Radiation dose estimation by automated chromosome biodosimetry

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Study Goal: Radiation exposure dose can be interpolated from the frequency of dicentric chromosomes (DC) per cell using a calibration curve fit to the known DC frequency at multiple exposure levels. Both the DC counts for the curve and of test samples are manually determined, as available autonomous systems tend to be inaccurate, particularly at low dose exposures. There is an acute need for accurate, automated biodosimetry calibration curve generation and analysis of samples exposed to undisclosed radiation levels.

Abstract: We apply the Automated Dicentric Chromosome Identifier (ADCI), software that detects and discriminates DCs from monocentric chromosomes and other objects, to compute biodosimetry curves and determine the radiation dose exposure for blinded samples. Results are then compared with standard curves derived by two different reference laboratories for these same samples. Blood samples from both labs were exposed simultaneously to a single radiation source; then, metaphase cell preparations were prepared, imaged, and analyzed separately. The manually scored images at each dose level (0 - 4 Gy) from each lab were then reanalyzed with the automated system. ADCI applies a Support Vector Machine classifier (SVM) trained on image segmentation features to determine DCs/cell. At each dose, 1000 calibration curves were bootstrapped by random sampling of 500 images at each dose. Only images with >25 and <70 segmented objects were selected. The SVM tuning parameter was optimized (σ = 1.4 or 1.5, for both datasets), based on the respective fit to a linear-quadratic function (R² = 0.96 to 0.98) and Poisson distribution of DCs/cell (1.0 ≤ dispersion ≤ 1.3; -2 ≤ μ ≤ 3). Accuracy was determined using independent cytogenetic data of known dose and synthetic datasets of proportionate mixtures from different doses. Estimated doses were analyzed by solving the quadratic function with observed DCs/per cell. Calculated exposures (in Gy) were consistent with those obtained from standard biodosimetry curves [Actual: estimated ±S.D.]: [0.5: 0.8±0.3], [1.0: 1.0±0.2], [2.0:2.1±0.3], [3.0:2.7±0.3], [4.0:3.9±0.2]. Correct intermediate exposures within 0.2 Gy of expected values were interpolated from equal mixtures of cells exposed to 2 different doses. Finally, an independently collected cells exposed at 1Gy gave an estimated dose of 1.6Gy using ADCI.

Conclusion: ADCI can determine radiation dose, with accuracies comparable to standard biodosimetry. Calibration curves were generated from image data using Desktop software in 1-2 days, and dose estimation required <2 hr per sample. For high quality image data, a single instance of ADCI is suitable for supervised processing and generates estimated doses at moderate throughput. Multiple software instances or parallelization may be an effective response to a mass casualty radiation event.

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