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Comparison of Monte Carlo Simulations and Experimental Results for the Measurement of Complex DNA Damage Induced by Ionizing Radiations of Different Quality

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Abstract : Complex DNA damage consisting of a combination of DNA lesions, such as Double Strand Breaks (DSBs) and non-DSB base lesions occurring in a small volume is considered as one of the most important biological endpoints regarding ionizing radiation (IR) exposure. Strong theoretical (Monte Carlo simulations) and experimental evidence suggests an increment of the complexity of DNA damage and therefore repair resistance with increasing linear energy transfer (LET). Experimental detection of complex (clustered) DNA damage is often associated with technical deficiencies limiting its measurement, especially in cellular or tissue systems. Our groups have recently made significant improvements towards the identification of key parameters relating to the efficient detection of complex DSBs and non-DSBs in human cellular systems exposed to IR of varying quality (γ-, X-rays 0.3-1 keV/μm, α-particles 116 keV/μm and 36Ar ions 270 keV/μm). The induction and processing of DSB and non-DSB-oxidative clusters were measured using adaptations of immunofluorescence (γH2AX or 53PB1 foci staining as DSB probes and human repair enzymes OGG1 or APE1 as probes for oxidized purines and abasic sites respectively). In the current study, Relative Biological Effectiveness (RBE) values for DSB and non-DSB induction have been measured in different human normal (FEP18-11-T1) and cancerous cell lines (MCF7, HepG2, A549, MO59K/J). The experimental results are compared to simulation data obtained using a validated microdosimetric fast Monte Carlo DNA Damage Simulation code (MCDS). Moreover, this simulation approach is implemented in two realistic clinical cases, i.e. prostate cancer treatment using X-rays generated by a linear accelerator and a pediatric osteosarcoma case using a 200.6 MeV proton pencil beam. RBE values for complex DNA damage induction are calculated for the tumor areas. These results reveal a disparity between theory and experiment and underline the necessity for implementing highly precise and more efficient experimental and simulation approaches.

Keywords : complex DNA damage, DNA damage simulation, protons, radiotherapy
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