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AN UPDATE OF THE WHO BIODOSENET: DEVELOPMENTS SINCE ITS INCEPTION

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In 2007 the World Health Organization established an international network of biodosimetry laboratories, the BioDoseNet. The goal of this network was to support international cooperation and capacity building in the area of biodosimetry around the world, including harmonisation of protocols and techniques to enable them to provide mutual assistance during a mass casualty event. In order to assess the progress and success of this network, the results of the second survey conducted in 2015 that assessed the capabilities and capacities of the members of the network, were compared to the similar first survey conducted in 2009. The results of the survey offer a unique cross-section of the global status of biodosimetry capacity and demonstrate how the BioDoseNet has brought together laboratories from around the world and strengthened the international capacity for biodosimetry.

INTRODUCTION

There are numerous productive uses of ionising radiation in the world including medical and industrial applications, however, due to the widespread existence of radioactive material and radiation emitting devices, there is also potential for their misuse, leading to accidental exposures or their use in terrorist events. In these cases, where no physical dosimetry is present, it is important to be able to assess the dose received by individuals in order to provide the appropriate medical care to mitigate the effect of exposure.

Biodosimetry can be used in these situations to provide a dose estimate based on damage to biological material taken from the potentially exposed individuals. There are several biodosimetry methods that can be used; the most widely used being the dicentric chromosome assay (DCA)[1, 2]. Although this assay is highly specific and sensitive for ionising radiation, it is limited by the time it takes for analysis. One way to overcome this limitation is through the establishments of networks that can share the workload during a mass casualty event. In response to the recognition of this need for networking, and in line with the implementation of the International Health Regulations (IHR)[3] the World Health Organization (WHO) established a global biodosimetry laboratory network in 2007[4]. Shortly thereafter, in 2009, a survey was conducted to assess the baseline capacities and capabilities of the WHO BioDoseNet (BDN) which provided information on the state of emergency cytogenetic biodosimetry capabilities around the world at that time[5].

Since the time of the first BDN survey, there has been much progress in the field of biodosimetry with the recognition of new methods[6–8], the growth of web-based scoring, the creation of new biodosimetry laboratories and the formation of new regional networks[9]. In 2015, in preparation for the 4th Coordination Meeting of the WHO BDN, the survey was repeated to assess how biodosimetry has changed over the past six years. The survey was designed to collect data that could be compared to the 2009 survey results while including collection of data indicating how the field has changed. To this end, there is still a large focus on the DCA but additional information on other assays and statistical methodologies was also collected.

MATERIALS AND METHODS

The BDN survey was originally developed and conducted in 2009 using a simple MS Word format. In 2015, the survey was further elaborated, as described below, and an online tool was used for completion of the questionnaire. The link to the survey was sent to the list of 67 members of the WHO BDN. As in the original survey, the questions were organised into groups that focused on the most important aspects of a functional cytogenetic biodosimetry laboratory and infrastructure, including staff, equipment, supplies, capacity, operating procedures from blood sample collection to dose estimation, communication with attending physicians, techniques used, Quality Assurance and Control (QA\QC) compliance, general experience and experience with performing

emergency dosimetry in exercised and actual emergencies. Questions pertinent to international activity of surveyed laboratories, collaboration and networking, the most pressing needs of the laboratories, contributions to and expectations from the BDN membership were also included. The main modification to the 2009 survey was the addition of more detailed questions about methods other than the DCA and questions related to statistical analysis (see Annex for survey questions).

The total of 62 laboratories from 44 countries around Europe, Asia, the Americas, Africa and Australia responded to the survey, representing a 92% response rate. This was an increase from 57 of 65 laboratories from 38 countries responding to the first survey (87%).

RESULTS AND DISCUSSION

The survey was sent to 67 laboratories that were listed as members of BDN with 62 responding. The locations of the respondents are shown in Figure 1. Although there was an increase in response to the survey, this actually represents 15 laboratories who responded to the 2009 who did not respond to the current survey while 20 additional laboratories responded. The 62 laboratories are situated in different types of institutions, mostly belonging to government (61% of responders), emergency preparedness organisations (39%), radiation protection authorities (34%), civilian research institutes (29%) and universities (26%). Fewer of the laboratories are part of hospital based institutes (21%) or the defence sector (13%). Many of the institutions with cytogenetic laboratories belong to more than one of the categories.

From blood sample to dose estimation

Similar to the 2009 paper, survey questions addressed all steps involved in the biodosimetry process including the organisation of blood sample collection, packaging and shipping from the site of the patient to the laboratory, through to sample processing and presenting the resultant dose estimate. Questions included requests for information on the procedures in each laboratory and their capacity for analysis during a mass casualty event.

Collection and shipment of samples

The survey asked laboratories how the collection of blood samples for biodosimetry is organised. Almost all laboratories (90%) had some procedures in place; many with detailed written protocols. This is a great improvement from 2009 where fewer (<75%) laboratories had protocols in place for sample collection. Most blood sampling occurs in the laboratory or a hospital with some laboratories having processes

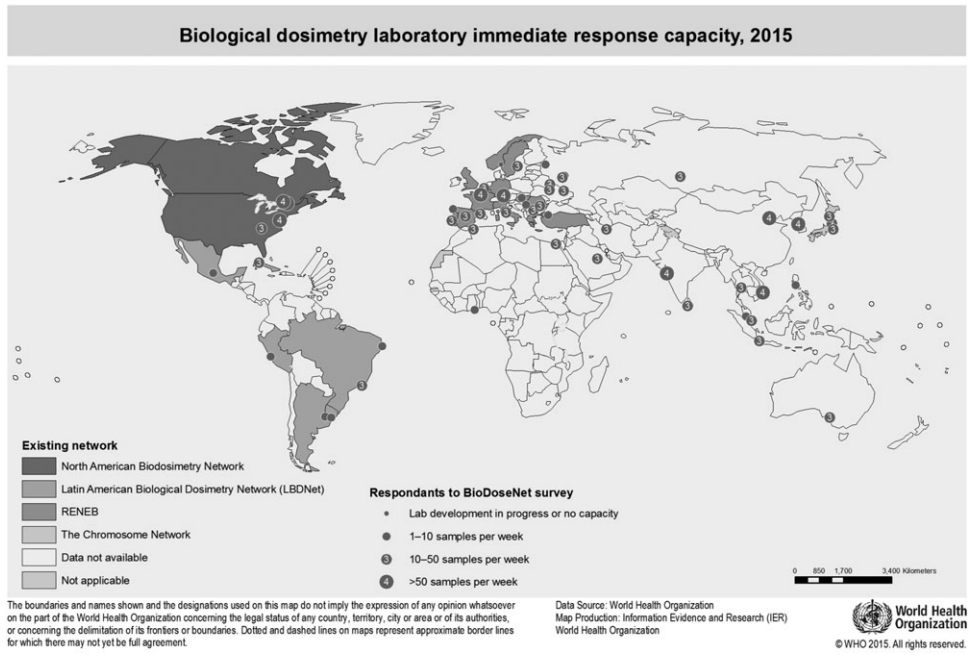

Figure 1. Geographical locations of biodosimetry laboratories who responded to the survey. The size of the symbol represents the weekly scoring capacity of each laboratory.

established for collection in the field or through their emergency response organisations during an emergency event. It was also determined from the survey that, similar to the 2009 survey, the majority of laboratories have a pre-arranged organised relationship between their laboratory and medical doctors and that samples collected outside of the laboratory were often transported by a courier service which sometimes included air transportation. There are very specific requirements for shipping biological specimens stipulated by the International Air Transport Association and described by the WHO[10] which must be carefully followed to maintain the quality of the blood samples. Guidelines for proper shipping conditions are described in detail in the 2011 IAEA Cytogenetic Dosimetry technical report[1]. There was a great improvement in the awareness of these regulations which increased from about 74% of the responding laboratories in 2009 to 89% in this survey. Of those that were not aware of them, no shipments of samples by air were occurring. With respect to dealing with international shipments, the laboratories need to be prepared to receive samples through customs. Again, there was a large improvement over the 2009 survey results in that the percentage of laboratories with predetermined arrangements for dealing with international shipment and customs increased from 35 to 52%. Overall, there seemed to be a much improved preparedness for shipping and receiving samples, even internationally, with more laboratories having established protocols and being aware of shipping requirements by air.

Sample processing

When samples are received, depending on the expertise in the laboratory, one or more of several assays may be used to determine the dose to the individual. When asked how many samples each laboratory could score using DCA in triage mode (50 cells/sample) during a mass casualty event, taking into account the normal holding of consumables, the results were actually lower than in 2009. In 2009 it was reported that about 3900 samples could be processed among the 57 responding laboratories (average of 68/laboratory) as compared to 3000 samples in 62 laboratories (average of 59/laboratory) reported in the current survey. There are two main explanations for the decrease since 2009, the first being the design of the survey. In 2009, the survey was paper based and had an open field for answering this question so that any number could be inserted. In the current survey, which was conducted online, there were predefined answers that could be selected with the greatest number being 100. In the 2009 survey a few laboratories reported having over 200 and up to 800 sample capacity which would not have been captured in the current survey. The second possible explanation for the decrease in the DCA capacity is that many laboratories have developed alternative methods so that, even if the DCA capacity has decreased, the overall biodosimetry capacity increased. As these data were not collected in the first survey, it is difficult to compare with this survey. The results from the current survey are presented in Figure 2 indicating that all but one laboratory have some capacity for processing samples for the DCA while many laboratories have large DCA capacity. Many also have a significant capacity for processing samples using the Cytokinesis-Block Micronucleus (CBMN) assay, however, there are 20 laboratories reporting no CBMN capacity. For translocation analysis as measured by Fluorescence *In Situ* Hybridisation (FISH), Premature Chromosome Condensation (PCC) and γ-H2AX, few laboratories have these assays established as demonstrated by the number of laboratories reporting zero capacity. Finally, with Electron Paramagnetic Resonance (EPR) there are only 4 laboratories that reported having any capacity. If the capacity for all assays is totalled, the overall sudden-request capacity is over 10 000 samples. It should be noted that from the survey it was not clear whether laboratories could process samples using all assays simultaneously.

The capacity for providing immediate response biodosimetry is dependent on the availability of consumables for each laboratory. Over 80% of the laboratories responded that it would be easy to restock consumables in a timely manner. Similar to the 2009 report, most of the laboratories that reported difficulty with obtaining supplies were in Eastern Europe, however, there was a change in the reporting from some Latin-American countries that previously reported being able to obtain consumables easily but are now having more difficulty. Only one laboratory that reported having difficulty obtaining supplies in 2009 now reported that consumables were easily obtained.

Another factor affecting the laboratory capacity is the availability of human resources. The laboratories were asked to report on the number of personnel trained and available for sample culturing, scoring and data analysis, specifically for the DCA. Figure 3 presents the results of these questions with the data from both the 2009 and 2015 surveys shown. There was little difference in the average number of staff laboratory capable of performing each step of the DCA process with capacity for culturing remaining the highest (3.8/laboratory in both surveys), followed by scoring capacity (3.5/laboratory in both surveys). There was a slight increase in the capacity for data analysis from 2.2/laboratory in 2009 to 2.3/laboratory in 2015. The main improvement over the past 6 years was that all laboratories have some capability in all aspects of the process whereas in 2009, there were a few laboratories that reported no capacity in each of the steps.

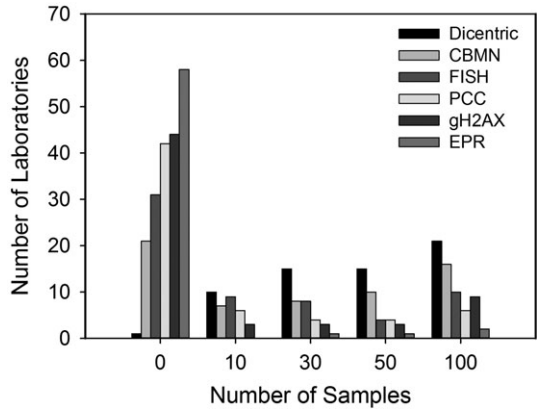

Figure 2. Number of samples that could be processed in a sudden request scenario for different biodosimetry techniques.

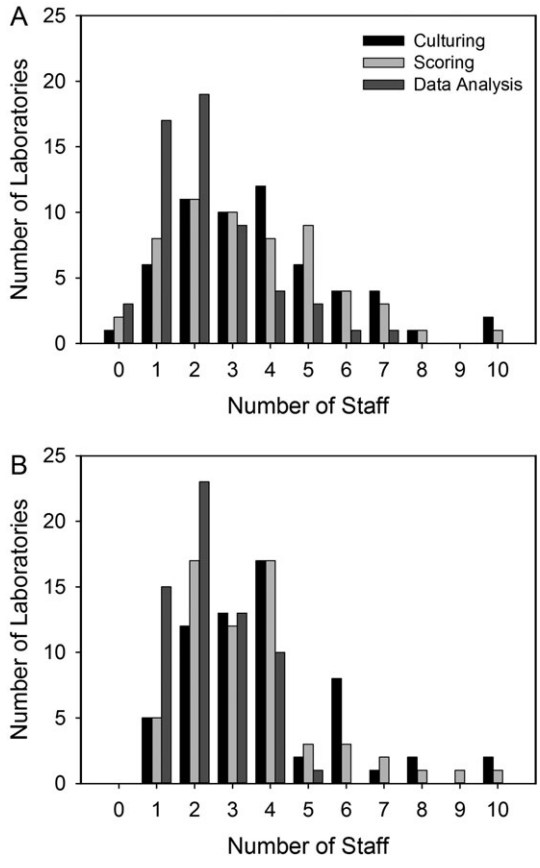

Figure 3. Number of trained staff in each laboratory for conducting cell culturing, sample scoring and data analysis in (**A**) 2009 and (**B**) 2015.

Overall capacity

The overall capacity of each laboratory was also assessed, taking into account all aspects of the analysis, again focusing on the DCA. The question asked for the weekly and monthly capacity for sample analysis when scoring 50 metaphases for each patient taking into account that some staff would also be performing the 'wet work'. This question was meant to capture the functional throughput capacity of each laboratory for triage biodosimetry that would be used in a mass casualty situation[11, 12]. The results from both surveys are presented in Figure 4 illustrating the number of laboratories with different levels of scoring capacity per week and per month. Although the weekly capacity did not change significantly (a decrease of 53 to 52 samples/laboratory), there was an increase in the monthly capacity, increasing from an average of 170 to 200 samples/laboratory. This indicates that the laboratories have improved their ability to sustain their capacity over a longer time. This could be due to the increase in use of semi-automated scoring systems that allows scoring capacity to be maintained while minimising scorer fatigue. While the increase in the percentage of laboratories owning an automated metaphase finder increased only slightly from 60 to 63% over the past 6 years, there was a greater increase in the number of systems from 63 to 88 including satellite scoring systems. Overall, the total international capacity increased slightly from ~3000/week to ~3200/week while the monthly capacity increased from ~10 000 to ~12 000. While this increase in capacity is promising, it is still not sufficient to deal with a very large mass casualty radiological event.

Techniques

As mentioned, there are several techniques besides the DCA that are becoming more widely used for biodosimetry. In the order of reported frequency of use, these include the CBMN assay, FISH, PCC, γH2AX and EPR (Figure 5). The three most common of these include FISH for detection of translocations, CBMN assay and PCC, all of which are described in detail in an IAEA technical report[1].

In Figure 5A, the percentage of laboratories which have working methods for each of the most common techniques is presented comparing the 2009 and 2015 survey results. In contrast, Figure 5B compares the percentage of laboratories that have calibration curves for each of these methods. The DCA remains the most commonly used assay for biodosimetry with almost all laboratories reporting well-developed capability with calibration curves generated. Overall, there was an increase in the percentage of laboratories performing all of the techniques, the greatest

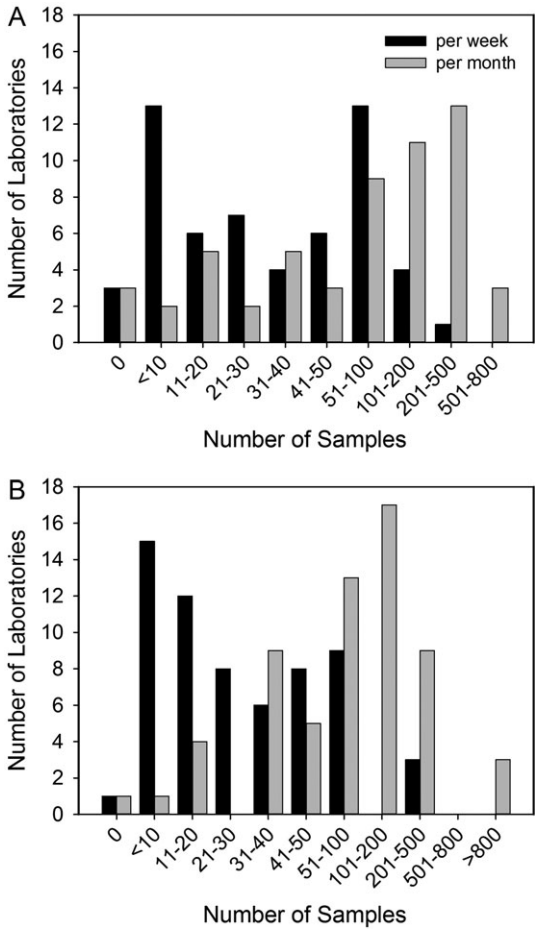

Figure 4. Number of samples that can be analysed using triage quality scoring of 50 spreads per week and per month in (**A**) 2009 and (**B**) 2015.

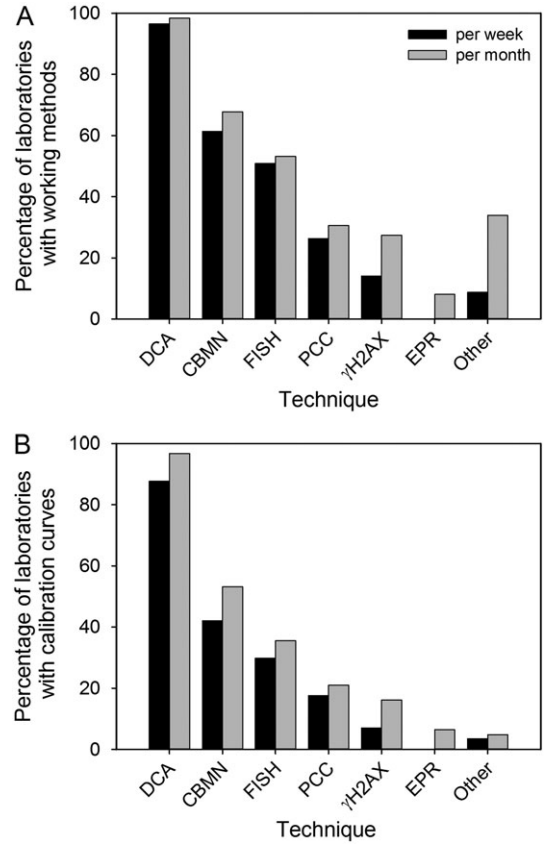

Figure 5. The most common techniques used for biodosimetry in each laboratory. (**A**) Percentage of laboratories with each technique. (**B**) Percentage of laboratories with calibration curves for each technique.

increases being for the CBMN and γH2AX assays. Furthermore, the percentage of laboratories having calibration curves for each technique has also increased over the past six years. There is still a small discrepancy between those reporting to have the capacity for an assay and having a calibration curve, however, this pertained mostly to assays other than the DCA. Other methods were reported in the survey including Optically Stimulated Luminescence (OSL), multi-FISH, gene expression, differential blood counts, reticulocyte micronucleus assay and nucleoplasmic bridges. This is an increase in alternative methods reported over the previous survey but it should be noted that few of these have established calibration curves.

Many laboratories have capabilities for performing more than one technique as shown in Figure 6. While there is a slight increase in the average number of techniques available per laboratory (2.6/laboratory in 2009 vs. 2.9/laboratory in 2015), there was a much larger increase in the average number of techniques with calibration curves since 2009 (1.9/laboratory in 2009 compared to 2.8/laboratory in 2015). In addition, no laboratories reported having no techniques and even more importantly, all laboratories reported having at least one calibration curve.

The comparison between the calibration curves in the laboratories over the two surveys is shown in Figure 7. There has been an increase in the percentage of laboratories having calibration curves since 2009 over all qualities of radiation with low LET (Linear Energy Transfer) curves being most prevalent (Figure 7A).

Almost all (98%) of laboratories have either a gamma or X-ray curve as compared to 88% in 2009, with gamma radiation calibration curves being the

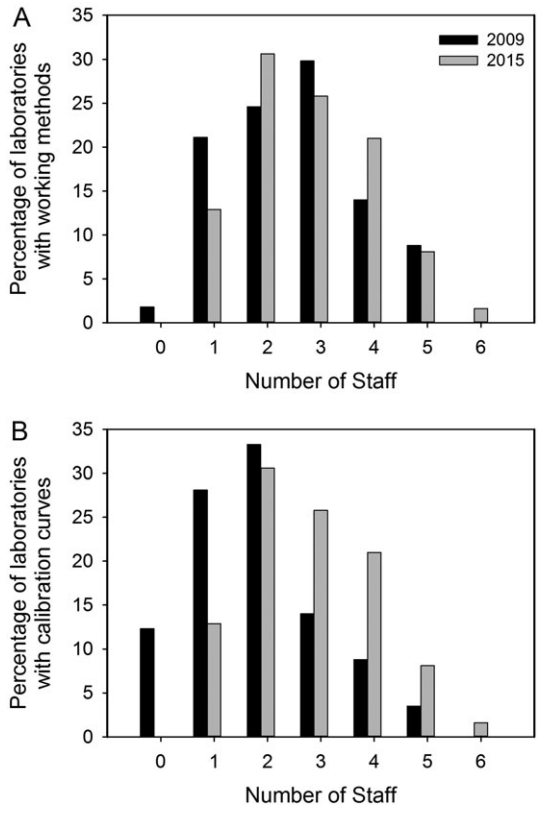

Figure 6. Number of techniques functioning in each laboratory. (**A**) Working methods in place. (**B**) calibration curves generated for the technique Types of calibration curves.

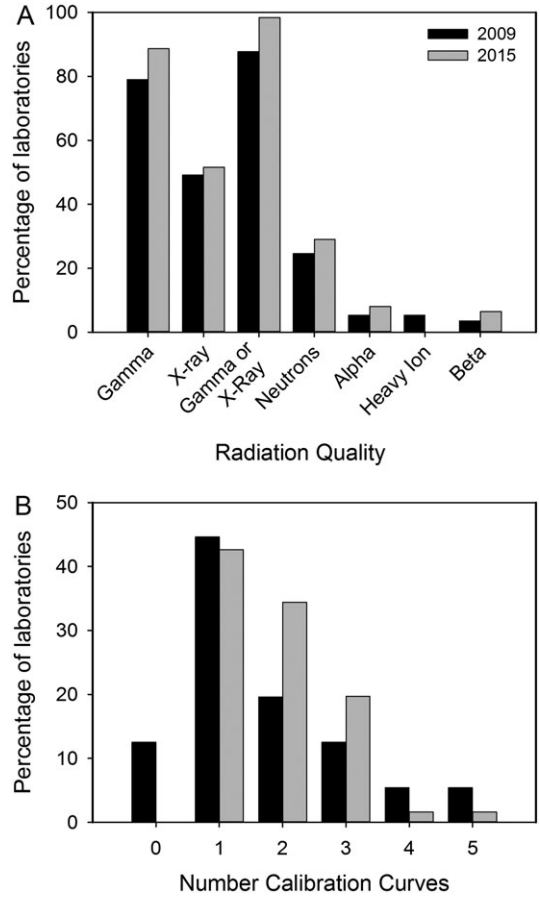

Figure 7. (**A**) Most common types of calibration curves in surveyed laboratories. (**B**) Number of calibration curves per laboratory.

most common (89%). There was an increase in the percentage of laboratories having two or three calibration curves for different radiation qualities (Figure 7B). Of those laboratories with three calibration curves (20%), they all included a gamma, X-ray and a high LET radiation (neutron or alpha) as recommended by IAEA[1]. Overall there has been much progress in the development of calibration curves in BDN laboratories which is an indication that there is more experience in conducting techniques which should result in more accurate biodosimetry worldwide.

Statistics

As discussed in the analysis of our previous survey, there are two components to the calculation of the uncertainty on the resultant estimates of individuals' dose: one from the calibration curve and one from the Poisson nature of the yield of aberrations, both of which are clearly outlined in the IAEA technical report[1]. All laboratories reported employing some sort of statistical analysis either with software created specifically for biodosimetry, other statistical analysis software or calculated manually. Overall, 78% of the laboratories reported that they used software for curve fitting and 80% for dose estimation. The most common freely available specific software packages were the 'Dose Estimate' software (52% for curve fitting and 60% for dose estimates) created by Public Health England[13] and CABAS software (52% for both curve fitting and dose estimates) created by Deparas *et al.*[14] This is an improvement since 2009 where 14% of the laboratories reported having no statistical methods in place, and only 60% used software for the dose estimations. When asked whether laboratories had a statistician in the laboratory to help analyse complex cases, 55% responded that they did. There is a clear improvement in statistical analysis methodology since the inception of

BDN which is likely due to improved communication and collaboration between the laboratories

Quality assurance and quality control

Quality Assurance and Control (QA/QC) are important aspects of providing accurate and reliable biodosimetry[15]. Guidelines for QA/QC for biodosimetry have been published by the International Organization for Standardization (ISO) for the DCA[2, 12] and for the CBMN assay[16]. In addition, a standard for FISH is currently being drafted. Respondents to the survey were asked whether they were in QA/QC compliance, whether their QA/QC procedures were formalised and whether their laboratory has been nationally accredited. About half of the respondents indicated that they were QA/QC compliant with almost 40% being nationally accredited and 6 laboratories being ISO accredited. This is an improvement from 26% being QA/QC compliant and 2 laboratories being ISO accredited in 2009. About half of the respondents, however, stated that they were at least following the guidelines of the ISO standards and the IAEA technical report without actually having gone through the administrative processes of acquiring formal accreditation.

Experience with *in vivo* biodosimetry

Once a laboratory has all procedures in place for conducting biodosimetry, it is important to gain some experience with *in vivo* exposed samples. The survey asked what type of *in vivo* exposures had been studied in each laboratory and whether any accidental or suspected exposure cases had been analysed. Ninety-five percent of the laboratories reported having some experience with *in vivo* exposures (80% in 2009) and 71% had experience with accidental or suspected exposures (65% in 2009). Of the *in vivo* studies, most experience was with occupational (76%), accidental (42%) and medical exposures (39%), while fewer laboratories had experience with retrospective dosimetry cases (28%). Since the 2009 survey, some of these cases have been related to recent accidents in Fukushima[17], Bulgaria[18], Ecuador, El Salvador, Venezuela and Peru, to name a few. The experience with *in vivo* biodosimetry has been growing over the past six years, providing laboratories with necessary experience to maintain and validate their expertise and demonstrating the need and utility for biodosimetry.

Intercomparisons and exercises

Biodosimetry laboratories devote substantial effort to setting up procedures, building calibration curves and ensuring they have a robust QC/QA system. It is important to continually apply these techniques to real-life situations or else risk the loss of capability through inactivity. Many laboratories have active research programmes that use the biodosimetry techniques but in the case of a purely service laboratory, there is a risk of losing the expertise if it is not used. In addition, many laboratories are now becoming members of networks which require validation that all laboratories are providing comparable biodosimetry analysis. Both of these issues can be addressed by conducting regular exercises and intercomparisons that will both maintain and validate capabilities while comparing biodosimetry analysis between laboratories. These exercises and intercomparisons form an essential part of maintaining biodosimetry laboratories in a state of readiness.

The survey addressed the involvement of laboratories in intercomparisons and exercises on national, regional and international levels. The results of this question are shown in Figure 8 in comparison to the results from the 2009 survey. Overall, there was an increase in exercise participation, particularly at the national and regional levels. At the international level, a few laboratories participated in a recent North Atlantic Treaty Organization (NATO) exercise that involved multiple assays[19–22]. The increase on the regional level can mostly be attributed to the formation of the Realising the European Network of Biodosimetry (RENEB) network which conducted several exercises over the past few years involving multiple assays and involved 18 of the responding laboratories[9, 23, 24]. As well, the Canadian Network was expanded to include the USA[25]. There have also been several intercomparisons based on scoring electronically transmitted images shared between laboratories[26–28]. Overall the number of laboratories having performed at least one intercomparison remained the same as in 2009 but still 17% of laboratories that are not participating in any type of intercomparison. Many of these laboratories are fairly

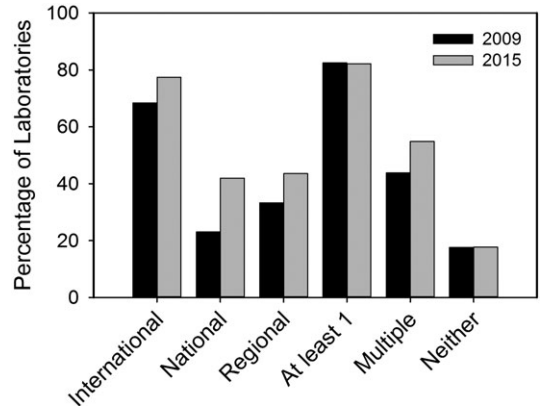

Figure 8. Number of laboratories participating in intercomparison exercises.

new or reside in countries with limited resources for performing their own exercises. Therefore they should be encouraged to participate in future international exercises to validate their biodosimetry capabilities. This could be easily accomplished through intercomparisons based on scoring electronically transmitted images, which can be done with minimal cost while providing training and improving capabilities.

Networks

As mentioned, many countries and regions are forming biodosimetry networks. The goal of networking is to enhance capacity for performing biodosimetry through standardisation, communication and intercomparisons so that, if one laboratory becomes overwhelmed, samples can be sent to others with confidence that dose estimations will be comparable[5, 25].

To gather information on the participation in networks, the laboratories were asked whether they participate in any networks other than BDN (Figure 9A). As of 2009, there were already some well-established national networks with 17 laboratories (30%) reported belonging to existing national biodosimetry networks. There has been a substantial drop in national network membership to five laboratories (8%) however this has been counterbalanced by an increase in membership of the European regional network which increased from three laboratories with belonged to the Tripartite Network (France, Germany and the UK) to 19 laboratories reporting being members for the newly formed RENEB[9, 23]. This demonstrates a tendency of participating in the European Regional Network versus national networks, which may perhaps be explained by the advantages of international cooperation. Membership in the Latin-American Biological Dosimetry Network[29] has remained stable with six of their laboratories responding to the survey. Overall, there was an increase in the percentage of laboratories belong to at least one network from 58% in 2009 to 66% in the current survey, which is not surprising with the growing number of international projects and networks world-wide.

The laboratories were also asked whether they belong to, or would consider joining either the WHO-Radiation Emergency Medical Preparedness and Assistance Network (REMPAN)[30] or the IAEA-Response Assistance Network (RANET)[31]. As shown in Figure 9B, more laboratories have joined RANET since 2009, which is almost balanced by the decrease in the number considering joining, whereas for REMPAN, there is an increase in both laboratories joining REMPAN and considering joining REMPAN. This may be explained by the fact that the two agencies' networks are very different in

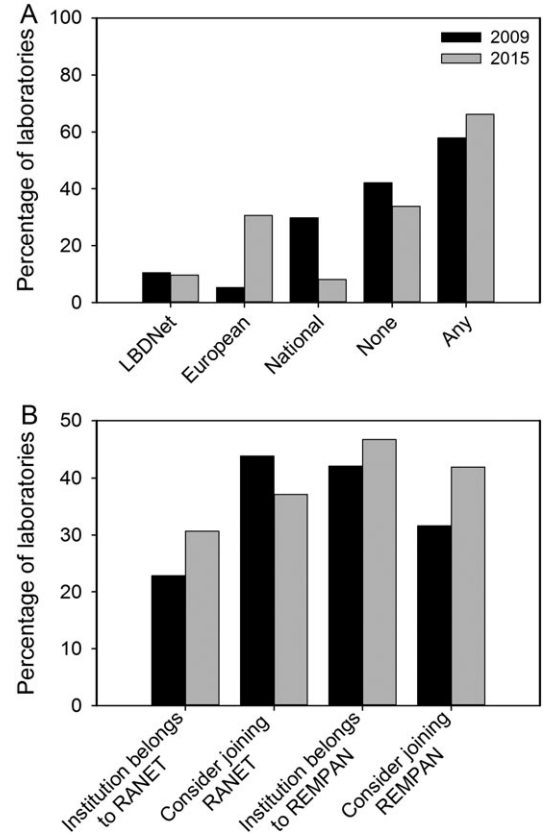

Figure 9. Laboratories whose institution belongs to (**A**) specific networks or (**B**) RANET or REMPAN or is considering joining RANET or REMPAN.

their nature, roles and the process for joining them. RANET requires a formal agreement between a Member State and the IAEA that offers a specific response capacity in assisting another country in the case of a nuclear accident or radiological emergency. Whereas, REMPAN is a semi-formal network with different levels of membership and the procedure for joining ranging from a formal relationship (WHO Collaborating Centers) to an informal relationship (Liaison Institutes and Observers), with the main purpose to support national and regional capacities building, to provide an information platform and to advise to WHO in case of actual emergencies.

Overall, of the 62 laboratories that responded to the survey, 41 are members of some sort of network, but still 21 laboratories remain with no participation in networks. To address this issue, in 2012, the IAEA established a Coordinated Research Project entitled 'Strengthening of "Biological dosimetry" in IAEA Member States: Improvement of current techniques and intensification of collaboration and networking

among the different institutes' which has been running since 2012 and will close in 2016. The major aim of this CRP was to increase preparedness of biological dosimetry laboratories in IAEA and Member States to react to a radiation accident nationally and in the region. Many of the participants of the CRP were laboratories that did not previously belong to any network outside of BDN. As part of this project, a technical meeting was held in Japan in September, 2015, entitled 'Future of biodosimetry in Asia: Promoting a Regional Network'. As eight of the laboratories identified in this survey as 'not belonging to a network' are from the Asia region, this CRP activity has helped fill this gap by promoting the development of an Asian Network. These types of activities highlight the synergy between WHO and IAEA that can help develop biodosimetry in all regions and connect laboratories from around the world.

International activities

Other than international activities already mentioned, laboratories reported involvement with collaborative projects, membership on the ISO TC85/SC2/WG18 biological dosimetry committee, involvement with the NATO, involvement with other European Union initiatives (e.g. EURADOS, Multibiodose, MELODI, etc.), exchange programmes for training, involvement with the recently formed International Association of Biological and EPR Radiation Dosimetry (IABERD: http://iaberd.org/) and with many international agencies of emergency response and health effects of radiation (e.g. International Commission on Radiological Protection, United Nations Scientific Committee on the Effects of Atomic Radiation, etc.). Overall, 48 (77%) of the laboratories are involved in some type of international activities, the vast majority of them through the IAEA and WHO.

Needs of the laboratories

Although many laboratories report being well established for biodosimetry, there remain outstanding requirements. To get a better understanding of these requirements, the laboratories were asked to describe their most pressing needs. The responses clearly identified these to be personnel (32%), automated analysis systems (30%) and equipment and consumables (19%). Overall, 43% require at least some kind of equipment or reagents; a decrease from 50% since 2009. There was little change in the requirement for staff since 2009 and training of staff still remained a priority. Not surprisingly, the need for more funding was identified, but only by 11% of the respondents. Other needs reported included calibration curves or access to radiation sources, better links and communication with the emergency response community and opportunities for intercomparison.

Improvement in BDN

In 2009, when BDN was in its infancy, the members were asked about their prospects and expectation from participation in BDN. At that time, laboratories were asking for improvements in emergency response support, standardisation of techniques, collaboration and information exchange. Overall, laboratories were hoping to develop better links within the biodosimetry community.

Now, with the BDN having been active for 8 years, the respondents were asked how the work of the BDN Secretariat could be improved. The majority of the laboratories either did not respond, stated that there were no improvements or were very happy with the work of the secretariat. Similar to the expectations of the BDN stated in 2009, others responded that they would like the BDN to assist in running intercomparisons, to improve communication and interactions between laboratories, and to coordinate standardisation, training and the establishment of regional networks. Several of the laboratories stated that they would like some documentation from the WHO that would help them justify their activities to their national authorities.

CONCLUSIONS

In 2007, the WHO developed an international biodosimetry network under the name of BioDoseNet which comprised of 65 biodosimetry laboratories from around the world. The goal of the WHO BDN was to bring together cytogenetic biodosimetry laboratories to share experience, assist countries in developing their capacities and capabilities and to provide a network of laboratories that could provide assistance in a large scale event. Since then, the membership has grown slightly to 67 laboratories, however this represents the combination of some laboratories closing and others being established. Based on the responders, there were 15 laboratories that responded in 2009 and did not respond to the present survey while there were 20 new laboratories responding to this survey. Overall, 62 laboratories responded to the current survey representing a 92% response rate.

This survey was designed to evaluate how the BDN has evolved over the last six years and determine whether the goals of the BDN are being met. As for capacities and capabilities, based on the responses received, the total international capacity for biodosimetry has increased since 2009. This is due to several factors including continuous cooperation under BDN umbrella, the development of new regional projects and networks, such as RENEB

which considerably strengthened biodosimetry throughout the EU, adoption of new techniques and efforts toward increasing throughput using automation and improved communication between laboratories which has led to information sharing, harmonisation, training and intercomparisons.

Many of the issues that were identified in 2009 have been addressed. For example, more laboratories have working techniques along with calibrations curves for multiple radiation qualities. In addition, more laboratories have established QA/QC procedures, many more have experience with *in vivo* cases and are also participating in intercomparisons. Freely available statistical packages have also improved data analysis. These are strong indicators that biodosimetry laboratories are gaining more experience in conducting the techniques which will lead to validation of their capabilities and more confidence in their dose estimates.

There still remain some issues identified in 2009 such as the lack of equipment, funding and training, however the reporting of these issues has decreased. Overall there was a strong feeling of satisfaction with the BDN and a good indication that the links developed through membership have enabled cooperation and assistance between laboratories. The results of this survey have clearly demonstrated the advantages of international networking and how the WHO has fostered the strengthening of the links between biodosimetry laboratories and supported countries in implementing IHR (2005) through building their national laboratory capacities for strengthening preparedness for radiological and nuclear emergencies.

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REFERENCES

1. IAEA. Cytogenetic Dosimetry: Applications in Preparedness for and Response to Radiation Emergencies. EPR-Biodose 2011. 2011. Vienna, IAEA.
2. International Organization for Standardization. Radiation protection - Perfomance criteria for service laboratories performing biological dosimetry by cytogenetics. ISO 19238. 2014. Geneva, ISO.
3. WHO. International Health Regulations (Geneva: WHO) (2005). [Available online at http://apps.who.int/iris/bitstream/10665/43883/1/9789241580410_eng.pdf; last accessed February 2016].
4. Blakely, W. F. *et al. WHO 1st Consultation on the Development of a Global Biodosimetry Laboratories Network for Radiation Emergencies (BioDoseNet)*. Radiat. Res. **171**(1), 127–139 (2009).
5. Maznyk, N. A., Wilkins, R. C., Carr, Z. and Lloyd, D. C. *The capacity, capabilities and needs of the WHO biodosenet member laboratories*. Radiat. Prot. Dosim. **151**(4), 611–620 (2012).
6. Flegal, F. N., Devantier, Y., Marro, L. and Wilkins, R. C. *Validation of QuickScan dicentric chromosome analysis for high throughput radiation biological dosimetry*. Health Phys. **102**(2), 143–153 (2012).
7. Karachristou, I., Karakosta, M., Pantelias, A., Hatzi, V. I., Karaiskos, P., Dimitriou, P., Pantelias, G. and Terzoudi, G. I. *Triage biodosimetry using centromeric/telomeric PNA probes and Giemsa staining to score dicentrics or excess fragments in non-stimulated lymphocyte prematurely condensed chromosomes*. Mutat. Res. Genet. Toxicol. Environ. Mutagen. **793**, 107–114 (2015).
8. Rodrigues, M. A., Beaton-Green, L. A. and Wilkins, R. C. *Validation of the Cytokinesis-block Micronucleus Assay Using Imaging Flow Cytometry for High Throughput Radiation Biodosimetry*. Health Phys. **110**(1), 29–36 (2016).
9. Kulka, U. *et al. Realising the European Network of Biodosimetry (RENEB)*. Radiat. Prot. Dosim. **151**(4), 621–625 (2012).
10. WHO. Guidance on regulations for the transport of infectious substances 2009–2010 (Geneva: WHO) (2008).
11. Lloyd, D. C., Edwards, A. A., Moquet, J. E. and Guerrero-Carbajal, Y. C. *The role of cytogenetics in early triage of radiation casualties*. Appl. Radiat. Isot. **52**(5), 1107–1112 (2000).
12. International Organization for Standardization. Radiation protection – Performance criteria for laboratories performing cytogenetic triage for assessment of mass casualties in radiological or nuclear emergencies – General principles and application to dicentric assay. ISO 21243. 2008. Geneva, ISO.
13. Ainsbury, E. A. and Lloyd, D. C. *Dose estimation software for radiation biodosimetry*. Health Phys. **98**(2), 290–295 (2010).
14. Deperas, J. *et al. CABAS: a freely available PC program for fitting calibration curves in chromosome aberration dosimetry*. Radiat. Prot. Dosim. **124**(2), 115–123 (2007).
15. Voisin, P. *Standards in biological dosimetry: A requirement to perform an appropriate dose assessment*. Mutat. Res. Genet. Toxicol. Environ. Mutagen. **793**, 115–122 (2015).
16. International Organization for Standardization. Radiation protection -Performance criteria for laboratories using the cytokinesis-blocked micronucleus assay in blood lymphocytes for biological dosimetry. ISO 17099. 2013. Geneva, ISO.
17. Suto, Y., Hirai, M., Akiyama, M., Kobashi, G., Itokawa, M., Akashi, M. and Sugiura, N. *Biodosimetry of restoration workers for the Tokyo Electric Power Company (TEPCO) Fukushima Daiichi nuclear power station accident*. Health Phys. **105**(4), 366–373 (2013).

18. Gregoire, E. *et al. Biological dosimetry assessments of a serious radiation accident in Bulgaria in 2011*. Radiat. Prot. Dosim. **155**(2), 418–422 (2013).
19. Badie, C. *et al. Laboratory intercomparison of gene expression assays*. Radiat. Res. **180**(2), 138–148 (2013).
20. Beinke, C. *et al. Laboratory intercomparison of the dicentric chromosome analysis assay*. Radiat. Res. **180**(2), 129–137 (2013).
21. Romm, H. *et al. Laboratory intercomparison of the cytokinesis-block micronucleus assay*. Radiat. Res. **180**(2), 120–128 (2013).
22. Rothkamm, K. *et al. Laboratory Intercomparison on the gamma-H2AX Foci Assay*. Radiat. Res. **180**(2), 149–155 (2013).
23. Kulka, U. *et al. Realising the European network of biodosimetry: RENEB-status quo*. Radiat. Prot. Dosim. **164**(1–2), 42–45 (2015).
24. Barnard, S. *et al. The first gamma-H2AX biodosimetry intercomparison exercise of the developing European biodosimetry network RENEB*. Radiat. Prot. Dosim. **164**(3), 265–270 (2015).
25. Wilkins, R. C., Beaton-Green, L. A., Lachapelle, S., Kutzner, B. C., Ferrarotto, C., Chauhan, V., Marro, L., Livingston, G. K., Boulay, G. H. and Flegal, F. N. *Evaluation of the annual Canadian biodosimetry network intercomparisons*. Int. J. Radiat. Biol. **91**(5), 443–451 (2015).
26. Garcia, O. *et al. Interlaboratory comparison of dicentric chromosome assay using electronically transmitted images*. Radiat. Prot. Dosim. **154**(1), 18–25 (2012).
27. Livingston, G. K., Wilkins, R. C. and Ainsbury, E. A. *Pilot Website to Support International Collaboration for Dose Assessments in a Radiation Emergency*. Radiat. Meas. **46**(9), 912–915 (2011).
28. Sugarman, S. L. *et al. The Internet's role in a biodosimetric response to a radiation mass casualty event*. Health Phys. **106**(5 Suppl 2), S65–S70 (2014).
29. Garcia, O. F., Ramalho, A. T., Di, G. M., Mir, S. S., Espinoza, M. E., Manzano, J., Nasazzi, N. and Lopez, I. *Intercomparison in cytogenetic dosimetry among five laboratories from Latin America*. Mutat. Res. **327**(1–2), 33–39 (1995).
30. Carr, Z. *WHO-REMPAN for global health security and strengthening preparedness and response to radiation emergencies*. Health Phys. **98**(6), 773–778 (2010).
31. IAEA. Response and Assistance Network (Vienna: IAEA) (2005).