AIR² Access to INFRASTRUCTURES for Radiation protection Research

Issue 7
May 2016

Editorial

Each edition of the AIR² bulletin includes a section called "The floor to …", which discusses the importance of infrastructures. Having started with contributions from CONCERT WP leaders, this section will now be broadened to include contributions from leaders of the European platforms: MELODI, ALLIANCE, NERIS, EURADOS, Medical Use…, as well as CONCERT grantees, POMs, ESFRI representatives, national contact points for infrastructures, etc. The valuable variety of viewpoints, comments, advice and sharing of experience that will result will not only enrich CONCERT concepts, but will provide inspiration for infrastructure strategy and for the yearly action plans and long term roadmaps. If you would like to suggest a potentially valuable contributor to "The floor to…", please contact our editorial team. **- Dr Laure Sabatier**

The floor to...

The Education and Training Workpackage in CONCERT is primarily dedicated to developing and maintaining the expertise of the scientific research community engaged in the work within the various research areas under the CONCERT umbrella. WP7 has a programme designed to attract new students into the field to ensure continuity in the essential disciplines of radiobiology, epidemiology, and radiation physics. The programme offers student travel grants and one-to-one mentoring for MSc and PhD students, and there is an annual call for short focused courses in order to give potential research students an opportunity for hands-on experience of the research work underway in specialist research institutes. The short courses continue the series on low-dose radiation risks begun during the DoReMi Network of Excellence. These were directed towards the interests of the MELODI platform, and proved very successful. Under CONCERT the range of topics is expanded to include all the areas of research interest relevant to NERIS (emergency response), ALLIANCE (radioecology) and EURADOS (radiation dosimetry).

Another priority of WP7 is to broaden the experience and knowledge of working research scientists into new disciplines related to the radiation protection field, possibly from areas not traditionally associated specifically with radiation, such as some new areas of molecular biology, immunology, systems biology, bioinformatics, etc.

In the ability to respond to new directions, WP7 can be of particular help in promoting the use of European research infrastructures by participants in the CONCERT research programme. In many cases the advantage of using newer, larger, faster, more powerful infrastructures is not taken because of the learning threshold needed to gain familiarity and confidence in their use. Certainly there are other factors, such as cost, location, and accessibility that may well be the main determinants as to whether the research is confined to the home-based facilities. However, the provision of teaching initiatives to give researchers personal experience of the possibilities offered by the available infrastructures may be just what is needed. WP7 will work closely with WP6 to ensure full advantage is taken of the possibilities.

> **"WP7 can be of particular help in promoting the use of European research infrastructures "**

Dr Andrea Ottolenghi and Dr Vere Smyth —UniPv
CONCERT WP7 Leader
« Education and Training »

Photos: G. Baiocco & V. Smyth/UniPv

CONCERT CORNER

Future events:

19 Sept 2016: ExB meeting, 1:00-3:00pm, Oxford, UK

23 Sept 2016: MB meeting, 9:00am-3:00pm, Oxford, UK

WP 6 News:

Update of AIR²D²:
- Please complete the online form(s) to register your infrastructure(s) in the database.
- A new option to add document for featuring your infrastructure is now available.

11 July 2016: "Harmonization and Exercise" Pesentation Day, Brussels, Belgium

12 July 2016: Task 6.2 presentation day, Brussels, Belgium

Contents:

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June 2016

This project has received funding from the Euratom research and training programme 2014-2018 under grant agreement No 662287

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.

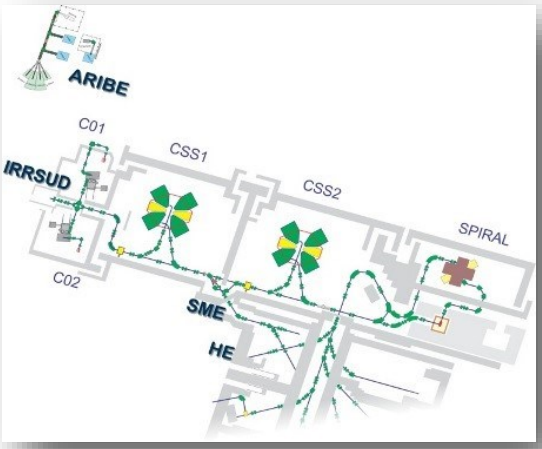


Photo: GANIL

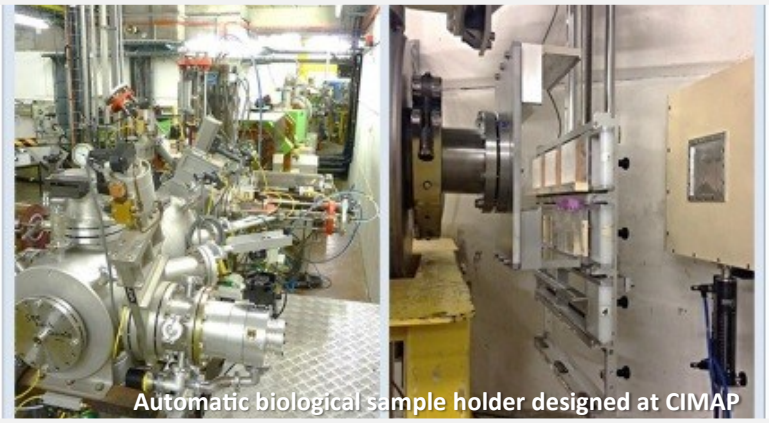
The 4 beamlines for the interdisciplinary researches corresponding to 4 exits at different locations on the ion accelator. ARIBE is located outside the GANIL INB, whereas IRRSUD, SME and HE are inside the INB on the GANIL facility.

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

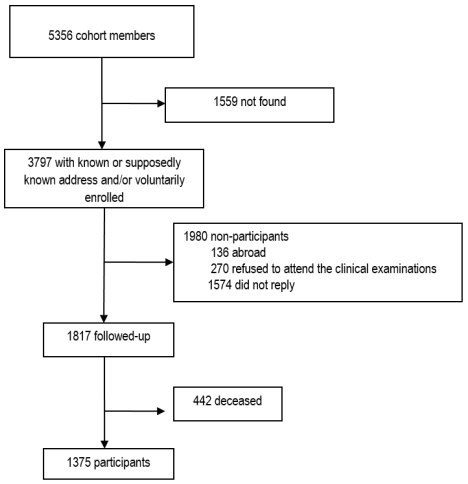
DOSIMETRY FOR RADIOBIOLOGY EXPERIMENTS AT GANIL. Durantel et al. NIM A. 2016.

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.

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.

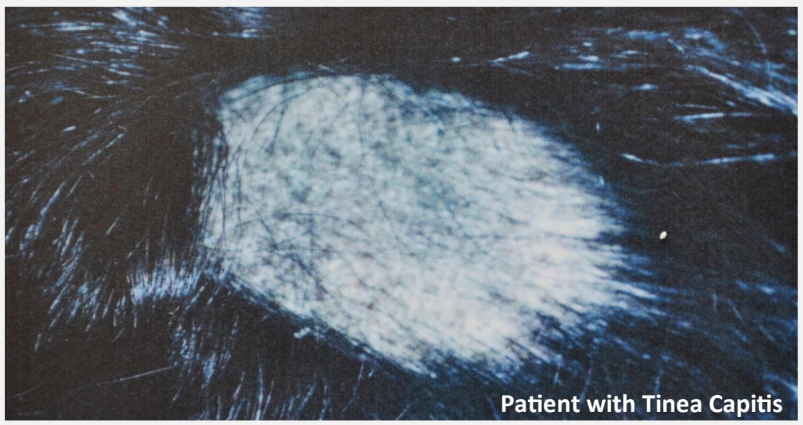
Photo: M. Gomes

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

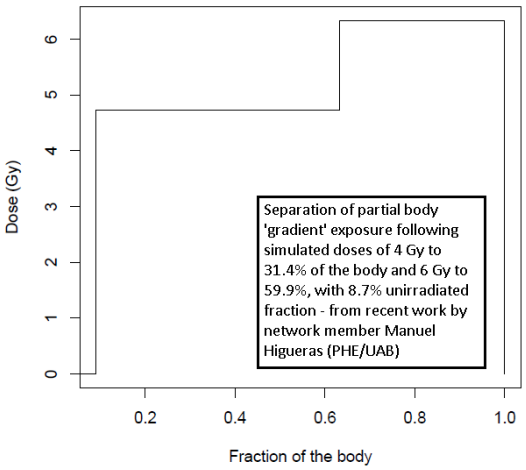
Contact:
Paula Boaventura
mboaventura@ipatimup.pt;
R. Júlio Amaral de Carvalho, 45, 4200-135 Porto, Portugal

Related to:
MELODI

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:

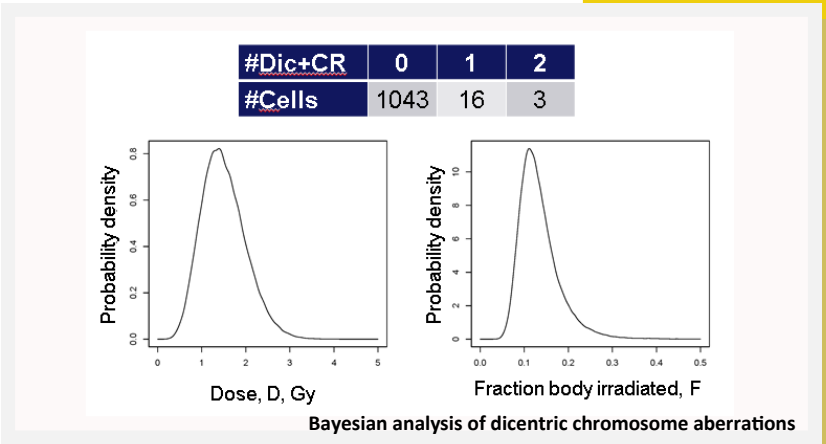
Photo: K. Rothkamm/PHE

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 .

AIR²

Access to INFRASTRUCTURES for Radiation protection Research

Issue	Exposure platforms	Databases, Sample banks, Cohorts	Analytical platforms, Models & Tools
Published to date:			
Oct 2015, #1	FIGARO	FREDERICA	RENEB
Nov 2015, #2	B3, Animal Contamination Facility	The Wismut Cohort and Biobank	The Hungarian Genomics Research Network
Dec 2015, #3	Cosmic Silence	STORE	Metabohub
Feb 2016, #4	SNAKE	French Haemangioma Cohort and Biobank	Dose Estimate, CABAS, NETA
Mar 2016, #5	Radon exposure chamber	3-Generations exposure study	ProFI
Apr 2016, #6	Biological Irradiation Facility	Wildlife Transfer Database	Radiobiology and immunology platform (CTU-FBME)
May2016, #7	CIRIL	Portuguese Tinea Capitis Cohort	LDRadStatsNet
Coming soon:			
Jun 2016, #8	Mixed beams facility	ELFE Cohort	ERICA-Tool

Future events:

9-13 May 2016: 14th Congress of the International Radiation Protection Association, IRPA14, Cape Town, South Africa
Registration open until 1st May 2016

17-18 May 2016 : Health Effects of Chernobyl: Prediction and Actual Data 30 Years after the Accident, Obninsk, Russia

31 May 2016: Registration deadline for Msc Radiation Biology Programme. See website

1-3 June 2016: 2nd International Conference on Risk Perception, Communication and Ethics of Exposures to Ionising Radiation, RICOMET 2016, Bucharest, Romania

13-17 June 2016: OPERRA training course: PCR-based Techniques in Radiobiology and Low-Dose Risk Research,Budapest, Hungary

15-17 June 2016: COMET Workshop "Models fit for purpose", focussed on modelling in radioecology. Seville, Spain

4-8 July 2016: CONCERT Course on Uncertainty Analysis for Low Dose Research, Barcelona, Spain.
Registration until 3 June 2016

4-8 Sept 2016: 42nd Annual Meeting of the European Radiation Research Society, ERR2016, Amsterdam, Netherlands
Registration open

19-23 Sept 2016: Radiation Protection Week, RPW2016, Oxford, UK.
Registration open

3-5 Oct 2016: International Conference on Research Infrastructures, ICRI2016, Cape Town, South Africa

5-7 Dec 2016: 8th EAN_{NORM}, Stockholm, Sweden.

Editorial Committee: Jean-Michel Dolo, Elisabeth May, Laure Piqueret-Stephan, Laure Sabatier

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