# New Frontiers in radiobiology, ion-beam science and radiotherapy

*through discovery, innovation and co-creation*

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*For the LhARA collaboration*[i].

**Primary EPSRC Theme:** Healthcare Technology

**Indicative cost and duration:** £xxxM; 6 years

## 1. Vision and strategic ambition

Radiotherapy is an effective tool in the treatment of cancer. It is used in 50% of treatments and is instrumental in 40% of cancer cures. This outstanding clinical impact is built on phenomenological parameterisations of the impact of ionising radiation on tissue. However, the fundamental biology that determines the response of normal and cancerous tissues to ionising radiation is not well understood. New techniques are required to measure the evolution of the biological response of cells, tissues, and organisms to the physical characteristics of the beam. The goal of such studies will be to understand the biological processes and to exploit this understanding to enhance treatment regimens in state-of-the-art facilities and to develop transformative techniques to exchange the range and efficacy of radiotherapy.

Radiotherapy is most often provided using X-ray or electron beams. The benefits of radiotherapy delivered using proton and ion beams is widely recognised. Recent results indicate that delivering the dose at ultra-high dose-rate (FLASH) and spatially fractionated radiotherapy underline both the importance of these unknowns and the opportunities that advances in fundamental understanding could create for cancer treatment.

Recent advances in high-power pulsed laser technology, plasma-based accelerator techniques, microscopy, automation and machine learning create an unprecedented opportunity to transform experimental radiobiology. The LhARA collaboration has been formed to exploit these advances to develop a uniquely flexible laser-hybrid accelerator facility dedicated to fundamental radiobiological research. LhARA, the Laser-hybrid Accelerator for Radiobiological Applications, will combine a laser-driven source of intense, pulsed proton and ion beams with strong-focusing plasma lenses and a fixed-field alternating-gradient accelerator. The resulting flexibility in particle species, energy, intensity, temporal structure and spatial distribution will make it possible to investigate radiation-induced biological processes under conditions that are difficult or impossible to achieve using conventional sources. The knowledge gained will lay the foundations for new approaches to proton- and ion-beam therapy.

With this proposal we seek the resources to establish and sustain a six-year, multidisciplinary programme of scientific discovery, technological innovation and co-creation that will push back three interconnected frontiers:

- The frontiers of experimental radiobiology: developing advanced automation, precision irradiation control and time-resolved live-cell microscopy to enable systematic, quantitative investigations of the mechanisms governing cellular response to ionising radiation.
- The frontiers of accelerator science: developing and demonstrating electron-plasma lenses capable of providing the strong focusing required to capture, transport and manipulate intense, pulsed proton and ion beams, thereby advancing a critical enabling technology for laser-hybrid acceleration.
- The frontiers of radiotherapy technology: co-creating with industry, in particular Leo Cancer Care, the technologies required for automated radiation delivery and in-situ, real-time measurement of the delivered dose and its spatial distribution, with the ambition of enabling more precise, adaptive and ultimately personalised radiotherapy.

Benefits of a programme grant ... the three frontiers cannot be advanced effectively through a series of independently funded projects. Their scientific and technological challenges are interdependent, the required expertise is distributed across institutions and sectors, and the direction of the research must evolve as experiments reveal new phenomena and technological demonstrations establish new possibilities.

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[i] The **LhARA** collaboration:

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