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NATO BIODOSIMETRY STUDY

Comparison of Established and Emerging Biodosimetry Assays

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Rapid biodosimetry tools are required to assist with triage in the case of a large-scale radiation incident. Here, we aimed to determine the dose-assessment accuracy of the well-established dicentric chromosome assay (DCA) and cytokinesis-block micronucleus assay (CBMN) in comparison to the emerging γ-H2AX foci and gene expression assays for triage mode biodosimetry and radiation injury assessment. Coded blood samples exposed to 10 X-ray doses (240 kVp, 1 Gy/min) of up to 6.4 Gy were sent to participants for dose estimation. Report times were documented for each laboratory and assay. The mean absolute difference (MAD) of estimated doses relative to the true doses was calculated. We also merged doses into binary dose categories of clinical relevance and examined accuracy, sensitivity and specificity of the assays. Dose estimates were reported by the first laboratories within 0.3–0.4 days of receipt of samples for the γ-H2AX and gene expression assays compared to 2.4 and 4 days for the DCA and CBMN assays, respectively. Irrespective of the assay we found a 2.5–4-fold variation of interlaboratory accuracy per assay and lowest MAD values for the DCA assay (0.16 Gy) followed by CBMN (0.34 Gy), gene expression (0.34 Gy) and γ-H2AX (0.45 Gy) foci assay. Binary categories of dose estimates could be discriminated with equal efficiency for all assays, but at doses ≥1.5 Gy a 10% decrease in efficiency was observed for the foci assay, which was still comparable to the CBMN assay. In conclusion, the DCA has been confirmed as the gold standard biodosimetry method, but in situations where speed and throughput are more important than ultimate accuracy, the emerging rapid molecular assays have the potential to become useful triage tools.

INTRODUCTION

Whenever a person may have been exposed to significant levels of ionizing radiation, it is important to estimate the dose received to determine any short- or long-term health implications and provide the evidence base for counseling. Such overexposure cases are typically rare and involve only one or a few potential casualties. The main focus for such isolated cases is to provide the most accurate dose estimate, taking into account exposure characteristics such as radiation type and quality as well as uniformity, duration and timing of the exposure (*1, 2*).

The dicentric chromosome assay (DCA) and the cytokinesis-block micronucleus assay (CBMN) have been established as the main biodosimetry tests for ionizing radiation exposure (*3*). These two cytogenetic methods combine high (DCA) or reasonable (CBMN) specificity, sensitivity of the order of 100 mGy and persistence of the signal for several months. Dozens of laboratories around the world have established calibration curves that enable chromosome aberration yields to be converted to dose estimates, and the quantitative impact of the specific exposure characteristics listed above on aberration yields and distributions has

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