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Gamma-H2AX irradiation induced foci (IRIF) in cells exposed to a mixed beam of X-rays and alpha particles.

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Increasing exposure of cancer patients to a mixed beam of high and low linear energy transfer (LET) ionizing radiation is an issue of growing concern. Little is known about the health effects of exposing organisms and cells to mixed beam irradiation. The effect of combined exposures has mainly been assessed with clonogenic survival or cytogenetic methods, and the results are contradictory. The gamma-H2AX assay has up to now not been applied in this context, and is thus a promising tool for investigating the early cellular response to mixed beam irradiation. In this study, VH10 human fibroblasts were irradiated with 241Am alpha particles, X-rays, or a combination of both at 37 °C. Gamma-H2AX ionizing radiation-induced foci (IRIF) were scored for repair kinetics 0.5, 1, 3 and 24 h after irradiation (one dose per irradiation type), and for dose response at the 1 h time point. For dose response the effect of mixed beam was additive, and the relative biological effectiveness (RBE) for alpha particles (as compared to X-rays) was of 0.76 ± 0.52 for IRIF, and 2.54 ± 1.11 for large foci (LF). The repair kinetics for total number of IRIF in cells exposed to mixed beam irradiation was intermediate to that of cells exposed to alpha particles and X-rays. However, for mixed beam-irradiated cells the frequency and area of LF were initially lower than predicted and increased during the first 3 hours of repair (while the predicted number and area did not). Moreover, LF in mixed beam-irradiated cells were not phosphorylated to their full extent until 1 h after exposure. We hypothesize that the presence of low LET-induced damage engages the DNA repair machinery leading to a delayed repair of the more complex DNA damage induced by alpha particles.

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