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Beam temporal structure of laser-driven VHEE beams affects biological response

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Laser-Plasma Accelerators (LPAs) can reliably generate Very High Energy Electrons (VHEE, >50 MeV), a promising radiotherapy modality due to their favorable depth-dose profiles and potential for ultra-high dose-rates required for FLASH therapy. While most biological studies involving LPAs focus on beam energy and dose target, the temporal structure of radiation delivery, specifically the electron bunch repetition rate, remains unexplored. This timing parameter, tunable according to machine configuration, may play a critical role in shaping biological effects.

To investigate this aspect, we optimized a 150TW LPA to deliver electrons in the 50–100 MeV range, with an average charge exceeding 500 pC/shot and a dose of ~350 mGy/shot. We systematically varied the repetition rate (1-0.5-0.2-0.1 Hz), while keeping the electron energy and average dose constant. Biological effects were assessed *in vitro* (healthy fibroblasts, MRC5; colorectal cancer cells, HCT116) and *in vivo* (zebrafish embryos), using survival and developmental toxicity as endpoints.

Results showed that beam temporal structure strongly modulates biological response: higher repetition rates (1 Hz) reduced toxicity in healthy models, while tumor cells exhibited the opposite trend. These findings identify bunch repetition rate as a key accelerator parameter for tuning radiobiological outcomes, with direct implications for the development of LPA-based preclinical applications.

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