Validation of the dicentric chromosome assay for radiation biological dosimetry in South Korea

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ABSTRACT

The dicentric chromosome assay (DCA) is a well-established biodosimetry test to estimate exposure to ionizing radiation. The Korea Institute of Radiological and Medical Sciences (KIRAMS) established a DCA protocol as a medical response to radiation emergencies in South Korea. To maintain its accuracy and performance, intercomparison exercises with Health Canada (HC) have been conducted; herein, we aimed to validate our capacity of DCA analysis based on those results. Blood samples irradiated at HC were shipped to KIRAMS to assess the irradiation dose to blinded samples using conventional DCA full scoring and triage-based techniques (conventional DCA scoring in triage mode and DCA QuickScan method). Actual doses fell within the 95% confidence intervals of dose estimates for 70–100% of the blinded samples in 2015–2018. All methods discriminated binary dose categories, reflecting clinical significance. This DCA can be used as a reliable radiation biodosimetry tool in preparation for radiation accidents in South Korea.

Keywords: dicentric chromosome assay; intercomparison exercises; biological dosimetry; radiation exposure; triage

INTRODUCTION

In a large-scale radiological accident, thousands of individuals would potentially be exposed to ionizing radiation, and medical management would be required to identify those with severe exposure (>1.5 Gy). This would help provide immediate clinical treatment efficiently and enable better use of limited clinical resources by helping prevent the worried well from overwhelming the health infrastructure [1–3]. Biological dosimetry is a valuable tool for determining dose received by an individual: confirming, complementing, or replacing physical dosimetry when it is missing or in dispute [4]. The dicentric chromosome assay (DCA) is a well-established biodosimetry test used to estimate exposure to ionizing radiation [5–7]. Dicentric chromosomes are considered to be specific to radiation exposure as they are primarily generated by ionizing radiation and only a few radiomimetic drugs. Because background levels of dicentric chromosomes are low in non-exposed individuals, the DCA is able to assess irradiation doses as low as 0.1 Gy [6]. Due to the advantages of DCA, this assay is considered to be the gold standard of radiation biodosimetry [6]. Significant effort has been invested in optimizing and standardizing the DCA protocol over the past years [8–11]. The International Atomic Energy Agency (IAEA) provides technical information for DCA for radiation biodosimetry [9], and the International Organization for Standardization (ISO) selected DCA as the recommended method for biological dosimetry, and published guidelines for cytogenetic service laboratories performing radiation biological dosimetry [10]. Based on IAEA and ISO guidelines, many countries have developed a system for biological dosimetry in preparation for radiological accidents or mass casualties [12] in which each laboratory should have established well-defined protocols and analytic processes for DCA, and laboratory performance is validated to maintain accuracy and throughput.

Interlaboratory comparison is a valuable tool for evaluating assay performance among individual laboratories. It helps to harmonize detailed protocols, including experimental conditions, scoring criteria, a method for generating dose–response curves and statistical analyses, which are essential to validation of assay systems [12, 13]. It is crucial to establish networks in preparation for a large-scale...
radiological accident in which the number of potentially exposed subjects could exceed the capacity of local service laboratories for DCA [12, 13]. For this reason, biodosimetry networks in Europe, Canada, Latin America, China, Japan and elsewhere have conducted many intercomparison exercises to maintain the accuracy and capacity of the DCA within the network, and assess the feasibility of the use of geographically dispersed laboratories for dose assessment [14–20].

The National Radiation Emergency Medical Center (NREMC) in the Korea Institute of Radiological and Medical Sciences (KIRAMS), South Korea, was built as a ‘control tower’ for medical response to radiation emergencies in South Korea. The KIRAMS has operated a laboratory of biological dosimetry to estimate the irradiation dose to potentially exposed individuals. Based on ISO and IAEA guidelines, this laboratory has established a DCA for which it obtained national accreditation for a medical testing laboratory in accordance with the recognized International Standard ISO/15189 (Medical Testing No. KM000-0, Korea Laboratory Accreditation Scheme). The goal of the present study was to validate our DCA system for radiation biodosimetry. We have been performing intercomparison exercises to evaluate the performance of the DCA since 2014. The accuracy and performance of our DCA was tested based on the results of intercomparison studies with Health Canada (HC), one of the primary institutes hosting intercomparison exercises for radiation biodosimetry. We confirmed that the conventional DCA full scoring and triage-based scoring techniques, including conventional DCA scoring in triage mode (triage-DCA) and DCA QuickScan method performed at NREMC in KIRAMS, are suitable for radiation biodosimetry.

MATERIALS AND METHODS

Sample preparation
All blood donors were volunteers who willingly responded to an advertising call for participation in a research protocol approved by HC Research Ethics Board. Ten donors gave informed consent, and none had a recent history of ionizing radiation exposure. X-irradiation was performed at HC: lithium-heparinized blood was irradiated at a dose rate of 0.36 Gy using an X-RAD 320 device (Precision X-ray Inc., North Branford, CT, USA) operated at 250 kVp and 15 mA. Following incubation of these blood samples at 37°C for 2 h to allow DNA repair, 10 coded samples were shipped to KIRAMS in South Korea by air with FedEx according to packaging instructions 650 of the International Air Transportation Association (IATA). The duration of shipment from HC to KIRAMS was ~3 days. The package was labeled to indicate that it should not be frozen or X-rayed at airport security checkpoints. As a quality control measure, the package included a temperature data logger for monitoring temperature (which showed that the samples remained at between 14 and 27°C during transit) and an optically stimulated luminescence (OSL) dosimeter (to rule out X-ray screening at airports). The actual radiation dose to each sample was kept confidential until analysis was completed.

Cell culture and harvest
Samples were cultured according to methods recommended by the IAEA [9] and ISO [10]. Briefly, whole blood was cultured in RPMI 1640 medium (Gibco, Thermo Fisher Scientific, Waltham, MA, USA) supplemented with 20% fetal bovine serum (JR Scientific Inc., CA, USA), 1% antibiotics (Gibco) and 2% phytohemagglutinin (Gibco) at 37°C for 48 h in a humidified atmosphere of 5% CO2 in air. Colcemid solution (Gibco) at a concentration of 0.07 μg/ml was added to the medium 24 h before harvesting. The fluorescence plus-Giemsa (FPG) staining technique coupled with 15 μM BrdU (Invitrogen, Thermo Fisher Scientific, Waltham, MA, USA) in cultures and Hoechst 33 258 (Invitrogen) allows identification by the differential staining of second-division metaphase spreads. Blood samples were treated with 0.075 M KCl for 20 min at 37°C, followed by fixation with cold methanol and acetic acid (3:1). Fixed cells were spread onto slides, which were stored for 12 h at 60°C. The slides were stained with Giemsa solution (Sigma-Aldrich, St Louis, MO, USA). Metaphase images were captured using the Metafer 4 (Metasystems GmbH, Altlussheim, Germany) and analyzed by well-trained scorers.

DCA scoring
Conventional DCA scoring adhered to the recommended guidelines of the IAEA [9] and ISO [10]. For conventional DCA full scoring, a total of 1000 metaphases or 100 dicentrics were scored in first metaphase cells. For triage-DCA, each scorer recorded the number of dicentrics in the first 50 metaphases or stopped scoring when it reached 30 dicentrics. DCA QuickScan scoring was performed according to the method described by Flegal et al. [21], in that scorers examined the metaphase spreads for obvious damage without counting individual centromeres. Fifty metaphases or 30 dicentrics were scored.

Dose estimation
Dose estimates were calculated using dose–response curves (60Co, 0.5 Gy/min) previously generated using a weighted Poisson regression formula following IAEA guidelines as follows [9]: the yield of dicentrics, Y = (0.00146 ± 0.00038) + (0.0269 ± 0.0051) × D + (0.0717 ± 0.0033) × D^2 for year 2014–2015; and Y = (0.00105 ± 0.00010) + (0.0355 ± 0.0041) × D + (0.0644 ± 0.0027) × D^2 for years 2016–2018, where D is the dose. These two calibration curves were developed by different scorers. The accuracy of reported dose estimates was measured by comparing the actual dose and reported dose. When the actual dose falls within the 95% confidence interval (CI) of a dose estimate, or a reported dose is within 0.5 Gy of the actual dose, dose estimates are considered to be correct. Mean absolute difference (MAD) between estimated dose and actual dose was also calculated.

Evaluation of discriminatory power
According to Rothkamm et al. [3], actual doses were merged into binary categories reflecting clinical, diagnostic, and epidemiological significance, using corresponding threshold doses of 0.1 and 1.5 Gy:

- Classification 1: never versus ever single radiation exposure (0 Gy/≥0.1 Gy) to avoid clinical resources being occupied by the ‘worried well’ (i.e. unexposed individuals who are concerned they may have been exposed);
• Classification 2: marginal versus higher single radiation exposures (≤0.1 Gy/ >0.1 Gy) to distinguish groups such as those who do not need clinical support from others, where deterministic or stochastic effects in adults may occur or become detectable using epidemiological methods; and
• Classification 3: lower versus medium-high single radiation exposure (≤1.5 Gy/ >1.5 Gy) to identify the group of patients who will likely experience acute radiation syndrome several days after radiation exposure.

Accuracy, sensitivity and specificity were calculated on the basis of dose estimates as indicators to assess the discriminatory power of the DCA, as follows: Accuracy = (True positive + True negative) ×100/Total; Sensitivity = True positive × 100/(True positive + False negative); and Specificity = True negative × 100/(True negative + False positive). 'Positive' is defined as a true dose of ≥0.1 Gy, >0.1 Gy and >1.5 Gy in case of Classification Groups 1, 2 and 3, respectively. 'Negative' is defined as a true dose of 0 Gy, ≤0.1 Gy and ≤1.5 Gy in each corresponding classification.

RESULTS

Accuracy of dose estimates using conventional DCA full scoring

To evaluate the accuracy of dose estimates according to a conventional DCA full-scoring method in KIRAMS, actual doses and estimated doses were compared. Figure 1 illustrates the number of samples for which the correct dose was identified in 2014–2018. Actual doses in 3 of 10 samples tested in 2014 were within the 95% CIs of dose estimates, which was considered to be a correct dose estimate. The number of samples with correct dose estimates increased in 2015–2018 [8 of 9 (2015); 7 of 10 samples (2016); and 8 of 10 (2018)]. As shown in Table 1, dose estimates (%) within ±0.5 Gy of true dose were >60% in 2015–2018 [67% (2015); 90% (2016); and 70% (2018)], and MAD values to illustrate differences between actual dose and reported dose were <0.5 Gy in 2015–2018 [0.26 (2015); 0.21 (2016); and 0.40 (2018)].

Accuracy of dose estimates using the DCA in triage mode

To evaluate the performance of the DCA in triage mode, 50 metaphase cells were scored using the Triage-DCA and DCA QuickScan methods in triage mode. Figures 2 and 3 illustrate doses estimated using the two methods. More than 70% samples were within the 95% CI in 2014–2018 using both methods. As shown in Table 1, samples (%) within 0.5 Gy interval of actual dose or 95% CI tended to be increased in 2015–2018, compared with 2014. The difference between actual dose and estimated dose—indicated by MAD value—was smaller than that in 2014.

Fig. 1. Doses estimated using the conventional dicentric chromosome assay (DCA) full scoring method. The symbols and error bars represent dose estimates and corresponding 95% confidence intervals. The dotted/dashed lines represent actual physical doses and their ±0.5 Gy intervals.
Table 1. Accuracy of dose estimation according to dicentric chromosome assay scoring methods

|                      | Year 2014 | Year 2015 | Year 2016 | Year 2018 |
|----------------------|-----------|-----------|-----------|-----------|
| **Conventional DCA full scoring** |           |           |           |           |
| % within 95% CI      | 30        | 89        | 70        | 80        |
| % within ±0.5 Gy     | 60        | 67        | 90        | 70        |
| MAD (Gy)             | 0.56      | 0.26      | 0.21      | 0.40      |
| **DCA–Triage (Triage mode)** |           |           |           |           |
| % within 95% CI      | 70        | 89        | 80        | 90        |
| % within ±0.5 Gy     | 50        | 78        | 60        | 60        |
| MAD (Gy)             | 0.60      | 0.39      | 0.40      | 0.41      |
| **DCA QuickScan* (Triage mode)** |           |           |           |           |
| % within 95% CI      | 80        | 100       | 75        | 100       |
| % within ±0.5 Gy     | 50        | 100       | 70        | 75        |
| MAD (Gy)             | 0.58      | 0.28      | 0.36      | 0.36      |

*Averaged value from one or two scorers were displayed. DCA = dicentric chromosome assay.

Fig. 2. Doses estimated using the dicentric chromosome assay (DCA)–Triage method. The symbols and error bars represent dose estimates and corresponding 95% confidence intervals. The dotted/dashed lines represent actual physical doses and their ±0.5 Gy intervals.
DCA performance in clinical/diagnostic/epidemiological significant settings

To test DCA performance in clinical and epidemiological significant settings, dose estimates were merged into binary categories reflecting clinically relevant aspects, and the accuracy, sensitivity and specificity were determined for the classifications. The sensitivity, specificity, and overall accuracy based on measurements using the conventional DCA full scoring method are summarized in Table 2. This scoring method categorized never-/ever-exposed individuals into the corresponding subgroup correctly (accuracy 100%, sensitivity 100% and specificity 100% in all years). Accuracy and specificity for other binary categories decreased somewhat; however, 100% sensitivity and more than ~90% accuracy was maintained for all categories in all years. When these calculations were performed using pooled samples from 2014 to 2018, similar results were observed, as shown in Table 2.

The ability of the DCA in triage mode to distinguish binary dose categories reflecting clinical, diagnostic, and epidemiological significance was also evaluated, as shown in Table 3. Triage-DCA yielded 100% sensitivity for all binary categories in all years. The QuickScan method demonstrated somewhat decreased sensitivity in 2016; however, it resulted in >90% sensitivity in most years. Both scoring methods demonstrated >80% accuracy for binary categories.

DISCUSSION

The DCA is considered to be the gold standard for radiation biological dosimetry. The NREMC in KIRAMS, South Korea, is the ‘control tower’ for medical responses to radiation emergencies, and has established a DCA to determine irradiation dose to potentially exposed individuals. We performed intercomparison work with HC in 2014–2018 to validate our DCA methods. The accuracy of dose estimation using our DCA methods, and the ability to distinguish clinically significant groups, were evaluated in this study.

The accuracy of dose estimation was assessed by verifying whether the 95% CI of the dose estimates contained the actual dose. For approximately 70–89% of samples, the actual dose was within the 95% CI in 2015–2018. Even samples that were not correctly estimated were only slightly outside the 95% CI. According to Romm and colleagues, 75% of the actual dose fell within the 95% CI of the estimated dose for data from five laboratories [4], which is comparable with our intercomparison results, except in 2014. Unlike the results in 2015–2018, the accuracy of dose estimation using DCA full scoring was relatively low in 2014 when we began the intercomparison exercises. However, the doses of the samples in 2014 appeared to be slightly overestimated. When the results from 2014 were converted to dose using a calibration curve generated at HC, where the blood samples were irradiated, 70% were within the CI. Samples that were not within the range were only slightly

![Fig. 3. Doses estimated using the dicentric chromosome assay (DCA) QuickScan method. The symbols and error bars represent dose estimates and corresponding 95% confidence intervals. The dotted/dashed lines represent actual physical doses and their ±0.5 Gy intervals.](image-url)
outside the confidence limit (data not shown). This indicates that the issues in 2014 were not due to poor scoring but to a poorly matched calibration curve. This finding demonstrates that the DCA using the conventional full scoring in KIRAMS can provide accurate dose estimations.

In a large-scale radiological accident, many potentially exposed individuals would require dose estimation. Instead of the full scoring method, a DCA scoring method to score only 50 metaphases has been recommended for triage in a mass casualty event [22]. Flegal et al. suggested another scoring method, known as DCA QuickScan to reduce scoring time, demonstrating that QuickScan scoring be completed in approximately one-sixth of the time [21, 23]. In the present study, we evaluated the accuracy of the DCA scoring methods in triage mode, as well as the full scoring method. Both triage methods were able to estimate the correct dose (within the 95% CI) for 70–100% of blinded samples. Previous reports have suggested that scoring 50 metaphases in triage mode could provide dose estimates with an accuracy of 0.5 Gy, which would be adequate for determining appropriate medical intervention [17, 22]. As additional indices for examining the accuracy of our DCA method, we evaluated the percentage of samples within the 0.5 Gy interval and MAD values. When using the triage methods, dose estimates in 60–100% of samples in 2015–2018 fell within the 0.5 Gy interval of the actual dose, and their MAD values (0.28–0.41) were <0.5 Gy, which corresponds well with the uncertainty interval. Canadian biodosimetry network intercomparison work reported that >60% of their dose estimates fell within a ±0.5 Gy interval of the actual dose [24]. MAD values of laboratories participating in a North Atlantic Treaty Organization intercomparison exercise were <0.61 for DCA [3]. These findings demonstrate that our DCA is comparable with methods used in other laboratories within the international biodosimetry network, which suggests that the DCA would be a valuable tool for mass casualty events.

From the dosimetry perspective, it is desirable to estimate doses as accurately as possible. From the clinical point of view, however, dose ranges often provide sufficient information to address urgent clinical or diagnostic needs [3]. In the current study, we tested whether our DCA methods have the discriminatory power of clinically relevant doses in preparation for a radiation emergency. Irradiation doses were merged into binary dose categories representing clinically, epidemiologically and diagnostically relevant groups using a classification threshold (i.e. 0.1 Gy and 1.5 Gy) [3], and we evaluated the accuracy, sensitivity and specificity for the classifications. Radiation exposure to <0.1 Gy is known to induce no detectable difference between exposed and non-exposed individuals. Distinguishing a high dose– from a never- or marginal-exposed group would help prevent the worried well from overwhelming health infrastructure and enable more efficient use of limited resources. Individuals exposed to >1.5 Gy need to initiate therapy with cytokines, antimicrobial agents, blood transfusion, or frequent outpatient follow-up with laboratory monitoring [25]. Confirmation of a whole-body dose of >1.5 Gy is important in order to care for patients who will likely experience acute radiation syndrome after radiation exposure. Our DCA full scoring method demonstrated

Table 2. Accuracy, sensitivity and specificity of dicentric chromosome assay into binary categories of clinical and epidemiological significance

|                      | Year 2014 | Year 2015 | Year 2016 | Year 2018 | Overall (2014–2018) |
|----------------------|-----------|-----------|-----------|-----------|---------------------|
| Conventional DCA full scoring |           |           |           |           |                     |
| Never vs ever        |           |           |           |           |                     |
| Accuracy             | 100       | 100       | 100       | 100       | 100                 |
| Sensitivity          | 100       | 100       | 100       | 100       | 100                 |
| Specificity          | 100       | 100       | 100       | 100       | 100                 |
| Marginal vs higher   |           |           |           |           |                     |
| Accuracy             | 100       | 89        | 90        | 100       | 95                  |
| Sensitivity          | 100       | 100       | 100       | 100       | 100                 |
| Specificity          | 100       | 50        | 50        | 100       | 67                  |
| Lower vs Medium higher|           |           |           |           |                     |
| Accuracy             | 90        | 89        | 100       | 90        | 92                  |
| Sensitivity          | 100       | 100       | 100       | 100       | 100                 |
| Specificity          | 67        | 86        | 100       | 75        | 86                  |

Accuracy = (True positive + True negative) × 100/(Total).
Sensitivity = True positive × 100/(True positive + False negative).
Specificity = True negative × 100/(True negative + False positive).

DCA = dicentric chromosome assay.
Validation of the dicentric chromosome assay

Table 3. Accuracy, sensitivity and specificity of dicentric chromosome assay in triage mode into binary categories of clinical and epidemiological significance

|                      | Year 2014 | Year 2015 | Year 2016 | Year 2018 | Overall (2014–2018) |
|----------------------|-----------|-----------|-----------|-----------|----------------------|
| **DCA–Triage (Triage mode)** |           |           |           |           |                      |
| Never vs ever        |           |           |           |           |                      |
| Accuracy              | 100       | 100       | 100       | 100       | 100                  |
| Sensitivity           | 100       | 100       | 100       | 100       | 100                  |
| Specificity           | 100       | 100       | 100       | 100       | 100                  |
| Marginal vs higher    |           |           |           |           |                      |
| Accuracy              | 100       | 89        | 90        | 100       | 95                   |
| Sensitivity           | 100       | 100       | 100       | 100       | 100                  |
| Specificity           | 100       | 50        | 50        | 100       | 67                   |
| Lower vs Medium higher|           |           |           |           |                      |
| Accuracy              | 90        | 89        | 90        | 90        | 90                   |
| Sensitivity           | 100       | 100       | 100       | 100       | 100                  |
| Specificity           | 67        | 86        | 86        | 75        | 81                   |
| **DCA QuickScan (Triage mode)** |           |           |           |           |                      |
| Never vs ever        |           |           |           |           |                      |
| Accuracy              | 100       | 100       | 80        | 100       | 94                   |
| Sensitivity           | 100       | 100       | 78        | 100       | 93                   |
| Specificity           | 100       | 100       | 100       | 100       | 100                  |
| Marginal vs higher    |           |           |           |           |                      |
| Accuracy              | 100       | 89        | 90        | 100       | 94                   |
| Sensitivity           | 100       | 100       | 88        | 100       | 96                   |
| Specificity           | 100       | 50        | 100       | 100       | 82                   |
| Lower vs Medium higher|           |           |           |           |                      |
| Accuracy              | 90        | 89        | 95        | 95        | 93                   |
| Sensitivity           | 100       | 100       | 100       | 100       | 100                  |
| Specificity           | 67        | 86        | 93        | 88        | 87                   |

\(^a\)Accuracy = (True positive + True negative) × 100/(Total)
\(^b\)Sensitivity = True positive × 100/(True positive + False negative)
\(^c\)Specificity = True negative × 100/(True negative + False positive)
\(^d\)Averaged value from one or two scorers were displayed.

High accuracy and sensitivity in all time periods (≥90%). Notably, our conventional DCA full scoring method yielded 100% sensitivity for all binary categories in every year it was performed. Both triage methods also resulted in >80% accuracy and sensitivity overall. Our findings demonstrate that our DCA methods have the capability to successfully identify exposed individuals who may require medical treatment or monitoring, which suggests that our DCA method in KIRAMS could be useful for triage in radiological events. When a large-scale radiological accident occurs, local cytogenetic laboratories would not be capable of screening vast numbers of
individuals exposed to ionizing radiation. One strategy to cope, however, would be to increase throughput by forming a cooperative network for dose assessment. Collected blood samples can be processed in multiple laboratories in parallel, which enables an increase in total biodosimetry capability [4]. This strategy, however, requires quality control exercises within the networks. Various biodosimetry networks have conducted many intercomparison exercises to validate the DCA within their network and assess the feasibility of geographically dispersed cytogenetic laboratories [14–19]. In the present study, DCA methods in KIRAMS were validated using blood samples provided by HC. This suggests KIRAMS has the capability to assist dose assessment for radiation mass casualty incidents occurring even in a geographically dispersed area.

Taken together, our findings demonstrate that DCA performed in KIRAMS has the ability to provide accurate dose assessment and to discriminate exposed persons who need medical treatment. The use of the Triage-DCA and DCA QuickScan scoring methods enabled rapid classification of clinically significant groups. Therefore, DCA in KIRAMS can be used as a reliable radiation dosimetry tool in preparation for radiation incidents in South Korea. Furthermore, we have demonstrated that KIRAMS has the capability to provide the biodosimetric support for radiological mass casualty events occurring in other countries.

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CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

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SUPPLEMENTARY DATA

Supplementary data are available at Journal of Radiation Research online.

REFERENCES

1. Blakely WF, Salter CA, Prasanna PGS. Early-response biological dosimetry—recommended countermeasure enhancements for mass-casualty radiological incidents and terrorism. Health Phys 2005;89:494–504.
2. Jarrett D, Sedlak R, Dickerson W et al. Medical treatment of radiation injuries—current US status. Radiat Meas 2007;42:1063–74.
3. Rothkamm K, Beinke C, Romm H et al. Comparison of established and emerging biodosimetry assays. Radiat Res 2013;180:111–9.
4. Romm H, Wilkins RC, Coleman CN et al. Biological dosimetry by the triage dicentric chromosome assay: potential implications for treatment of acute radiation syndrome in radiological mass casualties. Radiat Res 2011;175:397–404.
5. Edwards AA. The use of chromosomal aberrations in human lymphocytes for biological dosimetry. Radiat Res 1997;148:539–44.
6. International Atomic Energy Agency (IAEA). Cytogenetic Analysis for Radiation Dose Assessment: A Manual. Technical Report 405, Vienna: IAEA, 2001.
7. Romm H, Oestreicher U, Kulka U. Cytogenetic damage analysed by the dicentric assay. Ann Ist Super Sanita 2009;45:251–9.
8. Voisin P, Barquinero F, Blakely B et al. Towards a standardization of biological dosimetry by cytogenetics. Cell Mol Biol 2002;48:501–4.
9. International Atomic Energy Agency (IAEA). Cytogenetic dosimetry: applications in preparedness for and response to radiation emergencies. EPR-biodosimetry, Vienna: IAEA, 2011.
10. International Organization for Standardization (ISO). Radiation protection—performance criteria for service laboratories performing biological dosimetry by cytogenetics. ISO 19238, Geneva: ISO, 2014.
11. Voisin P. Standards in biological dosimetry: a requirement to perform an appropriate dose assessment. Mutat Res Genet Toxicol Environ Mutagen 2015;793:115–22.
12. Blakely WF, Carr Z, Chu MC et al. WHO 1st consultation on the development of a global biodosimetry laboratories network for radiation emergencies (BioDoseNet). Radiat Res 2009;171:127–39.
13. Di Giorgio M, Barquinero JF, Vallerga MB et al. Biological dosimetry intercomparison exercise: an evaluation of triage and routine mode results by robust methods. Radiat Res 2011;175:638–49.
14. Oestreicher U, Samaga D, Ainsbury E et al. RENEB intercomparisons applying the conventional Dicentric Chromosome Assay (DCA). Int J Radiat Biol 2017;93:20–9.
15. Liu JX, Pan Y, Ruan JL et al. Intercomparison in cytogenetic dosimetry among 22 laboratories in China. Genome Integ 2016;7:6.
16. Wojcik A, Lloyd D, Romm H et al. Biological dosimetry for triage of casualties in a large-scale radiological emergency: capacity of the EU member states. Radiat Prot Dosimetry 2010;138:397–401.
17. Wilkins RC, Romm H, Kao TC et al. Interlaboratory comparison of the dicentric chromosome assay for radiation biodosimetry in mass casualty events. Radiat Res 2008;169:551–60.
18. Miller SM, Ferrarotto CL, Vlahovich S et al. Canadian Cytogenetic Emergency network (CEN) for biological dosimetry following radiological/nuclear accidents. Int J Radiat Biol 2007;83:471–7.
19. Garcia OF, Ramalho AT, Di Giorgio M et al. Intercomparison in cytogenetic dosimetry among five laboratories from Latin America. Mutat Res 1995;327:33–9.

20. Yoshida MA, Hayata I, Tateno H, et al. The chromosome network for biodosimetry in Japan. Radiat Meas 2007;42:1125–7.

21. Flegal FN, Devantier Y, Marro L et al. Validation of QuickScan dicentric chromosome analysis for high throughput radiation biological dosimetry. Health Phys 2012;102:143–53.

22. Lloyd DC, Edwards AA, Moquet JE et al. The role of cytogenetics in early triage of radiation casualties. Appl Radiat Isot 2000;52:1107–12.

23. Flegal FN, Devantier Y, McNamee JP et al. Quickscan dicentric chromosome analysis for radiation biodosimetry. Health Phys 2010;98:276–81.

24. Wilkins RC, Beaton-Green LA, Lachapelle S et al. Evaluation of the annual Canadian biodosimetry network intercomparisons. Int J Radiat Biol 2015;91:443–51.

25. Waselenko JK, MacVittie TJ, Blakely WF et al. Medical management of the acute radiation syndrome: recommendations of the Strategic National Stockpile Radiation Working Group. Ann Intern Med 2004;140:1037–51.