Low dose radiation hypersensitivity and clustered DNA damages in human fibroblasts exposed to low dose and dose rate protons of $^{137}$Cs $\gamma$-rays; abstract

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Low dose radiation hypersensitivity and clustered DNA damages in human fibroblasts exposed to low dose and dose rate protons or $^{137}$Cs $\gamma$-rays

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Effective radioprotection for human space travelers hinges upon understanding the individual properties of charged particles. A significant fraction of particle radiation astronauts will encounter in space exploratory missions will come from high energy protons in galactic cosmic radiation (GCR) and/or possible exposures to lower energy proton flux from solar particle events (SPEs). These potential exposures present major concerns for NASA and others, in planning and executing long term space exploratory missions. We recently reported cell survival and transformation (acquisition of anchorage-independent growth in soft agar) frequencies in apparently normal NFF-28 primary human fibroblasts exposed to $0-30$ cGy of $50\text{MeV}$, $100\text{MeV}$ (SPE-like), or $1000\text{MeV}$ (GCR-like) monoenergetic protons. These were modeled after 1989 SPE energies at an SPE-like low dose-rate (LDR) of $1.65$ cGy/min or high dose rate (HDR) of $33.3$ cGy/min delivered at the NASA Space Radiation Laboratory (NSRL) at BNL [1].

We now report on studies including matched doses and dose rates of $^{137}$Cs $\gamma$-rays, an important reference radiation for calculating relative biological effectiveness (RBE). Analysis of clonogenic survival results reveal a window of low dose radiation hypersensitivity (HRS) with all four radiation species tested. This is suggestive of an HRS-like “induced repair” survival response [2]. Transformation frequencies (TFs) are maximal ($<25\text{cGy}$) for HDR protons. TFs for LDR protons did not peak in the low dose range, but continued to increase with the accumulation of dose ($50\text{cGy}$-$100\text{cGy}$). In contrast, TFs produced by $^{137}$Cs $\gamma$-rays which increase linearly with increasing dose accumulation.

On the hypothesis that protons may induce DNA damages that are more complex thus more refractory to repair or removal than those produced by $^{137}$Cs $\gamma$-rays levels of DNA double strand breaks (induction and removal) were measured, electrophoretically and by $\gamma$-H2AX pS139 focus detection. Induction and removal of oxidative bystranded clustered damages, which are mutagenic [3], were also measured for both HDR and LDR cell exposures. Slopes of clustered DNA damage induction and removal incurred in apparently normal human fibroblast strain 28 by proton radiation vs. $^{137}$Cs $\gamma$-rays at HDR vs. LDR to be presented.


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