The Distribution of Chromosomal Aberrations in Human Cells as Predicted by a Generalized Model of Radiation-Induced Aberration Formation

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We formulated a generalized model of chromosomal aberrations based on a stochastic Monte Carlo approach and calibrated the model using the relative frequencies and distributions of chromosomal rings and dicentrics predicted by the experiment. The extrapolation of the data on aberrations to smaller objects, such as smaller chromosomal rings is possible. Such smaller rings cannot be noticeable in established experimental techniques (Giemsa staining and fluorescence in-situ hybridization (FISH)), and only hypotheses abound about their true number. The chromosomal-aberrations model based on the previously developed DNA-fragmentation model for high- and low-LET radiations provides an explanation and prediction of the statistics of rare and more complex aberrations. The model simulates a stochastic process of chromosomal aberration formation from DNA fragments and gives predictions of the distribution of dicentrics and rings. The impact of the DNA loops has been studied on the aberration formation. Auxiliary data are presented for complex chromosomal aberrations, dicentrics, centric rings, inversions, translocations and exchanges. The relation between deletions and rings is analyzed, as these aberrations are closely related. The fraction of DSBs participating in aberrations is predicted. The theoretical analysis provides the consistent distributions of variety of aberrations classes (dicentrics, acentric and centric rings, translocations, exchanges and complex aberrations). We assess the differences in the scoring of different classes of aberrations using 2- or 3-color FISH to scoring with the complete genomes as done with M-FISH. Many of the aberrations considered are detrimental to cell survival, including transmissible aberrations that can contribute to the risk of carcinogenesis.