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The radiobiology of laser-driven particle beams: focus on sub-lethal responses of normal human cells

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Proton-based radiotherapy has become an increasingly common cancer treatment modality. The clinical exploitation of accelerated protons relies on their superior ballistic properties compared to photons, which translates in advantageous dose distribution to tumor and sparing of normal tissue. The need for cost and size reduction of particle accelerating machines, which would arguably benefit protontherapy adoption on a larger scale, is driving interdisciplinary research efforts towards novel, compact, single-room accelerators. Optical ion acceleration based on laser-plasma interaction has opened new scenarios as a possible alternative to classic accelerators in the future. Particle beams produced by laser-matter interaction consist of extremely pulsed particle bursts of ultra-high dose rates (≥ 109 Gy/s), largely exceeding those currently used in conventional proton therapy. Since the biological effects of ionizing radiation are strongly affected by the spatio-temporal distribution of DNA-damaging events, the unprecedented physical features of such beams may well impact the cellular outcome and any clinical application of laser-generated particles must be therefore validated by careful assessment of their radiobiological effectiveness. To date, the majority of studies carried out in this new field have either used rodent cell lines or have focussed on cancer cell killing being local tumour control the main objective of any radiotherapy strategy. The results thus far obtained seem to indicate no significant difference between laser-driven and conventionally accelerated proton beams. However, very little or no data at all exist on (sub)-lethal cellular effects of relevance to normal tissue integrity such as cytogenetic damage and premature cellular senescence. We shall therefore briefly discuss their role in particle-based therapy and present preliminary data on survival and cellular senescence of normal human cells following exposure to a laser-driven proton beam.

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