multibiodose

BULLETIN
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Multi-disciplinary biodosimetric tools to manage high scale radiological casualties MULTIBIODOSE

Which one of them received a radiation dose that will influence his/her immediate or long-term health?

www.multibiodose.eu

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

To demonstrate the results of the project to the emergency preparedness and health protection authorities in Europe, an operational guide will be developed. The guide will give advice regarding the use of the developed biodosimetry approaches for different emergency response scenarios.

It is envisaged that the project will result in an establishment of a biodosimetric network that is fully functional and ready to respond in case of a mass casualty.
More information about the MULTIBIODOSE project is available on the project webpage, www.multibiodose.eu, and in the 1st bulletin, which can also be downloaded from this web page.
This 2nd bulletin will focus on the progress of the project as whole and its work packages during the first year.

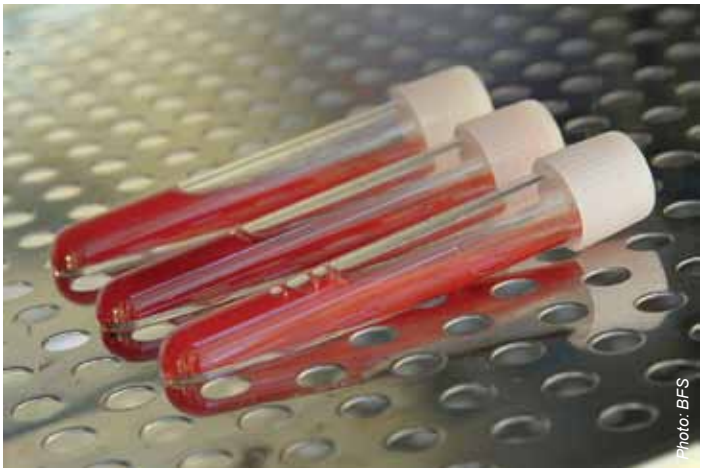


Photo: BFS

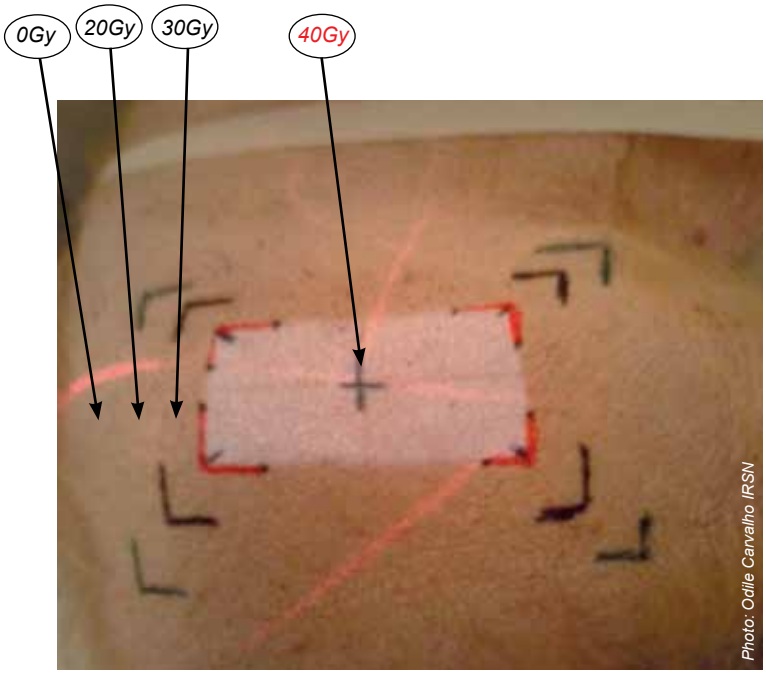
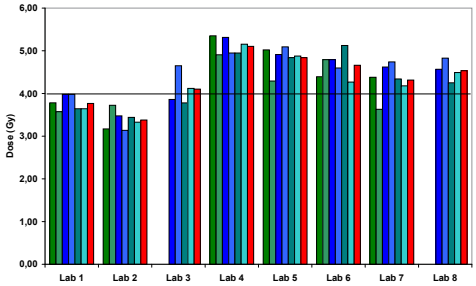


Photo: Odile Carvalho /RSN


Photo: M. Discher, HMGU

The progress of work during the first year (split in work packages (WP):

WP1: The dicentric assay lead by Bundesamt für Strahlenschutz (BfS)



Inter-laboratory comparison of the performance of the conventional dicentric assay used in triage mode in 8 laboratories; acute whole body irradiation with 4Gy; each colour bar represents one blood sample.

focused on validation and training in conventional dicentric assay in 8 consortium laboratories, using the triage mode (i.e. with a shortened scoring step that is normally time-consuming). This step was necessary to ensure homogeneity of dose estimations between the laboratories, as well as to test the logistics of transporting the blood samples in Europe. To achieve this task, blood samples from 33 healthy donors were taken at University of Gent and shipped blind coded to the 8 laboratories in portions of 5-6 samples. The irradiation of samples prior to shipment simulated three types of exposure: acute whole body, whole body dose gained over 16 hours, and acute partial body. Each laboratory analysed the samples using its own protocol.

For acute whole body exposures, there was good agreement with real irradiation doses in all laboratories. This was generally also the case for protracted whole body exposures. For partial body exposures, doses in the low dose-range could not be estimated precisely, when the triage mode of scoring (50 cells) was used. There was, however, good agreement between the laboratories in estimating partial body doses of 4 Gy and higher.

WP2: The micronucleus assay lead by the University of Gent (UGent)

had the primary task to validate and adapt the micronucleus assay (MN) for automated scoring by using one protocol that was developed by UGent and BfS, and the one software for automated MN scoring. A description of this work is already published in the International Journal of Radiation Biology (Willems et al. 2010), and it is also described in deliverable 2.1 of MULTIBIODOSE project. It was validated by analysing both images from a reference gallery and the 33 blood samples (the same samples as in WP 1) Criteria for automatic and semi-automatic scoring of the MN, as well as a fine-tuned MN

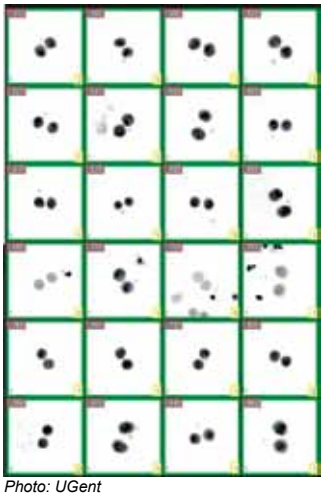


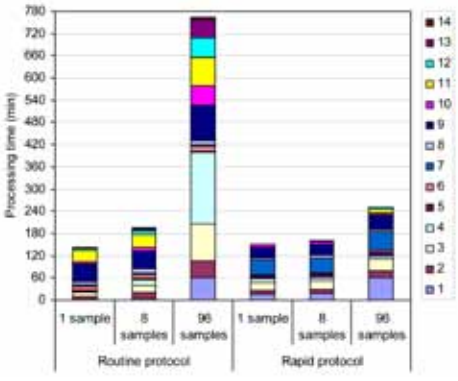
Photo: UGent

One of the galleries of the set of binuclear cells with indication of MN frequencies. Such galleries had been distributed among the five participating laboratories, with the purpose to harmonize the scoring criteria.

protocol were agreed upon during a working meeting of the WP participants.

It is generally concluded that the fully automated scoring of micronuclei gives acceptable results in the medium and high dose range. For lower doses, semi-automatic scoring could be a better option. Work on developing common dose-response curves for different exposure conditions is in progress.

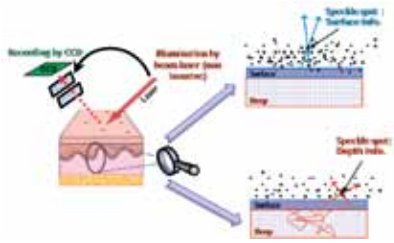
WP3: Gamma H2AX assay lead by the Health Protection Agency (HPA)



The graph shows processing time for 1, 8 and 96 blood samples, taken for the detection of the gamma H2AX foci. The numbers in the legend on the right side correspond to experimental steps described in SOP.

focused in this period on developing optimised standard operating procedures (SOPs) for blood sampling, transport and processing for the application of radiation-induced gamma-H2AX foci as a rapid radiological triage tool. This procedure was developed and reported as the deliverable 3.1. The work with developing a high throughput fluidic fluorescence intensity analysis system for this method is in progress, and a manuscript with conceptual and technical details has been accepted for publication in Radiation Measurements.

WP4: Skin Speckle Assay and Serum Protein Assay lead by Institutde Radioprotection et de Sûreté Nucléaire (IRSN)



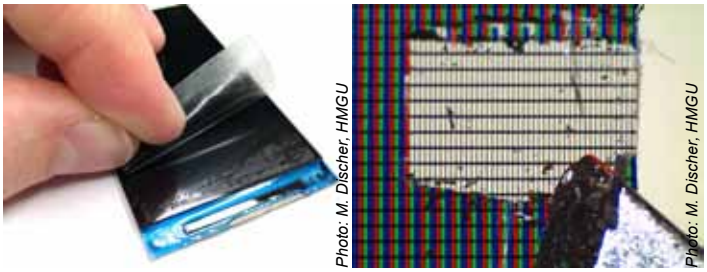
Principle of SSD assay used to estimate the dose to the skin validated on rat model.

Irradiation of the skin of the rat.

worked in this period on validating the two assays: a non-invasive and fast skin speckle assay (SSA) and a semi-invasive and fast serum protein assay (SPA). These assays can help to detect exposures to small areas of skin and thus complement the assays from the other WPs, which are not sensitive in cases of exposure to small proportion of the body. Both the SSA and the SPA are new biodosimetric tools that first require validation on animal models. Doses that are considered for medical interventions for small areas of the skin are much higher than doses to larger parts of the body; therefore, the doses tested in this WP are also higher.

The SSA was validated on a hairless rat model. On the basis of experiments performed in this model, it was concluded that the SSA is a promising non-invasive tool that allows discrimination between the irradiated and non-irradiated skin areas during the latent period, i.e. before the clinical signs appear. The next step in the validation of this assay will be the use of a preclinical model. The SPA validation has been performed on irradiated mice models. Changes in the expression of the serum proteins in blood samples taken 3 and 7 days after exposure were investigated using proteomic tools. Candidate 34 proteins were identified by mass spectrometry. A selection of these proteins will be validated further on a human model (radiotherapy patients) at the University of Stockholm.

WP5: Electron Paramagnetic Resonance and Optically Stimulated Luminescence lead by Istituto Superiore di Sanità (ISS)



Preparation of the mobile phone glass for EPR measurements.

worked in the first year on validating the suitability of different mobile telephones and their components for assessing the doses attained by people carrying these items by using Electron Paramagnetic Resonance (EPR) and Optically Stimulated Luminescence (OSL). Measurements of 75 telephones of 61 types were performed. Approximately 50% of these telephones were of the touch screen type. It was identified that the glass of mobile telephones is suitable for EPR measurements, while a variety of electronic components were suitable for OSL. A database for the classification of mobile components was created (deliverable 5.1 of MULTIBIODOSE).

WP6: Statistical Software Tool lead by the Health Protection Agency (HPA)

worked, in the first year, on comparing existing data analysis methods for the assays described in WP 1 to 5 with the purpose of identifying the state of the art of these methods as well as their current shortcomings. The results of these investigations are described in deliverable 6.1 of Multibiodose. It was concluded that the data analysis protocols for dicentric and MN assays were well defined and that no further work will be required, whereas for the gamma-H2AX, SSA, SPA and EPR and OSL assays, further development of the analysis methods is needed.

An example of the window of the statistical software that will bee developed for Multibiodose tools

WP7: Guidance and Dissemination lead by the Norwegian Radiation Protection Authority (NRPA)

established and continuously maintains the project web page. The NRPA has published the 1st MULTIBIODOSE bulletin, which was distributed both in almost 900 print copies among relevant organisations in and outside Europe and electronically via the webpage. WP 7 is also the editor of the current issue. The project had been presented on numerous international meetings (among others, the European Radiation Research meeting, EPRBiodose 2010, WHO REMPAN 13th Coordination Meeting and EURADOS 2010) and several national meetings.

WP8: Project management (lead by SU)

organised two yearly General Assembly Meetings and four meetings for Executive Board, either in connection with the large scientific meetings relevant for the project or via phone conferences. WP 8 is in close contact with the Multibiodose Advisory Committee to ensure the scientific quality of the project as whole, and also takes care of the reporting and financial and legal issues.

The General Assembly 2011 meeting of MULTIBIODOSE

The meeting took place at Hotel Eden Roc, Sant Feliu de Guixols, Spain, 4 - 6 May, 2011, was organised by WP 8 and Joan Francesco Barquinero from Universitat Autònoma de Barcelona. During the meeting, the progress of all work packages was presented by the WP leaders. Subsequently, there were meetings in each WP on the specific topics and with discussions/planning of the next steps/work of the project.

The General Assembly concluded that the project is performing according to the plan, and no major changes are needed. The meeting was organised in beautiful Catalonia, and both the scientific and the social parts of the event were very successful.

Photos: Andrzej Wojcik, Inger Nergaard

Presentations of Multibiodose on international meetings:

- EPRBioDose 2010 and WHO Bio-DoseNet meeting in Mandelieu, October 2010
- WHO REMPAN meeting in Wurzburg, December 2010
- REMPAN coordination meeting in Nagasaki, February 2011
- EURADOS meeting in Prague, February 2011
- Nuclear Defence Mechanisms in Munich, May 2011

Consortium Member institutions:

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

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