AIR²
Access to Infrastructures for Radiation protection Research

Issue 40
September 2019

Editorial

We have now arrived at the 40th and final issue of the AIR² newsletter. Since the beginning of this adventure, we have presented 120 infrastructures, fulfilling our commitment to the CONCERT project. It has been an exciting adventure which could have gone on for longer as there are still many more infrastructures to be highlighted. However CONCERT ends in 9 months' time and we have to finish the remaining tasks in WP6. Thus our efforts will now focus on preparing a number of special issues dedicated to a specific project or theme, or to presenting the initial results of the projects selected *via* the CONCERT calls. With these bonus issues which go beyond our deliverables commitments, we aim to maintain a regular rendezvous with our readers on the topic of European research in radiation protection. Meantime, we hope you enjoy reading this last 'classic' issue of AIR².

Dr Laure Sabatier, CEA

The floor to...

ERPW 2019: Radiation protection research in the Nordic countries

Radiation protection has a long tradition in the Nordic countries. Indeed, the International Commission on Radiological Protection (ICRP) was founded in Stockholm in 1928 and Rolf Sievert was its first chair. At his initiative, the Nordic Society for Radiation Protection was established in 1964, with members from all five Nordic countries (Denmark, Finland, Iceland, Norway and Sweden). It became a member of IRPA (the International Radiation Protection Association) the same year. The society is dedicated to the development and dissemination of knowledge and experience on protection against ionizing and non-ionizing radiation. This covers radiation protection for workers, patients subjected to irradiation for diagnostics or therapeutic purposes, and protection of the public in general.

Another Nordic organization related to radiation protection is the NKS, which aims to facilitate a common Nordic view of nuclear and radiation safety and create networks that can be easily activated, e.g. in the case of a nuclear accident. Cooperation builds on the foundation of a common cultural and historical heritage and a long tradition of collaboration between the five Nordic countries.

Each Nordic country has its own radiation protection and nuclear safety authority: the "Strålebeskyttelse" in Denmark, STUK in Finland, GR in Iceland, DSA in Norway, and SSM in Sweden. In contrast to many analogous authorities around the world, the Nordic authorities have no laboratories for basic radiation protection research. Basic research is outsourced to universities. The authorities do have laboratories, but these focus on radiation metrology and emergency preparedness.

A major radiological hazard in the Nordic countries is radon and long-lived radionuclides in drinking water. Exposure to natural radiation sources is among the highest in the world. Consequently, the biological effects of low-dose exposure to people and the environment are at the focus of research. Low-activity exposure facilities have been installed in Norway and Sweden. Moreover, STUK and Stockholm University have played important roles in creating the European Strategic Research Agendas and research platforms within the Euratom research and training program.

The Nordic countries have also hosted several international radiation research meetings. Annual meetings of the ERRS were held in Stockholm in 1956, 1993, and 2010. The 2010 European IRPA and MELODI 2012 meetings were held in Helsinki. This year, the European Radiation Protection Week (ERPW 2019) will be held in Stockholm, 14-18 October, and is jointly organized by the Nordic countries. Everybody is warmly welcomed!

The ERPW 2019 is jointly organised by radiation protection researchers from the Nordic Countries and the venue is the Stockholm University.

CONCERT CORNER

Future events:

Call for Travel Grants
Next deadline: 30th September
Information

14-18 October
ERPW 2019
Stockholm, Sweden
14th October: MB & ExB/ESAB

NFRP2019-2020
Deadline: 25th September
Information

WP 6 News:

Next WP6 meeting:
16th October, Stockholm, Sweden

The first version of CONCERT's Web-handbook (D6.4) is now online!

AIR²D²:
- Please complete the online form(s) to register your infrastructure(s) in the database.

Follow STORE on Twitter: @STOREDatabase

Contents:

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

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

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.

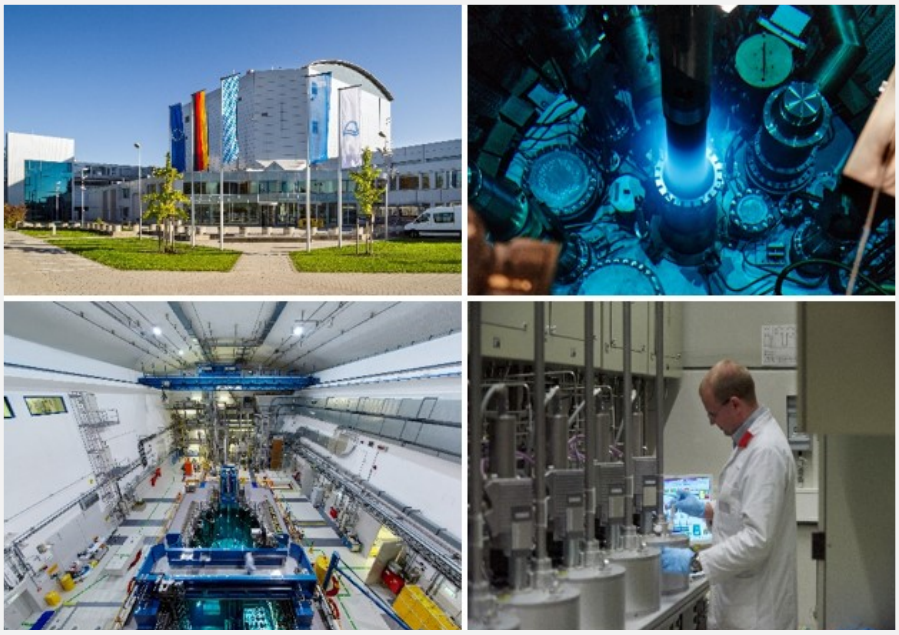
Photo: Schürmann/TUM

Florian Jeschke

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

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Related to:
EURADOS

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.

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.

Photo: University of Manchester

Dr Catharine West

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

REQUITE

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

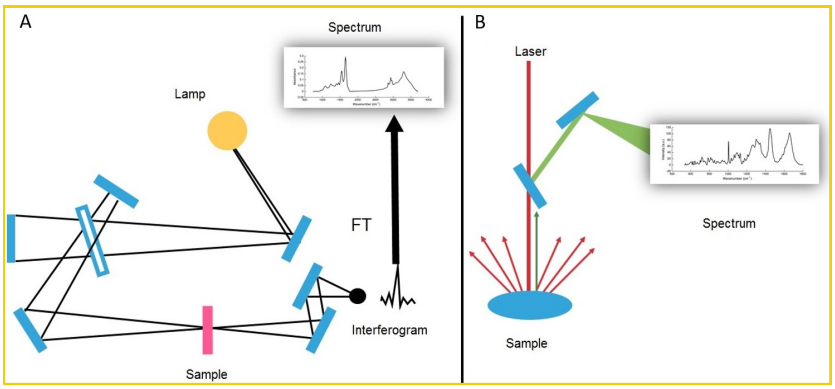
Related to:
MELODI
EURAMED

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

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.



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.

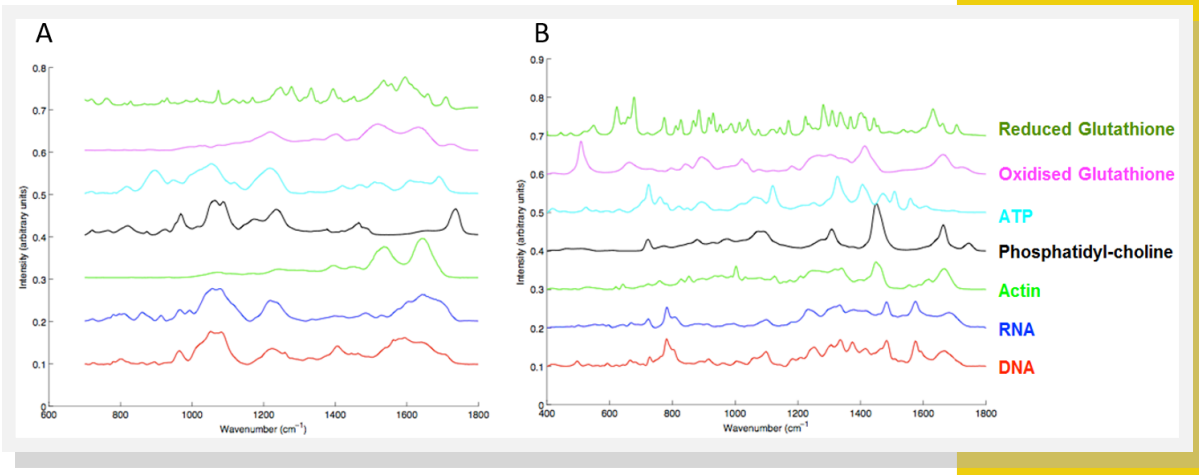
The Radiation and Environmental Science Centre (RESC) is housed in the FOCAS Research Institute, a 3200 m^2 facility with state of the art core laboratory support in microscopy and spectroscopy, in Technological University Dublin (TU Dublin). FOCAS houses a suite of spectroscopic instruments, including 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.

Photo: TU DUBLIN

Prof Fiona Lyng & Dr Aidan Meade

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:
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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

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	Pulex 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 TransferDatabase	Radiobiology and immunology platform (CTU-FBME)
May2016, #7	CIRIL	Portuguese Tinea Capitis Cohort	LDRadStatsNet
Jun 2016, #8	Mixed alpha and X-ray exposure facility	Elfe Cohort	ERICA Tool
Jul 2016, #9	SCRS-GIG	RES^{3}T	CROM-8
Sep 2016, #10	Facility radionuclides availability, transfer and migration	INWORKS cohort	France Génomique
Oct 2016 #11	LIBIS gamma low dose rate facility ISS	JANUS	Transcriptomics platform SCKCEN
Nov 2016, #12	Microtron laboratory	EPI-CT Scan cohort	CATI
Dec 2016, #13	Nanoparticle Inhalation Facility	UEF Biobanking	The Analytical Platform of the PREPARE project
Feb 2017, #14	Infrastructure for retrospective radon & thoron dosimetry	Chernobyl Tissue Bank	HZDR Radioanalytical Laboratories
Special Issue 1	1st CONCERT Call: CONFIDENCE, LDLensRad, TERRITORIES	1st CONCERT Call: CONFIDENCE, LDLensRad, TERRITORIES	1st CONCERT Call: CONFIDENCE, LDLensRad, TERRITORIES
Mar 2017, #15	Alpha Particles Irradiator Calibration Laboratory at KIT		SYMBIOSE
Apr 2017, #16	Changing Dose rate (SU) Low dose rate (SU)		Advanced Technologies Network Center
May 2017, #17	Chernobyl Exclusion Zone	Chernobyl clean-up workers from Latvia	BfS whole and partial body Counting
Jun 2017, #18	MELAF	Belgian Soil Collection	INFRAFONTIER
Jul 2017, #19	MICADO'LAB	Estchern Cohort	ECORITME
Sep 2017, #20	DOS NDS		CERES

Future events:

CONCERT Short Courses

9-11 September 2019

CONFIDENCE WORKSHOP: Do Process-Based Models have a role in human food chain assessments? CIEMAT, Madrid, Spain

Contact:
Lindis Skipperud
Lindis.skipperud@nmbu.no

4-7 November 2019

LEU-TRACK course "Essentials of Radiation Leukaemogenesis", Centre for Radiation, Chemical & Environmental Hazards, PHE, Didcot, Oxfordshire, UK

Contact:
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christophe.badie@phe.gov.uk

2-5 December 2019

CONFIDENCE Dissemination workshop: Coping with uncertainties for improved modelling and decision making in nuclear emergencies, Bratislava, Slovak Republic

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See also on CONCERT website

Editorial Committee: Maria Panagiotopoulou, Jean-Michel Dolo, William Hempel, Laure Sabatier

Issue 40
September 2019

AIR2

Access to INFRASTRUCTURES for Radiation protection Research

Issue	Exposure platforms	Databases, Sample banks, Cohorts	Analytical platforms, Models & Tools
Published to date:			
Oct 2017, #21	CALLAB Radon Calibration Laboratory		CORIF
Nov 2017, #22	Calibration and Dosimetry Laboratory (INTE-UPC)	German airline crew cohort	Centre for Omic Sciences (COS)
Dec 2017, #23	NMG	Techa River Cohort (TRC)	iGE3
Special Issue 2	MEDIRAD	MEDIRAD	MEDIRAD
Feb 2018, #24	UNIPI-AmBe	Greek interventional cardiologists cohort	SNAP
Special Issue 3	2nd CONCERT Call: LEU-TRACK, PODIUM, SEPARATE, VERIDIC, ENGAGE, SHAMISEN-SINGS	2nd CONCERT Call: LEU-TRACK, PODIUM, SEPARATE, VERIDIC, ENGAGE, SHAMISEN-SINGS	2nd CONCERT Call: LEU-TRACK, PODIUM, SEPARATE, VERIDIC, ENGAGE, SHAMISEN-SINGS
Mar 2018, #25	IRRAD	MARiS	BIANCA
Apr 2018, #26	Forest observatory site in Yamakiya	BBM	OEDIPE
May 2018, #27	Belgian NORM Observatory Site	The German Thorotrast Cohort Study	VIB Proteomics Core
Jun 2018, #28	CERF	Mayak PA worker cohort	Geant4-DNA
Jul 2018, #29	TIFPA	RHRTR	D-DAT
Sep 2018, #30	HIT	The TRACY cohort	COOLER
Oct 2018, #31	PTB Microbeam	The BRIDE platform	BRENDA
Nov 2018, #32	AGOR Facility at KVI-CART LNK		MARS beamline at SOLEIL
Dec 2018, #33	PARISII	The ISIBELa cohort	CIEMAT WBC
Feb 2019, #34	The MIRCOM microbeam	The ISE cohort	EFFTRAN
Special Issue 4	NSRL	LSAH & LSDA	GeneLab
Mar 2019, #35	IRSE Experimental Farm	The MWF database	DSA Environmental Laboratory
Apr 2019, #36	PG stack at Barreiro, Portugal	CONSTANCES	The MCDA Tool
May 2019, #37	LERF	IMMO-LDRT01 cohort	Radiochemical and Radioactive Analysis Laboratory (INTE-UPC)
Jun 2019, #38	FAIR	The BACCARAT study	CIEMAT *In Vitro* Internal Dosimetry Laboratories
Jul 2019, #39	AMBIC	LSS	LRM
Sep 2019, #40	FRM II	REQUITE	TU Dublin Analytical Platform

Future events:

Other Events

8-13 September 2019
ENVIRA 2019: 5th International Conference on Environmental Radioactivity, Prague, Czech Republic

11-13 September 2019
ENGAGE final project workshop:
Enhancing stakeholder participation in the governance of radiological risks for improved radiation protection and informed decision making, Bratislava, Slovak Republic
Registration here
Contact:
Tatiana Duranova
tatiana.duranova@vuje.sk

16-20 September 2019
RADECS 2019: Radiation and its Effects on Components and Systems, Montpellier, France

23-27 September 2019
9th International Symposium on NORM, Denver, USA

28-30 October 2019
ICRA 2019: International Conference on Radiations and Applications 2019, Algiers, Algeria

4-7 November 2019
International Conference on Effective Regulatory Systems for Nuclear and Radiation Safety 2019, Vienna, Austria

12-14 November 2019
TERRITORIES final event,
Aix en Provence, France
Open to TERRITORIES scientists and stakeholders
Pre-register your interest here

26-29 November 2019
19th EAN WORKSHOP jointly organised with the PODIUM project: Innovative ALARA tools, Athens, Greece
Contact:
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11-13 March 2020
CONCERT Final Meeting

Editorial Committee: Maria Panagiotopoulou, Jean-Michel Dolo, William Hempel, Laure Sabatier

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