

Biophysical Modeling Radiation-Induced Chromosomal Aberrations as Biomarkers of Exposure

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A mechanistic model and Monte Carlo (MC) computer code were developed for evaluating radiation-induced chromosomal aberrations in human lymphocytes aimed to investigate the role played by the stochastic track structure, organization of interphase DNA and rejoining algorithm. The model was based on the assumption that only clustered DNA breaks (CB) can produce observed aberrations whereas all simple breaks are repaired. The induction of single- and double-strand breaks was simulated and further classified by complexity with previously developed MC code [1]. An induced CB are distributed in lymphocyte nucleus according to stochastic track structure. Each of 46 human chromosomes was modeled as a 3D random polymer inside spherical 3 μm radius sphere composed of cubic non-overlapping boxes. A spatial coordinates of CB were stored and compared with the coordinates of cubic boxes to evaluate initial chromosome lesions. Then Revell's exchange hypothesis is applied assuming that only chromosome lesions with initial distance smaller 1.5 μm can interact and form aberrations. It was used the scoring criteria adopted for Giemsa-stained chromosomes useful for biological dosimetry, namely dicentrics, rings, translocations and complex exchanges. The small fragments were neglected in order to reproduce experimental conditions. In vitro dose-response curves for dicentric and centric rings induced by gamma-rays were simulated and compared with experimental data including own results [2]. The model showed good agreement between theoretical curves and available experimental data from lymphocyte irradiation. The obtained results suggest that CB are critical events for chromosomal aberration induction and interphase chromosome structure of cell nuclear is an important factor in the mechanism of aberration formation.

References.

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2. Sevankaev A.V., Khvostunov I.K., Mikhailova G.F. et al. (2000) Novel data set for retrospective biodosimetry using both conventional and FISH chromosome analysis after high accidental overexposure, Applied Radiation and Isotopes 52, 1149-1152.