Particles with similar LET values generate DNA breaks of different complexity and reparability: a high-resolution microscopy analysis of γH2AX/53BP1 foci

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Biological effects of high-LET (linear energy transfer) radiation have received increasing attention, particularly in the context of more efficient radiotherapy and space exploration. Efficient cell killing by high-LET radiation depends on the physical ability of accelerated particles to generate complex DNA damage, which is largely mediated by LET. However, the character of DNA damage and repair upon exposure to different particles with similar LET parameters remains unexplored. We employed high-resolution confocal microscopy to examine phosphorylated histone H2AX (γH2AX)/p53-binding protein 1 (53BP1) foci streaks at the microscale level, focusing on the complexity, spatiotemporal behaviour and repair of DNA double-strand breaks generated by boron and neon ions accelerated at similar LET values (~135 keV/μm) and low energies (8 and 47 MeV/n, respectively). Cells were spatially (3D) fixed and irradiated using a sharp-angle geometry to maximize the resolution of these analyses. Both high-LET radiation types generated highly complex γH2AX/53BP1 foci clusters with a larger size, increased irregularity and slower elimination than low-LET γ-rays. Surprisingly, neon ions produced even more complex γH2AX/53BP1 foci clusters than boron ions, which is consistent with DSB repair kinetics. Although cells exposed to γ-rays and boron ions eliminated a vast majority of foci (94 % and 74 %, respectively) within 24 h, this value was only 55 % in cells irradiated with neon. Our calculations suggest that the complexity of DSB damage critically depends on the particle track core diameter. Thus, different particles with similar LET and energy may generate different types of DNA damage, which should be considered in future research.

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