Radiobiology with laser-driven ions at ultra-high dose rate

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Background: Cancer ranks as a leading cause of death worldwide, motivating research in developing more advanced and effective forms of therapy. Treatment of cancer using radiation (radiotherapy) is particularly important in this context, and is delivered most commonly employing x-ray- photons, but also, in its more advanced form, employing high energy protons or carbon ions. An emerging radiotherapy concept currently attracting a phenomenal amount of research interest is the so-called FLASH approach, where radiation dose is delivered to the patient in short pulses, at a dose rate of 10 to 1000s Gray/second. In animal models, FLASH delivery has been seen to result in significant sparing of the healthy tissues surrounding the tumour and a remarkable decrease in side effects, while maintaining a pronounced effectiveness in destroying the cancerous cells. These results have triggered a broader fundamental interest in the investigation of the biological effects of highly pulsed radiation beams. Laser-acceleration of ions, a technique pioneered by our group at QUB, provides particle pulses with an intrinsically ultrashort (typically of picosecond order or less) temporal duration. This offers the opportunity to irradiate samples at extreme dose rates never reached before, many orders of magnitude higher than even in the FLASH regimes discussed above. This opens to investigation unexplored regimes of radiobiology, where preliminary data highlight a complex scenario which challenges established understanding of radiation interaction with cellular media and requires new hypotheses and models, highlighting this regime as particularly promising for future radiotherapy.

Project description: The project will be devoted to the investigation of the biological effects of exposure to ultra-high dose rate, laser-driven ion beams. During our recent research, we have developed and perfected irradiation platforms and techniques which can now be transferred across a variety of facilities for maximum scientific exploitation. The project will test, employing the latest developments in particle acceleration and delivery, as well as a range of relevant assays in cell and tissue models, the quality and quantity of cellular damage produced by ultrashort burst of protons and carbons. Key questions to be addressed are how the extreme spatio-temporal density of ionization tracks affects the cellular response, whether the ultrashort delivery affects the cell oxygenation, and how this is affected by the cellular microenvironment. We also aim to assess whether FLASH-type differential response between healthy and cancerous cell can be extended to the ultra-high-dose rate regime. These interdisciplinary studies will take advantage of the excellent and unique capabilities available at the partner institution's facilities.
The project offer the student the unique opportunity for training at the interface between physics and biology, which will be enhanced by specific expertise available at the partner's institution (e.g. in particle transport , numerical modelling, radioprotection and laser operations) . There is potential for acquiring skills and knowledge in a broad range of areas, including laser-plasma interaction experimental techniques; particle diagnostics and dosimetry; cell culture and handling; cell exposure techniques; biological assays; data analysis techniques in physics and biology; Montecarlo modelling of particle transport. Throughout the project, the student will have access to research capabilities and facilities at the leading edge internationally. We envisage that a large fraction of the research will be carried out at the ELI Beamlines facility, which is emerging as the leading European centre for the provision of laser-accelerated particle beams. At ELI Beamlines, the student will contribute to the flagship experimental activities carried out within the framework of the EU-funded IMPULSE project. Research will also be carried out in the UK, mainly at the STFC Central Laser Facility (CLF), of which our group is a major user. CLFs' VULCAN Petawatt and GEMINI lasers are also internationally leading systems which will provide unique capabilities to the student's research.

Funding: The studentship will be supported for 3.5 years through EPSRC funding, and will include a top-up of £2K per year (sponsored by ELI Beamlines) above the baseline studentship salary.

Background reading:

P. Chaudhary et al, *Radiobiology Experiments With Ultra-high Dose Rate Laser-Driven Protons: Methodology and State-of-the-Art*, Front. Phys., **9**, 624963 (2021)

F. Hanton, et al., *DNA DSB Repair Dynamics following Irradiation with Laser-Driven Protons at Ultra-High Dose Rates*, Sci.Reports. **9**, 4471 (2019)

D. Margarone, et al., *ELIMAIA: A Laser-Driven Ion Accelerator for Multidisciplinary Applications*, Quantum Beam Sci., **2**, 8 (2018)