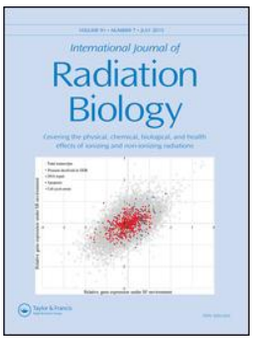

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Realizing the European Network of Biodosimetry (RENEB) – concluding remarks

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The past

Just over half a century has elapsed since dicentric aberrations in blood lymphocytes were first used at Oak Ridge to investigate a few accidental overexposures to ionising radiation. The scientific community was quick to realise the potential of this new biological approach to dose estimation that was quite independent of the existing physical methods. Some of those 1960s' American cases involved criticality accidents for which physical dosimetry for neutrons was, and indeed still is, far from straight forward. This spurred several other countries, notably in Europe, soon to commission their own biodosimetry laboratories. The intervening years have seen extensive research, developments and expansion in the field such that biological dosimetry has become established as an integral part of the radiation protection and emergency preparedness infrastructure in many countries.

Fast-forwarding to 30 years ago, the radiation protection world had a massive 'wake-up call' – Chernobyl, followed a year later by the Goiania accident; two quite different events but both involving a lot of people. Until then biodosimetry laboratories usually had needed to deal with events involving a single irradiated person or occasionally a few. The surge capacity of any lab was very limited; few countries had more than one lab and many had none. For responding to the Chernobyl accident, the former Soviet Union was fortunate in that there were several biodosimetry laboratories in Russia, Belarus and Ukraine and they were able to mobilise and jointly mount a creditable early response to the catastrophe. At Goiania, the biodosimetry task fell to a single laboratory but help was offered from several others, including from Europe, mediated mainly by prior personal contacts.

In national biodosimetry laboratories the question was asked; 'How would we cope if a big accident happened here?' and so was born the beginnings of networking. It was around this time that the IAEA began an active role in biodosimetry through Co-ordinated Research Programmes that have led to some important outcomes such as the well-known *Manual on Biodosimetry* now in its third revised edition. In the context of networking, another noteworthy IAEA initiative was to foster cooperation between a number of Latin American laboratories from which a highly effective and well-managed mutual assistance network has developed. Meanwhile in Europe three institutions; BfS in Germany, IPSN (now IRSN) in France and NRPB (now PHE) in UK set up a mutual assistance agreement, via a Memorandum of Understanding (MoU), such that should a major event occur in one of the countries, the other two would respond to a request for biodosimetry assistance. This became known as the Tripartite Network although there was a tacit understanding that they would also offer to respond to serious events in other neighbouring European countries and so, through personal contact, the STUK laboratory in Finland was considered to be a partner too.

That is how formal provision for cross border assistance in biodosimetry remained for many years in Europe and, thankfully, the tripartite laboratories never needed to mobilise their resources to deal with mass casualties. Meanwhile research continued apace along different lines on ways to alleviate the problem of small labs being able to respond rapidly to a sudden surge. These included computer driven microscopy-metaphase finders; working-up the cytokinesis-blocked micronucleus assay and criteria for operating the dicentric assay in rapid response triage mode. Added impetus was gained from the 9/11 outrages in USA where, despite no radiation being involved there, the malevolent use of stolen radiation sources was now judged to be an additional serious risk to the public.

The present

Now in the European Union (EU) countries we have RENEB – Realizing the European Network of Biodosimetry. It started with a small EU-funded initiative, with the acronym TENEB, which explored the possibility of creating a European network. Potential partner laboratories were identified and their capabilities assessed. Importantly, their institutional bodies, governmental, university and so on, and their national radiological safety organisations were contacted and asked whether they would be willing to participate in biodosimetry networking. The responses were

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overwhelmingly positive and so the message went back to the EU that Europe was ready, willing and able to network. Four-year funding was obtained from the EU's EURATOM programme and the network (of 23 laboratories in 16 countries) was created with the overall coordination by BfS in Germany.

RENEB has proved to be extremely successful in several respects. One obvious measure is the number of scientific publications that have come from the collaboration. Apart from the contents of this journal's special issue, there were 16 other peer-reviewed publications during the course of the contract plus about 100 oral presentations and posters at international congresses. The many activities within RENEB, some described within this special issue, have been wide-ranging. They included more obvious tasks such as the production of a QA/QC manual together with quality assurance inter-comparison exercises using the well-established assays: dicentrics, micronuclei and FISH. Newer methods were inter-compared too: web-based aberration telescoring; performance of semi- and fully- 'hands-off' aberration and micronucleus scoring with Metafer systems; premature chromosome condensation (PCC) and the gamma-H2AX foci assays. These inter-comparisons threw up some interesting laboratory differences, which were generally resolved, whilst overall there was a gratifyingly good measure of agreement.

At the outset, the capabilities of the partners were reasonably varied particularly regarding the numbers that were able to use the less frequently employed techniques such as PCC and gamma-H2AX; assays which have been identified as having special value in rapid response triage biodosimetry. The network commenced a very valuable training programme that has markedly improved the European expertise in these methods. Another noteworthy improvement that required a training effort was to ensure that all partners reached a required ability in statistical analyses and interpretation of data. In recent years this has been made easier by the development of freely available software tools developed by a few of the partner labs. These enable easier curve fitting and dose estimations together with their statistical uncertainties, the evaluation of complicated scenarios such as inhomogeneous exposure and, in the context of rapid response networking, a tool to collate initially limited scant biodosimetry and clinical data to provide a 'traffic-light' triage sorting of mass casualties.

One important objective that RENEB set itself was to identify other methods for determining individual doses apart from the traditional cytogenetic assays and to incorporate them into the network. A task group identified immediately deployable candidates plus near- and far-horizon possibilities. Where possible these were incorporated into the activities such as inter-comparison exercises. This has resulted in a more versatile network. Particularly noteworthy is the joining forces of the biological methods with physical techniques. Electron paramagnetic resonance, optically stimulated luminescence and thermoluminescence dosimetry can be deployed on a number of materials within mobile phones, credit cards and so on that individuals may fortuitously have on them when overexposed. Indeed RENEB is leading the world in the way that these methods have been incorporated into a front-line biodosimetry response network. It was accomplished relatively easily because of existing strong links between the biological and physical labs within EURADOS.

The future

Now that the EU 'pump-priming' funding has finished, Europe is left with the strongest and most versatile regional network in the world and the partners can be congratulated on having achieved all their set objectives. The future of RENEB now has to be considered. There is an obvious enthusiasm among the partners to continue and the immediate way forward has been to link up with an MoU. To date, 18 of the partners and seven new candidate partners have signed the MoU and this will probably increase slightly. In the longer term it is to be hoped that the MoU could be converted into something stronger. The idea of a non-profit association registered under the law of one of the Member States looks most promising. This would give RENEB a firmer status, akin to EURADOS, and enable it to perform more effectively in the European radiation research arena.

RENEB, keeping the acronym but with the slightly altered full name to reflect the inclusion of the physical methods, 'Running the European Network of Biological Dosimetry and Physical Retrospective Dosimetry', with a firm standing within Europe will perform many functions. Firstly, of course, it will be available to respond rapidly to a major disaster. For maintaining readiness it will provide a vehicle for laboratory inter-comparisons which are essential for maintaining QA/QC and are a formal requirement of accreditation bodies and the ISO standards. RENEB, as a highly regarded and legally recognised entity, could explore the possibility to issue certificates of competence to laboratories or even their individual staff members.

New developments in the field will inevitably arise and RENEB is well placed and structured to take them up as appropriate. Good examples of near-horizon assays already being worked upon are: (a) the detection of up and down regulation of particular combinations of sentinel genes by gene expression assays, and (b) combining PCC with FISH to highlight telomeres and centromeres. Moves to automate this assay will add to the more rapid provision of dose estimates already inherent in the PCC method. Far-horizon scanning for new methods is a function also within the RENEB remit, an example already being watched is application of Raman spectroscopy.

Given that the frequency of radiation accidents is thankfully low, most of the RENEB laboratories already devote much of their time to research. They have in many cases a long and successful history of undertaking research, both singly and in collaboration. MULTIBIODOSE, a project that worked towards development and fed into RENEB, is an excellent example of such collaboration. Many of the assays used have research applications that extend well beyond biodosimetry and the consortium is an ideal European resource to support future research projects. RENEB would

be able to contribute effectively in many of the objectives of other EU platforms such as research undertaken by NERIS, MELODI, ALLIANCE and a new medical radiation research initiative. Therefore it is gratifying to note that RENEB has been recognised by CONCERT. RENEB has produced a Strategic Research Agenda and it is very important to update it continually to demonstrate to other EU platforms what expertise can be offered.

Over the 4 years of funding RENEB has strengthened the communication and interaction between Europe and the biodosimetry community elsewhere in the world. In particular it has been important to cooperate with the international organisations, IAEA and WHO and their networks, such as RANET, BioDoseNet and REMPAN which are dedicated to responding to radiological emergencies. The biodosimetric strength of Europe has much to offer to the rest of the world and RENEB has become a natural point of reference for maintaining professional contact with the wider community of biodosimetry.

In conclusion, the RENEB consortium can be congratulated for what it has achieved over the 4 years of EU funding. A structure has been set up for which the way ahead is clear both as a pivotal body of excellence in biodosimetry and as a resource for many applications in radiation research.

Appendix

Abbreviations and acronyms not defined in the text:

ALLIANCE	The European Radioecology Alliance
BfS	Bundesamt für Strahlenschutz
BioDoseNet	WHO global network of biodosimetry laboratories
CONCERT	The European Joint Programme for the Integration of Radiation Protection Research
EURADOS	The European Radiation Dosimetry Group
EURATOM	The European Atomic Energy Community
FISH	Fluorescence in situ Hybridization
Gamma-H2AX	Phosphorylated form of the histone protein H2A
IAEA	International Atomic Energy Agency
IPSN	Institut de Protection et de Sûreté Nucléaire
IRSN	Institut de Radioprotection et de Sûreté Nucléaire
ISO	International Organization for Standardization
MELODI	Multidisciplinary European Low Dose Initiative
MULTIBIODOSE	Multi-disciplinary Biodosimetric Tools to Manage High Scale Radiological Casualties
NERIS	European Platform on Preparedness for Nuclear and Radiological Emergency Response and Recovery
NRPB	National Radiological Protection Board
PHE	Public Health England
QA/QC	Quality Assurance and Quality Control
RANET	Response and Assistance Network
REMPAN	Radiation Emergency Medical Preparedness and Assistance Network
STUK	Radiation and Nuclear Safety Authority in Finland
TENEB	Towards a European Network of Biodosimetry
WHO	World Health Organization