

**Which of these individuals  
will be the first priority  
for biodosimetry?**



# The aim of MULTIBIODOSE is to analyse a variety of biodosimetric tools and adapt them to different mass casualty scenarios

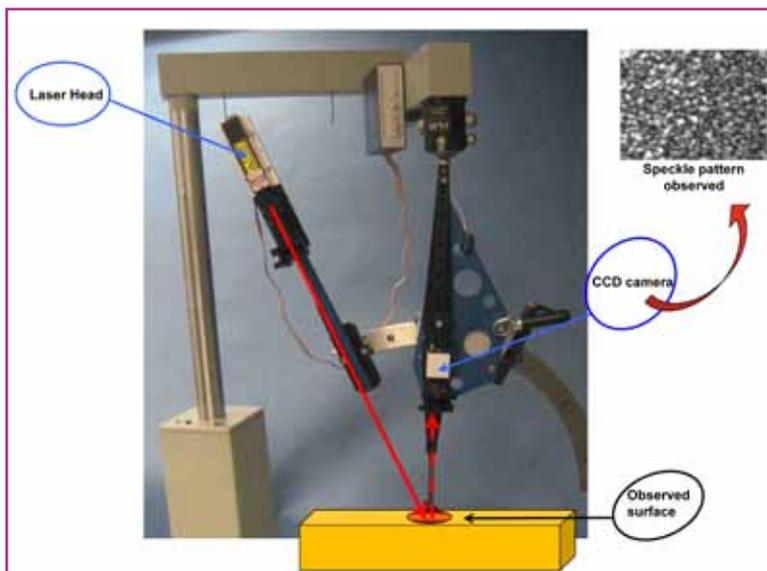
This project aims to establish the scientific and technical basis for a European biodosimetry network that is fully functional and ready to respond in case of a mass casualty.

Freeware software package will be developed for integrated statistical analysis of data from each of MULTIBIODOSE developed tools.

An operational guide, published in the end of the project, will give advice about the use of the developed biodosimetric approaches in different emergency response scenarios. This guide is meant primarily for the emergency preparedness and health protection authorities in Europe.



A practical training in automation of dicentric assay was performed at BfS in June 2011. Scoring criteria of each laboratory were investigated using a gallery of 80 cells.(pictures BfS).



Skin Speckle Assay Device (picture IRSN).



The software of Multibiodose will be implemented onto sharable platform available on the web (picture HPA).

# The progress of work in the second year of the project

## WP1: Dicentric Chromosome Assay

Since May 2011, the task was to establish and to validate the usefulness of a semi-automatic dicentric scoring system. Initially, the scoring criteria for dicentrics were adjusted between the participants using a gallery of 80 high resolution images containing dicentrics. Then gamma ray dose effect curves were established in 6 participating laboratories according to ISO standards. The scoring was done semi-automatically with the DCSore module of the Metasystems image analysis system using auto-captured high resolution images. The calibration curves were successfully established with different classifiers, specific for 3 or 24 hours of colcemid treatment during the processing of the samples. The validation steps of the curves with blind samples yielded promising results. The semi-automated dicentric assay may be a helpful tool for screening large sample numbers in a large scale radiation accident. With the generated images, a gallery of about 23,000 images was set up for the next task where web-based scoring will be tested.

## WP2: Micronucleus Assay

WP2 partners worked during this period on two tasks. The first was to establish common dose effect curves for automatic scoring of micronuclei (MN) for different exposure conditions i.e.: acute whole body dose, partial-body and protracted dose.

The second task was to set up a database of spontaneous micronucleus frequencies in the non-exposed population. Blood samples of 200 individuals were collected and analysed by WP partners according to the protocol described earlier in the MULTI-BIODOSE Deliverable 2.1. The effect of gender, smoking and the age dependency on the spontaneous micronucleus yield was analysed for this population.

Generally, it was concluded that the combination of the spontaneous MN and the MN dose response data obtained within this work package point to the superiority of the semi-automated scoring procedure for large scale biodosimetry in a multicentre setting to manage large scale radiological casualties.

## WP3: Gamma-H2AX Assay

WP 3 focused on gamma-H2AX based dose estimation for whole and partial body radiation exposures. The reference data sets were generated in HPA, and in the other four partners' laboratories for different exposure conditions, i.e. acute, protracted and partial body, and different times after exposure. Influence of the logistics aspects, like blood shipment, on the performance of the assay was tested. It was concluded that for rapid biodosimetry in a triage scenario following radiation exposure, microscopic scoring of gamma-H2AX foci offers great potential. It has satisfactory sensitivity up to several days post exposure, ability to determine critical partial body exposure and low inter and intra-variation in donors. A paper about gamma-H2AX based dose estimation for whole and partial body radiation exposures is already published (PLoS One 2011 6(9) e25113).

## WP4: Serum Protein Assay and Skin Speckle Assay

For the serum protein assay WP4 established a list of eight specific murine proteins that are similar to human proteins, to be tested in patient receiving radiotherapy. These eight circulating proteins were found to be discriminative and predictive of the severity of the cutaneous lesions. These proteins will be measured in samples from radiotherapy patients at the University of Stockholm. Blood serum is collected from patients before, during and after therapy. The analyses will show the dose-specificity of the changes in protein expression.

A paper «Alteration of the serum N-glycome of mice locally exposed to high doses of ionizing radiation» is submitted, and a book chapter «Serum and plasma proteomics and its possible use as detector and predictor of radiation diseases» (Radiation Proteomics, ed. D. Leszczynski, Elsevier) has been accepted for publication. Another paper on proteomic data in mice with the title «Serum proteome analysis for profiling predictive protein markers associated with the severity of skin lesions induced by ionizing radiation» is in preparation.

A paper on skin speckle assay carried out with mini-pigs was submitted to Radiation Research.

### **WP5: Electron Paramagnetic Resonance (EPR) and Optically Stimulated Luminescence (OSL)**

An international intercomparison of physical methods of retrospective dosimetry has been launched in the framework of MULTIBIODOSE, through the European Radiation Dosimetry Group (EURADOS).

The scope of the comparison is to test the transferability to other laboratories of the procedures implemented in the framework of WP5 of MULTIBIODOSE. These procedures are aimed at assessing dose retrospectively using components of mobile phones, specifically display glass (measured by EPR) and circuit board components (measured by OSL).

The exercise will start in November 2012. A preliminary meeting among potential participants took place in Vienna, February 6th - 7th, during the EURADOS Annual Meeting. Another meeting is foreseen in the autumn 2012.

All laboratories with experience in either EPR or OSL are invited to participate in the comparison exercise. For more information, please contact [paola.fattibene@iss.it](mailto:paola.fattibene@iss.it)

### **WP6: Statistical Analysis Software**

WP6 worked on developing methods for combining the results from MULTIBIODOSE assays and supporting decisions regarding assignation of radiological triage status of individuals in a mass casualty emergency scenario. The analysis included combination of errors in general, combination of random and systematic uncertainties, combination of errors from different measurements, combination of results from different laboratories (weighting by inter-laboratory variation) and at least but not last combination of results from different assays. This work is described in MULTIBIODOSE Deliverable 6.3.

### **WP 7: Dissemination**

WP 7 continuously maintains the project web page. In June 2011 the second MULTIBIODOSE bulletin was published. The bulletin was distributed both in almost 750 print copies and electronically via web page, among relevant organizations, emergency preparedness and biodosimetry community inside and outside Europe. WP 7 is also the editor of the current issue. MULTIBIODOSE was presented on numerous international and national scientific meetings.

### **WP 8: Project management**

WP 8 organized the General Assembly meeting in Lillehammer (May 2012), and several meetings of the Executive Board, either in connection with international meetings relevant for the project or via phone conferences. In January 2012 the mid-term meeting with the EC reviewer took place in Stockholm. The Review Report of this meeting concludes that the project proceeds according to plan and that now more effort should be allocated to dissemination of the project results.

# The General Assembly 2012 meeting of MULTIBIODOSE

The meeting, that took place in Lillehammer from 8th to 10th May 2012, was organized by WP 8 and Norwegian partners from NRPA. The meeting started with technical discussions about specific topics in each of the work package, and with planning of the next steps/work in the project. Subsequently, the progress of work in all work packages was presented by the WP leaders. There were also fruitful discussions about the statistical software and guidance to be developed at the end of the project.

The General Assembly Meeting concluded that the project is proceeding according to the plan, and no major changes are needed. The meeting was organized in the 1994 Olympics town of Lillehammer, and both the scientific and the social parts of the event were successful.



## Publications of the Multibiodose project:

- Willems P et al. (2010) Automated micronucleus (MN) scoring for population triage in case of large scale radiation events. *Int. J. Radiat. Biol.*, Vol. 86(1) pp. 2–11.
- Pope, IA et al. (2011) A portable microfluidic fluorescence spectrometer device for gamma-H2AX-based biological dosimetry. *Radiat Meas* 46:907-911.
- Horn S, Barnard S, Rothkamm K (2011) Gamma-H2AX-Based Dose Estimation for Whole and Partial Body Radiation Exposure. *PLoS ONE* 2011 6(9): e25113.doi:10.1371/journal.pone.
- Book chapter accepted: Guipaud O. Serum and plasma proteomics and its possible use as a detector and predictor of radiation diseases. In *Radiation Proteomics*. D. Leszczynski (ed.), Springer SBM, The Netherlands.

There are several papers from the MULTIBIODOSE project and its work packages that are already submitted, or will be submitted in the near future, and several other papers are planned.

## Presentations of Multibiodose on international meetings from June 2011 to May 2012:

- 14th International Congress of Radiation Research, 28th August -1st September 2011, Warsaw (3 lectures and posters)
- 6th Security Research Conference (SRC'11), 20th - 21st September 2011, Warsaw (poster)
- Third International MELODI workshop, 2nd – 4th November 2011, Rome, (poster)
- The Nuclear Renaissance and the Risks of Nuclear Proliferation in Asia, Royal Swedish Academy of Sciences (KVA), Stockholm, in cooperation with Comprehensive Nuclear-Test-Ban Treaty Organization (CTBTO) and Embassy of Japan in Sweden, May 2nd – 4th 2011, Stockholm (lecture)
- 13th International Congress of the International Radiation Protection Association (IRPA), 13th -18th May 2012, Glasgow (2 lectures and a poster)

## Consortium Member institutions:

	Stockholm University (SU), Sweden		Radiation and Nuclear Safety Authority (STUK), Finland
	Bundesamt für Strahlenschutz (BfS), Germany		Universitat Autònoma de Barcelona (UAB), Spain
	Université de Gand (UGent), Belgium		Institute of Nuclear Chemistry and Technology (INCT), Poland
	Health Protection Agency (HPA), United Kingdom		Helmholtz Zentrum München (HMGU), Germany
	Institut de Radioprotection et de Sécurité Nucléaire (IRSN), France		Bundeswehr Institut für Radiobiologie in Verbindung mit der Universität Ulm (BIR), Germany
	Istituto Superiore di Sanità (ISS), Italy		Gray Institute for Radiation Oncology and Biology, University of Oxford (UOXF), United Kingdom
	Norwegian Radiation Protection Authority (NRPA), Norway		European Radiation Dosimetry Group (EURADOS), European network registered in Germany

## CONTACT INFO

Multibiodose Coordinator: Andrzej Wojcik, Prof. D.Sc.  
 Centre for Radiation Protection Research  
 Department of Genetics, Microbiology and Toxicology  
 Stockholm University  
 Svante Arrhenius väg 20C, room E515  
 106 91 STOCKHOLM  
 SWEDEN  
 Tel: +46 8 16 1217  
 Fax: +46 8 16 4315  
 Tel mobile: + 46 762 122 744

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[www.multibiodose.eu](http://www.multibiodose.eu)