ERC Advanced Grant 2020

Research proposal [Part B1][[1]](#footnote-1)

*(Part B1 is evaluated both in Step 1 and Step 2,*

*Part B2 is evaluated in Step 2 only)*

Super-efficient ion capture to harness laser-hybrid accelerators for science, innovation, and society

CaptureLhARA

**Cover Page:**

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* Name of the PI's host institution for the project : Imperial College London
* Proposal duration in months : 60

X-ray therapy is central to cancer treatment and is most often delivered using a source that rotates around the patient. The energy deposited by X-rays falls exponentially with depth, limiting the dose that may be delivered to a tumour without exposing healthy tissue to unacceptably high radiation levels.

Proton and ion beams overcome the fundamental limitation of X-ray therapy because the bulk of the energy is deposited in the ‘Bragg peak’ that occurs as the beam comes to rest. This allows a large dose to be delivered to the tumour while sparing healthy tissue. The maximum instantaneous dose that can be delivered today is limited at the ion source because of the mutual repulsion of the low-energy (approximately 60 keV) of the ions produced. At such low energies the repulsion between the ions causes the beam to diverge rapidly and limits the capture efficiency. I propose to overcome this fundamental limitation by using a laser to create ions with energies of up to ~15 MeV and capturing them using a strong-focusing plasma lens.

I propose to develop a novel, as-yet unproven, source of proton and ion beams by exploiting state-of-the art technologies that to-date have only been demonstrated independently. The particle flux produced by a high-power short-pulse laser has a broad energy spectrum, is highly divergent, and contains a variety of particle species. I will construct a highly efficient capture system that exploits novel electron-plasma lenses to turn the divergent laser-generated proton and ion flux into a beam. To prove the principle of the technique, I will use my system to initiate a programme of radiobiology exploiting the laser-hybrid technique.

A system capable of delivering high instantaneous dose rate will have broad applicability. The laser-hybrid technique will allow radiotherapy to be carried out in completely new regimes, exploiting a variety of ion species, energy spectra, time structures, and spatial configurations at ultra-high dose-rate.

1988 of 2000 characters

Explain and justify the cross-panel or cross domain nature of your proposal, if a secondary panel is indicated in the online proposal submission forms. There is a limit of 1000 characters, spaces and line breaks included.

**Section a: Extended Synopsis of the scientific proposal (max. 5 pages, references do not count towards the page limits)**

1. Mission Need

Cancer is the second most common cause of death globally [1]. In 2018, 18.1 million new cancer cases were diagnosed, 9.6 million people died of cancer-related disease, and 43.8 million people were living with cancer [2,3]. It is estimated that 26.9 million life-years could be saved in low- and middle-income countries (LMIC) if radiotherapy capacity could be scaled up [4]. Novel techniques incorporated in facilities that are at once robust, automated, efficient, and cost-effective are required to deliver the required scale-up in provision.

Radiation therapy (RT), a cornerstone of cancer treatment, is used in over 50% of cancer patients [5]. The most frequently used types of radiotherapy employ photon or electron beams with MeV-scale energies. Proton and ion beams offer substantial advantages over X-rays because the bulk of the beam energy is deposited in the Bragg peak. This allows dose to be conformed to the tumour while sparing healthy tissue and organs at risk.

The benefits of proton and ion-beam therapy (PBT) are widely recognised. PBT today is routinely delivered in fractions of ~2 Gy per day over several weeks. Usually, each fraction is delivered at a low dose rate (<10 Gy/min) deposited uniformly over the target treatment volume. Exciting evidence of therapeutic benefit has recently been reported when dose is delivered at ultra-high dose-rate, >40 Gy/s (“FLASH” RT) [6, 7], or provided in multiple microbeams with diameter less than 1 mm distributed over a grid with inter-beam spacing of ~3 mm [8]. However, the radiobiological mechanisms by which the therapeutic benefit is generated are not properly understood.

I have established a multi-disciplinary consortium dedicated to the creation of the Laser-hybrid Accelerator for Radiobiological Applications (LhARA) [9]. 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 [10]. The technologies demonstrated in LhARA have the potential to be developed to allow PBT to be delivered in completely new regimens. Through the delivery of LhARA the consortium seeks to:

* Create the capability to deliver particle-beam therapy in completely new regimes by combining a variety of ion species in a single treatment fraction and exploiting ultra-high dose rates, multiple ion species, and novel spectral and spatial-fractionation schemes; and
* Make “best in class” treatments available to the many by demonstrating in operation a system that incorporates dose-deposition imaging in a fast feedback-and-control system thereby reducing the requirement for an extensive beam-delivery system and large gantry.

LhARA will 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 laser-driven source allows protons and ions to be captured at energies significantly above the proton- and ion-capture energies that pertain in conventional facilities, thereby evading the current space-charge limit on the instantaneous dose rate that can be delivered [10]. The plasma (Gabor) lenses provide the same focusing strength as high-field solenoids at a fraction of the cost.

The success of the LhARA initiative rests on the efficient capture of the laser-driven ion flux. While the production of protons and light ions using a high-power laser has been demonstrated [11] and a number of plasma-lens schemes are under development [12], the integration of a laser-driven source with a strong focussing plasma lens has not been attempted to date. Therefore, with this proposal I seek the resources to:

* Prove the principle of laser-driven injection of a large instantaneous flux of high-energy protons and light-ions into a novel strong-focusing plasma lens;
* Demonstrate the efficient capture and transport of the laser-created ion beam; and
* Carry out initial in-vitro measurements of the radiobiological impact of proton beams using the unique proton beam that will be produced.

The programme I propose will prove in operation the basis of the laser-hybrid technique and lay the foundations for the development of laser-hybrid accelerator systems capable of serving the particle-beam therapy facilities of the future. Furthermore, by evading the current space-charge limit, I will create a new proton- and ion-beam source with wide application in future high-power accelerator facilities.

2. Ground-breaking enabling technologies and challenges

Recent advances in the laser-driven acceleration of particles at Imperial, Strathclyde, and elsewhere, make it possible to conceive of a novel, hybrid accelerator system in which laser interactions drive the creation of a large flux of protons or light ions which may be captured and formed into a beam. The proposed combination of laser-driven source and plasma-lens focusing, techniques for which prototypes have been built at Imperial, will remove the instantaneous-flux limitation of conventional ion sources to allow measurements over a wide range of dose-rate using a variety of ion species in a single facility. The successful exploitation of the proof-of-principle system proposed here will drive a step-change in capability that can be exploited to the benefit of high-intensity pulsed proton and ion beams for scientific and industrial application and may be developed to allow particle-beam therapy to be delivered in completely new regimens.

I propose to bring together novel technologies, developed in unrelated fields, to demonstrate and exploit a new concept for the creation of proton and ion beams. This programme carries significant technical risk as it includes the proof-of-principle demonstration of key accelerator technologies. A holistic, system-level approach will be taken to the integration of the accelerator, instrumentation, and dose-measurement systems. The innovative work I propose to carry out will lay the foundations for the systematic development of the laser-hybrid technique. I will ensure that the successful demonstration of the laser-hybrid technique realised using the resources requested here will be exploited by the LhARA consortium to deliver the first “proof-of-principle” based on the laser-hybrid technique.

The great advantage of the laser-driven source over conventional sources is that the protons or light ions are injected into the first accelerator structure at high energy (up to 15 MeV). However, the laser-driven source creates an intense, highly divergent flux. The natural divergence of the beam at source is exacerbated by the mutual repulsion of the ions. This mutual repulsion is referred to as the “space-charge effect”. Two novel, strong-focusing Gabor lenses will be used to capture and focus the highly-divergent flux and form it into a beam. Each Gabor lens contains an electron plasma contained by crossed electric and magnetic fields. The negatively charged plasma provides a strong focusing effect for positive ions and efficiently manages the space-charge effect created by the ions’ mutual repulsion. A prototype Gabor lens of the type required for the application proposed has been constructed at Imperial.

The beam emerging from the Gabor-lens capture system will be characterised using state-of-the art diagnostics. <Sentences summarising discussion on, e.g., MediPix from Alex Howard.> The dose to the sample will be measured shot-by-shot using novel micro-dosimeters that have been developed at the National Physical Laboratory and a fast feedback system will be implemented to allow the dose-rate to be adjusted to that required for a particular experiment. An automated, computer-controlled system with remote monitoring will be implemented to allow samples to be irradiated without the need for operator intervention in the radiation area. This will maximise the flexibility of the system in operation and minimise the beam-time lost in sample manipulation. The system-level integration of the novel laser-hybrid proton and ion source with the instrumentation, dosimetry, and real-time feedback and control is essential for the exploitation of the technique in LhARA and other clinical, scientific, and industrial applications.

3. Awareness and context

3.1 The unique advantages of the laser-hybrid approach

Beam is extracted at fixed energy from conventional cyclotrons such as those in use at particle-beam therapy centres in the Europe. The dose rate can be varied by adjusting the bunch intensity and the pulse length at the ion source. However, the instantaneous dose rate is limited by source brightness, losses at injection, bunch length, and losses during acceleration and extraction. A reasonable estimate of the maximum bunch intensity that can be achieved is approximately 1.2 × 107 protons-per-bunch. In order to vary the beam energy a degrader is used to intercept the beam after extraction. Multiple Coulomb scattering and energy straggling cause a significant reduction in beam quality. This can be recovered through collimation with an unavoidable loss in beam intensity. Changing the extraction energy is possible, but is extremely difficult as even a small change in magnet saturation strongly affects the isochronous acceleration. Variable-energy extraction achieved by varying stripper-foil position is possible for H— ions. However, the application of this technique to multiple ion species is challenging and is likely to require multiple extraction ports leading to issues in commissioning and operation. The acceleration of more than one ion species is possible by harmonic operation and tuning of the magnetic field, but is limited to ions with specific charge-to-mass ratios and cannot accommodate a full ion spectrum.

Conventional synchrotrons, such as that used, for example, at CNAO and MedAustron, can deliver beam over a range of energies. The dose delivered is controlled through the process of slow extraction which takes place over a period of around 1 s. The instantaneous intensity that can be achieved within a time window equivalent to the cyclotron bunch length considered above is approximately 4 × 108 protons-per-pulse. The MedAustron synchrotron has two ion sources, the first delivers H+ ions, the second C4+ ions. These ions have the same charge-to-mass ratio and, after short, ion-specific transfer lines, are injected into a single radiofrequency quadruple (RFQ). Electrons are stripped from the ions at injection. The use of other types of ion with the same charge/mass is possible in principle.

The laser-hybrid proton and ion sources offers a route to a compact, cost-effective solution for the delivery of proton and ion beams over a range of energy, dose-rate and ion species. The design study performed by the LhARA consortium has demonstrated that the source proposed here can be used as the basis of a facility in which the intensity of the bunch is varied by changing the laser-beam parameters. The dose can be delivered in a single 10 ns bunch with an intensity of ~109 protons-per-pulse or over 600 bunches at 10 Hz repetition rate. The energy can be varied by collimating the beam delivered by the very strong energy-dependent electrostatic focusing provided by the plasma lenses. Many species of ion can be accelerated in LhARA simply by changing the target. The laser-hybrid technique has the potential to become a uniquely flexible source for scientific, industrial, and biomedical applications.

3.2 Complementary initiatives to create laser-driven beams for radiobiology

European laboratories have established leading roles in the development of laser-driven sources for biomedical application. A number of groups are investigating the challenges related to the production and capture of ion beams with the desired characteristics. In Germany, the effort is led by the Helmholtz Zentrum Dresden-Rosendorf (HZDR), the Technical University of Munich, and GSI Helmholtzzentrum für Schwerionenforschung (GSI). Primary experiments are also now beginning at the ELIMAIA-ELIMED facility in the Czech Republic. The ELIMED project, a multi-billion euro collaboration to build and exploit next generation laser sources, has a dedicated programme for radiobiology research based on a laser-accelerated source. This project has close collaborations with researchers from a number of institutes in Italy. At the J-KAREN-P facility in Japan, with which CCAP members have an ongoing collaboration, the focus is on developing carbon ions for particle treatment.

Laser-driven ions have been posited as a source for radiobiological studies for a number of years. However, to date the ion energies, energy spread, and shot-to-shot variability of the flux produced has meant that such sources were not suitable to serve as a radiobiology resource. A number of radiobiology experiments have been conducted with laser-accelerated ions, but these have been limited in scope to single-shot illumination, either due to low laser repetition rates or the lack of a target suitable for operation at high repetition rate. Most of these experiments have been performed on facilities for which radiobiology has not been the highest priority. The UK has been a pioneer in the study of laser-accelerated ions for hadron therapy. The A-SAIL collaboration explored the underlying fundamental physics required to produce the proton and ion beams we require. The programme we propose will continue to benefit from the advances made in the UK and elsewhere.

The initiatives outlined above exploit conventional magnetic quadrupole or solenoid focusing to capture and transport the laser-generated beam. The capture and transport efficiency of the plasma-lens-based solution we propose is superior and we therefore expect to be able to deliver beams with a substantially higher instantaneous dose. In addition, once developed the capital cost of a Gabor lens of the strength required to capture and focus low-energy proton and ion beams is expected to be significantly smaller than that of the equivalent high-field solenoid magnet.

4. Laser-hybrid ion-capture proof-of-principle system

5. Programme of work

5.1 Workpackages and timeline

5.2 Milestones

5.3 Justification of resources

5.4 The project team

5.5 Principal risks and mitigations

6. Potential for scientific, societal, and economic impact

7. Summary

1. Instructions for completing Part B1 can be found in the ‘*Information for Applicants to the Advanced Grant 2020 Call’*. [↑](#footnote-ref-1)