The cytokinesis-blocked micronucleus assay: application in radiation biodosimetry

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\textbf{Study Goal:} An in vitro study of the dose responses of human peripheral blood lymphocytes is conducted with the aim of creating age and gender specific calibrated dose response curves measuring up to 4 Gy of gamma radiation using the cytokinesis blocked micronucleus assay. A validation study with CBMN was carried out for two overexposed industrial radiographers and the results were compared with the dose values obtained from a dicentric assay. The background frequency of MN has been determined in the population.

\textbf{Abstract:} The cytokinesis blocked micronucleus (CBMN) assay has been used and validated as an appropriate biodosimetry tool to evaluate in vivo radiation exposures. The CBMN assay was employed to obtain the frequencies of micronuclei (MN) per binucleated cell in blood samples from 16 healthy donors (8 males and 8 females) in two age ranges of 20–34 and 35–50 years. The data were used to construct the age and gender specific calibration curves. The dispersion index, normalized unit of this index, goodness-of-fit, and the chi-squared test for homogeneity were performed with the Dose Estimate software.

In order to validate the created dose-response curves, blood samples from two overexposed workers in industrial radiography centers for nondestructive testing of metal objects (A and B aged 22 and 29 years) and 3 irradiated blinded samples were measured. The dose was estimated for each subject using the previously generated calibration curve from our laboratory using dicentric assay and the created gender- and age-specific calibration curve of gamma-ray-induced micronuclei. The spontaneous MN frequency of 130 healthy non-exposed donors (77 men and 55 women, 20-60 years old divided in four age groups) and the relationships of these frequencies to factors such as age and gender have been established.

The comparison of the results obtained by the two techniques indicated a good agreement between the dose estimates. Biologically estimated doses for case A were 0.808 ± 0.092 Gy by dicentric analysis vs. 0.810 ± 0.107 with 95% CI of 0.599-1.020 Gy by CBMN assay and for case B were 0.306 ± 0.083 by dicentric analysis vs. 0.319 ± 0.089 with 95% CI of 0.144-0.494 Gy by CBMN assay. The results of the u-test for MN distribution, none of the samples from the overexposed workers had a Poisson distribution. The average baseline frequency of micronuclei for the 130 individuals ranged from 6 to 21 MN per 1000 binucleated cells and MN frequencies were higher for women and for the older age group.

\textbf{Conclusion:} The results point out that the scoring of either dicentrics or micronuclei are reliable methodologies for biological dosimetry. However, as scoring of MN is faster and easier than chromosome aberrations, this assay may be more suitable for emergency responses to a large-scale accident and occupational bio-monitoring studies. Development of an automated MN scoring system and preparation of calibration curve by using a pancentromeric probe and applying FISH technique are currently underway in our laboratory.