study of Chernobyl clean-up workers was set up in 1992 at the Institute of Experimental and Clinical Medicine (now the National Institute for Health Development), in collaboration with US and Finnish colleagues and with major funding from the National Cancer Institute (USA). The aim of the study was to contribute to the knowledge on the long-term health effects of the Chernobyl accident. The cohort consists of 4,831 men from Estonia who worked in the Chernobyl area between 1986 and 1991. Initial information gathered for each individual includes name, date of birth, place of residence, date of arrival in and departure from Chernobyl, and documented whole-body radiation dose. Follow-up of the cohort members through the national population registry, to get unique personal identification numbers and update their vital status, is almost complete (0.4% of subjects untraced). By 31 December 2014, 108,331 person-years at risk (mean 22.5) had accumulated. Two-thirds of the men were sent to the contaminated area in 1986; their mean age was 31 years, mean duration of the service 102 days, and documented mean radiation dose 99 mGy.

Several sub-studies were carried out: 1) A self-administered questionnaire (1992–1995, 3,888 responses) was a major source of information on service in Chernobyl, health behaviour and socio-demographic characteristics, 2) Biodosimetry (1992–1996, blood samples from 3,197 men) which incorporated the GPA locus mutation assay and FISH chromosomal translocation analyses confirmed the low mean dose of 100–110 mGy, 3) Thyroid screening (1995, 1,984 screenees) did not reveal higher prevalence of thyroid nodules or thyroid cancers in the cohort, 4) Minisatellite mutation frequency among post-Chernobyl offspring (1999, 147 families) was slightly (not significantly) increased compared to their pre-Chernobyl siblings, 5) Follow-up for cancer incidence through the cancer registry (1986–2012, 369 cases) showed borderline overall cancer risk; there were 10 leukaemias *vs* 8.03 expected, and 4 thyroid cancers *vs* 1.93 expected; significant excess was evident for UADT* cancer, 6) Mortality in the cohort (1986–2014, 1,176 deaths) was similar to that expected; the risk of suicide among clean-up workers has been persistently 30 % higher than in the male population (94 suicides *vs* 72.15 expected), 7) Non-cancer morbidity analysis (2004–2012, 3,680 clean-up workers *vs* 7,631 unexposed men) revealed an elevated risk for diseases of the thyroid gland (not related to year of arrival) and ischaemic heart disease; clean-up workers experienced an excess of alcohol-induced conditions and external causes of morbidity, and 8) A mental health questionnaire (2010, 614 clean-up workers *vs* 706 unexposed men) demonstrated the increased risk of suicide ideation, depressive disorders and alcohol dependence in the cohort.

No clear evidence of adverse health effects of radiation exposure among clean-up workers has been observed, however small risks may have been undetectable.

*Upper AeroDigestive Tract



Cancer incidence and mortality in the cohort of Chernobyl clean-up workers in comparison with the Estonian male population

Photo: K.Rahu (selfie)

Dr Kaja Rahu

Thyroid screening of Chernobyl clean-up workers in Tallinn, 27 March 1995

Photo: M.Rahu/NIHD

ID Card:

Cohort type:
Chernobyl clean-up workers from Estonia; individual records of 4,831 men exposed to low-dose ionising radiation after the Chernobyl accident

Age/follow-up:
Age at exposure: 18–68 years; follow-up for site-specific cancer incidence and cause-specific mortality

Biobank available: Yes

Sample type:
Primary lymphocytes (from 3,197 clean-up workers)

Sample storage conditions:
-80°C, liquid nitrogen

Conditions of use:
External use possible

Access:
Subject to permission from the Scientific Resource Committee

Internet link:
http://www.tai.ee

Contact:
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Tel. +372 659 3943

Related to: MELODI

Rahu K, Rahu M, Tekkel M, Veidebaum T, Hakulinen T, Auvinen A et al. (2015) Chernobyl cleanup workers from Estonia: cohort description and related epidemiological research. J Radiol Prot;35:R35–R45.

Rahu K, Auvinen A, Hakulinen T, Tekkel M, Inskip PD, Bromet EJ et al. (2013) Chernobyl cleanup workers from Estonia: follow-up for cancer incidence and mortality. J Radiol Prot 2013;33:395–411.

German airline crew cohort

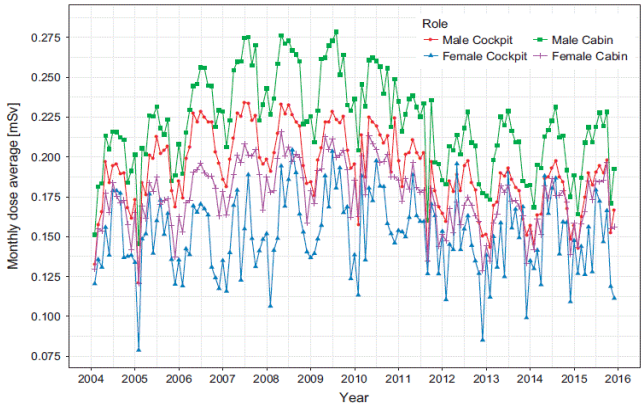
The use of radiation registry data in the 3rd follow-up study

Commercial airline crews are one of the occupational groups with the highest exposure to natural radiation of cosmic origin. Several national airline personnel cohorts in Europe and North America were established in the 1990s with the aim of investigating the occupational health risks of cockpit and cabin crew, and in particular to identify radiation-associated cancer. As one of the largest national studies (n= 26,846), the German cohort study is currently concluding its third follow-up investigation with an additional 10 years of observation, up to the end of 2014, and with an overall follow-up time of up to 55 years (1960-2014).

Photo: BIPS

Pr Hajo Zeeb

et al., 2017). In this third follow-up period, exposure data from 26,805 cohort members was available, compared to n=5,995 in the previous analyses. SMR and RR analyses are currently underway and results will be submitted for publication in international peer-reviewed journals in the first part of 2018.



Mean monthly effective aircrew dose from 2004 to 2015, stratified by sex and role.
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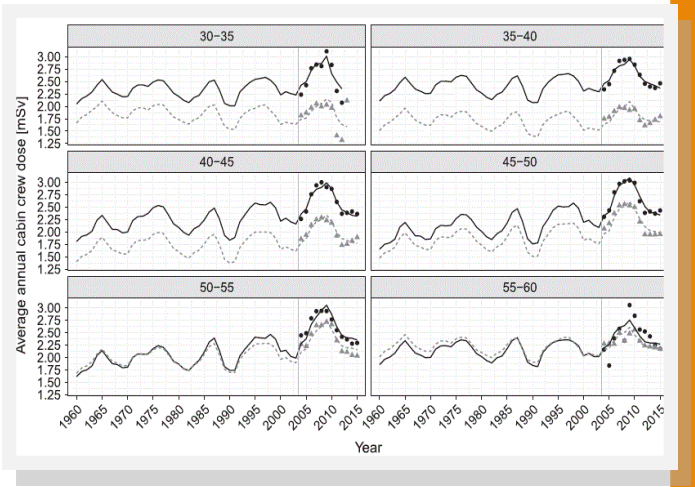
To our knowledge this is the first mortality follow-up study using SSR registry data in Germany. The data availability further enables convenient and quality assured exposure assessment via data-linkage for (possible) future follow-up studies of this cohort and/or the set-up of a new generation of aircrew cohorts, as working conditions have changed since the initial cohort started in terms of flight frequencies, ranges and routes, thus resulting in higher lifetime radiation doses compared to those individuals who started in the pre-jet era. Also, follow-up work will be more convenient as unique registry identifiers are used, which will ensure cohort retention and nearly complete exposure assessment. Furthermore, SSR data may also be used to ascertain vital status if SSR data availability exceeds the cohort time-inclusion criteria, which also leads to cost reduction.

In the previous follow-up studies, exposure assessment was based on dose reconstructions using a job-exposure matrix approach based on company flight records, to estimate individual radiation doses for the cockpit personnel only. Cabin crew were not included as detailed flight records were not available. Following regulatory changes in 2003, aircrews in Germany are now systematically monitored, and individual monthly effective doses have been documented by the Federal Radiation Registry (SSR) since mid-2003 (complete data availability: start of 2004).

Thus, in this follow-up study, the newly available exposure data are now included for cockpit and cabin cohort members, for exposures during the period from 2004 to 2014. In addition, the estimated radiation exposure of the cabin crew for the years from 1960 to 2003 has been modelled as a function of age, sex, job category, solar activity and male pilots' dose, to provide the opportunity to conduct dose-response analyses for the full cohort (Wollschlaeger



Predicted (lines) and observed (points) average annual effective cabin crew dose plotted from 1960 to 2015, stratified by sex and 5-year age groups.
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ID Card:

Cohort type:
German airline cockpit and cabin crew with 26,805 individual occupational exposure records

Age/follow-up:
Age at exposure: 18-62 years; mortality follow-up for radiation-related cancers and other disease outcomes

Biobank available:
No

Access:
To be discussed with the research team

Internet link:
https://www.bips-institut.de/en/home.html

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Related to:
MELODI

Estimated radiation exposure of German commercial airline cabin crew in the years 1960-2003 modeled using dose registry data for 2004-2015, Wollschlaeger D., Hammer G. P., Schafft T., Dreger S., Blettner M., Zeeb H. (2017), J Expo Sci Environ Epidemiol., doi: 10.1038/jes.2017.21.
Mortality from cancer and other causes in commercial airline crews: a joint analysis of cohorts from 10 countries, Hammer G. P., Auvinnen A. et al. (2013), Occup. Environ. Med. 71, 313-322

The Techa River Cohort (TRC)

Cohort study of general population exposed on the Techa River

The Techa River Cohort (TRC) includes individuals born before 1950 and who lived in any of the 41 villages situated along the Techa River (Russia) between 1950 and 1960. The TRC members were affected by external γ-radiation from contaminated river sediments and flood plain soil, and by internal exposure to radionuclides, including ^{89}Sr, ^{90}Sr and ^{137}Cs, due to consumption of local water, milk and food products which were contaminated following the release of radioactive waste into the Techa River by the Mayak Radiochemical Plant between 1949 and 1956.

Table 1. Demographic characteristics of TRC

Parameters	n	%
Sex		
Male	12,558	42%
Female	17,172	58%
Ethnicity		
Tatars & Bashkirs	5,950	20%
Slavs	23,780	80%
Age at January 1, 1950		
<1	1,032	3%
1-14	8,824	30%
15-59	17,279	58%
60 & older	2,595	9%
Total TRC	29,730	100%

Table 2. Vital status of TRC members

Vital status as of 31/12/2007	People
Alive in catchment area	5,684
Dead	17,307
% known cause of death	91%
Lost of follow-up	6,739
Including: migrants	4,696
persons with unknown status	2,043
Total TRC	29,730

The first specialised medical examinations of the residents of the Techa riverside villages took place in 1951. From 1955 to present, the residents of these villages have been followed up by the physicians of the Clinic of the Urals Research Centre for Radiation Medicine (URCRM), under the Federal Medical-Biological Agency.

A Registry of exposed persons and a medical dosimetry database were created at the URCRM in the 1970s. Between the late 1960s and the 1980s, URCRM researchers conducted an extensive review of official documents including tax records, vital statistics, medical records and population surveys, to identify potential cohort members. The demographic characteristics are shown in Table 1. Follow-up of vital status (Table 2), and of cancer incidence and mortality of TRC members, covers a period of more than 50 years and is based on the addresses provided by the bureau of information, the death certificates from the statistical offices of Chelyabinsk and Kurgan oblasts and cancer notification forms from the Chelyabinsk oblast oncology dispensary. The start date of the follow-up and the catchment areas used in the studies were dependent on data access.

Individualised organ doses for TRC members over the whole follow-up period were calculated by the URCRM dosimetry team using specially developed software (Techa River Dosimetry System-TRDS). The results presented are based on TRDS-2009, a software version which incorporates recent advances in radionuclide intake reconstruction, external exposure assessment and reduction in the uncertainty of dose estimates. Development work is in progress to further improve TRDS.

Photo: Krestinina L./URCRM

Dr Lyudmila Krestinina

The TRC is a unique resource for estimating cancer risks following chronic exposure to low-medium doses in the general population. It is one of the few human populations affected by protracted strontium exposure, a radionuclide which concentrates in the bone and is thus of great relevance for leukaemia studies. Studies of cancer incidence and mortality in this cohort have been undertaken in Russian-American projects (NCI: 1995-2013; DOE under JCCRER: 1996-2018) and in a European project (SOUL: 2006-2009). Results of radiation effects studied in the TRC show significant excess relative risk for all leukaemias, and also for leukaemias excluding chronic lymphatic leukaemia (CLL), as well as for solid cancer mortality in the TRC and for solid cancer incidence in the Chelyabinsk subcohort of the TRC. The study of non-cancer effects in the TRC (SOUL project) also showed significant risk for all diseases of the circulatory system and for ischaemic heart disease (Table 3).

Table 3. Dose response in Techa River Cohort

Parameters	Solid cancer			Leukemia		Cardio-vascular diseases (CVD)	
	Mortality[1]	Incidence[2]		Incidence[3]		Mortality[4]	
People	29,730	Techa River Incidence cohort 17,435		28,223		29,735	
Follow-up period	1950-2007	1956-2007		1953-2007		1950-2003	
Cases, n	2,303	1,933		99	72	7,595	3,194
Person-years	927,743	472,788		847,877		901,563	
Lag period, years	5	5	5	2		15	
ERR/Gy	0.61	0.87	Smoking adjusted 0.77	All leukemias 1.1	Leukemias Non-CLL 2.2	All CVD 0.36	Ischemic heart diseases 0.56
95% CI	0.04-1.3	0.2-1.6	0.13-1.5	0.4-2.4	0.8-5.4	0.02-0.74	0.01-1.19
P	0.03	0.008	0.02	<0.001	<0.001	0.04	<0.05
Model	linear	linear		linear			
Excess cases	50 (2.2%)	69 (3.6%)	61 (3.1%)	29 (30%)	34 (47%)	73 (1%)	49 (1.5%)

1- Schonfeld et al., 2013, Radiat Res (179); 2- Davis et al., 2015, Radiat Res (184); 3-Krestinina et al., 2013, BJC (109); 4-Krestinina et al., 2013, Radiat Environ Biophys (52)

ID Card:

Cohort type:
Approx. 30,000 persons from the general population, born before 1.1.1950 and resident in the Techa Riverside villages during 1950-1960, environmentally exposed to protracted low- and medium doses (<1 Gy) to soft tissues and to low-high doses to red bone marrow (<7 Gy).

Age/follow-up:
- at exposure: 0-90> years
- current age(2017): 67-90> years
- mean age of those alive at the end of 2014: 74.7 years

Mortality follow-up: 1950-2014.
Cancer incidence: 1956-2014

Biobank available:
Yes

Sample type:
Cells, DNA, fixed slides

Sample storage condition:
(-80°C, liquid nitrogen…)

Access:
The database is owned by URCRM. Access to coded (impersonalized) data is subject to permission from URCRM Commission of Experts.

Internet link:
www.urcrm.ru

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Urals Research Center for Radiation Medicine (URCRM), 68-a, Vorovsky Street, Chelyabinsk 454076, Russia

Related to:
MELODI

Leukaemia incidence in the Techa River Cohort: 1953–2007, Krestinina L. Y., Davis F. G., Schonfeld S., Preston D. L., Degteva M., Epifanova S. et al. (2013), British Journal of Cancer, 109, 2886–2893
Solid cancer mortality in the Techa River Cohort (1950–2007), Schonfeld S. J., Krestinina L. Y., Epifanova S., Degteva M. O., Akleyev A. V., Preston D. L. (2013), Radiation Research, 179, 183–189

Greek interventional cardiologists cohort

Estimation of eye lens doses in Greek cardiologists

The Greek Atomic Energy Commission is the national regulatory authority for radiation safety, and is responsible for maintaining the National Dose Registry (NDR) for workers occupationally exposed to ionising radiation.

Eye lens doses seem to be of great concern, especially for staff working in interventional cardiology, due to a decrease in the eye lens dose limit for occupational exposure, as set out in the latest European Basic Safety Standards Directive 2013/59/EURATOM. For this reason, efforts have been made in the present cohort to retrospectively estimate the eye lens doses in interventional cardiologists, based mainly on the whole body dose data kept in the NDR since 1989.

Photo: EEAE

Dr Eleftheria Carinou

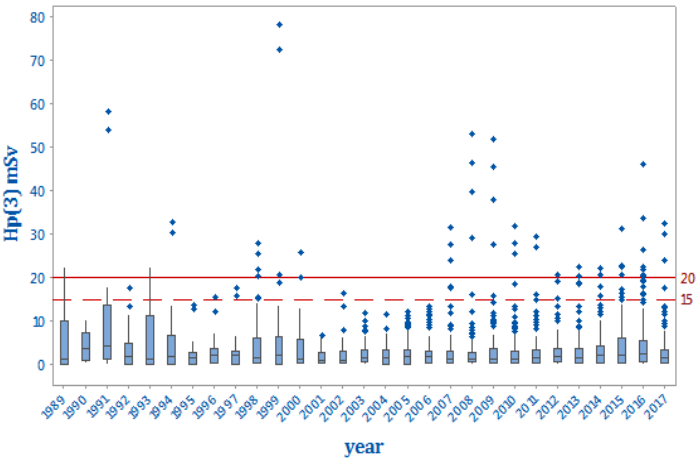

Photo: EEAE

Box plots showing the evolution of the annual Hp(3) in mSv.

A short questionnaire has also been used to collect data on the type and number of procedures, the X-ray system configuration and the use of protective measures during the respective exposure periods. All the relevant data for active interventional cardiologists in the cohort have been extracted from the NDR. Of the 530 cardiologists contacted, 150 completed the questionnaire. The eye lens dose was estimated using the second approach developed in the EURALOC project (OPERRA). For each cardiologist, the distribution of the possible cumulative eye lens doses was estimated individually and separately for each eye. The above graph shows the evolution of the annual Hp(3) dose for the cohort since 1989. From the questionnaires and the estimated eye lens dose values, it can be concluded that:

- The use of personal protective equipment is increasing. More specifically, an increase in the use of protective shields was noted in the 1990s. The use of lead glasses is also increasing; however 30% of the cardiologists are still not using lead glasses.
- Whole body doses seem to have increased over the last 15 years (from 5.3 mSv to 10.6 mSv). The estimated eye lens dose values indicate that the new annual eye lens dose limit has been exceeded in some cases.
- The maximum cumulative eye lens dose is estimated at 700 mSv.

The present approach used for estimation of the eye lens doses has the advantage that is based on individual measurements (i.e. whole body doses) for each cardiologist; however, there are also serious disadvantages, mostly related to the constant use of the personal dose meter in the past, and to its position on the worker's body.

Moreover, the findings in the present cohort underline the importance of keeping an NDR, which has proved to be a powerful tool for the retrospective estimation of eye lens doses in interventional cardiologists.

The research leading to these results has received funding from the European Atomic Energy Community's Seventh Framework Programme under grant agreement n° 604984.

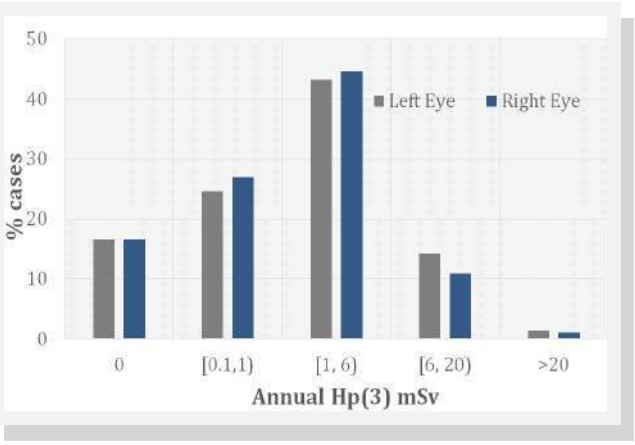

Photo: EEAE

Distribution of the estimated annual Hp(3) for both eyes.

Eye lens radiation exposure in greek interventional cardiology personnel, Thrapsanioti Z., Askounis P., Datseris I., Diamanti R. A., Papathanasiou M., Carinou E. (2017), Radiation Protection Dosimetry, 175 (3), 344–356

The influence of operator position, height and body orientation on eye lens dose in interventional radiology and cardiology: Monte Carlo simulations versus realistic clinical measurements, Principi S., Farah J., Ferrari P., Carinou E., Clairand I., Ginjaume M. (2016), Physica Medica, 32 (9), 1111–1117

EEAE ΕΛΛΗΝΙΚΗ ΕΠΙΤΡΟΠΗ ΑΤΟΜΙΚΗΣ ΕΝΕΡΓΕΙΑΣ GREEK ATOMIC ENERGY COMMISSION

ID Card:

Cohort type:
Interventional cardiologists
530 contacted; 150 replied

Age/follow-up:
Age at exposure: 30-67 years old
Data extracted from the National Dose Registry database starting from 1989

Biobank available:
N/A

Access:
Contact E. Carinou for possible external use of the cohort data

Internet link:
https://eeae.gr/en/

Contact:
Dr Eleftheria Carinou
Eleftheria.carinou@eeae.gr
+30 2106506718

Related to:
EURADOS, MELODI

The German Thorotrast Cohort Study

Cohort study on internal exposure to alpha radiation

Thorotrast was the trade name of the radioactive radiographic contrast agent containing 25% colloidal solution of thorium dioxide, widely used in the period 1930 - 1950 in Germany and other countries. The main application of Thorotrast was as an intravascular injection for cerebral angiography. Thorotrast is retained by the reticuloendothelial system, with a biological half-life of several hundred years. Thus, patients suffer lifetime exposure to internal alpha radiation. The potential risks of Thorotrast were recognised several years after the first application, on the appearance of sarcoma. It was banned in 1949 -1950.

Photo: https://media.springernature.com/lw785/springer-static/image/art%3A10.1007%2Fs00117-016-0186-7/MediaObjects/117_2016_186_Fig1_HTML.gif

Original 12 ml vial from the company Heyden (right) and a vial for animal experiments from a U.S. company (left)

Thorotrast patients have been followed-up in epidemiological surveys. Five cohort studies were carried out with patients from Japan, Portugal, Denmark, the USA and Germany. The largest of these was the German Thorotrast Study that started in 1968 with a follow-up until 31 December 2004.

The aim of this study was to determine the long-term health consequences of the incorporated colloidal thorium dioxide and the resulting radiation exposure through epidemiological surveys as well as clinical, radiological and biophysical examination of the patients. The study comprised 2,326 Thorotrast patients and 1,890 patients from a matched control group. The 899 Thorotrast patients and 662 controls who were alive at the start of the study in 1968 were followed-up through clinical examinations on a biannual basis.

At the end of 2004, only 9 of the 2,326 exposed individuals and 151 of the 1,890 controls were still alive. For all deceased individuals, causes of death were collected in various ways and coded according to ICD-10. When the exposed group was compared with the control group, based on post-mortem examinations and pathology, high relative risks were observed for liver cancer, leukaemia, myelodysplastic syndromes (MDS) and carcinoma of the extrahepatic bile ducts. SMR analyses were conducted based on national rates. They showed a strong life-shortening effect, with increased mortality being observed in particular for liver cancer, but also for bone cancer and malignancies of the haematopoietic system, but not for lung cancer.

Photo: BfS

Dr Mandy Birschwilks

Leukaemias appeared 5 yr after injection and continued to increase subsequently, while liver cancers did not appear until almost 20 yr after injection and then increased very rapidly. Dose-effect relationships were calculated for various endpoints showing different shapes of dose-response. A 2016 paper (DOI 10.1007/s00411-016-0651-8) describes the cohort, important results on dosimetry, medical examinations and chromosomal aberrations, and also asks some open questions. The data from the German Thorotrast Study are available to any interested researchers through the STORE database (http://storedb.org). Information on individual patients, including X-ray films, is available from the German Cancer Research Center, Heidelberg.

German Thorotrast Study – patients' vital status (at end of follow-up Dec. 2004)

	Thorotrast patients				Comparison group			
Vital status	male	female	sum	%	male	female	sum	%
alive	6	3	9	0.4%	99	52	151	8.0%
deceased	1,709	604	2,313	99.4%	1,305	428	1,733	91.7%
lost to follow-up	2	2	4	0.2%	-	-	6	0.3%
sum	1,717	609	**2,326**	100.0%	1,408	484	**1,890**	100.0%
	73.8%	26.2%			74.4%	25.6%		

(Based on Becker et al. 2008, numbers for lost to follow-up by sex are not available in the comparison group)

The German Thorotrast Cohort Study: a review and how to get access to the data, Grosche B., Birschwilks M., Wesch H., Kaul A., van Kaick G. (2016), Radiat Environ Biophys, 55 (3), 281–289

The German thorotrast study: recent results and assessment of risks, van Kaick G., Dalheimer A., Hornik S., Kaul A., Liebermann D., Lührs H., Spiethoff A., Wegener K., Wesch H. (1999), Radiat Res, 152 (6), S64–S71

Bundesamt für Strahlenschutz

ID Card:

Cohort type:
Thorotrast®, Germany
Thorotrast Study: 2,326 Thorotrast patients and 1,890 patients from a matched control group.

Biobank available:
N/A

Conditions of use:
Researchers interested in the cohort data should send a proposal describing the envisaged study design or type of analysis.

Access:
Will be granted after approval through the STORE website.

Internet link:
http://storedb.org

Contact:
Dr Mandy Birschwilks
store@bfs.de
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Related to:
MELODI, EURAMED

Mayak PA worker cohort (MWC)

Cohort study of workers employed at the Mayak Production Association

The Mayak Production Association (PA) is a large-scale, Russian nuclear enterprise set up to produce weapon-grade plutonium and located in the Southern Urals (Russian Federation), close to the city of Ozyorsk. When it commenced operations in June 1948, the Mayak PA consisted of a main production facility with industrial reactors, radiochemical and plutonium production plants, as well as auxiliary facilities.

Photo: SUBI

Dr Tamara V. Azizova

Table 1 – Characteristics of the cohort of Mayak PA workers employed between 1948 – 1982 (first employment) – data as of 31.12.2017

Cohort size	22,377
Known vital status	95 %
Deceased workers	63 %
Autopsy performed	34 %
Alive (Ozyorsk residents)	32 (19) %
Cumulative dose from external gamma-rays (Hp10)	0 – 8.4 Sv
Cumulative lung absorbed dose from internally deposited alpha-particles	0 – 26.3 Gy
Cumulative liver absorbed dose from internally deposited alpha-particles	0 – 38.0 Gy
Available data on initial health status	90 %
Medical history data on disease incidence	96 %
Available data on non-radiation factors (smoking, alcohol consumption, body mass index, blood pressure, etc.)	80 – 90 %
Available data on family members (offspring)	59 %
Available biological material	13 %

Once the first reactor came into operation, all Mayak PA workers were monitored for individual doses of external gamma-rays, however regular monitoring of internal alpha-activity in workers exposed to alpha-active aerosols containing transuranium radionuclides did not begin until the 1960s. Individual organ-absorbed doses from external gamma-rays and internally deposited alpha particles were estimated based on the improved and updated dosimetry and biokinetics models used in the Mayak Workers Dosimetry Systems of 2008 and 2013 (MWDS-2008 and MWDS-2013).

Workers of the Mayak PA were subjected to special health supervision following standard protocols, which included mandatory pre-employment and annual medical health examinations throughout the entire follow-up period.

The raw data collected enabled the creation of a unique resource, the "Clinic" medical dosimetry database of Mayak PA workers and their family members. These data provide the basis for numerous studies aimed at assessing tissue reactions (deterministic effects) and stochastic events following external and internal radiation exposure (cancer and non-cancer effects).

The Mayak Worker Cohort (MWC) includes 22,377 workers (25% female) whose first employment was at one of the main facilities during the period 1948-1982. Table 1 summarises the cohort characteristics as of the end of 2017.

The MWC has a number of strengths including its large size, long follow-up period (70 years), individually measured doses from external and internal radiation exposure, heterogeneity by sex, age, ethnicity and pre-employment health status, completeness of information on health effects and vital status, and available data on non-radiation factors as well as stored biological samples.

Tissue reactions, such as acute radiation sickness, chronic radiation syndrome, plutonium-induced pulmonary fibrosis, radiation-induced cataracts and local radiation injuries, were recorded in MWC members during 1948–1960, and evidence was reported of increased radiation-induced risks for leukemia, lung, liver and bone cancers, circulatory diseases, chronic obstructive pulmonary disease and senile cataract as well as cataract subtypes.

Table 2 – Dose-response for non-cancer incidence in MWC

Outcome (number of cases)	ERR per Gy of external gamma-rays (95% CI)	ERRper Gy of internal alpha-radiation (95% CI)
Cardiovascular diseases (7225)	0.10 (0.04, 0.17)	0.02 (n/a, 0.10)
Cerebrovascular diseases (8717)	0.46 (0.37, 0.57)	0.28 (0.16, 0.42)
Lower extremities diseases (938)	0.19 (0.05, 0.39)	0.16 (n/a, 0.50)
Chronic obstructive pulmonary diseases (2135)	0.14 (0.02, 0.28)	1.19 (0.32, 2.53)
Senile cataracts (4159)	0.28 (0.20, 0.37)	–
posterior subcapsular	0.91 (0.67, 1.20)	–
cortical	0.63 (0.49, 0.70)	–
nuclear	0.47 (0.35, 0.60)	–
Hypertension (8425)	0.14 (0.09, 0.20)	-0.10 (n/a, 0.05)

The "Clinic" medical-dosimetric database of Mayak production association workers: structure, characteristics and prospects of utilization, Azizova T. V., Day R. D., Wald N., Muirhead C. R., O'Hagan J. A., Sumina M. V., Belyaeva Z. D., Druzhinina M. B. et al. (2008), Health Phys, 94 (5), 449–458
Risk of cataract incidence in a cohort of Mayak PA workers following chronic occupational radiation exposure, Azizova T. V., Bragin E. V., Hamada N., Bannikova M. V. (2016), PLoS One, 11 (10):e0164357

ID Card:

Cohort type:
Individual data on Mayak PA workers occupationally exposed to external gamma- and internal alpha-radiation at wide dose ranges over prolonged periods.

Age/Follow-up:
Age at exposure (first employment): 15–65 years
Mean age at the end of the follow-up: 66 years
Mean duration of follow-up: 42 years; 939,811 person-years

Biobank available:
Yes

Sample type:
Tumour and non-tumour tissues (formalin-fixed, paraffin-embedded tissues blocks, histology slides), peripheral blood and its components, DNA

Sample storage conditions:
18 - 20°C, -20°C, -80°C, liquid nitrogen

Access:
MWC database is owned by SUBI. Access to anonymous data is restricted and subject to approval by the SUBI Institutional Review Board.

Internet link:
http://rhtr.subi.su

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Involved in:
- "Epidemiological Studies of Exposed Southern Urals Populations" (SOLO, FP7)
- "Combining epidemiology and radiobiology to assess cancer risks in the breast, lung, thyroid and digestive tract after exposures to ionizing radiation with total doses in the order of 100 mSv or below" (EpiRadBio, FP7)
- "Cardiovascular Risk from Exposure to Low-dose and Low-dose-rate Ionizing Radiation" (PROCARDIO, FP7)

Related to:
MELODI

The TRACY cohort

A French cohort of uranium workers with detailed risk factors data

Cohorts of workers monitored for internal contamination have a strong potential for solving several current key questions in radiation protection, in particular on the effects of protracted low-dose and internal exposure to ionising radiation, the different types of radiation (e.g.: α, γ) and the heterogeneity of energy deposition. Uranium (U) is one of the internal emitters most frequently encountered in occupational exposure situations. However, the potential health effects of chronic exposure to U are not well characterised. This is notably due to the complexity of reconstructing individual doses from U exposure, as compared to external exposure, and to the rarity of large cohorts that provide such information.

The TRACY (TRAvailleurs du CYcle) cohort includes 12,649 workers involved in various activities throughout the nuclear fuel production cycle in France, i.e. purification and conversion of natural U, enrichment of U, fuel manufacturing and activities such as storage and decontamination. The TRACY study is conducted in the context of a collaboration between IRSN and ORANO, with agreement from the French Data Protection Authority (CNIL). Vital status, dates and causes of death (from both cancer and non-cancer causes) have been obtained from national registries for the period 1968-2008, and this follow-up is being extended. Specific efforts are devoted to the reconstruction of lifetime internal dosimetry following U exposure.

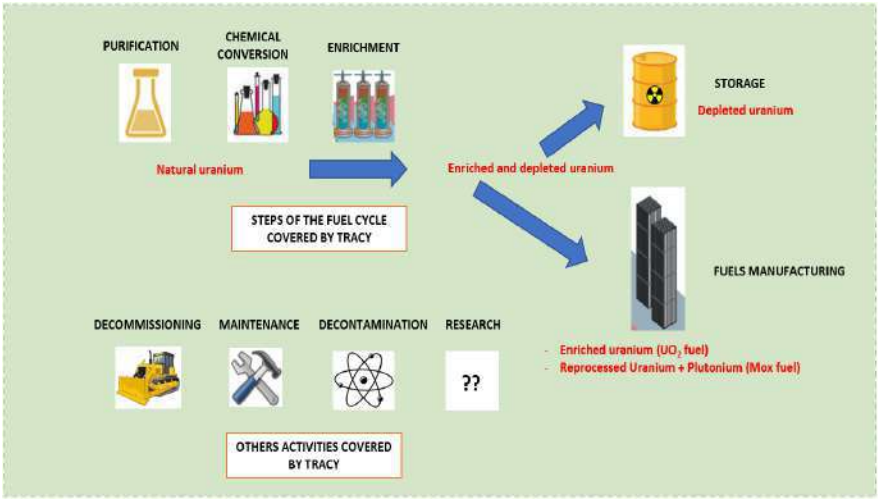
Job exposure matrices have been developed to characterise exposure to various types of U compounds (chemical forms, isotopic compositions …) and also, for more than 5,000 workers, to non-radiological occupational risk factors. Bioassay data on U exposure monitoring and records of external doses are progressively being collected from medical records and computerised. Protocols for internal dose reconstruction, developed in collaboration with other European research groups as part of the DoReMi Concerted Uranium Research in Europe (CURE) project, have also been applied and refined. In addition, methodological developments are underway in close collaboration with dosimetrists, biostatisticians and epidemiologists to account for dosimetric uncertainties in the estimation of dose-risk relationships.

Photo: IRSN

Eric Samson

Information on individual risk factors noted in medical records (e.g. smoking, body mass index, blood pressure, diabetes, cholesterol, glycemia and other blood parameters) have been computerised for 4,500 workers and this collection of data is being extended to the entire cohort. Such data will be valuable for exploring the potential influence of individual risk factors on dose-risk relationships. A nested case-control study of mortality from circulatory diseases has already been conducted using this data, and similar studies are being performed as part of a larger cohort analysis. In the long term, the TRACY cohort will help to improve characterisation of the health effects of occupational U exposure, and more generally of α-particles and low doses of ionising radiation.

Figure: IRSN



Main steps of the nuclear fuel cycle and related activities covered by the TRACY cohort

ID Card:

Cohort type:
Individual data on 12,649 workers employed between 1958 and 2006 in French companies involved in the production of nuclear fuel.

Workers monitored for external gamma and internal alpha-radiation from uranium exposure at low doses over prolonged periods.

Age:
At exposure: 18-65 years
Attained: the mean age at the end of the current follow-up (to end of 2008) is 60 years. The follow-up is being extended.

Biobank available:
No, but full protocol developed as part of the Concerted Uranium Research in Europe (CURE) DoReMi FP7 project

Address:
Institut de Radioprotection et de Sûreté Nucléaire - IRSN

31 Avenue de la Division Leclerc
92260 Fontenay-aux-Roses
France

Access:
Access to the data is restricted according to rules defined by the French Data Protection Authority (CNIL)—agreement number DR-2012-611. The principal investigator can be contacted to explore opportunities for scientific collaboration.

Internet link:
http://www.irsn.fr/FR/Larecherche/Organisation/equipes/radioprotection-homme/Lepid/Pages/Lepid-cohorte-Tracy.aspx#.W3pq5qNOKUk

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Involved in:
CURE

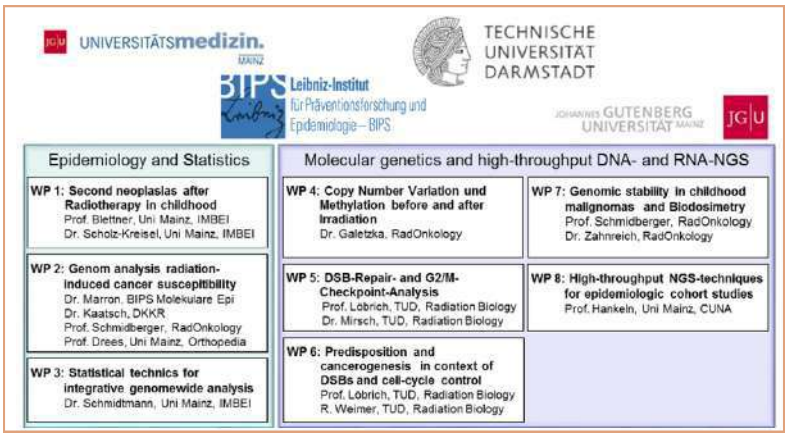
Related to:
MELODI

Cancer and non-cancer mortality among French uranium cycle workers: the TRACY cohort, Samson E., Piot I., Zhivin S., Richardson D. B., Laroche P., Serond A. P., Laurier D., Laurent O. (2016), BMJ Open, 6 (4): e010316
Circulatory disease in French nuclear fuel cycle workers chronically exposed to uranium: a nested case-control study, Zhivin S., Guseva Canu I., Davesne E., Blanchardon E., Garsi J. P., Samson E., Niogret C., Zablotska L. B., Laurier D. (2018), Occup Environ Med, 75 (4), 270–276

The ISIBELa cohort

An interdisciplinary study on radiation induced second cancer

Second primary neoplasms (SPN) are one of the most severe late effects of a first primary neoplasm (FPN) in childhood. Nearly one in ten former cancer patients develops an SPN within 35 years of the occurrence of an FPN. Although radiotherapy and chemotherapy are well known risk factors for SPN, there seems to be an intrinsic genetic sensitivity, making some patients more susceptible to radiation-induced cancer than others.



The ISIBELa project partners and working packages

The ISIBELa cohorts are based on the cohort of the German Childhood Cancer Registry (GCCR) which was established in 1980 to collect all cases of childhood cancer in Germany occuring below the age of 15. Since 2009, cases occurring between age 15 and 18 are also included. The GCCR is 96 % complete and patients are actively followed up for survival and SPNs. As GCCR is an epidemiological register, it does not store therapy data. However, 95 % of all cases of childhood cancer are treated in clinical therapy studies.

The ISIBELa Dosimetry cohort SCAR (Second Cancer After Radiotherapy) contains 1,244 SPN cases occurring after childhood cancer and 4,000 age and sex-matched controls of childhood cancer patients without SPN. Individual radiotherapy doses are gathered by reconstruction of the treatment arm of each patient from the particular clinical study involved. This is done in collaboration with the German Society for Pediatric Oncology and Hematology (GPOH), and provides a database containing all pediatric clinical therapy studies. For patients not included in a study or for whom the data could not be retrieved, therapy data have been gathered from hospital medical records.

Individual organ doses are estimated using the University of Florida Hybrid Phantom family developed by Lee et al. (1, 2) and the Eclipse V.15.1 therapy planning system (Varian Medical System, Palo Alto, CA).

Chemotherapy data is provided by the ISIBELa partner study STATT (Second Tumours After Tumour Therapy), conducted by the GCCR.

The molecular epidemiologic ISIBELa study, KIKme, contains 104 cases of patients with SPN and 377 former childhood cancer patients with no SPN, matched by sex, age at first cancer and follow-up duration, and 137 controls with no cancer diseases, matched by sex and age.

Photo: University Mainz

Dr Peter Scholz-Kreisel

All participants are asked to provide a skin tissue sample and a saliva sample, and to fill out a questionnaire on their family history including cancer and other diseases, radiation exposure and lifestyle factors. The skin sample is used to create non-tumour fibroblast cell lines from each patient. Whole RNA-sequencing before and after irradiation and whole genome sequencing is performed for 65 triplets (1 SPN, 1 Non-SPN, 1 Control). Sequencing of a triplet is done on an Illumina Sequencer in a single batch to minimise batch effects.

The study also includes experiments on double-strand breaks, chromosomal aberrations, single nucleotide polymorphisms and methylation, to get close to the full picture of the differences in handling radiation exposure in radiosensitive and non-sensitive persons respectively. The study is sponsored by the German Federal Ministry of Education and Science (BMBF), Study No. 02NUK042A-D.

The ISIBELa research group

Photo: B. Hof- Barocke/University Mainz-Medical Department

ISIBELA Intrinsische Strahlenempfindlichkeit: Identifikation biologischer und epidemiologischer Langzeitfolgen

ID Card:

Cohort type:
Childhood cancer survivors with and without a second primary neoplasm, partly exposed to radiotherapy (6-90Gy). Dosimetry reconstructed for 5,200 patients by analysing treatment protocols and hospital medical records.

Fibroblast samples for 104 second neoplasm patients, 377 first neoplasm patients and 137 age and gender-matched, cancer-free controls.

Age:
- at exposure: 0-15 years (treatment of first neoplasm)
- current age: 18-45 years

Biobank available:
Yes

Sample type:
Non-tumour fibroblasts, saliva

Sample storage conditions:
Fibroblasts: liquid nitrogen

Saliva: room temperature

Access:
Due to data protection issues, no external access is currently possible.

Internet link:
www.unimedizin-mainz.de/isibela
(German language)

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Related to:
MELODI

Second malignancies following childhood cancer treatment in Germany from 1980 to 2014, Scholz-Kreisel P., Kaatsch P., Spix C., Schmidberger H., Marron M., Grabow D., Becker C., Blettner M. (2018), Dtsch Arztebl Int, 115 (23), 385-392
Searching for gene expression differences in primary fibroblasts between patients with one and two neoplasms in childhood, Victor A., Weis E., Messow C. M., Marron M., Haaf T., Spix C., Galetzka D. (2013), Pediatr Hematol Oncol, 30 (1), 33-45

The ISE cohort

Individual sensitivity to radiotherapy for breast cancer

In Germany, between 1998 and 2001, a total of 476 breast cancer patients aged 26-87 years were recruited to the ISE cohort following breast-conserving surgery and prior to adjuvant radiotherapy (RT). Patients who had received chemotherapy were not eligible. Radiotherapy was delivered to the whole breast 5x/week, at fractions of 1.8 or 2.0 Gy up to 50 Gy (or 56 Gy), with an additional boost (6-16 Gy) to the surgical site for most patients. Acute toxicity was assessed prospectively during and at the end of RT (ISE-1 study), and late toxicity was evaluated after a median time of 51 months (ISE-2 study: N=416) and 139 months (ISE-3 study: N=294).

ISE-1 study: Detailed documentation is available for acute side effects with an adapted CTC Score at 5 time points: Before RT, at 36 to 42 Gy, at 44 to 50 Gy, at end of RT, 6 weeks after RT.

Cancer treatment details in ISE-1	N	(%)
Hormone therapy	394	(82.8)
Radiotherapy (RT):		
Whole breast <50 Gy	13	(2.7)
Whole breast 50 - 50.4 Gy	426	(89.5)
Whole breast >50.4 - 56 Gy	37	(7.8)
No boost	48	(10.1)
Boost up to 10 Gy	238	(50.0)
Boost > 10 Gy	190	(39.9)
Interstitial boost	3	(0.6)
Boost range (Gy)	5 - 25	

Adapted CTC score:

0= No side effects
1= Faint or dull erythema; dry desquamation
2a= Tender or bright erythema; moderate oedema
2b= Severe erythema
2c= At least one moist desquamation or interruption of radiotherapy due to side effects
3= Several or confluent moist desquamation
4= Ulceration, hemorrhage, necrosis.

13% of the patients developed acute side effects grade 2c or 3.

Available **data and samples** from the ISE cohort:

In addition to evaluation of acute and late side effects by a study physician, detailed data was collected on the tumour, operation, treatment, medical history, lifestyle factors, quality of life (EORTC-QLQ-C30), fatigue, recurrence and second tumours. Genotype data is also available.

The primary **aim** of the prospective ISE study was to assess radiotherapy-related side effects. Thus the **study design** took into account the following considerations:

- Female patients who received radiotherapy after breast-conserving surgery for primary breast carcinoma: Objective evaluation of radiation therapy in the treated breast field compared to the untreated contralateral side to reduce interindividual differences, for example, age-related degenerative changes.

Photo: DKFZ

Prof. Jenny Chang-Claude

- Exclusion of the influence of chemotherapy on radiotherapy-related side effects.
- The follow-up examinations were conducted by a single physician to avoid any interexaminer differences.
- In follow-up examinations, the location of fibrosis was separately documented for fibrosis within and outside the surgical area. This reduces the risk of confounding late side effects of the radiation with side effects of the operation, such as wound healing and scar formation. It also enables a distinction to be made between high boost dose areas and lower dose areas.

Some selected **results** from the ISE 1-3 studies:

- For certain genotypes, the risk for acute toxicity may be higher with higher levels of oxidative stress (e.g. GSTP1).
- Age, acute skin toxicities and long term smoking increased the risk of teleangiectasia after 5 years.
- Polymorphisms near TNFalpha were associated with an increased risk for teleangiectasia.
- Using a radiation-induced lymphocyte assay (RILA), low values of $CD4^+$ T lymphocytes were found to be associated with an increased risk for fibrosis and teleangiectasia after 10 years.

Characteristics study population	ISE-1 (RT) N=476	(%)	ISE-3 (139 months FU) N=294	(%)
Age (years):				
26-49	51	(10.7)	1	(0.3)
50-69	342	(71.9)	124	(42.2)
70-91	83	(17.4)	169	(57.5)
Range	26 - 87		48 - 91	
Median	60		71	
BMI >25 kg/m²	230	(48.3)	150	(51.0)
Hypertension yes	152	(31.9)	144	(49.0)
LENT-SOMA Late toxicity scores:				
Teleangiectasia >1cm² within OP area	--		26	(8.8)
Teleangiectasia >1cm² outside OP area	--		11	(3.7)
Fibrosis score ≥ 2 within OP area	--		87	(29.6)
Fibrosis score ≥ 2 outside OP area	--		26	(8.8)
Quality of Life Questionnaire	457	(96.0)	294	(100)
Fatigue Assessment Questionnaire	--		293	(99.7)
Tumor contralateral side	6	(1.3)	4	(0.8)
Recurrence	--		22	(4.6)
Death due to breast cancer	--		32	(6.7)
Death due to other	--		39	(8.2)

ISE

ID Card:

Cohort type:
German cohort of 476 breast cancer patients who, after breast-conserving surgery, received adjuvant radiotherapy at a dose of 50-66 Gy. Detailed documentation on acute side effects during radiotherapy (ISE-1). Active follow-up after a mean of 51 (ISE-2) and 137 months (ISE-3) with assessment of vital status and radiotherapy-related toxicity of the skin and soft tissue.

Age:
- at exposure to radiotherapy (1998-2001): 26-87 years
- second follow-up (2011): 48-91 years

Biobank available:
Yes

Sample type:
DNA, RNA

Sample storage conditions:
-80°C

Access:
The database is owned by the DKFZ. Access to pseudonymised data and samples is subject to acceptance of a project proposal and signature of a material transfer agreement.

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www.dkfz.de

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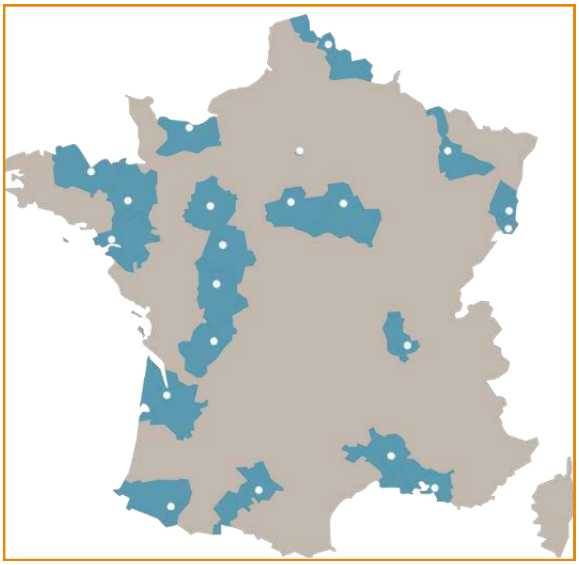
Related to:
MELODI

Association of $CD4^+$ radiation-induced lymphocyte apoptosis with fibrosis and telangiectasia after radiotherapy in 272 breast cancer patients with >10-year follow-up, Veldwijk M. R., Seibold P., Botma A., Helmbold I., Sperk E. et al. (2018), Clin Cancer Res, doi: 10.1158/1078-0432.CCR-18-0777
Predictive factors for late normal tissue complications following radiotherapy for breast cancer, Lilla C., Ambrosone C. B., Kropp S., Helmbold I., Schmezer P., von Fournier D., Haase W., Sautter-Bihl M. L., Wenz F., Chang-Claude J. (2007), Breast Cancer Res Treat, 106 (1), 143-150

CONSTANCES

The CONSTANCES population-based cohort

CONSTANCES is a general-purpose, population-based cohort for research and public health, which serves as an epidemiological research infrastructure for the scientific community. Its focus is on occupational and social factors, as well as chronic disease and aging; it also provides useful information to the French public health authorities. CONSTANCES is designed as a randomly selected, representative sample of the French adult population; its members were aged between 18-69 years at inclusion. The cohort comprises 200,000 subjects recruited over a six-year period.



The CONSTANCES recruitment centers

At recruitment stage, the selected subjects were invited to complete several questionnaires and to undergo a comprehensive medical examination at one of the 22 Health Screening Centres (HSC) run by the general Social Security Scheme in different regions of France. Work is currently in progress to set up a biobank. Follow-up of cohort members includes the completion of a yearly self administered questionnaire, a visit to an HSC every 4 years, and annual linkage to national administrative databases (SNDS-SNIIRAM for health data, and CNAV for social and professional data).

Participant data collected includes social and demographic characteristics, socioeconomic status, life events, behaviour, and environmental and occupational factors. The health data covers a wide spectrum: self-reported health scales, prevalence and incidence of disease, long-term chronic disease and hospitalisation, sick leave, handicap, limitations, disabilities and injuries, ulitilisation of the healthcare system and specific services used, and cause of death.

Photo: Personal archive

Dr Marie Zins

In order to take into account non-participation at recruitment stage and attrition throughout the longitudinal follow-up, a cohort of non-participants was set up, and this cohort will be followed up through the same national databases as the participants. Recruitment of participants began at the end of 2012 and was completed in February 2019. The main socioeconomic variables in the CONSTANCES sample closely match those of the general adult population in France and include a relatively diverse distribution of occupations and working conditions, lifestyle factors and health conditions.

Any research group (public or private), in France or elsewhere, can apply to develop a nested project within CONSTANCES and to access its database. Projects are evaluated by the CONSTANCES Scientific Committee based on feasibility of the study and scientific quality criteria. A Charter has been established outlining the rules for use of the CONSTANCES infrastructure, and includes legal aspects, data confidentiality and security, ethics, access to the database, dissemination of data and results, and publications and authorship. To date more than 80 projects, covering a wide range of topics, have been proposed and approved by the Scientific Committee.

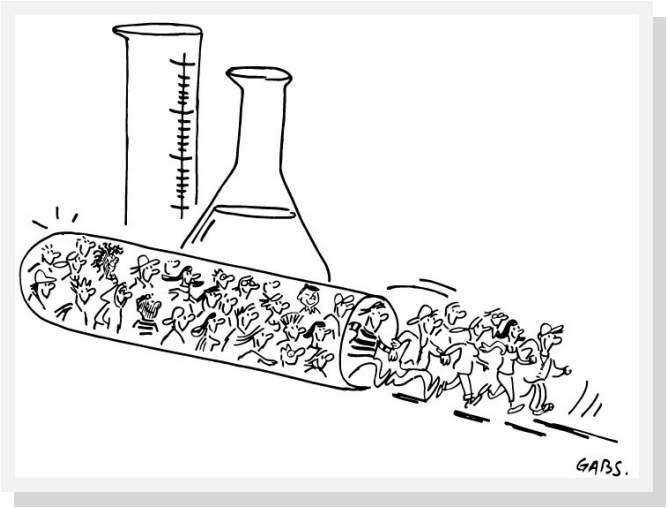


Photo: GABS

CONSTANCES, a human epidemiological laboratory

ID Card:

Cohort type:
Population-based, epidemiological cohort (200,000 members)

Age:
Range: 18-69 years at inclusion

Biobank available:
Yes

Sample type:
Blood, urine

Sample storage conditions:
Liquid nitrogen

Conditions of use:
External use possible

Access:
Subject to approval by project selection committee, which meets twice per year

Internet link:
http://www.constances.fr

Contact:
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+33 6 83 85 01 31

Related to:
MELODI

The French CONSTANCES population-based cohort: design, inclusion and follow-up, Zins M., Goldberg M. and CONSTANCES team (2015), Eur J Epidemiol, 30 (12), 1317–1328
CONSTANCES: a general prospective population-based cohort for occupational and environmental epidemiology: cohort profile, Goldberg M., Carton M., Descatha A., Leclerc A., Roquelaure Y., Santin G., Zins M., CONSTANCES team (2017), Occup Environ Med, 74 (1), 66-71

IMMO-LDRT01 cohort

Cohort of locally low-dose irradiated patients with chronic degerative, inflammatory joint diseases

Low Dose Radiation Therapy (LDRT) has been used for the treatment of chronic degenerative joint diseases for more than a century. The success of the treatment has been described in many retrospective studies and pattern of care studies.

Photo: M. Rabenstein/Universitätsklinikum Erlangen

The team of the Radiation Immunobiology performing immunophenotyping of whole blood of patients of the IMMO-LDRT01 study.

Today, the affected region is irradiated mostly using orthovoltage techniques (120-220 kV, 10 mA, own filter 4 mm Al; additional filter: 0.1-1mm Cu). A cycle of LDRT consists of six single fractions with a single dose per fraction of 0.5 Gy, delivered over a period of three weeks with an interfractional radiation-free interval of at least two days. In cases where there is no remission of pain or only partial remission six weeks after the end of the first cycle, a second cycle of radiation can be administered. In most cases, low dose radiation administered locally (targeting only the painful joint) results in significantly reduced pain perception, not only immediately after therapy, but also for a duration of more than 12 months.

Moreover, patients experience enhanced mobility and increased quality of life. Recent pre-clinical work has revealed that local and systemic osteoimmunological mechanisms are triggered by LDRT depending on the basal inflammatory state.

The IMMO-LDRT01 study aims, for the first time, to provide a detailed analysis of the immune status of patients suffering from inflammatory, chronic joint diseases before, during and after LDRT; this will be done on a longitudinal basis. The established and optimised multi-colour flow cytometry-based assay developed for the cohort allows over 30 immune cell subsets to be determined, in addition to their activation status.

Photo: Universitätsklinikum Erlangen

Prof. Dr. Udo Gaipl

The IMMO-LDRT01 study (NCT02653079) is a prospective and observational study which does not influence the standard therapeutic scheme and will provide hints on the effects of LDRT, not only on the local cells in the irradiated area, but also on the systemic inflammatory response. The analyses are conducted before LDRT (day 0), at the end of first round of LDRT (usually at a total dose of 3 Gy), and at month 3 after completion of the therapy. This scheme is repeated if the patient receives additional rounds of LDRT for relapse treatment.

As a primary outcome measure, changes in circulating immune cells and their phenotype are followed up in patients monitored with deep immunophenotyping. As a secondary outcome measure, changes in joint pain are monitored, and patients also retrospectively comment on their pain sensation and quality of life. All patients have to give their informed consent before starting LDRT. In addition, serum and plasma are stored in our quality-controlled in-house biobank at -80°C (500 µl aliquots). The remaining whole blood cells after serum/plasma retrieval are also stored as frozen peripheral blood mononuclear cells (PBMC) for future functional analysis.

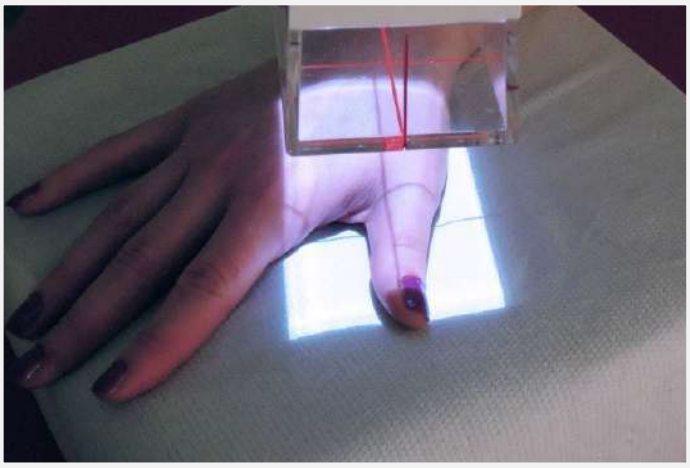


Photo: B. Frey/Universitätsklinikum Erlangen

Irradiation of joints with orthovoltage X-rays.

The Erlangen Dose Optimization trial for low-dose radiotherapy of benign painful elbow syndrome. Long-term results., Ott O. J., Hertel S., Gaipl U. S., Frey B., Schmidt M., Fietkau R. (2014), Strahlenther Onkol, 190 (3), 293-297

Immunomodulation by ionizing radiation-impact for design of radio-immunotherapies and for treatment of inflammatory diseases, Frey B., Rückert M., Deloch L., Rühle P. F., Derer A., Fietkau R., Gaipl U. S. (2017), Immunol Rev, 280 (1), 231-248

Universitätsklinikum Erlangen

ID Card:

Cohort type:
Liquid biopsies of patients with benign diseases after LDRT

LDRT: irradiated using orthovoltage techniques (120-220 kV, 10 mA, own filter 4 mm Al; additional filter: 0.1-1mm Cu); 6x0.5Gy that can be repeated once

Age:
- at exposure: at least 18 years old
- current age: >18 years old

Biobank available:
Yes

Sample type:
Serum, plasma and frozen PBMC

Sample storage conditions:
-80°C

Conditions of use:
Mainly restricted to internal use. External use possible upon submission of a request with project plan

Access:
Selection committee

Internet link:
https://clinicaltrials.gov/ct2/show/NCT02653079

Contact:
Prof. Dr. Udo Gaipl
udo.gaipl@uk-erlangen.de
0049 9131 85 44258

Related to:
MELODI

The BACCARAT study

Early cardiotoxicity after radiotherapy for breast cancer

Radiotherapy (RT) for breast cancer can lead to secondary effects to the heart due to the presence of neighbouring normal cardiac tissue within the irradiation field and is associated with long-term radiation-induced cardiovascular diseases. Little is yet known concerning early cardiotoxicity, which can appear long before the onset of clinically significant cardiac events.

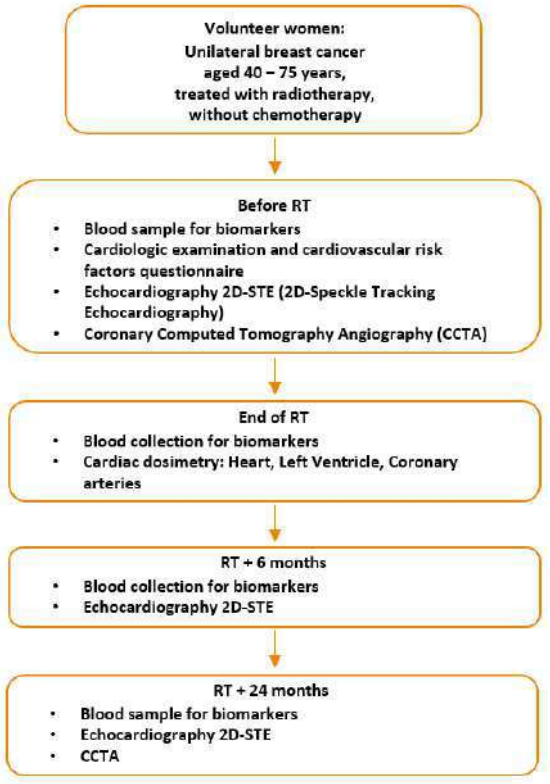


Photo: IRSN

BACCARAT Study flowchart

The BACCARAT study (BreAst Cancer and Cardiotoxicity induced by RAdioTherapy) is based on a two-year follow-up prospective cohort of breast cancer patients treated with RT. It aims to improve our knowledge on the early detection and prediction of RT-induced subclinical cardiac dysfunction and lesions and the biological mechanisms that are potentially involved through functional and anatomical cardiac imaging combined with the simultaneous assessment of multiple circulating biomarkers and precise cardiac dosimetry.

The study includes 114 female patients, aged 40 to 75 years old, treated with 3D-conformal radiotherapy RT for left or right unilateral breast cancer, without chemotherapy, in the Pasteur Clinic of Toulouse, France. Exclusion criteria were a history of coronary artery disease, myocardial infarction or a major cardiac event, or prior cancer treated with chemotherapy or RT. The inclusion period lasted from October 2015 to December 2017. The two-year follow-up of patients is still ongoing, the end is foreseen for early 2020.

Once included, the women's follow-up protocol was implemented (see Figure Flowchart):

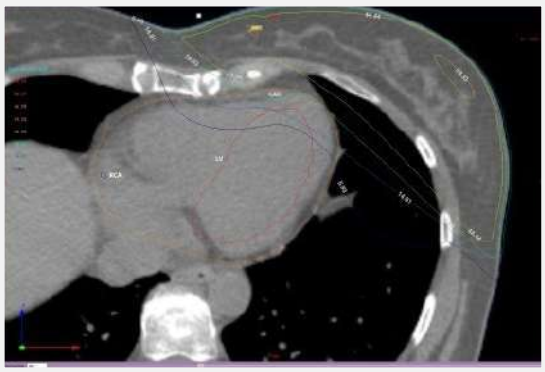
Photo: IRSN

Dr Sophie Jacob

- Two-dimensional speckle tracking echocardiography (2DSTE) performed at baseline before RT, RT+6 months, and RT+24 months: to evaluate myocardial dysfunction (in particular, the left ventricular ejection fraction) and assess myocardial deformation (with longitudinal myocardial strain).
- CT coronary angiography (CTCA) performed at baseline and RT+24 months: to evaluate coronary artery lesions by assessing morphological information, including plaques and stenosis of the arteries, and determination of the coronary artery calcium score.
- Plasma sampling (PLASMA) performed at baseline, the end of RT, RT+6 months, and RT+24 months: for the analysis of circulating biomarkers, including classical biomarkers of cardiac injury, inflammatory cytokines, markers of endothelial activation and dysfunction, microparticles, and microRNAs.
- Collection of information on traditional risk factors of cardiac diseases (e.g. systolic and diastolic blood pressure, hypertension, diabetes, cholesterol, tobacco use, and body mass index) performed at each visit of the follow-up.
- Individually-determined cardiac dosimetric evaluation performed at the end of RT: dose distributions (dose-volume histogram) were generated for the whole heart, left ventricle, left main coronary artery, left anterior descending artery, left circumflex artery, and right coronary artery.

BACCARAT is the result of a multidisciplinary collaboration to enhance knowledge on early breast RT-induced cardiotoxicity.

Photo: IRSN



CT-based dose-planning scan for left tangential breast irradiation, showing isodoses and delineated structures: heart (orange circle), left ventricle (LV), left anterior descending coronary artery (LAD), and right coronary artery (RCA).

IRSN
INSTITUT DE RADIOPROTECTION ET DE SÛRETÉ NUCLÉAIRE

ID Card:

Cohort type:
Prospective observational cohort study of 114 breast-cancer patients treated with RT without chemotherapy. Inclusion before RT, follow-up of 2 years, including 3 time points: end of RT, end of RT+6 months, end of RT+24 months. Blood samples are collected and cardiac imaging examinations performed at baseline and during follow-up. Cardiac dosimetry is available for the whole heart, left ventricle, and coronary arteries.

Age:
- at exposure: 40-75 years
- follow-up: 2 years

Biobank available:
Yes

Sample type:
Plasma

Sample storage conditions:
-80°C

Access:
Due to data protection, access to the data is restricted. S. Jacob can be contacted to explore opportunities for scientific collaboration.

Internet link:
https://clinicaltrials.gov/ct2/show/NCT02605512

Contact:
Sophie Jacob
sophie.jacob@irsn.fr
+33 5 61 14 56 08

Involved in:
MEDIRAD EARLY-HEART study

Related to:
MEDIRAD

Is mean heart dose a relevant surrogate parameter of left ventricle and coronary arteries exposure during breast cancer radiotherapy: a dosimetric evaluation based on individually-determined radiation dose (BACCARAT study), Jacob S., Camilleri J., Derreumaux S. et al. (2019), Radiat Oncol, 14 (1), 29
Early detection and prediction of cardiotoxicity after radiation therapy for breast cancer: the BACCARAT prospective cohort study, Jacob S., Pathak A., Franck D., Latorzeff I., Jimenez G., Fondard O., Lapeyre M., Colombier D. et al. (2016), Radiat Oncol, 11 (54), doi: 10.1186/s13014-016-0627-5 231-248

Life Span Study (LSS)

Cohort study of atomic bomb survivors of Japan

After the catastrophic atomic bombings of Hiroshima and Nagasaki, the Life Span Study (LSS) cohort of the survivors was set up using the information of a supplemental survey by the National Census of Japan in 1950 and others by the Atomic Bomb Casualty Commission (ABCC), the predecessor organization of the Radiation Effects Research Foundation (RERF). The members of the LSS cohort were selected from people who were alive and lived in the cities of Hiroshima and Nagasaki in 1950. The cohort includes four groups: (1) survivors who were located within 2 km of the hypocenter at the time of the bombings, (2) survivors from 2 to < 2.5 km away, (3) survivors from 2.5 to < 10 km away, and (4) people who were not in either city (*i.e.*, > 10 km from the hypocenters) at the time of the bombings.

Photo: K. Ozasa/RERF

Dr Kotaro Ozasa

status of the LSS members has been followed up by Japan's official family registry system since 1950. The death certificate is used to record the cause of death. Cancer incidence information has been collected by linkage with population-based cancer registries in Hiroshima and Nagasaki since 1958.

A marked excess of leukemia cases emerged in the early period, while the risk of solid cancers increased later and continues to be elevated today. The risk of all solid cancers was approximately 40 to 50% per Gy higher than that of the non-exposed baseline for both mortality and incidence for a person aged 70 years who was exposed at age 30. The dose-response is linear, but a significant concave curvature has appeared recently for men. Certain noncancer diseases have shown positive associations with radiation dose.

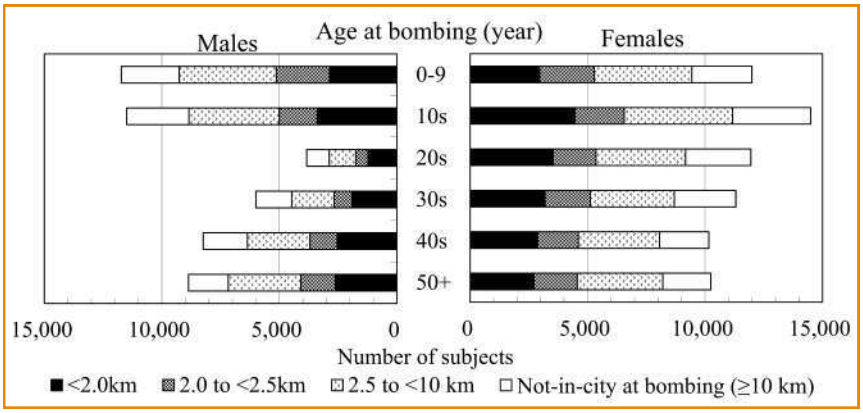


Photo: RERF

Distribution of LSS subjects by sex, age at bombings, and distance from hypocenters

Groups (1) and (2) included all affected people, whereas groups (3) and (4) were selected by matching for sex and age to those of group (1). After some additions, the LSS cohort consists of 120,321 subjects. There was a general lack of young men, who were thought to be out of the cities due to military duties and related jobs.

Radiation from atomic bomb explosions is classified into initial radiation and residual radiation. The ABCC-RERF developed a series of dosimetry systems for atomic bomb radiation and investigated survivors' shielding conditions at the time of the bombings. Radiation risk has been estimated based on individual radiation doses derived from the initial radiation. We do not think that exposure to residual radiation should have a large influence on radiation -risk estimates. The vital

In addition to the tragic memories of atomic bombings among survivors and citizens in Hiroshima and Nagasaki, some or many survivors were displeased with activities of the ABCC, an organization of the country of the bombings, for investigating the health effects of atomic bombings on them. LSS subjects are not voluntary participants in the study, and were included in the study regardless of their willingness. So, we continue to strive for the understanding of the cohort members.

Photo: K. Ozasa/RERF

Hiroshima Peace Memorial Park on 25 May 2019, a usual quiet morning

放影研 RERF

ID Card:

Cohort type:
Atomic bomb survivors in Hiroshima and Nagasaki. Individual records of 120,321 men and women exposed to from zero to several grays of gamma-rays, with a small proportion of neutrons, within several tens of seconds

Age:
- at exposure: 0 to 90 years
- current: 73 to > 100 years (in 2018)

Biobank available:
No

Condition of use:
Aggregated data of published papers are available at: https://www.rerf.or.jp/en/library/data-en/

Access:
Users are required to register at https://www.rerf.or.jp/en/library/data-en/

Internet link:
https://www.rerf.or.jp/en/

Contact:
Kotaro Ozasa
Department of Epidemiology
Radiation Effects Research Foundation, Hiroshima, Japan
ozasa@rerf.or.jp

Japanese Legacy Cohorts: The Life Span Study atomic bomb survivor cohort and survivors' offspring, Ozasa K., Grant E. J., Kodama K. (2018), J Epidemiol, 28 (4), 162-169
Solid cancer incidence among the Life Span Study of atomic bomb survivors: 1958–2009, Grant E. J., Brenner A., Sugiyama H., Sakata R., Sadakane A., Utada M., Cahoon E. K., Milder C. M., Soda M., Cullings H. M., Preston D. L., Mabuchi K., Ozasa K. (2017), Radiat Res, 187 (5), 513-537

REQUITE

4,438 radiotherapy patients with centralised data and samples

Many models and biomarkers were reported to have potential to predict a cancer patient's risk of toxicity following radiotherapy, but the challenge is to validate them for clinical application. Validation requires access to well-annotated big datasets. The European Union FP7 funded REQUITE project (G601826) was established with the aim of carrying out a prospective, longitudinal, multi-centre study to compile a large centralised, standardised dataset and biorepository for validating models and biomarkers that predict a cancer patient's risk of radiotherapy toxicity.

Photo: University of Manchester

Dr Catharine West

Characteristics		Breast	Prostate	Lung
Number of patients		2,057	1,760	530
Age	Mean (range), years	58 (23-90)	70 (42-88)	69 (39-91)
Body mass index	Mean±sd kg/m²	26.5±5.6	27.6±4.5	26.6±4.8
Smoking	Current	365 (18%)	249 (14%)	213 (40%)
	Former	514 (25%)	821 (47%)	290 (55%)
	Never	1156 (56%)	683 (39%)	23 (4%)
Comorbidities	Diabetes	127 (6%)	236 (13%)	88 (17%)
	Heart disease	143 (7%)	372 (21%)	161 (30%)
Family history	First degree relatives	410 (20%)	320 (18%)	94 (18%)
Tumour size	in situ	252 (12%)	0	0
	T1-T2	1728 (84%)	1133 (64%)	319 (60%)
	T3, T4	16 (1%)	467 (27%)	193 (36%)
Nodal status	Negative	1488 (72%)	1308 (74%)	235 (44%)
	Positive	394 (19%)	134 (8%)	289 (55%)
Chemotherapy		652 (32%)	0	271 (51%)
Hormone therapy		1574 (77%)	1221 (69%)	0
Radiotherapy	IMRT	1018 (49%)	246 (14%)	140 (26%)
	Arc Therapy	0	1161 (66%)	70 (13%)

Baseline characteristics & treatment information of the REQUITE cohort. (Only includes patients where comprehensive cancer treatment data were available.)

An international prospective cohort study recruited patients in 26 hospitals in eight countries across Europe and the US. Eligible patients had breast, lung or prostate cancer and planned potentially-curable radiotherapy. Although radiotherapy was prescribed according to local regimens, centres used standardised data collection forms (at baseline, during treatment and follow-up) and collected pre-radiotherapy blood samples from all participants. Patients were followed prospectively for a minimum of 12 (lung) or 24 (breast/prostate) months. Between 2014 and 2017, the study recruited 2,069 breast, 1,808 prostate and 561 lung cancer patients. Jenny Chang-Claude's team at the German Cancer Research Centre (DKFZ) in Heidelberg did an excellent job leading the observational study, chasing centres to minimise missing data and performing data validation and QC to create clean locked datasets. The centralised, accessible database includes an impressive amount of data: physician- (47,025 forms) and patient- (54,901) reported outcomes; 11,563 breast photos; 17,107 DICOM and 12,684 DVH files (as of October 2018). Imputed genotype data from the Illumina Infinium OncoArray-500K beadchip and imputed using the 1000 Genomes Project (v3 as a reference panel) are available for 4,223 patients with European ancestry (1,948 breast, 1,728 prostate, 547 lung). Radiation-induced lymphocyte apoptosis (RILA) assay data are available for 1,319 patients. DNA (n = 4,409), RNA (n=1,837) and PAXgene whole bloods (n = 1,202) are stored in the centralised biobank at The University of Manchester.

REQUITE developed a standardised approach for collecting and curating radiotherapy data linked with a biorepository. The outputs of REQUITE are already serving as a high quality resource for REQUITE partners and the wider radiobiology community to address further research questions in the field. A public data discovery platform enables researchers to search on numbers of patients with various attributes collected by the consortium (www.requite.eu). Access to the resource is *via* submission and approval of a Concept Form. A cost recovery model was implemented to support this as a sustainable (not-for-profit) resource that will provide researchers with access to stored patient samples and high quality data.

Contact REQUITE (requite@manchester.ac.uk) for more information on access and pricing.

Photo: REQUITE

Members of the REQUITE consortium

ID Card:

Cohort type:
Human N=4, 438 breast, prostate, lung cancer patients from Europe and the US receiving radiotherapy between 2014 and 2017

Age:
- at exposure: 23-91 years

Biobank available:
Centralised repository based in Manchester

Sample type:
Germline DNA, RNA, whole blood PAXgene tubes

Sample storage condition:
DNA, RNA & whole blood PAXgene tubes stored at -80°C

Condition of use:
Accessible; a cost recovery model has been implemented to ensure sustainability

Access:
Process for access available at: https://www.requite.eu/node/203.

Requires completion of a Concept Form and review by a committee that meets as required. Cost to access the resource. Data (& material) transfer agreement required.

Internet link:
www.requite.eu

Contact:
REQUITE@manchester.ac.uk

Related to:
MELODI
EURAMED

The REQUITE project: validating predictive models and biomarkers of radiotherapy toxicity to reduce side-effects and improve quality of life in cancer survivors, West C., Azria D., Chang-Claude J., Davidson S., Lambin P., Rosenstein B., De Ruysscher D., Talbot C. et al. (2014), Clin Oncol, 26 (12), 739-742
REQUITE: A prospective multicentre cohort study of patients undergoing radiotherapy for breast, lung or prostate cancer, Seibold P., Webb A., Aguado-Barrera M. E., Azria D., Bourgier C., Brengues M., Briers E., Bultijnck R., Calvo-Crespo P., Carballo A. et al. (2019), Radiother Oncol, 27 (138), 59-67

Chapter 3: Analytical platforms, Models & Tools

Chapter 3: Analytical platforms, Models & Tools

The nature and complexity of the societal challenges related to low-dose research require an international approach to answer the open questions in the radiation community. For this purpose, it is essential to have access to best platforms with cutting-edge technologies in order to achieve not only scientific excellence but also public health impact. Such technologies, but also models and tools to optimise the data analysis, increase the value of analytical platforms. This web handbook introduces some European platforms together with suitable models and tools as described in the next sessions.

(a) Analytical platforms

Research infrastructures, including analytical platforms, are at the core of the knowledge triangle of research, education and innovation and therefore play a vital role in the advancement of science, knowledge and technology. Analytical platforms play a key role in the construction of an efficient research and innovation environment and are one of the most efficient tools to facilitate European cooperation in radiation research.

In the low-dose research, analytical platforms are often designed to address questions related to systems biology studies with the goal to understand the mechanisms underlying radiation response. Analytical platforms described in this handbook are using different technologies and tools to answer challenging biological questions. This will allow the implementation of systems-based analyses that often generate large data sets [1]. These, in their turn, require resources for safe storage and management of information in the long term.

Several criteria need to be considered regarding such infrastructures. Firstly, performance is an important aspect for analytical platforms. The platform should have high score performance with constant quality controls included. In addition, detailed operating procedures should exist since they help the user to perform the work correctly, naturally with the help of the local user.

Secondly, the platform should be easily accessible for guest scientists to perform their analysis. Alternatively, the platform should provide a core-service type analysis. The security of access and the reliability of the experimental processes should be well managed and monitored all times. The user should be able to give feedback, both positive and negative, as suggestions how to improve a platform are often very useful. All collected data should be well documented and well governed *via* storage in secure open-access databases such as the STORE DB [1].

Strong investment in research and innovation is needed to address pressing societal challenges in radiation protection. Analytical platforms play an important role in addressing these challenges. However, it is essential to enhance collaboration between the different fields of radiation research in order to optimise the use of scarce resources for increasingly expensive facilities, in order to overcome the problems arising from fragmented funding in research infrastructures across Europe.

(b) Models & Tools

The category ‘Models & Tools’ encompasses a wide range of mathematical, statistical, biological (*in vitro*, *ex vivo* and *in vivo*), biochemical and physical models and tools, created and maintained by partners across the CONCERT consortium and wider collaborators, to support radiation protection research. As is clear from the CONCERT joint roadmap and related strategic research agendas of the radiation protection platforms [2, 3], models and the tools that support their use are essential to maintain innovative scientific research and development across the different platforms and projects in the field of radiation protection. For example, in the field of biological dosimetry and biomarker research (RENEB Analytical Platform) [4], ISO standard methodologies exist for translation of biological and biochemical observations into estimates of dose to support both emergency response (NERIS platform) [5] and medical management (EURAMED) [6] of individuals. Wider use of these techniques for molecular epidemiology, for example in the MELODI platform [7], is supported by provision of user-friendly tools such as Dose Estimate, NETA and CABAS. Continuing with the emergency response theme, the Severe Nuclear Accident Program (SNAP) tool provides a means to identify unknown sources of radiation, indicated by elevation in normally measured levels. The Multi Criteria Decision Analysis (MCDA) tool gives

guidance to decision makers regarding selection of concerted emergency response strategies. For non-human populations (ALLIANCE platform) [8], the Environmental Risk Assessment tool (ERICA) supports environmental risk assessment and the Biological Radiation Effects for Non-human Dose Assessment (BRENDA) model facilitates estimation of the non-stochastic effects of radiation on repairable radiation damage, reproductive ability and mortality.

In the field of physical modelling of radiation effects, several bespoke radiation transport codes have been created and further models which attempt to provide accurate representations of the biological and biochemical consequences of exposure are now in existence. Examples include the now relatively well established GEANT4-DNA, BIophysical ANalysis of Cell death and chromosome Aberrations (BIANCA) and COmputation Of Local Electron Release (COOLER) tools. Extending computational support to the medical protection research field (EURAMED platform), the OEDIPE tool, for example, supports personalised dosimetry in nuclear medicine.

The CONCERT project and the joint SRAs clearly indicate the need for interdisciplinary research to address the key research lines. As the radiation research community continues to grow and flourish, it is likely that its members will need to work more and more across disciplinary boundaries. The utility of such user-friendly models and tools in this context is clear, as it is in the context of emergency response when tools to support fast and effective decision-making will be invaluable.

References Chapter 3

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Chapter 3 : Analytical platforms, Models & Tools	
Subcategories	Infrastructure
(a) Analytical platforms	RENEB
	The Genomic Medicine and Bioinformatics Core Facility
	MetaboHUB
	ProFI
	Radiobiology and immunology platform (CTU-FBME)
	France Génomique
	The SCK•CEN Genomics platform
	CATI
	HZDR–Radioanalytical Laboratories
	Advanced Technologies Network (ATeN) Center
	BfS In Vivo Measurement Facilities
	ECORITME
	Consolidated Radioisotope Facility (CORiF)
	Centre for Omic Sciences (COS)
	The iGE3 Genomics Platform
	VIB Proteomics Core
	MARS beamline at Synchrotron SOLEIL
	CIEMAT Whole Body Counter (WBC)
	DSA Environmental Laboratory
	Radiochemical and Radioactive Analysis Laboratory (INTE-UPC)
	CIEMAT In Vitro Internal Dosimetry Laboratories
	LRM
	TU Dublin Analytical Platform
Add-on section	NASA Genelab
(b) Models & Tools	Dose Estimate, CABAS and NETA
	LDRadStatsNet
	ERICA Tool
	CROM-8
	The Analytical Platform of the PREPARE project
	Symbiose
	INFRAFRONTIER
	The CERES Platform
	The Severe Nuclear Accident Program (SNAP)
	The BIANCA code
	OEDIPE
	Geant4-DNA

	D-DAT COOLER BRENDA The EFFTRAN code The MCDA Tool

Table 9: Analytical platforms, Models & Tools cross table with tags for each infrastructure

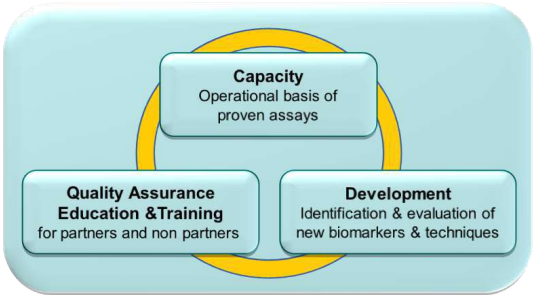
Chapter 3: Analytical platforms, Models & Tools

a) Analytical platforms

RENEB

A network for emergency preparedness and scientific research

RENEB is a European Biodosimetry Network, able to perform large scale rapid biodosimetric dose estimation. Specialized to handle a large number of samples, RENEB contributes to radiological emergency preparedness and large scale research projects. The network infrastructure is based on reliable assays and techniques combined with high performance standards. To enhance the effectiveness of the network, RENEB is linked to global emergency preparedness and response systems as well as to the European radiation research area.



The network was initiated in January 2012 with 23 partners from 16 European countries with the support of the EC (EURATOM FP7, GA 295513). At this time the focus was on emergency preparedness with the aim to significantly increase dose reconstruction capacities in case of large-scale radiological scenarios. Individual dose estimation based on biological samples and/or inert personalized devices has been optimized to support the rapid categorization of many victims according to the received dose. Communication and cross-border collaboration was standardized and cooperation with national and international emergency and preparedness organizations such as IAEA and WHO were initiated.

The value of RENEB to support topics also outside emergency preparedness is now evident. With established strategies to guarantee consistent performance between the partner laboratories, the network has the ability and capacity to contribute to large scale research projects with the analysis of exposure biomarkers. This includes studies on the effects of low doses, group related radiation sensitivity, contribution to non-cancer diseases, and epidemiological studies where sampling and handling of bioprobes is included. RENEB also drives the development and evaluation of new exposure markers with special view to their applicability for addressing acute or protracted exposures as well as exposures dating back years or decades.

As such, RENEB as an analysis platform is of special interest for the Emergency Preparedness Platform NERIS by adding preparedness in the field of individual dose estimation. Moreover it benefits MELODI and EURADOS by providing capacity for radiation research and specialized biomarker development. Concerning the latter, the radioecological Platform ALLIANCE will also profit from RENEB. Last but not least, RENEB provides intercomparisons, specialized courses and seminars open also to laboratories outside the network, thus being of relevance for E&T in the CONCERT-EJP.

Photo: ISS/A. Campa

Ulrike Kulka

RENEB was never meant to be a "time limited or closed club" and strategies were developed to identify "candidates" and integrate them as solid partners. Currently, RENEB comprises 22 partners and 7 candidates from 17 European countries. 16 have already signed a MoU, and thus form the nucleus of a unique growing infrastructure, combining high quality standards in the application and validation of biomarkers and maintenance and advancement of scientific and technical competence.

RENEB Consortium: BfS* Germany, BIR Germany, CEA France, ENEA Italy, HMGU Germany, ICHTJ Poland, INSP* Romania, IRSN France, ISS Italy, IST* Portugal, LAFE* Spain, NCRRP* Bulgaria, NCSRD Greece, OKK-OSSKI Hungary, NRPA* Norway, PHE* United Kingdom, SERMAS* Spain, STUK Finland, ,SU-CRPR* Sweden, UAB* Spain, UGent* Belgium, UNITUS* Italy

RENEB candidate: AMVRC* Italy, DIT* Irland, FZ Jülich Germany, INFN Italy, RPC* Lithuania, SCK•CEN* Belgium, US Spain

**MoU signed*

Photo: ISS/A. Campa

ID Card:

Analytical platform type:
biodosimetry, markers of exposure, retrospective dosimetry on biological and inert samples

Main techniques proposed:
panel of cytogenetic assays, gene expression assay, gamma H2AX assay, EPR/OSL dosimetry

Capacity:
emergency situation: up to 1000 samples per week, depending on assay;
research: up to 500 samples per week for several weeks, depending on assay;

Delay to start:
Emergency situation: immediately, no delay;
Research: dependent on the project

Intercomparison exercise options:
possible for all network assays and techniques

Training options:
possible for all network assays and techniques

Access:
Emergency situation: regulated by national authorities;
Research: selection by members

Internet link:
http://reneb.eu

Contact:
Ulrike Kulka
reneb@bfs.de
+49 30 18333 2210

Related to:
Emergency preparedness: NERIS,
Research: EURADOS, MELODI,

REALISING THE EUROPEAN NETWORK OF BIODOSIMETRY: RENEB—STATUS QUO. U. Kulka, et al. Radiat Prot Dosimetry. 2015 Apr;164(1-2):42-5.
THE FIRST GAMMA-H2AX BIODOSIMETRY INTERCOMPARISON EXERCISE OF THE DEVELOPING EUROPEAN BIODOSIMETRY NETWORK RENEB. S. Barnard, et al.Radiat Prot Dosimetry. 2015 Apr;164(3):265-70.

The Genomic Medicine and Bioinformatics Core Facility

Hungarian Genomics Research Network

The Genomic Medicine and Bioinformatics Core Facility (http://genomics.med.unideb.hu) was established in the year 2000 to provide access to cutting edge genomics technologies and foster collaborations between basic science and clinical research groups, as well as small and large pharma companies in the area of clinical genomics. The Centre now has 20 staff members working in the areas of biobanking, gene expression profiling, epigenetics, next generation sequencing and bioinformatics. The Centre is a national leader in the field of genomics. It is a

Photo: UD/Sandor Nagy

Standardized epigenetics workflow based on robotics

designated key national infrastructure, coordinator of the Hungarian Genomics Research Network, and leader of the National Genomics Technology Platform (http://www.genomika.net/gntp/home.html).

The main research infrastructure comprises:

- Next Generation Sequencing (Illumina HiScan) (Exome Sequencing, RNA-Seq, ChIP-Seq, RNA-Seq)
- Microarray Technologies (Affymetrix and Illumina Arrays, gene expression, genotyping and cytogenetics)
- Biobanking system, sample processing using robotics (Qiagen), lN_2 storage and -70°C storage for over 20,000 samples
- Pipetting robots for sample preparation and processing (Tecan, IPStar)
- UNIX server for data analysis and storage

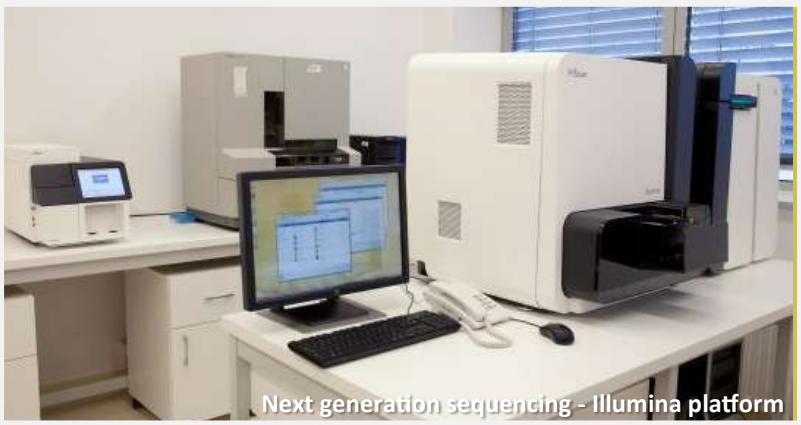
The Centre's long-standing technology and twinning partner in the MOLMEDREX project is the Gene Core at EMBL, Heidelberg. This partnership consists of regular bidirectional visits and transfer of know-how from GeneCore (EMBL). In addition, the Centre has been involved as an external partner (access user) in the European Sequencing and Genotyping Infrastructure Project (ESGI: http://www.esgi-infrastructure.eu/) and was invited to undertake continued collaboration on the project.

Photo: UD/Sandor Nagy

Laszlo Nagy

To date, the Centre has successfully completed projects for pharma and biotech companies such as Pfizer Global Research (EUR 340 K), Richter Hungary (Schizo Biobank EUR 2,900 K) and Csertex (EUR 1,000 K). Besides the pharma contacts, the Centre has provided services to dozens of Hungarian research groups, as well as groups from Poland, Romania, Lithuania, Taiwan, Greece, etc.

The Genomic Medicine and Bioinformatics Core Facility is located in the "In Vitro Diagnostic Building", together with the Laboratory of Medicine, the Molecular Diagnostic Laboratory and Microbiology Institutes. The Molecular Diagnostic Laboratory performs DNA analysis for monogenic disorders using sequencing, targeted mutation analysis, MLPA, trinucleotide repeat analysis, next-generation sequencing on the Roche Junior sequencer and clinical exome sequencing. It is one of the largest genetic centres in Hungary, performing 6,000 genetic tests annually including prenatal analysis. This close connection with the clinical units also ensures access to clinical samples.



Next generation sequencing - Illumina platform

Photo: UD/Sandor Nagy

ID Card:

Analytical platform type:
Genomics

Main techniques proposed:
Next Generation Sequencing (RNA-seq, DNA-seq, ChIP-seq) microarray (gene expression, SNP, CNV), clinical sample collection and processing (biobanking)

Delay to start:
None

Duration of experiment:
Technique-dependent

Training proposed:
See details on website

Address:
University of Debrecen, Medical and Health Science Center
Debrecen Clinical Genomic Center
4032 Debrecen, Hungary, Nagyerdei krt. 98. Pf. 6.

Access:
Genomics and biobanking core facility

Internet link:
http://genomics.med.unideb.hu

Contact:
Balint L. Balint:
lbalint@med.unideb.hu
+36-52-411-600 (ext. 65734)
Laszlo Nagy:
nagyl@med.unideb.hu
+36-52-411-717 (ext. 50015)

Related to:
MELODI, ALLIANCE, CARPEM

PRMT1 AND PRMT8 REGULATE RETINOIC ACID-DEPENDENT NEURONAL DIFFERENTIATION WITH IMPLICATIONS TO NEUROPATHOLOGY. Z. Simandi Z et al., Stem Cells. 2015 Mar;33(3):726-41.
THE ACTIVE ENHANCER NETWORK OPERATED BY LIGANDED RXR SUPPORTS ANGIOGENIC ACTIVITY IN MACROPHAGES. B. Daniel, et al. Genes Dev. 2014 Jul 15;28(14):1562-77.

MetaboHUB

French National Infrastructure for Metabolomics and Fluxomics

MetaboHUB is the French national facility in metabolomics and fluxomics selected in 2012 in the framework of the programme "Investissement d'Avenir" for a 7 years funding. It proposes advanced research services in metabolomics and fluxomics to provide opportunities for integration into other European infrastructures. The MetaboHUB infrastructure offers tools and services to academic research teams and industrial partners in the fields of nutrition and health, agriculture and biotechnology.

Photo: L. Lizet/INRA

Metabolomics relies on NMR and MS based technologies coupled with data mining tools

The objectives of the MetaboHUB infrastructure are fourfold: (i) to identify metabolites in human biofluids, as well as in plants, microorganisms and animal cell extracts, through the implementation, curation and maintainance of centralised, open spectral repositories for metabolite annotations, (ii) to provide high-throughput, quantitative technologies for biochemical phenotyping of large sets of samples and for systems biology, (iii) to develop large-scale flux profiling and subcellular fluxomics, and (iv) to attract a new generation of scientists and users by promoting metabolomics through education and training.

The MetaboHUB infrastructure will be developed in two interlinked phases: a construction phase and an operational phase. The construction phase (the first four years) is dedicated to harmonising, implementing and upgrading the four existing platforms with common metabolomics and fluxomics tools and methods, in order to build a world-class research centre and database in the field of metabolomics. To this end, the work plan is organised into 6 work packages (WP): Multi-site implementation of analytical chemistry for metabolite detection, quantification and identification (WP1); Fluxomics (WP2); Shared bioinformatics tools for data management and mining (WP3); Quality management (WP4); Coordination of services, governance and access to infrastructure (WP5), and Communication, training and technology transfer (WP6). The operational phase will be dedicated to handling the rise in the day-to-day activity of this national infrastructure which will operate as a world-class research centre in metabolomics, open to both academic and private partners. Activities and services will include providing spectral databases, centralised data repositories, standardised analytical methods for metabolomics, reagents for absolute quantification of metabolites, data mining tools and platforms capable of analysing large numbers of samples from large-scale projects.

Photo: S. Leblois/CEA

Christophe Junot

The French MetaboHUB project includes the four main French metabolomics platforms accredited with the national IBiSA quality standard. These are: the Bordeaux Metabolomics Platform (BMP, INRA and University of Bordeaux), the MetaboHUB-Paris Platform (Paris area - CEA and Pierre et Marie Curie University), the MetaToul Platform (Toulouse, Paul Sabatier University, INSA, INRA, CNRS and INSERM) and the Metabolism Exploration Platform (PFEM at Clermont-Ferrand, INRA and Blaise Pascal University). These four partners develop shared tools and expertise for basic and applied research projects.

Bordeaux, November 2013

Photo: INRA

ID Card:

Analytical platform type:
Nuclear Magnetic Resonance (NMR), Mass Spectrometry (MS), Statistical analyses and data mining, bioinformatics

Main techniques proposed:
- Targeted metabolite analyses
- Metabolite identification
- Non targeted metabolomics
- Non targeted lipidomics
- ^{13}C fluxomics
- Metabolic network analysis

Capacity:
Dependent on the application. MetaboHUB is able to handle cohorts of a few hundreds of samples for untargeted and targeted metabolomic studies.

Delay to start:
Dependent on the project.

Duration of experiment:
Dependent on the project.

Intercomparison exercise proposed:
Not available for the moment. Analyses of reference material such as NIST plasma are envisaged.

Training proposed:
Specific trainings on MS, NMR and data mining tools can be proposed by MetaboHUB platforms.

Address:
MetaboHUB, INRA center of Bordeaux
71 avenue Edouard Bourleaux
33140 Villenave d'Ornon, France

Access:
Projects can be submitted to the executive management board at any time.

Internet link:
www.metabohub.fr/

Contact:
contact@metabohub.fr

Related to:
MELODI, ALLIANCE, CARPEM, RENEB

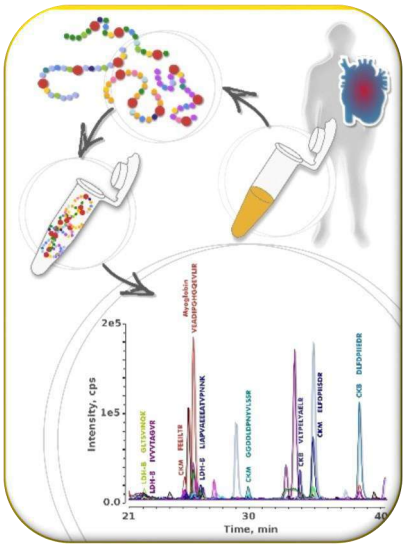
ANALYSIS OF THE HUMAN ADULT URINARY METABOLOME VARIATIONS WITH AGE, BODY MASS INDEX, AND GENDER BY IMPLEMENTING A COMPREHENSIVE WORKFLOW FOR UNIVARIATE AND OPLS STATISTICAL ANALYSES. Thévenot EA et al., J Proteome Res. 2015;14(8):3322-35.

COORDINATION OF STANDARDS IN METABOLOMICS (COSMOS): FACILITATING INTEGRATED METABOLOMICS DATA ACCESS. Salek RM et al., Metabolomics. 2015;11 (6):1587-1597.

ProFI

French National Infrastructure for Proteomics

Initially devoted to protein identification, proteomics today aims to provide in-depth characterization of proteomes for functional proteomics and clinical applications. This leads to new challenges, including how to quantitatively determine variations within the proteome as a result of various stimuli or different cellular states, how to detect low abundance proteins important for biology or health, how to identify protein complexes and study their dynamics, and how to analyse post-translational modifications that play a key role in protein function. Within this highly challenging context, France has created ProFI, the French national proteomics facility. ProFI was selected for funding in 2012 through the government program, "Investments for the Future", and awarded 7 years' funding (€15m). ProFI is a joint infrastructure which regroups the three best known French proteomics platforms: the Laboratory for Exploration of the Dynamics of Proteomes (CEA, INSERM and Grenoble Alps University), the Laboratory for Bioorganic Mass Spectrometry (CNRS and Strasbourg University) and the Proteomics and Mass Spectrometry of Biomolecules research group (CNRS and Toulouse Paul Sabatier University). The objectives of ProFI are two-fold: (1) to undertake R&D activities in quantitative proteomics and bioinformatics; (2) to make the services of ProFI widely available both to the scientific community and industrial sector by setting up a highly technical environment compatible with the production and processing of high quality data at very high throughput, within the context of ISO 9001 quality assurance certification.



Picture: V. Brun/CEA

Biomarkers detection and quantification using multiplex SRM Mass Spectrometry

Photo: E. Begouen/INSERM

Jérôme Garin

Using a proteomics approach to study biological or clinical problems requires access both to the protein repertory of the samples involved in the study and to the information on the abundance of these proteins and their post-translational modifications. To carry out quantitative proteomics analysis, ProFI platforms use two complementary strategies: large-scale proteomics studies without preconceptions ("shotgun" proteomics using Orbitrap mass spectrometers) and targeted quantitative studies on a few proteins of interest ("Selected Reaction Monitoring" multiplex analyses). Both the nature of the biological material and the type of questions asked will determine which of these strategies to use.

Increasing the power of computing and bioinformatics in the proteomics field is one of the main aims of the infrastructure. ProFI has developed a fully shared computing environment between Grenoble, Toulouse and Strasbourg, with the aim of facilitating data exchange and constituting a shared platform for the development of new software. ProFI has made this software environment available to the whole scientific community via its web site. Regular training sessions are offered to allow staff from academic and industrial proteomics platforms to familiarize themselves with this new environment. In this way, the resources allocated to ProFI benefit a wide community.

Proteomics lab in Grenoble

Photo: P. Latron/INSERM

ID Card:

Analytical platform type:
-Mass spectrometry
-Nano and micro liquid chromatography
-Bioinformatics

Main techniques proposed:
-Shotgun proteomics
-Targeted proteomics
-Identification of post translational modifications

Capacity:
Hundreds of samples a month

Delay to start:
Dependent on the project

Duration of experiment:
Dependent on the project. For small projects, results can be obtained in less than a month

Intercomparison exercise proposed:
Standard protein mixtures and ProFI MS data obtained on those samples are available

Training proposed:
Specific training courses are proposed (see website)

Address:
CEA Grenoble, Bat42,
17 rue des Martyrs,
38054 Grenoble Cedex, France

Access:
Projects can be submitted via the website

Internet link:
http://www.profiproteomics.fr

Contact:
Jérôme GARIN,
jerome.garin@cea.fr

Related to:
MELODI, ALLIANCE, CARPEM, NERIS

BENCHMARKING QUANTITATIVE LABEL-FREE LC–MS DATA PROCESSING WORKFLOWS USING A COMPLEX SPIKED PROTEOMIC STANDARD DATASET. Claire RAMUS et al. Journal of Proteomics (2015) 132: 51-62

MASS SPECTROMETRY-BASED WORKFLOW FOR ACCURATE QUANTIFICATION OF ESCHERICHIA COLI ENZYMES: HOW PROTEOMICS CAN PLAY A KEY ROLE IN METABOLIC ENGINEERING. Mathieu TRAUCHESSEC et al. Mol. Cell Proteomics (2014) 13, 954–9

Radiobiology and immunology platform (CTU-FBME)

Analytical platform for immunology and radiobiology

The immunological laboratory of CTU FBME, located in Prague, disposes of SPF animal facility for small rodents breeding and in vivo experiments, and of the tissue culture laboratory. Experimental animals are housed in different levels of barrier protection including GMO Class I and Class II (Optimice racks with IVC cages).

We can analyze radiation induced changes, i.e. the health condition of animals, the phenotype

Photo: CTU FBME

SPF animal facility

and functional analyses of immune cells; proliferation or cytotoxicity evaluated on established cell lines, biological samples and primary cultures employing Core facility for cytometry FACS (LSRII), confocal microscopy (Olympus FV-1000), ELISA reader (Tecan Infinite), and evaluation of gut microflora (MALDI, Bruker). We can offer various experimental mouse models for cancer, inflammation or autoimmunity as well as newly generated mouse strains with different sensitivity to radiation. We can also provide frozen sections of biological material for further analyses.

In cooperation with small enterprise (APIGENEX Ltd.) we are developing safe radioprotectants (nor-muramyl lipoglycopeptides derived from bacterial cell wall peptidoglycans) for restoration of hematopoiesis, and thus prevention of leukopenia evoked by radiotherapy. APIGENEX Ltd. company is focused to research and development for foreign companies (e.g. Novo Nordisk, Pfizer, GSK, Schering Plough) in the development of innovative pharmaceuticals.

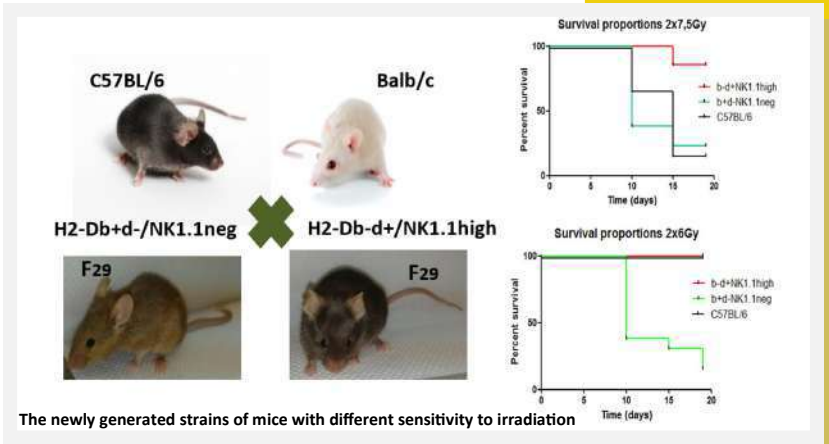
Photo: Fiser/CTU FBME

Anna Fiserova

The irradiation of mice will be performed using Microtron MT-25 (NPI ASCR v.v.i.) that will serve as a source of relativistic electrons (primary electron beam), secondary photon beams (bremsstrahlung), and neutrons from nuclear reactions. The accelerator applications involve radiation resistance testing studies in well controlled and monitored conditions, whole body or local irradiation of animals using collimator. Advanced neutron and photon activation analysis (PAA) will be applicable for determination of large number of elements in biological samples. Further we have access to ^{60}Co-irradiator for low doses irradiation.

Moreover, we have close collaboration with clinical departments employing radiodiagnostics or radiotherapy of patients (CT, X rays, ^{60}Co, ^{137}Cs, and proton therapy). Taken together, we can perform clinical, immulogical, and immunopharmacological examination of small rodents and humans. For obtained data processing we have specialist for bioinformatics.

We are open for collaboration with other infrastructures, preferentially focused to genomics, and CONCERT partners for common research.



The newly generated strains of mice with different sensitivity to irradiation

Picture: CTU FBME

ID Card:

Analytical platform type:
Imunology and radiobiology

Main techniques proposed:
Flow cytometry, confocal microscopy, immunological assays (ELISA, proliferation, cytokine synthesis), functional tests of cytotoxicity, antibody formation, microbiom

Delay to start:
None

Duration of experiment:
Design of experiment and assay-dependent

Training proposed:
Work with small rodents, isolation of biological material (organs, cells), cell culture, FACS analysis, ELISA

Address:
Immunological Laboratory of FBME CTU is located at National Institute of Public Health, Šrobárova 48, 10042 Prague 10, Czech Republic

Access:
National Institute of Public Health, Centre of Toxicology and Health Safety, NRL for Welfare of Laboratory Animals, Building 31

Internet link:
Under construction

Contact:
Anna Fiserova
anna.fiserova@fbmi.cvut.cz
+420 724127666

Related to:
MELODI, DoReMi, CONCERT

THE EVOLUTION OF RECTAL AND URINARY TOXICITY AND IMMUNE RESPONSE IN PROSTATE CANCER PATIENTS TREATED WITH TWO 3DCRT TECHNIQUES. Vránová J, et al. 2011. *Radiat Oncol*; 6:87.
COLLAGEN-INDUCED ARTHRITIS: SEVERITY AND IMMUNE RESPONSE ATTENUATION USING MULTIVALENT N-ACETYL GLUCOSAMINE. Richter J, et al. 2014. Clin. Exp. Immunol ;177:121-33.

France Génomique

French National Infrastructure for Genomics

Over the last 20 years, Life Sciences has hugely benefited from the spectacular developments in genome sequencing technologies which have rendered data acquisition faster, easier and cheaper. This has resulted in research discoveries and progress in all fields (biology, medicine, agronomy, biodiversity, etc.) that were beyond reach only a few years ago.

The sequencing of the human genome (3 billion bases) was officially completed in 2003 after more than 10 years of work. Today, the complete resequencing of an individual can be done within days, at a cost of only a few hundred euros. Given these developments, which are radically transforming our approach to the life sciences, it was deemed essential for French research to remain independent and competitive in the genomics field in order to retain ownership of its results. This led to the creation of France Génomique.

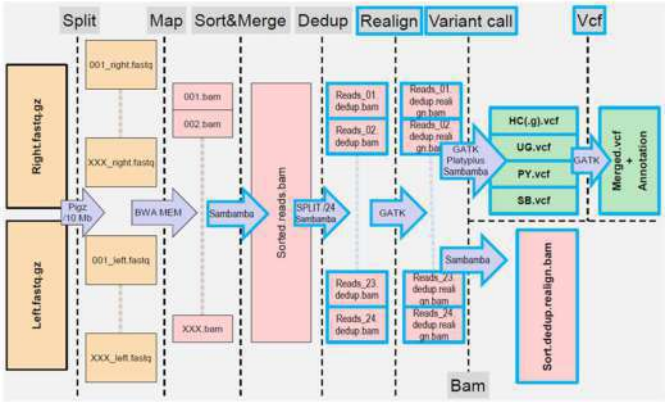


Photo: V. Meyer / IG

The VarScope 2.0 pipeline for whole-genome analysis

Created in 2011 through grant support from the French government programme "Investments for the Future", France Génomique (FG) is a national genomics infrastructure born out of the desire to maintain France at the highest level of competitiveness and performance, at the cutting edge of the field of genomics production and data analysis, thus reinforcing France's visibility in the international genomics landscape. The FG infrastructure brings together the majority of the French sequencing and bioinformatics platforms: CEA (coordinator), INRA, CNRS, Inserm, INRIA, Pasteur Institute, Curie Institute, ENS Paris and IGBMC Strasbourg.

The FG infrastructure offers: (1) an integrated structure and governance, providing greater visibility and higher functionality to the network in general and to each of its platforms, (2) access to a network facility of sequencing and/or bioinformatics platforms that have been operational for many years and have each developed complementary expertise, (3) the opportunity to undertake ambitious projects with strong visibility, through submission to the FG "large projects" call for proposals and selection on the basis of scientific excellence by external scientific review committees, (4) a critical mass to generate innovation collectively through continual survey, evaluation and development of new sequencing and bioinformatics methodologies and technologies, (5) access to competitively priced genomics services and associated bioinformatics with state-of-the-art, permanently upgraded data production, storage and processing systems and (6) access to a high performance computing centre and to data storage systems at the CEA/TGCC, equipped with large scalable capacity that is adapted to the exponential growth of the data being generated.

Photo: P Le Ber / CEA

Pierre Le Ber

An essential mission of FG is to disseminate its expertise, knowledge and know-how within the FG community but also more importantly to the wider French life sciences community: regular training sessions and workshops are organised by the FG platforms to allow students and researchers to improve their skills in this highly strategic field.

Genomics platform in Evry

Photo: F. Rhodes

ID Card:

Analytical platform type:
- Genomics
- Bioinformatics

Main techniques proposed:
- Next-Generation Sequencing (NGS): genome (de novo / resequencing), transcriptome, epigenome …
- 3rd generation sequencing (long reads, single molecule)
- Genotyping
- High-throughput data processing

Capacity:
100+ Terabases/month

Waiting time:
Depends on the project (sample availability)

Duration of experiment:
Depends on project size and complexity

Training proposed:
Various general or specific training courses (wet lab techniques and/or data processing and analysis)

Address:
CEA/Institut de Génomique, 2 rue Gaston Crémieux, 91057 Evry Cedex, France

Access:
Although international projects are accepted, the project PI has to be from a French laboratory. Projects can be submitted continuously via the Web portal or directly to the platforms. Very large projects can be submitted via the "large scale projects" call for proposals (every 18 months).

Internet link:
www.france-genomique.org

Contact:
Pierre Le Ber
contact@france-genomique.org

Related to:
MELODI, ALLIANCE, CARPEM

EUKARYOTIC PLANKTON DIVERSITY IN THE SUNLIT OCEAN. De Vargas C, et al., Science (2015) 348 (6237): 1261605.

CHARACTERISATION OF MUTATIONS OF THE PHOSPHOINOSITIDE-3-KINASE REGULATORY SUBUNIT, PIK3R2, IN PERISYLVIAN POLYMICROGYRIA: A NEXT-GENERATION SEQUENCING STUDY. Mirzaa GM et al., Lancet Neurol (2015) 14 (12): 1182-1195.

The SCK•CEN Genomics platform

Exploring the genomic changes induced by radiation

Since the discovery of the DNA (Deoxyribonucleic acid) double helix in the 1950's, several techniques were developed to study this mysterious molecule and to illustrate its role in the cell and in life. The human genome consists of (44 + XX/XY) chromosomes, made out of supercoiled and compacted stretches of DNA. These DNA sequences contain coding and non-coding areas. The coding genes are regulated at different levels to fine-tune their expression into effector proteins.

Photo: R. Benotmane/SCK•CEN

Quality control of RNA samples

Since the 1950's, genetics has been the discipline that studies the structure and function of single genes while genomics, which emerged in the new millennium after the full sequencing of the human genome, addresses the functioning of all genes and their interactions. Thus genomics seeks to understand the influence of genes on the development and growth of organisms, as well as in cancer and other diseases. The term "omics" has come to refer generally to the study of large, comprehensive biological data sets.

The Genomics Platform at SCK•CEN was established in 2003, based on microarray technology to study global gene expression. Initially, the platform was equipped with a DNA spotting robot (MicroGrid, UK) producing homemade spotted glass slide arrays. The genomics platform was later upgraded through acquisition of Affymetrix technology (Santa Clara, USA), for which precast arrays are commercially available. The Affymetrix GeneChip arrays cover quite a large variety of sequenced and well-annotated genomes from different species for transcriptomics (gene expression and alternative splicing). In addition, other applications can now also be performed, including microRNA quantification and chromatin immunoprecipitation (ChIP) for epigenetic studies, as well as genotyping (SNP, CNV) and tiling. This upgrade has provided a wider genomic vision and more in-depth knowledge with which to uncover the hidden layers of the genome in different biological systems.

Photo: R. Benotmane/SCK•CEN

Rafi Benotmane

When considering an experiment with replicates and different conditions and time points, translating these data into a biological hypothesis becomes challenging. Data analysis is therefore a critical step in genome-wide analysis involving statistics and bioinformatics. Advanced statistical methods help to reduce the complexity of the data to reveal highly significant changes between two conditions (treated *vs.* untreated). On the other hand, bioinformatics is a new discipline that emerged in parallel with genomic studies, and which provides biological meaning to the numerical variations. It involves data mining to identify gene interactions and regulatory networks leading to pathway inference. The Genomics Platform at the Radiobiology Unit of the Belgian Nuclear Research Centre has been involved in several EU-funded projects for more than a decade. The long-term expertise gathered has led to high quality, reproducible data, and to the development of dedicated bioinformatics pipelines for optimal data analysis.

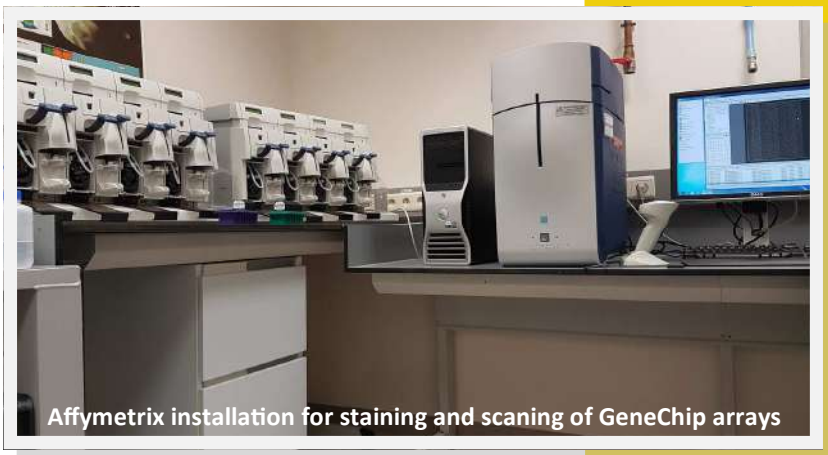


Photo: R. Benotmane/SCK•CEN

Affymetrix installation for staining and scaning of GeneChip arrays

ID Card:

Analytical platform type:
Microarray platform for transcriptomic, microRNA, LncRNA, methylation and tiling analyses

Main techniques proposed:
Gene expression quantification using microarray technology

Capacity:
50 to 100 array per week

Delay to start:
at least a month in front

Intercomparison exercise options:
Several quality controls are run by Affymetrix (the array provider) and many other controls are assessed in house

Training options:
possible

Access:
Selection (no more than 4 persons at once)

Internet link:
www.sckcen.be

Contact:
Rafi Benotmane
abenotma@sckcen.be

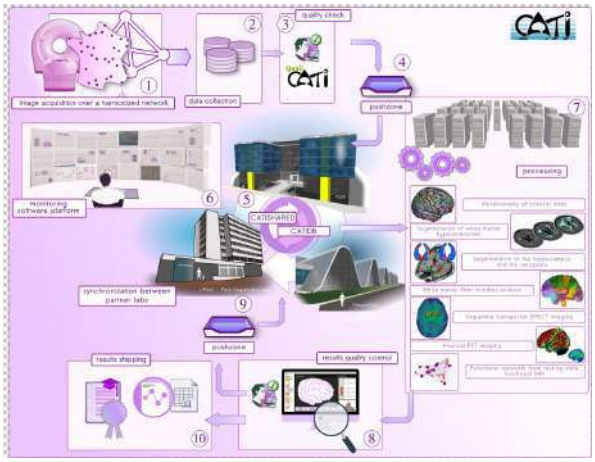
Related to:
MELODI and many other EU radiation research projects

IDENTIFICATION OF NOVEL RADIATION INDUCED p53 DEPENDENT TRANSCRIPTS EXTENSIVELY REGULATED DURING MOUSE BRAIN DEVELOPMENT
Quintens R, Verreet T, Janssen A, Neefs M, Leysen L, Michaux A, Verslegers M, Samari N, Pani G, Verheyde J, Baatout S, Benotmane MA. . Biol Open. 2015 Feb 13;4(3):331-44
TRANSCRIPTOMIC AND PROTEOMIC ANALYSIS OF MOUSE RADIATION INDUCED ACUTE MYELOID LEUKAEMIA (AML)
Badie C, Blachowicz A, Barjaktarovic Z, Finnon R, Michaux A, Sarioglu H, Brown N, Manning G, Benotmane MA, Tapio S, Polanska J, Bouffler SD. .Oncotarget. 2016 May 26. doi: 10.18632/oncotarget.9626. PubMed PMID: 27250028

CATI

A large infrastructure for the neuroimaging of cohorts

CATI was born from the collaborative efforts of a consortium of neuroimaging research laboratories with complementary expertise: NeuroSpin (the French high-field MR imaging centre of the CEA) and four teams located at the Pitié-Salpêtrière Hospital: ARAMIS and CENIR (the neuroimaging analysis research team and the neuroimaging platform of the Brain and Spine Institute), the Institute for Memory and Alzheimer's disease (IM2A) and LIB (an Inserm/UPMC unit focusing on functional imaging research). These teams, who had been collaborating for several years, were granted EUR 9 million in 2011 by the French Alzheimer's disease initiative to create CATI, a national platform which aims to support multicentre neuroimaging studies. Services offered by CATI include the standardisation of MRI and PET/SPECT data acquisitions, the transfer of data to a centralised database, monitoring, quality control and image analysis. Initially designed to address the specific needs of Alzheimer's disease, the platform is now open to academic research projects and therapeutic trials targeting any neuropsychiatric disorder. The CATI infrastructure stretches across France, collecting additional know-how from all the French groups and organisations involved in neuroimaging, in order to offer the best tools for scientific projects.



Picture:G. Operto, Neurospin, CEA

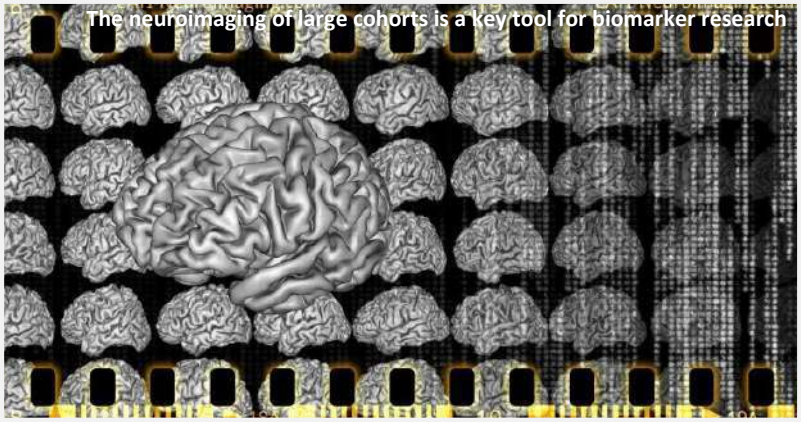
CATI is a large infrastructure which seamlessly integrates a large network of imaging facilities and a very rich portfolio of image analysis pipelines.

In agreement with the French societies of Neuroradiology, Radiology and Nuclear Medicine, CATI currently harmonises imaging acquisitions across more than 40 French sites and this network can be expanded according to demand. In addition, 20 European sites will join the network starting from 2015. Although data accessibility policy is specifically chosen by the PI of each study, CATI aims to facilitate data sharing across studies and to promote this as much as possible. The platform is currently responsible for the imaging protocols of more than 30 large French multicentre studies, including several therapeutic trials and the Memento cohort of the French Alzheimer initiative. Three European projects have also been using the platform since 2015. In the context of Memento, which images 2300 subjects with isolated memory complaints or mild cognitive impairment, CATI has close links with the French network of memory centres.

Photo: private source

Jean-François Mangin

CATI embeds a team of MRI and PET physicists, engineers and researchers in charge of standardising acquisitions and monitoring MRI and PET scanners within the CATI network. The Keosys Company deals with the secure transfer of imaging data to the CATI central database through a web service that is accessible from imaging acquisition sites. A team of research assistants performs quality control of the incoming raw datasets. For data analysis, CATI provides broad expertise in image processing and statistical meta-analysis tools, which are operated by engineers and technicians. CATI can provide assistance at any stage of a study and can perform additional imaging harmonisation or dedicated algorithmic R&D for new facilities upon request.



The neuroimaging of large cohorts is a key tool for biomarker research

Photo: JF Mangin, Neurospin, CEA

ID Card:

Analytical platform type:
Neuroimaging

Main techniques proposed:
MRI (T1, T2, T2*, resting state, fMRI, ASL, diffusion, Melanine), PET (FDG, amyloid), SPECT (DATSCAN)

Capacity:
Up to several thousand patients per project

Waiting time:
A few months if using existing network facilities; 6 months if new facilities have to be harmonized

Duration of experiment:
Usually several years

Address:
Neurospin, CEA, 91191 Gif sur Yvette, France

Access:
Academic research projects and therapeutic trials – service fees apply

Internet link:
http://CATI-neuroimaging.com

Contact:
jfmangin@cea.fr

Related to:
MELODI, EURAMED

CATI: A LARGE DISTRIBUTED INFRASTRUCTURE FOR THE NEUROIMAGING OF COHORTS. Grégory Operto et al., Neuroinformatics, 2016.
OPTIMIZATION OF BRAIN PET IMAGING FOR A MULTICENTRE TRIAL: THE FRENCH CATI EXPERIENCE. Marie-Odile Habert et al., EJNMMI Phys, 2016.

HZDR-Radioanalytical Laboratories

Valuable tools for the spectroscopy of radioactive samples

The reliable protection of people and the environment from the hazards caused by radionuclides requires a detailed knowledge of their migration and transfer behaviour in the environment. Hence, a molecular understanding of the chemical reactions of the contaminants in the geosphere and biosphere is indispensable. Comprehensive molecular information can be obtained by a multi-method approach and – in case of radioactive samples – where the spectroscopic techniques are located in an appropriate infrastructure.

Photo, O. Killig/HZDR

Rossendorf Beamline (ROBL) at the ESRF in Grenoble

The Institute of Resource Ecology of the Helmholtz-Zentrum Dresden-Rossendorf (HZDR-IRE) provides experimental and technical equipment for officially licensed work with radionuclides up to a limit of 5×10^9 Bq. The institute uses a broad range of analytical methods, all of which are performed in modern radiochemical laboratories with state-of-the-art equipment. Additionally, some of the laboratories are S1-classified, allowing the handling of genetically modified organisms in a radiation protection area.

The radioanalytical laboratories at HZDR focus mainly on sophisticated spectroscopic techniques in combination with conventional radioanalytical methods. The main research infrastructure comprises:

- Laser spectroscopy: Time-resolved laser fluorescence spectroscopy (TRLFS) with tunable nanosecond and femtosecond laser systems (excitation wavelength: 220 –1,800 nm, detection range: 300–1,500 nm, maximum time resolution in the picosecond range); Cryo-TRLFS (sample cooling: ≥ 4 K), Confocal Laser Scanning Microscopy (excitation wavelength: 350–650 nm); Laser-Induced Photoacoustic Spectroscopy (LPAS)
- NMR spectroscopy – liquid/solid state (400/600 MHz)
- Vibrational spectroscopy – FT-IR (in situ ATR technique, mid/far-IR), FT-Raman
- UV-vis-NIR spectroscopy (conventional and long pass flow cell, maximum path length: 2,500 mm)
- X-ray diffraction for single crystals and powder samples
- Standard and inert gas glove boxes suitable for work with radionuclides, in particular alpha-emitting nuclides, as well as with Schlenk lines for chemical synthesis
- Classical radioanalytical methods (α-, β-, γ-spectroscopy) and elemental analysis (ICP-MS, AAS, IC)
- Methods for characterisation of colloids
- (Micro-)Calorimetry, Isothermal titration calorimetry
- State-of-the-art microbiological and biochemical methods including conventional separation techniques (HPLC, CE)

Photo: private

H. Foerstendorf (left)

A.C. Scheinost (right)

Furthermore, the IRE runs the Rossendorf Beamline (ROBL) at the European Synchrotron Radiation Facility (ESRF) in Grenoble (France). ROBL is the first research facility at a public synchrotron to be dedicated to radionuclide work. The brilliant X-ray flux of the ESRF is used to perform:

- X-ray absorption spectroscopy: EXAFS and (high-resolution) XANES
- X-ray emission spectroscopy (XES) and resonant inelastic X-ray scattering (RIXS)
- Powder and single crystal diffraction
- Surface diffraction (CTR) and resonant anomalous X-ray reflectivity (RAXR)

Radiochemical experiments in glovebox

Photo: O. Killig/HZDR

ID Card:

Purpose:

Spectroscopic and radioanalytical studies of actinides and fission products in biological and geological environmentally relevant systems

Access:

HZDR Radioanalytical Laboratory: Applications are available under surveillance of experienced staff scientists of HZDR. Technical equipment is provided for radionuclide activities up to $5x10^9$ Bq.

ROBL: Beamtime is offered upon scientific merit of the submitted proposal, which is evaluated by review panels of HZDR or ESRF.

Housed on:

Helmholtz-Zentrum Dresden-Rossendorf, Institute of Resource Ecology, Dresden, Germany

Rossendorf Beamline (ROBL) at ESRF, Grenoble, France

Address:

Helmholtz-Zentrum Dresden Rossendorf, Institute of Resource Ecology
Bautzner Landstraße 400
01328 Dresden, Germany

Internet link:

www.hzdr.de/FWO

Contact:

HZDR: Harald Foerstendorf
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+49 351 260 3664

ROBL: Andreas C. Scheinost
scheinost@esrf.fr;
+33 476 88 2462

Related to: ALLIANCE

Günther, A., Raff, J., Merroun, M. L., Roßberg, A., Kothe, E., Bernhard, G., 2014. Interaction of U(VI) with Schizophyllum commune studied by microscopic and spectroscopic methods. Biometals 27, 775-785.

Kvashnina, K. O., Scheinost, A. C., 2016. A Johann-type X-ray emission spectrometer at the Rossendorf beamline. Journal of Synchrotron Radiation 23, 836-841.

Advanced Technologies Network (ATeN) Center

A large research infrastructures for advanced biotechnologies

The Advanced Technologies Network (ATeN) Center, directed by Prof. Maurizio Leone, is a centre of excellence of the University of Palermo (Sicily) which provides cutting-edge research, development and service activities for technological transfer to the public and private sectors. The Center consists of three macro-areas (Cellular and Molecular Biotechnology, In vivo Analysis, Biocompatible Materials and Systems) in which scientists with different backgrounds (e.g. biotechnology, biology, chemistry, physics, engineering, medicine, bioinformatics) work together to produce the technological know-how needed to achieve highly competitive scientific results. Due to its sophisticated structure and equipment (25 laboratories housed in 2500 m² with approx. 100 instrumentation facilities), ATeN is among the few centres in the world able to provide a production chain ranging from the synthesis of materials to in vivo tests.

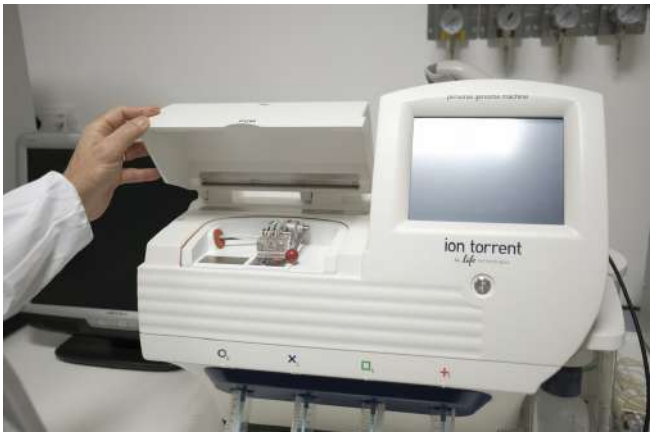

Photo: Agenzia CMC Studio

Ion PGM™ System for Next-Generation Sequencing

The macro-area of Cellular and Molecular Biotechnologies deals with the production and propagation of stem cells and primary cell cultures, large-scale analysis of DNA, RNA and proteins. The laboratory of genomics and proteomics provides molecular analysis at advanced technological level. The laboratory works in different advanced sectors through the analysis of large families of genes, proteins, enzymes and metabolites. These sectors include: development and technological improvement of drugs including proteins, vaccines and monoclonal antibodies, which are largely obtained from targeted application of genetic modification techniques and personalised medicine; characterisation, through the analysis of genetic and protein profiles and of molecular pathways, experimental cellular and animal models of disease; identification of specific response markers of cells and tissues to exposure to ionising radiation and/or molecules with biological activity and potential pharmacological activity; validation of products for molecular diagnostics; development of services for advanced diagnostics and for drug discovery; development of bioinformatics products (acquisition, storage, distribution, analysis and interpretation of the data mainly for molecular biology, genetics and biochemistry).

Photo: Agenzia CMC Studio

Maurizio Marrale

The In Vivo Analysis macro-area, with two enclosures containing small animals and zebrafish, carries out analyses on the effects of ionising radiation and the testing of drugs, biomaterials, biomarkers and radiopharmaceuticals, as well as functional analyses for the production of primary cultures from transgenic organisms and 3D imaging.

Multiple bioimaging techniques are available to explore the biological structure and function of molecules in live cells and in tissues by means of 3D and 4D measurements.

Confocal and multiphoton microscopy, atomic force microscopy, together with advanced spectroscopy techniques (e.g. Raman, EPR, NMR) can be applied to analyse biological, physical and chemical phenomena in order to characterise the material properties.

Photo: Agenzia CMC Studio

Laboratory of Pulsed Electron Paramagnetic Resonance

CHAB mediterranean center for human health advanced biotechnologies

ID Card:

Analytical platform type:
Biological dosimetry and physical retrospective dosimetry, exposure markers, proteomics, genome sequencing, transcriptome sequencing, transcriptomics, metabolomics, exosomes, small molecules

Main techniques proposed:
Panel of cytogenetic assays, gene expression assay, protein markers, EPR/TL dosimetry, gamma spectrometry, microscopy

Capacity:
20 measurements per week

Waiting time:
None

Duration of experiment:
Dependent on experiment and assay

Address:
Viale delle Scienze Edificio 18 I-91128 Palermo (Italy)

Access:
Free

Internet link:
http://www.chab.center/home-en

Contact:
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maurizio.marrale@unipa.it
+39 091 23899073

Related to:
MELODI, EURADOS, RENEB

MONITORING FEW MOLECULAR BINDING EVENTS IN SCALABLE CONFINED AQUEOUS COMPARTMENTS BY RASTER IMAGE CORRELATION SPECTROSCOPY (CADRICS). G. Arrabito, F. Cavaleri, V. Montalbano, V. Vetri, M. Leone, B. Pignataro, Lab on a Chip, 16 (2016), 4666-4676

PRELIMINARY APPLICATION OF THERMOLUMINESCENCE AND SINGLE ALIQUOT REGENERATION METHOD FOR DOSE RECONSTRUCTION IN SODA LIME GLASS. M. Marrale, A. Longo, A. Bartolotta, M. D'oca, and M. Brai, Nuclear Instruments and Methods in Physics Research Section B: Beam Interactions with Materials and Atoms, 297 (2013), 58-63

BfS IN VIVO MEASUREMENT FACILITIES

Whole and partial body counting and Quality Assurance

Incorporated gamma-emitting radionuclides can be determined in humans using gamma ray spectrometry to measure the radiation that leaves the body. Since this test is performed on living persons, this type of measurement is called in vivo method. Radionuclides that are (more or less) distributed throughout the body, for example Cs-137 and K-40, are determined by whole-body counters. Nuclides that tend to concentrate in specific organs, especially nuclides such as iodine isotopes in the thyroid or inhaled small plutonium dioxide particles in the lung, are determined by partial body counters.

Photo: O Meisenberg/BfS

Available phantoms including a brick phantom and skull, neck and torso phantoms

The counting efficiency of an in vivo counter is normally determined using a calibration phantom. This phantom is similar in size and shape and has similar attenuation characteristics to those of the body of the real person to be screened, and also contains radioactive sources. For whole-body counting, brick phantoms are often used. In vivo counting is a routine method used for monitoring employees who have been potentially exposed to internal radiation. Special applications include, for example, follow-up studies of exceptional incorporation cases or the monitoring of special population groups.

The BfS operates two incorporation monitoring laboratories at its sites in Berlin/Karlshorst and Oberschleißheim/ Neuherberg (near Munich). Each facility permanently operates a stretcher type whole-body counter (WBC), performing about 500 to 700 measurements per year each. The persons monitored come from research and nuclear power reactors, radionuclide production companies and nuclear waste final repositories. In addition, a reference group of unexposed persons from the population is also monitored. Standard counting time is 20 minutes. The WBC in Neuherberg is equipped with four stationary HPGe detectors, and the WBC in Berlin is equipped with two detectors which are used in a scanning mode. In addition, each facility keeps a partial-body counter in readiness. These counters are kept 'ready-to-use' for emergency preparedness and special measurements.

Photo: U Gerstmann/BfS

Dr Udo Gerstmann

In accordance with the German Radiation Protection Ordinance, the BfS offers in vivo intercomparison analysis for the incorporation monitoring laboratories in Germany. These laboratories have to identify and quantify radionuclides in phantoms. Currently, brick, thyroid, skull and torso phantoms are available. For emergency preparedness, the BfS has begun to produce more radioactive sources with a broader variety of radionuclides. In 2017, the production of special components for phantoms using 3D printing was launched.

Photo: O Meisenberg, S Helbig/BfS

The three main in-vivo measurement facilities: whole- and partial-body counter in Neuherberg and scanning whole-body counter in Berlin

Bundesamt für Strahlenschutz

ID Card:

Analytical platform type:
Internal Dosimetry

Main techniques proposed:
Whole body counting and organ counting (e.g. thyroid, lung, liver, bone…)

Source:
Large range of radionuclides with gamma ray emission (Cs-134/137, I-131, Ba-133, Am-241, Eu-152…)

Intercomparison exercise proposed:
Annual in vivo intercomparison offered

Address:
Bundesamt für Strahlenschutz,
Ingolstädter Landstrasse 1,
85764 Neuherberg, Germany

Bundesamt für Strahlenschutz,
Köpenicker Allee 120-130,
10318 Berlin, Germany

Internet link:
http://www.bfs.de/EN/topics/ion/service/incorporation/incorporation_node.html

Contact:
Udo Gerstmann
ugertsmann@bfs.de
+49 89 18333-2430

Related to:
MELODI, EURADOS

A PUZZLING CASE OF CONTAMINATION WITH Am-241, A. Giussani, P. Nogueira, N. El Faramawy, W. Buchholz, U. C. Gerstmann, M. Hartmann, O. Meisenberg, D. Noßke und W. Rühm, J. Radiol. Prot., 36, (2016), 391-404

RETROSPECTIVE ESTIMATION OF EXPOSURE TO SHORT LIVED Rn-222 PROGENY BY MEASUREMENT OF Pb-210 IN THE SKULL, R. Scheler, K. Dettmann, J. Brose, Radiat. Prot. Dosim., 79, (1998), 129-132

ECORITME

ECOtoxicology of Ionising Radiation and Trace Metals

The **ECORITME** platform is specialized in the field of "**ECO**toxicology of **M**etals and **I**onising **R**adiation". It combines analytical tools, modeling developments and advanced statistics. **ECORITME** offers all the required skills for performing and improving predictive ecological risk assessment for chronic exposure to low doses of ionising radiation. It is also designed for studying complex toxicant exposure (from the external media to the molecular targets including dynamic transformations, biokinetics, and interactions in mixtures) through the development of advanced and innovative in vitro models and analytical methods.

Photo: C. Adam-Guillermin/IRSN

Dr Christelle Adam

ECORITME allows the controlled exposure of experimental units from micro- to large-scales, to external gamma irradiation and/or internal contamination with alpha- or beta-radionuclides alone or in combination with metals or organic compounds. It offers the possibility to use various biological models such as unicellular algae, plants, invertebrates (e.g. the waterflea *Daphnia magna*, the nematode Caenorhabditis elegans) or fish (e.g. the zebrafish *Danio rerio*, including fish cells such as ZF4). A phytotron and growth-chambers complement the platform for the research on plants and experiments with contaminated soils. **ECORITME** includes 1200 m^2 of laboratory space (plus 1600 m^2 of associated technical zones and radioactive waste/effluent treatment areas). The laboratories are authorized to host experiments using a wide spectrum of radionuclides (82 radioisotopes including ^{3}H, ^{14}C, ^{137}Cs, isotopes of Pu, Am, U…) in compliance with the current regulations.

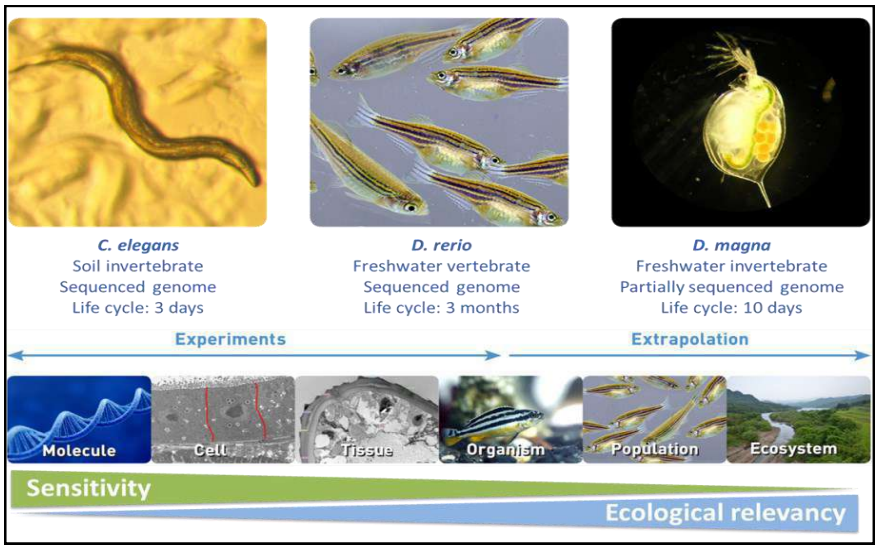

Photo: IRSN

Main biological models used in the ECORITME platform and various levels of biological organisation at which effects are measured, combining sensitive and ecologically relevant responses

ECORITME offers supports as follows: (i) Modeling skills and tools for : speciation and bioavailability (Biotic Ligand Model), dosimetry (**EDEN** model), dose-effects, mixture exposure and effects, individual to population effect extrapolation, biostatistics for field data, bioinformatics and system biology, ecological risk; (ii) An integrated technical platform (analytical equipment, organism husbandry, and exposure laboratories). This platform allows experiments to be performed under controlled conditions for various biological models with or without the use of radioactive tracers and/or ionising radiation, and/or any chemical elements such as metals; (iii) A unique tool with **MICADO'Lab** equipment (see Exposure platform page 2). An innovative field of application of this equipment is to that is allows perfect control of the delivered energy. Thus enabling manipulation of the red-ox status of any biological object.

Photo: IRSN

Devices used to detect low concentrations of metals and their chemical forms (top), and Transmission Electronic Microscope used for histological and microlocalisation analyses (bottom)

ID Card:

Analytical platform type:

Use of biochemistry, immunochemistry, microscopy, transcriptomics, proteomics to characterize biological responses:

- DNA damages
- Oxidizing stress,
- Neurotoxicity,
- Immunotoxicity…

Quantification of trace and major elements, radionuclides and their speciation in environmental and biological matrices

Main techniques proposed:

- Coulter-Counters,
- Flow cytometer,
- Epifluorescence microscope,
- Apotome,
- Transmission Electronic Microscope with EDAX probe for elementary analysis,
- Confocal microscope (ZOOM plateau),
- Ultramicrotome,
- Cryomicrotome,
- PCR, Rt-qPCR,
- 2D-electrophoresis,
- Incubators for cell culture or organisms maintenance,
- ICP-MS, ICP-OES,
- HPLC,
- Gamma spectrometry,
- Liquid scintillation,
- SLRT…

Access:

Analytical tools available for joint research collaborations only

Internet link:

http://www.irsn.fr/EN/Research/Research-organisation/Research-units/environment-unit/LECO/

Contact:

christelle.adam-guillermin@irsn.fr

Related to: ALLIANCE, MELODI

Alonzo F., Hertel-Aas T., Réal A., Lance E., Garcia-Sanchez L., Bradshaw C., Vives i Batlle J., Oughton D. H., Garnier-Laplace J. (2016). Population modelling to compare chronic external gamma radiotoxicity between individual and population endpoints in four taxonomic groups. Journal of Environmental Radioactivity 152: 46-59

Armant O., Kewin Gombeau, Sophia Murat El Houdigui, Magali Floriani, Virginie Camilleri, Isabelle Cavalie, and Christelle Adam-Guillermin (2017). Zebrafish exposure to environmentally relevant concentration of depleted uranium impairs progeny development at the molecular and histological levels. PLoS One 12(5): e0177932.

Consolidated Radioisotope Facility (CORiF)

Environmental radioactivity and X-ray fluorescence analysis

Environmental radiation, often termed "background radiation", has been present everywhere in our surroundings since the formation of the earth and originates from naturally occurring or man-made radiation sources. High concentrations of both natural and synthetic radioisotopes have been detected in soils, in the sea and in river slit, especially in close proximity to contaminated sites. Thus, environmental monitoring of radioactivity levels is essential for radiation protection.

Photo: Plymouth University

Pr William Blake Dr Alex Taylor

Photo: Plymouth University

EG&G Ortec Well (GWL-170-15-S) HPGe Gamma spectrometry system and PANalytical Axios Max WD XRF system

The ISO 9001-2008-certified Plymouth University Consolidated Radio-isotope Facility (CoRiF) is a dedicated laboratory for the manipulation and analysis of natural and enhanced radioactive materials. CoRiF has a licence to hold and dispose of alpha, beta and gamma radionuclides, which are used to support a wide range of research or consultancy services to external academic, public and private sector clients. Data quality is assured through regular participation in external proficiency tests.

Measurement of gamma-emitting radioisotopes is undertaken using three EG&G Ortec gamma spectrometry systems, all of which are suitable for low-level ^{210}Pb determination. The detector geometries allow a wide range of sample types to be analysed: 1 x planar (GEM), 1 x coaxial (GMX) and 1 x well detector (GWL), with typical in-house applications including contaminated land assessment, sediment-contaminant source fingerprinting and sediment and peat geochronology.

X-ray fluorescence spectrometry provides complementary major and minor element geochemical analyses using a wavelength dispersive X-ray fluorescence (WD XRF) spectrometer (PANalytical Axios Max) with facility to prepare and run soil and sediment samples as fused beads (using PANalytical Eagon 2 fusion system), pressed pellets and loose powders.

Alpha and beta emitting radioisotopes are analysed using two Beckman Coulter automated Liquid Scintillation 6500 Counters with facility to prepare and analyse environmental samples and solids and liquids relating to high activity radio-tracer studies (which can be undertaken in-house as required).

Services offered by CoRiF include investigations of contaminated land and aquatic ecosystems, geochemical tracer studies using radiochemicals, investigation of eco- and geno-toxic effects of radionuclides, sediment and peat geochronology, sediment and contaminant source apportionment (fingerprinting), soil erosion and sediment budget evaluation, and complementary research involving non-radiometric analyses.

In relation to environmental forensics, CoRiF is currently involved in the EU Horizon 2020 funded project IMIXSED, in which researchers are applying fallout radionuclide and wavelength dispersive X-ray fluorescence tools to track eroded sediment through a degraded river basin in East Africa.

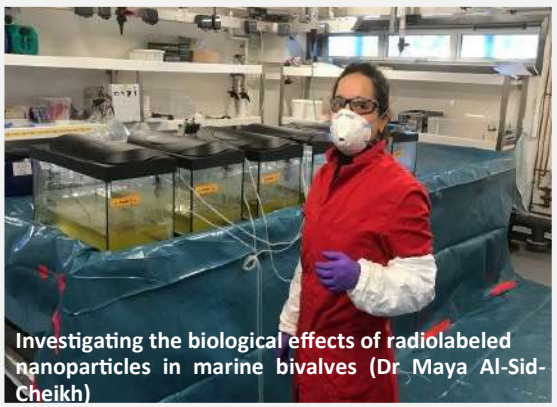

Photo: Plymouth University

Investigating the biological effects of radiolabeled nanoparticles in marine bivalves (Dr Maya Al-Sid-Cheikh)

SUCCEED WITH PLYMOUTH UNIVERSITY

ID Card:

Analytical platform type:
Dedicated laboratory for the manipulation and analysis of natural and enhanced radioactive materials and applications of radioactivity in material analysis

Main techniques proposed:
Gamma spectrometry, Wavelength dispersive X-ray fluorescence (WD XRF), Liquid scintillation counting, Laser particle sizing, Inductively coupled plasma mass spectrometry & optical emission spectrometry (ICP MS & ICP OES)

Capacity:
Hundreds samples per month

Delay to start:
Depends on technique-please enquire

Duration of experiment:
Dependent on the techniques applied

Address:
Consolidated Radio-isotope Facility, Plymouth University, Plymouth University, Plymouth PL4 8AA, United Kingdom

Access:
The analytical facility is accessible to joint research collaborators and scientists of the public or private sector after selection.

Internet link:
https://www.plymouth.ac.uk/schools/school-of-geography-earth-and-environmental-sciences/consolidated-radio-isotope-facility

Contact:
Professor Will Blake:
william.blake@plymouth.ac.uk
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+44 1752 585969

Related to:
ALLIANCE

Bioaccessibility of U, Th and Pb in solid wastes and soils from an abandoned uranium mine, Foulkes M., Millward G., Henderson S., Blake W. (2017), J Environ Radioact, 173:85–96

Mobilization of Technetium from Reduced Sediments under Seawater Inundation and Intrusion Scenarios, Eagling J., Worsfold P.J., Blake W., Keith-Roach M.J. (2012), Environ Sci Technol 46:11798–11803

Centre for Omic Sciences (COS)

A unit for metabolomics, proteomics, genomics and transcriptomics

EURECAT is the major Technology Centre of Catalonia, Spain. EURECAT provides the industrial and business sectors with differential technology and advanced expertise; it offers solutions to their innovation needs and boosts their competitiveness in a fast-paced environment. The range of services offered by the centre is primarily focused on key strategic sectors of the Catalan economy: Food, Health, Energy and Resources, Industrial Systems, Design-based Industries, Industries related to Sustainable Mobility and the Cultural Industries.

Photo: EURECAT

Dr Nuria Canela

Non targeted metabolomics unit

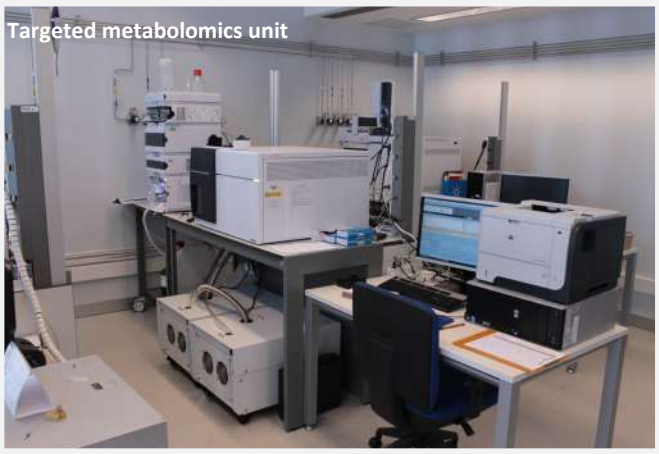
Photo: COS

The centre serves over a thousand businesses, participates in over 200 national and international R&D&I high level strategic projects, holds 73 international patents and owns 9 technology-based companies. It comprises eight centres in Catalonia and one in Latin America (Brazil).

EURECAT has 3 main technology divisions: digital, industrial and biotechnologies. Its biotechnologies division manages the Centre for Omic Sciences (COS). COS is a joint Unit comprising the University Rovira i Virgili (URV) and EURECAT. COS hosts a large, well-equipped analytical facility for high throughput omic studies which focuses on metabolomics but also includes proteomics, transcriptomics, genomics, imaging and research facilities for organisms and cells, based on an initial equipment investment of more than 10 million euros.

EURECAT-COS is a singular facility, unique in Spain, due to its equipment set-up and its approach to biochemical problems. COS provides support services to both companies and academia. These services are underpinned by state-of-the-art technologies, comprising a microarray platform, a next generation sequencing platform, 9 high-end mass spectrometers including MS-Imaging systems, 2 NMR instruments, an SPR protein interaction analysis system and various robots and high throughput technologies, as well as computing infrastructures and other analytical tools. Moreover, the biotechnologies infrastructure has acquired new facilities to develop in silico, in vitro and in vivo research studies and human intervention studies to validate the efficacy and non-toxicity of new bioactive compounds and extracts.

The vision of COS is to become a hub facility for omic sciences based on a metabolomics approach, and to become a European reference centre for omic science research and services applied to the field of food and nutrition. The facility is unique because its approach to biological problems begins with metabolomics in order to generate new hypotheses for molecular mechanisms that can then be validated using the other omics (proteomics, transcriptomics and interactomics) and in vivo models. Additionally, the integrated information from the different omics provides a novel means of investigating biomarkers and understanding biological processes related to the consumption of healthy foods.



Targeted metabolomics unit

Photo: COS

COS Centre for Omic Sciences

ID Card:

Analytical platform type:
Scientific operator in the world of omic technologies fully equipped with cutting-edge metabolomics, proteomics, transcriptomic, and genomic tools. We offer scientific advice and support from experimental design prior to omic assessment complete with facilities with in-vitro and in-vivo models and a Human Nutrition Unit available to our clients.

Main techniques proposed:
DNA sequencing & fragment analysis (Sagner DNA Sequencing), Next generation sequencing (Ion Torrent PGM), Microarray analysis, Automated real-time PCR analysis, Targeted proteomic profiling (SRM assays), MALDI tissue imaging, Luminex bead array and others.

Capacity:
Hundreds samples per month

Address:
Centre for Omic Sciences
Avda. Universitat no 1
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Related to:
MELODI, ALLIANCE

Hydroxytyrosol and its complex forms (secoiridoids) modulate aorta and heart proteome in healthy rats: Potential cardio-protective effects, Catalán Ú., Rubió L., López de Las Hazas M. C., Herrero P., Nadal P., Canela N., Pedret A., Motilva M. J., Solà R. (2016), Mol Nutr Food Res 60(10), 2114-2129
Analytical methods in sphingolipidomics: Quantitative and profiling approaches in food analysis, Canela N., Herrero P., Mariné S., Nadal P., Ras M. R., Rodríguez M. Á., Arola L. (2016), J Chromatogr A 1428, 16-38

The iGE3 Genomics Platform

Cutting-edge Genomic Technologies to support research

The iGE3 (**i**nstitute of **G**enetics and **G**enomics of **G**eneva) genomics platform of the University of Geneva provides access to a wide array of state of the art technologies ranging from high-throughput genomics to very targeted analysis. Established in 2002 as the "Frontiers-in-Genetics" genomics platform of the Swiss National Centers of Competence in Research (NCCR), its services were initially restricted to the research groups of the NCCR consortium. It rapidly became a reference laboratory in the genomics field and access was extended to all laboratories, including the private sector. In 2012, the platform joined the newly created interdisciplinary iGE3 consortium.

Photo: Brice Petit/Brice Petit Photography

Dr Mylène Docquier

years ago) the nCounter analysis system (nanoString Technologies); iGE3 is the third site in Europe to offer this technology. The nCounter allows digital counting of individual molecules using molecular barcodes with very high dynamic range, reproducibility and specificity, and with no enzymatic reaction.

Photo: Brice Petit / Brice Petit Photography

Next Generation Sequencing using Illumina HiSeq 4000

The main activity of the iGE3 genomics facility is Next Generation Sequencing (NGS). Illumina HiSeq 4000, 2500 and MiSeq sequencers allow sequencing of whole genomes, exomes and transcriptomes as well as more targeted sequencing (of enriched regions). The laboratory has also implemented a single-cell NGS approach using the Fluidigm C1 prep station, which enables high parallel (800 single cells at a time) transcriptome analysis or targeted DNA sequencing. The applications of this high throughput single-cell technology include cell classification (Telley L. et al. 2016, data illustrated in the Figure below), tissue heterogeneity studies and CRISPR-Cas9 screening.

The platform is also equipped with Illumina and Affymetrix microarray technologies for Single Nucleotide Polymorphism (SNP) analysis (Genome-wide association studies and cytogenetics), DNA copy number profiling, DNA methylation status and expression profiling, including miRNA.

For projects requiring expression analysis of smaller gene sets, or specific metabolic pathway genes, the platform offers (since 8

For targeted expression analysis, the facility proposes the widely used real-time PCR technology. In response to growing interest in digital PCR, the platform has also implemented the QuantStudio3D digital PCR system (Thermo Fisher Scientific) for rare variant detection, absolute quantification, biomarker analysis and viral or bacterial detection.

All data generated by the platform can be further analysed by the bioinformatics team. Particular attention is given to understanding the projects and needs of each individual user in order to optimise the analysis pipeline, and new tools are developed as needed. For users who want to analyse their data themselves, guidelines and informatics tools are available.

The provision of proximity services is another of the strengths of the iGE3 platform. Every project and experimental design is directly discussed with the users. Additionally, in order to adapt platform capacity to match demand, continuous efforts are made to optimise protocols and develop and implement new technologies.

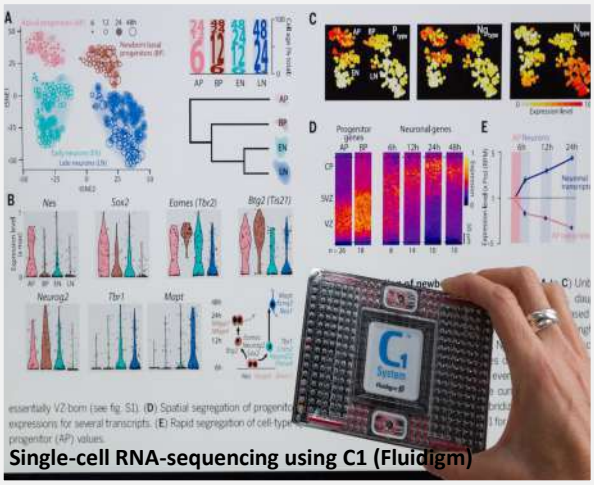

Photo: Brice Petit / Brice Petit Photography

Single-cell RNA-sequencing using C1 (Fluidigm)

ID Card:

Analytical platform type:
Genomics

Main techniques proposed:
-Next Generation Sequencing (RNA, DNA, exome-seq…)
-Microarrays (SNP, CNV, methylation, expression)
-nCounter (nanoString)
-q- and d-PCR

Capacity:
Several hundred NGS libraries and arrays per week

Delay to start:
None

Duration of experiment:
Depends on the request (maximum 1.5 months including the analysis)

Intercomparison exercise proposed:
Illumina Phix quality
Affymetrix spikes

Training proposed:
On request

Address:
University of Geneva
CMU 6 - laboratory A06.2707
Rue Michel Servet, 1
CH-1211 Geneva 4
Switzerland

Access:
Free

Internet link:
https://ige3.genomics.unige.ch

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+41 22 379 50 31

Related to:
MELODI

Metagenomics analysis of red blood cell and fresh-frozen plasma units, Lau P., Cordey S., Brito F., Tirefort D., Petty T. J., Turin L., Guichebaron A., Docquier M. et al. (2017), Transfusion, 57 (7) , 1787-1800
Sequential transcriptional waves direct the differentiation of newborn neurons in the mouse neocortex, Telley L., Govindan S., Prados J., Stevant I., Nef S., Dermitzakis E., Dayer A., Jabaudon D. (2016), Science, 351 (6280), 1443-1446

VIB Proteomics Core

State-of-the-art proteomics service facility in Belgium

The VIB Proteomics Core (PRC), located at the VIB-UGent Center for Medical Biotechnology in Ghent, Belgium, provides contemporary mass spectrometry (MS)-based proteomics services to academic and non-academic users. The PRC started in 2005 as a spin-off service unit of the proteomics laboratory of Prof. Dr Kris Gevaert. Today, it has evolved from a research-oriented facility to a service-oriented platform and has become a reference centre for proteome research in Belgium and beyond.

Photo: VIB

Dr Francis Impens

In addition to these routine applications, customised services are provided including the identification of proteolytic processing sites, the development of targeted proteomics assays (e.g. by SRM/PRM) and mass determination of intact proteins. Samples can be isotopically labelled (e.g. by SILAC or TMT labelling) for optimal quantitation accuracy or sample multiplexing, in addition to the standard label-free workflows.

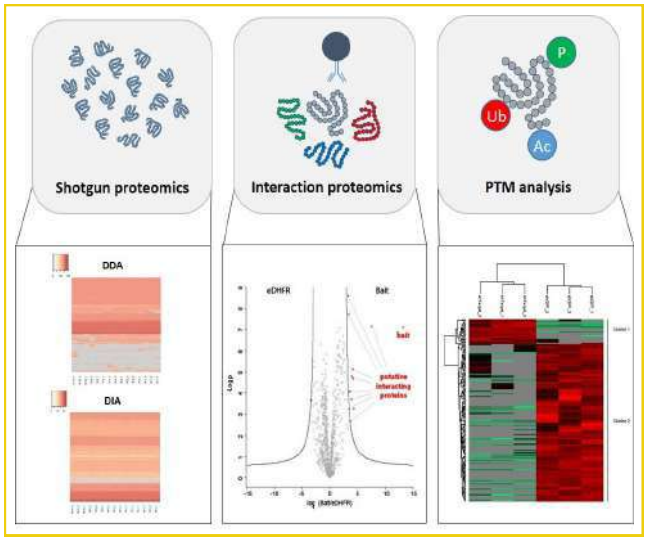

Photo: Teresa Maia/VIB

Main analysis types at the VIB Proteomics Core

Significant advances in the development of LC-MS/MS instrumentation and data analysis software over recent years have set the stage for clinical proteomics. In order to keep pace with these developments and to take an active role in biomarker discovery, the PRC recently implemented a novel analysis pipeline based on Data Independent Acquisition (DIA). This pipeline ensures improved detectability and quantitation of proteins, and is ideally suited for high-throughput screening of patient samples.

Six state-of-the-art orbitrap mass spectrometers coupled with nano-LC chromatography systems are available to perform LC-MS/MS analyses at the PRC. These instruments run 24/7 and can process several hundred samples/month. In addition, the PRC has a triple quadrupole mass spectrometer for targeted proteomics, as well as a MALDI-TOF MS/MS instrument.

The PRC is operated by an experienced, international team composed of MS engineers, biochemists and data analysts, and applies constant monitoring procedures including daily MS quality control and continuous benchmarking of implemented protocols. Thus the facility is able to deliver high quality services at all times, encompassing every step of a proteomics experiment. Users are guided from sample collection to data analysis, and receive assistance from the PRC team to formulate biological conclusions that are easy to interpret for the non-proteomics expert.

As part of its routine services portfolio, the PRC offers three main types of proteomics applications in modern life sciences: 1) Shotgun analysis which generates comprehensive proteomic profiles that reveal differences in protein levels associated with a particular cellular state or experimental condition; 2) Affinity purification mass spectrometry (AP-MS) experiments which allow the characterisation of protein complexes and the discovery of novel protein interactions; 3) Mapping of common protein post-translational modifications such as acetylation, phosphorylation and ubiquitination, for which the PRC has extensive experience.

Orbitrap LC-MS/MS systems

Photo: Delphi Van Haver/VIB

ID Card:

Analytical platform type:
Proteomics

Main techniques proposed:
- Mass spectrometry-based proteomics (LC-MS/MS)
- Shotgun proteomics by DDA & DIA
- Analysis of common post-translational modifications (e.g. phosphorylation, ubiquitination, acetylation)
- Characterisation of protein complexes and interaction partners (e.g. AP-MS, Bio-ID)
- Targeted proteomics by SRM & PRM

Capacity:
Hundreds of samples per month

Delay to start:
Dependent on the scale of the project, typically 1 to 2 weeks

Duration of experiment:
Dependent on the scale of the project, typically 5 to 6 weeks

Intercomparison exercise proposed:
Daily quality control *via* QCloud (https://qcloud.crg.eu)

Training proposed:
On request

Address:
VIB Proteomics Core
Albert Baertsoenkaai 3 - 9000 Gent, Belgium

Access:
For academic and non-academic users

Internet link:
https://corefacilities.vib.be/pec

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Related to:
VIB, Core for Life, EU-LIFE, UGent-CRIG

Quality control in mass spectrometry-based proteomics, Bittremieux W., Tabb D. L., Impens F., Staes A., Timmerman E., Martens L., Laukens K. (2017), Mass Spectrometry Reviews, doi:10.1002/mas.21544
Phase separation of C9orf72 dipeptide repeats perturbs stress granule dynamics, Boeynaems S., Bogaert E., Kovacs D., Konijnenberg A., Timmerman E., Volkov A., Guharoy M., De Decker M., Jaspers T., Ryan V. H., Janke A. M., Baatsen P., Vercruysse T., Kolaitis R. M. et al. (2017), Mol Cell, 65 (6), 1044-1055

MARS beamline at Synchrotron SOLEIL

X-ray analyses of radioactive samples

Photo: SOLEIL

D. Menut P.L. Solari M. Hunault

Radioactive samples for environmental and nuclear energy research require to be characterised at the atomic or molecular level. This can be done using X-ray synchrotron techniques such as those of the MARS beamline at the French national synchrotron SOLEIL facility.

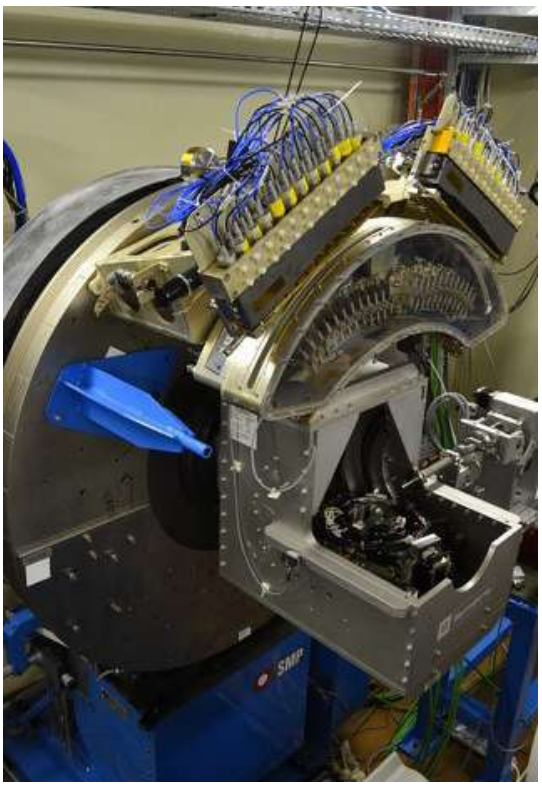

Photo: SOLEIL

Figure 1: High resolution diffractometer.

MARS is a hard X-ray beamline, dedicated exclusively to the study of radioactive samples. Since September 2013, analyses can now be performed on radioactive samples at ambient temperature and pressure, with activities up to 20,000 times the French exemption limit (thus for actinides, activities of up to 200 MBq). Yet, the ultimate aim is to extend this exemption limit to a wider range of experiments, and to activities of up to 18.5 GBq, in order to perform experiments on highly radioactive samples such as spent nuclear fuel. It is also possible to conduct analyses at high and low temperature, at high pressure, and on chemical reactions, but only for activities currently below the exemption limit.

The beamline, which was built through a partnership with the CEA, is located on a bending magnet source of SOLEIL's storage ring, and operates in the energy range of 3.5 keV to 35 keV. Currently, six different types of experiments are available on two different experimental end-stations. The first end-station is a special diffractometer dedicated to High-Resolution X-Ray Diffraction (HRXRD) analyses (Figure 1). It was specially designed in collaboration with CEA, to analyse irradiated nuclear fuel with specific shielding.

The second end-station is more versatile (Figure 2), and is mainly dedicated to X-ray Absorption Spectroscopy (XAS) both in standard mode and in High-Resolution mode (HRXAS) using a crystal analyser spectrometer. X-ray absorption spectroscopy technique allows determining the electronic state and local structure of specific elements in samples to be studied irrespective of their physical form. It can thus be used, for example, to study actinide or radionuclide elements in solutions down to sub-millimolar concentrations. The same end-station can also be used to perform Transmission X-Ray Diffraction (TXRD). Small and Wide Angle X-ray Scattering (S/WAXS) analyses have also been recently developped.

Finally, the use of a specific refocusing setup allows performing X-ray microbeam analyses, e.g. X-ray fluorescence imaging (XFR), microXAS and microXRD, with a beamsize of 15 by 15 micrometers.

The main research studies conducted at SOLEIL are in the areas of structural materials of interest for nuclear power plants, actinide oxides in relation to nuclear fuels, actinide and other radionuclide solutions of interest in nuclear fuel reprocessing, different types of glass of interest for nuclear waste storage, and radionuclide-containing samples of biological or environmental interest.

Photo: Photo: V. Moncorgé

Figure 2: Dr M. Hunault and Dr P.L. Solari positioning a sample-holder on the XAS experimental end-station.

Characterization of radioactive materials using the MARS beamline at the synchrotron SOLEIL, Sitaud B., Solari P. L., Schlutig S., Llorens I., Hermange H. (2012), J Nucl Mater, 425 (1-3), 238-243

X-ray absorption spectroscopy investigations on radioactive matter using MARS beamline at SOLEIL synchrotron, Llorens I., Solari P.L., Sitaud B., Bes R., Cammelli S., Hermange H., Othmane G., Safi S., Moisy P., Wahu S., Bresson C., Schlegel M. L. et al. (2014), Radiochim Acta, 102 (11), 957-972

ID Card:

Analytical platform type:
Synchrotron beamline dedicated to the analysis of radioactive samples with X-rays.

Main techniques proposed:
X-ray Absorption Spectroscopy, X-ray Diffraction, X-ray Fluorescence.

Capacity:
Total activity of the samples should be lower than 20,000 times the exemption limit.

Delay to start:
Experiments are usually scheduled in advance for the semester that follows the selection process (see Access).

Duration of experiment:
Usually experiments last one week (5 working days).

Address:
Synchrotron Soleil
L'Orme des Merisiers
Saint Aubin - BP 48
F-91192 Gif-sur-Yvette Cedex
France

Access:
Call for proposal opens twice a year.

Internet link:
https://www.synchrotron-soleil.fr/en/beamlines/mars

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Related to:
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CIEMAT Whole Body Counter (WBC)

In vivo monitoring of gamma emitters retained in the body

CIEMAT WBC can perform *in vivo* monitoring of radionuclides emitting X-ray and/or gamma radiation, which are incorporated into the human body through inhalation, ingestion, injection or a wound. The activity (Bq) detected in the exposed person is interpreted in terms of committed effective dose E(50) (mSv) in an internal dosimetry frame. The CIEMAT Internal Dosimetry Service is ISO/IEC 17025 accredited (since 2012), validating its technical competence for *in vivo* and *in vitro* monitoring and dose assessment for internal exposures.

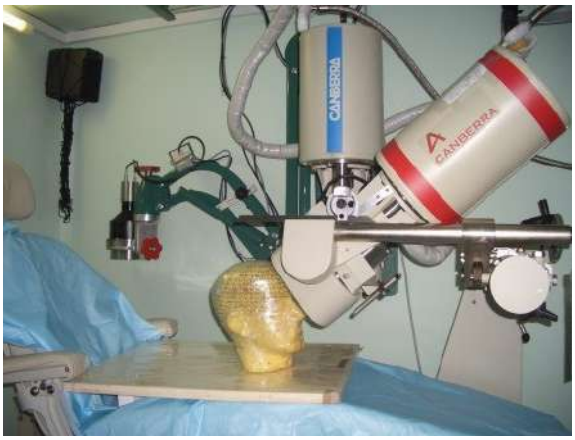

Photo: CIEMAT WBC

Measurement of Am-241 in a USTUR skull phantom with CIEMAT LE Ge detector. EURADOS Intercomparison

Workers at risk of intake of radioactive materials in the workplace, or members of the public affected by a radiological or nuclear accident, can be included in individual monitoring programmes for the identification and quantification of internal contaminants, at the CIEMAT WBC laboratory. Fission and activation products distributed in total body are evaluated using a high efficiency FASTSCAN Counter (2 NaI(Tl) detectors) in routine programmes (count time of 5 minutes).

The CIEMAT WBC facility also includes a shielded room constructed in 1967 with steel walls lined with Pb, Cd, and Cu to perform low-background measurements. One large NaI(Tl) detector and 4 LE Ge detectors of high resolution are used inside the shielded room for different applications.

Photo: CIEMAT

B. Pérez M. A. López J. F. Navarro

The equipment is calibrated by measuring appropriate calibration phantoms simulating the internal contamination of total body or of specific organs (LLNL torso phantom, BOMAB total body phantom, Spitz knee phantom, Cohen skull phantom, ANSI thyroid phantom, IRSN wound phantom) depending on the biokinetics of the radionuclides of interest. Determination of enriched uranium in the lungs is performed with the LE Ge system in the case of incidents where workers have been internally exposed through inhalation during fabrication of nuclear fuel elements for the Spanish Nuclear Power Plants. Thyroid monitoring for radioiodine (I-125, I-131) can be performed with all the detection systems mentioned above.

CIEMAT WBC techniques are validated on a regular basis through participation in intercomparison exercises, mainly organised by IRSN (France) and EURADOS (European Radiation Dosimetry Group). Other methods have been developed as a result of research projects or international actions such as for the determination of contaminants in wounds or of Am-241 in bone (skull and knee), with important feedback from Monte Carlo simulations on the measurement geometries using voxel phantoms, e.g. for improving counting efficiency.

The remaining research activities of CIEMAT WBC are focused on developing capabilities for monitoring populations of different gender and age involved in a radiological or nuclear event (e.g. CAThyMARA Project, EC OPERRA). In these cases, calibration efficiencies are provided in scale for groups of populations according to the ICRP89 publication, to improve the reliability of the results of activity and the dose assessment of the radionuclides detected.

Photo: CIEMAT

CIEMAT Whole Body laboratory. Shielded room and FASTSCAN Counter.

ID Card:

Analytical platform type:
Internal Dosimetry

Main techniques proposed:
In vivo monitoring of exposed persons:
- Radioiodine in thyroid
- Actinides in lungs
- Gamma emitters in total body
- Gamma emitters in a wound by gamma spectrometry

Capacity:
Max. 600 persons per year

Duration of experiment:
Max. 45 min

Intercomparison exercise proposed:
IRSN intercomparisons
EURADOS intercomparisons

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Related to:
EURADOS

Methodology at CIEMAT Whole Body Counter for *in vivo* monitoring of radioiodine in the thyroid of exposed population in case of nuclear emergency, Pérez B., Navarro J. F., López M. A. (2018), Radiat Prot Dosimetry, doi: 10.1093/rpd/ncy045

Efficiency study of a LEGe detector system for the assessment of ^{241}Am in skull at CIEMAT Whole Body Counter, Pérez B., Navarro J. F., López M. A., Nogueira P. (2016), Radiat Prot Dosimetry, 170 (1-4), 231-236, doi: 10.1093/rpd/ncv404

DSA Environmental Laboratory

Norwegian Radiation and Nuclear Safety Authority Environmental Lab

The Laboratory for Environmental Radioactivity at the Norwegian Radiation and Nuclear Safety Authority (DSA) is a non-commercial laboratory, with a staff of 7. The laboratory has facilities suitable for radiochemical work with low activity environmental samples, and a low background gamma spectrometry laboratory. DSA also has two laboratories in Northern Norway with gamma spectrometry and emergency preparedness capacity.

In total, approximately 1200 samples are analysed annually by gamma spectrometry while a few hundred are analysed by alpha spectrometry or liquid scintillation counting following radiochemical separation (for example, Pu, Am, U, Po, Sr and Tc). Since the early 2000s, methods for radiochemical separation of NORM radionuclides (uranium, thorium, Ra-226) have also been established. Sample measurements with gamma spectrometry have been accredited according to the standard EN ISO 17025 since 2000, and the laboratory is also active in the IAEA ALMERA and RANET networks. As part of its quality assurance programme, the laboratory participates annually in several intercomparison exercises organised by IAEA, NPL, Nordic Nuclear Safety Research (NKS) and other bodies.

Most of the current samples come from national monitoring programmes and radio ecological research, but the laboratory also acts as a support for the Section for Emergency Preparedness and Response and the Section for Nuclear Safety and Pollution Control. Sample types analysed include sediment, soil, seawater and seaweed as well as various types of biota. Air filters from several air sampling stations in Norway are also prepared and analysed in the laboratory.

In recent years, the laboratory has also employed field measurements, such as *in situ* gamma spectrometry and characterisation of nuclear materials using high-resolution gamma spectrometry.

Photo: T. Kolstad/DSA

T. B. Aleksandersen
B. Lind & T. T. Gäfvert

Moreover, since 2004, the laboratory has operated a mobile laboratory for emergency purposes, with facilities for sample preparation, gamma spectrometry, simple radiochemistry procedures, LSC and whole body counting.

Major detector equipment available at the DSA laboratories includes:

- 11 HPGe-detectors in a low-background counting room
- 4 Portable HPGe-detectors for *in situ* measurements
- 8 NaI-detectors
- 2 Canberra Alpha Analyst spectrometers with a total of 24 PIPS-detectors for alpha spectrometry of U-isotopes, Th-isotopes, Pu-238, Pu-239+240, Am-241 and Po-210
- 2 Risø beta counters for Tc-99
- 1 Quantulus LSC for Ra-226, Sr-90/Y-90 and H-3
- 1 Canberra iSOLO300L for total alpha/beta.

Photo: B. Johnsen/DSA

Collage of our staff and equipment

ID Card:

Analytical platform type:
Radioactivity analysis

Main techniques:
Radiochemistry
Alpha spectrometry
Beta counting
Gamma spectrometry

Capacity:
Ranges from a few hundred to several thousand samples per year, depending on the type of analysis required

Intercomparison exercise:
IAEA ALMERA
NKS
NPL

Address:
Norwegian Radiation and Nuclear Safety Authority
Grini Næringspark 13
1361 Østerås
Norway

Access:
Non-commercial laboratory

Internet link:
www.dsa.no

Contact:
Merete Hannevik
Merete.hannevik@dsa.no

Related to:
ALLIANCE

InSiCal - A tool for calculating calibration factors and activity concentrations in *in situ* gamma spectrometry, Mauring A., Vidmar T., Gäfvert T., Drefvelin J., Fazio A. (2018), J Environ Radioact, 188, 58-66
Radon tightness of different sample sealing methods for gamma spectrometric measurements of ^{226}Ra, Mauring A., Gäfvert T. (2013), Appl Radiat Isot, 81, 92-95

Radiochemical and Radioactive Analysis Laboratory (INTE-UPC)

Environmental radioactivity analyses

The Environmental Radiation Analysis Laboratory (LARA) of the Institute of Energy Technologies (INTE) at the Polytechnic University of Catalonia (UPC) has been working in the field of low-level measurements of radioactivity in environmental samples since 1982. The LARA has been accredited by the Spanish National Accreditation Service (ENAC) under ISO 17025 since June 2002 and is registered in the Directorate General of Food Quality and Agro-Food Industries of the Department of Agriculture, Food and Rural Action of the Government of Catalonia.

Water treatment plant

Photo: INTE-UPC

The laboratory equipment at LARA includes 3 germanium detectors, 1 low-background liquid scintillation system, 4 silicon detectors, 6 solid scintillation ZnS detectors and 20 low-background proportional detectors. Natural and artificial alpha, beta and gamma emitters are analysed in more than 600 samples every year.

LARA offers an environmental radioactivity control service which enables the measurement of radionuclides in water, air, food, soil, sediments, milk, vegetation and animal tissue samples for customers interested in checking compliance with national legislation or requirements to export products. Moreover, the laboratory develops new radiochemical methodologies for the determination of low levels of radioactivity and contributes to radiological studies in water treatment plants.

LARA collaborates with organisations such as the Spanish Nuclear Safety Council (CSN), as one of the sparse network laboratories, and with the Health Protection Department of the Government of Catalonia, the Service for Coordination of Radioactive Activities (SCAR) of the Industrial Safety Department of the Government of Catalonia where it contributes, for example, to the Environmental Radiological Survey Plan of the Ascó and Vandellós nuclear power stations. The history and extensive experience of this laboratory has generated long-term collaboration agreements (over 30 years) with renowned institutions and companies such as the CSN and Aigües de Barcelona.

Photo: INTE-UPC

Dr Antonia Camacho

The main research activities of the laboratory are linked to the INTE´s Dosimetry, Medical Radiation and Environmental Physics group (DRMA). LARA takes part in investigations on the physical, chemical and meteorological processes responsible for spatial and temporal variations of radionuclide concentrations in the environment, as well as the improvement of radioactivity measurement methods. Some relevant projects include "Study of the problems in determining the gross alpha activity index in drinking water", "Environmental radiological impact of products related to water treatment, “Risk evaluation due to radioactive components" and the FRESA programme for the study of the impact of dust-laden African and stratospheric air masses in the Iberian Peninsula. Further information about research projects, doctoral theses and publications can be found on the INTE website (www.upc.edu/inte).

Counting room

Photo: INTE-UPC

Removal of radionuclides in drinking water by membrane treatment using ultrafiltration, reverse osmosis and electrodialysis reversal, Montaña M., Camacho A., Serrano I., Devesa R., Matia L., Vallés I. (2013), J Environ Radioact, 125, 86-92

Medically-derived radionuclides levels in seven heterogeneous urban wastewater treatment plants: The role of operating conditions and catchment area, Mulas D., Garbayo A., Devesa R., Duch M. A. (2019), Sci Total Environ, 663, 818-829

UNIVERSITAT POLITÈCNICA DE CATALUNYA BARCELONATECH

ID Card:

Analytical platform type:
Laboratory equipped with 3 germanium detectors, 1 low-background liquid scintillation detector, 4 silicon detectors, 6 solid scintillation ZnS detectors and 20 proportional detectors. The laboratory carries out low-level radioactivity determination of all types of environmental samples, including water, soil, air particles, milk, vegetation and animal tissue samples for public administrations as well as private companies.

Main techniques proposed:
Gross alpha and beta activities using proportional counters.

Natural and artificial gamma emitter activity by gamma spectrometry.

Activity of ^{238}U, ^{234}U, ^{235}U, ^{210}Po, ^{230}Th, ^{232}Th, by alpha spectrometry.

Capacity:
More than 500 assays per year.

Address:
Technical University of Catalonia (UPC)
Institute of Energy Technologies (INTE)
Environmental Radiation Analysis Laboratory (LARA)
Avda. Diagonal,
647. 08028 Barcelona, Spain

Access:
Joint research collaborations, service contracts

Internet link:
https://inte.upc.edu/en/services/laboratories/radiochemical?set_language=en

Contact:
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Related to:
ALLIANCE

CIEMAT *In Vitro* Internal Dosimetry Laboratories

Spanish reference laboratories for *in vitro* monitoring

The CIEMAT *In Vitro* Internal Dosimetry Laboratories consist of the Bioelimination Laboratory and the Mass Spectrometry Laboratory, both reference facilities in Spain for *in vitro* bioassay of internal emitters. They can monitor alpha and beta emitters in urine and faecal samples that have been incorporated into the body through inhalation, ingestion, injection, or a wound. The activity measured in the excreta (mBq/d or Bq/L) is interpreted in terms of the committed effective dose E(50) mSv. Approximately 140 internally exposed workers are monitored per year at CIEMAT using *in vitro* bioassay techniques.

Photo: CIEMAT (Madrid, Spain)

Inductively Coupled Plasma Sector Field Mass Spectrometer (ICP-SF-MS). Element XR (Thermo Finnigan).

The Bioelimination Laboratory (BIO) has been accredited according to the ISO 17025 Standard since 2012 (ENAC 144/LE1836). Alpha emitters (Pu, Am, Th, Cm, U) in urine and faecal samples are analysed by alpha spectrometry after radiochemical separation. The uranium content in urine can also be determined by mass measurement by kinetic phosphorescence analysis (KPA). Beta emitters in urine samples can be measured by liquid scintillation counting (LSC) by direct measurement (H-3, C-14, S-35) or by performing radiochemical separation procedures (Sr-90).

The most recent research activities of the CIEMAT Bioelimination Laboratory have been focused on developing rapid methods for the determination of Pu, Am, Th, Cm, U, and/or Sr-90 in an emergency scenario. Future challenges of the laboratory are the implementation of the gamma spectrometry technique for the determination of gamma emitters in urine samples and the analysis of alpha emitters in nasal swabs.

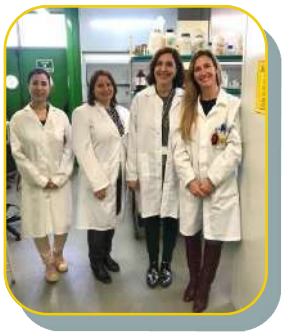

Photo: CIEMAT (Madrid, Spain)

P. Lorente, C. Hernández, I. Sierra, A. I. Barrado

The Mass Spectrometry Laboratory (ICP) consists of a measurement laboratory, containing a high-resolution mass spectrometer with an inductive coupling plasma source, magnetic sector, and double focus (XR Element, Thermo Finnigan), and a laboratory for the preparation and treatment of samples, in which measurements of various radioisotopes are carried out.

The ICP Laboratory is in the process of being accredited and is currently authorized by the CSN (Nuclear Safety Council) for the determination of activity in urine samples. Due to the high sensitivity of the XR Element, U and Th measurements are performed directly after dilution. Pu-239 analysis requires radiochemical separation and a special nebulization chamber to increase the sensitivity of the analysis (ARIDUS II).

The CIEMAT *In Vitro* Internal Dosimetry Laboratories participate in national and international R&D programs (e.g. ICP lab in the DARK MATTER Project), European initiatives (e.g. BIO Lab in EURADOS Emergency Intercomparisons), technological and/or knowledge transfers, and education & training activities. In addition, the Bioelimination Laboratory has coordinated and prepared several proficiency tests for public and private Spanish laboratories. The CIEMAT *In Vitro* Internal Dosimetry Laboratories also participated in the elaboration of the document "Technical Recommendations for Monitoring Individuals for Occupational Intake of Radionuclides" - EC Radiation Protection Report 188 (2018).

Photo: CIEMAT (Madrid, Spain)

CIEMAT Bioelimination Laboratory facilities and equipment

Rapid procedure for actinides and ^{90}Sr analysis in emergency urine spot samples applied in the GHSI-RNWG emergency intercomparison exercise, Hernández C., Sierra I. (2019), Appl Radiat Isotopes, 144, 19-23

Retrospective method validation and uncertainty estimation for actinides determination in excreta by alpha spectrometry, Hernández C., Sierra I. (2016), Radiat Prot Dosim, 170 (1-4), 39-44

ID Card:

Analytical platform type:
Internal dosimetry *in vitro* laboratories

Main techniques proposed:
In vitro monitoring of alpha and beta emitters in urine and faecal samples using:
- Alpha Spectrometry
- Liquid Scintillation Counting
- Kinetic Phosphorescence Analysis
- Inductively Coupled Plasma Sector Field Mass Spectrometry
- Rapid emergency methods

Capacity:
300-600 samples per year, depending on the required analysis

Duration of experiment:
From 1 hour to 2-3 weeks, depending on the sample type and analytical procedure

Intercomparison exercise proposed:
- PROCORAD intercomparisons
- BfS intercomparisons
- Emergency intercomparisons

Training proposed:
Technical Recommendations for Monitoring Individuals for Occupational Intake of Radionuclides. European Commission Radiation Protection Report 188 (2018)

Address:
CIEMAT, Internal Dosimetry.
Avda. Complutense 40.
E36. 28040 – Madrid, Spain

Access:
The analytical facility is open to joint research collaborations

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+34 914962588

Maria Antonia López (Int. Dosim.)
ma.lopez@ciemat.es
+34 914962580

Related to:
EURADOS

LRM

Low-Level Radioactivity Measurement Laboratories of the SCK•CEN

The laboratories of the Low-Level Radioactivity Measurements (LRM) group of the SCK•CEN in Mol, Belgium are specialized in low-level radioactivity measurements for environmental monitoring, characterization of NORM and TENORM, food and feed control, monitoring of drinking water, and bioassay measurements for nuclear workers. Additionally, our laboratories analyze radioactivity in samples in support of radiation protection, research and development, and the exploitation of nuclear facilities at SCK•CEN and play a role in emergency preparedness.

The LRM group is also an active partner in the ALMERA network of the IAEA. A staff of 22 people conduct more than 10,000 radioactivity analyses annually. The LRM laboratories have been involved in environmental monitoring of the Belgian territory since the late sixties. Currently, the Federal Agency of Nuclear Control (FANC) coordinates and supervises environmental monitoring of the Belgian territory. The LRM laboratories conduct the yearly monitoring plan created by the FANC together with the laboratories of IRE Elit.

The LRM laboratories are organized according to an integrated management system (IMS), including quality management according to ISO 17025 and environmental management according to ISO 14001 standards. Accreditation for testing was first obtained in 1995 for a number of analyses and has been gradually extended to cover all relevant analyses. The integrated management system is process-oriented and autonomous processes are consistent with the various measurement techniques that are applied.

These processes run sequentially or in parallel to cover all analytical tasks of the LRM laboratories. The processes are coupled to a central laboratory information management system (C-LIMS) that keeps track of all tasks and in which all samples and subsamples are registered. In addition to the information in the C-LIMS, some laboratories also have a dedicated laboratory LIMS that is used to register specific information related to a measurement technique and automate the measurements using software modules for data exchange with hardware and analysis software.

Since 2019, the LRM laboratories have been hosted in a new building with laboratories designed according to their activities.

The major infrastructure components of the LRM laboratories comprise:

Photo: SCK•CEN

Dr Michel Bruggeman

- 2 vehicles and sampling equipment (automatic water samplers, small volume air samplers, a large volume air sampler (Snow White))
- Laboratories for primary sample preparation (drying, freeze drying, calcinating, milling, sieving, subsampling)
- 1 cooling room, freezing cell, and dry storage rooms for conditioned storage of pretreated samples
- 1 counting room with 20 HPGe detectors
- 1 counting room with 20 ZnS counters for gross alpha counting
- 1 counting room with 16 ZnS counters for measuring ^{222}Rn and ^{226}Ra (using Lucas cells)
- 4 proportional counters with sample changer (gross alpha & beta counting)
- 1 low background proportional counter (4 detectors)
- 1 counting room with 5 liquid scintillation counters (+ one portable).

Photo: SCK•CEN

View of the different counting rooms and detectors and that of a preparation laboratory with a pyrolyser

ID Card:

Analytical platform type:
Low Level Radioactivity Measurements

Main techniques proposed:
Radiochemistry
Gross alpha & beta counting
Alpha particle spectrometry
Liquid Scintillation counting
Gamma-ray spectrometry

Capacity:
More than 10000 assays per year

Address:
SCK•CEN
LRM laboratories
Boeretang 200
2400 Mol
Belgium

Access:
On commercial basis or in the framework of common research

Internet link:
https://www.sckcen.be/nl/Services_Consulting/Analyses_Measurements/Low_level_measurements

Contacts:
Michel Bruggeman
mbruggem@sckcen.be

Related to:
ALLIANCE

Characterization of the natural radioactivity of the first deep geothermal doublet in Flanders, Belgium, Vasile M., Bruggeman M., Van Meensel S., Bos S., Laenen B. (2017), Appl Radiat Isot, 126, 300-303

Determination of ^{210}Pb, ^{210}Po, ^{226}Ra, ^{228}Ra and uranium isotopes in drinking water in order to comply with the requirements of the EU 'Drinking Water Directive', Vasile M., Loots H., Jacobs K., Verheyen L., Sneyers L., Verrezen F., Bruggeman M. (2016), Appl Radiat Isot, 109, 465-469

TU Dublin Analytical Platform

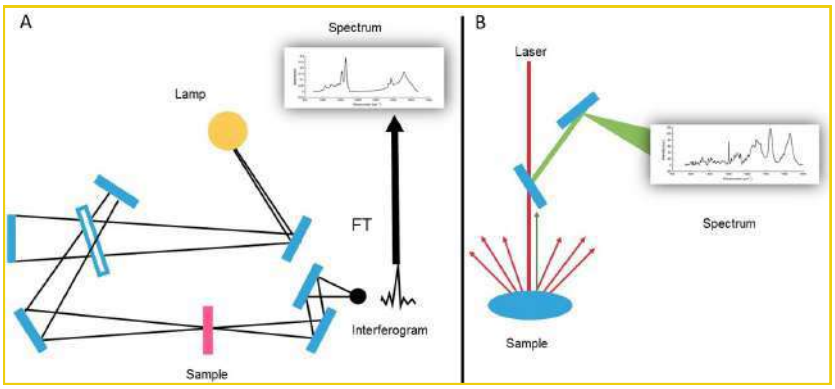
Spectroscopic platform for radiation biology and biodosimetry

Vibrational spectroscopy (Infrared (IR) and Raman) analyses vibrations within a molecule and the spectrum of vibrational energies can be used to characterise a molecular structure (Figure 1 and 2). IR spectroscopy is based on the absorption of infrared radiation by the sample and the fact that molecules absorb specific frequencies of the incident light which are characteristic of their structure. Raman spectroscopy is based on inelastic light scattering where the coupling of the light generates vibrations within the material, which are again characteristic of the chemical structure, and the energy of the scattered light is reduced by an amount equal to the vibrational energy.

Photo: TU DUBLIN

Prof Fiona Lyng & Dr Aidan Meade

The RESC has a suite of spectroscopic instruments, including two Fourier Transform infrared microscopes and three multi line Raman spectroscopic microscopes, including one with upright and inverted geometry for *in situ* AFM and/or fluorescence imaging. In the RESC 200 m^2 laboratory, two Raman microscopes are available as well as full cell culture, molecular biology and immunocytochemistry facilities.



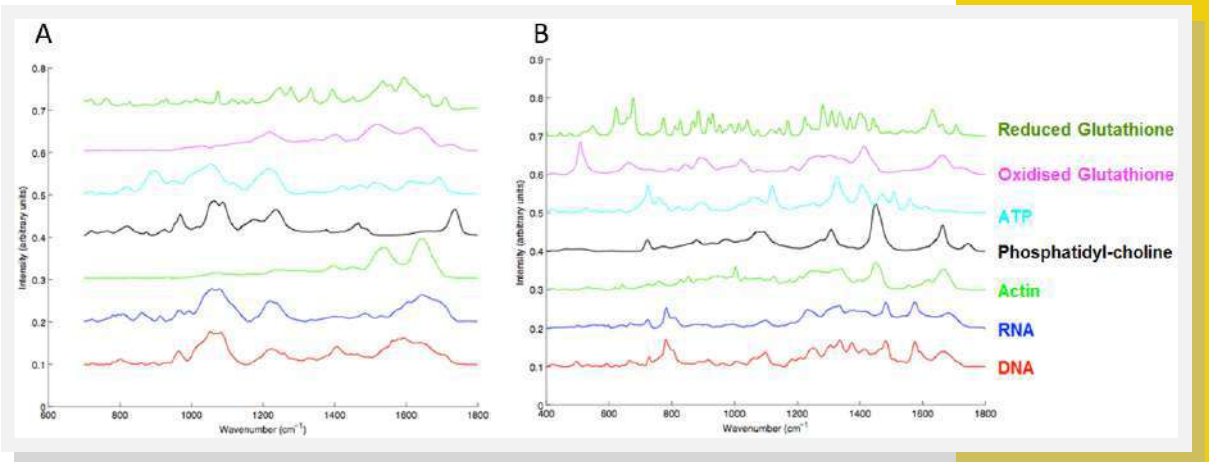
Schematic showing the process involved in collection of (A) Infrared spectra and (B) Raman spectra.

Raman and IR spectroscopy are complementary techniques offering advantages over cellular and –omics assays in terms of minimal sample preparation, speed and cost and can provide multiplex signatures of the proteome, lipidome, and metabolome of a biological sample. Spectroscopic analysis of tissues, cells or biofluids, such as blood plasma/serum and urine, can provide unique spectral markers or signatures of radiation response.

The Radiation and Environmental Science Centre (RESC) is housed in the FOCAS Research Institute, a 3200 m^2 facility with state of the art core laboratory support in microscopy and spectroscopy, in Technological University Dublin (TU Dublin). FOCAS houses a suite of spectroscopic instruments, including two Fourier Transform infrared microscopes and three multi line Raman spectroscopic microscopes, including one with upright and inverted geometry for *in situ* AFM and/or fluorescence imaging. In the RESC 200 m^2 laboratory, two Raman microscopes are available as well as full cell culture, molecular biology and immunocytochemistry facilities.

High end computing facilities associated with the Science Foundation Ireland ADAPT centre at TU Dublin are also available comprising a high-performance Research Computing Cluster housed in a state-of-the-art Data Centre in TU Dublin's new Grangegorman Campus. Data modelling experiments using images, high content and multi-omics data with traditional machine learning and modern deep learning analyses are routinely conducted on this platform.

The core expertise of the RESC is in radiobiology and recent RESC research has involved applications of vibrational spectroscopy in radiation biology and biodosimetry using cell lines and tissues and blood samples from patients receiving radiotherapy.



(A) Infrared spectra and (B) Raman spectra of typical biochemical components, DNA, RNA, phosphatidylcholine, ATP, glutathione and actin.

ID Card:

Analytical platform type:
Spectroscopic platform for radiobiology and radiation biodosimetry

Main techniques proposed:
Raman spectroscopy
FTIR spectroscopy
Multivariate analysis
Data mining

Capacity:
Dependent on sample type (tissues, cells, biofluids)

Delay to start:
Dependent on project

Duration of experiment:
Dependent on experiment

Intercomparison exercise proposed:
Intercomparison possible with other assays

Training proposed:
Specific training in spectroscopic measurements and data analysis

Address:
Radiation and Environmental Science Centre, FOCAS Research Institute, Technological University Dublin, Kevin Street, D08 NF82, Ireland

Access:
Joint research collaboration

Internet link:
www.dit.ie/resc

Contact:
Fiona Lyng
fiona.lyng@tudublin.ie

Aidan Meade
aidan.meade@tudublin.ie

Monitoring radiotherapeutic response in prostate cancer patients using high throughput FTIR spectroscopy of liquid biopsies, Medipally D.K.R., Nguyen T.N.Q., Bryant J., Untereiner V., Sockalingum G.D., Cullen D., Noone E., Bradshaw S., Finn M., Dunne M., Shannon A.M. et al. (2019), Cancers, 11 (7), 925
Prediction of DNA damage and G2 chromosomal radio-sensitivity *ex vivo* in peripheral blood mononuclear cells with label-free Raman micro-spectroscopy, Meade A.D., Maguire A., Bryant J., Cullen D., Medipally D., White L., McClean B., Shields L., Armstrong J. et al. (2019), Int J Radiat Biol, 95 (1), 44-53

Chapter 3: Analytical platforms, Models & Tools

b) Models & Tools

Dose Estimate, CABAS and NETA

Statistical and software tools for cytogenetic biodosimetry

Cytogenetic methods of biological dosimetry are crucial for triage of individuals following suspected radiation overexposure and also to support large scale research projects where biological markers of exposure and effect are required (see issue 1 – RENEB). The biological and statistical methods for dose estimation in radiation cytogenetics are now extremely well defined. To facilitate dosimetry, calibration data are collected and fitted under

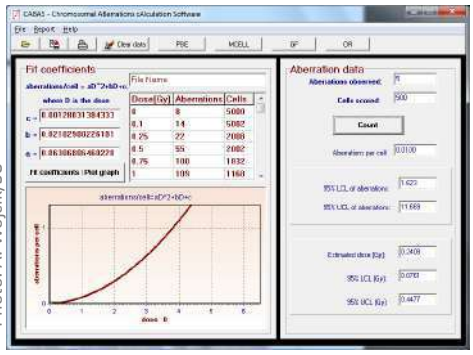


Photo: A. Wojcik/SU

The interface of CABAS

Poisson assumptions to a linear or linear quadratic model and the coefficients are then used to calculate doses. Full details of this classical procedure can be found in the International Atomic Energy Agency manual (http://www-pub.iaea.org/MTCD/publications/PDF/EPR-Biodosimetry%202011_web.pdf).

Statistical methods for analysis of cytogenetic data can be complex – for instance iteratively reweighted or maximum likelihood methods to fit calibration curves - however good statistical analysis is crucial to ensure that accurate dose and uncertainty estimates are produced. Thus in recent years there has been a lot of work on developing computational tools to support implementation of the IAEA statistical analysis methods. In particular, Dose Estimate and CABAS allow users to fit calibration curves and estimate whole or partial body doses in acute or protracted scenarios. Both tools contain graphic user interfaces for ease of use, come with full instructions, and have been extensively tested. Dose Estimate can be obtained by emailing liz.ainsbury@phe.gov.uk and CABAS from http://www.ujk.edu.pl/ibiol/cabas/. In addition, there are a large number of inhouse tools developed at the various biodosimetry laboratories in Europe, for instance GLIM (UAB), MLREG (BfS), BIODOSEUAB and DOSGEN (CPHR).

Photo: left to right:K. Rothkamm/ Hamburg University; A.Wojcik/SU

Liz Ainsbury - Andrzej Wojcik

Limitations in the traditional methods, for instance departure from Poisson distribution in partial body exposures, have led to development of new analysis methods based on alternative models to Poisson. NETA allows users to test whether data are Poisson or Neyman A distributed, for example: http://www.ujk.edu.pl/ibiol/neta/. Bayesian analysis is a very attractive solution to characterise cytogenetic doses, as the results are given in terms of probability distributions which intrinsically include uncertainty information. CytoBayesJ (liz.ainsbury@phe.gov.uk) and the R software radir (https://cran.r-project.org/web/packages/radir/index.html) are simple tools for this purpose.

Software tools have also been developed to assist in triage categorisation – including the Multibiodose EU FP7 project software (http://www.multibiodose.eu/software.html) and outside the EU, BAT and FRAT (https://www.usuhs.edu/afrri/biodosimetrytools).

Finally, in addition to defined tools, the retrospective dosimetry community has a number of biostatisticians devoted to analysing data and developing statistical analysis methods and tools. These experts are very happy to collaborate going forward – contact the authors or through RENEB (reneb@bfs.de).

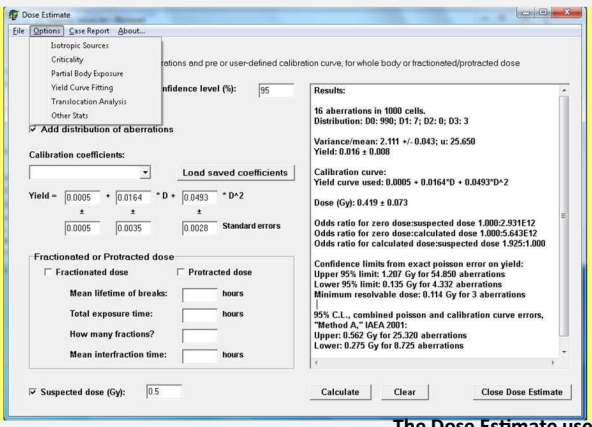


Photo: L.Ainsbury/PHE

The Dose Estimate user interface

ID Card:

Purpose:
Cytogenetic radiation dose and uncertainty assessment

Capacity:
N/A - freeware

Use:
Graphic user interface providing simple tools to fit calibration curves and estimate cytogenetic radiation doses

Housed by:
Dose Estimate: PHE;
CABAS: SU and JKU

Training proposed on the software:
Full instructions and example data are provided, but adhoc training can be given if needed

Access:
Dose estimate: Free, by emailing liz.ainsbury@phe.gov.uk;
CABAS: Free to download from: http://www.ujk.edu.pl/ibiol/cabas/ or by emailing andrzej.wojcik@su.se

Contact:
Dose Estimate: liz.ainsbury@phe.gov.uk, 0044 1235 825105;
CABAS: Andrzej.wojcik@su.se, 00468161217

Related to:
MELODI, EURADOS, CARPEM,

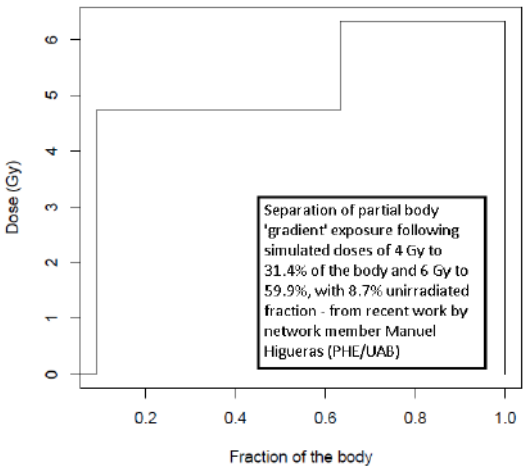
CABAS - A FREELY AVAILABLE PC PROGRAM FOR FITTING CALIBRATION CURVES IN CHROMOSOME ABERRATION DOSIMETRY. Deperas, J., et al. Radiat. Prot. Dosim. 2007 124:115-23.

DOSE ESTIMATION SOFTWARE FOR RADIATION BIODOSIMETRY. Ainsbury EA, Lloyd DC. Health Phys. 2010 98(2):290-5.

LDRadStatsNet

Network of statisticians interested in low dose IR research

Uncertainties, both quantitative and conceptual in nature, have been identified as key to addressing the remaining research questions in EU low dose radiation research. Sophisticated techniques are in use across the different disciplines, however, there seems to be little commonality and, furthermore, the proportion of individuals with formal mathematical and statistical training compared to the other scientific disciplines appears relatively low. In order to address this, DoReMi collaborators from PHE and CREAL, together with colleagues from Universitat Autonoma de Barcelona (UAB) and Durham University (DU), organized a workshop to bring together researchers from the low dose radiation fields and invited expert mathematicians and statisticians with an interest in applied uncertainty analysis. The meeting was funded by EU FP7 DoReMi and the Centre de Recerca Matemàtica (CRM) which is a consortium between the UAB and several institutions and was held at CREAL, Barcelona, in September 2015.



DoReMi low dose radiation experts outlined the key research questions and the associated problems, together with the solutions that are currently being applied in DoReMi and the other EU low dose radiation research consortia, under the general headings of radiation biology, modelling and epidemiology research. The invited external statistical experts then outlined their own current research – the idea being to stimulate exchange of ideas. Focused discussions then took place to attempt to identify areas in which standard or indeed novel statistical methods can be applied to solve EU low dose radiation research questions going forward under MELODI and CONCERT.

The conclusions from the meeting were broad, but can be summarised as follows:

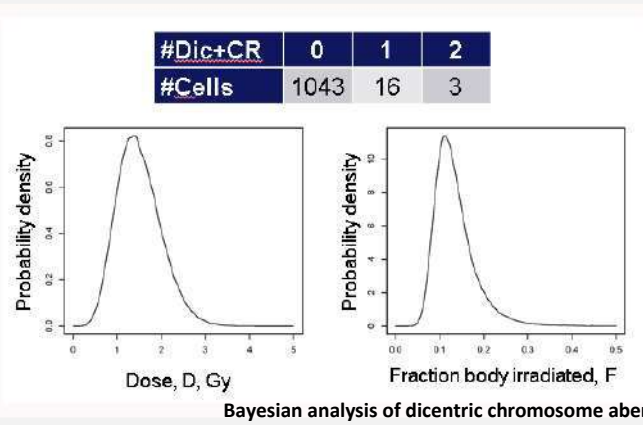
Photo: K. Rothkamm/PHE

Liz Ainsbury

1) It will be very important to consider and account for uncertainty in order to solve the remaining low dose research questions, identified in the relevant strategic research agendas. Statisticians must work closely with scientists from the other disciplines, indeed communication in interdisciplinary research can be supported by statistical expertise, e.g. in communication of what information is needed / what is available.

2) Training courses and workshops will clearly play a role in ensuring adequate statistical support for radiation research going forward, but the focus should be on opening a dialogue between scientists from different fields and at different stages of their careers, rather than on the purely instructive format of traditional training courses. A CONCERT funded course will take place in July - details here.

3) The meeting attendees all supported creating an informal network of scientists interested in the formal analysis of uncertainties in radiation research questions - resulting in the birth of 'LDRadStatsNet'. Individuals interested in joining the informal network or in drawing on the expertise of network members should contact Liz Ainsbury (liz.ainsbury@phe.gov.uk) for futher information in the first instance.



Bayesian analysis of dicentric chromosome aberrations

Graph: calibration data from Vinnikov et al., 2013

ID Card:

Purpose:
To support statistical analysis in EU low dose radiation research projects

Capacity:
Project dependent

Use:
Statistical analysis, statistical modelling, epidemiological analysis, etc…

Housed at:
Administered by PHE, UK

Training proposed:
Adhoc as required

Access:
Contact Liz Ainsbury in the first instance

Internet link:
Further details available at: http://www.doremi-noe.net/meetings_and_events.html#LDRadStats

Contact:
Liz Ainsbury, liz.ainsbury@phe.gov.uk

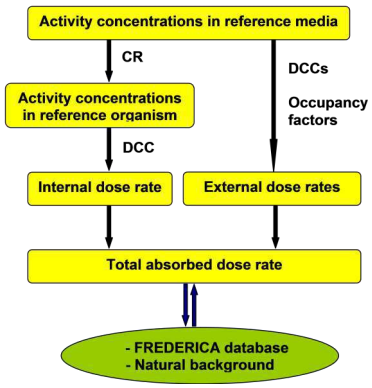
Related to:
EURADOS, RENEB and many other EU radiation research projects

RADIR PACKAGE: AN R IMPLEMENTATION FOR CYTOGENETIC BIODOSIMETRY DOSE ESTIMATION. Moriña D, et al. J Radiol Prot. 2015;35(3):557-69.
ZERO-INFLATED REGRESSION MODELS FOR RADIATION-INDUCED CHROMOSOME ABERRATION DATA: A COMPARATIVE STUDY. Oliveira M, et al. Biom J. 2016 58(2):259-79 .

ERICA Tool

The ERICA Tool supports adept environmental risk assessment

A key component of the ERICA Integrated Approach was the quantification of environmental risk involving, as an initial step, the combination of data on environmental transfer and dosimetry to provide a measure of wildlife exposure. These values, in the form of dose rates or corresponding activity concentrations for screening purposes, could then be compared with benchmarks, derived from exposure levels at which detrimental effects are known to occur, for the estimation of risk. In view of the large data sets underpinning the assessment approach and the potential to introduce errors when performing numerous calculations by hand, a supporting computer-based tool, the ERICA Tool, was developed as described in Brown et al. (2008). The Tool gives the option to cover a comprehensive list of radioisotopes and organism types, and has particular emphasis on the assessment of planned routine discharges of radionuclides and existing exposure situations.



Source: NRPA

Components within the assessment part of the ERICA Tool

The ERICA Tool adopts a tiered structure. There are two generic screening tiers and a third site-specific tier. The first Tier is very simple, based around Environmental Media Concentration Limits, EMCLs, defined as the activity concentration of a given radionuclide in media (soil, sediment water) that will result in a dose-rate to the most exposed reference organism equal to the screening dose-rate. This Tier requires minimal input from the assessor. The second Tier, although still a screening tier, is used to calculate dose rates explicitly and requires more detailed input from the assessor allowing for scrutiny and editing of default parameters in the process. A key procedural element of Tier 2 involves the application of Uncertainty Factors, UFs. Such factors reflect knowledge concerning probability distribution functions and provide a way of incorporating conservatism into the assessment by allowing the consideration of high percentile values in underlying parameters. Tier 3 allows a fully probabilistic analysis to be undertaken.

Photo: Justin Brown/NRPA

Justin Brown

The ERICA Tool has been further evaluated in numerous studies and has been widely applied by the scientific community. Examples include: consideration of potential environmental impacts from deep geological disposal facilities in various European countries; scoping analyses in line with newly introduced environmental regulations; in quantifying environmental impacts from operating and planned nuclear power stations and assessments of the impact of near-surface radioactive waste repositories in Europe and Australia.

Training in the use of the Tool has been relatively comprehensive (see: https://wiki.ceh.ac.uk/x/dIPJBg) with a bespoke 'Questions & Answers' webpage having been developed (see: https://wiki.ceh.ac.uk/x/r48ZBw). The software is freely available for download (http://www.erica-tool.com and http://www.erica-tool.eu/) with the newest version of the software described in Brown et al. (2016).

Web-page at http://www.erica-tool.com

Source: NRPA

ID Card:

Purpose:
Environmental risk assessment

Information available type:
Radionuclide transfer, eco-dosimetry and biological effects for wildlife (summarised from published literature)

Use:
Individuals can download and use the software themselves for screening assessments, but may need a specialist for site specific analyses

Training proposed on the software:
Training in the use of the Tool has been relatively comprehensive (see: https://wiki.ceh.ac.uk/x/dIPJBg) and is ongoing – see website for details

Access:
Free

Internet link:
http://www.erica-tool.com and http://www.erica-tool.eu/

Contact:
Justin Brown
Justin.brown@nrpa.no;
+47 67162500

Nicholas Beresford
nab@ceh.ac.uk
+44 1524 595856

Related to:
Alliance

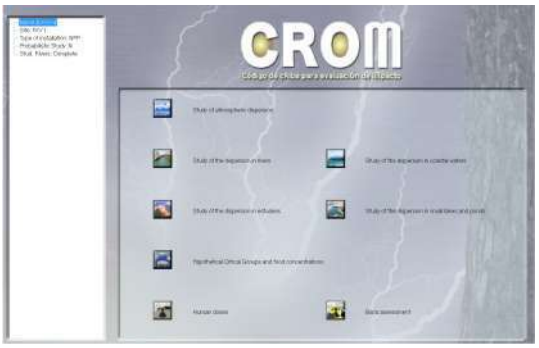
The ERICA Tool. Brown, J.E., et al. (2008). J. Environ Radioact, 99, pp.1371-1383.

A new version of the ERICA Tool to facilitate impact assessments of radioactivity on wild plants and animals. Brown J.E., et al. (2016). J. Environ Radioact, 153, pp. 141-148.

CROM-8

A code to integrate dose assessments for humans and biota

CROM code was initially designed as a computational tool to implement the more complex models described in the Safety Report Series No 19 (SRS-19) of the International Atomic Energy Agency (IAEA), but has evolved to include new capabilities. The SRS-19, published in 2001, compiles the generic models for the transport of radionuclides in the environment (produced as a discharge in an installation) and all their associated parameters.



Picture: CIEMAT

Figure 1 : Main screen of CROM8

In 2007, CROM 6, a stable version, quality controlled by the IAEA, was distributed by the Agency worldwide as the basis for the calculation of these models. This was followed by CROM 7, created to propagate the uncertainties of the measurements and parameters through the models, and then almost immediately by a new version, CROM 8, to include the protection of the biota, in accordance with the requirements of the IAEA and the EU. All these versions are freely available at ftp://ftp.ciemat.es/pub/CROM.

CROM 8 (Figure 1), a tool for integrated assessment of effective doses for humans and absorbed doses for biota, was developed on the basis that both approaches require contamination levels of environmental media, such as air, freshwater, soil, etc, as inputs. Therefore, the use of common models to derive these concentrations from the discharges produced in a nuclear, radioactive or even a NORM installation, would allow simultaneous calculations to be performed. CROM 8 includes default data for 162 radionuclides for humans and 63 for biota. Two sets of Reference Animals and Plants are also available: one from ICRP and accepted by the IAEA, and another from ERICA. The code does not include the screening levels (tiers) specified in the SRS-19 for humans nor those in the ERICA-Tool for biota. The code does allow assessments to be performed in rivers, lakes and marine environments and in contaminated atmosphere and soils.

Photo: JC Mora/CIEMAT

Juan Carlos Mora

The CROM tool was developed by the CIEMAT and the Polytechnic University of Madrid and co-sponsored by CIEMAT, ENRESA, IAEA and STAR.

Simultaneous to the development of CROM 8, parallel development began on the Open Platform CROM (OP-CROM), with the aim of creating a flexible tool that would allow implementation of any model, including the SRS-19 models, and which could be run on different computer platforms (operating systems and computer architecture). Another aim of OP-CROM was to enable all data and parameters to be input or generated as separate text files, rather than use an established database as is the case in the CROM family. Further, the tool would be freely distributed and would follow the open software philosophy, allowing others to contribute to its development.

In fact, OP-CROM has exceeded these aims (Figure 2), and plans exist to: generate new modules with advanced models; develop modules allowing dynamic calculations; include additional default parameters, or additional graphical user interfaces to allow the results to be presented in maps integrated into other tools such as Google Earth.

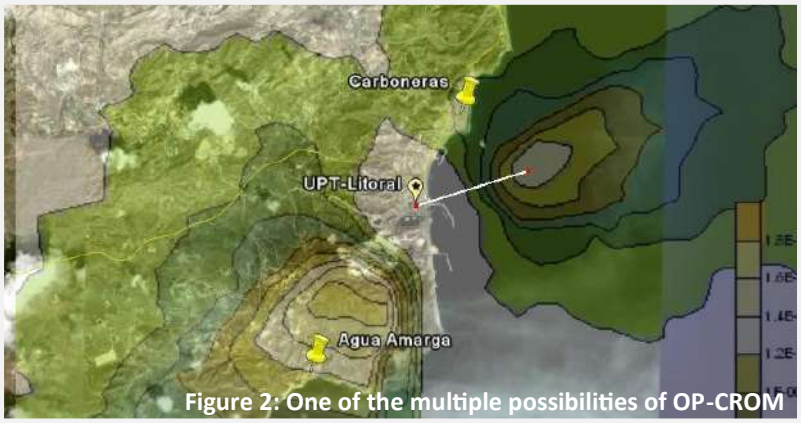


Figure 2: One of the multiple possibilities of OP-CROM

Picture: CIEMAT

ID Card:

Purpose:
Dose estimation in humans and biota.

Capacity:
N/A (freeware)

Use:
Integrated assessment of effective doses for humans and absorbed doses for biota.

Housed at:
CIEMAT

Software Training: Manuals available in English and Spanish. CIEMAT provides training upon request.

Address:
CIEMAT, Av Complutense 40, Madrid 28040, Spain

Access:
Free

Internet link: ftp://ftp.ciemat.es/pub/CROM

Contact:
Juan-Carlos Mora
jc.mora@ciemat.es
+34 91 346 6751

Related to:
ALLIANCE

CROM. Intellectual Property Registry No M-000481/2006. Registration Entry 16/2011/3841. 12 of May of 2011. (2011)
GENERIC MODEL FOR COMBINED TIER-1 ASSESSMENTS FOR HUMANS AND WILDLIFE. Juan C. Mora, et al. STAR (Contract Number: Fission-2010-3.5.1-269672) DELIVERABLE (D-N°3.1) (2015)

The Analytical Platform of the PREPARE project

Web based information exchange for emergency management

The European project PREPARE (Innovative integrated tools and platforms for radiological emergency preparedness and post-accident response in Europe) is aimed at closing gaps that have been identified in nuclear and radiological preparedness following the first evaluation of the Fukushima disaster. Among other measures, a so-called Analytical Platform (AP) has been developed to explore the scientific and operational means of improving information collection, information exchange and the evaluation of such types of disasters.

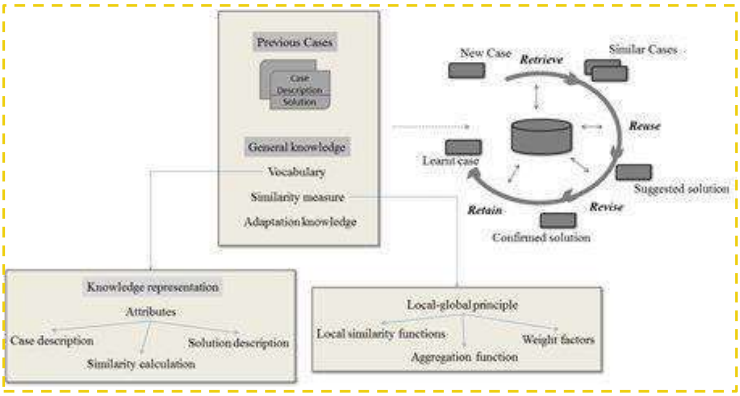


Photo: KIT

Knowledge database and CBR cycle

The AP provides a framework to allow discussion between experts and to disseminate congruent information on the current situation to the public. The AP is composed of three types of tools. Module 1 supports the expert-to-expert interactions in analysing an ongoing incident. Components include:

- A knowledge database and case-based reasoning (CBR) functionalities with machine-learning algorithms to find solutions for events that are not part of the existing knowledge database.
- A multi-criteria analysis tool for evaluating the effects of potential sets of measures to be taken.
- A means of communication to allow experts to analyse an on-going event (virtual meeting room).

The toolbox is completed by a web-crawling facility, which allows the collection and processing of information from all possible sources, and an "Ask the expert" tool to communicate information to the public about assessments.

The AP is designed to be installed centrally and access is provided via a web browser from any mobile or stationary computer. The AP was designed to be applicable in all phases of an emergency. The knowledge database contains more than 100 scenarios and historical cases for early phase countermeasures, and several dozen for the late phase. These can be used as a starting point for the evaluation of an on-going event. Internal communication is supported by the virtual meeting room that allows experts to communicate on particular topics. This communication is secure and only visible to those who have been assigned to this task. The forum and web-crawling facilities serve to support communications with the public.

Photo: KIT

Wolfgang Raskob

Application areas of the AP include situations where information is sparse and uncertain, for example, if the accident has happened in a neighbouring country. Training of decision-makers and other experts is also a possible field of application, as the AP contains lots of information for many different scenarios and provides vast knowledge not only on historical consequences but also on particular events from the scenario database.

Now that the Analytical Platform has been developed, the next step is to explore its application and usability. To facilitate this, an "Information, participation and communication" working group has been established under NERIS (http://www.eu-neris.net/). Among other tasks, the group intends to establish adequate rules of conduct and the basis for maintenance of the platform.

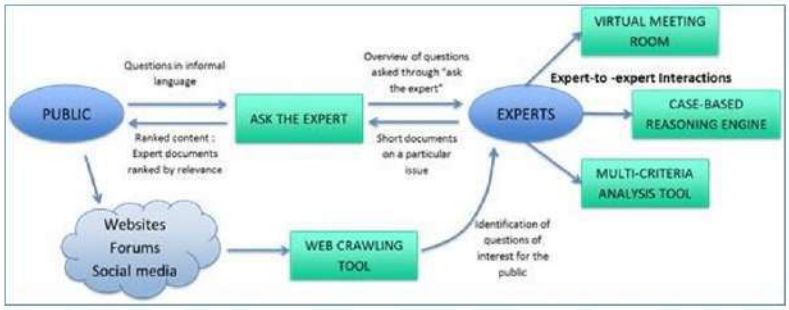


Photo: KIT

Interactions with the public and the experts through the PREPARE AP tools

ID Card:

Purpose:
Information collection and exchange to analyse an ongoing nuclear emergency

Capacity:
No limitation

Use:
Installed centrally and accessed via web browser. Possible to install it locally for training

Housed at:
Virtual installation (Virtual Box)

Address:
If applicable

Access:
Installed centrally at KIT, user can request access. Access is free

Internet link:
Will be provided after registration

Contact:
Wolfgang Raskob,
Karlsruhe Institute of Technology (KIT), Germany
Tel: +49 721 608 22480
Wolfgang.Raskob@kit.edu

Related to:
NERIS

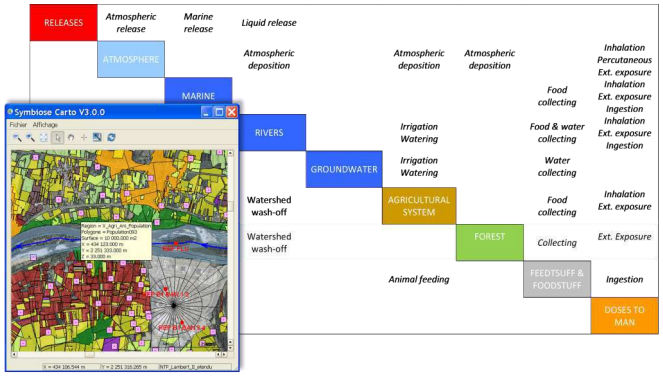
PREPARE: INNOVATIVE INTEGRATED TOOLS AND PLATFORMS FOR RADIOLOGICAL EMERGENCY PREPAREDNESS AND POST-ACCIDENT RESPONSE IN EUROPE. Raskob et al. Radiation Protection Dosimetry, 164(2015), pp.170-174

STRUCTURING AND REUSING KNOWLEDGE FROM HISTORICAL EVENTS FOR SUPPORTING NUCLEAR EMERGENCY AND REMEDIATION MANAGEMENT. Moehrle, S. et al. Eng. Appl. Artif. Intel. (2015)

Symbiose

A Modeling Platform for Environmental Radiological Assessment

SYMBIOSE is a simulation platform that aims at modelling the fate and dispersion of radioactive substances in environmental systems, and assessing their impact on humans and biota, accounting for uncertainty and variability. This platform can be used in a wide range of situations for assessing risks induced by radioactive releases from nuclear facilities under normal operational, accidental, or decommissioning conditions. As shown in Figure 1, environmental models in SYMBIOSE address atmospheric, terrestrial, freshwater and marine systems, as well as the main transfer processes at their interfaces.



SYMBIOSE: matrix featuring the environmental systems (diagonal boxes) and the interactions between them (off-diagonal boxes), which depict exchanges of mass, energy or information; example of landscape around an NPP for spatial predictions

The modelled exposure pathways for humans are external irradiation (plume shine and ground shine) and internal contamination (inhalation, percutaneous transfer for tritium, ingestion).

SYMBIOSE deals with several hundreds of radionuclides, derived from up to 70 chemical elements including chlorine, hydrogen and carbon, for which specific non-equilibrium approaches have been proposed. Outputs such as concentrations, activities, stocks and fluxes of pollutants or (a)biotic mass obey mainly to mass conservation equations (ODE & PDE ordinary and partial differential equations). When the previous approach is not possible, empirical parameterisations such as transfer factors or transfer functions are adopted. Spatial predictions are produced for a given sub-system on a specific spatial frame (i.e. collection of points, polylines or polygones). The specification of these frames, along with the spatial interactions between the frames, defines a landscape model.

SYMBIOSE has been developed in the context of an R&D project led by IRSN and co-funded by Electricité de France (EDF). Each of the co-owners (IRSN and EDF) are able to provide SYMBIOSE to licensees for specific purposes. The industrial version is regularly upgraded to take account of user feedback. The most recent version, SYMBIOSE V2.3, was released in early 2017. As shown in Figure 2, the SYMBIOSE platform, which runs under Windows/Linux OS, in French/English language, features a highly flexible and modular architecture. This consists of four major components:

Photo: M.A. Gonze, C. Mourlon,IRSN

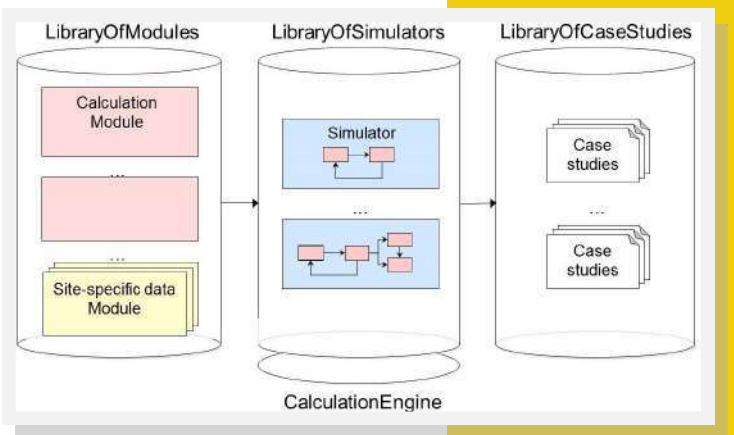
M.A. Gonze, C. Mourlon

-A library of modules, a module being an autonomous/reusable piece of software that models an environmental sub-system and encapsulates related parameters (generic/site-specific and deterministic/probabilistic values),

-A library of simulators, a simulator being a fit-for-purpose code that addresses a specific environmental problem, built by instantiating and connecting pre-existing modules through a graphical user interface,

-A library of case studies for the various existing simulators, and

-The application itself for managing modules and simulators or performing simulations through the use of a powerful calculation engine capable of dealing with complex space and time dynamics.



Simplified scheme displaying the architecture of SYMBIOSE platform

Simon-Cornu M. et al., 2015, Evaluating variability and uncertainty in radiological impact assessment using SYMBIOSE, Journal of Environmental Radioactivity, 139, p91-102

Gonze M. A. et al., 2016, Modeling the dynamics of ambient dose rates induced by radiocaesium in the Fukushima terrestrial environment, Journal of Environmental Radioactivity, 161, p22-34

ID Card:

Purpose:
A Modeling and Simulation Platform for Environmental Radiological Impact Assessments

Use:
Restricted to co-owners (IRSN and EDF) and licensees; some skills and initial training needed.

Training proposed on the software:
One or two sessions per year for co-owners (IRSN and EDF) or licensees

Access:
Licenses for specific needs (possibly free for certain uses)

Internet link:
https://gforge.irsn.fr/gf/project/symbiose/

Contact:
symbiose@irsn.fr

Related to:
ALLIANCE

INFRAFRONTIER

High quality resources for biomedical research

INFRAFRONTIER is the European Research Infrastructure for the developement, phenotyping, archiving and distribution of model mammalian genomes. It is a pan-European **non-profit** endeavour by more than 25 public research centres and private companies from 14 European countries and Canada, and the European Molecular Biology Laboratory. In INFRAFRONTIER these partners join forces to **advance the understanding of human health and disease.**

The INFRAFRONTIER Research Infrastructure offers **open access to unique scientific platforms, resources and services**, and to the extensive expertise of the INFRAFRONTIER partners:

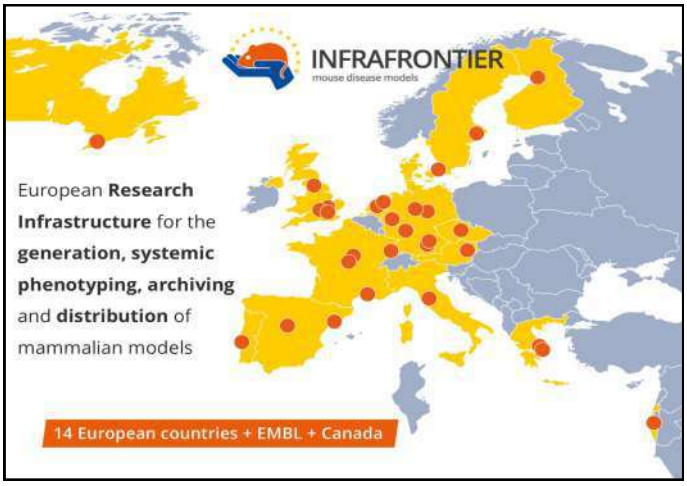


Photo: INFRAFRONTIER/Helmholtz Zentrum München

- Scientifically valuable mutant mouse strains are archived by the **European Mouse Mutant Archive (EMMA)** and distributed to interested researchers around the globe.
- Rodent **model generation** (mouse and rat) is offered using gene targeting in embryonic ES-cells or CRISPR/Cas9 technologies
- **Systemic phenotyping** of mutant mice offers a whole-organism view on gene function and pleiotropic effects. In-depth phenotyping (e.g. immuno-phenotyping, metabolic phenotyping) provides further insights.
- **Germ-free (axenic) mice** reveal the contribution of the gut microflora to phenotype-genotype interactions.
- The GEMM-ESC archive at the Netherlands Cancer Institute offers a rapid target gene validation in **complex cancer mouse models**.
- **Training** courses teach the state-of-the-art in the generation, cryopreservation and phenotyping of mouse models under strict animal welfare standards and promote the 3R -principles.

The INFRAFRONTIER Research Infrastructure has a **global user community**. All resources and services can be accessed at INFRAFRONTIER's central web portal www.infrafrontier.eu. In 2016, biomedical researchers requested more than 600 mouse strains from the European Mouse Mutant Archive (EMMA).

Photo: INFRAFRONTIER/Helmholtz Zentrum München

Dr Martin Hrabě de Angelis

The INFRAFRONTIER Partners share a **common European spirit and goal**: Advancing the understanding of human health and disease using mammalian models. They actively work together to provide high-quality platforms, resources and services for the biomedical research community, and to disseminate and share knowledge and expertise. This pan-European effort is coordinated by the **INFRAFRONTIER GmbH**, located in Munich, Germany, which guides the development of:

- **common standards and procedures** to ensure highest quality and reliability
- **common technology development** to further improve the INFRAFRONTIER resources and services
- **common outreach activities** to spread the word about INFRAFRONTIER
- **common training activities** to disseminate knowledge to current users and the next generation of biomedical researchers.

INFRAFRONTIER fully embraces the **3R principles: Replacement** - Supporting methods which avoid or replace the use of mice in research; **Reduction** - Using methods which minimise the number of mice used per experiment; **Refinement** - Applying methods which minimise suffering and improve animal welfare. By providing centralised access to high-quality resources, it adds the **INFRAFRONTIER Rs: Reproducibility, Reliability and Responsibility**.

Photo: INFRAFRONTIER/Helmholtz Zentrum München

INFRAFRONTIER

mouse disease models

ID Card:

Resources and Services:

- Rodent model development (mouse and rat)
- Systemic phenotypic and specialised phenotyping
- Archiving and distribution of mutant mouse strains
- Axenic (germ-free) mice
- Cancer mouse models
- Training and consulting

Central coordination:
INFRAFRONTIER GmbH,
Ingolstaedter Landstrasse 1,
85764 Neuherberg
Germany

Internet link:
www.infrafrontier.eu

Contact:
info@infrafrontier.eu

Related to:
MELODI, EURAMED

ESFRI European Strategy Forum on Research Infrastructures

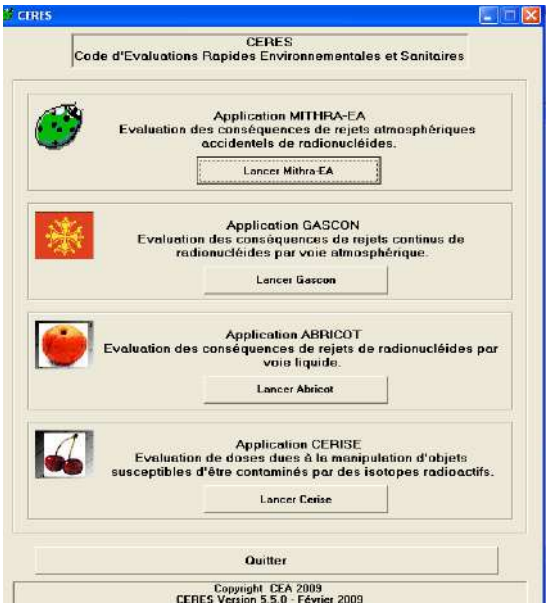
INFRAFRONTIER Consortium. 2015. "INFRAFRONTIER–Providing Mutant Mouse Resources as Research Tools for the International Scientific Community." Nucleic Acids Research 43, p1171–D1175. doi:10.1093/nar/gku1193

Raess, Michael, Ana Ambrosio de Castro, Valérie Gailus-Durner, Sabine Fessele, Martin Hrabě de Angelis, and the INFRAFRONTIER Consortium. 2016. "INFRAFRONTIER: A European Resource for Studying the Functional Basis of Human Disease.", Mammalian Genome 27 (7), p445–50, doi:10.1007/s00335-016-9642-y

THE CERES® PLATFORM

A rapid environmental and sanitary assessment code

The Radioanalysis, Chemistry, Environment Division of the French Alternative Energies and Atomic Energy Commission (CEA) is in charge of the development of methods and tools to estimate the impact of accidental or routine pollutant releases (radionuclides or chemicals) on human health and the environment. It has developed the CERES® tool (Code d'Evaluations Rapides Environnementales et Sanitaires) of Environmental sanitation) to ensure that all impact evaluations of CEA installations releases are carried out in the same way. The CERES® platform houses a database containing the characteristics of approximatively 800 isotopes or pollutants (dose coefficients, transfer coefficients from soil to plants, from plants to animals…) and can be used either in emergency situations or for safety files.



Main interface of CERES® platform

Currently, CERES® focuses on the integration of chemical reactions during atmospheric transfer, the development of heavy gas models and the use of topography in accidental situations.

For accidental atmospheric releases, atmospheric transport modelling is performed using the Gaussian puff model, MITHRA. Different standard deviation equations are used such as Doury's formula (default option), function of travel time. The activity emitted from a facility into the environment is evaluated using the ERASTEM system which is a box model, that takes into account transfers between different compartments of the installation. For routine atmospheric emissions, dispersion calculations are performed using the GASCON model, which is based on the Gaussian puff model described above. In this case, the release over time rate is constant and the different meteorological data acquired near the sites over a period of one or more years is based on observations. For normal releases in rivers, the ABRICOT model which assumes immediate dilution, is used.

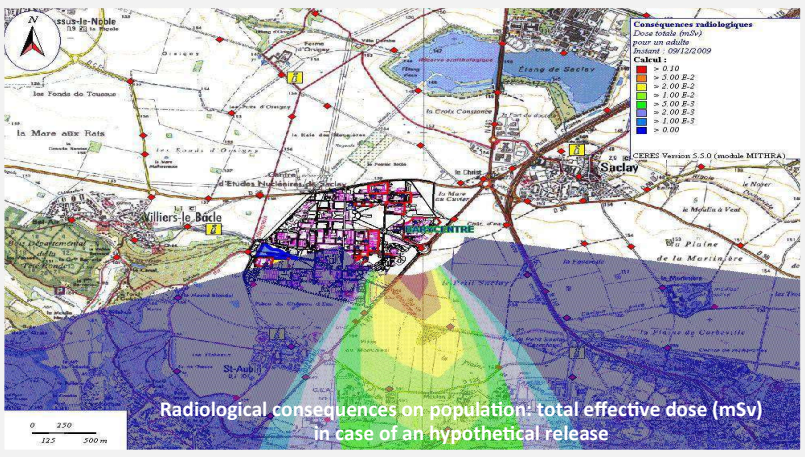
Dr Marguerite Monfort

Impact evaluations are performed in population groups whose characteristics are made available in a "site" dependent database containing stacks, measurement points, dietary habits, etc. The consequences in terms of effective dose or dose to the thyroid in accidental situation only, are estimated for the following pathways:

- immersion in the plume, which leads to internal exposure by inhalation and external exposure by irradiation following atmospheric release,
- presence on the deposits, which leads to external radiation exposure,
- inhalation of resuspended deposits in the case of liquid releases,
- ingestion of water or fish following liquid releases,
- consumption of plants, whose activity comes from the deposits of aerosols and rainfall or from ground transfers *via* root uptake,
- consumption of contaminated animal products.

In the case of tritium emissions, the modes of exposure differ in that immersion in the plume leads to internal exposure by inhalation and passage through the skin. Tritium is a low energy pure β emitter and does not cause external exposure via radiation deposits. Contamination can also occur through inhalation or ingestion *via* the food chain.

For accidental releases, the intervention levels for radiological emergencies defined by decree are highlighted if reached. The external exposure dose coefficients are derived from the Federal Guidance Report n°12, while the internal ones are either from the decree of September 1, 2003 or from ICRP publications: transfer coefficients in food chain are those proposed by international literature - TRS 472, AIEA, 2010.



Radiological consequences on population: total effective dose (mSv) in case of an hypothetical release

ID Card:

Purpose:
Dose assessment on population

Use:
need a specialist

Housed on:
CEA

Training proposed on the code:
Yes

Delay to start:
No

Access:
On demand (not free)

Internet link:
www.dase-cea.fr

Contact:
Marguerite Monfort
Marguerite.monfort@cea.fr
33 1 69 26 46 19

Address:
CEA DAM Ile de France
Bruyères le Châtel
91297 Arpajon
France

Related to:
MELODI, EURADOS, NERIS

Eckerman K. F., Ryman J. C., (1993) External exposure to radionuclides in air, water and soil. Federal Guidance Report 12-EPA 402-R-93-081

ICRP Publication 72 (1995) Age-dependant doses to members of the public from intake of radionuclides-Part 5 Compilation of Ingestion and Inhalation Dose Coefficients

The Severe Nuclear Accident Program (SNAP)

A Norwegian model for nuclear emergency

The Norwegian Meteorological Institute (MET) is responsible for modelling atmospheric dispersion of radioactive debris in the event of a nuclear emergency related to a nuclear accident or detonation. An additional task of the MET in a nuclear emergency is to identify unknown sources of radiation indicated by elevated levels of measurement. The basic tool used by the MET for such events is the Severe Nuclear Accident Program (SNAP).

Photo: Jan Terje Rausand/MET

Dr Jerzy Bartnicki **Dr Heiko Klein**

The SNAP model can be run in different domains, ranging from the local domain with a resolution of 2.5 km to the hemispheric domain with spatial resolution of approximately 10 km. Once released into the air, radioactive gases and particles are subject to advection, turbulent diffusion and deposition (dry and wet). In the model calculations, the advection process is immediately followed by the diffusion process. A random walk approach is used to parameterise horizontal and vertical diffusion. When large and dense particles are released, gravitational settling is more effective than vertical diffusion and this process is taken into account. The effectiveness of dry deposition is mainly a function of atmospheric stability which is calculated based on the Local Richardson Number. Wet deposition is a function of precipitation intensity and type, as well as particle size.

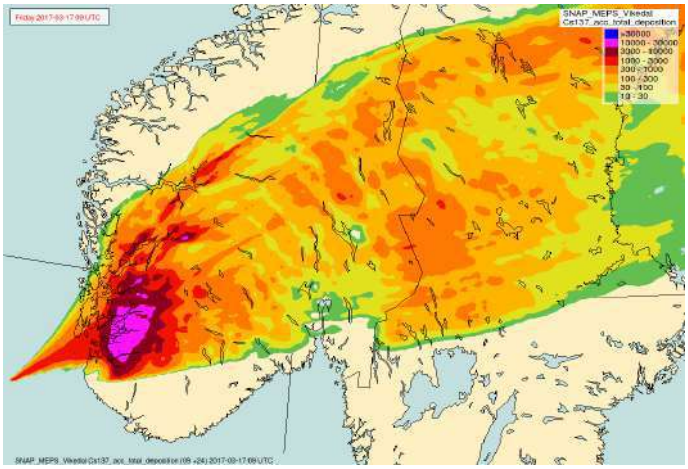


Photo: H. Klein /MET

SNAP dispersion results from a hypothetical accident on a floating nuclear powerplant transported along the Norwegian coast.

The SNAP model was developed at the MET in 1994 as a Lagrangian particle model. The present version is fully operational at the MET and takes into account atmospheric transport and deposition of gases, noble gases and particles of different size and density emitted during nuclear accidents or explosions. SNAP can also be run remotely by experts from the Norwegian Radiation Protection Authority (NRPA) where the Norwegian Crisis Committee is located.

In the event of a nuclear accident, the source term for the model runs is usually provided by NRPA. This source term includes the magnitude of release which is time dependant, the elevation, time profile of release and the nuclides released. In the case of a nuclear explosion, the source term depends on the explosive yield. In this type of event, radioactivity is transported mainly as particles of different sizes. A large variation of the particle size in the initial cloud is represented by 10 discrete classes with a characteristic particle radius ranging from 2 µm to 200 µm. All meteorological input is available on-line at the MET from different operational Numerical Weather Prediction (NWP) models, e.g. from the ECMWF forecast or from the regional Norwegian/ Swedish MetCoOp Ensemble Prediction System (MEPS).

The SNAP model has been used both for simulations of historical events (e.g. nuclear detonations in Novaya Zemlya, Chernobyl Accident) and real time simulations (e.g. Fukushima accident). It was tested in the ETEX experiment and showed good agreement with observations (ETEX 1). It has also been used for tracing unknown sources of radioactivity (e.g. recent ^{106}Ru case). SNAP is the dispersion model currently used by the MET in the CONFIDENCE project and also in CERAD CoE.

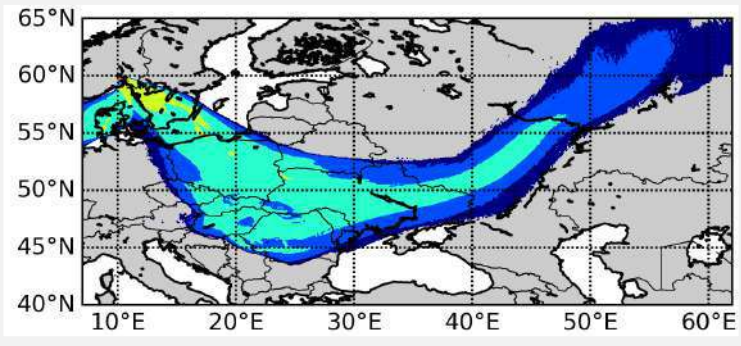


Photo: H. Klein/MET

Inverse SNAP dispersion calculations (-156h) of ^{106}Ru measurements in Oslo on 2/10/2017.

ID Card:

Purpose:
Atmospheric dispersion of radioactivity

Use:
Needs a specialist

Housed at:
Norwegian Meteorological Institute (MET)

Training proposed on the software:
None

Address:
Norwegian Meteorological Institute,
Henrik Mohns Plass 1
0313 Oslo, Norway

Access:
Open source

Internet link:
https://github.com/metno/snap

Contacts:
Heiko Klein
heiko.klein@met.no

Jerzy Bartnicki
Jerzy.bartnicki@met.no

Related to:
NERIS

Atmospheric transport of radioactive debris to Norway in case of a hypothetical accident related to the recovery of the Russian submarine K-27, Bartnicki J., Amundsen I., Brown J., Hosseini A., Hov Ø., Haakenstad H., Klein H., Lind O. C., Salbu B., Szacinski Wendel C. C., Ytre-Eide M. A. (2016), Journal of Environmental Radioactivity, 151, 404-416.
Operational SNAP model for remote applications from NRPA, Bartnicki J., Haakenstad H. and Hov Ø. (2011), Met.no report No. 12/2011. Norwegian Meteorological Institute, Oslo, Norway

The BIANCA code

BIophysical ANalysis of Cell death and chromosome Aberrations

BIANCA (BIophysical ANalysis of Cell death and chromosome Aberrations) is a biophysical model/MC code that simulates cell death and chromosome aberrations by different radiation types, including those of interest for radiation protection (e.g. alpha particles) and cancer hadron therapy (protons and C-ions). The model/code is developed and maintained at the University of Pavia (UniPv) and the National Institute of Nuclear Physics (INFN) in Pavia, Italy.

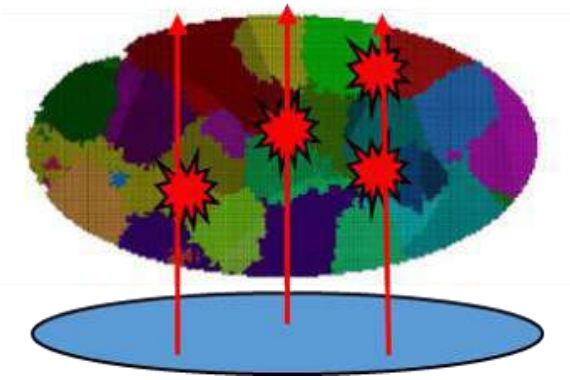


Photo: F. Ballarini and M. Carante/UniPv and INFN

Simulation of light-ion irradiation of a cell nucleus by the BIANCA code

The model, which ascribes a pivotal role to DNA cluster damage, is based on the following assumptions:

- Ionising radiation can induce DNA "Cluster Lesions" (CLs), where a CL is defined as critical DNA damage that produces two independent chromosome fragments.
- Distance-dependent mis-rejoining (or un-rejoining) of chromosome fragments produces chromosome aberrations.
- Certain aberrations (dicentrics, rings and large deletions) lead to cell death.

The CL yield, which mainly depends on radiation quality but is also modulated by the cell features, is adjusted by comparisons with experimental data. The fragment un-rejoining probability (or the characteristic distance of the fragment mis-rejoining probability, depending on the model version) is the second, and last, adjustable parameter.

The genomes (number of chromosomes and chromosome sizes) of human, hamster and rat cells have been implemented, and others can be added. The cell nucleus can be modelled either by a cylinder (for cell monolayers) or by a sphere (for cell suspensions), and the nucleus size can be chosen by the user. Each interphase chromosome-arm domain is described explicitly by the union of 0.1-µm-size voxels.

Photo: UniPv and INFN

Prof. F. Ballarini **Dr M. Carante**

The model has been recently applied to V79 cells (which are widely used in radiobiology, also to characterise hadron therapy beams) and AG01522 cells exposed to protons, He-ions and C-ions over a wide range of LET values. The good agreement between simulations and data allowed the creation of a database of particle- and LET-dependent CL yields; by fitting these yields, cell death and chromosome aberrations can be predicted also at LET values where experimental data are not available.

In view of hadron therapy applications, this allows an almost continuous set of α and β cell-survival parameters to be produced, which can be read by a radiation transport code and/or a TPS. In parallel, to elucidate the DNA damage repair mechanisms, the dependence of the fragment (mis-) rejoining probability on the (initial) fragment distance was investigated in human lymphocytes and fibroblasts. An exponential function of the form $\exp(-r/r_0)$, which is consistent with chromatin free -end diffusion, was found to better describe proximity effects with respect to both a step function and a Gaussian function. Furthermore, the results supported the use of the F-ratio (dicentrics to centric rings) and/or the G-ratio (interstitial deletions to centric rings) as "fingerprints" of low-dose, high-LET exposure, which can have applications for radiation protection.

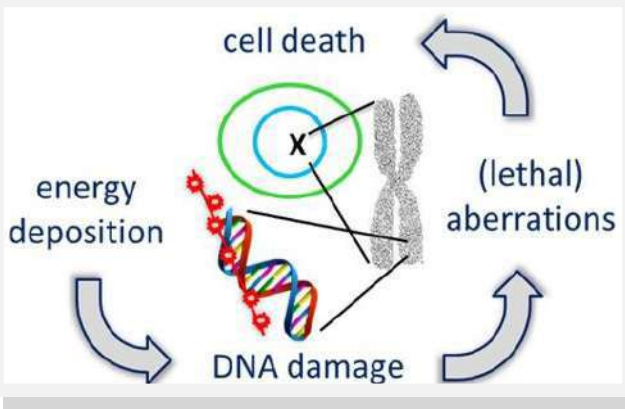


Photo: F. Ballarini and M. Carante/UniPv and INFN

Scheme of the main steps included in the BIANCA model

Chromosome aberrations and cell death by ionizing radiation: Evolution of a biophysical model, Ballarini F., Carante M. P. (2016), Radiation Physics and Chemistry, 128, 18-25

Proximity effects in chromosome aberration induction by low-LET ionizing radiation, Tello Cajiao J. J., Carante M. P., Bernal Rodriguez M. A., Ballarini F. (2017), DNA Repair, 58, 38-46

ID Card:

Purpose:
Calculation of cell death and chromosome damage probabilities

Use:
Use of the BIANCA code needs some initial skills and further training

Housed at:
- University of Pavia (UniPv)
- National Institute of Nuclear Physics (INFN)

Training proposed on the software:
N/A

Address:
University of Pavia, Physics Department
via Bassi 6, I-27100 Pavia, Italy

INFN-Section of Pavia
via Bassi 6, I-27100 Pavia, Italy

Access:
Currently the code is not freely available. Researchers interested in BIANCA should contact F. Ballarini and M. Carante.

Internet link:
http://fisica.unipv.it/ricerca/RicAppl/ENG/EN_SFB_Radio_computazionale.htm

Contacts:
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+39 0382 987949

Related to:
MELODI

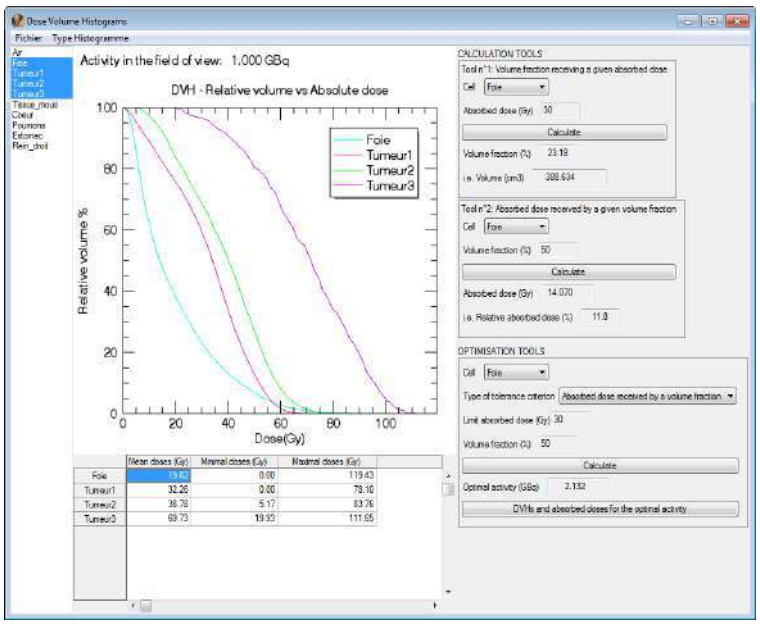
OEDIPE

A software tool for personalised dosimetry in nuclear medicine

Nuclear medicine is currently a rapidly evolving sector, particularly due to the discovery of new tumour-specific biomarkers and the availability of previously unconsidered radionuclides. Therapeutic procedures are of particular interest in this context, and one of the challenges is how to determine the individual activity to be administered to each patient. Currently, the administered activity is still largely standard, and sometimes tailored to patient weight or body surface area, although the European Directive 2013/59/Euratom emphasises that individual dose planning should be performed.

Photo: Céline Lelache/IRSN

Dr Aurélie Desbrée



Dose-volume histograms for regions of interest and treatment planning optimisation tools

Since biological effects, both in terms of response and toxicity, are primarily dependent on dose rather than administered activity, it is crucial to determine the personalised absorbed doses delivered to healthy tissues.

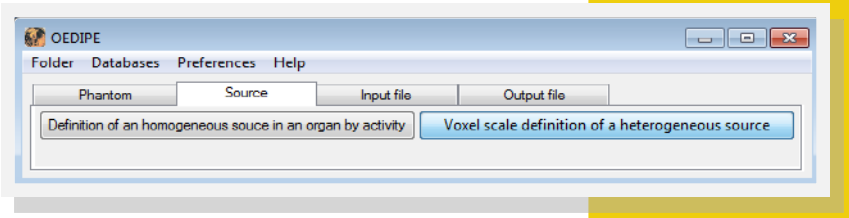
Only these estimations can ensure that healthy tissue irradiation will not lead to unacceptable toxicity, and can optimise treatment planning by calculating the maximal activity that can be safely administered to each patient. This activity is determined according to tolerance criteria for organs at risk, either for mean absorbed doses, dose-volume fractions or maximal absorbed doses.

The OEDIPE software offers a user-friendly graphical interface to carry out dosimetry, and a treatment planning tool for clinical applications of nuclear medicine. This tool has been developed to drive nuclear medicine treatment planning towards the refinements proposed in external dosimetry. OEDIPE creates an input file that must be run with the MCNPX Monte Carlo code, and it provides tools to process the results.

Mean absorbed doses to the regions of interest, isodose curves and dose-volume histograms can be obtained from data describing the patient's anatomy, based on CT or MRI images, and activity distribution data, based on PET or SPECT images. The distribution of Biological Effective Dose (BED) at the organ or voxel level can also be derived from the heterogeneous absorbed dose distribution. For treatment planning optimisation, tools have been implemented to provide the maximal injectable activity that can be administered to the patient according to tolerance criteria for organs at risk, expressed in terms of mean absorbed doses or dose-volume fractions.

Moreover, it is possible to calculate the maximal injectable activity for fractionated protocols, based on a BED tolerance criterion and depending on the number of fractions, the activity administered at each fraction, and the time delays between fractions.

In particular, this tool has been applied to selective internal radiation therapy (SIRT) in collaboration with the George Pompidou European Hospital in Paris. Therapy consists of injecting microspheres labelled with ^{90}Y into the lesions *via* the hepatic artery to treat unresectable hepatic cancers. This has allowed a 3D personalised dosimetry evaluation to be performed, based on patient-specific data and Monte Carlo calculations, and evaluated retrospectively on clinical data.



Main interface of the OEDIPE software

ID Card:

Purpose:
Dose assessment in nuclear medicine

Use:
Need some skills in the field

Housed at:
Administered by IRSN, France

Training proposed on the software:
N/A

Address:
IRSN
31 avenue de la Division Leclerc
92260 Fontenay-aux-Roses
France

Access:
On demand/through collaboration

Internet link:
http://www.irsn.fr/EN/Research/Scientific-tools/Computer-codes/Pages/OEDIPE-Personalised-dosimetric-evaluation-tool-3443.aspx

Contacts:
Dr Aurélie Desbrée
aurelie.desbree@irsn.fr
+33 1 58 35 80 36

Related to:
MELODI
EURADOS

OEDIPE, a software for personalized Monte Carlo dosimetry and treatment planning optimization in nuclear medicine: absorbed dose and biologically effective dose considerations, Petitguillaume A. et al. (2014), Radioprotection, 49 (4), 275-281
Three-dimensional personalized Monte Carlo dosimetry in ^{90}Y resin microspheres therapy of hepatic metastases: nontumoral liver and lungs radiation protection considerations and treatment planning optimization, Petitguillaume A. et al. (2014), J. Nucl. Med., 55, 405-413

Geant4-DNA

An extension of Geant4 for simulations in radiobiology

Accurate modelling of biological damage induced by ionising radiation at the scale of the DNA molecule remains a major challenge for radiobiology research today. In order to provide the community with an easily accessible mechanistic simulation platform, it was decided to extend the usage of the general purpose, open source "Geant4" Monte Carlo simulation toolkit, developed under the "Geant4-DNA" project initiated by the European Space Agency.

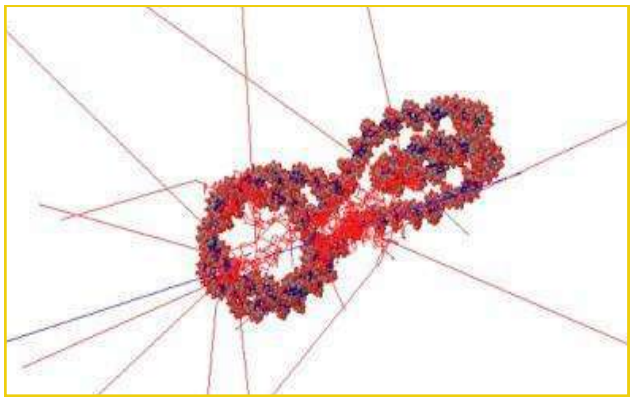


Photo: Geant4-DNA Collaboration

Geant4-DNA simulation of the irradiation of a dinucleosome with a single 100 keV proton

Geant4-DNA offers Geant4 users a set of functionalities which allow detailed simulation of particle-matter interactions in biological media. These functionalities include physical, physico-chemical and chemical processes that can be combined with nanometer-size geometries of biological targets in order to predict early DNA damage.

The key developments currently being undertaken by the Geant4-DNA Collaboration cover three main areas:

- Physical processes: Several sets of physical processes are available to describe the dominant step-by-step physical interactions of electrons, protons, hydrogen atoms, alpha particles and their charged states in liquid water, the main component of biological media. They can be combined with existing Geant4 physical processes in order to describe other processes such as photon interactions.
- Physico-chemical and chemical processes: These processes can simulate water radiolysis from physical interactions, that is, the creation, diffusion and mutual reactions of molecular species in liquid water, up to 1 microsecond after irradiation. An illustration of water radiolysis around a single electron track, simulated using Geant4-DNA, is shown in the figure on the right.
- Detailed geometries of biological targets: Given the benefits of Geant4 geometry modelling capabilities, it is now possible to simulate accurate geometries of biological targets such as the DNA molecule and even neurons.

Photo: Personal archive

Dr Sébastien Incerti

The figure in the left panel illustrates the implementation of a dinucleosome geometry extracted from the Protein Data Bank™ database.

These developments can be combined to predict early DNA damage. In particular, we have recently demonstrated that it is possible to predict early direct and indirect DNA damage in bacteria and cells.

Most of the features described above are already fully accessible through the Geant4 simulation toolkit and can also be run using a freely downloadable Geant4 virtual machine. Their inclusion in Geant4 makes them accessible to other Geant4-based simulation platforms such as GATE and TOPAS. Several application examples are also provided in Geant4. We hope that this simulation platform and its future developments will be useful for the further mechanistic understanding of ionising radiation effects in biological targets, especially when high spatial resolution (nanometer) and low energy (tens of electronVolts) track structure simulations are required.

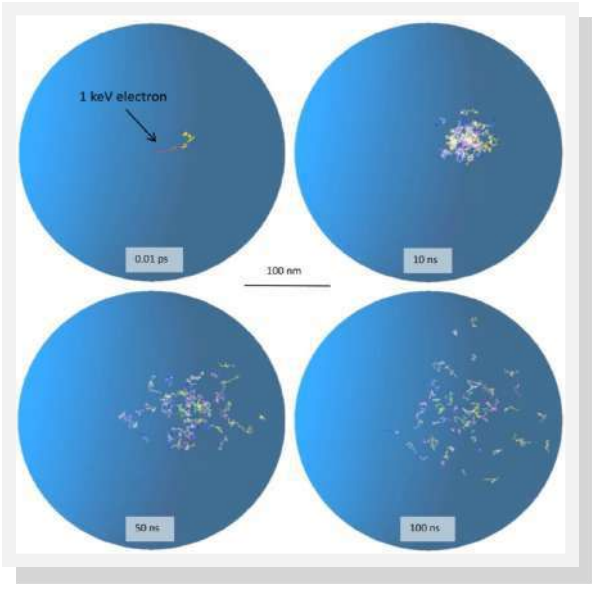


Photo: Geant4-DNA Collaboration

Molecular species diffusing in liquid water around a single electron track of 1 keV

GEANT4-DNA

ID Card:

Purpose:
Open access toolkit for the simulation of 3D track structures, water radiolysis, geometrical models of biological targets, and early biological damage.

Use:
Anyone familiar with the Geant4 Monte Carlo simulation toolkit.

Housed at:
Software repository at CERN, coordinated by CNRS/IN2P3, France, and developed by an international Collaboration.

Training proposed on the software:
http://geant4-dna.org

Access:
Open access, fully included in Geant4 (http://geant4.org) and also available through a virtual machine (http://geant4.in2p3.fr).

Internet link:
http://geant4-dna.org

Contact:
Dr Sébastien Incerti
incerti@cenbg.in2p3.fr
+33 5 57 12 08 89
(Geant4-DNA Collaboration spokesperson)

Involved in:
GATE and TOPAS Monte Carlo simulation platforms

Related to:
MELODI

Track structure modeling in liquid water: A review of the Geant4-DNA very low energy extension of the Geant4 Monte Carlo simulation toolkit, Bernal M. A., Bordage M. C., Brown J.M.C., Davídková M., Delage E., El Bitar Z., Enger S. A. et al. (2015), Phys. Med., 31 (8), 861-874

Comparison of Geant4 very low energy cross section models with experimental data in water, Incerti S., Ivanchenko A., Karamitros M., Mantero A., Moretto P., Tran H. N., Mascialino B., Champion C., Ivanchenko V. N., Bernal M. A., Francis Z., Villagrasa C., Baldacchino G. et al. (2010), Med. Phys., 37 (9), 4692-4708

D-DAT

Dynamic Dose Assessment and Transfer model for marine biota

In many situations involving radionuclide discharges to the ocean, activity levels in biota are not in equilibrium with fluctuating levels in the surrounding water. There are many processes at play, such as oceanographic, sediment and biological processes. D-DAT is a successful model designed to represent them and make predictions for radiological assessment. The model was initially developed for application to the Sellafield site and is now adapted for Fukushima to calculate time-variable ^{131}I, ^{134}Cs, ^{137}Cs and ^{90}Sr concentrations and doses in fish, crustaceans, algae, plankton and molluscs.

Photo: Personal archive

Prof. Jordi Vives i Batlle

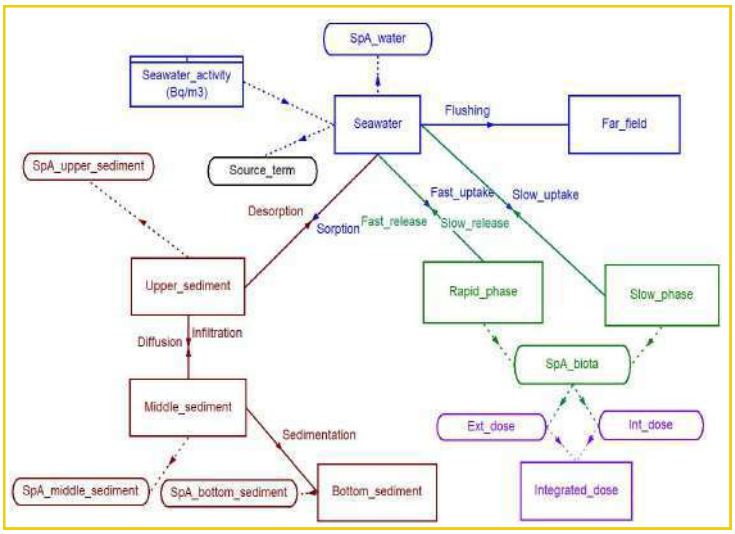


Photo: Jordi Vives i Batlle/SCK•CEN

D-DAT conceptual model showing the relevant aquatic, sediment and biological compartments (rectangles), fluxes (arrows) and variables (rounded rectangles)

At the heart of D-DAT is a biokinetic model comprising two biological compartments that exchange radionuclides individually with the water via a slow and a fast process respectively, with two biological half-lives as the key parameters. At equilibrium, the ratio of concentration in biota to that of seawater approaches the concentration factor.

The current version of D-DAT, developed during the EC COMET project, includes a module to represent radionuclide interactions between particulates, water and three layers of sediment (upper, middle and bottom). Particle scavenging and mixing, diffusion, pore water mixing and sedimentation processes regulate radionuclide migration across sediments. With this addition, the model can now deduce correctly the initial amount of radionuclides released during the accident, using a mass balance approach.

Using the calculated time-dependent biota concentrations, D-DAT generates internal and external dose rates to the biota using dose rate per unit concentration (DPUC) values for the relevant radionuclides and marine reference organisms, derived from a template run of the ERICA assessment tool. The time-dependent dose rates obtained are integrated to obtain the total dose received by a marine organism over the acute discharge period.

D-DAT uses real-time seawater concentrations from hydrodynamic files as its primary input. In addition, the model uses a biokinetic-allometric database of transfer parameters, oceanographic parameters and dose coefficients purposely optimised for Fukushima.

The model was successfully applied in the first international UNSCEAR assessment of the impact of Fukushima on the marine environment (2011-12). It was found that doses to marine organisms were generally below levels causing measurable effects on populations except for ^{131}I in macroalgae near the discharge point in the earliest days after the accident. In the subsequent COMET project, D-DAT was perfected, as described, to better match the biota concentrations observed in the long term (2012-17) and to assess exposures found to be below thresholds for population effects.

In summary, D-DAT can represent the complex time evolution of radionuclides in highly dynamic ocean environments, bringing more realism to the predictions. Therefore, we are readier now than before the Fukushima accident in terms of having models to assess accident situations.

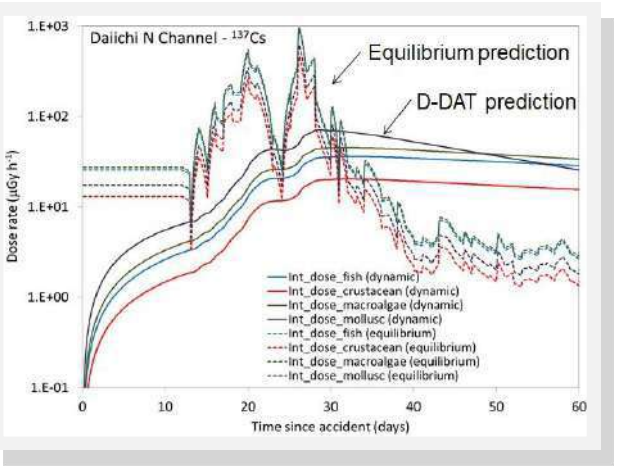


Photo: Jordi Vives i Batlle/SCK•CEN

Output of dynamic model D-DAT compared with calculation assuming instantaneous equilibrium of biota with seawater

ID Card:

Purpose:
Dynamic model for the calculation of radionuclide concentrations and assessment of dose to marine biota

Capacity:
Simultaneous assessment for six species of biota: fish, crustaceans, macroalgae, plankton and mollusk, and six radionuclides: ^{90}Sr, ^{129}I, ^{131}I, ^{134}Cs, ^{137}Cs and ^{236}U. It is also able to perform calculations in seawater and sediments as well as source term estimations

Use:
Requires some skills in marine radioecology to parameterise the model for a specific situation/ radionuclide/species

Housed at:
Current model version 6 is implemented on the ModelMaker 4 for Windows® modelling platform and resides at the host institute (SCK•CEN)

Address:
Belgian Nuclear Research Centre (SCK•CEN)
Boeretang 200,
2400 Mol, Belgium

Access:
D-DAT v.6 code is proprietary to SCK•CEN but SCK•CEN can perform model runs and share results as part of scientific collaborations
An Excel-based version 2 with more basic capabilities is freely available for use and can be downloaded from the Radioecology Exchange (https://wiki.ceh.ac.uk/display/rpemain/Marine+dynamic+model)

Internet link:
www.sckcen.be

Contact:
Prof. Jordi Vives i Batlle
jvibatll@sckcen.be

Involved in:
COMET

Related to:
ALLIANCE

The impact of the Fukushima nuclear accident on marine biota: Retrospective assessment of the first year and perspectives, Vives I Batlle J., Aono T., Brown J. E., Hosseini A., Garnier-Laplace J., Sazykina T., Steenhuisen F., Strand P. (2014), Sci Total Environ, 487, 143–153
Dynamic modelling of radionuclide uptake by marine biota: application to the Fukushima nuclear power plant accident, Vives i Batlle J. (2016), J Environ Radioact, 151, 502-511

COOLER

COmputation Of Local Electron Release

The effects of ionising radiation are typically summarised by Relative Biological Effectiveness (RBE) values. They guide the selection of radiation weighting factors, which are adopted in radiation protection and sometimes by legal regulations to estimate risks. Since RBE is defined as the ratio of the absorbed doses required by two radiations to cause the same effect, it is extremely important to be able to calculate precise dose values.

Photo: Personal archive

Dr Mattia Siragusa

addition, it contains (but it is not limited to) cellular models that ideally represent V79 cells, cultured under adherent or suspension growing conditions.

COOLER has been developed from monoenergetic electron sources, but it can also work with beta decay spectra. Extension of the code to other particles is possible, as well as to radionuclides that generate mixed field radiation or initiate a decay chain, provided that decay and spatial energy deposition data are implemented. As Monte Carlo codes are sometimes beyond the practical reach of the preclinical and clinical researcher, the use of analytical tools such as COOLER should be preferred.

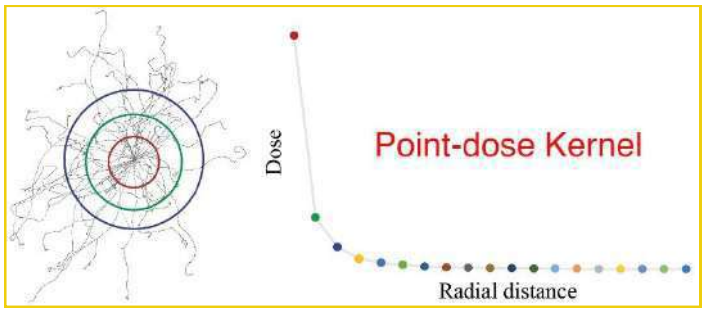


Photo: Mattia Siragusa/DTU-Nutech

Multiple electron tracks are generated in water, isotropically from a point source, using the Monte Carlo track structure code PARTRAC. The amount of energy delivered within consecutive spherical shells, concentric with the source, is scored and then divided by the volume of the corresponding shells. In COOLER, this is called a point-dose kernel.

Thanks to a partnership between The Hevesy Laboratory at The Technical University of Denmark and the Radiation Biophysics and Radiobiology group at the University of Pavia, a new tool, named COOLER, has been defined for dosimetry assessment at the subcellular scale. This tool is suitable to convert given distributions of administered low-energy electron-emitting radionuclides to radiation doses, a critical step in risk/benefit analysis for advancements in internal radiotherapy.

COOLER provides absorbed dose values *via* convolution of a geometrical term with a physical one. The geometrical part includes information on the cell type (e.g. the growing condition, the nuclear and cellular diameters ...) and the activity distribution. The physical term contains Monte Carlo-derived stopping power information which has been tabulated and stored in COOLER in the form of monoenergetic point-dose kernels. In its current version, the software can handle electron energies up to 50 keV. In

COOLER is a valuable tool for experiments carried out on living cells. In a recent application, it was used by the authors to study a realistic case of cellular contamination with tritiated water, that is, a radioactive form of water where stable H atoms are replaced with tritium. The software was employed to investigate the cell growing conditions and the tritium full beta-decay spectrum impact on absorbed doses, and subsequently on the RBE for clonogenic cell survival experiments.

To summarise, COOLER can perform accurate absorbed dose calculations for different cellular models, electron energy inputs and activity distributions. Hopefully this tool, and future versions of it, will be of benefit to research projects aimed at assessing the role of low-energy electrons in, for example, therapeutic applications and radiation protection scenarios.

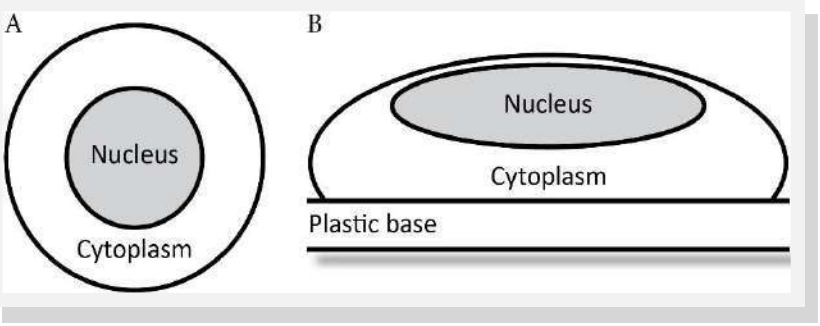


Photo: Mattia Siragusa/DTU-Nutech

Schematic representation of the cellular geometries included in COOLER. The suspension cell is spherical (panel A), while the adherent cell (panel B) is represented as an ellipsoid with the cytoplasm deformed by attachment to the cell culture flask; the nucleus is considered an ellipsoid.

ID Card:

Purpose:
General purpose: Absorbed dose calculation tool for subcellular energy depositions by internal electron emitters

Use:
Anyone familiar with MATLAB

Housed at:
Software repository at DTU-Nutech

Training proposed on the software:
On request

Access:
Open access. Licensed under the terms of the MIT licence

Internet link:
www.nutech.dtu.dk/english/research/medical-isotopes/open-source-software

Contact:
Dr Mattia Siragusa
masir@dtu.dk

Related to:
MELODI
EURADOS
EURAMED

The COOLER code: a novel analytical approach to calculate subcellular energy deposition by internal electron emitters, Siragusa M., Baiocco G., Fredericia P. M., Friedland W., Groesser T., Ottolenghi A., Jensen M. (2017), Radiat Res, 188 (2), 204–220
Radiobiological effects of tritiated water short-term exposure on V79 clonogenic cell survival, Siragusa M., Fredericia P. M., Jensen M., Groesser T. (2018), Int J Radiat Biol, 94 (2), 157-165

BRENDA

Biological Radiation Effects for Non-human Dose Assessment

BRENDA is a continuous, ordinary differential equations, dual life stage, logistic model for generic populations of wildlife, which is designed to assess the non-stochastic effects of radiation on repairable radiation damage, reproductive ability and mortality. Population change is modelled as a function of survival, fecundity, natural mortality and low density 'Allee' effects. Radiation-induced damages in young and adult life stages are modelled by means of a recovery pool representing the organism's repair system, which can itself be depleted by radiation or recover in a logistic manner. The direct effect of radiation on fecundity is also incorporated in the model.

Photo: Personal archive

Prof. Jordi Vives i Batlle

that the same model is also applicable for that type of radiation.

BRENDA is set-up in the ModelMaker 4 platform and, in this format, it has been extended for species with four life stages (benthic crustaceans). Further developments are underway to study radiation effects at the level of the ecosystem, such as time-dependent resources, inter-connected populations of different radiation sensitivity (predator/prey competition), migration of species between contiguous and unequally contaminated areas, and how historical doses can have effects over the generations (transgenerational effects, epigenetics and adaptation).

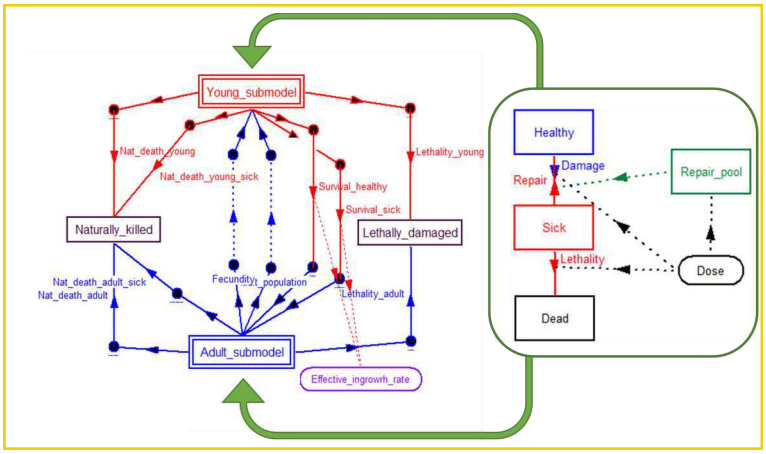


Photo: Jordi Vives i Batlle/SCK•CEN

BRENDA conceptual model in ModelMaker format (left) and detail of the repair mechanism present in both young and adult submodels (right), showing the relevant compartments (rectangles), fluxes (arrows) and variables (rounded rectangles).

The potential of BRENDA to assess the defensibility of screening values for the protection of wildlife has been evaluated in the course of the IAEA project MODARIA, where additionally BRENDA has been inter-compared with other population effects models. It remains a strong tool to assess protection at the level of ecosystems, helping to test the validity of the radiation protection benchmarks proposed at the ecosystem level.

The model has been tested against radiation effects data for freshwater fish and small mammal populations, predicting approximately the observed mortality, morbidity and reproductive changes for fish and mouse populations at various doses of γ-radiation as reported in the FREDERICA radiation effects database for wildlife. Experimental doses at which effects were observed, and those for which the model predicts the same effect, are well correlated. Limited data for low-energy β-exposures in mammals suggests

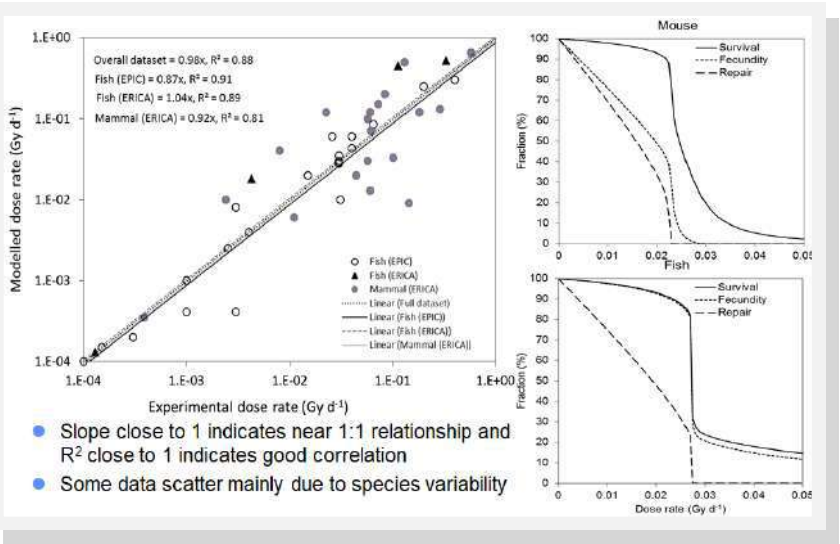


Photo: Jordi Vives i Batlle/SCK•CEN

Results of BRENDA simulation for external exposure of mice and fish to gamma rays.

ID Card:

Purpose:
Dynamic model for the assessment of the effects of radiation on repairable radiation damage, reproductive ability and mortality for age-structured populations of non-human biota.

Capacity:
The model has been applied to lobsters, mammals (mice, rabbits, wolves and deer), fish and phyto/zooplankton populations. It has been tested against radiation effects data at various doses of γ-radiation as reported in the FREDERICA radiation effects database for wildlife. The model has also been applied to cases involving α- and β-radiation.

Use:
Requires knowledge on how to use ModelMaker and some ability to configure the model for a population with a specific age structure, life history and radiosensitivity.

Housed at:
Current model versions for different species are implemented on the ModelMaker 4 for Windows® modelling platform, and reside at the host institute (SCK•CEN)

Training proposed on the software:
A training session has been given with a 2-age structure version of the model as part of the IAEA project MODARIA

Address:
Belgian Nuclear Research Centre (SCK•CEN)
Boeretang 200,
2400 Mol, Belgium.

Access:
The model is proprietary to SCK•CEN but we can perform model runs and share results as part of scientific collaborations.

Internet link:
www.sckcen.be

Contact:
Prof. Jordi Vives i Batlle
jvibatll@sckcen.be

Related to:
ALLIANCE

Dual age class population model to assess radiation dose effects on non-human biota populations, Vives i Batlle J. (2012), Radiat Environ Biophys, 51 (3), 225-243

An approach to the assessment of risk from chronic radiation to populations of European lobster, Homarus gammarus (L.), Vives i Batlle J., Wilson R.C., Watts S. J., McDonald P., Jones S. R., Vives-Lynch S. M., Craze A. (2010), Radiat Environ Biophys, 49 (1), 67-85

The EFFTRAN code

Efficiency transfer and TCS corrections for γ-ray spectrometry

EFFTRAN is a freely available computer code for the calculation of efficiencies and true coincidence summing correction factors in gamma-ray spectrometry. It has an MS Excel-based user interface, with VBA providing a link to the computational routines written in FORTRAN. Installation is very straightforward and full source code is provided as part of the package.

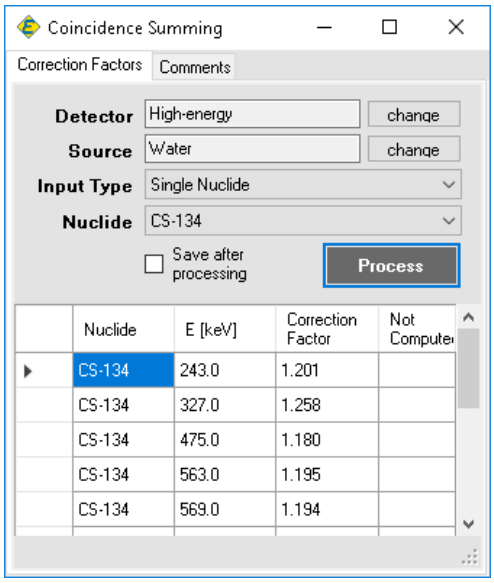


Photo: T. Vidmar/SCK•CEN

Calculation of coicindence summing correction factors with EFFTRAN.

In EFFTRAN, the efficiency transfer method is used for the calculation of efficiencies, and a calibration with a standard source is therefore required. The measured efficiency can then be transferred to a sample that differs from the standard, in size, composition and density. The computation of true coincidence summing correction factors does not require any measured data. However, with both methods, the parameters of a detector and source model need to be provided.

The coincidence library contains decay data on 300 radionuclides. True coincidence summing correction factors are provided for gamma rays, and gamma-gamma and gamma-X coincidences are taken into account.

Photo: T. Vidmar/SCK•CEN

Tim Vidmar

Calculations take only seconds to perform and can therefore be done routinely during the analysis of a measured spectrum. Materials can be defined as compounds and mixtures, and used for the construction of detector and source models.

Coaxial and planar detectors can be modelled, and the course types supported include cylindrical sources, point sources, filters and Marinelli beakers.

The code is primarily aimed at gamma-ray spectrometry laboratories that perform routine measurements and analysis of environmental samples. To date, the code has been used by some 300 such groups, many of whom are from developing countries.

Export and import of the efficiencies and the coincidence summing correction factors from Canberra's GENIE 2000 files and libraries is also provided.

EFFTRAN has been successfully validated and tested against similar codes of its kind and against experimental and synthetic data. Typical accuracy of the computed efficiencies and coincidence summing correction factors is a few percent. Its performance and algorithms have been described in several peer-reviewed articles published in international journals.

The code is available from the author upon request and completely free of charge.

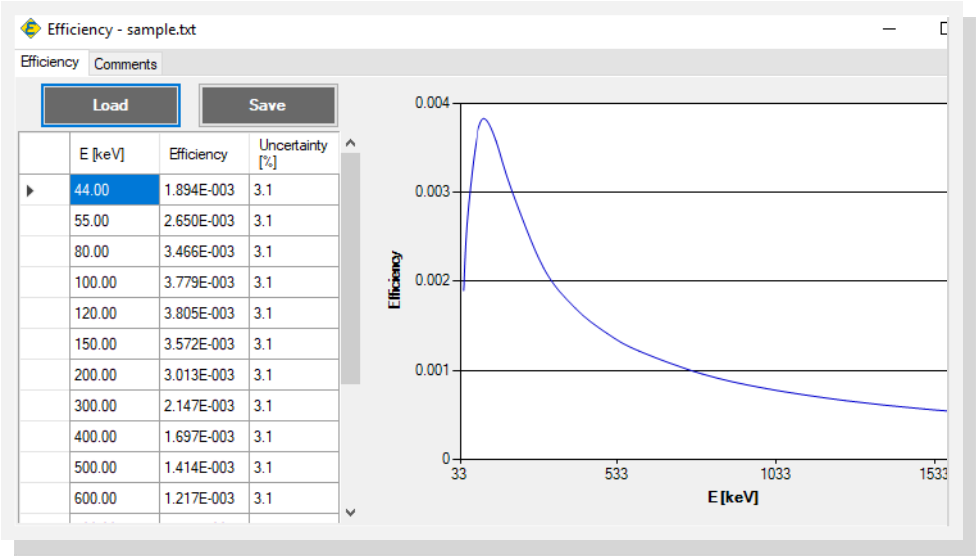


Photo: T. Vidmar/SCK•CEN

Displaying an efficiency curve in EFFTRAN.

EFFTRAN - A Monte Carlo efficiency transfer code for gamma-ray spectrometry, Vidmar T. (2005), Nucl Instrum Methods Phys Res A, 550 (3), 603-608

Calculation of true coincidence summing corrections for extended sources with EFFTRAN, Vidmar T., Kanisch G., Vidmar G. (2011), Appl Radiat Isot, 69 (6), 908-911

ID Card:

Purpose:
Efficiency transfer and calculation of true coincidence summing correction factors in gamma-ray spectrometry

Capacity:
No limitations

Use:
Installation of a local copy; expertise in gamma-ray spectrometry required; user friendly interface

EFFTRAN can be accessed remotely from the user's own institute, if necessary with help from a specialist. It is easy to use for anyone with basic skills in the field

Housed on:
Local computer

Training proposed on the software:
EC- and IAEA- organised courses on gamma-ray spectrometry

Address:
SCK•CEN
Belgian Nuclear Research Centre
Boeretang 200
2400 Mol
Belgium

Access:
Freely available from the author upon request

Internet link:
www.efftran.com

Contact:
Tim Vidmar
tim.vidmar@sckcen.be
+32 14 33 21 10

Related to:
ALLIANCE

The MCDA Tool

Providing decision support considering uncertainties

In crisis management, decision-makers may be presented with several possible strategies that can be applied to a given scenario. Usually many different criteria have to be considered to determine the benefit of each strategy, in order to select the most appropriate strategy. The decision process becomes more difficult if, instead of a single decision-maker, it involves a group of decision-makers, each with different opinions on the significance and weight of the criteria. The complexity is further increased if criteria and opinions are affected by uncertainty, which is frequently the case.

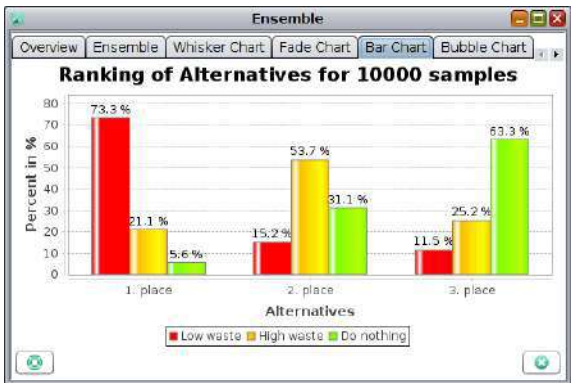


Photo: KIT/IKET

Ensemble evaluation for 3 strategies with 4 criteria all affected by uncertainty

Multi Criteria Decision Analysis (MCDA) is a method that supports a group of decision-makers in finding a consensus of opinion by systematically analysing the benefit of the strategies for the various criteria and ranking these strategies. MCDA was implemented as a Java application and was enhanced for the CONFIDENCE project to enable it to handle uncertainties.

The application provides an interactive user interface. At the start, the possible strategies are determined by the decision-makers. Next, the group has to agree on the criteria they want to consider. Then the group is asked to determine the weights of the criteria in a moderated discussion. Finally, for each strategy developed, the criteria have to be input along with measured, computed or estimated values. In the evaluation step, the criteria values are normalised to make them comparable, and are then summed for each strategy according to their weight. Thus for each strategy, a value is computed (the higher the value, the better) and the strategies are ranked accordingly. The results can be visualised in different types of charts or as a textual report. The screenshot of the tool shows 4 windows displaying, for example, the matrix tree of strategies by criteria, a result bar chart, a human readable summary and the weight management. As the set up takes some time to run, the MCDA tool is better suited to long term decision-making in situations where there is no time pressure.

Photo: KIT/IKET

Dr Tim Müller

Criteria and weights can be defined as uncertain, e.g. by determining probabilistic distributions or by histograms derived from measurements or surveys. These uncertainties can be evaluated using ensemble techniques. For this, numerous deterministic MCDAs are generated randomly from the probabilistic MCDA. They are then evaluated iteratively and the results are statistically aggregated. The visualisation example shows an aggregation of 10,000 samples. As computational effort was very low here, the evaluation took less than a second to finish. As can be seen, the strategy “Low waste” was ranked in 1st place in 73% of all cases, in 2nd place in 15% of cases, and in 3rd place in 11% of cases. Thus this strategy seems to be the best choice, as it is on average the best strategy. Besides a textual summary, several other means are available for ensemble visualisation.

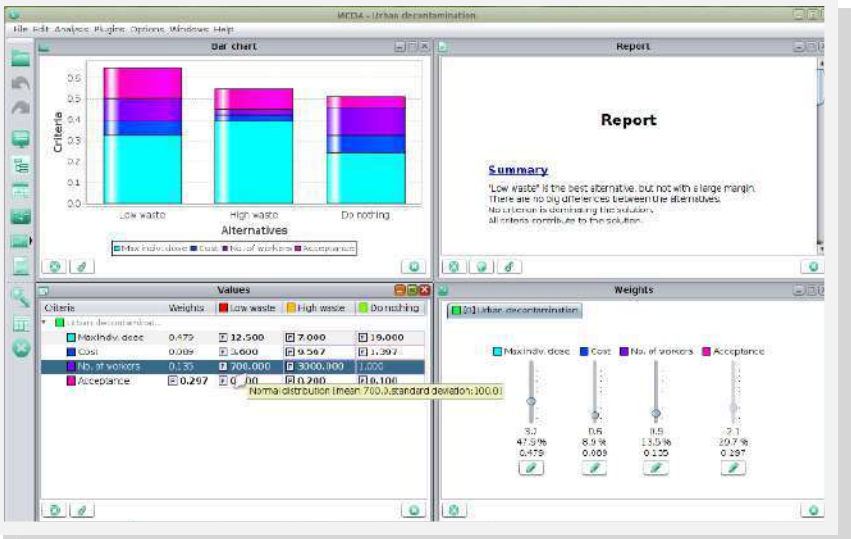


Photo: KIT/IKET

The GUI provides means for editing preferences (weights) and values of criteria as well as analytical tools like charts, human readable summary, or stability analysis

CONFIDENCE: Dealing with uncertainties in multicriteria decision analysis tools, Raskob W., Müller T. (2018) in RICOMET

A transparent approach for prioritising security measures, Müller T., Meng S., Raskob W., Wiens M., Schultmann F. (2015), Future Security, 217-224

ID Card:

Purpose:
To support a group of decision-makers in reaching a consensus.

Capacity:
A group of decision-makers is supported to elaborate common preferences in the choice of decision criteria. Possible strategies are ranked according to the weight of the chosen criteria. Uncertainties of preference and criteria can be taken into account.

Use:
The application can be used to define criteria and strategies according to a given scenario. It allows interactive discussion between decision-makers to decide common preferences for the selection of criteria. Results are presented as reports and charts. Video tutorials and user guides are available online.

Address:
Karlsruhe Institute of Technology (KIT)
Hermann-von-Helmholtz-Platz 1
76344 Eggenstein-Leopoldshafen
Germany

Access:
The tool is a Java application and is provided free of charge for non-commercial use. It can be downloaded from the web site indicated below.

Internet link:
https://portal.iket.kit.edu/MCDA/

Contact:
Dr Tim Müller
Tim.Mueller@kit.edu
+49 721 608 24691

Related to:
NERIS

Add-on: Infrastructures from Special Issues

NASA Space Radiation Laboratory (NSRL)

GCR simulations and Solar Particle Event simulations

The NASA Space Radiation Laboratory irradiation facility was commissioned in 2003 to simulate the space radiation environment for biological experiments as well as physics, dosimetry and electronics testing. The facility is owned by NASA and managed by Brookhaven National Laboratory (BNL) for the US Department of Energy. NSRL operates ~1,200 hours per year in three cycles (spring, early summer and autumn).

Photo: BNL

NSRL principal investigator Dr Adam Rusek checks the beam alignment

Beams of ions from protons to gold are extracted from the Booster Accelerator and transported to a shielded target area. The 400-ft^2 target area houses a 10-ft long optical bench, beam handling and sample changing equipment, and dosimetry. Beam energy ranges are 50-2500 MeV for protons and 50-1500 MeV/n for ions between He and Fe. Heavier ions from Z=27-79 are limited to ~350-500 MeV/n.

Beam spots with dimensions up to 20 x 20 cm^2 and 95% - 99% uniformity are typical, with a maximum dose rate of 10 Gy/min. For low fluence studies, rates as low as 100 and 2000 particles/cm^2 per spill for HZE ions and protons, respectively, are possible. A "large-beam" configuration of 60 x 60 cm^2 and 90% - 95% uniformity also exists, with a maximum dose rate of ~0.5 Gy/min.

The target area connects to a 4,560- ft^2 support facility with biological experiment stations for cell culture and a short-term animal facility, as well as an area for physics/run-control use. Long-term laboratory space and an accredited animal facility is available in an adjacent building. On-site housing accommodations for users are also available.

Photo: BNL

Dr Peter Guida & Dr Adam Rusek

The NSRL can generate a spectrum of ion beams to approximate the primary and secondary GCR field experienced at human organ locations within a deep-space vehicle. The majority of the dose is delivered from protons (~60-70%) and alpha particles (~10-20%) with heavier ions (Z>3) contributing the remainder. The "NSRL GCR Simulator" consists of 33 beams including 4 proton energies plus degrader, 4 helium energies plus degrader, and the five heavy ions of C, O, Si, Ti, and Fe. A polyethylene degrader is used with the 100 MeV/n H and He beams to provide a distribution of low energy particles. A 500 mGy simulation, delivering doses from each of the 33 beams, requires 75-90 mins.

To more closely simulate the low dose rates found in space, sequential field exposures can be divided into daily fractions over 2-4 weeks, with individual fractions as low as 0.1-0.2 mGy. In the large beam, 54 special housing cages can accommodate 2-3 mice each for a 90 min duration or ~20-36 individually housed rats (depending on age, species, and orientation).

The NSRL Building

Photo: BNL

BROOKHAVEN NATIONAL LABORATORY

ID Card:

Exposure type:
External

Source:
Accelerator

Dose rate:
<10 Gy/min

Irradiation type:
Proton, Helium and heavy ions

Irradiated organism type:
Cells, animals (rodents, fish, invertebrates), plants

Address:
NASA Space Radiation Laboratory
at Brookhaven National Lab
Bldg. 958
Upton, New York 11973

Access:
NASA and non-NASA funded research

Supporting lab:
Cell/molecular biology, animal procedures

Internet link:
https://www.bnl.gov/nsrl/

Contact:
Adam Rusek
rusek@bnl.gov
+1-631-344-5830

Peter Guida
guida@bnl.gov
+1-631-344-2913

Reference field specification and preliminary beam selection strategy for accelerator-based GCR simulation, Slaba T. C., Blattnig S. R., Norbury J. W., Rusek A., La Tessa C. (2016), Life Sci Space Res (Amst), 8, 52-67

Overview of the NASA space radiation laboratory, La Tessa C., Sivertz M., Chiang I. H., Lowenstein D., Rusek A. (2016), Life Sci Space Res (Amst), 11, 18-23

CIEMAT External Dosimetry Service and Retrospective Luminescence Dosimetry Lab

The CIEMAT **External Dosimetry Service (EDS)** has provided dosimetry to Spanish customers since 1959. The CIEMAT EDS is currently approved by the Nuclear Safety Council (CSN), the Spanish regulatory body, and accredited according to the ISO-17205 standard by the Spanish National Accreditation Body (ENAC) for the determination of the personal dose equivalents $H_p(10)$ and $H_p(0,07)$ and the ambient dose equivalent $H^*(10)$.

For personal dosimetry, the thermoluminescent dosimetry system is based on a combination of two $Li_2B_4O_7$ and two $CaSO_4$ detectors, with different filters, for whole body dosimetry and on one $Li_2B_4O_7$ detector inside a ring hanger for extremity dosimetry. Dosimeters are read in two automatic readers with optical heating. Calibration is performed in a reference metrology laboratory in terms of the operational quantities and a ^{137}Cs panoramic irradiator is routinely used for periodic internal verification. The CIEMAT EDS manages approximately 1,000 whole-body and 100 extremity dosimeters a month.

For environmental and area monitoring, the dosimetry system is based on a combination of six LiF:Mg,Ti and four LiF:Mg,Cu,P thermoluminescent detectors, enclosed inside a holder designed and manufactured by CIEMAT. Dosimeters are read in two automatic readers that use hot nitrogen as a heating method. Two programmable ovens are used for annealing and pre-readout thermal treatment of the dosimeters. As for personal dosimeters, calibration is performed in a reference metrology laboratory. A ^{90}Sr beta irradiator is used for periodic routine verification. The CIEMAT EDS monitors approximately 100 environmental stations and 50 workplaces.

The CIEMAT EDS regularly participates in national and international intercomparison exercises for whole body, extremity, and environmental dosimeters, mainly organized by the CSN and the European Radiation Dosimetry Group (EURADOS). The results confirm the competence of the laboratory to produce valid results.

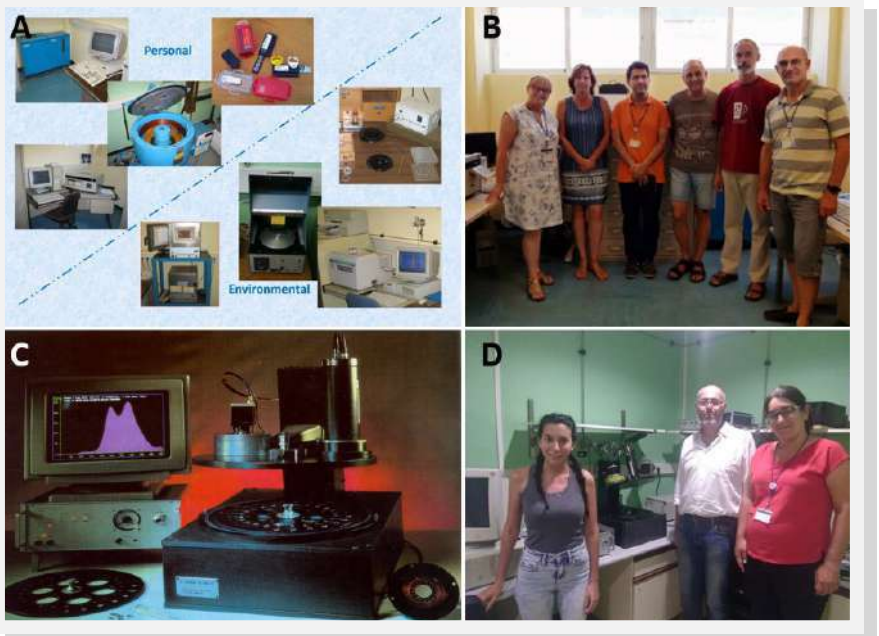
The CIEMAT EDS team is involved in two EURADOS Working Groups: Harmonization of Individual Monitoring and Environmental Dosimetry. These activities contribute to increasing quality and reliability in the protection of workers and the public against ionizing radiation.

Photo: CIEMAT

Ana Romero & Virgilio Correcher

The research activities of the laboratory are focused on the numerical analysis and simulation of thermoluminescence glow curves for improving dose assessment, the study and development of single-exposure neutron spectrometers for applications in workplace monitoring, and the implementation of a neutron-dosimetry system based on track detectors for personal monitoring.

The CIEMAT has a **Retrospective Dosimetry Laboratory** for the preparation of ceramic materials and later dosimetric evaluation by luminescent methods. Preparation includes mechanical, chemical, and thermal treatment to separate the components from the matrix or mineral phases with dosimetric properties. Evaluation stages apply thermoluminescence (TL) or optically-stimulated luminescent (OSL) techniques for situations in which there is no conventional dosimetry measurement system available (emergencies in radiological accidents), the detection of irradiated food, dating, spatial dosimetry, etc. The CIEMAT has access to experimental techniques for structural characterization of mineral phases under study in cooperation with the CSIC Museum of Natural Sciences.



A) CIEMAT EDS equipment for TL dosimetry B) CIEMAT EDS personnel: A. Romero, M. García, J.F. Benavente, J.L. López, A. González, R. Rodriguez. Not present: M. García, A. Hernanz, R. Martín
C) TL/OSL reader D) CIEMAT Retrospective dosimetry laboratory personnel: A. Zabala, V. Correcher, I. Sarasola

Ciemat EDS: ISO/IEC 17025 accreditation and 3 y of operational experience as an accredited laboratory, Romero A. M., Rodríguez R., López J. L., Martín R., Benavente J. F. (2016), Radiat Prot Dosim, 170 (1–4), 70–73
UV effect on the cathodo- and thermoluminescence properties of a gem-quality Cr-rich diaspore (α-AlOOH), Topaksu M., Correcher V., Boronat C., Garcia-Guinea J., Portakal Z. G., Akça S. (2018), Appl Radiat Isotopes, 141, 101-106

Ciemat
Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas

ID Card:

Platform type:
External Dosimetry Service
External dosimetry: personal and environmental

Retrospective Luminescence Dosimetry Lab
Retrospective Dosimetry

Main techniques proposed:
External Dosimetry Service
Thermoluminescence dosimeters: $Li_2B_4O_7$:Cu; $CaSO_4$:Tm; LiF:Mg,Cu,F; LiF:Mg,Ti

Retrospective Luminescence Dosimetry Lab
Thermoluminescence

Users:
External Dosimetry Service
~ 1,000 exposed workers using whole body dosimeters (monthly monitoring)
~ 200 exposed workers using extremity dosimeters (monthly monitoring)
~ 100 stations with environmental dosimeters (three-month period)
~ 50 points with area monitoring (one-month period)

Retrospective Luminescence Dosimetry Lab
Researchers

Address:
CIEMAT, External Dosimetry. Avda. Complutense 40, E34, P2-03
28040 – Madrid, Spain

Access:
The facility is open to joint research collaborations

Contact:
External Dosimetry Service
Ana M. Romero
ana.romero@ciemat.es
+34 913466250

Retrospective Luminescence Dosimetry Lab
Virgilio Correcher
v.correcher@ciemat.es
+34 913466322

Related to:
EURADOS

AIFIRA Microbeam

Study of radiation-induced response by targeted irradiation

The AIFIRA facility (Applications Interdisciplinaires des Faisceaux d'Ions en Région Aquitaine) is a small scale ion beam facility equipped with a single stage electrostatic accelerator delivering bright beams of light ions (H^+, D^+, He^+) in the MeV energy range. The facility, run by CENBG (Centre d'Etudes Nucléaires de Bordeaux-Gradignan, a laboratory of the University of Bordeaux and CNRS/IN2P3), provides ion beam irradiation, analysis and imaging techniques to academic research groups and companies.

Photo: H. Seznec/CENBG

Dr. Philippe Barberet

Recovery After Photobleaching) capabilities on the fluorescence microscope.

More recently, thin diamond detectors, developed in collaboration with CEA-LIST, have been inserted upstream the sample enabling a precise detection of every single delivered particle while preserving the microbeam lateral resolution. The combination of all these features allowed for example to measure the accumulation of DNA double strand break proteins in single alpha-particle tracks in the first minutes after irradiation (Muggiolu et al. 2017). The irradiation protocols were also recently extended to perform targeted irradiation of specific cells or organs in the *C. elegans* nematode (Torfeh et al. 2019).

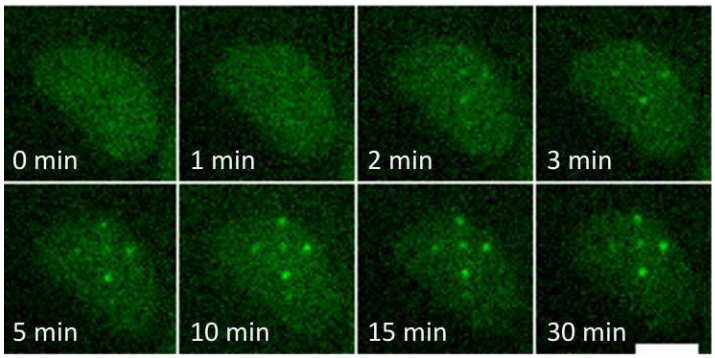


Photo: P. Barberet/University of Bordeaux

Online time-lapse microscopy of the RNF8-GFP protein (DNA double-strand breaks) in a nucleus irradiated with 5 single α-particles on the microbeam line. The irradiation takes place at t=0 and 5 α-particles are delivered on a cross pattern. Scale: 10 µm (source Muggiolu et al. 2017).

AIFIRA is open to external users and equipped with a microbeam line dedicated to targeted irradiation of living cells at the micrometer scale. This beamline was developed by the local research team ("Ionizing Radiation and Biology", iRiBio group) and the technical staff of CENBG. It is operational since 2013 and constantly upgraded. Irradiation of sub-cellular structures (nucleus/cytoplasm) can be conducted with protons (12 keV/µm) or helium ions (140 keV/µm) with an accuracy of about 2 µm. The early radiation-induced response can be measured online by following GFP- or RFP-tagged proteins using fluorescence time-lapse imaging. In the last years, technical upgrades have been conducted such as the installation of FRAP (Fluorescence

A L2 laboratory for cell culture and microbiological preparations was also developed by the local research team (iRiBio group) in close proximity to the microbeam facility. Access to the microbeam and the laboratory can be considered in the frame of collaborations with the iRiBio group at CENBG.

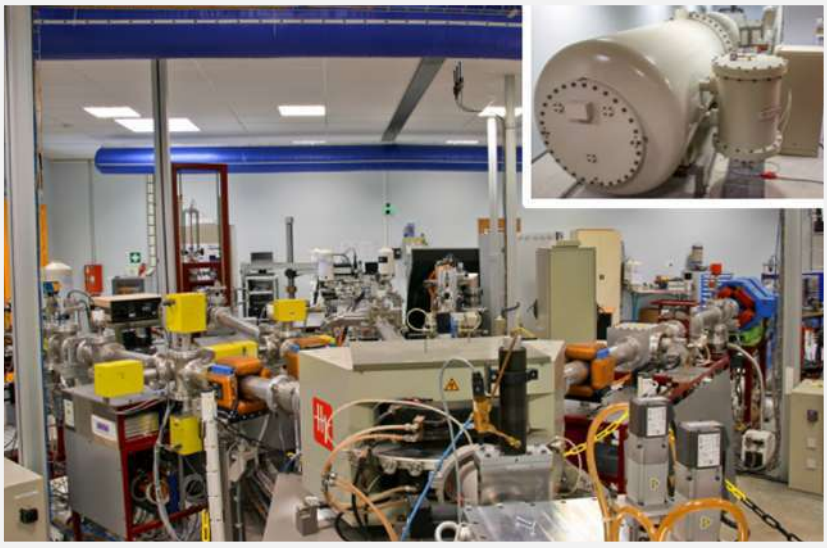


Photo: P. Barberet/University of Bordeaux

The AIFIRA facility and its 5 beamlines

ID Card:

Exposure type:
External

Source:
Single-ended 3.5 MV electrostatic accelerator (Singletron™, HVEE)

Dose rate:
Single ion irradiation

Irradiation type:
Proton and alpha-particles, up to 3 MeV. Horizontal beam.

Irradiated organism type:
Cells and *C. elegans*

Address:
19 chemin du solarium CS10120
33175 GRADIGNAN Cedex
FRANCE

Access:
Joint research collaborations

Supporting lab:
Cell culture lab, instrumentation lab

Internet link:
http://www.cenbg.in2p3.fr/-Plateforme-AIFIRA

Contact:
Dr. Philippe Barberet
barberet@cenbg.in2p3.fr

Dr. Hervé Seznec
seznech@cenbg.in2p3.fr

+33 5 57 12 09 03

Related to:
MELODI

Single α-particle irradiation permits real-time visualization of RNF8 accumulation at DNA damaged sites, Muggiolu G., Pomorski M., Claverie G., Berthet G., Mer-Calfati C., Saada S., Devès G., Simon M., Seznec H., Barberet P. (2017), Sci Rep, 7, 41764

Monte-Carlo dosimetry and real-time imaging of targeted irradiation consequences in 2-cell stage *Caenorhabditis elegans* embryo, Torfeh E., Simon M., Muggiolu G., Devès G., Vianna F., Bourret S., Incerti S., Barberet P., Seznec H. (2019), Sci Rep, 9, 10568

The Calliope Facility

^{60}Co gamma irradiation facility at ENEA Casaccia Research Centre

The Calliope facility at the ENEA-Casaccia Research Centre in Rome, Italy, was built in 1967-1968. Since the '80s the facility has been involved in radiation processing research on materials and devices to be used in hostile radiation environments such as nuclear plants, Space and High Energy Physics experiments.

The plant is a pool-type irradiation facility with a ^{60}Co (energy= 1.25 MeV) radioisotopic source in a high volume (7.0 x 6.0 x 3.9 m^3) shielded cell. The maximum licensed activity is 3.7 x 10^{15} Bq (100 kCi) and the current facility activity is 2.2 x 10^{15} Bq (December 2019) with a maximum dose rate of 9.6 kGy/h (December 2019).

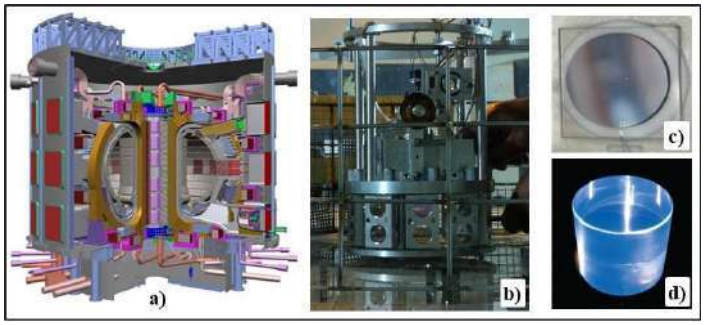


Photo: ENEA - FSN

a) ITER scheme; b) irradiation set-up of optical filters and customized piezoelectric motor for the In-Vessel Viewing System (IVVS); c) single-crystal diamond and d) plastic scintillator for the ITER Radial Neutron Camera (RNC).

The facility has dedicated set-ups, diagnostic and monitoring systems. The irradiation tests can be performed in special environmental atmosphere (such as vacuum, gas mixtures other than air) or at different temperatures and with remote monitoring and acquisition.

A dosimetric laboratory is available at the Calliope facility. Depending on the absorbed dose range of interest, several dosimetric systems are used: Fricke solution (20 – 200 Gy), Red Perspex (5 – 50 kGy) and radiochromic (1 kGy – 3 MGy), alanine-ESR (1 Gy – 500 kGy), Thermo Luminescent Dosimetry TLD (0.1 mGy – 100 Gy) and RADFET (0.01 – 1000 Gy) dosimeters. Among them, the relative solid-state and electronic dosimeters (Red Perspex, radiochromic, alanine-ESR, TLD and RADFET) are periodically calibrated with the Fricke absolute dosimeter. The relative dosimetric systems are used to determine the dose rate value when the Fricke solution is not applicable.

For each test, specific irradiation and dosimetric certifications are issued to the customers.

Photo: ENEA - FSN

Irradiation cell with ^{60}Co sources rack and the platform for sample positioning (photo acquired during an irradiation test by local remote camera acquisition).

A. Cemmi I. Di Sarcina G. Ferrara

The Calliope is deeply involved in qualification and research activities, in the framework of international projects and collaborations with industries and research institutions (CMS ECAL at LHC CERN, Belle II at SuperKEKB, SPARK Project H2020, IAEA, ITER, F4E, EUROFUSION). Qualification tests, in compliance with the international standard specifications (such as ESA/SCC 22900, Issue 5 and MIL-STD-883), are mainly performed on components, devices and systems for applications in hostile environments, such as nuclear plants and aerospace, and on concrete matrices for nuclear waste disposal and storage.

The Calliope irradiation plant is the Italian gamma facility recommended by the European Space Agency (ESA) for the Space qualification tests in the framework of the ASIF Programme (Italian Space Agency Supported Irradiation Facility).

Research activities are focused on the investigation of gamma irradiation induced effects on chemical and physical properties of different materials, such as radiation detectors, scintillating crystals, glasses and polymers, for applications in nuclear plants, aerospace and High Energy Physics experiments. Material characterization and biological research are also carried out on conservation and preservation of cultural heritage artifacts, agriculture, AgroSpace and environmental field.

ID Card:

Exposure type:
External

Source:
Gamma source (energy ~1.25 MeV)

Dose rate:
0 – 9.6 kGy/h

Irradiation type:
^{60}Co radioisotopic source

Irradiated organism type:
Inorganic materials, components and devices, biological matrices

Address:
Calliope Facility
ENEA, Casaccia Research Center
Via Anguillarese 301 – 00123
Rome, Italy

Access:
Fee-based for services;
free for scientific collaborations/ projects

Supporting lab:
Dosimetric laboratory; optical (UV-VIS-IR), spectroscopic (ESR) and fluorescence characterizations; climatic chamber for ageing tests

Internet link:
www.enea.it/en

Contact:
Alessia Cemmi
alessia.cemmi@enea.it
+39 06 3048 3169

Related to:
EURADOS

Gamma irradiation Calliope facility at ENEA-Casaccia Research Centre (Rome, Italy), Baccaro S., Cemmi A., Di Sarcina I., Ferrara G., ENEA Report ENEA-RT-2019-04, ISSN 0393-3016

Rad-hard properties of the optical glass adopted for the PLATO space telescope refractive components, Corso A. J., Tessarolo E., Baccaro S., Cemmi A., Di Sarcina I., Magrin D., Borsa F., Ragazzoni R., Viotto V., Novi A., Burresi M., Pellowski F., Salatti M. et al. (2018), Opt Express, 26 (26), 33841-33855

ZATU (Zone Atelier Territoire Uranifère)

A place for interdisciplinary research on (TE)-NOR

Member of European and International Long Term Ecological Research Infrastructures, the French national network of Zones Ateliers (RZA) labelled by CNRS develops a specific scientific approach based on observations and experiments on workshops sites, to conduct multidisciplinary research in the long term. It enables to survey the complex relationships between human activities and the functioning of ecosystems to be studied. The RZA is recognized by ALLENVI, as a Long-Term Experimentation and Observation System for Research in Environment: the SOERE RZA. The RZA is also a member of eLTER Europe and of iLTER for the international.

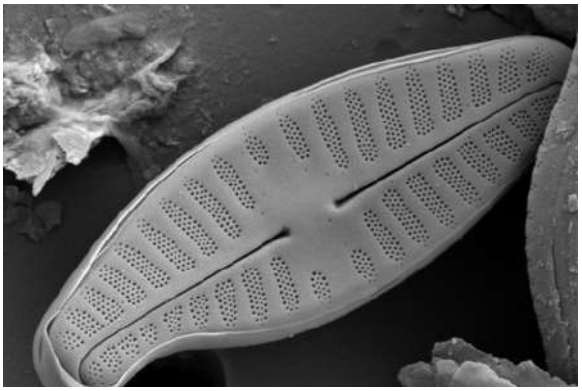


Photo: ERIN, LIST

SEM observations of teratological valves for a diatom species, *Planothidium frequentissimum*, living in radioactive spring water.

Labelled in January 2015, the Zone Atelier Territoires Uranifères (ZATU) focuses on the environments characterized by chronic radiation of natural or enhanced natural origin. A contaminated wetland downstream of a mine tailings repository located in a small watershed and the presence of natural radioactive mineral sources nearby provide an ideal setting to conduct long-term radioecological research in NOR and TE-NOR contaminated sites.

The multidisciplinary fundamental research program builds upon multiple expertise (radiochemists, physicists, geochemists, biologists, ecologists, and researchers in human and social sciences) supported by long-term observation through site instrumentation (radon detectors, piezometers, ...). Focused on adaptation and evolution of life in the presence of enhanced natural radioactivity, on transport and transfer of radionuclides in food webs, and the perception of the associated risk, the research program has for main aim to integrate the data into a Socio-Ecological System (SES) model to help decision makers and stakeholders for the territorial management.

Researchers aim at opening the following locks:

- How to achieve "multi-scale" approaches, from the past to the future *via* the present, from the sample studied in the laboratory to the watershed of a mining site, from the molecule to the ecosystem scale?
- How can mechanistic approaches be integrated/taken into account in impact assessment codes?
- What are the effects of radioactivity on adaptive or evolutionary processes in living organisms (recent vs chronic long-term exposure)?
- How can the effect of radioactivity on living organisms be distinguished from other confounding factors and how can the effects of radiation be dissociated from chemical effects?
- What are the socio-cultural dimensions of risk?

Photo: Personal archive

Gilles Montavon

Recently renewed for 2020-2024, the ZATU involves 22 laboratories from various research organizations (CNRS, CEA, IRSN, BRGM) and French universities. Among the priority actions of ZATU, comparing the methods/results with similar approaches applied to other contaminated sites could help assess whether the risks of low doses to the environment can be effectively addressed. The ZATU is also open to collaborators from the ALLIANCE platform.

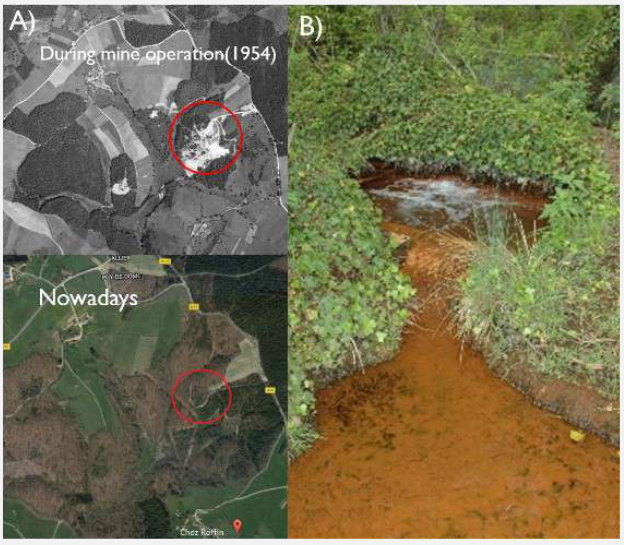


Photo: IGN and Google maps for (A), GEOLAB (UMR CNRS 6042) for (B)

Study of TE-NOR on the 'Atelier site' (Old uranium mine of Rophin (A)) of the ZATU and of the NOR in its observatories (i.e. radioactive mineral springs (B))

ID Card:

Type of ecosystem contaminated:
Wetland, forest, natural springs

Compartment of environment contaminated:
Water, soil, sediments

Contamination source:
NOR and TE-NOR (U, Ra, Rn, Po)

Radioactivity or dosimetric characteristics:
Concentrations: e.g. 2000 ppm ^{238}U, 40 Bq/g ^{226}Ra, 4 kBq/L ^{222}Rn....
Dose rates: up to 2000 nSv h^{-1}

Total contaminated area:
Watershed, ~5 km^2

Species exposed/present in the site:
Microorganisms, diatoms, chickadees, invertebrates, trees...

Authorized related data/samples:
Permission to access and work at the site has to be obtained *via* ZATU and is subject to signature of a working agreement. Contact Patrick.chardon@clermont.in2p3.fr.

Presence of an associated contamination:
Heavy metals (As, Pb, ...)

Supporting lab:
No laboratory infrastructure available on site.

Address:
LTSER "Zone Atelier Territoires Uranifères", Clermont-Ferrand, France

Internet link:
https://zatu.org/

Contact:
David Biron
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+33 (0)4 73 40 74 58

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Patrick.chardon@uca.fr
+33 (0)4 73 40 72 25

Gilles Montavon
montavon@subatech.in2p3.fr
+33 (0)2 51 85 84 20

Related to:
ALLIANCE

The effect of natural radioactivity on diatom communities in mineral springs, Millan F., Izere C., Breton V., Voldoire O., Biron D. G., Wetzel C. E., Miallier D., Allain E., Ector L., Beauger A. (2019), Bot Lett, 167 (1), 95-113

Uranium quantification of oak tree rings (*Quercus petraea*) from a former uranium mining site by High Resolution Inductively Coupled Plasma Mass spectrometry in Laser Ablation and Solution modes, Loni Y. H., David K., Larrue S., Grambow B., Corona C. et al. (2019), Spectrochim Acta B, 161, 105709

NASA's LSAH and LSDA repositories

Enabling use of archived data

Jessica A. Keune, PhD & Diedre M. Thomas

The Human Health and Performance Directorate (HH&P) at Johnson Space Center (JSC) is charged with optimizing astronaut crew health and performance and mitigating spaceflight risks through countermeasures, habitability, environmental factors research, medical operations, and directorate support functions that enable mission success.

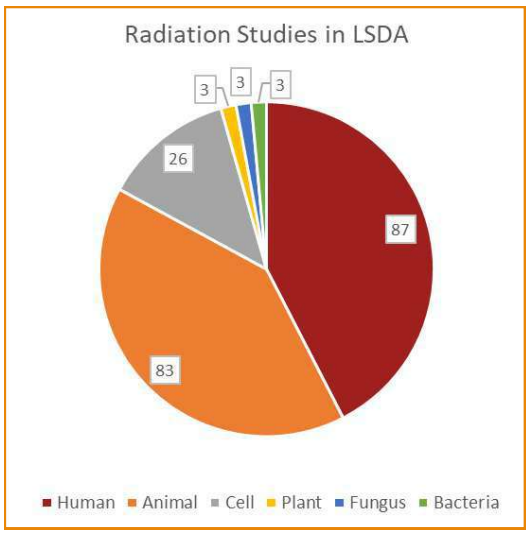


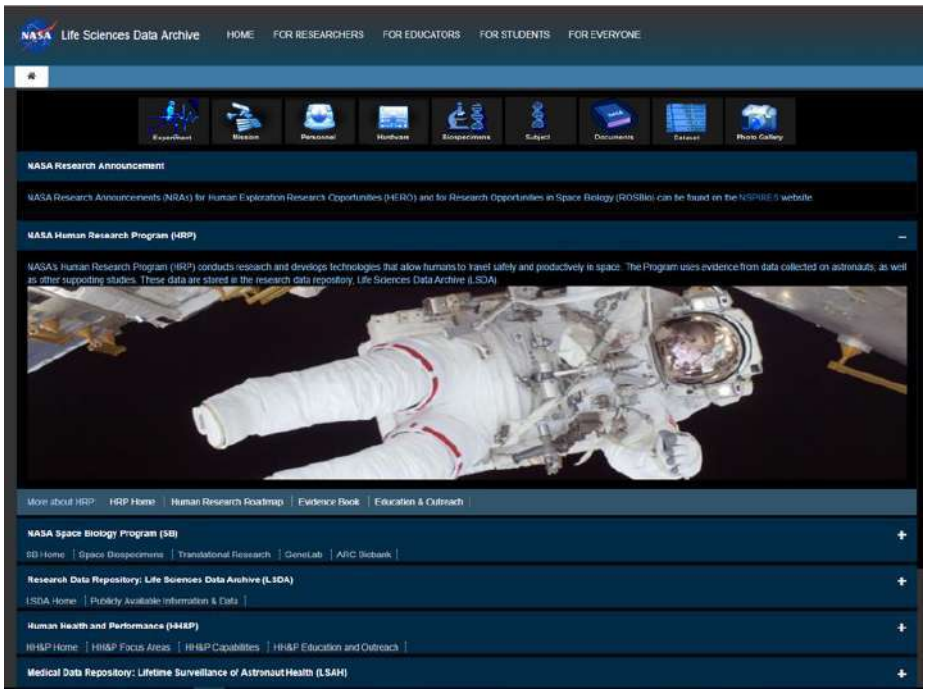
Photo: NASA

The HH&P houses over 50 years of records, archives, and databases of NASA's human spaceflight experience. Two groups within HH&P are working together to implement processes outlined in the HH&P Data Sharing Policy: the Lifetime Surveillance of Astronaut Health (LSAH) program and the Life Sciences Data Archive (LSDA). These groups have made great strides in sharing astronaut data with the spaceflight operational, clinical, and research communities.

Medical and research life sciences data are housed in two separate systems of LSAH and LSDA. The LSAH data system holds all ground and flight medical data for astronauts, vehicle environmental data, and data from non-flight assignable former astronauts who return to JSC annually for occupational health surveillance monitoring. The LSDA holds all research data collected through NASA-funded life sciences investigations, including data collected on astronauts, control and ground analog subjects, plants, animals, and cells. The human data held in both systems are subject to the Privacy Act of 1974, and the agency also voluntarily adheres to the applicable elements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Data from both LSAH and LSDA systems are accessible by request through a single, integrated web-based process. The access point for all data is through the public website.

With regard to space radiation, LSAH primarily contains effective doses of radiation exposure reported from dosimeters and medical devices. LSDA contains records of over 200 radiation-related studies addressing these risks to not only humans, but also to a variety of animals, bacteria, and plants. Additionally, the LSDA enables access to over 7,000 irradiated animal specimens that are available by request to approved researchers. More information on the specimens can be found through the listed biobank link (https://lsda.jsc.nasa.gov/Home/).

LSDA website interface



ID Card:

Database topic:
LSAH: Astronaut Health Information

LSDA: NASA-sponsored life sciences experiments

Information available type:
NASA Medical and Research Data, with supporting information

Data type:
LSAH: Medical record numeric and image data

LSDA: Experiment descriptions with results, numeric and image data, and animal biospecimens

Link with a biobank:
Yes - https://lsda.jsc.nasa.gov/Biospecimen

Exportable:
No

Species:
Various – human, animal, bacteria, fungus, cells

Internet link:
https://lsda.jsc.nasa.gov/MRID

https://lsda.jsc.nasa.gov

https://www.nasa.gov/ames/research/space-biosciences/alsda

Access:
Publicly accessible

Contact:
https://lsda.jsc.nasa.gov/Common/Feedback

LSAH
Jessica A. Keune
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LSDA
Diedre M. Thomas
jsc-lsda-archive@mail.nasa.gov

NASCA report 2: Longitudinal study of relationship of exposure to space radiation and risk of lens opacity, Chylack L. T. Jr., Feiveson A. H., Peterson L. E., Tung W. H., Wear M. L., Marak L. J., Hardy D. S., Chappell L. J., Cucinotta F. A. (2012), Radiat Res, 178 (1), 25-32

LSAH and LSDA Repositories: Enabling use of archived NASA data, Lee L. PowerPoint presentation

The 'hematopoietic system' database for Mayak nuclear workers chronically exposed to ionizing radiation

Hematopoietic effects following chronic radiation exposure

The hematopoietic system is known to be highly sensitive to ionizing radiation. A number of papers describe effects of acute radiation exposure in the hematopoietic system considering various populations. Meanwhile, studies of hematopoietic effects induced by chronic low-dose radiation exposures are sparse.

To facilitate studies of dose and dose rate effects of chronic occupational exposure on the human hematopoietic system we developed a database for hematopoietic data for the worker cohort employed at the Mayak PA, the first Russian nuclear production facility. The cohort was described in details earlier [1, 2]. It should be highlighted that the medical follow-up of the workers was performed since the very first days of the Mayak PA operation and included a pre-employment and regular mandatory examinations by various medical specialists and laboratory tests.

In 1948-1953 complete blood counts were performed 4 times a year, in 1954-1960 – 2 times a year and after 1961 – once a year through the entire follow-up. If persistent changes in hematological parameters were observed for a worker, he/she was examined by a haematologist and, if need, a sternal puncture and/or trephine biopsy were carried out. This unique monitoring allowed to collect a lot of raw clinical data on the hematopoietic system. Structurally the medical and dosimetry database 'Clinic' contains a number of blocks that directly correspond to the hematopoietic system, such as 'Incidence', 'Peripheral blood', 'Red bone marrow'.

'Incidence' block stores data on all diseases experienced during the follow-up period including a first diagnosis date, detailed diseases statements, a diseases code in accordance with the International Classification of Diseases (ICD-9).

'Peripheral blood' block stores the following data: examination date, quantitative counts of the morphological blood content (RBC, WBC, PLT and others).

'Red bone marrow' block stores raw data on RBM analyses: examination date, myelogram results and a hematologist's conclusion.

Photo: SUBI

Dr. Tamara V. Azizova

As of 31.12.2019, 212 tumors of the lymphoid and hematopoietic tissues and 3180 blood and blood-forming organ diseases were verified in the study cohort. The Table below provides the totality of hematopoietic data in the 'Clinic' database as of 31.12.2019.

To sum up, the database for the hematopoietic system developed at SUBI might be used for future updates of risks of early and late effects in the human hematopoietic system, such as tumors of the lymphoid and hematopoietic tissues and diseases of the blood and blood-forming organs related to radiation exposure, for dose-response and dose-rate-response assessments considering non-radiation factors, for estimations of dose thresholds and associated uncertainties for certain tissue reactions occurring in the lymphoid and hematopoietic systems due to chronic low dose-rate radiation exposure, and for investigations of mechanisms of chronic exposure effects on the human hematopoietic system, etc.

Photo: SUBI

Descriptive characteristics	Males	Females	Both sexes
Complete blood counts			
Number, total	381246	172682	553928
Portion of individuals for whom counts were performed, %	8289 (95.09%)	3358 (93.83%)	11647 (94.72%)
Mean number of counts per person ± SE (minimum : maximum)	45 ± 39.98 (1 : 347)	51 ± 43.92 (1 : 327)	47 ± 41.23 (1 : 347)
RBM examinations			
Number, total	3647	2192	5839
Portion of individuals for whom examinations were carried out, %	1084 (12.44 %)	642 (17.94 %)	1726 (14.04 %)
Mean number of examinations per person ± SE (minimum : maximum)	3.00 ± 2.46 (1 : 20)	3.00 ± 2.62 (1 : 26)	3.00 ± 2.52 (1 : 26)

Data on complete blood counts and bone marrow examinations provided by the 'Clinic' database as of 31.12.2019

[1] Mayak PA worker cohort (MWC), Azizova T. V. (2018), AIR² Issue n°28, P3

[2] The "Clinic" medical-dosimetric database of Mayak production association workers: structure, characteristics and prospects of utilization, Azizova T. V., Day R. D., Wald N., Muirhead C. R., O'Hagan J. A., Sumina M. V., Belyaeva Z. D., Druzhinina M. B. et al. (2008), Health Phys, 94 (5), 449–458

ID Card:

Database topic:
Radiation epidemiology, radiobiology

Information available type:
Type of exposure, doses, dose rates, demographic data, family history, medical history, occupational history, social habits, etc.

Data type:
Cohort data

Link with a biobank:
Radiobiological Human Tissue Repository (RHTR)
http://rhtr.subi.su/

Access:
The database is owned by SUBI. Access to anonymous data is limited and should be approved and granted by SUBI Institutional Review Board.

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456780 Ozyorsk,
Chelyabinsk region

Related to:
MELODI

NASA GeneLab

Open Science for Life in Space

GeneLab (http://genelab.nasa.gov) is a NASA initiative designed to accelerate open-science biomedical research, to support human exploration of space and to help improve life on Earth. The initiative includes a core staff of space biologists, data scientists with expertise in omics (genomics, transcriptomics, proteomics, metabolomics) data, and computer scientists. The GeneLab Data System (GLDS) architecture is illustrated below.

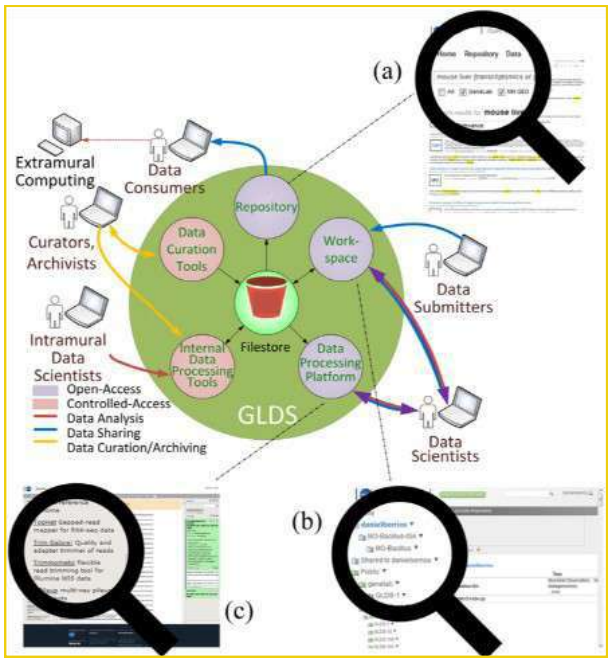

Photo: D. Berrios/NASA Ames Research Center

Schematic representation of the GLDS. Web interfaces for the GeneLab Data Repository (a), Collaborative Workspace (b), and Analysis Platform (c) are also shown.

Phase I of the three-phase GeneLab project emphasized key capabilities for submission, curation, search, and retrieval of omics data from biomedical research experiments conducted in space, or from space-related studies (i.e. radiation and simulated microgravity studies).

The development focus for Phase II included federated search and retrieval of space-related omics data across other open-access systems, so that users are able to conduct biological meta-investigations. Such meta-investigations aim to corroborate findings from many kinds of assays and translate them into systems biology knowledge and, eventually, therapeutics, including countermeasures to support life in space. Phase II development also included a Collaborative Workspace for users to upload, store, and share space-related omics data to promote scientific collaboration.

Phase III introduced a free, open-access *in silico* analysis platform for omics data, based on the open-source Galaxy platform. The GeneLab Analysis Platform provides a tool-shed that includes many widely used bioinformatics tools, a simplified list of tools and workflows, and some tools customized for meta-analysis of spaceflight experiments or for spaceflight data visualization (visualization of microarray illustrated below). A dedicated visualization portal is currently under development for customized browsing of spaceflight omics data with the ability to filter for various experimental factors specific to space (e.g. space radiation doses and radiation quality, environmental conditions like carbon dioxide levels on the International Space Station, species, and strains).

Photo: NASA

Dr Sylvain V. Costes

In addition, GeneLab has expertise in preparing bio-samples from model organisms for omics assays using a state-of-the-art Sample Processing Lab (SPL). GeneLab requests any unused tissues and samples from biological experiments conducted in space through the NASA Life Sciences Data Archive. The SPL uses specialized protocols to process the unused spaceflight (and respective ground control) samples to generate omics data. All of the protocols used for nucleic acid (and protein) extraction, library preparation, and sequencing were established in collaboration with the scientific community and are setting standards for the entire Space Biology community. In an effort to better control variation between experiments due to differences in methodology, the SPL has also become a state-of-the-art sequencing facility with automated sample processing and nucleotide sequencing equipment.

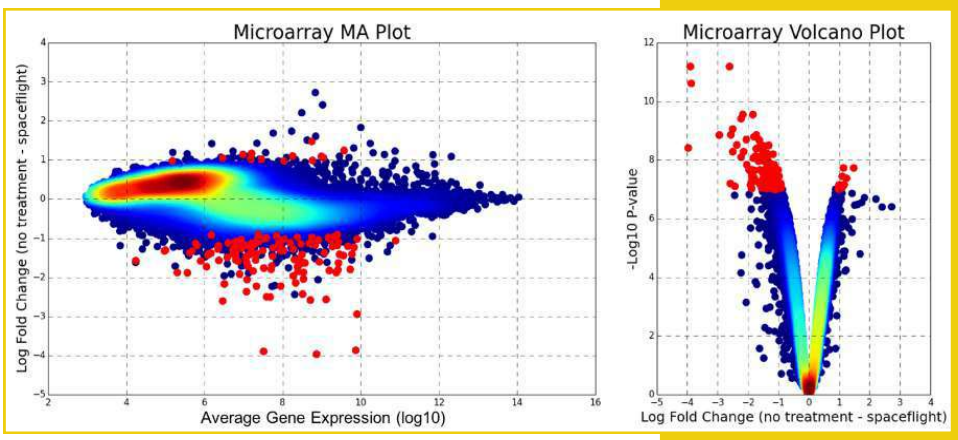

Photo: J. Rubin, D. Mattox/NASA Ames Research Center

Microarray analysis of GLDS-21 samples. MA (left) and Volcano (right) plots comparing gene expression of gastrocnemius muscles from mice flown on the STS-108 shuttle flight (11 days, 19 hours) (spaceflight) *versus* mice maintained on Earth (no treatment) for the same period were generated using the Microarray Analysis tool on the GeneLab Analysis Platform. Dots are colored based on kernel density estimate and differentially expressed genes are colored in red.

ID Card:

Analytical platform type:
Open source, web-based platform for spaceflight-relevant data (genomic, proteomic, metabolomic, epigenomic)

Main techniques proposed:
Nucleotide sequencing computational analysis (e.g. differential gene expression, genome methylation analysis, informatics for mass spectrometry-based proteomic)

Capacity:
Default configuration: 256 GB of storage – CPU and RAM provided for running pipelines are adapted based on user load

Training proposed:
GeneLab provides online tutorials:
- RNA-Seq Analysis pdf tutorial
- GeneLab RNA-Seq Analysis video tutorial

Address:
NASA Ames Research Center
Moffett Field
CA 94035, USA

Access:
Free, open

Internet link:
http://genelab.nasa.gov

Contact:
Sylvain V. Costes
sylvain.v.costes@nasa.gov
+1-650-604-5353

GeneLab: Omics database for spaceflight experiments, Ray S., Gebre S., Fogle H., Berrios D. C., Tran P. B., Galazka J. M., Costes S. V. (2018), Bioinformatics, doi:10.1093/bioinformatics/bty884

NASA GeneLab project: Bridging space radiation omics with ground studies, Beheshti A., Miller J., Kidane Y., Berrios D., Gebre S. G., Costes S. V. (2018), Radiat Res, 189 (6), 553-559, doi:10.1667/RR15062.1

Conclusions and perspectives

In this deliverable, 120 infrastructures, published till September 2019 in the 40 Issues of AIR² are presented. We have added also 8 infrastructures published in 2 Special Issues presented in the "Add-on" section. This web handbook consists of 3 main chapters, representing the 3 categories that AIR² readers are already familiar with: "Exposure platforms", "Databases, Sample banks, Cohorts", "Analytical platforms, Models & Tools". Each chapter has been divided into subcategories aiming to facilitate researchers and students in the field of Radiation Protection research finding information about potential infrastructures they need. First level of information with detailed technical characteristics, access conditions and a contact are provided about "well known" but also for "newly-developed" infrastructures. They have been described going beyond CONCERT partners and even including non-EURATOM countries in order to more accurately draw the radiation protection infrastructure landscape.

Europe has many high quality infrastructures to support Radiation Protection research. It will nevertheless be important to identify gaps and remain responsive to new requirements that may emerge with scientific and technological developments. Some categories of infrastructures are quite straightforward, while others, such as "Databases, Sample Banks and Cohorts", are more complex. Exposure platforms are the cornerstone of most radiation protection research activities, indeed we feature 45 of them in comparison to 35 "Databases, Sample banks, Cohorts" and 40 "Analytical platforms, Models & Tools". Some less visible infrastructures are also the most fragile. Frequently created during a European project to answer a particular need, they fall dormant afterwards through lack of sustainable funding, when they could have been so useful for future research if kept active and updated. AIR² focused its efforts in keeping them under the spotlight. Similarly, efforts will be focused to enlarge the scope to other subcategories such as, for example, infrastructures for image-guided small animal radiotherapy, microbeams, internal contamination facilities, observatory sites, sample banks and so on.

Most of the infrastructures needed for Radiation Protection research exist across Europe (and sometimes outside). CONCERT promotes the visibility of those infrastructures and recommends their use. One of the roles of CONCERT has been to ensure the availability of and facilitate access to operational "state-of-the-art" research infrastructures required to support the research efforts of Radiation Protection researchers. The priority is promote the use of mature infrastructures and avoid unnecessary duplication. The open approach of CONCERT involves the use of infrastructures, which fulfil recommended criteria. They are integrated on the voluntary basis into a searchable available database AIR²D² (http://www.concert-infrastructures.eu/home) that can be updated to include new candidates. At the time being, the best way to achieve the sustainability of these infrastructures is to use them for research projects. The web-handbook answers also to enforce their visibility and increase their funding potential through European projects. The web-handbook may be seen as the funding preliminary act of a dedicated virtual open network to support Radiation Protection research.

The web-handbook is based on the 40 classic issues of AIR², together with additional research. It is a result of "ongoing" work and we can easily imagine a possible future with revised and extended version because infrastructures like other research labs disappear and sometimes new ones are created.

Future extensions are possible: various hyperlinks with the future extended AIR²D² database and more direct actualized information issued directly from owners and why not, directly other links using tools already available through Internet. It is sure that it could become a continuous integrative tool for researchers to find their suitable platform but also for reviewers to evaluate and control the quality of this type of support/partners for European projects financially supported by the EC. It could become a strong recommendation to obtain the highest value in the evaluation of the scientific excellence, if not a requirement.

The web-handbook is a great tool to analyse the actual landscape and open-mindedness of infrastructures. This is a key point, which by this construction shows inherently its strengths and weaknesses. It is the first time that they accept to be together without a competitive spirit. Each owner considers only that this visibility increases its chances of continuation. Nevertheless, it also shows that they are not organized; they do not constitute a

network and are more competitors than partners. Today, the competition is focused on the visibility of their specificity.

The help of the entire Radiation Protection Research community is required to cover all the radiation protection related present and future topics of research: low dose, radioecology, dosimetry, emergency situations, medical use, social sciences, etc….

Surely, these 120 collected infrastructures are among the top listed ones, however it is not an exhaustive description of the entire landscape of the potentially available infrastructures in Europe. Shortly, this is not a “closed” web-handbook and we will hopefully open it and revise it on a continuous basis in the future.

Infrastructure	Exposure platforms						Databases, Sample banks, Cohorts			Analytical platforms, Models & Tools	
	Low doses and low dose rates	Microbeams	Particular radiation qualities: ions, neutrons, alpha…	Internal contamination	Observatory sites	Metrology exposure platforms	Databases	Sample banks	Cohorts	Analytical platforms	Models & Tools
FIGARO	■			■							
PULEX-Cosmic Silence	■		■								
Silesian Centre for Environmental Radioactivity (SCRS-GIG)	■		■	■							
LIBIS	■										
Microtron Laboratory	■										
Low dose rate facility at Stockholm University	■										
MICADO'LAB Experimental Platform	■										
LERF	■										
AMBIC	■										
The Calliope facility	■										
SNAKE		■									
PTB-Microbeam, ion and neutron fields		■									
The MIRCOM microbeam		■									
AIFIRA		■									
Radon Exposure Chamber	■		■	■							
Biological Irradiation Facility (BIO)	■		■								
CIRIL			■								
Mixed alpha and X-ray exposure facility			■								
Alpha particles irradiator			■								
Changing dose rate exposure facility			■								
Proton IRRADiation facility (IRRAD)			■			■					
CERF			■								
TIFPA			■								
HIT			■								
The AGOR Facility at KVI-CART			■								
FAIR			■								
Research Neutron Source Heinz Maier-Leibnitz (FRM II)			■								
NASA Space radiation Laboratory (NSRL)			■								

B3, Animal Contamination Facility											
Facility radionuclides availability, transfer and migration											
Nanoparticle Inhalation Facility											
PARISII											
The Chernobyl Exclusion Zone											
Forest observatory site in Yamakiya											
Belgian NORM Observatory Site											
IRSE Experimental Farm, Kazakhstan											
Phosphogypsum stack at Barreiro, Portugal											
ZATU (Zone Atelier Territoire Uranifère), France											
Laboratory for retrospective Radon and Thoron dosimetry											
Calibration Laboratory at KIT											
MELAF											
Radiation Metrology Laboratory (DOS)											
Laboratory for Dosimetry Standards (NDS)											
CALibration LABoratory(CALLAB)											
Radon Calibration Laboratory of BfS											
Calibration and Dosimetry Laboratory (INTE-UPC)											
The Nuclear Metrology Group (NMG)											
UNIPI neutron irradiation facility											
Laboratory for Nuclear Calibrations at SCK•CEN											
CIEMAT External Dosimetry Service and Retrospective Luminescence Dosimetry Lab											

Table 10: Summary table for the category Exposure Platforms

Infrastructure	Exposure platforms						Databases, Sample banks, Cohorts			Analytical platforms, Models & Tools	
	Low doses and low dose rates	Microbeams	Particular radiation qualities: ions, neutrons, alpha…	Internal contamination	Observatory sites	Metrology exposure platforms	Databases	Sample banks	Cohorts	Analytical platforms	Models & Tools
FREDERICA							■				
STORE							■				
RES³T							■				
Wildlife Transfer Database							■				
JANUS Animal Radiobiology Archive							■				
MARiS – MARine Information System							■				
The BRIDE platform							■				
Database of Mayak workers' families							■				
NASA's LSAH and LSDA repositories							■				
The "hematopoietic system" database for Mayak nuclear workers							■	■			
Biobank of Eastern Finland								■			
Chernobyl Tissue Bank								■			
Belgian Soil Collection								■			
The Bank of Biological Materials of SBRC								■			
Russian Human Radiobiological Tissue Repository (RHRTR)								■			
The Wismut Cohort and Biobank								■	■		
French Haemangioma Cohort and Biobank								■	■		
3-Generation exposure study								■	■		
Portuguese Tinea Capitis Cohort								■	■		
French longitudinal study of children (Elfe)								■	■		
INWORKS Cohort									■		
EPI-CT scan cohort									■		
Chernobyl clean-up workers from Latvia									■		
ESTCHERN Cohort								■	■		
German airline crew cohort									■		
The Techa River Cohort (TRC)								■	■		
Greek interventional cardiologists cohort									■		

The German Thorotrast Cohort Study											
Mayak PA worker cohort (MWC)											
The TRACY cohort											
The ISIBELa cohort											
The ISE cohort											
CONSTANCES											
IMMO-LDRT01 cohort											
The BACCARAT study											
Life Span Study (LSS)											
REQUITE											

Table 11: Summary table for the category Databases, Sample banks, Cohorts

Infrastructure	Exposure platforms						Databases, Sample banks, Cohorts			Analytical platforms, Models & Tools	
	Low doses and low dose rates	Microbeams	Particular radiation qualities: ions, neutrons, alpha…	Internal contamination	Observatory sites	Metrology exposure platforms	Databases	Sample banks	Cohorts	Analytical platforms	Models & Tools
RENEB											
The Genomic Medicine and Bioinformatics Core Facility											
MetaboHUB											
ProFI											
Radiobiology and immunology platform (CTU-FBME)											
France Génomique											
The SCK•CEN Genomics platform											
CATI											
HZDR–Radioanalytical Laboratories											
Advanced Technologies Network (ATeN) Center											
BfS In Vivo Measurement Facilities											
ECORITME											
Consolidated Radioisotope Facility (CORiF)											
Centre for Omic Sciences (COS)											
The iGE3 Genomics Platform											
VIB Proteomics Core											
MARS beamline at Synchrotron SOLEIL											
CIEMAT Whole Body Counter (WBC)											
DSA Environmental Laboratory											
Radiochemical and Radioactive Analysis Laboratory (INTE-UPC)											
CIEMAT In Vitro Internal Dosimetry Laboratories											
LRM											
TU Dublin Analytical Platform											
NASA Genelab											
Dose Estimate, CABAS and NETA											
LDRadStatsNet											
ERICA Tool											

The Analytical Platform of the PREPARE project											
CROM-8											
Symbiose											
INFRAFRONTIER											
The CERES Platform											
The Severe Nuclear Accident Program (SNAP)											
The BIANCA code											
OEDIPE											
Geant4-DNA											
D-DAT											
COOLER											
BRENDA											
The EFFTRAN code											
The MCDA Tool											

Table 12: Summary table for the category Analytical platforms, Models & Tools

Index (alphabetical order)

The ISE cohort – 2b, 2c
The ISIBELa cohort – 2b, 2c
The MCDA Tool – 3b
The MIRCOM microbeam – 1b
The Nuclear Metrology Group (NMG) – 1f
The SCK●CEN Genomics Platform – 3a
The Severe Nuclear Accident Program (SNAP) – 3b
The Techa River Cohort (TRC) – 2c, 2b
The TRACY cohort – 2c
The Wismut Cohort and Biobank – 2c, 2b
TIFPA – 1c
UNIPI neutron irradiation facility – 1f, 1c
VIB Proteomics Core – 3a
Wildlife Transfer Database – 2a
ZATU (Zone Atelier Territoire Uranifère), France – 1e