The Laser-hybrid Accelerator for Radiobiological Applications

R&D proposal for the preliminary, pre-construction phases

The LhARA collaboration

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Executive summary

The LhARA collaboration's long-term vision [1] is to transform the clinical practice of proton- and ion-beam therapy (IBT) by creating a fully automated, highly flexible system to harness the unique properties of laser-driven ion beams. Such a facility will be capable of delivering particle-beam therapy in completely new regimens by combining a variety of ion species from proton to carbon in a single treatment, exploiting ultra-high dose rates and novel temporal-, spatial- and spectral-fractionation schemes. The automated, laser-hybrid system will integrate patient, soft-tissue and dose-deposition imaging with real-time treatment planning to trigger the delivery of dose tailored to the individual patient in real time. The automated, triggerable system we propose has the potential to remove the requirement for a large gantry, thereby reducing the size and therefore the cost, of a clinical IBT facility and to follow movement of patient and tissue, thereby increasing patient throughput and reducing the cost of IBT per patient.

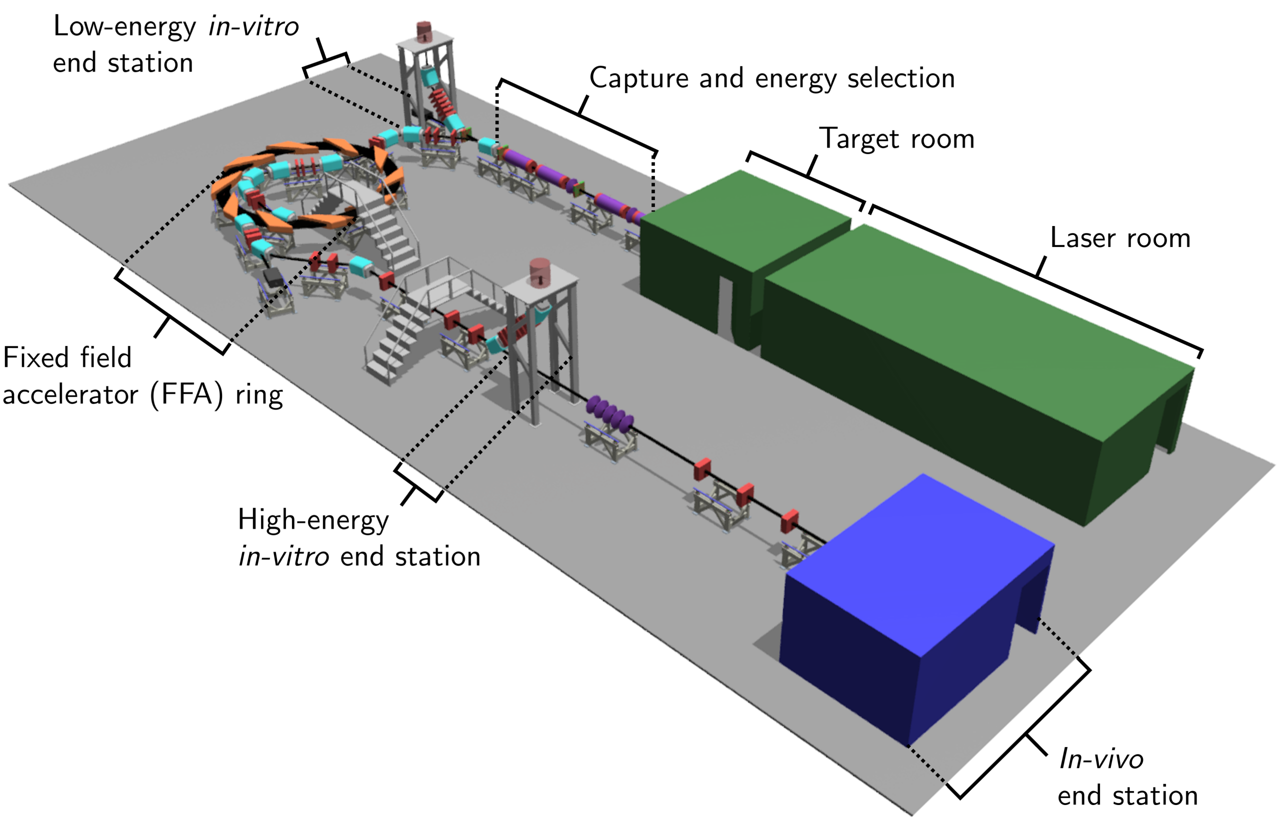


Figure 1: LhARA—the Laser-hybrid Accelerator for Radiobiological Applications. Two separate shielded areas are planned to accommodate the laser and target system. After the 'Capture and energy selection' section of the beamline, the beam is directed either to the vertical *in-vitro* end station or injected into the fixed-field alternating-gradient (FFA) ring. After post-acceleration, the beam is extracted from the FFA and directed either to the high-energy *in-vitro* end station or to the *in-vivo* end station.

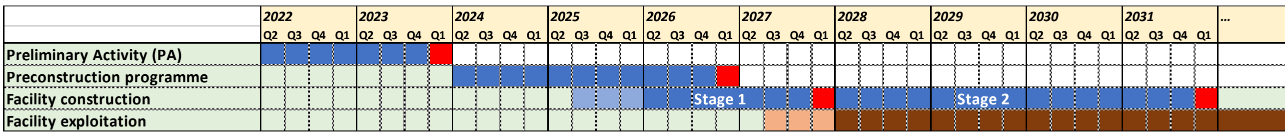
We propose to develop LhARA [2, 3], the Laser-hybrid Accelerator for Radiobiological Applications, to serve the "Ion Therapy Research Facility" (ITRF) [4]. LhARA is conceived as the new, highly flexible, source of radiation that is required to explore the vast "terra incognita" of the mechanisms by which the biological response to ionising radiation is determined by the physical characteristics of the beam [5]. The LhARA collaboration's concept, shown in figure 1 is to exploit a laser to create a large flux of protons or light ions which are captured and formed into a beam by strong-focusing plasma lenses. The triggerable, laser-driven source allows protons and ions to be captured at energies significantly above the capture energies of conventional facilities, elegantly circumventing the current space-charge limit on the instantaneous dose rate that can be delivered [6]. The plasma (Gabor) lenses provide the same focusing strength as high-field solenoids at a fraction of the cost. Post-acceleration using a fixed field alternating gradient accelerator (FFA) preserves the unique flexibility in the time, energy, and spatial structure of the beam afforded by the laser-driven source.

The multi-disciplinary LhARA collaboration [7, 8] consists of clinical oncologists, medical, particle, plasma, laser, ultrasound, and optical physicists, accelerator, computer, and instrumentation scientists, radiobiologists, industrialists, and patient representatives. With this proposal, the collaboration seeks to initiate its broad and ambitious, multi-disciplinary programme to:

- Demonstrate the feasibility of the laser-hybrid approach in a facility dedicated to biological research; and
- Create the national and international partnerships necessary for LhARA to become a multidisciplinary research centre of excellence in the UK.

LhARA formed the basis of a recent proposal to the UK Research and Innovation (UKRI) Infrastructure Advisory Committee to create an "Ion Therapy Research Facility" (ITRF) [4]. The proposed ITRF "*. . . will be a unique, compact, single-site national research infrastructure delivering the world's first high-dose-rate ions from protons through oxygen and beyond, at energies sufficient for both in-vitro and in-vivo studies.*" The ITRF proposal notes that a "*. . . laser-hybrid proton/ion source, as proposed by the existing, UK-led, international LhARA collaboration . . . can deliver this and meet the needs of the ITRF.*" The proposal is for a two-year Preliminary Phase activity and identifies the need for a subsequent three-year pre-construction phase. The timeline for the development of LhARA to serve the ITRF defined in the proposal is shown in table 1.

Table 1: Timeline for the development of LhARA to serve the Ion Therapy Research Facility presented in the proposal to the UKRI Infrastructure Advisory Committee [4].



We propose that LhARA be developed to serve the ITRF in two stages [2, 3]. In Stage 1, the laser-driven beam, captured and transported using plasma lenses and bending magnets, will serve a programme of *in-vitro* experiments with proton beams of energy of up to 15 MeV. In Stage 2, the beam will be accelerated using an FFA. This will allow experiments to be carried out *in vitro* and *in vivo* with proton-beam energies of up to 125 MeV. Ion beams (including C^{6+}) with energies of up to 30 MeV per nucleon will also be available. The beam energy at LhARA has been specified to allow *in-vitro* experiments and *in-vivo* studies using small mammals. The LhARA collaboration's hybrid approach will allow the unique properties of the laser-driven source—extremely high instantaneous flux in an extremely short pulse over a tiny area—to be preserved and exploited to deliver radiobiological investigations in completely new regimens.

The collaboration will build on its present industrial links to ensure appropriate industrial engagement from the outset. Such engagement is essential if the technology-development programme is to yield practical, cost-effective solutions. As the LhARA build-phase becomes established, the collaboration's will continue to work with its industrial partners to develop a laser-hybrid system capable of clinical deployment. This approach will ensure timely development of industrial capability and provide the opportunity for UK industry to take pole position in the delivery of the IBT systems of the future.

With this proposal, we seek the resources to deliver the Preliminary Activity and Preconstruction Phase of the programme necessary for LhARA to serve the ITRF. Over the first two years the Preliminary Phase will:

- Deliver the Conceptual Design Report for LhARA to serve the Ion Therapy Research Facility;

- Demonstrate the feasibility of the laser-driven creation of the requisite proton and ion flux through measurement and simulation;
- Create the detailed specification of a second Gabor-lens prototype through a programme of experiment, simulation, and design;
- Experimentally prove the principle of ion-acoustic dose-profile measurement; and
- Create a detailed specification for the *in-vitro* and *in-vivo* end stations through peer-group consultation, design and simulation.

The Preconstruction Phase will be carried out over years three to five and will deliver Technical Design Reports for LhARA Stage 1 in year 3 and LhARA Stage 2 in year 5. The programme of technical-risk mitigation will continue and will culminate in the production of complete designs for a proton and ion production target and capture system capable of 10 Hz operation, the detailed design of the Stage 2 FFA, and the beam-line and end-station instrumentation necessary to provide fast feedback and control to the accelerator components.

The proposed five-year programme will lay the foundations for the establishment of an entirely new technique for delivery of proton and ion beams for science and innovation. Serving the ITRF, LhARA will be a unique, compact, research infrastructure delivering ions from protons to carbon at energies sufficient for both *in-vitro* and *in-vivo* studies. Fundamentally new biological mechanisms in radiation treatment and immune response which underpin the clinical efficacy of future proton- and ion-beam therapy will be elucidated. Exploitation of LhARA at the ITRF will promote the disruptive accelerator, diagnostic, imaging, and computing technologies required radically to transform clinical practice.

Lay summary

The LhARA collaboration's mission is to revolutionise ion-beam radiotherapy (IBT). The ambition is to greatly improve the accuracy and effectiveness of IBT in destroying cancer cells while minimising the risk of damage to healthy tissue. Integral to the vision is the development of the novel instrumentation and diagnostics required to automate the treatment facility. Such automation is essential to increase throughput. As a crucial first step towards its goals the collaboration proposes the construction and exploitation of a research facility that will exploit emerging new laser-plasma accelerator technology to deliver beams of protons and ions onto biological materials to study their cancer-killing properties. This will prove the principle of the new technologies and allow the best space and time structures of the beams to be evaluated.

The clinical need is clear. In the UK it is anticipated that 1 in 2 people will develop cancer and the present incidence of 17 million new cases per year globally is predicted to increase to 27.5 million new cases per year by 2040. Radiotherapy is used in treatments of 50% of cancer patients and results in 40% of cancer cures, second only to surgery. The UK currently sits at the bottom of the league of cancer survival for high income countries and the UK Government has recently announced that it wants a War on Cancer and is committed to increasing cancer cures. For many years, radiotherapy using beams of high energy X-rays has been the main way of delivering radiotherapy. This has proved to be very effective for many types of cancer although there is a risk of damage to non-cancerous tissues. Recently, proton-beam-based radiotherapy has been used. In the UK, the NHS has brought into action two proton-beam machines, one in Manchester and one in London. Many more proton-beam therapy centres are in operation in other countries. There is a clinical need for increased UK coverage and to reduce the cost per patient while improving the effectiveness of the therapy and reducing its side effects.

Exciting recent results indicate that short pulses of ions and protons confined in very narrow beams have excellent therapeutic effect while significantly reducing damage to healthy tissue. This is new science which needs to be researched and tested thoroughly to enable the next step of designing and manufacturing a new class of radiotherapy machines for clinical use to be taken. The new class of machine has the potential to reduce a course of radiotherapy to period of days rather than weeks and to enable more patients to be treated.

The LhARA collaboration of accomplished physicists, engineers, medical scientists and clinicians from several universities and research institutes will bring together their expertise and experience to build and operate this world-leading research facility. This would lead both to significant advances in our understanding of cancer biology as well as the establishment of technology to greatly improve cancer treatments to the benefit of patients all around the world at a reduced cost per patient. Specific tasks include the development of the laser-driven production of the required fluxes of protons and ions, the production of beams and their focussing using electron plasma lenses (Gabor lenses), the acceleration of the beams using a fixed-field alternating-gradient accelerator and beam guidance onto laboratories for biological experiments where the research into radiobiology will be carried out.

LhARA will be a UK investment which, serving the Ion Therapy Research Facility, will attract scientists from around the world, create jobs in engineering, construction, science and technology (lasers, electron-plasma lenses, accelerator physics, ion-acoustic imaging, robotics, chemistry, and biology), it will develop increased international collaboration including with CERN in Switzerland, and the National Institute of Radiological Sciences in Japan, with the potential to attract crucial inward and external industrial funding. This would facilitate the production of new machines for clinical use to be sold throughout the world.

References

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[8] "The Laser-hybrid Accelerator for Radiobiological Collaboration institute slide." `https://ccap.hep.ph.ic.ac.uk/trac/raw-attachment/wiki/Research/DesignStudy/2021-05-11-Institute-slide-v8.pdf`, May, 2021. Accessed: 2021-12-22.