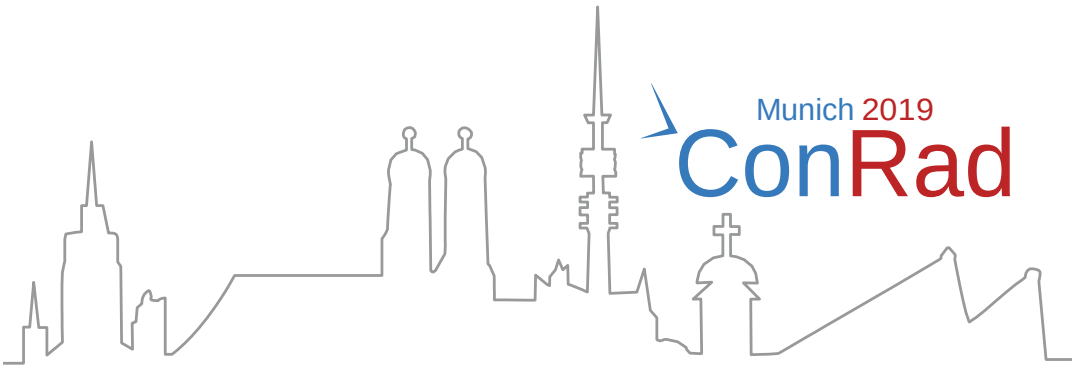

Conference on Radiation Topics | 23rd Nuclear Medical Defence Conference

Abstractbook

Global Conference on Radiation Topics Munich 2019

Preparedness | Response | Protection | Research

organized by

Bundeswehr Institute of Radiobiology affiliated to the University of Ulm

Contents

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The ConRad Logo and the cover page have been designed with friendly support of Ms. Isabell Schütz
(Dez VI 5; Zentrum für Geoinformationswesen der Bundeswehr, Euskirchen, Leiter: Hr. Venker-Metarp)

Welcome address by the Director of the Bundeswehr Institute of Radiobiology affiliated to the University of Ulm
on the occasion of the
23rd Nuclear Medical Defence Conference - ConRad 2019

Dear Colleagues,

It is a pleasure for us to welcome you to ConRad 2019, the 23rd Nuclear Medical Defence Conference, from May 13th to 16th 2019 in Munich. This series of conferences with their specialist focus have been hosted by the Bundeswehr Institute of Radiobiology affiliated to the University of Ulm in Munich since 1988.

There will be two main sessions in this conference, each introduced by a brief overview and then followed by several selected presentations. The first session will describe different aspects of 'living in contaminated areas'. The second contains presentations on several new developments in 'radiation preparedness'. We are sure that the information provided will be relevant for our guests and we expect some inspirational discussion to follow.

As we have found successful in previous years, additional presentations are also being included which provide up to date insight into many topics associated with medical protection against ionizing and non-ionizing radiation, as well as the newest developments in radiation biology. Once again, we have a poster exhibition and a scheduled session where you should be able to speak with many of the authors. As usual we are also pleased to be able to invite you to several social events.

A broad spectrum of national and international experts is attending from both military and civilian organisations. The conference therefore offers an excellent opportunity for education and continuing professional development, as well as providing a forum for professional and multidisciplinary exchange. We are very pleased to host representatives from many nations around the world. Despite some new unfortunate, political obstacles, we also believe that science, particularly in the field of medical preparedness, offers a chance for boundless collaboration - or at least exchange.

We can no longer include an industrial exhibition in our conference because our new anti-corruption guidelines do not permit civilian companies to advertise themselves on German military premises. Nevertheless, several scientists working within industry will be presenting some of their scientific results. Each contribution has been overseen by our scientific committee and I have requested that all presenters refrain from any discussion not motivated by the advancement of scientific knowledge.

For a second time we are welcoming our students from the Technical University of Munich international mastercourse in Radiation Biology to the conference. Please engage personally with our new generation – they are eager to develop our specialist area of science. Also, please consider if any areas of collaboration or exchange maybe possible with your institution – e.g. perhaps an internship, a masters or a doctoral thesis? They are presenting a poster during the conference.

We are certain that you will enjoy being in Munich, the capital city of the Free State of Bavaria, for this exciting conference. We look forward personally welcoming you as a participant to this further key event dealing with radiation topics relevant to us all.

Yours sincerely,

Colonel (MC) Prof. Dr. Matthias Port
Chair, ConRad 2019
Director Bundeswehr Institute of Radiobiology
affiliated to the University of Ulm

Welcome address by the Commander of the Bundeswehr Medical Academy
on the occasion of the
23nd Nuclear Medical Defence Conference - ConRad 2019

Dear participants of ConRad 2019, the 23rd Nuclear Medical Defence Conference.

It is my great honor and pleasure to welcome you all in Munich. With more than 200 participants from almost 30 nations attending, the prospects for this meeting are fantastic. As the Commander of the Bundeswehr Medical Academy, I am both delighted and proud to have you all here with us once again since I fully recognize this conference for its reputation and role as a scientific platform of international standing.

Let me share some recent activities around the Bundeswehr Institute of Radiobiology. It was evaluated in 2018 by the German Council of Science and Humanities. Well known experts from different areas of radiation protection science assesed the accomplishments of the Institute in the areas of science, teaching, radiation preparedness and political counselling. Public information and scientific information exchange was a key issue. Therefore, we are proud that the Bundeswehr and especially the Bundeswehr Medical Academy serve once more as a sponsor and host of the 2019th *Conference on Radiation Topics*, ConRad. The results of the evaluation will be available within the next months.

Let me come back to the conference: A number of topics are going to be addressed that are relevant for both military and civilian exposure scenarios. These include the issue of 'living in contaminated areas', radiation preparedness for accidents, and criminal or terrorist use of radiation. I expect fruitful and inspiring discussions. These topics are perhaps more relevant than ever now due to recent political events worldwide and the potential for the technical skills and knowledge of terrorists to be developing.

The conference is an excellent opportunity to exchange thoughts and knowledge between scientists dedicated to health protection from radiation and radioactive materials. New scientific findings should never remain the exclusive property of any nation. Their translation into medicine leads directly to the diagnosis and treatment of patients and we all have obligations to follow ethical principles such as those published by the International Red Cross or Red Crescent.

With the Institute of Radiobiology and other military departments, we as the Medical Service of the Bundeswehr, strive to develop the knowledge and materials required to meet the needs of humans exposed to ionizing radiation. Matthias Port, as the director of the Institute, and his team work hard to improve the options to counteract medical radiation threats. Their research will be shared during the conference as will the equally relevant and important results of our honorable guests.

I´m especially delighted to welcome representatives from national and international institutions at this year's conference, including our partners from International Atomic Energy Agency, North Atlantic Treaty Organization, Strahlenschutzkommission, French Armed Forces Biomedical Research Institute, Armed Forces Radiobiology Research Institute, the Universities of Ulm, Munich, Stockholm or Würzburg, Bundesamt für Strahlenschutz, Institut de Radioprotection et de Sûreté Nucléaire, Helmholtz Research Institutes, National Research Center for Radiation Medicine of National Academy of Sciences of Ukraine and many more.

Progress and continuity of science in the field of radiobiology, just like anywhere else, are very much dependent on the younger generation who represent the means by which our work can move forward into the future with enthusiasm and modern approaches. In this context, it is my great pleasure to welcome, for the second time, ten students from the International Master Study Program "Radiation Biology" of the Technical University Munich under the lead of Univ.-Prof. Dr. med. Stephanie Combs and Prof. Mike Atkinson.

I´m sure that you will enjoy the different topics and surely the key sessions on 'Living in contaminated areas' and 'Latest developments in radiation preparedness'.

Finally, let me thank you for joining us in Munich and once again wish you a successful conference.

Major General (MC) Dr. Gesine Krüger,
Commander of the Bundeswehr Medical Academy

MONDAY, 13.05.2019

TIME	CONFERENCE OFFICE	BALLROOM SERGEANTS' MESS
from 10:00 AM	Registration and Check In	
7:00 PM - 9:00 PM		"Ice Breaker"
until 12:00 PM (midnight)		

TUESDAY, 14.05.2019

TIME	LECTURE HALL	BASEMENT
8:15 - 8:45 AM	Welcome addresses	Poster exhibition
8:45 - 9:00 AM	Group photo	
9:00 - 10:00 AM	Radiation health effects and medical countermeasures I	
10:00 - 10:30 AM	Coffee break	
10:30 AM - 12:00 noon	Key Session I "Living in contaminated areas" Part I	
12:00 noon - 1:00 PM	Lunch break	
1:00 - 3:00 PM	Key Session I "Living in contaminated areas" Part II	
3:00 - 3:30 PM	Coffee break	
3:30 - 5:15 PM	Radiation biology/Radiation physics I	
6:00 PM Departure to "Bräustüberl Weihenstephan" Freising		

WEDNESDAY, 15.05.2019

TIME	LECTURE HALL	BASEMENT
8:00 - 10:05 AM	Key Session II "Latest developments in radiation preparedness"	Poster exhibition
10:05 - 10:35 AM	Coffee break	
10:35 - 11:50 AM	Radiation protection	
11:50 - 12:50 AM	Lunch break	
12:50 - 1:50 PM	Radiation accident management	
1:50 - 3:00 PM	Poster presentation (basement)	
3:00 - 3:30 PM	Coffee break	
3:30 - 5:15 PM	Radiation emergency medical preparedness and response	
Free time to explore Munich, suggestions and flyer available at the conference office		

THURSDAY, 16.05.2019

TIME	LECTURE HALL
8:00 - 9:20 AM	Radiation health effects and medical countermeasures II
9:20 – 9:50 AM	Effects of electromagnetic fields
9:50 - 10:20 AM	Coffee break
10:20 – 11:05 AM	Effects of low dose ionizing radiation
11:05 – 11:25 AM	Radiation risk perception of the public/External exposure assessment
11:25 AM – 12:05 PM	Radiation biology/Radiation physics II
12:05 – 12:15 pm	Closing remarks
12:15 - 1:15 PM	Lunch break

Monday, May 13th 2019

Arrival	**Conference office opened from 10:00 am until 12:00 pm**
7:00 pm	**Icebreaker (Seargents` mess ballroom, build. no. 07)**

Note:

In the following time schedule only presenting authors are mentioned.

Co-authorships are outlined in the abstracts section.

Tuesday, May 14th 2019

8:15 – 8:45 am	**Welcoming addresses**
8:45 – 9:00 am	**Group photo**
9:00 – 10:00 am	**Radiation health effects and medical countermeasures I**
10:30 am – 3:00 pm	**Key Session "Living in contaminated areas"**
3:30 – 5:15 pm	**Radiation biology/Radiation physics I**

8:15 – 8:45 am **Welcoming addresses**

Colonel (MC) Prof. Dr. Matthias Port
Bundeswehr Institute of Radiobiology affiliated to the University of Ulm, Munich, Germany
Conference Chairperson

Brigadier General (MC) Dr. Hans-Ulrich Holtherm, MSc
Director, Military Medical Science and Medical Service Capability Development and Deputy Commandant Bundeswehr Medical Academy, Munich, Germany

Navy Captain (MC) (res) Prof. Dr. Johann Wilhelm Weidringer
Executive Officer Bavarian Chamber of Physicians, Munich, Germany

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8:45 – 9:00 am **Group photo inside the lecture hall**

9:00 – 10:00 am **Radiation health effects and medical countermeasures I**

Chairpersons *Dr. Christophe Badie and LTC (MC) Dr. Stefan Eder*

9:00 – 9:15 am
Prevention and management of long-term adverse health effects associated with exposure to ionizing radiation: an occupational medicine perspective
S. Eder, Bundeswehr Institute of Radiobiology, Germany

9:15 – 9:30 am
Multisite de novo mutations in human offspring after paternal exposure to ionizing radiation
P. Krawitz, Institute for Genomic Statistics and Bioinformatics, University Bonn, Germany

9:30 – 9:45 am
Measuring response to radiation exposure by real-time differential gene expression sequencing analysis
C. Badie, Public Health England - Centre for Radiation, Chemicals and Environmental Hazards (PHE-CRCE), United Kingdom

9:45 – 10:00 am
The German Uranium Miners Biobank – a treasure chest for radiation research
M. Gomolka, Bundesamt für Strahlenschutz, Germany

10:00 – 10:30 am **Coffee break**

10:30 am – 12:00 noon **Key Session I "Living in contaminated areas" Part I**

Chairperson *Dr. Florian Gering and COL (MC) Prof. Dr. Michael Abend*

10:30 – 10:40 am
Introduction
M. Abend, Bundeswehr Institute of Radiobiology, Germany

10:40 – 11:00 am
Application of the Radiological Protection System in Post-Accident Situations - An update on ICRP Publications 109 and 111
A. Nisbet, Public Health England - Centre for Radiation, Chemical & Environmental Hazards, (PHE-CRCE) United Kingdom

11:00 – 11:20 am
Individual dose estimation based on radiation measurements in the environment (and it's relation to the environmental monitoring strategy)
F. Gering, Bundesamt für Strahlenschutz, Germany

11:20 – 11:40 am
Countermeasures, radiological surveillance and evolution of regulations in Belarus, after the Chernobyl accident
V. Averyn, Faculty of Biology at the University of Francisk Skaryna, Belarus

11:40 am – 12:00 noon
"Experiences on reduction of external dose to inhabitants of contaminated areas"
K. Andersson, DTU NUTECH Center for Nuclear Technologies, Technical University of Denmark

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12:00 noon – 1:00 pm **Lunch break**

1:00 – 3:00 pm **Key Session I "Living in contaminated areas" Part II**

Chairperson *Prof. Dr. Hajo Zeeb and COL (MC) Prof. Dr. Michael Abend*

1:00 – 1:20 pm
Coping with radiological exposure in daily life following a nuclear accident: Lessons from the ETHOS and CORE projects in Belarus
T. Schneider, European Platform on preparedness for nuclear and radiological emergency response and recovery (NERIS), France

1:20 – 1:40 pm
Towards a holistic approach to protection of inhabitants of contaminated environments: the role of non-targeted effects
C. Mothersill, Department of Biology, McMaster University, Canada

1:40 – 2:00 am
High natural background radiation and health: an overview of current evidence
H. Zeeb, Leibniz Institute for Prevention Research and Epidemiology – BIPS, Germany

2:00 – 2:20 pm
How dangerous is living in contaminated areas? Epidemiological thoughts on risks and further studies
P. Scholz-Kreisel, Institute of Medical Biostatistics, Epidemiology and Informatics (IMBEI); University Medical Center of the Johannes Gutenberg University Mainz, Germany

2:20 – 2:40 pm
Social and medical preparedness and response against nuclear accident in Japan; lessons learned from Fukushima thyroid examination
S. Yamashita, Fukushima Medical University/Nagasaki University, Japan

2:40 – 3:00 pm
Risk communication - a significant contribution to long-term psychosocial support of affected populations
C. Pölzl-Viol, Bundesamt für Strahlenschutz, Germany

3:00 – 3:30 pm **Coffee break**

3:30 – 5:15 pm **Radiation biology/Radiation physics I**

Chairperson *Prof. Dr. Günther Dollinger and PD. Dr. Reinhard Ullmann*

3:30 – 3:45 pm
DNA damage interaction on both nanometer and micrometer scale determine overall cellular damage
G. Dollinger, Universität der Bundeswehr München, Germany

3:45 – 4:00 pm
Mutational patterns and gene expression signatures in a cell line resistant to cytostatics and irradiation
R. Ullmann, Bundeswehr Institute of Radiobiology, Germany

4:00 – 4:15 pm
Radiation –induced mutational changes in the genome, exome and transcriptome of human fibroblasts
A. Kuss, University Medicine Greifswald, Germany

4:15 – 4:30 pm
Biological interaction of a static magnetic field (SMF) with ionizing irradiation
S. Bartzsch, Institute of Innovative Radiotherapy, Helmholtz Zentrum München, Neuherberg, Germany

4:30 – 4:45 pm
Research in radiotoxicology and the 3Rs - Replace, Reduce and Refine – observations
N. Griffith, CEA, France

4:45 – 5:00 pm
Automatic scoring of dicentric chromosomes and the detection of partial body exposure: Statistical considerations
D. Endesfelder, Bundesamt für Strahlenschutz, Germany

5:00 – 5:15 pm
Is there any similarity in gene expression profile in response to radiation therapy, independently of the cancer type?
J. Polanska, Silesian University of Technology, Gliwice, Poland

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6:00 pm **Departure to conference dinner at "Bräustüberl Weihenstephan"**

Wednesday, May 15th 2019

8:00 – 10:05 am	**Key session II: Latest developments in radiation preparedness**
10:35 – 11:50 am	**Radiation protection**
12:50 – 1:50 pm	**Radiation accident management**
1:50 – 3:00 pm	**Poster presentation in the poster exhibition (basement)**
3:30 – 5:15 pm	**Radiation emergency medical preparedness and response**

8:00 – 10:05 am **Key session II: Latest developments in radiation preparedness**

Chairpersons *BG (MC) Dr. Michel Drouet and COL (MC) Prof. Dr. Matthias Port*

8:00– 8:05 am
Introduction
M. Port, Bundeswehr Institute of Radiobiology, Germany

8:05 – 8:20 am
Development of automated high throughput biodosimetry tools for radiological/nuclear mass casualty incidents
A. Balajee, Oak Ridge Institute for Science and Education, USA

8:20 – 8:35 am
Integration of local, national and international medical responses in a mass casualty radiological/nuclear incident
N. Dainiak, Yale University School of Medicine, USA

8:35 – 8:50 am
Radioprotective effect of vitamin C as an antioxidant
M. Kinoshita, National Defense Medical College Japan

8:50 – 9:05 am
Rapid high through-put diagnostic triage after a mass radiation exposure event using early gene expression changes
M. Abend, Bundeswehr Institute of Radiobiology, Germany

9:05 – 9:20 am
Circulating Cell-Free DNA (cfDNA) Correlates with integral dose and identifies radiotherapy patients who develop gastrointestinal toxicity
P. Okunieff, University of Florida, USA

9:20 – 9:35 am
Assessment of the radiological effects from a "dirty bomb" scenario in urban areas on a metrological microscale
K. Folger, Bundesamt für Strahlenschutz, Germany

9:35 – 9:50 am
MSC-derived extracellular vesicles: New emergency treatment to limit the development of radiation-induced hematopoietic syndrome?
D. Riccobono, French Armed Forces Biomedical Research Institute, France

9:50 – 10:05 am
Genomic intability and DNA-repair predicting radiosensitivity?
C. Streffer, University Medicine Essen, Germany

10:05 – 10:35 am **Coffee break**

10:35 – 11:50 am **Radiation protection**

Chairpersons *Prof. Dr. Dimitry Bazyka and Dr. Christina Beinke*

10:35 – 10:50 am
Misuse of a medical isotope: Playing cards contaminated with I-125, German experience
E. Kroeger, Bundesamt für Strahlenschutz, Germany

10:50 – 11:05 am
Biodosimetry and biodosimetry networks for managing radiation emergency
U. Oestreicher, Bundesamt für Strahlenschutz, Germany

11:05 – 11:20 am
Biodosimetry of internalized irradiation exposures using transcriptional analysis from relapsed and refractory neuroblastoma patients from a NANT11-01 study treated with 131I-MIBG.
M. Coleman, Lawrence Livermore National Laboratory, USA

11:20 – 11:35 am
Imidazolyl Ethanamide Pentandionic Acid for the Treatment of Acute Radiation Syndrome
M. Czajkowski, Myelo Therapeutics GmbH, Germany

11:35 – 11:50 am
Radiation risks of medical exposure in Russia: current status of the problem within international and national standards
V. Kashcheev, A.Tsyb Medical Radiological Research Center (MRRC), Russia

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11:50 am – 12:50 pm Lunch break

12:50 – 1:50 pm Radiation accident management

Chairpersons *Prof. Dr. Harold Swartz and Prof. Dr. Manabu Kinoshita*

12:50 – 1:05 pm
SEED, a deployable numerical dosimetric reconstruction tool
F. Entine, French defense radiation protection service, France

1:05 – 1:20 pm
Metrology for mobile detection of ionising radiation: The EMIR project 16ENV04 "Preparedness"
S. Neumaier, Physikalisch-Technische Bundesanstalt, Germany

1:20 – 1:35 pm
The accuracy of biological dose reconstruction in case of criticality accident
E. Gregoire, Institut de Radioprotection et de Sûreté Nucléaire, France

1:35 – 1:50 pm
Radiation exposure biomarkers in the practice of the medical radiology: Cooperative research and the role of the International Atomic Energy Agency (IAEA) biodosimetry/radiobiology laboratory
O. Belyakov, International Atomic Energy Agency, Austria

1:50 – 3:00 pm **Poster presentation in the poster exhibition (basement)**

3:00 – 3:30 pm **Coffee break**

3:30 – 5:15pm **Radiation emergency medical preparedness and response**

Chairpersons *Prof. Dr. William Blakely and Prof. Dr. Ann Barry Flood*

3:30 – 3:45 pm
Update on AFRRI's cytogenetic Biodosimetry activities – enhancement of throughput
W. Blakely, Uniformed Services University/Armed Forces Radiobiology Research Institute (AFRRI), USA

3:45 – 4:00 pm
Comparative effectiveness of biomarkers: Expanding a framework to include organ-specific predictions of Injury
A. Flood, Dartmouth Medical School, USA

4:00 – 4:15 pm
Resolution of homogeneity and dose distribution under emergency conditions using Electron Paramagnetic Resonance (EPR) measurements of finger/toe nails in vivo
H. Swartz, Geisel College of Medicine at Dartmouth & Clin-EPR, LLC, USA

4:15 – 4:30 pm
The STORE database; a platform for data and resource sharing in radiation biology, radioecology and epidemiology
P. Schofield, University of Cambridge, United Kingdom

4:30 – 4:45 pm
Natural history of disease progression in a rabbit model of acute radiation sickness following total body irradiation
I. Jackson, University of Maryland School of Medicine, USA

4:45 – 5:00 pm
Developing entolimod, a TLR5 agonist, as a medical countermeasure against acute radiation syndrome
V. Krivokrysenko, Cleveland BioLabs, Inc., USA

5:00 – 5:15 pm
Development of a METREPOL-based response category (RC) algorithm for H-ARS severity triage in a baboon radiation model involving gamma ray and mixed-field (i.e., 5.5 neutron to gamma ray) exposures
D. Bolduc, Uniformed Services University/Armed Forces Radiobiology Research Institute (AFRRI), USA

Free time to explore Munich, suggestions and flyer available at the conference office

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Thursday, May 16th 2019

8:00 – 9:20 am	**Radiation health effects and medical countermeasures II**
9:20 – 9:50 am	**Effects of electromagnetic fields**
10:20 – 11:05 am	**Effects of low dose ionizing radiation**
11:05 – 11:25 am	**Radiation risk perception of the public/External exposure assessment**
11:25 am – 12:10 pm	**Radiation biology/Radiation physics II**
12:10 – 12:20 pm	**Closing remarks**

8:00 – 9:20 am Radiation health effects and medical countermeasures II

Chairpersons *Prof. Dr. Vijay Singh and Dr. Lanyn Taliaferro*

8:00 – 8:15 am
Plasma proteins as new biomarkers of irradiation in humans
A. Tichy, University of Defence, Faculty of Military Health Sciences, Czech Republic

8:15 – 8:30 am
Molecular markers of occupational exposure at area contaminated after radiation accident
D. Bazyka, National Research Center for Radiation Medicine of the National Academy of Medical Sciences of Ukraine, Ukraine

8:30 – 8:40 am
Cataract type and magnitude in mouse is highly dependent on dose and age at irradiation
D. Pawliczek, Helmholtz Zentrum München, Germany

8:40 – 8:55 am
Biomarkers for assessing radiation injury identified using the nonhuman primate model
V. Singh, Uniformed Services University/Armed Forces Radiobiology Research Institute (AFRRI), USA

8:55 – 9:10 am
Radiation-induced cardiovascular disease: 10 years lessons learned from heart proteome analyses
O. Azimzadeh, Helmholtz Zentrum München, Germany

9:10 – 9:20 am
Diagnostic performance of 68Gallium-PSMA PET/CT in a large cohort of patients with biochemical recurrence of prostate carcinoma
M. Hoffmann, Bundeswehr Medical Service Headquarters, Germany

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9:20 – 9:50 am **Effects of electromagnetic fields**

Chairpersons *Prof. Dr. Marcus Stiemer and MAJ (MC) Dr. Andreas Lamkowski*

9:20 – 9:35 am
Examining cell proliferation and differentiation in primary human dermal fibroblasts to ensure EMF exposure experiments under comparable condition
V. Franchini, Scientific Department of Army Medical Center, Italy

9:35 – 9:50 am
Precise and Reproducible SAR-Dosimetry for Electromagnetic Field Exposure Tests
R. Hollan, Universität der Bundeswehr Hamburg, Germany

9:50 – 10:20 am **Coffee break**

10:20 – 11:05 pm **Effects of low dose ionizing radiation**

Chairpersons *Prof. Dr. Harry Scherthan and Dr. Tanja Popp*

10:20 – 10:35 am
Canceled

10:35 – 10:45 am
Risk assessement in Siberian group of chemical enterprises personnel
R. Takhauov, Seversk Biophysical Research Center of the Russian Federal Medical and Biological Agency, Russia

10:45 – 10:55 am
Low dose irradiation by low and high LET emitters discriminated by DNA damage geometry
H. Scherthan, Bundeswehr Institute of Radiobiology, Germany

10:55 – 11:05 am
Molecular imaging for longitudinal in vivo prediction of cell death and tissue regeneration after exposure to ionizing radiation
S. Ziegler, Department of Nuclear Medicine, LMU Munich, Germany

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11:05 – 11:25 am Radiation risk perception of the public/External exposure assessment

Chairpersons *Prof. Dr. Prakash Hande and Dr. Tanja Popp*

11:05 – 11:15 am
Advanced CT-protocols in clinical routine: CTA-Subtraction-Technique in detection of pulmonary embolism. A benefit for patients or only an increase in dose?
K. Nestler, Department for Radiology and Neuroradiology, Bundeswehr Central Hospital, Koblenz, Germany

11:15 – 11:25 am
Reevaluation of the dose effect curve from low to high doses using the standard micronuclei technique in association with a telomere/centromere FISH staining
C. Herate, CEA, France

11:25 am – 12:10 pm Radiation Biology/Radiation Physics II

Chairpersons *Dr. Ales Tichy and MAJ (MC) Dr. Patrick Ostheim*

11:25 – 11:35 am
Using mRNA and small RNA gene expression changes in the peripheral blood for easy detection of Ra-223 incorporation
P. Ostheim, Bundeswehr Institute of Radiobiology, Germany

11:35 am – 11:45 am
Accident with a Se-75 source
*V. Kaufmann and P. Adler***,** NucTecSolutions GmbH, Germany

11:45 – 11:55 am
Protecting skin keratinocytes from ionizing radiation with Bardoxolone-methyl
C. Hermann, Bundeswehr Institute of Radiobiology, Germany

11:55 – 12:05 pm
CT irradiation induced changes of RNA profiles within peripheral blood cells and exosomes
H. Kaatsch, Bundeswehr Institute of Radiobiology, Germany

12:05 – 12:15 pm **Closing remarks**

Colonel (MC) Prof. Dr. Matthias Port, conference chairperson

Bundeswehr Institute of Radiobiology, Germany

12:15 – 1:15 pm **Lunch**

Conference lectures

Available online: www.radiation-medicine.de and www.sanitaetsdienst-bundeswehr.de (short link: http://bit.ly/ConRad2019)

Session Radiation health effects and medical countermeasures I

Abstract ID 27399

Prevention and management of long-term adverse health effects associated with exposure to ionizing radiation: an occupational medicine perspective

S. Eder [1,2], A. Lamkowski[1,2], A. Rump[1], M. Port[1]

[1] Bundeswehr Institute of Radiobiology affiliated to the University Ulm, Munich, Germany

[2] Institute and Outpatient Clinic for Occupational, Social and Environmental Medicine, Inner City Clinic, University Hospital of Munich (LMU), Munich, Germany

According to European and German guidelines for the medical screening of persons occupationally exposed to radiation authorized physicians are made responsible for the execution of preventive examinations, consultations and evaluations of concerned employees as well as for recommendations with regard to the initiation of medical countermeasures in case of radio-nuclear overexposure.

Contrary to the public perception, received exposure estimates of previous radiation incidents most predominantly lay within the low-dose range raising medical concerns for long-term rather than acute health effects.

Not least based on the experiences e.g. from insufficient radiation protection procedures of former military radar technicians and operators during the 1960s and early 1970s combined with resulting compensation claims there is a present awareness within German military services with respect to the implementation of preventive radiation protection measures. Here we present current examples of environmental radiation risk assessments for occupational missions abroad including exposure to elevated levels of natural background activity, solar UV-light or Ru-106.

Furthermore, we highlight the need for scientific studies regarding potential biological effects of electromagnetic fields generated by military devices and present first results from experiments using a mini-TEM cell.

Abstract ID 29208

Multisite de novo mutations in human offspring after paternal exposure to ionizing radiation

M. Holtgrewe, A. Knaus, F. Brand, G. Hildebrand, J.-T. Pantel, M. Rodriguez de los Santos, K. Neveling, J. Goldmann, M. Schubach, M. Jäger, M. Coutelier, S. Mundlos, D. Beule, K. Sperling, P.M. Krawitz

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A genome-wide evaluation of the effects of ionizing radiation on mutation induction in the mouse germline has identified multisite de novo mutations (MSDNs) as marker for previous exposure. Here we present the results of a small pilot study of whole genome sequencing in offspring of soldiers who served in radar units on weapon systems that were emitting high-frequency radiation. We found cases of exceptionally high MSDN rates as well as an increased mean in our cohort: While a MSDN mutation is detected in average in 1 out of 5 offspring of unexposed controls, we observed 12 MSDNs in altogether 18 offspring, including a family with 6 MSDNs in 3 offspring. Moreover, we found two translocations, also resulting from neighboring mutations. Our findings indicate that MSDNs might be suited in principle for the assessment of DNA damage from ionizing radiation also in humans. However, as exact person-related dose values in risk groups are usually not available, the interpretation of MSDNs in single families will benefit from larger molecular epidemiologic studies on this new biomarker.

Abstract ID 27797

Measuring response to radiation exposure by real-time differential gene expression sequencing analysis

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In the hypothesis of a large-scale event leading to acute ionising radiation exposure, high-throughput methods would be requested to assess individual dose estimates for triage purposes. Blood-based gene expression biomarkers are of great potential (Kabacik et al. 2011; Manning et al. 2013) as they can be used to provide rapid dose estimates for a large number of individuals. Gene expression has now been validated through multiple NATO and RENEB exercises (Badie et al. 2013, Abend et al. 2016, and Manning et al. 2016). For the management of such radiological emergencies, time is a crucial component while the shipment of blood samples to relevant laboratories is an issue. In this study, in collaboration with Oxford Nanopore Technologies, we have performed differential gene expression analyses to detect radio-inducible genes. Briefly, blood was drawn from nine healthy volunteers and each sample was divided in two equal volumes (one control and one ex vivo irradiated with a 2 Gy X-rays dose). Following peripheral blood mononuclear cells isolation, the irradiated samples were incubated along with the controls for 24 hours at 37 degrees. Following total RNA extraction, and poly A RNA isolation, we generated PCR cDNA data using the PCS-109 kit for the three paired biological replicates (~40-75 million aligned reads per sample) and analysed the reads using a snakemake pipeline modified to handle paired samples (Love et al. 2018). The pipeline maps the reads to the transcriptome using minmap2 and estimate per-transcript read counts. Transcript read counts are filtered and aggregated into gene counts. We found that some genes are expressed at very high level (around 900,000 reads each e.g. TMSB10, Beta2M, CCL24). For one of the most radiation-responsive genes in humans in vivo, FDXR (O'Brien et al 2018), the mean number of counts before normalisation was 103 (control) and 2065 (irradiated), giving after normalisation to HPRT housekeeping gene, a 20 fold increase in expression, which is broadly similar to what we previously reported by quantitative PCR (Manning et al. 2013). In summary these data show that although further development is required, this sequencing technology could be applicable for high throughput biological dosimetry purposes.

Abstract ID 27895

The German Uranium Miners Biobank – a treasure chest for radiation research

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The Federal Office for Radiation Protection (BfS) operates a unique biobank dedicated for radiation research purposes. The biobank encloses biological human samples from blood or tissue from former uranium miners of one of the world largest uranium mining companies, the SAG/SDAG Wismut located in eastern Germany. Between 1946 and 1990 more than 400.000 workers were employed in the uranium mining process. Especially in the early years, workers were highly exposed to ionizing radiation, mainly radon and radon progeny.

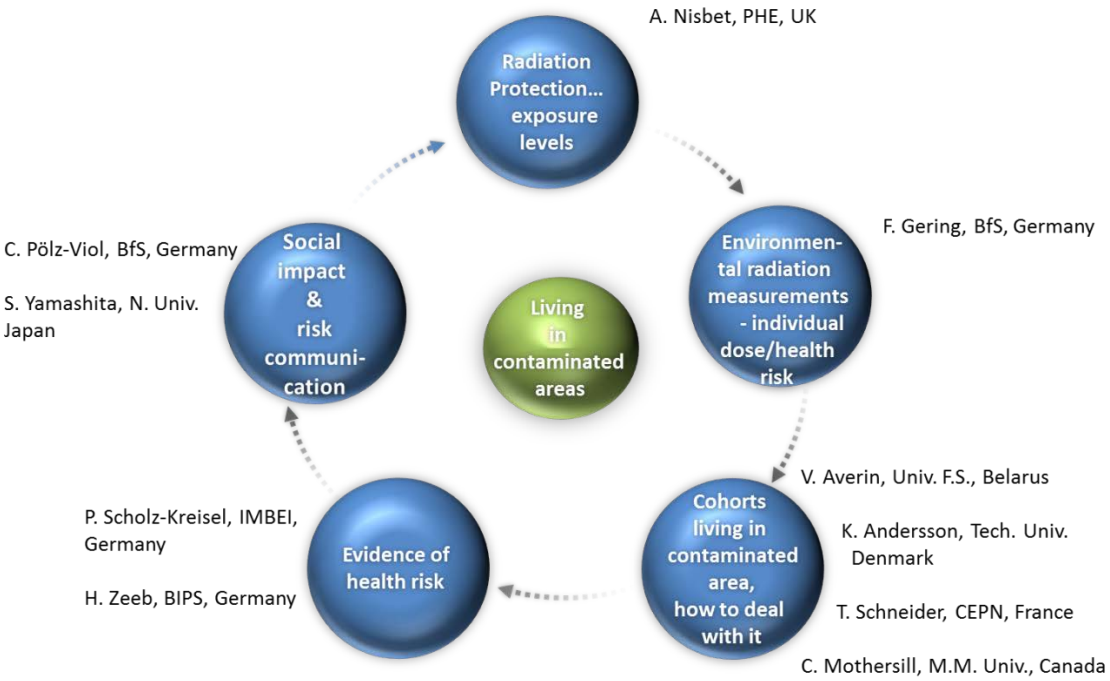
The BfS started a biobanking initiative in 2008. High quality blood samples from more than 400 former miners have been collected. DNA, RNA and peripheral blood leukocytes have been isolated and stored as well as plasma samples and PAXgene tubes. In addition, DNA and RNA samples have been isolated from tumor and normal tissue from more than 600 lung cancer cases of former miners. Individual data are available for radon and gamma radiation exposure, silica dust and arsenic, smoking, medical information on diseases and medication at the time of sample collection. Experimental data on SNPs (Oncoarray), whole genome gene expression (Affymetrix) and

chromosomal aberrations by mFISH analyses have been generated for the whole biobank samples or for a subgroup. Experimental data are also available via STORE after application.

First studies have been performed on individual radiation sensitivity, past exposure related gene expression and microRNA induction and chromosomal aberrations. Lung cancer risk genes have been identified that are modulated by the radon exposure (Rosenberger et al. 2018), as well as gene expression signatures related to the gamma exposure of the red bone marrow. Part of the results have been published. Experimental data are available via STORE databank after application.

The biobank is open to researchers upon request. Material and data can be accessed after successful application. The biobank offers research opportunities for chronic low dose exposure to the red bone marrow (<700 mGy mean cumulative absorbed red bone marrow dose) or high exposure to the lung (> 600 **W**orking **L**evel **M**onth mean cumulative) by radon.

Key-Session I Living in contaminated areas



Abstract ID 27355

Application of the Radiological Protection System in Post-Accident Situations - An update on ICRP Publications 109 and 111

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The ICRP system of radiological protection is a fundamental framework for dealing with any exposure situation in a systematic and coherent manner. ICRP Publications 109 and 111 are focussed on emergency and existing exposure situations resulting from nuclear accidents, and were built on the experience of managing the Chernobyl accident in Europe in 1986, but were published before the events at Fukushima Daiichi nuclear power plant in 2011. An ICRP Task Group (TG93) was established in 2013 to update Publications 109 and 111 in light of the lessons learned from the management of Fukushima and from the series of dialogue meetings organised by ICRP in co-operation with national and local stakeholders starting in 2011. This paper provides an overview of this widely anticipated update (The report produced by TG93 will be subject to public consultation before final publication), highlighting areas where clarification and modifications to previous recommendations have proved necessary. By considering emergency response and recovery in the same report, the evolution of radiological protection considerations along the timeline after an accident is covered by a consistent and overarching framework. The recommendations emphasise the importance of the justification of the protection strategy and its subsequent optimisation through the application of reference levels. During emergency response, the reference level for the protection of both responders and the population should not exceed 100 mSv for a short period or up to one year; lower values may be selected according to the severity of the accident. During recovery, the reference level for people living in long-term contaminated territories should not exceed 10 mSv/y; the objective being to progressively reduce exposures to around 1 mSv/y. The involvement of local communities during recovery is important in the development of a practical radiological protection culture, where individual lifestyles become a key factor in controlling exposures. Self-help protective actions can be undertaken to complement those implemented by the authorities and individual measurements using suitable devices support this approach. Finally, consideration of ethical, societal and environmental dimensions is necessary for the effective management of post-accident situations.

Abstract ID 27885

Radiation Measurements in the Environment and Individual Dose Estimates

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Assessing doses of individual persons affected by nuclear or radiological accidents is an important issue in emergency response. It enables the individual comparison of doses with e.g. reference levels, allowing for identification of those members of the affected population who require additional follow-up actions like e.g. medical follow-up. In addition, large-scale individual dose assessment can also provide a basis for epidemiological studies.

A software tool for dose reconstruction was recently developed by the German Federal Office for Radiation Protection. It makes use of all kinds of available environmental monitoring data, including gamma dose rate, air concentration and ground contamination measurements. Individual doses are computed based on the time and duration of stay of the respective person within the contaminated areas. The output of the tool comprises individual values for the effective dose and for the equivalent doses of the thyroid and red bone marrow.

This dose reconstruction tool is designated to be used in emergency care centers where potentially contaminated people arrive after an emergency exposure situation, and was successfully tested during several emergency exercise since 2017.

Abstract ID 25572

Countermeasures, radiological surveillance and evolution of regulations in Belarus, after the Chernobyl accident

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As a result of the Chernobyl accident, radioactive contamination affected 23.5 % of the territory of the Republic of Belarus (48.8 thousand square kilometers). During 1986, 24.7 thousand Belarusians were evacuated from 107 most affected settlements Gomel region.

Recommendations to reduce thyroid doses were disseminated straight after the accident: stop consuming milk and fresh leafy vegetables; stop cattle grazing on open pastures, feed with clean fodder and keep dairy cattle in stalls; process whole milk into storable products such as butter, or bring it for processing into dry or condensed milk.

In accordance with the USSR Ministry of Health resolution of 18 September 1986, it was decided to establish a permissible radiation dose to population of 10 rem (100 mSv) for the first year after the Chernobyl accident, including 5 rem (50 mSv) from internal exposure.

Agricultural countermeasures in the Republic of Belarus were implemented extensively with the aim to reduce radionuclide transfer into foods and guarantee 'clean' foodstuff production of crops (e.g. liming, application of increased rates of potash fertilizers, pastures improvement) and animal products (e.g. controlling the radionuclide contents in animal diets by means of feed management, applying cesium binders, using 'clean' feeds in finish rations). Food crops and grain legumes (vegetables, buckwheat, peas, etc.), previously covering the area of 6 thousand hectares, have been excluded from agricultural production in the areas with contamination densities above 40 Ci/km2.

Countermeasures can be only effective when there is a preliminary awareness of all possible pathways of human exposure, and when there is a high level of preventing preparedness to their implementation before the major part of the absorbed dose is formed. Dose effectiveness of countermeasures depends on the time of their implementation since the moment when environmental contamination occurred. Countermeasures implemented in the early period after the accident guarantee a high level of effectiveness, preventing from building significantly higher collective doses, comparing to those implemented in a later phase when the absolute concentrations of radionuclides in foodstuffs are lower. Economic effectiveness is also time-dependent, as the same amounts of expenses can prevent significantly different absorbed doses.

Abstract ID 26428

Experiences on reduction of external dose to inhabitants of contaminated areas

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Prior to the Chernobyl accident in 1986 it was considered highly unlikely that any plausible incident leading to airborne dispersion of radioactive contaminants would to any significant extent affect inhabited areas. Therefore, efforts made to that time to investigate countermeasures that might be implemented in case of a large

contaminating incident had almost entirely focused on rural land areas, and in particular agriculture. According to recent reviews, the long term ingestion and external dose contributions received by inhabitants of areas contaminated by the Chernobyl accident were estimated to be about equal in magnitude, whereas the long term external dose contribution to the public in areas contaminated by the Fukushima accident has been estimated to be of the order of 80-90 %, and the corresponding ingestion dose only 10-20 %. In preparedness for possible future nuclear power plant accidents, it is thus highly important to be able to implement effective recovery strategies for contaminated inhabited areas. The international state of unpreparedness in this context at the time of the Chernobyl accident is reflected in the generally poor results of efforts in the late 1980's to reduce external dose in the affected areas. Throughout the 1990's an experience base was formed through examination of a wide range of different countermeasures under different environmental conditions. On this basis, the first compendium describing important features of recovery countermeasures for contaminated inhabited areas in a standardised format emerged in 1995 from the European Experimental Collaboration Project No. 4. Since then, this work has undergone a large further development and today constitutes the backbone of the European recovery handbook for contaminated inhabited areas. The presentation gives an overview of today's knowledge and recovery management methods, and outlines current shortcomings, also in relation to the way recovery has been managed in the context of the Fukushima accident.

Abstract ID 27615

Coping with radiological exposure in daily life following a nuclear accident: Lessons from the ETHOS and CORE projects in Belarus

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The ETHOS and CORE projects, implemented in Belarus from 1996 to 2008 in Belarus, following the Chernobyl accident, highlighted the importance for the management of the recovery phase to involve local stakeholders living in contaminated territories for ensuring the effectiveness and sustainability of protective actions as well as allowing them to take informed decision. These projects were developed with the support of the Belarus Authorities and implemented by a European Team of experts, aiming at developing a sustainable improvement of the living conditions of the local population. Based on the direct involvement of the local populations in their own protection, in involved groups of teenagers, young mothers, farmers, teachers, health care professionals and foresters in several villages. They aimed at addressing their concerns for their daily life: i.e. management of the radiological quality of milk and meat; management of the radiological protection of children; management of the radioactive waste… In this context, the role of radiological protection experts was essential to favour the development of the radiological protection culture in order to: provide capabilities for identifying and having references regarding the presence of radioactivity in the day-to-day life; allow the interpretation of the measurements produced in the locality and/or at the regional level; and contribute to the decision-aiding process.

Abstract ID 26759

Towards a holistic approach to protection of inhabitants of contaminated environments: the role of non-targeted effects

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Recent moves within ICRP to develop an integrated approach to radiation protection of both humans and non-human biota are focused on regulating dose to exposed populations based on behaviour, size, lifestyle and "radiosensitivity". Currently man and 12 reference organisms are used covering various taxonomic groups,

behaviours, and exposure scenarios - e.g. marine, terrestrial, sediment or airborne. However most biologists agree that particularly in low dose exposure legacy sites, the factors determining effects and outcomes are far more complex that this simple framework suggests. The issue is developing reliable predictors of system or ecosystem health rather than relying on biomarkers that give information about effects on individual cells, organs or organisms. Approaches to this include the Adverse Outcome Pathway (AOP) developed as part of the CERAD project in Norway, which looks at multiple levels of organisation from gene to ecosystem building a comprehensive picture of effects at multiple levels of organisation in multiple species including humans. Various camera drone based ecosystem evaluation techniques have been developed in other areas of environmental management. These could be applied at legacy sites where damage to for example tree canopies or river flow patterns can be used to assess ecosystem health much like a CAT or MRI scan reveals structural changes in individual organisms systems. Another more focused approach used by our group is to look at the role of non-targeted effects such as genomic instability (GI) and bystander effects (BE). These mechanisms involve transmission of information between different levels of organisation. In the case of BE signals from exposed to unexposed cells or organisms coordinate response at higher levels of organisation permitting population responses to radiation to be optimised. GI is more complex as it involves not only signalling but also trans-generational transmission of genetic or epigenetic changes and may lead to long-term adaptive evolution. GI may also be involved in memory or legacy effects, which contribute a further component to the dose effect measured in legacy sites. Our recent analysis the contributions of memory and legacy effects to the total effect using data sets from Chernobyl and Fukushima (voles, birds and butterflies) suggest this type of analysis may help reduce uncertainties over lab to field extrapolations. Given the clear discrepancy between actual data measured in the field and dose effects generated using databases populated mainly with acute lab based experimental data, it is imperative that we strive to develop meaningful holistic systems for protection of those living in contaminated ecosystems.

Abstract ID 25549

High natural background radiation and health: an overview of current evidence

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Next to medical radiation, natural radiation is a major contributor to radiation exposure of the general population. Due to the specific regional geology, there are several areas in the world which are characterized by a comparatively high natural level of natural ionizing background radiation (HNBR). A current classification categorizes these areas according to the annual effective dose from natural background radiation: around 5 mSv = low, 5-20 mSv = medium level, 20-50mSv = high level, and levels above 50 mSv = very high. In the context of understanding low-dose radiation risks for humans, these areas have raised substantial interest of researchers as the populations living in these regions are constantly exposed to these elevated radiation levels. Studies to assess potentially associated health risks have been conducted in many of these areas, including in Brazil, Iran, China and India. With a view to the quality of available epidemiologic studies, a recent UNSCEAR report focused on investigations conducted in Kerala (India) and Yangjiang (China). In both regions large-scale population-based studies have been performed. The cohort in Kerala included some 70,000 persons, with radiation measurements taken in each household and follow-up of cohort members for cancer incidence and mortality. The somewhat smaller Chinese study used similar approaches, however, in the absence of cancer registry information, only mortality data was collected. The main results of published analyses overall do not indicate elevated cancer mortality or cancer incidence associated with radiation exposure. However, both studies have limitations that need to be considered when interpreting the data, and results for subgroups and with respect to cytogenetic studies in these populations will be presented and discussed in the presentation. Overall, HNBR present a useful, but challenging opportunity to assess low-dose-rate ionizing radiation exposure to humans. They augment studies

on occupational groups, on medically or environmentally exposed persons, and notably the study among survivors of the atomic bombings.

Abstract ID 25763

How dangerous is living in contaminated areas? Epidemiological thoughts on risks and further studies.

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Radioactive contamination can lead to many long term consequences for the inhabitants. The extent of these consequences can range from minor restrictions or precautions in the use of (wild-) food over social-economic embarrassments like reduced income or shunning to severe medical risks. A possible further consequence could be the risk of genetic alterations due to the prolonged radiation exposure and their long-term impact on a population. Here, we give an overview of the reported health effects of living in contaminated areas and discuss requirements and possibilities of further epidemiological studies. Results from several studies on existing cohorts of people living in or evacuated from contaminated areas after accidents like Mayak, Semipalatinsk, Chernobyl or Fukushima will be discussed.

Increased incidence of thyroid cancer, leukemia or brain tumors as well as elevated risk of cardiovascular and endocrinal diseases are dose-associated, but evidence regarding the effect of low doses like in Fukushima is still incomplete. Furthermore, psychological and socioeconomic issues like fear, isolation, poverty, or lack of infrastructure are leading to a number of additional medical problems, like psychiatric or cardiovascular diseases. These effects are not dose related and can also be found in successfully decontaminated and resettled areas.

Challenges to epidemiological studies include difficult dosimetry and a typically low individual exposure that makes adverse health effects hard to reliably identify. Migration away from the area is creating a major problem for the follow-up of the cohorts. The role of radiation in late health effects is often confounded by many other life style factors that may systematically differ in these areas.

Planning new epidemiological studies to assess health effects for people living in contaminated areas should not only focus on radiation-related outcomes but also investigate indirect effects. To achieve this, it is necessary to develop epidemiological studies using qualitative and quantitative methods to get a deeper insight into living behavior and resulting health issues. An important possibility to discriminate between direct and indirect effects could be the further development and use of biomarkers for radiation injury. This could be realized in combination with molecular-epidemiological studies on genetic alterations in inhabitants and their siblings.

Abstract ID 26023

Social and Medical Preparedness and Response against the Nuclear Accident in Japan; lessons learned from Fukushima Thyroid Examination

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Now eight years have passed since the complex disaster of the Great East Japan earthquake and its aftermath, the Fukushima Daiichi Nuclear Power Plant accident. Besides the necessity of well-preparedness and response theoretically against nuclear accidents, ways to engage with the problems of radioactive contamination, the so-called “existing exposure situation” (when both the exposure dose remains higher than public dose limit of 1mSv/year during normal conditions and extended periods of time are required to reduce the dose) have

practically manifested as changes in individual actions caused by a difference in recognition and understanding of these problems.

To overcome the difficulties in Fukushima, as one of the tools of risk communication, a sound scientific understanding of the relationship between radiation dose and health risk, especially “Radiation and Thyroid”, is needed to apply justified countermeasures against radiological and nuclear accidents. Here, in addition to the current situation of thyroid ultrasound examination in Fukushima, socio-psychological and ethical issues will be introduced and discussed, at the standpoint of “Resilience” and “Logical Approach”, in order to avoid misunderstanding or misinterpretation of high detection rate of thyroid cancer in young population of Fukushima Prefecture.

Abstract ID 27735

Risk communication - a significant contribution to long-term psychosocial support of affected populations

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Effects on mental health and social life have been identified as one of the most severe consequences of previous radiological emergency situations. There is broad consensus that crisis communication is an important factor to support affected populations in dealing with the crisis situation and the consequences of radiological emergencies, to reduce uncertainty and to strengthen self-help ability in emergency situations.

However, there is still a need for establishing ongoing communication about radiological risks also in the post-emergency and recovery phase. The public’s need for rapid, consistent and comprehensive information does not stop at the transition to the post-emergency phase. Affected people still need the possibility to express their concerns and information needs. For example, after the Fukushima Daiichi Nuclear Power Plant accident, risk communication and stakeholder involvement were seen as effective means to strengthen relevant knowledge, to improve self-help abilities, to provide a sense of control for affected population and to counteract stigmatization. Especially the possibility of exchange with local facilitators was found to be helpful by various stakeholders.

Though numerous guidelines have been developed which provide recommendations for a good crisis and risk communication, there are still a lot of challenges for integrating risk communication as part of long term health surveillance. The necessary attention, appropriate structures, expertise, personal resources and training landscape still have to be strengthened on all levels and in all phases of emergency response and recovery. One the one hand, long term research on the public’s perceptions and mental health effects have to be implemented. On the other hand, risk communication activities need to be monitored and evaluated in order to gain continuous knowledge on possible improvements.

The presentation will provide details on scientific knowledge about the relation between risk communication and subjective wellbeing. Approaches, experiences and challenges related to risk communication will be described.

Session Radiation biology/radiation physics I

Abstract ID 27882

DNA damage interaction on both nanometer and micrometer scale determine overall cellular damage

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DNA double strand breaks (DSB) play a pivotal role for cellular damage, which is a hazard encountered in toxicology and radiation protection, but also exploited e.g. in eradicating tumors in radiation therapy. It is still debated whether and in how far clustering of such DNA lesions leads to an enhanced severity of induced damage. Here we investigate - using focused spots of ionizing radiation as damaging agent - the spatial extension of DNA lesion patterns causing cell inactivation. We find that clustering of DNA damage on both the nm and µm scale leads to enhanced inactivation compared to more homogeneous lesion distributions [1]. A biophysical model interprets these observations in terms of promoted DSB production and DSB interaction, respectively. We decompose the overall effects quantitatively into contributions from these lesion formation processes, concluding that both processes coexist and need to be considered for determining the resulting damage on the cellular level.

[1] T. Friedrich, K. Ilicic, C. Greubel, S. Girst, J. Reindl, M. Sammer, B. Schwarz, C. Siebenwirth, D.W.M. Walsh, T.E. Schmid, M. Scholz and G. Dollinger; Scientific Reports 8 (1) (2018) 16063.

Abstract ID 27600

Mutational patterns and gene expression signatures in a cell line resistant to cytostatics and irradiation

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HaCaT is an immortal cell line originating from adult skin keratinocytes. In previous work we took advantage of the adaptive potential of HaCaT to generate a derivative cell population with increased tolerance towards sulfur mustard (SM). Follow up studies unearthed that resistance was not limited to the initial stressor that triggered resistance, but extended to irradiation and at least further nine cytostatica currently used in tumor therapy. Against this background, comparative analysis of mutational patterns and gene expression signatures in the original and resistant cell population, respectively, promises new insights into basic mechanisms of cellular resistance to genotoxic stress.

Proceeding from whole genome sequencing data we have characterized the specific mutational patterns and additionally determined their overlap with previously published mutation signatures. Deep Sequencing was also employed to profile the transcriptomes of HaCaT and its resistant derivative, and to monitor irradiation associated changes of gene expression after exposure to 6 Gy.

The characteristic mutation patterns enabled the distinction of both HaCaT cell populations by means of unsupervised hierarchical clustering of their cosinus similarities. Comparison to previously published mutation signatures revealed a dominance of single nucleotide variant patterns associated with age, but failed to identify

the characteristic signatures for exposure to UV or alkylating agents. Gene set enrichment analysis based on the list of differentially expressed genes highlighted expected biological processes such as oxidoreductase activity and cellular defense response as well as processes not previously linked to resistance to environmental stress, which we will investigate in more detail by functional follow up studies.

Abstract ID 27135

Radiation-induced mutational changes in the genome, exome and transcriptome of human fibroblasts

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Little is known about the mutational impact of ionizing radiation (IR) exposure on a genome-wide level. Recent advancements in sequencing technology, however, have provided powerful tools to perform exome-, genome- and transcriptome-wide analyses of genetic variation. This also opened up new avenues for studying and characterizing global genomic IR-induced effects. Here, we present our investigation of putative IR-induced mutation signatures in whole genome, exome and transcriptome sequencing datasets of human gingiva fibroblasts (HGF) that were exposed to escalating doses of X-radiation in combination with different post-exposure repair periods.

For our analyses we developed a bioinformatics workflow incorporating three stringent filtering steps for the removal of non-IR induced variants, to remove sequencing errors and to remove variants with low sequencing coverage. We studied the accumulation of single nucleotide variants (SNVs) as well as insertions and deletions (Indels) in the DNA-based datasets and statistically analyzed the accumulation of variants with respect to different genomic features such as cytogenetic bands and topologically associating domains (TAD). We observed the highest accumulation of IR-induced SNVs on chromosome 19 in both the genome and exome datasets. SNVs showed low transition/transversion (Ti/Tv) mutation ratios, while the number of deletions exceeded the number of insertions. Variant distribution in TAD regions was variable across the respective domains. SNVs in gene sets related to stress response and DNA-repair were situated mostly in intronic, up- or downstream regions and sequence ontology analyses showed that they were mostly harmless with no effect on protein function.

Taken together, our results provide strong evidence for a characteristic meta-signature of variants after IR exposure of genomes. Furthermore, structural and/or functional chromatin domain related effects of particular chromosomal areas were noted that may relate to repair pathway choice.

Abstract ID 27167

Biological interaction of a static magnetic field (SMF) with ionizing irradiation

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Purpose

During the last decade there have been several technical developments in radiotherapy, like the development of integrated magnetic resonance imaging (MRI) in a linear accelerator. However, in literature the interaction of a

static magnetic fields (SMFs) with radiation as part is still controversially discussed. Interactions could lead either to aneugenic damages, induced by alteration in the mitotic spindle, as well as clastogenic damages produced by chromosome breaks. In this study, a clonogenic cell survival assay was performed to measure the interaction of a static magnetic field with radiation. Additionally, the mechanism of a possible biological interaction was analyzed using multicolor fluorescence in situ hybridization (mFISH).

Methods

Human glioblastoma cells (LN-18) as well as human peripheral blood T-cell lymphocytes were seeded in petri dishes, which were placed inside a phantom. The irradiation was for cell survival test was performed with a 6 MV linac with doses of 0, 1, 2, 4, 6, and 8 Gy in the presence and absence of a SMF of 1 Tesla produced by a permanent magnet. For the chromosome aberration test, irradiations with 2 and 4 Gy in the presence and absence of a SMF of 1 Tesla were performed. Chromosome aberrations were analyzed in at least 300 metaphases per treatment group using Metafer4 software. For both experiments three technical as well as three biological replicates were performed.

Results

The survival curves were fitted using the linear quadratic model. The survival fractions in absence of an SMF exceed the ones in presence of an SMF for all dose points between 1 and 8 Gy by 12% to 31%. The statistical analysis showed a significant decline ($p \leq 0.05$, ANOVA test) of the overall cell survival when irradiation was combined with a static magnetic field. However, the chromosome aberration test did not show an induction of chromosome aberrations in general or a shift in the complexity or completeness of damages. The number of all chromosome aberrations was 0.71 +/- 0.05 without and 0.73 +/- 0.05 with a SMF during the 2 Gy irradiation.

Conclusion

Up to now, there are only very few studies that have investigated the combinational effect of a static magnetic field and radiation. Most of these studies were in line with our results showing that a static magnetic field increases the efficiency of the radiotherapy. Additionally, our study showed evidence that the altered cell survival is not caused by clastogenic DNA damages, which leads us to the hypothesis that aneugenic effects may cause the change in cell survival. Further experiments, including a micronucleus assay with centromere FISH and staining of the mitotic spindles by immunohistochemistry are proposed.

Abstract ID 25913

Research in Radiotoxicology and the 3Rs – *Replace, Reduce and Refine* – observations

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To characterize the health effects of incorporated radionuclides many experiments have been conducted using different animal models. These range from (1) applied (tissue uptake/retention determination, decorporation therapy efficacy), (2) fundamental (gene expression, cancer induction) and (3) biokinetic models for dose estimation. Importantly, the ICRP have used animal data, in part, for development of different biokinetic models for dose calculations in humans.

The concept of the 3Rs, *Replace* (use of alternative methods), *Reduce* (reduction in animal numbers) and *Refine* (better animal welfare) is now implemented in the guidelines and legislation for animal experimentation in many countries. Using examples for actinide lung contamination, this discourse has for objective to privilege the remit of

the 3Rs applied to animal ethics – namely Reduce, Refine and Replace in radiotoxicology. The aim here however is not to advocate prohibition of experiments using animals but to present examples of specific questions that may be answered by for example, using alternative methods or conversely where such methods require animals.

In radiotoxicology research it seems there is natural tendency to *Replace* given the possibility of data reuse (*in silico* approach) obtained from contamination cases in man and animal studies. Furthermore, and perhaps unique to radiotoxicology, the initiation of "registries" and "repositories" for nuclear industry workers (civil and military) is an excellent source of both data and tissues. Use of these repositories is a rich legacy for radiotoxicological measurements and certainly complies with 3Rs remit. Similarly *Reduction* in animal numbers can be achieved by good experimental planning with prior statistical analyses of animal numbers required to obtain robust data. Multiple measurements in the same animal over time (external body counting, excreta collection) with appropriate detection instruments also allow *Reduction* and so radiotoxicology research fulfils this aspect. In terms of *Refinement* this has become "de rigueur" and a necessity given the societal and legal concerns for animal welfare. For research in radiotoxicology, particularly long term studies, better housing conditions within the constraints of radiation protection issues for research workers, are an important concern. These are all pertinent considerations for future research in radiotoxicology with the caveat that no model has the perfect answer.

Abstract ID 26889

Automatic scoring of dicentric chromosomes and the detection of partial body exposure: Statistical consideration

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The dicentric chromosome assay is currently the gold standard for biological dosimetry. Manual analysis of dicentric chromosomes is very labour intensive and therefore only (limited) partially suitable for large scale radiation scenarios. In particular, to reliably detect partial body exposures based on the dicentric assay, a large number of metaphases have to be scored. Recently, semi-automated scoring of dicentric chromosomes has been successfully applied by several laboratories, enabling a significant reduction of the workload. Current statistical methods for the detection of partial body irradiation require that dicentric chromosomes observed in the irradiated fraction are Poisson distributed. However, for automatically counted dicentric chromosomes contradictory results have been published. For higher doses, a tendency for over-dispersed, non-Poisson distributed counts has been observed by some laboratories.

The aim of this study was to statistically validate the suitability of automatic dicentric chromosome analysis for the detection of inhomogeneous exposures especially for higher doses. For this purpose, two new calibration curves were established at the Federal Office for Radiation Protection, Germany (BfS), including doses up to 6 Gy, to investigate possible over-dispersion at higher doses, relevant for partial body exposures. Several statistical models for curve fitting were compared and applied to the newly established calibration curves as well as to published data.

Dose dependent over-dispersion was detected for automatically scored calibration curves, especially for higher doses. Standard statistical methods for the detection of partial body irradiation will therefore lead to inflated false positive assessments for the classification of exposure scenarios and therefore to overestimation of the dose. New statistical methods based on the Negative Binomial distribution were developed as a reliable method for the detection of partial body irradiations as well as for the estimation of the partial body dose and the fraction of irradiated cells.

Automatic scoring of dicentric chromosomes is a promising tool to speed up biological dose reconstruction. However, standard statistical methods for dose and uncertainty estimation might not be applicable, especially for

the detection of partial body exposures. The proposed statistical method provides a new opportunity to detect inhomogeneous exposures for over-dispersed data.

Abstract ID 27539

Is there any similarity in gene expression profile in response to radiation therapy, independently of the cancer type?

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Aim: To find candidate genes whose expression is consistently and significantly modified by radiation exposure independently of the cancer type.

Materials and Methods: Blood samples from 20 cancer patients (5 types of cancer: breast, endometrial, prostate, lung and oesophagus) were collected at four time points during radiotherapy: pre-exposure, 24 h after the 1st fraction, before 5th or 6th fraction and before the last fraction. nCounter was used to measure the expression of 249 inflammation genes. The data were normalized, and paired t-tests were performed to verify the hypotheses on mean value equality and modified Cohen's d statistics were calculated to estimate the effect size. Gene expression time courses were clustered according to their response pattern.

Results: Of 81 possible response pattern, those that determine monotonic increase, monotonic decrease or fast-response (u-shape) with at least medium effect size were selected. 131, 138, 146, 151 and 121 such genes were identified in breast, endometrial, prostate, lung, and oesophagus cancer patients respectively. In the case of breast cancer patients, the majority of genes showed a monotonic increase: 82 (62.6%), while for oesophagus it was only 11 genes (9.1%). For the latter patients, the most frequent response were monotonic decrease – 65 genes (53.7%) – and down-regulation U-shape – 43 genes (35.5%). The response profile for the remaining types of cancers was similar to breast cancer patients. C3AR1, MYC and PRKCA were found as showing a similar response pattern across all patients independently of cancer type, while BCL6, CD86, CEBPB, FOS, IL1R1, RAC1, CD40, PTGER2, PTGER4, TRADD were identified as having a similar monotonic response in at least four types of cancer (mainly breast, endometrial, lung and prostate). Functional analysis revealed overrepresentation of 61 KEGG and 27 Reactome pathways for those 13 genes (FDR <5%), among which MAPK signalling pathway, transcriptional misregulation in cancer, Toll-like receptor signalling pathway and signalling by interleukins were on the top of the lists.

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Key-Session II Latest developments in radiation preparedness

Abstract ID 25996

Development of automated high throughput biodosimetry tools for radiological/nuclear mass casualty incidents

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Incidental or intentional radiological /nuclear (R/N) mass casualty incidents can affect several hundreds and thousands of humans. In case of R/N scenario, individualized radiation dose assessment is often critical for predicting radiation induced health risks and for subsequent clinical/medical intervention involving mitigation of radiation associated injuries. Currently available cytogenetic biodosimeters are time consuming and laborious to perform making them impractical for triage scenarios. Therefore, it is imperative to develop automated high throughput techniques which will enable timely assessment of individualized absorbed radiation dose for making an appropriate “life-saving” clinical decision on those who need urgent care. To achieve this objective, several multidirectional initiatives have been undertaken at the REAC/TS CBL: (I) Development and automation of high throughput Dicentric Chromosome Assay in robotic platforms, (II) Increase the rapidity of dose assessment by automated DC scoring (III) Development of automated analysis of a novel biomarker, Pseudo-Pelger Huet Anomaly (pseudo PHA), (IV) Development of automation for the Premature Chromosome Condensation (PCC) technique for rapid dose estimation within 6-8 hrs of blood collection and (V) Development of electronic training tools to teach and train clinical laboratorians for increasing the surge capacity of dicentric chromosome scorers for validation of estimated radiation dose. Additionally, efforts are being made to optimize the interphase chromosome breakage analysis (ICBA) tool which can be efficiently performed on any human cell type for dose assessment. Development of automated high throughput techniques has a number of advantages: (I) Processing of a large number of samples, (II) Reduced turnaround time (TAT) for radiation dose assessment, (II) Consistency and reproducibility, (IV) cost effective and (V) Operational capacity at 24/7/365. Optimization of high throughput techniques in robotic platforms will enable a rapid assessment of absorbed radiation dose for several hundreds and thousands of exposed people. Our multidirectional approach using automated high throughput robotic platforms for cytogenetic tools will constitute an efficient radiation emergency response to fulfill the biodosimetry needs of R/N casualty incidents in the future.

Abstract ID 27966

Integration of local, national and international medical responses to a mass casualty radiological/nuclear incident

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Medical preparedness and response to a mass casualty radiological/nuclear (R/N) incident requires not only harmonization and consensus among medical experts regarding medical management (1-3) but also objective assessment of local, national and international capabilities (4). For example, subject matter experts at U.S. federal agencies have developed a Radiation Triage, Transport and Treatment (RTR) system as a conceptual model that focuses on rapid triage, emergency treatment and transportation of the injured (5). Since an individual’s biological dose will be used by clinicians to inform triage and medical decision-making, we have proposed that biological dosimetry be integrated into medical response planning, and we have presented a concept of operations for a U.S. dosimetry and biodosimety laboratory network that may be integrated into the RTR system (6). Protected health information will be provided to healthcare providers and aggregated data will be provided to Federal agencies for

use in the RTR system and population monitoring programs. Here, gaps are considered in medical response capabilities at the levels of public health planning, health care system integration, individual hospital/medical center response and emergency response in the field. Integration of medical response assets in medical specialties and subspecialties within communities, among national agencies/departments and between countries is required to save lives and reduce morbidity among victims of a mass casualty R/N incident. An overview of these issues will be presented and potential approaches to fill the gaps will be discussed.

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Abstract ID 26540

Radioprotective effect of vitamin C as an antioxidant

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Vitamin C is known as a potent antioxidant. We studied vitamin C as a radioprotective agent, focusing on its antioxidative effect. When the body is exposed to radiation, free radicals and reactive oxygen species (ROS) are produced and oxidize cell components, resulting in cell damage. Vitamin C has the potential to scavenge these radical products, thereby protecting against radiation-induced cell damage.

We investigated the effects of vitamin C on radiation-induced gastrointestinal (GI) syndrome in mice. The mice received whole-body irradiation (WBI) at 14 Grays (Gy) followed by bone marrow transplantation (BMT) 24 h after exposure. Despite avoiding bone marrow failure, the mice eventually died of GI syndrome. However, per os (p.o.) administration with high-dose vitamin C for 3 days before radiation rescued 42% of treated mice from lethal GI syndrome. Furthermore, combination therapy of vitamin C, consisting of p.o. administration for 3 days before radiation and 7 days after radiation and additional engulfment (one shot) at 8 h before radiation, rescued all treated mice from lethal GI syndrome after abdominal radiation at 13 Gy (100% survival).

However, these studies were prophylaxis study but not post-exposure therapy. We then investigated the effect of post-exposure treatment with vitamin C on radiation-induced hematopoietic syndrome (bone marrow dysfunction). After WBI at 7.5 Gy, mice were treated with high-dose vitamin C. Intraperitoneal administration with vitamin C, even at 24 h after radiation, was still effective in avoiding bone marrow dysfunction, thereby significantly increasing the survival after WBI (85% vs. 47% survival).

In conclusion, administration of high-dose vitamin C effectively reduced the radiation lethality in mice.

Abstract ID 25572

Rapid high through-put diagnostic triage after a mass radiation exposure event using early gene expression changes

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Radiologic exposure scenarios of large numbers of people require a rapid and high through-put method to identify the unexposed, and low- and high-exposed individuals. Those with high exposure, e.g. > 2 Gy and depending on host characteristics, may develop severe hematological acute radiation syndrome (HARS), requiring hospitalization and treatment. Previously we identified a set of genes that discriminated these clinically relevant groups. Here we examined the utility of gene expression changes to classify 1000 split blood samples into HARS severity scores H0, H1 and H2-4, with the latter indicating likely hospitalization. In several previous radiation dose experiments, we determined the HARS categories corresponded to unexposed, 0.5 and 5 Gy, respectively. Our main purpose was to assess the rapidity of processing the samples using targeted next generation sequencing (NGS). Peripheral blood from two healthy donors was X-irradiated in vitro and incubated at 37°C for 24 hours. The 1,000 samples were evaluated by laboratory personnel blinded to the radiation dose. Changes in gene expression of FDXR, DDB2, POU2AF1 and WNT3 were examined with qRT-PCR as positive controls. Targeted NGS (TREX, Illumina) was used on all samples for the same four genes. Agreement using both methods was almost 78%. Using NGS, all 1,000 samples were processed within 30 hours. Classifying the HARS severity categories corresponding to radiation dose had an overall agreement ranging between 90-97%. Depending on the endpoint, either a combination of all genes or FDXR alone (H0 HARS or unexposed) provided the best classification. Using this optimized automated methodology, we assessed 100 times more samples about three times faster compared to standard cytogenetic studies. We showed that a small set of genes, rather than a complex constellation of genes, provided robust positive (97%) and negative (97%) predictive values for HARS categories and doses of zero, 0.5 and 5 Gy. Our study supports the possibility of using early radiation-induced gene expression changes for high-throughput biodosimetry and to rapidly identify irradiated persons in need of hospitalization.

Abstract ID 27396

Circulating Cell-Free DNA (cfDNA) Correlates with Integral Dose and Identifies Radiotherapy Patients Who Develop Gastrointestinal Toxicity

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Background: Predicting radiotoxicity is critical for a Rad/Nuc event and for radiotherapy (RT) patients. Toxicity from radiation is related to physical factors and unknown biological factors (e.g., concurrent disease, trauma, infection). Although physicians employ dose-volume histograms (DVH) to predict toxicity, there is no method of identifying subgroups that will experience toxicity. To augment the DVH, we developed a method for personalized radiotoxicity detection.

Methods: Plasma was collected from prostate cancer patients (n=54) to measure their cfDNA levels before photon or proton RT and after each of the first 5 treatments. Patients were followed to determine acute (during RT) and late (>90 days after RT) gastrointestinal (GI), genitourinary (GU), and general toxicity using CTCAE v4. The correlation between cfDNA levels at time points with acute and late toxicity was analyzed by Chi-square test. cfDNA was measured using a proprietary bDNA-based method (RadTox®, DiaCarta Inc.).

Results: Average, peak, and day-2 cfDNA concentrations were significantly elevated in photon-treated compared to proton-treated patients ($p<0.05$). Increases of cfDNA were categorized as low (<15 ng/ml or ratio <1.5), medium (15-30 ng/ml or ratio 1.5 to 3), or high (>45 ng/ml or ratio >3). Integral dose showed a significant correlation with these categorizations (both $p<0.05$). Five (9%) and 3 patients (6%) experienced acute and late grade 2+ GI toxicity, respectively; 16 (29%) and 18 patients (35%) experienced acute and late grade 2+ GU toxicity, respectively. Acute grade 2+ GI toxicity was significantly correlated with cfDNA levels obtained on days 1, 2, 3, 4, and 5 of RT ($p<0.005$). Grade 2+ late GI toxicity was significantly correlated with cfDNA levels obtained on day 5 of RT ($p=0.017$ concentration, $p=0.034$ ratio). Bladder toxicity was not significantly correlated with cfDNA levels, perhaps due to low bladder mass.

Conclusions: We believe this is the first assay that has shown potential to detect individual subjects who go on to develop GI toxicity after receiving otherwise similar RT. A test of this hypothesis is in evaluation through an NCI-funded SBIR phase 2 trial.

**Dr. Okunieff is a founder of and a stockholder in DiaCarta, Inc., and a patent holder for the RadTox assay.*

Abstract ID 28031

Assessment of the radiological effects from a "dirty bomb" scenario in urban areas on a meterological microscale range

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In present times, even now more than in the past, there is a fear that terrorists might thread population, military forces or a State to enforce illegal demands. An often-discussed possibility is to disperse explosive material combined with radioactive substances somewhere in public or military areas (dirty bomb- or RDD- (Radiological Dispersive Device) scenario). These areas consist generally of urban structures, with a range of smaller buildings like housing areas to complex buildings like areas in the center of big cities or military camps.

A decision support model (LASAIR) has been developed to simulate atmospheric dispersion of radionuclides after an accidental release and assist in such a case of malevolent threads to provide quick and relevant information on the radiation exposure. The microscale model with a model domain of 20 km x 20 km and a smallest grid size of 5 m based on a well-accepted mathematical procedure (Lagrange-particle procedure), with a state of the art turbulence parameterisation (developed in 2017).

For adequate consideration of urban effects, the dimensions of houses or buildings have to be taken into account as they might change the wind direction and wind speed as well as generate additional mechanical turbulence which influences the dispersion. Therefore LASAIR uses the free system Open Street Map from which the two dimensions or sometimes even three dimensions of buildings can be extracted. In an operational mode, these data can be gained via the internet within a few minutes. Based on this, a diagnostic wind field model (lprwnd) together with the Lagrangian particle model (LASAT, [Lagrange Simulation von Aerosol-Transport]) computes the atmospheric dispersion.

The combined wind field and dispersion model LASAIR is able to assess the radiation exposure after explosion or short term releases with special consideration of the radiation dose from inhalation, cloud- and ground-shine as well as activity concentration and deposition as a function of time. The model is especially dedicated for operational use but can be applied as well for analysis of building structures in order to provide a maximum of shelter against attacks.

The presentation gives an overview on the model and especially on the influence of simple urban structures (e.g. urban areas, nuclear facilities, military camp) to the dispersion of radioactive substances and related radiation exposure.

Abstract ID 24878

MSC-derived extracellular vesicles: New emergency treatment to limit the development of radiation-induced hematopoietic syndrome?

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Nuclear accidents or acts of terrorism involving radioactive sources could lead to the irradiation of many victims. It therefore seems necessary for the Army Health Service to carry out research aimed at improving the care of irradiated persons by developing new medical countermeasures. The most vulnerable organ system to radiation exposure is the hematopoietic system which important depression of hematopoietic elements (radiation-induced hematopoietic syndrome RI-HS). Actually, CSF therapy is considered a valuable adjunct to treatment controls in certain irradiated patients. These overexposed patients with bone marrow eradication nevertheless have a minimal medullary territory that does not allow a complete resumption of hematopoiesis but leading to significant immunoreactivity following the allogeneic hematopoietic stem cell transplantation (HSC). The high morbidity and mortality of these overexposed patients is a reminder of the lack of effective HS treatment. The RI-HS remains the first therapeutic challenge.

In recent years have allowed to propose a mesenchymal stem cells (MSC) therapeutic approach for the care of victims of accidental irradiation. Preclinical research in animals has shown that MSCs, mainly by their secretory activity, contribute to the control of inflammation and promote tissue regeneration by accelerating the processes of angiogenesis and re-epithelization. MSCs' mode of action involves a strong paracrine component resulting from the high levels of bioactive molecules, they secrete in response to the local microenvironment. For this reason, MSCs' secretome, in particular the extracellular vesicles (Mev), have a more anti-inflammatory and regenerative phenotype (cell survival, vascularization, immunomodulation).

So, we investigated the potential effect of Mev to reduce the early toxicity of ionizing radiation on the bone marrow, by early anti-apoptotic therapy and vascular protect in RI-SH model. This main objective is to propose innovative non-patient specific therapeutic approaches adapted to the medico-military context of the RI-HS emergency treatment to limit allogeneic HSC.

Abstract ID 27423

Genomic Instability and DNA-repair predicting radiosensitivity?

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Radiation risk in low (<100 mGy) and medium (100-2.000 mGy) ranges of radiation dose is related to the causation of cancer. Many efforts are undertaken to predict radiosensitivity with respect to cancer induction. Due to the methodological possibilities of molecular biology today it is tempting to look for mutations in certain genes, expression of these genes and other sophisticated methods. From the scientific point of view these tasks are understandable. However, the diversity of these molecular, genetic changes is very high not only between various cancer entities but also between various cancer types of the same organ end even between individuals with the same cancer type.

Therefore it seems reasonable to study some cellular or molecular principles which may be involved in cancer development generally. When one considers the present knowledge about the mechanisms of cancer development one can postulate that DNA-repair and especially repair of double strand breaks (DSB) as well as genomic instability may be such general principles. DNA-repair of DSBs is important during the first hours or days after a radiation exposure and genomic instability will play an important role during years or decades of cancer development, as several mutations are needed in most cases of cancer.

DNA-repair of DSB was measured in lymphocytes of healthy persons and cancer patients by the comet assay technique with electrophoresis in a medium of pH 8.4 at 10° C. It is important not to do the electrophoresis at pH 10 or even higher pH-values. Under these latter conditions not only DSBs are measured but also single strand breaks (SSBs), whereas this is not the case with electrophoresis at the lower pH-value.

Genomic instability was determined by counting micronuclei in lymphocytes of healthy persons as well as cancer patients and differentiating between micronuclei with or without centromeres. Centromeres were analyzed by the FISH technique. The percentage of micronuclei with centromeres decreases when the genomic instability is increased. It could be shown that cancer patients have a higher genomic instability than healthy persons. It was also evident that uranium miners with high radiation exposures developed an increase of genomic instability several years after the exposure without having a cancer. In miners with cancer the genomic instability was even higher.

Session Radiation protection

Abstract ID 22939

Misuse of a medical isotope: Playing cards contaminated with I-125, German experience

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Over the last three years, the German Federal Office for Radiation Protection (Bundesamt für Strahlenschutz, BfS) has gathered considerable experience in the location, identification and analysis of playing cards contaminated with I-125, both at the scene and in the laboratory. This experience has been gained partly through the support the BfS has provided to the Brandenburg Criminal Police Office (LKA-Brandenburg) and the Berlin Criminal Police Office (LKA-Berlin) during their investigation of contaminated playing cards found in Brandenburg and Berlin. The aim of the work of the BfS is to contribute to the radiological forensics of the cards, which is a subtopic of nuclear forensics for the investigation of nuclear security events.

In this contribution, the world-wide phenomenon of radioactively-marked playing cards will be introduced and the advantages for gamblers of using this method will be explained. The radiological investigation carried out by the BfS into two cases in Germany, one from 2014 and one from 2016, will be detailed. These incidents occurred in Brandenburg, where circular pieces of playing cards contaminated with activities of I-125 over 1 MBq, along with other contaminated items, were found at an incinerator plant. The topic of radiation protection will be addressed, both for unwitting participants of radioactively-marked card games and for police and other forces handling the radioactively-marked cards. The information gained through the radiological forensics investigation of the finds by the BfS will be discussed, for instance if the source or supplier of the medical nuclide could be determined and the method used for marking the cards.

Further international finds of playing cards marked with I-125 show that the phenomenon remains an important and pressing topic for customs, police and radiation protection authorities. In addition, it is important for hospitals

to be aware that the misuse of I-125 is a current issue. Unfortunately, the security of I-125 from misuse is not guaranteed world-wide at the present time.

Abstract ID 24659

Regional and global biodosimetry networks and initiatives for managing radiation emergencies

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Various techniques are able to contribute to biological and retrospective physical dosimetry in the case of various exposure scenarios, especially in cases of unknown or conflicting irradiation situations. Thus estimated doses are generally well accepted by affected persons, due to the individual aspect of the applied methods. To be prepared for large scale radiological incidents, biodosimetry laboratories of different countries have joined forces and established regional and/or global networks, either on a formal or informal basis. This approach has resulted in a significant increase of the analysis capacity, but also of the methodological capability, which is needed to be prepared for various radiation scenarios. Fundamental for the acceptance and credibility of the networks is the accuracy, precision and reliability of the dose estimates in each participating laboratory. Also of importance is the reliability of the supporting infrastructure, such as consistent shipment of the samples and secure storage and communication of the results. Regular interlaboratory comparisons and related exercises are performed by the networks to ensure a persistent high quality and stability of the laboratories and of the infrastructure. The integration of established networks in existing national and international emergency preparedness and response systems is urgently required for sustainability, reliability, and efficiency in real radiological disasters.

An overview will be given about established regional and global biodosimetry networks and their activities. Also presented will be initiatives, which actively or indirectly support the activities and preparedness of these networks, either by bringing together relevant organisations or by supporting the transfer of knowledge and skills.
Introduced will be regional active networks in North America, Japan (Chromosome network council), China, Latin America (LBD), Europe (EURADOS WG 10, RENEB) and Asia (ARADOS WG03). These networks prepare for and are actively involved in dose estimation in the case of radiological accidents but also in testing and optimizing available biomarkers and techniques. Complementary to these networks, global informal initiatives such as GHSI, IABERD, WHO BioDoseNet and IAEA

Abstract ID 27940

Biodosimetry of internalized irradiation exposures using transcriptional analysis from relapsed and refractory neuroblastoma patients from a NANT11-01 study treated with ^{131}I-MIBG.

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The drug ^{131}I-Metaiodobenzylguanidine (MIBG) is used as a targeted radiation treatment for patients with neuroblastoma, the most common extracranial pediatric cancer. We have previously shown that radiation biomarkers can predict acute toxicity in response to 131I-MIBG treatment. We have also demonstrated that peripheral blood gene expression analysis in these patients can be used to estimate internalized ionizing radiation (IR) dose. In this study we tested the ability of the transcripts to discriminate between 0 vs. 2 Gy exposures using early (up to 5 days) after 131I-MIBG exposure in children. Total RNA was isolated from 62 patients treated with ^{131}I-MIBG. Samples were taken prior to treatment (baseline), as well as 72 -120 hours after exposure. Selected TP53-specific transcripts were measured and compared based on the significance and response profiles. At 72-120 hours, 13 of the 17 selected pathway-specific transcripts were differentially expressed. A majority of the transcripts were trending toward baseline at 120 hours. Three transcripts CDKN1A ($p<0.000001$), FDXR ($p<0.000001$), and DDB2 ($p=0.000001$) showed the highest up-regulation at 72 hours post-^{131}I-MIBG exposure. Next, we ran a decision tree classification for the samples identified as unexposed and > 2 Gy exposures (n=107), using Random Forrest Classification. This analysis showed that CDKN1A can split the samples into two nodes: one with (n=62) zero-dose samples and another with (n=39) >2 Gy exposure samples. The decision rule to assign samples to the >2 Gy group resulted in 100% predictive accuracy. Adding in additional transcripts such as CDKN1A, FDXR, GADD45A, XPC, BCLXL/BCL2L1, STAT5B, BCL2, BAX, DDB2 were used for Receiver-Operator area under the curve analysis, which ranged from 80-100% discrimination for 0 vs. 2 Gy in humans. The range varied depending on the classifier algorithms used. Our biodosimetry gene expression panel for internalized ^{131}I exposures is useful for identifying exposed individuals and sorting the worried well in the event of mass exposure scenario. Ongoing analyses will expand on these findings to identify late biomarkers associated with dose estimates and susceptibility factors predictive of treatment outcomes for children with high-risk neuroblastoma.

Abstract ID 25839

Imidazolyl Ethanamide Pentandioic Acid for the Treatment of Acute Radiation Syndrome

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Acute Radiation Syndrome (ARS) is a debilitating condition resulting from whole body exposure to high doses of ionizing radiation, as occurs in cases of nuclear attack or nuclear plant failures. The primary manifestation of ARS is depletion of hematopoietic stem cells, constituting one of the major causes for mortality. Three radiomitigators – G-CSF, Peg-G-CSF and GM-CSF – were approved by FDA as medical countermeasures (MCM) for hematopoietic-

ARS (H-ARS) but are only injected therapeutically after exposure to radiation doses above 2 Gy. The effect of G/GM-CSFs is limited to neutrophils and macrophages, which leaves an unmet need to protect lymphocytes and thrombocytes for functional hemostasis. Moreover, instability at room temperature and required subcutaneous/intravenous administration limit their wider use.

Imidazolyl Ethanamide Pentandioic Acid (IEPA, Myelo001) is a novel drug candidate developed as an MCM to decrease mortality and myelosuppression after exposure to radiation. IEPA is administered in a tablet form that is stable at room temperature for at least three years. Preclinical and clinical studies showed that IEPA has both prophylactic (pre-radiation) and therapeutic (post-radiation) efficacy at reducing hematopoietic symptoms caused by radiation and chemotherapy. In 5 radiation challenged studies, IEPA reduces the nadir and accelerates recovery of neutrophils, lymphocytes, thrombocytes and erythrocytes. IEPA's efficacy in radiated mice and rabbits on accelerating lymphocyte recovery suggests the use as a potential therapy in the prevention and treatment of viral infection and Delayed Effects of Acute Radiation Exposure (DEARE). In mice, orally administered treatment 24h post-radiation resulted in increased survival (86% IEPA vs. 56% control), faster bone marrow recovery and reduced body weight loss. Moreover, IEPA treatment prior to radiochemotherapy or chemotherapy led to a faster recovery of white blood cells in human subjects.

Comprehensive chronic toxicology and safety studies, as well as clinical studies in over 3,000 patients, displayed a positive safety and tolerability profile for IEPA. Thus, combined characteristics of IEPA make it a promising MCM candidate for prophylactic and therapeutic distribution to warfighters and self-administration in a broader population exposed to radiation. Future studies includes translatability to non-human primate models and investigating higher doses, altered posologies and polypharmacy approaches resulting in increased efficacy.

Abstract ID 26959

Radiation risks of medical exposure in Russia: current status of the problem within international and national standards

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According to Russian official statistics the annual average effective dose of radiation to members of the public is 3.7 mSv and up to 14% falls on medical exposure. More than 270 million procedures related to medical exposures are performed annually. Last years we have seen the dynamic increasing of the numbers of computed tomography (CT) and Positron Emission Computed Tomography (PET/CT) procedures. Nuclear medicine and CT make up only 3.6% of the total number of x-ray studies, but they contribute most to the total dose of medical exposure (up to 48% of total collective effective dose).

The IAEA's Basic Safety Standards of 2014 require registrants and licensees to ensure that the patient has been informed, as appropriate, of the expected diagnostic or therapeutic benefits of the radiological procedure as well as the radiation risks. The same requirement is present in the Russian Basic Sanitary Radiation Protection Standards of 2009 and in the Basic Sanitary Rules for Radiation Safety of 2010. It is the first time the requirements of estimating risk of late stochastic effects associated with medical radiologic exposure at the planning stage have been included in international and national regulatory documents.

ICRP Publication 103, recommends evaluating radiation risks associated with diagnostic imaging using doses to the individual tissues at risk. Effective dose can be used for comparing doses from similar diagnostic technologies and procedures in different medical clinics and countries, as well as for comparing different technologies for the same examination if reference patient groups are similar by age and sex.

Thus, the estimating of radiation risks and benefits as well as the Risk Communication in the cases of medical exposure are necessary.

The "global" goal of the scientific research recent started in MRRC is to develop a methodology for assessing the possible radiation health effects to patients when undergoing medical diagnostic procedures using CT and PET/CT.

The developing method for determination of radiation health effects when single and multiply pass PET/CT examination based on estimates of lifetime attributable cancer risks is highly topical and may find practical application in the current system of radiological protection.

Session Radiation accident management

Abstract ID 27438

SEED, a deployable numerical dosimetric reconstruction tool

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In the context of a radiological accident involving high doses of ionizing radiation, for irradiated patients, priority goes to the diagnosis because it is essential to know how the dose is distributed among the organs in order to sort the victims according to the severity of the exposure, and then lead them to the most appropriate health structures. At present there is only few field techniques that are capable of rapidly characterizing an external radiation exposure in case of an accident involving a large amount of victims. Nevertheless scientific, industrial and military applications as well as terrorist menace generate a significant probability of such an event. An operational dosimetric reconstruction tool is currently being developed as part of a collaboration between SPRA and IRSN. Called "SEED", it aims to take advantage of a powerful mobile calculator implemented by a team doctor / physicist.

The dosimetric reconstruction tool uses the Geant4 Monte Carlo code to provide dose maps in the area of an irradiation accident. The device is integrated in a militarized and hardened case, and it can be freed from any link to a remote computer cluster thanks to a powerful multicore calculator. Trained users can quickly design the whole scene of the accident using mostly the mouse and navigating in this 3D virtual world with a first person camera.

A first physical validation step in comparison with a reference calculation code, MNCPX, has been performed. The comparison of the results obtained showed an average relative difference of 2% between the two calculation codes. Moreover, SEED results were obtained much faster than using the reference code combining the time saved in modelling the accident scene and the time spent for the particle transport.

An experimental validation is planned, based on the irradiation of an anthropomorphic dummy equipped with thermoluminescent dosimeters using a high activity iridium192 source. Exposure conditions are close to one of the accidents that have occurred in the past. The same geometrical configuration is modeled on SEED and the calculated results are compared to the measured values.

Abstract ID 26295

Metrology for mobile detection of ionising radiation following a nuclear or radiological incident: The EMIR project 16ENV04 "Preparedness"

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During and in the aftermath of a nuclear or radiological emergency caused by accidents or terroristic attacks, adequate and fast governmental decisions for countermeasures and immediate protective actions are of key importance for the protection of the public against dangers arising from the release of radioactivity and the resulting ionising radiation. Therefore, in such disruptive scenarios, the reliable assessment of dose rates and ground contamination levels as well as the surveillance of the radioactivity concentrations in the air are of highest priority. The nuclear power plant accident in Chernobyl (1986) drastically demonstrated that for radiological measurements in the vicinity of the epicenter of an uncontrolled radioactive release, unmanned detection systems are required in order to reduce the risk for the health and life of first responders due to ionizing radiation and radioactive contaminations but also due to collapsing infrastructures or a complex topography of the area. The main objective of the Preparedness project therefore is the development and validation of detector systems and methods for the unmanned aerial collation of radiological data in radiological emergency scenarios. For this purpose, unmanned aerial vehicles UAVs (e.g. multi-rotor systems, commonly named 'drones' and unmanned helicopters) are used as carriers for novel spectrometric detectors. In line with that, transportable air-sampling systems will be developed, which allow a quick response to monitor the dispersion of a radioactive plume. Even years after a nuclear accident the long-term monitoring of contaminated areas is essential for the radiation protection of the public. Passive dosimetry systems are an appropriate tool for that. The reliability of commercially available passive dosimetry systems for that purpose will be investigated within the project. Finally, the feasibility to use non-governmental dosimetry detector networks for the surveillance of dose rate levels will be studied. The joint research project 16ENV04 "Preparedness" within the European Metrology Programme for Innovation and Research (EMPIR), co-funded by the European Commission and EURAMET, is comprised of 17 European institutions including 6 national metrology or designated institutes, as well as 11 universities, radiation protection agencies, regulatory bodies and private companies. The objectives of the project and its first outcomes will be presented.

Abstract ID 26440

The accuracy of biological dose reconstruction in case of criticality accident

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A key element for the evaluation of the risks associated with an exposure to ionizing radiation is an accurate estimation of the absorbed dose. However, depending on the radiation quality, a given absorbed dose could lead to different biological effects, the most prominent one being the level DNA damage it can cause. Nowadays, the analysis of chromosome aberrations (CA) is considered the most robust biological indicator of these effects as the complexity of CA can be correlated to the radiation quality. A criticality accident or use of atomic nuke could lead to people exposures to neutrons, and could challenge the accuracy of the biological dose reconstruction based on CA. To evaluate the level of CA complexity in case of neutron exposure, we performed exposure of human blood samples to neutron fields similar to those generated during this kind of accident. The comparison of CA complexity have been achieved using Multicolor fluorescence in situ hybridization (M-FISH) of chromosome spreads obtained

from blood samples exposed to 3 different radiation conditions: neutron field with a constant dose rate, pulsed neutron field and 4 MV X-rays of equivalent dose. As expected, more complex aberrations were observed in the peripheral lymphocytes exposed to neutrons compared to X-rays. The number of breaks per cell between X-ray and neutron exposure is significantly different. In addition, we observed the increase of the level complexity of CA for neutron exposure. Interestingly, we have also measured a higher rate of unrepaired chromosomal fragments, leading to the hypothesis of a delay or impairment in DNA damage repair processes in this case.

Abstract ID 27184

Radiation Exposure Biomarkers in the Practice of the Medical Radiology: Cooperative Research and the Role of the International Atomic Energy Agency (IAEA) Biodosimetry/Radiobiology Laboratory

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The problem of the limited efficacy of radiation dosimetric biomarkers in clinical practice of radiation medicine has been recently recognized in the extensive review of the relevant scientific literature organized by IAEA. A Human Health Series report based on this review is now in the stage of finalization for publishing.

To fill in gaps of current methodology of the clinical application of biodosimetry markers beyond radiation protection and radiation medicine, the experts involved in the review and the Report preparation underlined the necessity of international multicentre research. That became a rationale for launching the IAEA Coordinated Research Project (CRP) E35010 “Applications of Biological Dosimetry Methods in Radiation Oncology, Nuclear Medicine, and Diagnostic and Interventional Radiology”.

At the 2nd Coordination Meeting on the CRP (18-22 February 2019, Recife, Brazil) participants reported significant progress in various aspects of radiation biomarker applications for clinical purposes, particularly in the usage of biological dosimetry for genotoxicity assessment and/or individualization of radiotherapy treatment plans. Another important avenue of research discussed was the prognosis of normal tissue toxicity and cancer risk prediction using biomarkers yield measured in vivo or after ex vivo irradiation of patient’s cells. Other areas of interest are: mechanisms of cytogenetic radiation response; validation of new radiation biomarkers; development of innovative techniques, automated and high-throughput assays for biodosimetry; and improvement of the biodosimetry service. The latter issue is one of strategic aims of the CRP.

An important aspect of clinical application of biodosimetry is standardization of techniques and unification of approaches to data interpretation. The new IAEA Biodosimetry/Radiobiology laboratory, which is being established, will provide a support for this activity. The declared lab’s mission includes, among other tasks, a harmonization of the biodosimetry applications in clinical practice with relevant ISOs and the IAEA EPR-Biodosimetry-2011 manual.

Session Radiation emergency medical preparedness and response

Abstract ID 26769

Update on AFRRI's Cytogenetic Biodosimetry Activities – Enhancement of Throughput

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Cytogenetic biodosimetry using the IAEA manual and relevant ISO standards is the generally accepted method for radiation dose assessment in cases of suspected radiation over-exposures. The Armed Forces Radiobiology Research Institute (AFRRI) Biodosimetry Center provides biodosimetry capability based on the use of the dicentric chromosome aberration (DCA) and premature chromosome condensation (PCC) cytogenetic assays. In the last year the number of donors contributing to AFRRI's baseline for use of the dicentric chromosome aberration (DCA) assay has is 22, which improves our ability to assess potentially low-dose exposures. In 2016 we obtained a commercial software application to permit routine karyotyping of metaphase spreads in cases where radiation-induced chromosome aberrations are detected in order to evaluate for potential clonal aberrations. Protocols are in place to use an automated metaphase harvester and manual spreader. Our laboratory replaced its automated metaphase finder in 2017 and applied the use of the automated scoring software to develop dose-response calibration curves (i.e., 60Co gamma rays at 1.0 Gy/min, 0.6 Gy/min, and 0.1 Gy/min) that permits rapid scoring of dicentric aberrations in cases of suspected radiation accidents. In the last few years we have participated in multiple exercises/inter-comparisons and successfully demonstrated blood collection and shipping in a military deployment activity as well as the ability to use both the conventional- and QuickScan-DCA analysis methods for dose assessment. In addition, efforts to establish the premature chromosome condensation (PCC) assay are underway to provide the laboratory with a second cytogenetic biodosimetry assay with robust capability for assessment of partial-body and higher doses (>5 Gy). Blood was exposed to 137Cs gamma ray doses 0 – 26 Gy at 0.59 Gy/min. Cultures were incubated for 2 hr at 37°C following with 48 hrs in the presence of PHA with the final 0.5 hr. with 100 nM calyculin A. Dicentrics in PCC spreads were measured using the centromeric protein nucleic acid (PNA) probe using fluorescence in situ hybridization. Results from the analysis of excess PCC fragments, length ratios, rings, and dicentrics will be reported including the use of the analysis methods for partial-body and high-dose exposure cases.
[The views expressed in this abstract are those of the authors and do not necessarily reflect the official policy or position of DoD, AFRRI, USUHS, nor the U.S. Government. Funding support provided by AFRRI RBB4431318 and RBB4352318.]

Abstract ID 26881

Comparative Effectiveness of Biomarkers: Expanding a Framework to Include Organ-Specific Predictions of Injury

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Biodosimeters/biomarkers for triaging and medical response of victims in large radiation incidents have largely focused on predicting individual dose levels of potentially exposed victims to inform emergency responses. Because of variation in the intensity of resource use or time-dependency, some are better suited for triage (e.g., rapid results, easily performed in emergency settings) while others are better for treatment decisions (greater precision about dose, direct evidence of injury). We developed a comparative framework to evaluate the strengths

and time dependencies of biodosimetry methods and simulated the number of victims who could be processed based on their characteristics, as well as raising other moderating factors, e.g., type of radiation, concurrent disease, other injuries. Increasingly, there is a shift toward identifying biomarkers that predict acute or longterm injury, focusing on organs that may sustain life-threatening damage. Such biomarkers have great appeal because they would direct medical resources to help patients based on their projected injuries, irrespective of dose. However, the conversion of these principles into an effective plan for the response to a large-scale radiation incident raises new and quite challenging issues. In this presentation we expand our comparative framework to identify and evaluate what factors need to be considered when biomarkers focus on organ damage rather than dose. Some comparative concepts are similar for both types of biomarkers, e.g., the delay before and the period during which the biomarker can be validly sampled, the time from sampling to results reported to the decision-maker. Modifying factors are similar, e.g., how is the the biomarker affected by prior disease, heterogeneous exposure, non-radiological injuries, stress, radiation type; does its expression differ systematically by age, etc.? To accurately predict organ injury, biomarkers must also determine whether the whole organ was impacted, e.g., patients can recover with only some bone marrow. Our revised comparative effectiveness framework can address key questions that planners need to assess, including: Does a stand-alone organ-injury biomarker better inform what total medical responses are needed (including time delays before having the information to inform treatments)? What else is needed to perform effective response, e.g., knowledge about damage to all significant organ systems?

Abstract ID 26884

Resolution of homogeneity and dose distribution under emergency conditions using Electron Paramagnetic Resonance (EPR) measurements of finger/toe nails in vivo

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In a large scale radiation incident, military or civilian, identifying individuals at significant risk of radiation induced illness is key to carrying out effective triage and initiating appropriate treatment. For decisions about medical intervention to be effective for each individual, it is essential to have knowledge about dose and its homogeneity. If the exposure is not homogeneous, it is very desirable to have quantitative information on its distribution. EPR dosimetry of nails, based on measuring the radiation-induced free radicals generated in the keratin of human nails, now is capable of providing rapid and robust indications of homogeneity of the exposure by making measurements at four widely separated sites, i.e., using two hands and two feet). The technique can make this determination in vivo, within a few minutes, at the site of the incident as well as at the point of care. It also should be feasible to construct a dose distribution map for the whole body based on having four geometrically observed estimates. This information on dose would be very complementary to the growing capability for having biomarkers that predict biological damage to specific organs. This will be especially important in a large-scale event, where it will be essential to make informed decisions on the allocation of resources. Without information on dose distribution, actions taken that consider only evidence of damage to a specific organ will be suboptimal, because decisions on whether and how to carry out treatment for damage to a specific organ, need to consider what other organs systems are likely to have sustained significant biological damage. Because the biomarkers have a time dependent interval when they are reliable, while the measurements from the nails can be made at any time immediately after exposure and throughout the times when decisions would be made and treatment planned, the combined information will greatly facilitate decision-making. The measurements of the distribution of dose also will provide an index of suspicion for potential false positives and false negatives from biomarkers, if there is a discrepancy between the projected injury and what would be expected from the dose.

Abstract ID 27259

The STORE database; a platform for data and resource sharing in radiation biology, radioecology and epidemiology

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There is currently increasing concern about the availability of primary data from research in the biosciences. This is associated with the problem of reproducibility of published data and failure to realise the full value of public investment in the science commons. In addition the secure archiving of legacy data and recording the whereabouts of biosamples is poorly coordinated and in both cases there is a high degree of risk that unique data and resources might be lost.

In response to these concerns we initiated the development of the STORE database in 2009 following the successful completion of the ERA legacy database containing data from the large-scale experiments on animal radiation exposure carried out between the 1950s and the 1990s.

STORE is free to access and permits users to upload and share any type of data including links to data in other databases, in-house datasets and bioresources. Within a Study there are Datasets and within those individual Files or data elements. So a study might contain many datasets and each dataset many pieces of data, which can be of any type or size and annotated with standard metadata terms for retrieval and searching. Each Dataset and data item are assigned a persistent STORE accession ID using the STOREDB: namespace and an additional Digital Object Identifier (DOI). The IDs assigned can be used to reference data in publications instead of using journal supplementary information sites, and are much more stable as a consequence. Users can maintain control over its dissemination through Creative Commons licensing and user-defined security and privileges.

STORE is housed on the data platform of the Bundesamt fuer Strahlenschutz and consequently, as well as being very secure, is resilient to civil and emergency contingencies. This provides a platform for sharing data in real time in emergency scenarios and can be used as a common file storage for information that might need to be accessed by multiple distributed users. The project has developed a strategy for facilitating distributed biodosimetry with the RENEB consortium which might be a model for its future implementation as part of emergency preparedness.

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Abstract ID 27962

Natural history of disease progression in a rabbit model of acute radiation sickness following total body irradiation

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While classically acute radiation sickness (ARS) has been categorized based on the dose- and time-dependent manifestations of organ damage, the spectrum of clinical manifestations leading to multiorgan failure (MOF) cannot be explained by the decrease in white blood cell and platelet count alone. Among victims with ARS, hemorrhagic lesions with prolonged bleeding and coagulation times have been reported. The purpose of the current study was to assess the time-sequence of events leading to hemostatic dysfunction and MOF across the dose-range to induce ARS in the rabbit.

61 male New Zealand White rabbits were randomized to receive a single, uniform total body irradiation (TBI) dose of 7.0 Gy (n = 19), 7.5 Gy (n = 31) of 6 MV photons, or sham-TBI (n = 6). Animals were administered Buprenorphine and Enrofloxacin between day 1 – 45 postTBI. Tylenol was administered for fever >104.8oF. Blood was sampled at consecutive time points pre- and postIR for hematology, serum chemistry, traditional laboratory coagulation tests, viscoelasticity, and markers of vascular damage. At designated time points (day 5, 7, 10, 14, 20, 45), 3-4 animals were culled according to the preTBI randomization schedule. Macro and microscopic exam of tissues was performed.

5 animals in the 7.0 Gy cohort and 10 animals in the 7.5 Gy cohort met criteria for euthanasia between d1 and d20. All animals presented with classical myelosuppression following TBI. Signs of MOF included vascular breakdown, gastric dysmotility, renal failure, in some cases, rhabdomyolysis and subdural hematomas. Viscoelastic properties evaluated by rotational thromboelastometry suggested significant clotting abnormalities as indicated by increased clotting time and decreased maximum clot firmness. Analysis of circulating markers of endothelial injury and coagulopathy is ongoing.

Initial data analysis suggests the onset of hemostatic dysfunction occurs prior to, and in some part independent of, thrombocytopenia. Additional analysis is ongoing including determining the sensitivity and specificity of blood biomarkers via ROC analysis. In addition, positive predictive and negative predictive value to predict outcomes will be obtained to inform future medical countermeasure decisions.

Abstract ID 27993

Developing entolimod, a TLR5 agonist, as a medical countermeasure against acute radiation syndrome

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Protection of the human organism from ionizing radiation and treatment of the acute radiation syndrome (ARS) are the key problems in biodefense and radiation therapy. Entolimod (CBLB502) is a proprietary candidate medical radiation countermeasure (MRC). Entolimod acts via interaction with TLR5 receptor and subsequent induction of multiple protective and mitigating mechanisms, including production of hematopoietic cytokines (e.g. G-CSF, IL-6), and mobilization of immunocytes (e.g. neutrophils).

Because efficacy testing of MRC against lethal ARS in humans is ethically impossible, entolimod is developed under US FDA Animal Rule that combines efficacy testing in animals with safety evaluation in human subjects.

Entolimod was shown to be an effective MRC in both rodent and non-human primate (NHP) models: a single administration increased survival by at least 30-50% when administered within -24 to +48 hours relative to LD50-LD90 doses of radiation.

In a statistically robust pivotal study in 179 NHP, a single intramuscular injection of placebo or 0.3-120 µg/kg entolimod was given at 25 hours after LD70/60 dose of total-body irradiation, with minimal level of clinical support provided. Entolimod in ≥10 µg/kg doses significantly improved 60-day survival from 27.5% (11/40) in placebo group to 70-75% (14-16/20) ($P<0.0002$), reduced severity and duration of radiation-induced thrombocytopenia, neutropenia, and anemia ($P<0.002$), and mitigated gastrointestinal injury.

Safety studies of intramuscular entolimod in healthy volunteers demonstrated that drug-related adverse events are limited and transient, manifesting as a transient “flu-like syndrome” and hemodynamic changes that self-resolved within 24-36 hours.

Entolimod induced similar dose-dependent increases in G-CSF, IL-6, and neutrophils in healthy humans, healthy NHP, or irradiated NHP; in the latter, these biomarker responses were closely associated with survival efficacy. Thus, to calculate the efficacious human dose based on animal efficacy data, we developed a dose-conversion paradigm and a statistical model based on matching these biomarker responses across the species.

In summary, a single injection of entolimod significantly improved survival and reduced morbidities in animal ARS model simulating mass-casualty radiation disaster, supporting its benefits as MRC for protection and treatment of military and civilian victims of radiation emergencies. Potential dual-use applications of entolimod include cancer immunotherapy and reduction of cancer treatment toxicities.

Abstract ID 27206

Development of a METREPOL-Based Response Category (RC) Algorithm for H-ARS Severity Triage in a Baboon Radiation Model involving Gamma Ray and Mixed-field (i.e., 5.5 neutron to gamma ray) Exposures

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The use of hematological biomarkers represent the consensus approach in providing useful diagnostic information for assessment of hematopoietic acute radiation syndrome (H-ARS) severity. Forty-three baboons were evaluated in a radiation model that underwent either mixed-field total-body (neutron/gamma 5.5), total-body (gamma) or partial-body (gamma) irradiations at doses between 2 to 10 Gy (dose rates 6.25 cGy min and 32 cGy min) (Hérodin et al. 2012, 2014; Valente et al. 2015). H-ARS severity levels determined by an analysis of blood-count changes measured up to 200 d after irradiation were used to gauge overall H-ARS severity classifications (H-ARS 1 to 2(1.5), 2, 2 to 3 (2.5) or 3). A panel of hematologic biomarkers was measured from blood-cell samples collected at 0 to 200 d after exposure using a standard blood counter. The database was used in an initial stepwise logistic regression model-fitting approach, which resulted in the down selection of H-ARS relevant biomarkers for determining METREPOL based Response Categories (RC) of either 0 (≤ 2 H-ARS) or 1 (>2 H-ARS). The Triage RC model consisted of the following variables: lymphocytes log base 10 ($p< 0.001$), neutrophils log base 10 ($p< 0.0001$), platelets squared ($p< 0.0001$), and constant ($p <0.001$) with an overall model fit $p < 0.001$ (Nagelkerke $R2 = 0.7018$). The predicted RC representing the H-ARS severity outcome for the 200 day model using the dataset,

showed an AUC of 0.945 by ROC curve analysis. The percent of cases correctly classified was 89.84%. The resultant study supports the proof of concept that H-ARS RC algorithms using standard blood-cell parameters can provide rapid triage following gamma and mixed field exposures. On-going studies are to perform independent validation testing. (Funding support provided by AFRRI protocols RBB43523 and RBB44313. The views expressed in this abstract are those of the authors and do not necessarily reflect the official policy or position of the AFRRI, USUHS, DOD or the U.S. Government (USG).)

Session Radiation health effects and medical countermeasures II

Abstract ID 25919

Plasma proteins as new biomarkers of irradiation in humans

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Introduction

The increasing risk of acute large-scale radiological/nuclear exposures of population underlines the necessity of developing rapid and high throughput biodosimetric tools for estimation of received dose and initial triage as the current methods are time-consuming and lacking capacity.

Ionizing radiation triggers complex response on genome and proteome level; both were already reported as suitable indicators of radiation-induced damage *in vitro* or in animal models. Our goal is to verify this hypothesis in blood of total-body irradiated (TBI) leukaemia patients and to identify and quantify plasma proteins before and after irradiation using mass spectrometry targeted analysis.

Methods

Blood was taken before and 24 hours after TBI. Plasma samples of leukaemic patients (n=15) were pooled and immuno-depleted using MARS Hu-14 column (Agilent). Healthy donors (n=15) with corresponding sex and age were sampled in parallel to reduce bias caused by oncological condition and temporal effects.

Proteins were reduced, alkylated, and digested. Both “label-free” and iTRAQ relative quantification approaches were applied using RP-nanoLC-ESI-MS/MS system with Q-Exactive mass spectrometer (Thermo). Proteins were identified using Proteome Discoverer v.2.2 platform (Thermo). Proteotypic peptides for targeted Single Reaction Monitoring (SRM) were selected using PeptideAtlas (ISB, Seattle) and subsequent analysis was carried out using Skyline freeware (University of Washington).

Preliminary Data

We acquired a list of plasmatic proteins with statistically significant up-regulation (ratio ≥ 1.2) or down-regulation (ratio ≤ 0.83) 24 hours after irradiation. We ruled out proteins significantly up-regulated in non-irradiated patients when compared to healthy donors due to their possible association with the disease and also proteins that altered in healthy donors within 24 hours as unstabile. Finally, we obtained 23 proteins from label-free and 19 proteins from iTRAQ analysis, which were evaluated for radiobiological relevance and top 15 candidates were selected for further analysis. Another 5 radiation-responsive proteins were added based on literature search.

In total, 20 candidates were subjected to targeted analysis by SRM. An overview of identified proteins will be given. As this is an ongoing project, the validation is in the process.

Conclusion

This is the first attempt to identify radiation biomarkers from human plasma proteome with implications to biological dosimetry.

Abstract ID 27318

Molecular markers of occupational exposure at area contaminated after radiation accident

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Introduction. The state of nuclear and radiation safety determines the priority of search of the biological markers of radiation damage, such as gene expression changes and other molecular markers. Estimation of sensitivity or resistance to low dose radiation is of importance for personnel involved in transformation of the damaged reactor IV of Chornobyl NPP (object “Shelter”) into an environmentally safe system.

Patients and Methods. Study groups included 300 staff of “Shelter” (dose of external irradiation: 26.1 ± 18.1 mSv; age: 43.1 ± 10.3) and 69 control persons (age: 48.7 ± 5.9). Methods included RT-PCR, flow cytometry and relative telomere length by flow-FISH. Analysis was performed using radiation doses received during activities inside the exclusion zone and settlement doses if inhabiting at contaminated area.

Results. Changes were demonstrated in of gene regulation of adaptive-reparative processes: overexpression of TP53 and DDB2 genes, downregulation BRCA1-mediated pathway for DNA repair at doses below 35 mSv. A decrease of the expression of gene-regulation of signal transduction, imbalance of the cell cycle checkpoint system (reduced expression of *CCND1*, *CDKN1A*, *CDKN2A*, *TGFBR1*) and *TERT* overexpression were revealed at doses over 35 mSv. The correlation between the RQ of gene expression and radiation dose was registered for genes *BAX*, *CCND1*, *CDKN1B*, *CDKN2A*, *DDB2*, *MKNK2*, *TERF2*, *TP53*, *FASLG* for both groups of staff; *MKNK2*, *CDKN1B*, *NFKB1*, *CSF2*, *FASLG*, *TERF2* for exposed to doses less than 35 mSv and *BRCA1*, *CCND1*, *CDKN1A* genes for exposed over 35 mSv. An increase in counts of dicentrics, pair fragments and TCR- variant lymphocytes at doses over professional limits shows the need of biological dosimetry. The most sensitive markers include TCR-CD4+, γ-H2AX+ and CyclinD1+ cell counts. The study of the radiation workers with the history experience of chronic exposure in radiation area during 3-5 years demonstrates changes of compensatory origin, i.e. absence of telomere shortening, increased number of NK-cells in combination with lower.

Abstract ID 27540

Cataract type and magnitude in mouse is highly dependent on dose and age at irradiation

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Clouding of the eye lens (cataract) is one of the most abundant vision impairments. One noxious agent for this process is ionizing radiation (IR). For moderate doses up to or equal 2 Gy it is still unclear, whether opacification occurs in mouse model and if, how cataract development depends on the animals age at irradiation time.

Wild-type and heterozygous Ercc2+/--mice (Ercc2 = excision repair cross-complementation group 2) were whole-body-irradiated by 0.5 Gy. 1 Gy and 2 Gy of γ-radiation (Dose rate=0.3 Gy/min), 10 weeks after birth (P70). Another cohort was exposed to 2 Gy only 2 days after birth (P2). All cohorts were investigated in vivo by optical coherence tomography (OCT) and eyes were collected for histology after killing.

OCT revealed frequent lens alteration in the irradiated P2 and P70 mice. P70 mice lesions were located only posterior. Mean lens lesions of control mice were up to 0.008 mm². Whereas the mean lesion of 0.5 Gy-irradiated mice was at least 0.014 mm² ($p<0.01$) in size, mice exposed to 1 Gy had mean lesions of at least 0.019 mm² ($p<0.01$). Mice exposed to 2 Gy developed lesions of at least 0.033 mm² ($p<0.01$) of size.

Mice irradiated at P2 showed heavy scattering structures within the posterior cortex 10 weeks post irradiation (p.i.) and all along the interface of the cortex and nucleus 8.5 months p.i.. Those lesions were not quantifiable by OCT.

Histology of irradiated lenses (P70) unravelled OCT-detected lesions as cataractous accumulations of enlarged fibre cells, accompanied by subcapsular placed cells with nuclei. In contrast, lesions of P2 mice displayed clefts in the fibre cell structure of the inner cortex and posterior eruptions of lens material through the lens capsule.

Therefore, we concluded that ionizing radiation led to lens opacification in a dose-dependent manner starting at a dose of at least 0.5 Gy. Opacification magnitude was stronger in younger lenses after irradiation.

These results help to assess the sensibility of eye lenses for IR in case of exposure.

The LDLensRad project received funding from CONCERT under grant agreement No 662287.

Abstract ID 22595

Biomarkers for assessing radiation injury identified using the nonhuman primate model

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Exposures to ionizing radiation, whether they are intended or unintended, are currently an undeniable reality and carry potentially catastrophic health consequences. Therefore, medical preparedness and countermeasures are critical security issues, not only for the individual, but for the nation as a whole. Identification of biomarkers for radiation exposure is an urgent need. We have identified several promising biomarkers for radiation injury and radiation countermeasure efficacy using hematology, cytokine/chemokine/growth factors, microRNA, proteomics, transcriptomics, metabolomics, and lipidomics using the nonhuman primate (NHP) model.

We identified a unique signature of seven miRNAs that are significantly altered with irradiation in NHPs. A combination of three miRNAs (miR-133b, miR-215, and miR-375) can differentiate irradiated versus unexposed NHPs. We have also identified a 5-miRNA composite signature that has the potential to identify irradiated NHPs and predict their probability of survival. Our study revealed a highly dynamic temporal response in the serum lipidome after irradiation. Marked lipidomic perturbations occurred within 24 h post-irradiation along with increases in cytokines and C-reactive protein. A metabolomic study demonstrated that several metabolites are altered after irradiation, including compounds involved in fatty acid-β oxidation, purine catabolism, and amino acid metabolism. We have also studied metabolites in exosomes of irradiated NHPs. Exosomal profiling enabled detection and identification of low abundance metabolites that comprise exosomal cargo which would otherwise get obscured with plasma profiling.

Our study demonstrates that the biomarkers discussed above will definitely help to determine the dose of radiation with which a victim is exposed during any radiation/nuclear scenario. MicroRNAs appear specifically promising since we have developed a classifier based on two miRNAs (miR-30a and miR-126) that can reproducibly predict radiation-induced mortality. Such biomarkers will also play an important role in studying the efficacy of promising radiation countermeasures under development following the United States Food and Drug Administration Animal Rule. Such biomarkers are important for drug dose conversion from animal model to human.

Disclaimer: The views expressed do not necessarily represent the Armed Forces Radiobiology Research Institute, the Uniformed Services University of the Health Sciences, the Department of Defense, or the United states.

Abstract ID 26070

Radiation-induced cardiovascular disease: 10 years lessons learned from heart proteome analyses!

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Epidemiological studies clearly show that thoracic or whole body exposure to ionizing radiation increases the risk of cardiac morbidity and mortality. Radiation-induced cardiovascular disease (CVD) has been intensively studied but the underlying molecular mechanisms are only partly understood.

To address this issue, we used over the last 10 years a broad range of quantitative proteomics platforms including chemical and metabolic labelling as well as label-free analysis on different biomaterials ranging from organelles to cells and whole organs of animal and human. Using a variety of established and well-developed cutting-edge techniques technologies applied in proteomics, we could provide information on the molecular mechanisms involved in cardiac damage after radiation exposure.

Our proteomics data indicated that radiation-induced CVD is strongly associated with perturbation of cardiac metabolism. This impairment is accompanied by a persistent reduction in the activity of peroxisome proliferator-activated receptor (PPAR) alpha and its related signalling pathway. The alteration in PPAR alpha contributes to heart oxidative stress response, cardiac tissue remodelling and vascular endothelial dysfunction. Furthermore, the intervention of the PPAR alpha pathway attenuates the alteration of cardiac proteome after irradiation.

We expect that our proteomics observations in a good conversation with data obtained from other omics platforms will provide an important basis for further improving diagnosis and prevention of radiation-imduced heart disease in clinical settings.

Abstract ID 27358

Diagnostic performance of 68Gallium-PSMA PET/CT in a large cohort of patients with biochemical recurrence of prostate carcinoma

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Objectives

^{68}Gallium-prostate specific membrane antigen (PSMA) positron emission tomography/computed tomography (PET/CT) is a highly promising method for imaging primary and recurrent prostate cancer (PCa).
The aim of this study was to evaluate ^{68}Gallium-PSMA PET/CT for detecting and localizing PCa in patients with biochemical recurrence (BCR) and to evaluate the association to serum prostate specific antigen (PSA) levels and PSA kinetics.

Methods

Five hundred sixty-five BCR-patients referred for ^{68}Gallium-PSMA PET/CT were retrospectively evaluated. Relationships between PSA, PSA doubling time and PSA velocity were correlated with the detection rates of ^{68}Gallium-PSMA PET/CT.

Results

^{68}Gallium-PSMA PET/CT was positive in 426 of 565 patients (75%). The detection rates (DR) were positively associated with PSA levels. For patients with PSA <0.2 ng/ml, the DR was 64%.
Patients with PSA of 0.2-<0.5 ng/ml showed a DR of 55%. The DR was 61% for PSA of 0.5-<1.0 ng/ml, 74% for PSA of 1.0-<2.0 ng/ml, 83% for PSA of 2.0-<5.0 ng/ml and increased to 95% of PSA of ≥5.0 ng/ml.

In contrast, no positively association could be found for PSA doubling time (70% in <6 months, 72% in 6-<12 months, and 80% in ≥12 months).

However, PSA velocity (PSAvel) was associated with PSMA PET/CT positivity. The DR was 45% for patients with PSAvel <1 ng/ml/y, 62% with PSA 1.0-<2.0 ng/ml/y, 84% with PSA 2.0-5.0 ng/ml/y and increased to 97% at PSA >5 ng/ml/y.

Conclusions

Our data confirm the high performance of ^{68}Gallium-PSMA PET/CT for the detection of recurrent PCa in patients with BCR, even in patients with low PSA <0.2 ng/ml.

^{68}Gallium-PSMA ligand PET/CT may improve treatment planning and this may help guide to appropriate treatments (localized vs. systemic therapy).

Session Effects of electromagnetic fields

Abstract ID 27490

Examining cell proliferation and differentiation in primary human dermal fibroblasts to ensure EMF exposure experiments under comparable condition

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Primary human fibroblasts from dermal skin (HDFa) are cellular models widely used in several fields of research. In future studies we want to examine the impact of EMF exposure on these primary cell lines. The prerequisite of every meticulous in vitro study necessitates the characterization of the model before exposure. HDFa can be cultured in special media supplemented with cytokines (106 Medium) or using DMEM. It was the purposes of this study to systematically examine cell proliferation and differentiation processes of these cells in two different growth media and using different passage numbers. A time window should be identified where primary HDFa cells from different donors reflect comparable proliferation/differentiation characteristics, thus enabling reproducible EMF exposure under comparable cell status conditions. Cells were seeded with 0,5x106 cells/flask and incubated over 24 hours. Over the next 6 days growth curves, vitality, morphology as well as gene expression of genes coding for cell proliferation (*PCNA*, *CDKN2A*, *CDKN1A*, *SFN*) and differentiation (*PDGFRA*, *TGM2*, *ACTA2*, *PDPN*, *NTN1*, *MGP*, *PPP1R14*) were examined in both media and passage numbers 3-4, 5-6 and >6 and three independent experiments. At passage 3 a doubling time <48 hours could be observed in both media. However, cells incubated in DMEM over passages 4-5 and >6 remained to proliferate while cell numbers in 106 medium persisted around the seeded numbers. Vitality in all experiments ranged between 90-100%. Most differentiation marker remained at or close to control values, but *TGM2* (strongly expressed in reticular fibroblasts) revealed a 10-50 fold downregulation in both media and all passage numbers. A down-regulation of *SFN* (3-10 fold, known negative regulator of mitotic translation and cell differentiation) and *PCNA* (about 2-fold, known co-factor for DNA replication) coincided with proliferating HDFa cells. To better characterize known SFN mediated effects on epidermal formation (*TP63*) and wound healing (*MMP1*, *MMP3*) further genes will be examined and shown. In conclusion, *SFN* appears as a key

marker for differentiation and proliferation processes in HDFa cells. Further characterization of SFN related downstream processes might allow for a cell culture characteristic, thus, enabling reproducible EMF exposures on HDFa cells of comparable proliferation or differentiation status.

Abstract ID 27443

Precise and Reproducible SAR-Dosimetry for Electromagnetic Field Exposure Tests

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At present the so called 5G cell phone standard is going to be introduced in Germany. Its higher frequencies offer larger bandwidths and promise a higher data throughput necessary for “industry 4.0”, “smart home” and “autonomous driving”. For its implementation, additional antennas are needed due to low range of 5G. Environmental effects of both, electromagnetic exposition in general and the new frequencies at higher field magnitudes of corresponding antennas are still investigated. Existing results are contradictory, a dose-impact-relation cannot yet be determined. Differences of network coverage and exposition conditions (urban centres and rural regions) need to be investigated as well.

In this work, µTEM-cell cells and electromagnetic reverberations chambers (ERCs) are investigated as test environments for electromagnetic field exposure tests, which can be applied to a large variety of biological models including in vitro and in vivo setups. Predominant strategy of µTEM-cell cells is to provide an electromagnetic field defined in all parameters exclusive of all types of disturbances, e.g., due to probed biological samples. In contrast, ERCs rely on the stability of statistical means of ergodic time series of electromagnetic fields due to changes of the reverberation chamber’s geometry. The electromagnetic field homogeneity during exposition in any experimental set-up is of fundamental importance for both. Yet, field homogeneity is not the only relevant parameter. To guarantee comparable results, field dosimetry has (also) to be performed in terms of specific absorption rate (SAR). In this work a detailed investigation is presented, clarifying how multiple samples influence each other. SAR is determined by identification of the thermodynamical power balance between DUTs and environment via measurement of the temperature-time-profile.

To further investigate the applicability of the method, the interaction of the DUT with the exposition set-up and other DUTs is determined. With such measurements a three-dimensional SAR-field and the corresponding spatial variation of the relative distribution of the electromagnetic field strength can be deduced. This, exemplarily investigated for a µTEM-cell, will be applied to a mode stirred bio-reverberation chamber, ensuring homogeneity of SAR distribution and electromagnetic field. Hence, screening experiments with high numbers of exposed samples will become possible.

Session Effects of low dose ionizing radiation

Abstract ID 26452
Canceled

Abstract ID 27039

Risk assessment in Siberian group of chemical enterprises personnel

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Cancer risk assessment was performed in the cohort of Siberian Group of Chemical Enterprises (SGCE) (n = 61,005), who started to work between 01.01.1950 and 31.12.2000. The period of follow-up was from 01.01.1950 to 31.12.2014. Individual monitoring of external exposure was conducted for 18,976 employees, with 68 % having cumulative dose less 100 mSv.

An assessment of an excess relative risk (ERR/Gy) of solid cancers, excluding lung, liver and bone cancer, without taking into account the dose of internal exposure was performed.

A statistically insignificant increase of radiation risks with an increasing dose of external exposure with a five-year lag was estimated for solid cancer excluding lung, liver and bone cancer (ERR/Gy = 0.17, 95 % CI: –0.17; 0.59; n = 3,897 cancers; p-value = 0.34). All models were calculated taking into account age at risk, gender, calendar time, plant and duration of work at the SGCE, and smoking. Models with a lag of 0, 10, 15, and 20 years were also considered, but the results did not differ significantly.

The radiation risks of incident solid cancers, excluding cancer of lung, liver and bones, didn't change depending on gender, type of plant, age at risk or age of start of work. The radiation risks of smokers differed from the risks for those who never smoked (p = 0.02). We estimated statistically significant radiation risks for smokers (ERR/Gy = 0.71, 95% CI: 0.13; 1.42), while risks for non-smokers were not increased (ERR/Gy = –0.28, 95% CI: –0.61; 0.19).

It seems necessary to conduct an additional analysis of radiation risks in the cohort of SGCE personnel, taking into account internal exposure doses.

Abstract ID 27025

Low dose irradiation by low and high LET emitters discriminated by DNA damage geometry

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Radioactive fallout after NPP accidents, A-bomb deployment, and dirty bomb scenarios will lead to internal radionuclide exposures that are also the consequence of nuclear medicine procedures. Here we investigated and compared the DNA damage response of blood leukocytes to internal ex-vivo irradiation with the dissolved radionuclides I-131, Lu-177, Ga-68, Y-90, Tc-99m, Ra-223, which are the most frequently used radionuclides in Nuclear Medicine today, and Ra-224. We sought to correlate DNA double-strand breaks (DSBs) to the absorbed dose to the blood (ADBlood) and to investigate differences relating to radiation quality. To this end, blood sample

aliquots were mixed with radioactive solutions in different concentrations, and incubated for 1h at 37°C. The sample activities were measured with a calibrated germanium detector. Fixed leukocytes were immunofluorescently stained and investigated for DSB-indicating co-localizing γ-H2AX+53BP1 foci as well as α-induced DNA damage tracks. For the β-/γ-emitters, the calculation of ADBlood was based on a simulation of energy deposition by Monte Carlo simulation (Hänscheid et al. PMB 59, 2014). For α-emitters, ADBlood was calculated assuming local energy deposition of all non-penetrating particles for Ra and its progeny.

Cells irradiated with low LET β-/γ-emitters displayed randomly distributed small γ-H2AX+53BP1 foci of a dimeter of 0.3–1.2 µm, likely representing simple DNA double-strand breaks, Ra-223 and Ra-224 high LET α-irradiated cells also showed particle-induced DNA damage tracks and large foci (Ø1.2-1.6µm) likely harboring densely stacked DSBs and complex DNA damage. For Ga-68/Tc-99m/Y-90 β-irradiated samples, the number of radiation-induced foci (RIF) was proportional to ADBlood ranging from 0 to 108mGy, as known from Lu-177 and I-131 experiments (Eberlein et al. PlosOne 2015). For the α-irradiated samples, a linear relationship between the number of α-tracks and ADBlood (range: 0 to 142mGy) was observed. In all, it appears that focus and DNA damage track geometry allows for the discrimination of incorporated low or high LET emitters. While β-/γ-emitters can be identified by small round RIF with numbers proportional to ADBlood, the number of linear damage tracks proves a suitable parameter for describing the dose-response relationship for α-emitters

Abstract ID 27361

Molecular imaging for longitudinal in vivo prediction of cell death and tissue regeneration after exposure to ionizing radiation

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Positron emission tomography (PET) is a quantitative molecular imaging method with a very strong translational relevance, since the same methodology can be applied in mouse experiments as well as in the clinic using appropriate technology. Radioactive tracers are available for a wide range of biologically useful signals. Among others, 3'-deoxy-3'-[^{18}F]Fluorothymidine ([^{18}F]FLT) can be used for imaging proliferation, while 5-fluoropentyl-2-methyl-malonic acid ([^{18}F]ML-10) is a [^{18}F]-labeled marker of apoptosis. Thus, PET may offer in vivo detection and follow-up monitoring of cell death and proliferation after exposure to ionizing radiation.

In a previous study in normal mice, it could be shown that [^{18}F]FLT can provide dose-dependent information on proliferation in the bowel after total-body irradiation. The PET signal was measured up to 7 days after total-body photon irradiation with 1, 4, or 8 Gy.

Now, the novel apoptosis tracer [^{18}F]ML-10 will be used in combination with [^{18}F]FLT to study cell death and regeneration after low-dose irradiation. In a first study, mice will be irradiated with 0.5, 1.0 or 3.0 Gy in a total-body scheme. Serial PET measurements using [^{18}F]FLT and [^{18}F]ML-10 will be performed up to 6 days after irradiation to determine the maximum PET signal. In the main study, the animals are also irradiated with 0.5, 1.0, or 3.0 Gy, but PET measurements with both tracers will be repeated for up to 6 months to detect long-term effects. PET imaging data will be analyzed in comparison to animals without irradiation but identical handling. Quantitative measures of tracer uptake, e.g. standardized uptake values, will be analyzed for specified time points in various organs, including bone marrow. If correlation of total-body radiation dose, apoptosis, and proliferation signals is found, PET imaging may offer a non invasive tool for assessing potential long-term effects at an early time point after total body irradiation.

Session Radiation risk perception of the public /External exposure assessment

Abstract ID 24758

Advanced CT-protocols in clinical routine: CTA-Subtraction-Technique in detection of pulmonary embolism. A benefit for patients or only an increase in dose?

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Latest advantages in computed tomography come with enhanced diagnostic imaging and also sophisticated dose reduction techniques. However, overall exposure to ionizing radiation of patients in Germany slightly rises, which is mainly based on the higher number of performed CT scans. Furthermore, new possibilities in modern imaging, including 4D scans or perfusion protocols, offer new medical insights but require additional scans.

In this study, we re-evaluated data sets from patients undergoing CT examination because of suspected pulmonary embolism and compared doses and diagnostic results of the standard protocol to the additional modern CT subtraction technique.

Two groups of single-blinded radiologists were provided with CT data sets from 50 patients. One group (G1) had access to full datasets including CT subtraction with perfusion map. The other group (G2) only evaluated conventional CT angiography. Results were compared to final clinical diagnosis. Dose length product (DLP) of CT angiography was compared to CT subtraction technique, which consists of an additional non-contrast-enhanced scan and perfusion map. Effective dose was calculated using a Monte Carlo simulation based software tool (ImpactDose).

Interrater agreement of both groups was high (k = 0.896) and also agreement to final diagnosis was high for both groups (G1 k = 0.767 vs. G2 k = 0.848). Doses applied using CT subtraction technique were 34.8% higher than for CT angiography alone (G1 DLP 337.6 ± 171.3 mGy/cm; G2 DLP 117.4 ± 67.7 mGy/cm). Calculated effective dose was therefore significantly higher for G1 (G1 4.82 ± 2.2 mSv; G2 3.04 ± 1.3 mSv; $p < .0001$).

Our results suggest a rather low benefit of CT subtraction technique for the detection of pulmonary embolism in clinical routine but an explicit increase of administered dose.

New CT protocols should therefore always be applied carefully to specific clinical indications in order to maximize the potential for dose reduction and keep the administered dose as low as reasonably achievable.

Abstract ID 26665

Reevaluation of the dose effect curve from low to high doses using the standard micronuclei technique in association with a telomere/centromere FISH staining

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While the dicentric assay is the international gold-standard method for biological dosimetry and classification of genotoxic agents, micronuclei and PCC techniques are also developed to quantify radiation exposure as well as chemical toxicity. Telomere/centromere staining in PCC-fusions can be improved by using an alternate to CHO-fusion that showed huge interstitial telomeric signals. Biodosimetry network usually used the three techniques during intercomparisons and training for dose quantification. Here, the global project is to reestablish new dose

effect curves from 0 to 6Gy using the three techniques with a strong focusing on very low dose (4 points between 10mGy and 100mGy) which will make finally possible the evaluation of dose below 100mGy.

For micronuclei analysis, the standard technique approved by the AIEA consist in scoring micronuclei after DAPI staining in cytokinesis-blocked lymphocytes. In complement, the introduction of telomere and centromere staining renders the scoring of micronuclei more precise and informative with the establishment of 4 classes of micronuclei and their associated curves for the first time. Interestingly, micronuclei do not contain only acentrics fragments.

Here, we plan to score 7 donors at 3 different time points to check a possible variation of radiosensibility over time. At the end, the different curves will be established with 21 scoring using the 3 biodosimetry techniques. Dicentric assay on metaphasis and on PCC will be done after telomere and centromere staining (as published in MKacher et al. 2014,2015) while micronuclei will be established both with DAPI and telomere/centromere staining.

This new calibration curves could be used for biological dosimetry in radiation emergency medicine in our lab but also for all dosimetry labs.

Session Radiation biology/radiation physics II

Abstract ID 25798

Using mRNA and small RNA gene expression changes in the peripheral blood for easy detection of Ra-223 incorporation

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Background

Radiation analytics is the established method for detection of incorporated alpha-emitting radionuclides. It is laborious and time consuming. We wondered whether changes in gene expression measured in the human peripheral blood after radionuclide incorporation might serve as an easier approach for detection of incorporated radionuclides in a radiological or nuclear scenario.

Methods and Results

We received whole blood in PAXgene Blood RNA tubes from five patients suffering from multiple bone-metastatic, castration-resistant prostate cancer (without visceral or nodal involvement), who underwent treatment with the alpha emitting isotope radium-223 dichloride (Ra-223, Xofigo®). Patients received about 4 MBq per cycle and month and were treated ideally for six months.

In a first step, we employed next generation sequencing (NGS) for a whole genome screening of the transcriptome (mRNAs) as well as the post-transcriptome including small RNAs (e.g. long non-coding RNAs, snoRNAs and miRNAs) in one patient at 8 different time points during 6 cycles of Ra-223-therapy. This allowed us to identify specific candidate RNAs which are associated with the increased dose cumulated over the treatment time. Hereby, we could detect about 70 mRNAs and more than 120 small RNAs that were differentially up- or down-regulated (>2-fold, $p<0.05$) over the whole period of time after the first treatment with Ra-223 or that were deregulated with peaking profiles (>5-fold, $p<0.05$) at specific points in time.

In a second step, candidate mRNAs and small RNAs which appeared differentially up- or down-regulated in the screening samples were chosen for validation. This was performed by using the remaining patient samples (n=4 patients, each with up to 6 points in time) and shifting to more sensitive and specific qRT-PCR platform (low density arrays) at the same time.

Conclusion/Prospect

We will present and discuss the results on radiation-induced gene expression changes in whole blood which might serve as a simplified diagnostic tool for identification of incorporated radionuclides (Ra-223) in future.

Abstract ID 25958

Accident with a Se-75 Source

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On December 2016, a Service Company for Gammamat-Devices and X-Ray tubes near Cologne reported a release of the nuclide Se-75. The Se-75 Source, which is used in nondestructive material tests, was damaged due to a misjudgment.

The release of the radioactive Material caused contamination of building parts and the operational facility. The decontamination measures were taken right after the incident, and are still going on.

In the presentation we want to set our focus on the immediate decontamination measures, measurements for free release as well as the problems that we had to face.

One big challenge during this project were the not suitable environment as well as the anxiety of the staff involved.

For long-term security of the building and the still contaminated hot cell, an external air system was set up. This is used to put the buildings under negative pressure to secure that no further contamination is leaking out.

NucTecSolutions GmbH is as a radiation protection and dismantling service company prepared for emergency measures in all areas. Within the last 10 years our Team has worked on numerous dismantling and disposal projects. During this time, we had to face a total of seven emergencies.

Abstract ID 27169

Protecting skin keratinocytes from ionizing radiation with Bardoxolone-methyl

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Background

Skin injuries caused by ionizing radiation (IR) are one major threat in radiological and nuclear events. Moreover, they represent a limiting factor in cancer radiotherapy, and can also occur after extended fluoroscopically guided procedures. Therefore, drugs able to mitigate the harmful impact of IR on the skin are urgently needed. Here, we tested the efficacy and mechanisms of Bardoxolone-methyl (CDDO-Me), a triterpenoid which already showed radioprotective characteristics, in protecting normal human epidermal keratinocytes (NHEK) and squamous cell carcinoma cells (Cal-27).

Methods

Treatment with CDDO-Me was conducted by using a 10nM concentration versus solvent. Six hours after adding CDDO-Me or solvent to the cell culture medium, cells were exposed to 2 or 8Gy 240 kV X-rays and compared to non-irradiated cells. The ability of CDDO-Me to lower the intracellular reactive oxygen species (ROS) after irradiation was tested by adding 2',7'-dichlorofluorescin-diacetate (DCFDA). ROS were determined as fluorescence intensity after flow cytometry. Expression levels of Heme-oxygenase-1 (HO-1) were assessed using Western blot. DNA damage (double-strand-breaks) was estimated by counting colocalizing γ-H2AX+53BP1 foci following immunofluorescent staining.

Results

CDDO-Me did show a low cytotoxicity towards NHEK (IC_{50}=820nM) whereas it was higher for Cal-27 (IC_{50}=280nM). It was capable of lowering intracellular ROS in NHEK at radiation doses as high as 8Gy. Interestingly, CDDO-Me significantly increased the level of ROS in Cal-27 without radiation exposure, whereas this effect seemed to be overlaid by ROS generated by radiation. HO-1 expression levels in NHEK were significantly increased upon CDDO-Me treatment, whereas in Cal-27 HO-1 only showed a minor increase. The amount of DNA double-strand-breaks increased with radiation dose, but CDDO-Me could successfully lower them in both cell types.

Conclusion

CDDO-Me may be a potent radioprotector for normal keratinocytes; the increased toxicity and decreased protection of carcinoma cells could be exploited to selectively protect healthy cells when irradiating a skin carcinoma.

Outlook

Further research in the mechanism of radioprotection by CDDO-Me is desirable since other enzymes like HO-1 or chemokines may be likely involved. As CDDO-Me already showed detrimental effects after high systemic doses, the development of a locally applied ointment could provide interesting advantages.

Abstract ID 27606

CT irradiation induced changes of RNA profiles within peripheral blood cells and exosomes

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In medical imaging the computed tomography (CT) is an elementary pillar for the diagnosis of various diseases in everyday clinical practice, especially in emergency medicine. The continuous advancement of CT technology and the implementation of new methods into clinical routine result in an onward dose reduction for single examinations but an overall increase of administered dose because of the extended usage. At the same time, the molecular and biological processes triggered by low doses such as used in diagnostic radiology still remain elusive. Consequently, risk assessment in low dose range continues to be based upon the assumption of a linear cause-effect interrelation of exposure and adverse effects. Apart from monitoring DNA damages by e.g. DIC and γH2AX-assays, the analysis of irradiation associated gene expression changes promises further insights into the consequences of low dose exposure in the context of diagnostic procedures. This prompted us to investigate the impact of CT irradiation on the gene expression signature within peripheral blood cells and exosomes, which are protein and RNA containing extracellular vesicles implicated in intercellular communication.

We have exposed peripheral blood cells of three healthy donors ex vivo to X-ray radiation using a modern Dual-Source-CT-Scanner (SOMATOM Force, Siemens) with a tube voltage of 150 kV and a resulting dose-length product of 610 mGy*cm. RNA was isolated 1h and 6h after exposure, respectively. Subsequent RNA deep sequencing was employed in order to detect the transcriptomic response to low dose irradiation. First results of differential gene expression analysis indicate subtle changes within the gene expression profiles, which we will next compare to the microRNA content of exosomes.

Overview Poster per Topic

Radiation protection

Abstract ID 22063

How reliable is your measurement equipment? – Evaluation of measurement devices for radioactive and nuclear material

H. Friedrich, M. Risse
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Abstract ID 26091

MiniSzint, a handy, light-weight, very sensitive scintillation gamma-probe for finding and discriminating radioactivity in the field, in homes and in labs

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Abstract ID 27580

Cytogenetic Analysis after Temporary Residence in the Area of the Uncontrolled Ruthenium-106 Release in Russia in September 2017

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Abstract ID 27986

Repositioning Radiation Protection Institute of Ghana Atomic Energy Commission as an Efficient Technical and Scientific Support Organization

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Radiation biology/Radiation physics

Abstract ID 22901

Mechanisms and Challenges for Understanding Radiation Induced Changes in Chromatin Nanoarchitecture and Repair Complex Formation

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Abstract ID 24641

The influence of room-tempered physical plasma on the genome stability of fibroblast cells

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Abstract ID 25797

Measuring human RNA biomarkers in saliva for prediction of health effects in radiological/nuclear scenarios

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Abstract ID 26091

Uranium exposure increases spermatocytes metaphase apoptosis in rats: inhibitory effect of thymoquinone and N-acetylcysteine

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Abstract ID 27051

Local inhibition of rRNA transcription without nucleolar segregation after targeted irradiation of the nucleolus at the ion microbeam SNAKE

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Abstract ID 27189

Parp1-dependent DNA double strand break repair in late spermatocytes of irradiated mouse testicular germ cells

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Abstract ID 27576

Analysis of the Bardoxolone-methyl effect on radiation-induced gamma-H2AX foci and micronuclei formation in human blood lymphocytes in vitro

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Abstract ID 27582

Elucidation of CDKN1A participation in PHA-mediated lymphocyte stimulation after radiation exposure as a potential starting point of accelerating the cell cycle.

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Abstract ID 28934

Synergistic induction of malignant transformation of BEAS-2B cells by ionizing radiation and microgravity through β-arrestin1-FN1-YAP pathway

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Abstract ID 26991

Impact of bcl-2 and growth pattern on cell turnover, CAFs and EMT in basal cell carcinoma of the head and neck

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Radiation emergency medical preparedness and response

Abstract ID 24611

Development of new biokinetic-dosimetric models for the simulation of iodine blockade in the case of radioiodine exposure

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Abstract ID 24757

Detection of incorporated radioactive shrapnels after the explosion of a Radiological Dispersal Device in radiological emergency diagnostics

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Abstract ID 27594

The role of Nagasaki University in the nuclear disaster in Japan

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A**bstract ID 27205**

Emergency planning in Austria for the Treatment of Deterministic Effects - Revision of the National Medical Emergency Plan

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External exposure assessment

Abstract ID 27247

Radiation exposure of military personnel due to thoriated magnesium alloys in jet engines

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Abstract ID 27620

French military personnel translocation background levels

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Radiation accident management

Abstract ID 25097

Validating the gene expression assay for biological dosimetry in emergencies involving exposure to radiation of high and low LET radiation

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Abstract ID 25491

Developing a smartphone app for the prediction of the hematological acute radiation syndrome (HARS) based on changes in blood cell counts – the H-module App

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Abstract ID 27300

Cytogenetic biodosimetry for radiation accidents: application of image analysis and its advantage for emergency and expertise networks

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Abstract ID 30774

Emergency measurements of the population - a task for competent incorporation monitoring laboratories

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Decontamination measures and monitoring

Abstract ID 23848

Operational research and data mining methods for regulatory supervision of nuclear legacy site Andreeva Bay

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Abstract ID 25726

Skin and hair nuclear decontamination with the Cevidra® cream

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Abstract ID 25911

Determination of bioavailability of aged legacy actinides obtained from a contaminated glove box: application of a simple *in vitro* test

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Abstract ID 25954

Medical countermeasures following internal contamination with radionuclides

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Effects of electromagnetic fields

Abstract ID 27095

Acute and chronic biological effects of an anti-denial system exposure

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Effects of low dose ionizing radiation

Abstract ID 27040

The estimation of acute myocardial infarction risk in people exposed to occupational irradiation

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Abstract ID 27041

Association between gene polymorphisms and the increased frequency of cytogenetic abnormalities in the persons exposed to long-term irradiation (GWAS)

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Abstract ID 27482
Canceled

Abstract ID 27543
Canceled

Radiation health effects and medical countermeasures

Abstract ID 23923

NIH/NIAID Radiation and Nuclear Countermeasures Program (RNCP)

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Abstract ID 24871

RI-MODS/MOF : Overview of preclinical models and innovative therapies at IRBA

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Abstract ID 25575

Pharmacological treatment of inhalation injury after nuclear or radiological incidents: The Chinese and German approach

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Abstract ID 25871
Canceled

Abstract ID 26742

***In vitro* evaluation of the wound healing activity in primary human fibroblasts (HDFa) - a new approach**

M.E. Hotz, R. Zabold, M. Port
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Abstract ID 26979

Preventive reduction of oxidative stress might minimize the risk of thyroid carcinoma after radiation exposure

A.F. Rommel, S.F. Eder, R. Ridi, M. Port, C. Hermann
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Abstract ID 27440

The influence of human mesenchymal stem cells of the adipose tissue on the regeneration process of a radiation-induced wound healing disorder

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Abstract ID 27559

Small peptide mimetic of basic FGF for mitigation of gastrointestinal syndrome

S. Swarts, A. Zhang, S. Zhang, Z. Zhang, R. Lori, S. Vidyasagar, N. Lockney, K. Casey-Sawicki, A. Hope, Z. Daohong, D. Siemann, M. Akbar, G. Hochhaus, H. Derendorf, C. Hardik, P. Okunieff
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Abstract ID 27293

Changes of gene expression associated with non-cancer effects in Chornobyl clean-up workers in the remote period after exposure

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Abstract ID 27261

Effect of different antioxidants on X ray induced DNA double strand breaks (DSBs)

using γH2AX and "comet assay"

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Radiation risk perception of the public

Abstract ID 26606

Developing a CompRadRisk NATO App for improved risk communication of radiation exposures –actual status

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Abstract ID 27212

Educational Dialogue on Public Perception of Nuclear Radiation

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Abstract ID 28017

Emergency Readiness in the Current Nuclear Age - An Educational Challenge

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Poster abstracts

Available online: www.radiation-medicine.de and www.sanitaetsdienst-bundeswehr.de (short link: http://bit.ly/ConRad2019)

Radiation protection

Abstract ID 22063

How reliable is your measurement equipment? – Evaluation of measurement devices for radioactive and nuclear material

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In all areas correlated with radiation preparedness, e.g. radiation protection in disaster medicine, contamination and so on, one has to deal with measurement equipment for radioactive and nuclear material. Therefore it is necessary to know about the performance and reliability of the used devices. Predominantly one has to rely on the information given by the manufacturer, also due to the fact that there is no international quality label available. It is therefore desirable to have a reliable third party test result concerning the devices. This is especially interesting when thinking of the procurement of new devices and the comparison to existing old equipment.

Fraunhofer INT has a profound long-lasting experience in the assessment of measurement devices for the detection of nuclear and radioactive material.

Due to this experience Fraunhofer INT has been invited to participate in the Illicit Trafficking Radiation Assessment Program (ITRAP+10). ITRAP+10 is a program initiated by the European Union and the United States to evaluate the performance of commercially available radiation detection equipment against consensus standards and to improve these standards.

The ITRAP+10 effort accentuated the need to have accredited testing laboratories in the EU to perform testing against such standards in order to have reproducible test results, independent of the testing location. Therefore, the next step was to enable laboratories to work as testing locations. Initiated by the EU, this was carried out in ITRAP+10 Phase II in work package 2. Fraunhofer INT has conceived and built a test environment to perform the corresponding dynamic and static test measurements using neutron and gamma sources. The development of the testing facility as well as exemplarily tests of measurement devices are part of the present presentation.

The INT testing facility can be used to qualify new devices as well as to test already deployed ones. Therefore a reliable comparison between different devices is possible. This will be especially helpful for the procurement of additional components when the presently used version is no longer available or a replacement with new equipment has to be done.

Abstract ID 26091

MiniSzint, a handy, light-weight, very sensitive scintillation gamma-probe for finding and discriminating radioactivity in the field, in homes and in labs

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Objective: MiniSzint is a radiation detection system consisting of a probe with simple accessories. It is specially designed and has been successfully tested with several natural and artificial radionuclides. These may occur under various specific conditions in noticeable concentrations. Such as: Cs-137 in fallout and foodstuff and Ru-106 as in hot particles after nuclear accidents, U-238 as dust from ammunition used, radionuclides of potential for terrorists. The starting point of the authors was their more than 30-years' experience in developing simple, reliable methods to measure ceramics, glasses and radon decay products in air, water, and in and from solids.

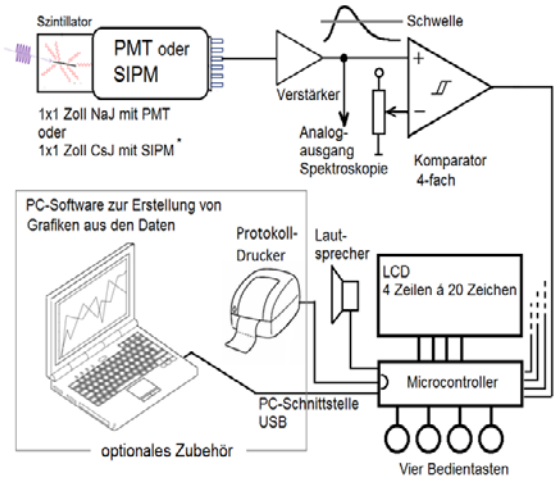
Scintillation probe: Single crystals of CsI function with low-voltage Si-photomultipliers, which facilitates handling as compared with NaI. The probe with a single crystal of CsI, Ø 25 mm, h = 25 mm, plus electronics in a 0.5 mm waterproof stainless steel casing, Ø 35 mm x 112 mm, weighs only 250 g. There are three types of shielding: 1) an electronic shielding for selecting Cs-137; 2) a 0.40 mm lead filter, 51 g, for calibrated dose rate measurements; 3) a 2 mm lead plus 2 mm steel encasing, 660 g, for measuring Rn decay products, reducing natural background from 21 cps to 7 cps. Small samples are placed in stainless steel mini-pots Ø 29 mm, h = 7 mm, 5 g, directly under the detector.

Control box: 12 x 18 x 4 cm^3, 500 g. User-friendly software allows to choose six types of measurement: calibrated dose rate in µSv/h; bulk material; Rn decay products in air; Rn-dps in water; Cs-137; search for radioactive sources. A thermo-printer, 317 g, records type of measurement, date, counting time, background, gross and net counts per 100 s, activity, and the calibration factor k [Bq/cps], chosen according to the sample. k is the reciprocal of the efficiency e = 1/k [cps/Bq] = [1]

Accessories: A stainless steel pot, 120 g, for 500 mL bulk material needs no shielding for Cs-137. An air sampler, 1200 g, collects 1 m^3 in 240 s on 50 mm glass fiber filters. For collecting Rn-dps electrostatically, a novel type of Philion Plate proved to be simple, efficient and reliable. A 50 mL glass cylinder for liquids serves also as a stand for the Philion Plate. A porcelain Büchner funnel for glass fiber filters weighs only 160 g, filtration time is 100 s for 100 mL. Small, simple, license-free test and calibration sources for all applications have been developed. An elegant olive-green, waterproof, linen shoulder bag with four zippers weighs 340 g.

Grass of '86 with Cs-137: 62 g pellets from Southern Bavaria with 7.3 Bq Cs-137 per g, as determined by gamma-spectrometry, make up 453 Bq. In a 100 mL plastic cylinder, they yield in 347 s: background 435 ± 12 cp100s; gross 650 ± 14 cp100s; net 215 ± 25 cp100s; 472 ± 56 Bq; activity 472 ± 56 Bq; calibration factor k = 220 [Bq/cps]; efficiency e = 1/k = 0.45 %. The result very highly significant > 99 %.

Rn-dps in water: The wet filter after filtration of 100 mL of water with 200 Bq/L Rn-dps, as determined by calibrated other instruments, yields in a minipot in 353 s: background 649 ± 16 cp100s; gross 774 ± 15 cp100s; net 125 ± 31 cp100s; activity 28 ± 7 Bq; k = 22 [Bq/cps]. The result is highly significant > 95 %.



* SIPM : Silizium-Photomultiplier (Avalanche-Diodenarray)
Vorteile gegenüber PMT: Keine Hochspannung (Sicherheit), Kein Glas, bruchfest, kleiner, leichter

Abstract ID 27580

Cytogenetic Analysis after Temporary Residence in the Area of the Uncontrolled Ruthenium-106 Release in Russia in September 2017

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In September/October 2017 an elevated atmospheric Ruthenium contamination was measured in several European countries. The most probable origin of this release of radionuclides was reconstructed to be the southern Ural. Five workers of a German company stayed during that time up to two weeks about 120 kilometers far from the Chelyabinsk region in Ekaterinburg (Russia). No clinical symptoms were reported during or after the suspected radiation exposure, and no internal contamination was found in whole body measurements. However, to follow radiation protection aspects and to clarify the workers` situation in order to reassure them as they planned to continue working in Ekaterinburg, our laboratory was urgently requested by the company's` occupational physician to perform biodosimetry using the dicentric analysis in order to examine if the workers have been exposed to radiation by incorporation of radionuclides. The workers` dicentric yields have been compared to reference data of background frequencies in unexposed individuals but as it is not reasonable to quantify individual absorbed radiation doses from internalized beta-emitters due to various confounding factors individual dose estimation has not been performed. Dicentric frequencies of two workers differed significantly from the mean laboratory's background level, which could have been induced by an exposure to incorporated radionuclides due to the beta-emission of 106Ru or the gamma irradiation by the daughter nuclide Rhodium-106. However, the maximum absorbed radiation doses calculated for a residence in the 106Ru contaminated area during that time does not correspond to the observed dicentric frequencies. It cannot be excluded that their dicentric frequencies were already elevated before September 2017 potentially induced by an earlier radiation exposure to diagnostic X-rays or even by chance.

Key words: dosimetry, internal exposure, ionizing radiation, ruthenium

Abstract ID 27986

Repositioning Radiation Protection Institute of Ghana Atomic Energy Commission as an Efficient Technical and Scientific Support Organization

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Organizations with technical and scientific expertise provide key support activities which is necessary to carry out regulatory functions. The Radiation Protection Institute (RPI) of the Ghana Atomic Energy Commission (GAEC) has a mandate to work in the area of Radiation Protection, Nuclear Safety and Security to assist in the overall fulfilment of the vision and mission of GAEC. RPI also collaborates with other Regulatory Agencies and stakeholders to achieve its mandate. In January 2016, the Nuclear Regulatory Authority (NRA), was established from GAEC as an independent nuclear regulatory authority by Act 895 of 2015 responsible for regulatory activities. Prior to the passage of Act 895 of 2015, RPI was serving both as a Regulator and a Technical Support Organization (TSO) for the acquisition and peaceful utilization of nuclear/radioactive materials in the country. With this development, RPI has repositioned itself as as a TSO providing scientific and technical services in Health Physics, Occupational Radiation Protection, Public Exposure Control, Nuclear Safety and Security, Non-ionising Radiation

Protection, Radioactive Waste Management and Decommissioning, as well as training in Radiation Protection, Safety and Security. In that regard, RPI is developing the human, technical, organizational and financial resources in order to execute its new mandate. The existence and role of technical and scientific support organizations (TSOs) in enhancing nuclear safety, nuclear security and safeguards as well as challenges faced such as the need to develop and manage specific tools to support nuclear and radiation safety and to maintain an up to date scientific knowledge base among others is discussed.

Radiation biology/Radiation physics

Abstract ID 22901

Mechanisms and Challenges for Understanding Radiation Induced Changes in Chromatin Nanoarchitecture and Repair Complex Formation

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The three-dimensional architecture of genomes on the meso- and nano-scale acts as an important supra-layer of gene regulation and fundamental biological processes such as DNA damage response and repair. In this context, chromatin and protein nanoprobing and super-resolution microscopy are powerful methods for structural analyses of genomic targets in native chromatin and repair protein complexes in single cells at resolutions of single antibodies, proteins, histones, short DNA stretches, etc. We used multi-color nanoprobing (specific antibodies, specific oligonucleotides) and single molecule localization microscopy to analyze the nano architecture and danamics of DNA damage and chromatin markers, DNA repair protein complexes in 3D-conserved nuclei of different cell types after exposure to various types (low-LET, high-LET; α-, β-particles) and doses of ionizing radiation. In an analogous approach, the effect of gold nanoparticles on extent and direction of radiation-induced DNA damage was assessed.

Our studies revealed a cell- and radiation type-specific nano-architecture of DNA damage foci with respect to γH2AX, Mre11 or 53BP1 and their dynamic molecular rearrangements during repair processes. Correlations to radio-sensitivity were identified. Localization microscopy of dispersed genomic Alu sequences resulted in linear-quadratic dose-effect curves for low to higher dose ranges, which may be related to DNA breakage events preferentially in these regions. In addition, the spatial distribution-changes of anti-H3K9me3-labelled heterochromatin clusters indicated a dose-independent chromatin relaxation upon radiation exposure. Preliminary results even show post-irradiation time dependent changes in Alu-FISH-marked chromatin, that warrants further investigation. We show, that single molecule localization microscopy can also be used to study damages along high LET particle tracks and the associated repair protein recruitment over time. Our studies contribute to the molecular understanding of cellular radiation responses at the sub-light microscopic chromatin levels, laying the basis for improved biological dosimetry and radiotherapies in the future.

Abstract ID 24641

The influence of room-tempered physical plasma on the genome stability of fibroblast cells

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Physical plasma is the fourth state of matter and corresponds to a highly energized gas. In contact with atmospheric air, numerous reactive molecular species like ROS and NOS as well as electromagnetic radiation are produced. Due to its antimicrobial, immunomodulating and anti-inflammatory effect, room-tempered ('cold') atmospheric plasma (CAP) is used in dermatology and increasingly tested for further medical applications, e.g. in oncology. Since the composition of CAP might suggest DNA damaging mechanisms, CAP-induced mutagenicity was investigated.

The hypoxanthine phosphorybosyl transferase (HPRT) assay was used to investigate gene mutations. DNA strand breaks were detected by TdT3'-end labeling (TUNEL) assay, microscopic γ-H2AX DSB focus assay and comet assay. A caspase 3/7 activity assay was performed to distinguish it from apoptotically induced DNA fragmentation. CAP was generated using a kINPen MED device (neoplastools, Greifswald) with Argon as carrier gas. Control cells were treated with Argon at the same flow rate. V79 fibroblasts were analyzed 0min, 5min, 1h, 4h , 8h, and 24h after CAP treatment and compared to control.

The absence of HRPT gene mutations after CAP exposure suggests that CAP is not mutagenic. Analysis of DNA integrity showed that DNA double strand breaks (γ-H2AX) and DNA fragmentation (comet, TUNEL) occurred within 1h. However, DNA damage was reduced after 4h incubation and only increased again after longer incubation times. This was accompanied by an increase in caspase 3/7 activity compared to controls after 24h incubation time, which may relate to cell cycle effects (DSBs are associated with stalled replication forks).

The present study highlights an important aspect of biological CAP effects on mammalian cells. While mutagenic effects can be excluded in view of therapeutic application, CAP induces apoptosis which likely contributes to the elimination of undesired mutagenic effects. Analysis of DNA integrity showed an initial but very short phase of DNA damage. This transient effect suggests that affected cells died rapidly and/or that DNA damage was repaired quickly. As a result, after a few hours DNA damage was absent, while its increase after 24h most likely relates to the onset of apoptosis due to cell cycle effects.

Abstract ID 25797

Measuring human RNA biomarkers in saliva for prediction of health effects in radiological/nuclear scenarios

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Background

Saliva, as the most non-invasive accessible bio fluid, has been already shown to contain RNA biomarkers (mRNA and miRNA species) for prediction and diagnosis of several diseases. The aim of our study is to identify radiation-induced gene expression changes in human saliva in order to predict later occurring health effects in a radiological or nuclear scenario.

Methods and Results

In the first stage we established the method and examined quantity and quality of RNA isolated from saliva. Bacterial contamination and cell debris represent challenges, which have to be taken into account first. For this issue, we modified the established workflow. Hereby, the crucial point is to isolate only the human RNA for cDNA-synthesis and preamplify the products before qRT-PCR. The degree of bacterial contamination can be estimated by calculating the quotient between 18S and 16S rRNA.

For detection of radiation-induced gene expression changes we take advantage of saliva stored from radiotherapy treated patients who suffered from head and neck cancer (n=8) or leukemia (n=4, additional patient recruitment is still in progress). After establishment of the method we will perform qRT-PCR for detection of mRNA expression for specific genes that are associated to radiation response. Furthermore, we will also employ a qRT-PCR platform (low density arrays) for simultaneous detection of 667 miRNAs. Independent validation will be performed on different patients.

Conclusion/Prospect

We will present results regarding the establishment of a method for detection of radiation-induced gene expression changes in an easy and non-invasive accessible biofluid, namely saliva considering confounders such as bacterial contamination and cell debris. The applicability of the method will be examined on stored saliva samples from radiotherapy patients and the results will be shown and discussed.

Key words

Gene expression changes, radiation biomarkers, radiotherapy, miRNA, mRNA, transcriptome, saliva, head and neck cancer, leukemia.

Abstract ID 26091

Uranium exposure increases spermatocytes metaphase apoptosis in rats: inhibitory effect of thymoquinone and N-acetylcysteine

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Uranyl acetate (UA), a commercial stock from depleted Uranium (DU), has a combined effect of chemical toxicity and mild radioactivity. Here, we investigated the potential antioxidant, antiapoptotic and cytoprotective effects of thymoquinone (TQ) and N-acetylcysteine (NAC) against UA-induced testicular damage in rats. UA reduced testicular superoxide dismutase (SOD) activity and nitric-oxide (NO) and glutathione (GSH) levels relative to the control group. Interestingly, the testicular SOD activity and NO and GSH levels of UA/TQ and UA/NAC treated groups were also significantly lower relative to the control. A marked increase in spermatocytes metaphase apoptosis was found (stage XIII) in UA treated rats, which is probably due to difficulties in segregation of homologous-chromosomes. This may clarify why UA exposure decreased round spermatids numbers and fertility in previous studies. To check the reason of partial metaphase arrest, the presence of DNA-damage-related γ-H2AX foci in late spermatocytes of all groups was checked, but only insignificant increase was found in UA treated group. TQ or NAC supplementation reduced the apoptosis and improved the testicular histological alterations. Thus, TQ and NAC attenuate UA adverse effects on the testicular microenvironement through anti-apoptotic and cytoprotective but not antioxidant effects.

Abstract ID 27051

Local inhibition of rRNA transcription without nucleolar segregation after targeted irradiation of the nucleolus at the ion microbeam SNAKE

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In their role as cellular stress sensors and as potential therapeutic targets for cancer treatment, nucleoli have recently gained interest. It is under debate, how and to which extent DNA double-strand breaks (DSBs) induced in nucleoli influence rRNA transcription or nucleolar organization. The agent to induce DSBs, the DSB frequency and the presence of DSBs in the vicinity but outside the nucleoli may strongly influence the effect.

We address the controversy by using the ion microbeam SNAKE to irradiate nucleoli with 1 to 100 carbon ions (0.3-30 Gy per nucleus). In the targeted nucleolus and in the other nucleoli of the same cell, no overall reduction of the ribonucleotide incorporation is caused by this localized irradiation. On the other hand, at the damaged nucleolar chromatin regions marked by γH2AX, 5EU incorporation and Parp1 protein level were locally decreased, which suggests a localized inhibition of rRNA transcription. Nucleolar segregation, a reorganization of the nucleolar structure and proteins, which is observed after treatment with other agents inhibiting rRNA transcription, e.g. actinomycin D or UV irradiation, does not accompany this locally transcriptional inhibition.
These results indicate that even multiple complex DSBs affect only a subnucleolar region, but not the whole nucleolus. Thus, it is assumed that only widespread transcription inactivation in the entire nucleolus causes nucleolar segregation.

Abstract ID 27189

Parp1-dependent DNA double strand break repair in late spermatocytes of irradiated mouse testicular germ cells

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Poly(ADP-ribose)polymerase-1 (PARP1) is a family member of nuclear proteins involved in several cellular processes, and is critical for the maintenance of the genome stability. A significant elevation of Parp1 level has been reported in several malignant tissues, thus recently, inhibitors of Parp have gained attention as rationally designed therapeutics for cancer. Homologous recombination (HR) repair is the predominant repair pathway during meiotic recombination of early meiotic testicular prophase. However, based on analysis of DNA repair kinetics in late meiotic prophase cells of SCID mice, Ku70 -/- and Rad54/Rad54B -/- mice models, we have previously demonstrated an interplay between HR and the conventional non-homologous enjoining (cNHEJ) repair pathways. Here, we evaluated the relative contribution of Parp1-dependant NHEJ in the repair of ionizing radiation (IR) induced DNA double strand breaks (DSBs) in late spermatocytes (late pachytene and early diplotene) after the completion of meiotic recombination. The disappearance of large DSB-related γ-H2AX foci was quantified at autosomes 1 and 8 h after 1Gy X-irradiation (IR) in late spermatocytes from wild-type and Parp1-inhibited mice (injected with DPQ, i.p.). In meiotic spreads and testicular sections of WT mice, 8h post IR, late spermatocytes repaired >80% of DSBs seen at 1h post IR. However, only 64% of foci disappeared in late spermatocytes of DPQ-

treated mice. Thus, it appears that both, alternative Parp-dependent and classical NHEJ contribute to DSB repair in late spermatocytes, with cNHEJ predominating early after IR, disclosing new insights in DNA repair pathway choreography during spermatogenic differentiation.

Abstract ID 27576

Analysis of the Bardoxolone-methyl effect on radiation-induced gamma-H2AX foci and micronuclei formation in human blood lymphocytes in vitro

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Ionizing radiation produces reactive oxygen species leading to cell damage. Synthetic triterpenoids, including Bardoxolone-methyl (CDDO-Me), exert antioxidant, anti-inflammatory and anti-cancer activities in in-vitro studies in part by enhancing the signaling of the DNA damage response. Therefore, CDDO-Me is discussed for the use as a potential anti-cancer treatment as well as a radioprotective agent for patients undergoing radiation therapy or for first responders in radionuclear scenarios.
As previously described pre-incubation of human peripheral blood lymphocytes with nanomolar concentrations of CDDO-Me for 6 hours provoked increased levels of antioxidative heme-oxigenase (HO)-1 as shown by immunoblotting. Subsequently, the effect of CDDO-Me towards radiation-induced DNA-damage in lymphocytes was analyzed using the gamma-H2AX foci assay and the cytokinesis-block micronucleus (CBMN) method. Additionally, we determined the nuclear division index (following mitotic stimulation and cell culture).
Surprisingly, we could not detect a reduced gamma-H2AX foci formation following irradiation. Consistently with this, we neither observed a decreased frequency of radiation-induced micronuclei nor an increased nuclear division index in the presence of CDDO-Me.
In summary, we could not verify radioprotective effects of CDDO-Me in human peripheral blood lymphocytes despite of up-regulated antioxidative HO-1 levels.
To further elucidate the potential radioprotective properties of CDDO-Me in human lymphocytes further experiments are required.

Key words: Bardoxolone-methyl, CDDO-Me, antioxidant, radioprotective activity, DNA damage, micronucleus assay, gamma-H2AX foci analysis

Abstract ID 27582

Elucidation of CDKN1A participation in PHA-mediated lymphocyte stimulation after radiation exposure as a potential starting point of accelerating the cell cycle.

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Objective: Dicentric chromosome analysis (DCA) is the gold standard for individual radiation dose assessment. However, DCA is limited by the time-consuming phytohemagglutinin (PHA)-mediated lymphocyte activation. We started to elucidate this process and sought to identify suitable gene or protein targets as a means of meeting our long-term objective of accelerating cell cycle kinetics to reduce DCA culture time.

Materials and Methods: The cell cycle kinetics of PHA-stimulated human peripheral blood lymphocytes was analyzed following exposure to ionizing radiation. At time points up to 36 h the PHA-related whole genome gene and single gene expression changes in irradiated lymphocytes after mitogenic stimulation was investigated.

Results: Various genes related to chemokine/cytokine expression, cell cycle progression as well as DNA replication and repair were identified to be differentially expressed following PHA stimulation. Among those, the mRNA of the cyclin-dependent kinase inhibitors coding genes *CDKN1A* (p21), *CDKN3* and *CDKN2A* (p16) was upregulated on the molecular level after stimulation with PHA in non-irradiated cells. Upregulated mRNA expression was also detected for *RBL-1/RBL-2, E2F2, Deaf-1,* which are genes known to be involved cell cycle regulation. *CDKN1A* mRNA was also upregulated in irradiated lymphocytes. Western Blot analysis showed that at different time points between 6 h and 48 h CDKN1A protein was expressed in non-irradiated as well as in irradiated lymphocytes. Until 18 h CDKN1A protein expression was greater in irradiated cells compared to non-irradiated cells. At 24 h up to 48 h there was no difference in protein expression observed.

Conclusion: Based on that analysis target genes for cell cycle acceleration in lymphocytes have been identified with CDKN1A being chosen as the first target gene to be investigated in further studies. It has to be determined whether the time expenditure for DCA can be reduced by influencing gene expression of one of these genes involved in the regulatory circuits controlling PHA-associated cell cycle entry and/or progression at a specific early cell cycle phase.

Key words: gene expression, whole genome microarray, qRT-PCR, dicentric chromosome analysis, mitogen, PHA, lymphocytes, proliferation, cell cycle, flow cytometry

Abstract ID 28934

Synergistic induction of malignant transformation of BEAS-2B cells by ionizing radiation and microgravity through β-arrestin1-FN1-YAP pathway

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For long-term deep space exploration missions, space radiation-induced tumorigenesis is the biggest challenge for astronauts. However, the combined effects of heavy ion radiation with microgravity on cellular malignant transformation as well as tumorigenesis have not been elucidated so far. In our study, fibronectin1(FN1) was found to be up-regulated significantly by both ionizing radiation and microgravity, and the two factors showed a synergistic effect. Then we investigated the effects of both ionizing radiation and microgravity on the expression of E2F1 and β-arrestin1, both of which have been shown to be key transcription factors for FN1. However, no expression change was found for their transcripts in cells exposed to either ionizing radiation or microgravity. However, β-arrestin1 was found to be induced to translocate into nucleus by both α particle irradiation and microgravity, between which there is a synergistic effect. Upregulation of FN1 expression has been reported to lead to rearrangement of the actin cytoskeleton. Thus we detected the morphology and distribution of actin cytoskeleton by staining with rhodamine-phalloidin in BEAS-2B cells after irradiation of alpha particles and/or simulated microgravity treatment. It was found that ionizing radiation and microgravity synergistically induced the rearrangement of actin cytoskeleton and led to degradation of fibrous actin into globular actin. Furthermore we found that the expression of YAP, a transcription coactivator in Hippo pathway, was synergistically upregulated by ionizing radiation and microgravity. Besides, the transcriptional activity of YAP was also found to be increased synergistically by using a luciferase reporter assay. Considering the important roles of β-arrestin1, FN1 and YAP in tumorigenesis and progression, we speculated that the effects of radiation and microgravity on malignant transformation and tumorigenesis are unified through β-arrestin1-FN1-YAP pathway, which is of great significance

to elucidate the molecular mechanisms underlying the malignant transformation and tumorigenesis induced by combined effects of space radiation and microgravity.

Abstract ID 26991

Impact of bcl-2 and growth pattern on cell turnover, CAFs and EMT in basal cell carcinoma of the head and neck

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Basal cell carcinomas are among the most common tumors of the head and neck characterized by their semi-malignant behavior with locally invasive growth and extremely low metastatic tendency. The proto-oncogene and regulatory protein of apoptosis, bcl-2 (B-cell-lymphoma-protein), is expressed in 60 to 100% of all basal cell carcinomas. It is increasingly expressed as a result of translocation, has an anti-apoptotic effect and leads to increased resistance to chemotherapy and radiation therapy in squamous cell carcinomas of the skin. In basal cell carcinomas, a positive correlation of bcl-2 expression with tumor cell proliferation, invasion, dedifferentiation and frequency of metastasis has been demonstrated. The aim of this study was to correlate growth patterns and bcl-2 expression with the presence of CAFs (cancer associated fibroblasts) and changes corresponding to EMT (epithelial to mesenchymal transition), thus explaining the different behavior of basal cell carcinomas and creating new approaches for future therapies. For this purpose, 74 basal cell carcinomas of 57 patients were immunohistochemically examined for the expression of bcl-2, the presence of CAFs, proliferation and apoptosis as well as marker proteins of EMT. Sclerodermiform and metatypical differentiated basal cell carcinomas showed only half of the bcl-2 expression of the nodular or superficial differentiated ones. Moreover a more malignant growth pattern was associated with tenfold increased expression of CAFs, in which the majority of them appeared to originate from the tumor cells themselves. Only minimal changes with increasing dedifferentiated growth pattern and reduced bcl-2 expression could be demonstrated for EMT. In terms of cell turnover, there was an increased proliferation with a concomitant reduction in the number of apoptosis in the less differentiated tumors compared to the better differentiated ones. Due to the large standard deviations, however, the results were nowhere significant. The impact of immunoreactivity and growth pattern on surgical resection showed no significance, too. Finally, there seems to be an association between malignant potential, growth pattern and tumor stroma, as known for EMT, but large interindividual differences were detectable, which requires an in-depth immunohistochemical study prior to the possible use of EMT-inhibitors for therapy.

Radiation emergency medical preparedness and response

Abstract ID 24611

Development of new biokinetic-dosimetric models for the simulation of iodine blockade in the case of radioiodine exposure

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In the case of a nuclear weapon detonation or a nuclear power plant accident, radioiodine will be liberated. After incorporation it accumulates in the thyroid gland and by internal irradiation enhances the risk of thyroid cancer occurrence. By administering a large dose of stable iodine the uptake of radioiodine into the gland can be inhibited ("iodine blockade"). Usual biokinetic models for radioiodine describe the uptake into the gland with first order kinetics. These models are not suited after the administration of 100 mg stable iodine as usually recommended for iodine blockade, as the uptake into the gland through the membrane of the follicular cells is mediated by a saturable active transport. For this purpose we integrated an uptake mechanism described by a Michaelis-Menten kinetic into a simple biokinetic model of the International Commission for Radioprotection. We moreover added a total uptake blocking mechanism representing the Wolff-Chaikoff effect becoming active when the gland is saturated with iodine. The thyroid equivalent dose was calculated using the method of Quimby/Marinelli and the validity of the model was ascertained by comparison with the results obtained with the commercial IMBA software. The competition of radioiodine and stable iodine at the carrier site in the membrane was modeled in analogy to the rate law for monomolecular irreversible reactions for competing substrates.

Our simulation results show that the competition mechanism for the uptake through the basolateral membrane of the follicular cells at the carrier site accounts for about 60 % and the saturation of the gland with iodine for over 35 % of the total protective efficacy that exceeds 95 %. Following a short term acute radioiodine exposure, it is preferable to administer a large single dose of stable iodine instead of repetitive smaller doses. In the case of a continuous radioiodine exposure, a single dose of stable iodine is less effective than after an acute radioiodine exposure and splitting the total available dose and shortening the dosage intervals enhance efficacy.

Model-based simulations may be an effective and efficient tool permitting to develop therapeutic dosage schemes for antidotes reserved to uncommon emergencies like nuclear or radiological incidents. They may also be used beyond the field of antidote treatment by giving indications if further measures (e.g. evacuation/sheltering) are required.

Abstract ID 24757

Detection of incorporated radioactive shrapnels after the explosion of a Radiological Dispersal Device in radiological emergency diagnostics

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The threat of a terroristic attack with a Radiological Dispersal Device is imminent and comes along with an immense challenge especially regarding medical treatment of combined injuries with incorporated radioactive fragments. In such scenarios the identification and surgical exploration of radioactive fragments is a major issue to prevent further radiation induced effects like wound healing disorders, onset of acute radiation syndrome, and as a late effect cancer. However, in a usual emergency setting it is unclear how this task can be achieved. Within this study we evaluated the feasibility of different radiological methods to identify and locate an incorporated radioactive fragment.

We placed two different Cs137 sources and several non-radioactive fragments representing sham control samples within a human spine phantom. Standard emergency imaging procedures were performed including plane radiography and different CT scans (64 row, 384 row dual energy, 320 row w/o iterative metal artifact reduction), respectively. Eight radiologists were blinded towards the results and asked to identify the radioactive fragments within the provided images.

For both sources correct identification was rather low (15.63%). Furthermore, none of the questioned radiologists (N = 0) stated that they were able to identify the radioactive shrapnel distinctly. Positive predictive value was accordingly low (15.63%). Most participants recommended a scintigraphy based technique for identification (12.5%) rather than radiographic procedures (3.25%).

Identification and location of incorporated radioactive fragments by standard radiological procedures prior to surgical exploration is not promising. Nevertheless, procedures which can achieve this aim are direly needed in the case of a terroristic attack with a radiological dispersal device and should be available in an emergency department.

Abstract ID 27594

The role of Nagasaki University in the nuclear disaster in Japan

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Since an accident of Fukushima Dai-ichi nuclear plant, the new nuclear medical system was established in Japan. Nagasaki University was designated as Advanced radiation emergency medical support center and Nuclear emergency medical support center. Nagasaki Unversity established headquarter for nuclear disaster response and preparedness in case of emergency from peace time.
At the time of a disaster, Nagasaki University is in charge of dispatching a nuclear emergency medical assistance team as a nuclear emergency support center, and as an advanced radiation emergency medical support center, it is responsible for accepting radiation and injured people who are difficult to respond at a nuclear emergency core hospital.

Regarding the activities of the nuclear emergency medical assistance team, we have modeled Japan DMAT(Disaster Medical Assistance Team) as a model, setting a limit on the number of active days, at the time of dispatch, entering under the command of the head of the nuclear emergency core hospital accepting acceptance, and providing emergency medical services to polluted injured patient
As a future task, it is required to efficiently improve the current system based on the feedback of troubles obtained by training.

A**bstract ID 27205**

Emergency planning in Austria for the Treatment of Deterministic Effects - Revision of the National Medical Emergency Plan

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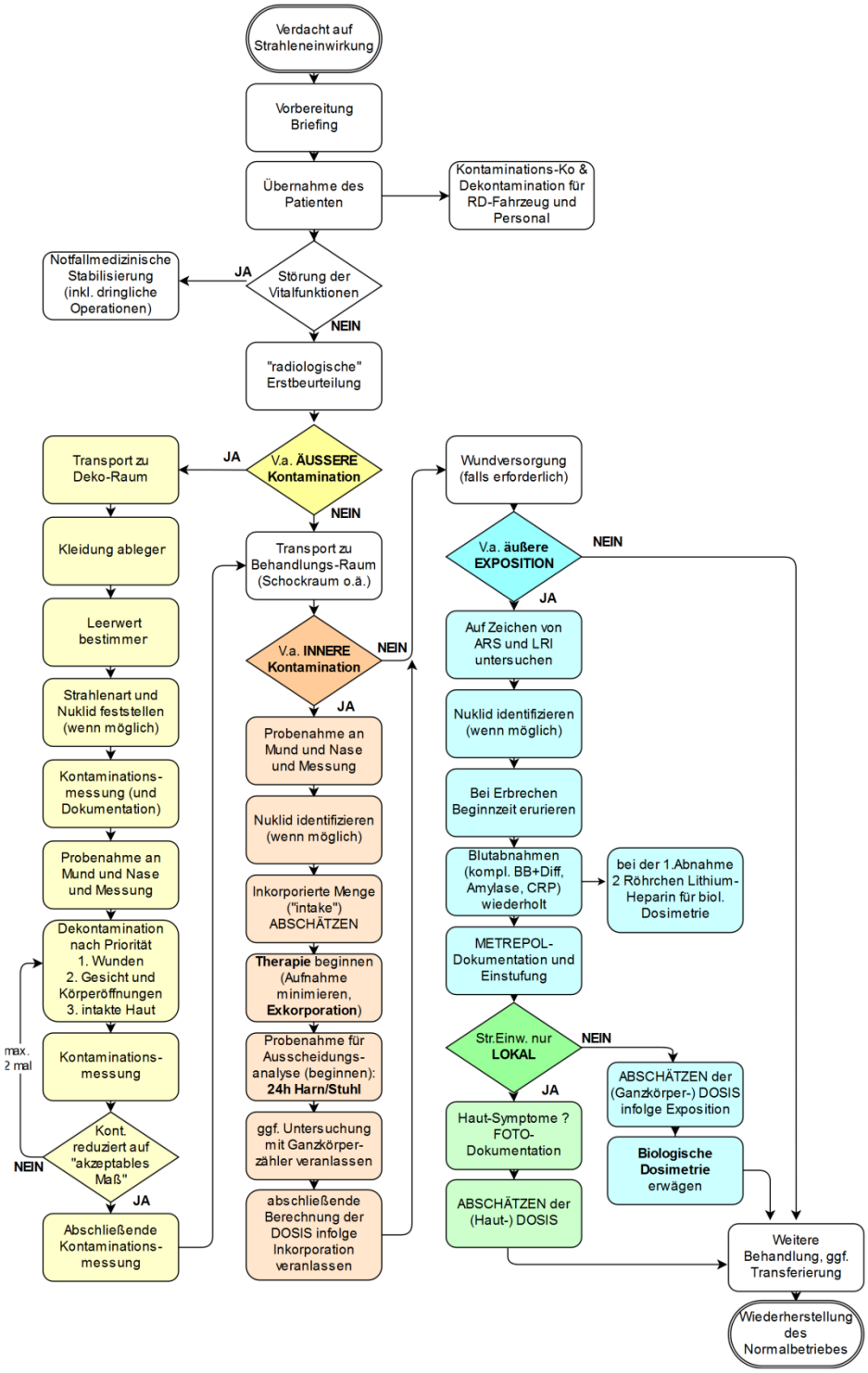
Given the low frequency of radiation accidents, the focus of nuclear emergency planning in Austria has traditionally been on mitigating effects of widespread contamination (e.g. after NPP accidents) by bilateral and international agreements on information exchange and by a 'Radiation Early Warning System'.
In 2008 the author was contracted by the Federal Ministry of Agriculture to create a 'Medical Radiation Emergency Plan'. This first version was mainly based on 'METREPOL approach', taking account also of publications by IAEA, REAC/TS, the Radiation Protection Commission of Germany, the Swiss-German Radiation Protection Association, UNSCEAR and ICRP.
While the content of that document was widely accepted, it was nevertheless only punctually translated into the emergency planning of the federal states, which have in Austria the prime responsibility in organising emergency services and the medical sector.
To enhance implementation, the National Medical Emergency Plan was revised in 2018. It was converted into 'Guideline for Medical Diagnostic and Therapy after Radiological Emergencies'.
The multi-level approach regarding hospitals was revised and clarified. 'Designated Hospitals' for care after radiation accidents are required to have an appropriate response plan to integrate their resources into a therapeutic networks, which include nuclear medicine and radiotherapy departments, haematology and bone marrow transplantation centres, ICUs, surgery and dermatology as well as biological dosimetry laboratories. Consultation within the IAEA/WHO REMPAN network is possible and desirable; yet it is required to involve the national competent authority and the appropriate contact point.
'Basic' hospitals need to prepare to properly refer patients while protecting themselves and performing initial steps of management.
Detailed flowcharts for radiological emergency medical management have been developed for 'designated' and 'basic' hospitals as well as for 'on scene response'. The presentation or poster will describe those in depth. An example is provided below.
The Guideline also aims to provide information on other issues like the organisation of biological dosimetry examinations, triage in multiple casualty situations, management of the worried well and long-term follow up. With this Guideline the federal authorities expect major progress in medical emergency preparedness in Austria.

Abstract ID 27205

Emergency planning in Austria for the Treatment of Deterministic Effects - Revision of the National Medical Emergency Plan



Example of flowchart

External exposure assessment

Abstract ID 27247

Radiation exposure of military personnel due to thoriated magnesium alloys in jet engines

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In light-weight Magnesium alloys with high-temperature properties suited for the use in aircraft engines Thorium has become an important constituent. It was widely used in the US and the UK for the production of jet engines. The mass concentration of Thorium ranged between 1.7 and 4 %. This results in an elevated dose rate near the engine as the decay products of Th-232 grow in after casting of the alloy. In this joint publication are dose rate data presented obtained from the aircraft engine J-79, which was widely used in different aircrafts. They comprise both, a compilation of former measurements with electronic dose rate meters and with passive dose meters (TLD). The electronic measurements cover a longer measuring period which contributes to lowering the uncertainty of the gamma dose rates while the TLD measurements show a higher spatial resolution and beta dose rates. The combined data describe the use of the J79 jet engine in NATO air forces. The data sets were compared and related to the reference dose quantities (H*(10) and Hp(10)), which are used for both retrospective dose assessments of former work places and work places in museums and collections.

Abstract ID 27620

French military personnel translocation background levels

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Biological dosimetry has a major role in triage and in the medical management of victims exposed to ionizing radiation (IR). It can confirm or even replace physical dosimetry for accidents that occurred in absence of a personal dosimeter or when the exposure context is poorly known.
Chromosome aberrations of circulating lymphocytes have been used in biological dosimetry of exposures to IR for decades. For exposures suspected to have occurred several months (or even years) before the expertise, the Fluorescence in situ Hybridization assay (FISH) with whole chromosome painting is often preferred (IAEA recommendation), as it allows the quantification of more stable aberrations like two-way translocations [1].
Here we present the results of an ongoing study to specifically characterize the background translocation levels of French Ministry of Defense personnel and compare different groups of people based on their different potential confounding factors: work conditions, sex and age.
Military operatives are recruited based on their good health conditions at a young age, are expected to work out regularly to maintain fitness and can go on missions abroad on conditions (stress, pollution, etc) different than those of the French territory. In this work, two types of work conditions are compared: operatives (military having done at least 3 months of a mission abroad) versus administrative personnel (military never having done long missions abroad).
Because sex and age have been found to influence background translocation levels, both “work condition groups” are separated in “Male”, “Female” and three age groups (“below 30 years”, “between 30 and 45”, “over 45 years”).

Circulating lymphocyte samples from over 80 individuals (blood donors not having gone through medical scans involving IR) were analyzed to date.

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Radiation accident management

Abstract ID 25097

Validating the gene expression assay for biological dosimetry in emergencies involving exposure to radiation of high and low LET radiation

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Following a large-scale nuclear accident or radiological emergency, the medical and radiological classification ("triage") of patients according to the degree of their injuries and the level of their radiation exposure will be required in the shortest possible time. In this context, the gene expression assay on peripheral blood lymphocytes (PBL) is a promising biological dosimeter because the results can be obtained within several hours after collecting blood. Indeed, the results of several studies show a good dose-response relationship for radiation-responsive genes in PBL exposed to gamma or X-ray radiation. However, a radiation emergency can involve combined exposure to radiations of different qualities, such as alpha particles (characterised by a high linear energy transfer – LET), neutrons (recoil protons and recoil nuclei characterised by a high LET) and gamma radiation (characterised by a low LET). It is therefore interesting to test the sensitivity of the gene expression assay to radiations of different qualities.

A dedicated mixed-beam exposure facility is installed and characterized at the Stockholm University, which allows exposing cells to 241Am alpha particles and X-rays in a combined or single manner. Experiments were carried out with human PBL collected from three donors. qPCR was used to measure the relative expression levels of the genes XPC, FDXR, BBC3 and GADD45a 24 and 48 hours following exposure to doses in the range of 0-2 Gy.

All analysed genes showed a positive dose response to the tested radiation types. Generally, alpha particles and mixed beams were strongest inducers of gene expression but the response was individually variable. Analyses are in the pipeline where the gene expression assay will be tested with neutrons of different energies in order to integrate the results whitin a comprehensive project on radiobiological and dosimetric approaches for protection of people in large-scale nuclear emergencies

Work supported by the Swedish Radiation Safety Authority SSM.

Abstract ID 25491

Developing a smartphone app for the prediction of the hematological acute radiation syndrome (HARS) based on changes in blood cell counts – the H-module App

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Novel treatment regimens for therapy of the acute radiation syndrome (ARS) were developed over the last years. Their application relies on an early and high-throughput diagnosis.

In previous studies, we examined the utility of blood cell counts (BCCs) in the first three days post irradiation to predict clinical outcome, specifically for the hematologic acute radiation syndrome (HARS). For the development of mathematical models using unconditional logistic regression analysis (hypothesis generating) we analyzed 454 BCC samples from 267 individuals along with their clinical outcome HARS severity scores (H1-4). The validation of the models was performed on another 275 BCCs from 252 individuals. The BCC and HARS severity scores originated partly from radiation accident victims and were stored in the SEARCH database, the System for Evaluation and Archiving of Radiation Accidents based on Case Histories (SEARCH). We for instance found an almost complete discrimination of H0 vs. irradiated individuals during model validation (negative predictive value, NPV > 94%) for all three days, while the correct prediction of exposed individuals increased from day 1 (positive predictive value, PPV 78-89%) to day 3 (PPV > 90%). Encouraged by these results we developed prediction model spreadsheets in previous studies to provide early and prompt diagnostic predictions and therapeutic recommendations including identification of the worried well, requirement of hospitalization or development of severe hematopoietic syndrome. These spreadsheets proved to be useful in two table-top exercises, but also some limitations became apparent. That was the reason to finally convert the spreadsheets into an App, called H-module App. Other than the collection of 16 spreadsheets (required to reflect different combination of daily BCCs and considering acute/chronic infections as a confounder on BCC counts) the H-module App integrates these inputs on one screen. The architecture of the App and functions will be presented.

Abstract ID 27300

Cytogenetic biodosimetry for radiation accidents: application of image analysis and its advantage for emergency and expertise networks

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Cytogenetic biodosimetry has been an important part of radiation accident countermeasures in public health fields. For institutions, clinics and authorities, involved in radiation emergencies preparedness and response activities, international cooperation and networking became an excellent choice to solve biological dosimetry tasks.
We suggested and applied the additions to the concept of biodosimetry service that becomes possible with modern technology and world tendency of networking. In a small previously established network which we positioned as virtual cytogenetic biodosimetry laboratory the main efforts were devoted to combination and unification of the expertise from different fields for biodosimetry purposes. We've concluded that the must have for a virtual laboratory is an image capturing system.
Several inter-comparison studies with increasing complexity have been conducted in order to determine the best ways of communication, sample collection, sample processing, image and microscopy analysis and data protection.

In all cases the captured images were sent as files to scorers at various locations or uploaded to the special secure web-site. It was shown that working with the images required some different skills than microscopy analysis. In order to use image analysis data we validated them with microscopy scoring.
The factors to be considered for scoring harmonization in emergency and expertise levels will be discussed. In several experiments was shown that image analysis required only 20% – 30% of time usually needed for microscopy analysis of the same cell amount, which is of great advantage for triage mode cytogenetic biodosimetry. Still several additional factors such as software parameters used have to be considered and will be discussed.
It was shown that for the expertise level when time is not so crucial the application of image analysis provided the opportunity to increase the number of cells for the better accuracy in dose estimation and for conducting the dose-response curves.
We can conclude that using image capturing systems provided much better opportunities to run the cytogenetic biodosimetry networks in both emergency and expertise levels. At the same time the distinctive features of image analysis have to be considered and further investigated for different radiation exposure scenarios.

Abstract ID 30774

Emergency measurements of the population - a task for competent incorporation monitoring laboratories

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After releases of radioactive substances in the atmosphere and the environment, incorporation monitoring of parts of the population is indispensable. At the Competent Incorporation Monitoring laboratory Jülich (CIMB-J), incorporation monitoring is performed by means of direct measurements (whole body counter), indirect measurements with radiochemical testing methods of excretion samples and internal dose assessment.

In order to gather in case of a radiological emergency information about a possible intake of radioisotopes quickly, it is necessary to use modified routine test methods. Depending on released radioactive substances fast testing methods such us ICP-MS, Low-Level Beta counting, LSC, Alpha spectrometry and whole-body counting can be used. There is a large range of radionuclides that are assessable. Examples in excretion analysis (urine, faeces) are among others Am-241, Cf-252, Sr-90, Po-210 and isotopes of Th, U and Cm. The whole-body counter can count γ-rays in the energy range of ~25 - 2000 keV and additionally perform organ measurements (e.g. thyroid). Typical radionuclides measured are Mn-54, Mn-56, Cr-51, Fe-59, Co-60, Zn-65, Tc-99m, I-125, I-133 and Cs-137. Testing parameters include activity, specific activity, mass (ICP-MS) and individual body dose.

The validation process of methods and procedures at CIMB-J includes proof of traceability to metrological standards, limits of detection and quantifications, precision and accuracy.

CIMB-J is just an example for how laboratories with comparable abilities could help in assessing the consequences of radiological emergencies. Several such laboratories exist in Germany, much more on an international scale. Especially excretion samples can be distributed easily also to foreign laboratories making use of international networks like EURADOS. Many laboratories have their methods accredited according to ISO/IEC 17025 such ensuring comparability, reliability and international recognition of the results.

Abstract ID 30880

Initial measurements of Iodine-131 in the thyroid in case of radiological emergencies – cross-border harmonization

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Forschungszentrum Jülich (FZJ) is geographically located near Aachen in the region of shared borders between the Netherlands, Belgium and Germany (Euregio Maas-Rhein).
FZJ has a specialized Division for Safety and Radiation Protection (S) This division provides an Emergency Response Team, which is able to react to different radiological situations. Not the least due to its expertise FZJ is a valued partner in the training of fire brigades and emergency services in radiation protection. As released activity will not necessarily stop at borders, partners from different countries must efficiently work together. Cross-border training is provided.
This poster will describe one of the tasks of emergency response teams, namely the initial measurements in case of radiological exposition. For an accident/incident scenario, it is important to be able to select those individuals out of the expectable huge amount of people arriving in an emergency shelter or collecting point, who need further care urgently (triage).
Beneath other measures, the detection of incorporated Iodine -131, which will accumulate in the thyroid, might be necessary. This poster will discuss the use of measurement devices common to fire brigades in the Euregio, Special emphasis is given to commonly used instruments from Automess. One output of our work are the calibration factors for different devices, which are needed to calculate the incorporated activity from measured dose or count rate. The cross-border training enables harmonization of procedures and furthers comparability of results.

Decontamination measures and monitoring

Abstract ID 23848

Operational research and data mining methods for regulatory supervision of nuclear legacy site Andreeva Bay

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The presentation describes radiation situation dynamics at the Andreeva Bay nuclear legacy site over 2002–2016, the period of preparation for the most critical phase of remedial work: removal of spent fuel assemblies. The analysis of aggregated indicators and data mining were used. Analysis of detailed data and aggregated indices relates to operational or OLAP-analysis (On-Line Analytical Processing). The integral of the ambient dose equivalent rate (ADER) over the technical site was taken as an aggregated index of the radiation situation. The dynamics of the integral of the ADER at the technical site was evaluated by the method of time series decomposition. Three components of time series were identified: trend, season and residual. The trend of the ADER integral over the technical site is a monotonic decreasing function, the initial and final values differ tenfold. Taking into account that 137Cs dominates the radiation situation on-site, it is clear that the ADER due to the radionuclide decay will have decreased by 1.4 times. Therefore, approximately a seven-fold decrease in dose rate is due to remediation activities of personnel. During the year, the seasonal component varies the ADER integral by a factor of two, due to snowfall. The residual component reflects the uncertainty of the ADER integral calculation and phases of active SNF and RW management. The optimal number and location of control points needed to ensure the sufficient accuracy of the radiation situation description is suggested. The fractal properties of the radiation field are studied using the Hurst index. The relationship between control points was assessed using the

method of searching for control point communities. It is shown that, with a reduction in the amount of control, it is first and foremost necessary to discard dead-end control points that have fewer connections with other points. The methods developed are used to support optimization of remediation work as well as regulatory supervision of occupational radiation protection.

Abstract ID 25726

Skin and hair nuclear decontamination with the Cevidra® cream

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IRSN (The French Nuclear Safety and Radioprotection Institute) demonstrated that an emulsion loaded with carboxylic calixarene is much more efficient to decontaminate a skin contaminated by actinides than the products used so far. After several years of research, this innovation has been patented by IRSN and an exploitation license has been granted to CEVIDRA, Pharmaceutical Laboratory. The efficacy of the IRSN product is based first on an active ingredient, the carboxylic calixarene, which is known to be a specific chelator agent to Actinides, and secondly on integrating this chelating agent in an emulsion.

The chelating properties of Carboxylic Calixarene towards Actinides were initially demonstrated by IRSN during studies on contaminated urine / water.

A cleansing formulation of this emulsion loaded with carboxylic calixarene has been developed by IRSN on the advice of the physicians of the nuclear industry. This cleansing emulsion of carboxylic calixarene demonstrated a similar efficacy to the patented emulsion, the product acting by chelating the radionuclides and by cleansing insoluble elements present on the skin/hairs.

Two years of development were necessary to market this cleansing & decontaminating emulsion, under the brand name of Cevidra®, cream for nuclear decontamination.

The safety studies performed on the active ingredient and performed on the CEVIDRA® cream, demonstrated the good tolerance and the very low toxicity of this product.

A recent study carried out by IRSN confirmed the ability of the Cevidra® cream to specifically decontaminate skin or hair contaminated with actinides and with cobalt, cesium and strontium.

After presenting a short review of these scientific data, it is interesting to review the first nuclear industry results on the uses of CEVIDRA® cream on real cases of skin and hair contaminations.

These results confirm the efficacy and the safety of the Cevidra® cream.

Based on these data, we will then discuss the benefits of using CEVIDRA® in the treatment of contaminations or suspicion of contaminations in different non-standard situations.

KEYWORDS: Cevidra®, Calixarene carboxylic, skin decontamination, cleansing emulsion, Actinides, Cobalt, Cesium, Strontium, IRSN

Abstract ID 25911

Determination of bioavailability of aged legacy actinides obtained from a contaminated glove box: application of a simple *in vitro* test

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Background: Following accidental dispersion of actinides filter swipe tests are used to adsorb and collect radioactive materials for isotopic and elemental analyses. Analyses of legacy nuclear material originating from industrial and weapon production facilities or contaminated areas are important given the likely changes in physicochemical properties of aged materials due to intrinsic irradiation. Understanding the modified properties of such potential environmental contaminants is a prerequisite to understanding biological handling and to tailoring appropriate treatment. Previous presented work demonstrated the utility of a simple in vitro test for actinide bioavailability determination in physiological conditions that mimic both physiological fluids and tissue components (ConRad 2015). The present work is a follow-up study to assess the bioavailability of aged legacy actinides recovered by filter swipe tests from a nuclear glove box destined for decommissioning.

Methods: This study describes uptake of different actinide forms onto filters, “swipe test”, followed by solvent dissolution of the filter. The resulting actinide-containing solution is then incorporated into the static phase of **agarose** gels in plastic culture wells and actinide transfer from static gel phase to dynamic fluid phase measured.

Results: To maximise actinide recovery several filter types were tested and the most efficient solvent was selected. Dissolution of standard Plutonium (Pu) or Americium (Am) solutions showed that inclusion of the filter extract did not alter actinide transfer from the gels. Different forms of Pu were tested and demonstrated the expected order of transfer - Pu citrate > Pu nitrate >Pu colloidal form. Swipe tests were then taken from glove boxes “legacy approach”. Elemental and isotopic analyses of the swipe tests showed different proportions of Pu and Am from two different glove boxes. Transfer of Pu and Am from the filters indicated the presence of mainly insoluble actinide forms.

Conclusions: This simple, rapid test for actinide bioavailability can be applied to filter swipe tests obtained from accidental scenarios, contaminated areas, decommissioning operations and nuclear weapon legacy material. The data indicate that it is possible to gain an insight not only on the physical properties but also on the biological behaviour of the radiocontaminant associated with a “filter swipe test”.

The authors are grateful to Orano for financial support.

Abstract ID 25954

Medical countermeasures following internal contamination with radionuclides

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Following a radiological or nuclear emergency, such as a malevolent act (explosion of a radiological dispersal device - “dirty bomb”) or an accident in research nuclear facilities, dispersion of radioactive substances may occur. External and internal contamination from actinide fallout may concern a great number of victims from both general public and first responders. Medical consequences of an internal contamination are usually described as long-term effects. They may result from breathing of contaminated air, ingestion of contaminated food or water, or being wounded by contaminated sharp objects, such as shrapnels shells. The route of contamination, the nature

and the physicochemical properties of the radionuclides are key determinants of their biodistribution. Furthermore, the efficacy of therapeutic agents is also dependent on these parameters.

Different categories of medical countermeasures can be described according to their mechanisms of action. Broadly, the three main aims are to i) limit the absorption of the contaminant from the site of entry to the blood, ii) limit the translocation from blood to the organs of retention and iii) increase the excretion. Both nonspecific (adsorptive agents, laxatives, diluting agents…) and specific approaches (stable isotopes, chelating agents…) are currently used.

In the present work, it will be presented the available medical countermeasures, their application and limits. In addition, potential improvement of therapeutic approaches regarding handling of mass casualties, including military forces as well as facilitated administration routes to be used on warfare or hostile terrain will be discussed.

Key words: internal contamination, radionuclides, CBRN, countermeasures, decorporation

Effects of electromagnetic fields

Abstract ID 27095

Acute and chronic biological effects of an anti-denial system exposure

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Introduction

Among the extensive Non-lethal weapons development, electromagnetic power emitting systems have been used for crowd control (ADS, anti-denial systems) (1).

These systems operate by emitting electromagnetic radiation (EMR) in millimeter band at 94 GHz inducing an intense burn sensation. The studies on biological effects of these systems are still limited.

The aim of this study is to identify the biological risks associated with acute and chronic exposures to the ADS weapons.

Methods

Acute and chronic exposures, corresponding to the "operational" (crowd dispersion, 3s to 10 000 W/m^2, rising skin temperature to 53°C) and occupational conditions (4 hours a day, for 5 days a week, for 6 months to 100 W/m^2) were performed on hairless male rats (n= 36, 16 weeks old), model close to human skin.

The power density (W/m^2) was evaluated through a numerical calculation and confirmed by the superficial thermal elevation recorded by an infrared thermal camera.

Each animal was exposed to EMR on a side and to capsaicin (positive control, 2 mg/cm^2, 30 minutes occlusive patch), activator of thermal pain receptors, on the contralateral side. Skin biopsies were taken after 3, 6 and 24h on anesthetized animals (n=6 rats for each biopsies collection time).

Histological analysis (hematoxylin phloxine saffron staining of biopsies included in paraffin) and inflammatory gene expression tests (PCR, *Micro-array*) have been done on skin biopsies.

Results

The 94 GHz acute exposure provoked the disappearance of the epidermis upper corneal layers and the increase of the inflammatory gene expression SOCS-3 after 3h. Neither histological nor genetic expression modification could be observed after chronic 94 GHz exposure and after an acute and a chronic capsaicin exposure.

Conclusions

After a powerful acute exposition a thermal effect is observable, resulting in a localized inflammatory response. After a chronic, low power exposition no effects appear on the target tissue.

Keywords: anti-denial systems, millimeter band, inflammation, PCR, Micro-array.

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Effects of low dose ionizing radiation

Abstract ID 27040

The estimation of acute myocardial infarction risk in people exposed to occupational irradiation

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The results of the prospective epidemiological study evaluating the risk of developing acute myocardial infarction (AMI) in people exposed to occupational irradiation, taking into account the effect of non-radiation risk factors for the development of cardiovascular diseases, are presented. The observation period is 1998–2013. The studied cohort included workers from the Siberian Group of Chemical Enterprises (SGCE) employed from 01.01.1950 to 31.12.1994. The total number of the cohort is 34,146, among them 23,659 are men and 10,487 are women; 1,252 people (321 women and 931 men) had the diagnosis of “acute myocardial infarction“ (codes according to ICD–X I 21.0–I 21.4); 6,334 men and 2,056 women of the entire cohort population were on individual dosimetric control for external exposure. Among the workers of the SGCE, who were subjected to an acute myocardial infarction, 630 people (529 men and 101 women) had external and internal dosimetry data. An increase in the relative risk of AMI morbidity by 7–17 % in male SGCE personnel who had contact with ionizing radiation sources in the workplace was found in comparison with non-irradiated workers. Combined exposure is accompanied by an increase in age-specific morbidity rates of AMI among the people of working age (in the age group 35–39 years and 50–54 years) and among men of the older age group (80–84 years). Regression analysis made possible to confirm the presence of a dose-effect relationship for the incidence of AMI in the observed cohort in the studied dose range.

Abstract ID 27041

Association between gene polymorphisms and the increased frequency of cytogenetic abnormalities in the persons exposed to long-term irradiation (GWAS)

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SNPs play an important role in mechanisms of individual radiosensitivity during the long-term exposure to ionizing irradiation.

We conduct the genome wide association study of the association of 750,000 SNPs and an increased frequency of different types of chromosomal aberrations induced by chronic irradiation to identify new genetic markers of individual radiosensitivity.

The study was conducted among Siberian Group of Chemical Enterprises healthy employees (n = 37) exposed to professional external γ-radiation in a dose ranging from 100 to 300 mSv. Mean dose – 188.8 ± 8.3 mSv, median – 185 mSv, interquartile range – 147.8–218.7 mSv, min – 103.4 mSv, max – 295.8 mSv. Genotyping of DNA samples from 37 employees was carried out by microarray "Affymetrix" (USA) "CytoScan™ HD Array", containing 750,000 SNP-markers of 36,000 genes. The standard cytogenetic analysis was performed in the entire examined group.

We have found that 8 SNPs (rs10779468, rs158735, rs158710, rs158712, rs11131536, rs528170, rs9533572, rs10512439) are associated with the frequency of aberrant cells. We also have identified four intergenic SNPs (rs10779468, rs158735, rs158710, rs158712) in the long arm of the 1st chromosome, that appear to be in an important regulatory region (1:222282882–1:222402787 between the *DUSP10* and *TAF1A* genes), which can act as an enhancer for downstream genes that define individual radiosensitivity, such as *PARP1*. *PARP1* is a possible candidate for regulation of 1:222282882–1:222402787 area, being at a range 4145604 bp from the region designated above. In addition, it is directly related to the individual radiosensitivity. *PARP1* together with the *BRCA1* and *BRCA2* genes are involved in the repair of double-stranded DNA breaks, which are formed under action of the radiation, and are the principal cause of aberrations of chromosomal type – the main markers of irradiation. We have found three intron polymorphisms (*PACRG* rs528170, *ENOX1* rs9533572 and *MYO1D* rs10512439), which are also can be potential regulators of individual radiosensitivity.

Thus, we have discovered polymorphic variants that are associated with the increased frequency of aberrant cells in workers of Siberian Group of Chemical Enterprises exposed to irradiation at a dose of 100–300 mSv. These polymorphic variants can be considered as potential markers of individual radiosensitivity.

Abstract ID 27482

The prevalence of the thyroid gland pathologies among the Armenian liquidators of the Chernobyl Nuclear Power Plant (CNPP) accident

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The results of the study of the prevalence of the thyroid gland pathologies among the Armenian liquidators of the CNPP disaster revealed during last two years, thus, 30 years after the irradiation, are presented. The number of Armenians among the liquidators is 100%. Among them (n = 82), the thyroid gland' function

abnormalities were diagnosed in 23.2% of cases, and nodular lesions- in 8.2% of cases. In the most cases, the nodules were up to 1 cm, and were of a tissue nature. In one case the relapse of multinodular goiter after subtotal resection of the thyroid gland (due to precancerous proliferation) was revealed. Most often, the pathologies were detected in the 61-70 year old age group. When comparing the presented data with the data of general Armenian population, no definite differences were revealed.
Thus, the possible impact of the radiation on the prevalence of the thyroid gland diseases among the Armenian liquidators of the CNPP accident has not been established.

Abstract ID 27543

Canceled

Radiation health effects and medical countermeasures

Abstract ID 23923

NIH/NIAID Radiation and Nuclear Countermeasures Program (RNCP)

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Radiation and Nuclear Countermeasures Program (RNCP), National Institute of Allergy & Infectious Diseases (NIAID), National Institutes of Health (NIH)

With the goal to accelerate the discovery and development of biodosimetry tools and medical countermeasures (MCMs) for use during a radiation/nuclear mass casualty incident, RNCP has built a robust suite of basic, translational and pre-clinical research awards. Through grants, contracts, and interagency agreements (IAAs), the program seeks to advance MCMs and biodosimetry devices from early stage to licensure. RNCP funding supports a wide variety of innovative approaches to treat acute radiation syndrome (ARS) and the delayed effects of acute radiation exposure; including growth factors, cellular therapies, fusion proteins and small molecules. In addition, RNCP has funded discovery and validation of novel biomarkers/bioassays for rapid and accurate assessment of exposure to inform medical intervention, as well as biomarkers of tissue/organ injury to predict outcomes of radiation exposure. The Centers for Medical Countermeasures against Radiation Consortium (CMCRC) and cooperative U01 grants sustain the drug development pipeline by orchestrating basic research to understand the pathology of radiation injuries, and mechanisms of action of promising treatments. For example, the CMCRs are optimizing the micronucleus assay, studying cell death inhibitors, and investigating MCMs for hematopoietic regeneration. Efficacy screening and animal model development conducted through an IAA with the Armed Forces Radiobiology Research Institute, encompasses research in mouse, minipig and NHPs, including hematopoietic and gastrointestinal ARS and combined injury. A Product Development Support Services contract awarded to SRI International supports advanced development of lead products through non-clinical studies and investigational new drug-enabling activities. Recently, platelet-targeting strategies to treat ARS have shown that Nplate®, alone or in combination with G-CSF, increases survival and accelerates platelet recovery in monkeys and mice. Together with government partners, RNCP future directions include continued animal model development, addressing treatment options for special populations and exploration of poly-pharmacy approaches, to accelerate the development of MCMs and biodosimetry devices for inclusion in the Strategic National Stockpile.

Abstract ID 24871

RI-MODS/MOF : Overview of preclinical models and innovative therapies at IRBA

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The RI-MODS/MOF concept has been introduced and intensively discussed following the Tokai-Mura nuclear industry accident in 1999 during which a group a workers were highly exposed to mixed neutron-gamma radiation fields. Two out of 3 victims were transplanted with HSPC but died on D82 and D211 in spite of some level of hematopoietic production. They exhibited complex clinical symptom combinations and terminal cardio pulmonary failure. This clinic reflects the systemic nature of the radiation disease resulting from direct damages and cross-talks between organs of different radio-sensitivity. In fact the current understanding of RI-MODS/MOF pathophysiology remains limited: associated burns, gastro intestinal damages, major fluid leakages, microcirculatory damages, hypoxia…

In this context the IRBA Radiobiology Department has developed for some years preclinical models in order to test new therapeutic strategies preventing RI-MODS/MOF. Among the different targets our work focused on preventing the hematopoietic syndrome, mitigating the entangled inflammatory and repair processes and reducing the vascular damages which could be considered a unique tissue as a whole. Current proposed tools combine pharmacologic agents administration and cell/gene therapy.

Abstract ID 25575

Pharmacological treatment of inhalation injury after nuclear or radiological incidents: The Chinese and German approach

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Inhalation injury is often associated with burns and significantly increases morbidity and mortality. The main toxic components of fire smoke are carbon monoxide, hydrogen cyanide and irritants. In the case of an incident in a nuclear power plant or recycling facility associated with fire, smoke may also contain radioactive material. Medical treatments may vary in different countries and in this paper we discuss the similarities and differences between China and Germany.

The treatment of carbon monoxide poisoning is by 100 % oxygen administration and, if available, by hyperbaric oxygenation in China as well as in Germany. Besides, antidotes binding the cyanide ions and relieving the respiratory chain are important. Methemoglobin-forming agents (e.g. nitrites, dimethylaminophenol) or hydroxocobalamine (Vitamin B12) are options. The metabolic elimination of cyanide may be enhanced by sodium thiosulfate. In China, sodium nitrite with sodium thiosulfate is the most common combination. The use of dimethylaminophenol instead of sodium nitrite is typical for Germany, and hydroxocobalamine is considered the antidote of choice if available in cases of cyanide intoxications by fire smoke inhalation as it does not further reduce oxygen transport capacity. A systematic prophylactic use of corticosteroids to prevent toxic pulmonary edema is not recommended, neither in China nor in Germany. Stable iodine is indicated in the case of radioiodine exposure and must be administered within several hours to be effective. The decorporation of metal radionuclides is possible with Ca(DTPA) or Prussian Blue that should be given as soon as possible. These medications are used in both countries, but it seems that Ca (DTPA) is administered at a lower dosage in China.

Although the details of the treatment of inhalation injury and radionuclide(s) decorporation may vary, the general therapeutic strategy is nevertheless very similar in China and Germany.

Abstract ID 25871

Canceled

Abstract ID 26742

***In vitro* evaluation of the wound healing activity in primary human fibroblasts (HDFa) - a new approach**

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Human dermal fibroblasts are responsible for producing the extracellular matrix, forming the connective tissue of the skin and play a crucial role during wound healing, especially in skin burns and ulceration after irradiation. Therefore adult human dermal fibroblasts (HDFa) provide an excellent model system to study many aspects of cell physiology and have been utilized in dozens of research publications, particularly those related to skin biology and reprogramming / induced pluripotency studies.

A new task in our lab is to study wound healing and basic cell biology after radiation exposure (2 and 4 Gy) with the new provided live cell imaging and analysis platform JuLI™ Stage (NanoEnTek) as a first step. At a later stage an ideal cell system of HDFa serum free human feeder layers for human mesenchymal stem cell cultures in a 3D hydrogel environment should be established. The used fibroblasts are cryopreserved as primary cells to ensure the highest viability and plating efficiency. Firstly, we acquired time-lapse images of cells in small cell culture dishes with removable culture-inserts (Ibidi) for wound healing assays on the JuLI™ Stage platform. JuLI™ Stage is a fully automated, digital fluorescence imaging analyzer that directly acquires cell images from cell culture plates placed in a cell culture incubator. The software of JuLI™ Stage allows image capturing, time-lapse recording with multi-position scanning, navigation function to figure out the optimal position and image stitching function to scan whole well at once. Cell-growth images were captured for 48 hours with intervals of 30 minutes, images were stitched and the monolayer confluence was analysed. Wound confluence was also be graphed to analyse quantitatively the recovering of the surface of the wound (bright field mode).

The first present results already indicate that using this platform *in vitro* insights into disease and pathology can be gained: IR or UV effects, stress-induced senescence, dermal integrity as well as wound healing.

Abstract ID 26979

Preventive reduction of oxidative stress might minimize the risk of thyroid carcinoma after radiation exposure

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Background
Ionizing radiation (IR) is one of the main risk factors promoting the development of thyroid carcinomas, as e.g. shown by the Chernobyl nuclear disaster. In addition to catastrophic events, however, dirty bombs are a possible source of IR. The purpose of the presented investigations was to reduce the oxidative stress in thyroid carcinoma cells, caused by IR, using the triterpenoid bardoxolone-methyl (CDDO-Me), to reduce tumorgenesis and to eleminate already dedifferentiated cells while simultaneously protecting healthy tissue.
Methods

After determining the therapeutic range of CDDO-Me for the cell line B-CPAP its impact on the expression of the antioxidant enzymes HO-1 (heme-oxygenase 1) and NQO1 (NAD-(P)-H-quinone acceptor oxidoreductase 1) was investigated by western blot depending on treatment with CDDO-Me and X-ray irradiation with 0, 2 and 8 Gy.
First Results
The lowest therapeutic concentration of CDDO-Me was determined as 10 nM.
In Western blot-analyses the tumor cell line B-CPAP showed an increased expression of HO-1 and NQO1 following treatment with CDDO-Me, whereas IR had no influence.
Conclusion
In summary, the expression of antioxidative enzymes can be increased by the treatment with CDDO-Me in thyroid carcinoma cell lines. Accordingly, it would be conceivable to use CDDO-Me as a radioprotectant in order to increase the resistance of tissue to radiation.
Outlook
In order to compare the reaction of carcinoma cell lines with the non-malignant cells further investigations on the cell line Nthy-Ori3 are planned. Furthermore, clonogenic survival assays should show a potential protective effect of CDDO-Me towards healthy thyroid tissue compared to the tumor cells. Immunohistochemical studies on tissue samples and further western blot-analyses for antioxidant enzymes are in progress. In addition, immunofluorescent staining for DNA repair foci are planned.
Since the use of dirty bombs or radiation accidents are usually unpredictable, the following investigations should clarify if the application of CDDO-Me also works after such an incident.
Moreover, the involvement of EMT (epithelial to mesenchymal transition) in the observed phenomena will be investigated in order to possibly establish EMT inhibitors in this context as potential therapeutic.

Abstract ID 27440

The influence of human mesenchymal stem cells of the adipose tissue on the regeneration process of a radiation-induced wound healing disorder

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Introduction

Irradiation of the skin leads to damage of proliferating and maturating dermal cells and causes amongst others, necrosis and ulcerations. Current conservative and surgical treatments of these painful poorly healing wounds have limitations. However, new therapeutic approaches using mesenchymal stem cells (MSC) may offer promising perspectives for future treatment regimes. Several animal and human MSC-studies revealed a significantly improved wound healing process and pain reduction along with lacking adverse health effects.
The goal of this research project is to elucidate the underlying molecular mechanisms of these positive effects, in order to implement this knowledge for future, targeted therapy.

Material & Methods

MSCs were isolated and enriched from human adipose tissue via plastic adherence and by antibody-mediated cell separation. Subsequently, cells were characterized via flow cytometry and adipogenic, chondrogenic and osteogenic differentiation. To investigate the wound healing disorder observed in vivo, scratch assays were performed using irradiated keratinocytes (NHEK) and fibroblasts (NHDF). Closing of the wounded area was monitored by live cell imaging of the irradiated cells. The healing-promoting effect of stem cells was assessed by comparing NHEK and NHDF cells treated with conditioned and unconditioned media of MSCs.
In addition, culture media of the different cell types were analyzed on protein level via multiplex immunoassays and the isolated RNA of the cells on gene expression level with qRT-PCR with the focus on the expression of various growth factors, pro-/anti-inflammatory interleukins, chemokines, extracellular matrix and proteases.

Results & Prospect

Primary keratinocytes and fibroblasts were much less sensitive to ionizing radiation compared to immortalized cells. Only at a dose of 40 Gy, NHEK and NHDF cells showed a significant 3.5 fold and 1.25 fold increase of closure time, respectively, compared to unirradiated cells. Doses between 10 – 30 Gy had no significant impact on cell migration. Furthermore, experiments with different cell numbers revealed significant differences with respect to the closure time.

Future experiments are planned to investigate on protein and gene expression level the influence of stem cells on angioneogenesis as well as the induction of stem cell senescence following exposure to ionizing radiation.

Abstract ID 27559

Small peptide mimetic of basic FGF for mitigation of gastrointestinal syndrome

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Introduction: An effective mitigation agent for acute gastrointestinal (GI) syndrome is currently missing from our clinical armamentarium for responding to a radiological or nuclear disaster. Basic FGF (FGF2) benefits both GI and hematopoietic syndromes in mouse models. However, natural FGF2 is severely depleted by total-body irradiation in humans, and replacement with hrFGF2 has logistical challenges and production costs that make clinical use and strategic stockpiling unrealistic. We hypothesize that FGF-P, a small FGF2 mimetic peptide, mitigates acute radiation-induced GI syndrome through a variety of cooperating mechanisms, including decreased mucosal cell loss, improved proliferation of small bowel mucosa and gut barrier function, and reduced bacterial translocation. It also helps maintain progenitor cells through signaling pathways that mimic natural FGFs.

Methods: Two of our FGF-2 mimetic peptides, FGF-P or FGF-PT, were administered at 10 mg/kg SC daily for three days beginning 24hr after irradiation in NIH Swiss mice and Wistar rats (human recombinant FGF-2 used as positive control). Animals received sub-total body (a hind leg out of field) gamma irradiation with doses ranging from 17 to 21.5 Gy. Hematopoietic factors, GI function, cellular proliferation and maturation parameters, and inflammation biomarkers were tested by various methodologies. Pharmacokinetic (PK) modeling of FGF-P was conducted in sham-irradiated and irradiated NIH Swiss mice and Wistar rats.

Results: A survival benefit accompanied by reduced GI bleeding and improved stool formation was seen in mice receiving FGF-P or FGF-PT at 10 mg/kg SC daily for 1 or 3 days. These results were most pronounced in animals receiving 3 daily doses. The PK of FGF-P was similar and linear in sham-irradiated and irradiated rats, with rapid absorption into systemic circulation, a short half-life, and rapid elimination. Single doses of FGF-P or FGF-2, given 24 hr after irradiation, induced GI and mitochondrial functional benefits that persisted for at least 30 days.

Conclusion: Administration of FGF peptides beginning 24hr after irradiation, produced survival benefits in GI syndrome mouse and rat models despite rapid clearance kinetics. FGF-2 and FGF peptides induced GI histological and mitochondrial changes that appear consistent with a common mechanism of action. These results indicate that the FGF peptides may be potential mitigation agents for radiation-induced acute GI syndrome.

Abstract ID 27293

Changes of gene expression associated with non-cancer effects in Chornobyl clean-up workers in the remote period after exposure

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The research was aimed at finding specific genetic mechanisms and markers that are involved in somatic pathology pathways and are simultaneously associated with the influence of ionizing radiation in the remote period after Chornobyl accident. We examined the peripheral blood leukocytes of Chornobyl clean-up workers after irradiation (n = 104, males) at different dose intervals: 0 – 100 mSv, 100 – 1000 mSv, > 1000 mSv and chronic somatic pathology, in particular diseases of the cardiovascular (ischemic heart disease, hypertension), nervous (cerebral atherosclerosis, dyscirculatory encephalopathy), respiratory (chronic bronchitis, chronic obstructive pulmonary disease) and endocrine systems (thyroid pathology, diabetes mellitus). Relative quantification of gene expression was performed with RT-PCR and TagMan sets (Applied Biosystems, USA) for genes-regulators of immune response, signal transduction, proliferation, apoptosis and cell aging (*BCL2, CDKN2A, CLSTN2, GSTM1, IFNG, IL1B, MCF2L, SERPINB9, STAT3, TERF1, TERF2, TERT, TNF, TP53, CCND1, CSF2, VEGFA*). Statistically significant and dose-dependent downregulation of genes *BCL2, SERPINB9, CDKN2A* and *STAT3* was maximal at doses above 1 000 mSv. Correlations were found between the *BCL2, SERPINB9, TP53* gene expression and dose irradiation, dose-dependent overexpressing of *MCF2L*, *TERT* and genes-regulators of immune inflammation - *IL1B, IFNG, TNF*.

It was established the association of respiratory diseases with the changes of *CLSTN2, GSTM1, SERPINB9, TERF1, TERF2, TNF, TP53, VEGFA* gene expression (OR: 1.06 – 9.16); cardiovascular pathology – with the changes of *CDKN2A, CLSTN2, CSF2, GSTM1, IFNG, TERF1, TNF, VEGFA* gene expression (OR: 1.00 – 3.50); endocrine pathology – with the changes of *GSTM1, MCF2L, VEGFA* (OR: 1.06 – 1.66) and cerebrovascular diseases – with changes of *CDKN2A, CLSTN2, CSF2, IFNG, ILB, TERF1, VEGFA* gene expression (OR: 1.0 – 8.00).
The results of our study demonstrate a violation of gene regulation of the immune response, in particular inflammatory reactions, cell proliferation, adhesion and angiogenesis, cell aging and death in cardiovascular, pulmonary, endocrine and cerebrovascular pathology. Changes in gene expression may contribute to the risk of non-cancer chronic diseases in the remote period after exposure.

Abstract ID 27261

Effect of different antioxidants on X ray induced DNA double strand breaks (DSBs) using γH2AX and "comet assay"

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Ionizing radiation exposure produces direct or indirect biological effects on genomic DNA. The latter are ionizing radiation mediated by induction of free radicals and oxygen species (ROS). The study was conducted to evaluate the dose-effect / time-effect of antioxidants treatments in reducing the induction of double-strand breaks in human blood lymphocytes.
The blood samples from healthy donors were irradiated with 10mGy before and after pre-incubation with different antioxidants (β carotene, vitamin E, vitamin C, N-acetyl-L cysteine), In order to assess their efficiency as prophylactic therapy for irradiation. Various concentrations and combinations of antioxidants, as well as different incubation times, have been evaluated. To assess double strand breaks induced by ionizing radiation the single cell gel electrophoresis assay (widely known as comet assay) and the phosphorylated histone γH2AX have been used.

A significant reduction in double strand breaks was observed with N-acetyl-L cysteine with a 1 hour incubation time, followed by vitamin C, β carotene and vitamin E.
The use of antioxidants, especially N-acetyl-L cysteine before irradiation significantly decreased the occurrence of double strand breaks, demonstrating the potential radiological protection for exposure to ionizing radiation.

Keyword: ionizing radiation, double strand breaks, antioxidants, comet assay, γ-H2AX

Radiation risk perception of the public

Abstract ID 26606

Developing a CompRadRisk NATO App for improved risk communication of radiation exposures –actual status

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The NATO HFM 222 research task group (RTG) on "Ionizing Radiation Bioeffects and Countermeasures" represents a group of scientist from military and civilian academic and scientific institutions working in the field of radiobiology. Among other tasks, the RTG intends to extend their work on risk estimation and communication to bridge the gap in appropriate judgement of radiation exposure health risks. The group has no explicit psychological background, but an expertise in radiobiology and risk assessment. The group believes that as one of the essential first steps in risk communication it is required to put radiation risk into perspective. Radiation risk requires a weight in comparison to already known risks. What we envision is to convert/***Comp***are ***Rad***iation exposure ***Risk***s (***CompRadRisk*** NATO App) with daily life risks such as cigarette smoking, driving a car, etc. Within this presentation, we will provide a status of data collected on risk communication approaches, our discussions and decisions to date.

Abstract ID 27212

Educational Dialogue on Public Perception of Nuclear Radiation

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In many countries, radiation education remains the fodder for back-burner debate, given the strong emotional attachment involved. After the Fukushima accident, the Division of Human Health (NAHU) at the IAEA emphasised the relationship between nuclear accidents and society, incorporating aspects of science-technology-society (STS) into medical education.

Radiation and Society is a seminar-style module at the Tembusu College, National University of Singapore, consisted of weekly 3-hour interactive sessions for 13 weeks. The undergraduate students were exposed to the themes and concepts related to radiation and society. It explored topics including the fear of radiation, its historical dimension, complexities in radiation disaster response, the psychology of radiation fear, radiation science, communicating risk and radiation in medicine. Discussions during the sessions covered a variety of topics including ionising radiation as a result of a nuclear fall-out, the historical contextualization of nuclear fear, and most importantly, the uses of radiation in biomedicine, STS and science communication. Field visits to research reactors and cancer centres were arranged for students to understand how nuclear radiation is used for peaceful

purposes in a variety of fields. Experts were invited to share their perspectives on matters including technological developments and societal impacts pertaining to radiation.

The facilitator-student interactive sessions helped educate young minds on the subject of nuclear radiation. A survey was conducted to obtain the opinions of enrolled students on the reliability and safety of nuclear energy, the effectiveness of the seminar/course and their opinion on where the different energy sources stand on different fronts. Overall findings of the survey showed that although nuclear energy was perceived to offer better safety and reliability, renewable energy was perceived to be the better option. Participants also felt that the sessions were effective in the stated objective of providing education on nuclear energy.

This seminar-style module is expected to equip the students with the analytical tools required to assess and question the sources of knowledge as well as social perceptions of radiation. Such educational communication efforts will groom future citizens to be aware of the pros and cons of nuclear radiation and to respond to nuclear and radiological emergencies.

Abstract ID 28017

Emergency Readiness in the Current Nuclear Age - An Educational Challenge

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In particular the current development of smaller tactical nuclear warheads is making regional military conflicts more likely and far less predictable. Resulting mass casualties and radioactive outfall with long term consequences for the biosphere pose a new nuclear threat scenario and possible grim future outlook. Educational strategies and practical efforts to raise citizens´ awareness, knowledge and understanding of the implications for nuclear conflict, radiation preparedness and management is warranted. Existing educational systems, such as schools, lend themselves for the purpose of introducing the younger generation to current and future challenges, as well as proactive preparedness strategies, within an adaptive framework that needs to be defined and supported by national and international leaders. Civil protection concepts have to become part of our daily lives in new forms of emergency preparedness and safety cultures. The pedagogic challenges are to engage youth in particular which needs to be addressed by educators in the light of threating scenarios. The core underlying question hereby is, if young people have a right to be educated about the possible future that they will shape, lead, work and live in and what their active role can be to process fears in a safe and positive way. This could start with workshops with the 16 to 18-year-old groups to explore their knowledge, information, feelings, fears about the world of threat and instability and address the underlying fears to be made conscious to transform fear that would otherwise be acted out in self-destructive and aggressive behaviours.

Dear Colleagues,
It is a pleasure to announce our first NATO workshop on:

StTARS 2019

'Software tools for Triage of the Acute Radiation Syndrome: a practical workshop'

which will take place in Brétigny/Paris from 9-11 October 2019

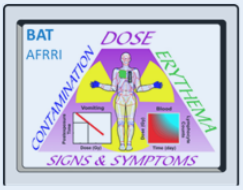
THE WORKSHOP

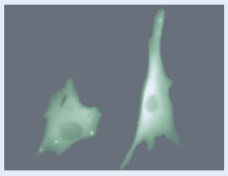
Within this workshop we will describe the purpose and function of ***software tools*** developed by scientific groups within NATO. These tools either allow an integrated estimation of dose (BAT, WinFRAT), or the prediction of ARS severity based on changes in blood cell counts (H-module) in the first days after an exposure to ionizing radiation. You will be introduced into these tools primarily by those who developed them, so that you will receive first hand tuition about their strengths and limitations.

As a short chapter you will also gain a deeper insight into ***diagnostic and therapeutic strategies that are currently under development*** - such as the use of mesenchymal stem cells to countermeasure radiation-induced local injury. These will also be presented by experts in their field.

Finally, you ***will practice your diagnostic skills*** by predicting clinically relevant degrees of the ARS using a ***database which includes real case histories*** – such as those arising from the Chernobyl incident and other accidental industrial exposures.

At the beginning of the course you will receive copies of the software tools and the case history database to download onto a personal laptop. The tools and dataset can then ***be used for teaching within your own nations***.



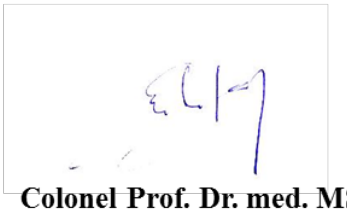


ORGANIZATIONAL DETAILS

- The workshop will take place in Brétigny sur Orge close to Paris from 9th to 11th of October 2019
- The workshop is for civilian or military personnel with a medical background or dealing with medical decision making in the field of radiological or nuclear threats
- You can pre-register at www.radiation-medicine.de
- Pre-registration will be closed on 31st May 2019
- The number of participants is restricted (30-40). Pre-registration does not imply participation, but in June 2019 you will receive a conformational letter of your participation
- The workshop fee is 200 € and has to be payed after having received the conformational letter in June 2019
- Cancellations can be accepted up till 31st May 2019 by written notification (including email)

We are looking forward to seeing you in Brétigny/Paris in 2019.

Sincerely,



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Dear Colleagues,
It is a pleasure to announce our introduction to the:

Master of Radiation Biology

Gwendolyn Marie Kaletka
Samantha Jo Stewart

Medical uses of radiation, as well as the broad social and political implications of radiation, are at the forefront of the master program "Radiation Biology" of the Technical University of Munich.

In the last decade, radiation biology has undergone a shift away from biophysical models of radiation interaction with DNA and is now more closely allied with molecular studies of cellular regulation and cell-cell interaction. These new areas are highlighted in teaching and research work.

The program aims to an interdisciplinary approach covering all relevant aspects of radiation including molecular biology, genetics, cancer biology, immunology, radiation-induced early and late morbidities, epidemiology, radiation physics, dosimetry and radiation protection.

Mandatory research practicals ensure that all necessary competences to work independently in a scientific environment are given.

Taught subjects and practical experiences combined form the basis of a possible career as a medical scientist for example in fundamental or translational research in radiation oncology, cancer biology, cell biology, environmental sciences, radiation medicine and other related disciplines.

Further Information

www.med.tum.de/en/master-program-radiation-biology

Contact

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In Cooperation with

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