Distribution of radiation-induced breaks in chromosomes: Effects of dose, dose rate and radiation quality

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The distribution of breakpoints in chromosomes has been an interest in cancer research as a large number of malignant diseases are associated with chromosome aberrations containing breaks in specific regions. To study the effects of low- and high-linear energy transfer (LET) radiation on break locations within a chromosome, we exposed human epithelial cells \textit{in vitro} to Cs-137 $\gamma$-rays at both a low and a high dose rate, secondary neutrons at a low dose rate, and 600 MeV/u Fe ions at a high dose rate. Breakpoints were identified using multicolor banding \textit{in situ} hybridization (mBAND), which paints chromosome 3 in 23 different colored bands, and allows identification of both inter- and intrachromosome aberrations. The distributions of the total breaks, as well as the breaks involved in inter- and intrachromosome exchanges were analyzed. Detailed analysis of the chromosome fragment ends involved in inter- or intrachromosomal exchanges revealed that only the fragment ends participating in interchromosomal exchanges contributed to the hot spots found for low-LET. For fragment ends participating in intrachromosomal exchanges, the distributions for all four radiation scenarios were similar. Analysis of the locations of the two fragment ends in chromosome 3 that joined to form an intrachromosomal exchange demonstrated that two breaks with a greater genomic separation can be more likely to rejoin than two closer breaks, indicating that chromatin folding can play an important role in the rejoining of chromosome breaks. Our study demonstrated that the gene-rich regions do not necessarily contain more breaks. The breakpoint distributions are associated with whether a chromosome fragment joins with another fragment in the same chromosome or with a fragment from a different chromosome.