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FLASH proton irradiation of normal and breast cancer cells

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Recent preclinical studies in mice and other animal models have demonstrated a protective effect of FLASH (very high dose-rate) radiotherapy in healthy tissues, while apparently not compromising its curative ability. Since clinical proton accelerators still require of hardware adaptation to produce FLASH rates, biological experiments on FLASH proton therapy (FLASH-PT) can be conducted on nuclear physics accelerators. The 5-MV tandem accelerator at CMAM (Madrid) offers an excellent setup for such experiments, with proton beams up to 10 MeV and hundreds of times more intense than clinical beams and the capacity to irradiate samples with sub-millimeter precision.

Using specifically designed pinhole collimators, we were able to obtain a range of dose rates from 0.1 to 1000 Gy/s, covering both FLASH and standard-rate protontherapy. We developed a smart irradiation system based on 3D-printed materials and robotic actuators, coupled with a specifically designed 2D treatment planning system for cell-culture samples. Dosimetry was performed using a Faraday cup combined with EBT3 films.

We used the irradiation system to deliver up to 8 Gy in healthy fibroblast cell lines (obtained from fresh mammary tissue from women undergoing mammoplasty), tumor associated fibroblasts and MDA-MB-231 (triple negative) breast cancer cells. Initial results show a clear negative spatial correlation between delivered dose and cell survival for tumour cells irradiated at FLASH rates. Full analysis of the irradiated samples (ongoing) will include determination of DNA damage by H2AX foci formation, proliferation using Ki67, and study of additional markers like HIF-1.

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