Search for chromosomal Biomarkers specific to a prior Exposure to densely ionizing Radiation

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Recently there has been considerable interest in identifying biomarkers of radiation exposure that allow both to estimate the dose to which an individual has been exposed and to determine, whether the initial exposure was to low or high LET radiation. However, published data are controversial, probably due to large inter-laboratory differences in aberration scoring.

To contribute to this issue, we reanalysed 35 data sets generated at GSI (Darmstadt) for human lymphocytes and fibroblasts as well as for Chinese hamster cells (V79, CHO-K1, xrs5). In the experiments cells were exposed in G1-phase to heavy ions (C, O, Ne, Ar, Kr, Fe and Au ions) covering an LET range of 13 to 4000 keV/μm. For comparison, X-ray experiments were performed. More than 80000 first generation metaphases were analysed, identified by BrdU incorporation and subsequent fluorescence-plus-Giemsa staining. To account for drastic cell cycle transition delays after high LET exposure, metaphases were collected at several post-irradiation sampling times. Then, for the analysis of data, the aberration yields were averaged over dose and time.

For all cell types tested, the aberration spectrum did not change up to LET value of about 200 keV/μm. Thereafter, LET-dependent changes occurred: For example, the fraction of dicentrics among all aberration-types detectable by Giemsa-staining declined, while the fraction of excess acentrics increased. Furthermore, an unexpected high number of chromatid-type aberrations was found, although cells have been exposed in G1-phase. This observation suggests that high LET radiation induces a significant number of single strand breaks and alkali-labile sites that remained unrepaired throughout G1 and are converted in double strand breaks during S-phase. As a consequence, chromatid-type aberrations are found in the subsequent mitosis. Interestingly, none of the observed changes showed a dose-dependence. Furthermore, our data demonstrate that the aberration spectrum is strongly influenced by the repair capacity of the cell type under study.

The potential of aberration measurements from solid stained metaphases to identify a fingerprint of high LET radiation will be discussed. Furthermore, recent data obtained for human lymphocytes exposed *in vitro* or *in vivo* to C ions or X-rays and analysed by Giemsa-staining and multicolour fluorescence in situ hybridisation (m-FISH) will be presented.