

**ERC Advanced Grant 2020**  
**Research proposal [Part B1]<sup>1</sup>**  
*(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:**

Name of the Principal Investigator (PI)	: Kenneth Long
Name of the PI's host institution for the project	: Imperial College London
Proposal duration in months	: 60

I propose to lay the technological foundations for a step-change in clinical practice. To do this I will prove the principle of the laser-hybrid acceleration technique in which novel strong-focusing electron-plasma (Gabor) lenses capture and focus the large flux of protons or ions which is created when a short pulse, high-power laser strikes a target. The laser-driven particle flux has a broad energy spectrum up to ~40 MeV and is highly divergent. I propose to capture the intense proton flux produced at 15 MeV with a novel, highly efficient, Gabor-lens based capture-and-focusing system that is compact and cost effective.

The mechanism by which proton and ion beams lose energy as they pass through tissue results in the bulk of their energy being deposited in the “Bragg peak” that occurs as the beam comes to rest. Appropriately positioning the Bragg peak allows a large dose to be delivered to the tumour while sparing healthy tissue. The efficacy of proton- and ion-beam therapy (PBT) depends on the beam characteristics: ion species; energy spectrum; dose and dose rate; and spatial distribution. However, PBT today is almost always delivered with proton beams, over a restricted range of beam characteristics, and at low dose rate. The maximum instantaneous dose rate that can be achieved in conventional facilities is limited at the low-energy (~60 keV) source by the mutual repulsion of the ions. The laser-hybrid technique I propose is capable of delivering a wide variety of ion species in almost arbitrary time, spatial, and spectral structures. Capturing the beam at high energy, 250 times that of conventional facilities, suppresses the effect of the mutual repulsion, evading the instantaneous dose-rate limitation of current sources.

By proving the principle of the laser-hybrid acceleration technique I will create a new source of proton and ion beams and the capability to deliver particle-beam therapy in completely new regimens.

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.

<sup>1</sup> Instructions for completing Part B1 can be found in the ‘*Information for Applicants to the Advanced Grant 2020 Call*’.

## Section a: Extended Synopsis of the scientific proposal

### a:1 Overview

#### *Ambition:*

Laser-driven proton and ion sources are disruptive technologies that offer enormous potential to satisfy the anticipated growth in demand for particle-beam therapy (PBT). A laser-hybrid system, in which strong-focusing electron-plasma (Gabor) lenses capture and transport the beam, will allow clinicians to deliver PBT in a completely new regimens, combining a variety of ion species in a single treatment fraction and exploiting ultra-high dose rates (up to  $10^9$  Gy/s [1] compared to conventional dose rates of  $< 10$  Gy/min). The transformative potential of the technique I propose is demonstrated in my pioneering concept for the Laser-hybrid Accelerator for Radiobiological Applications, LhARA [2].

I propose to prove the principle of the laser-hybrid technique and thereby lay the technological foundations for a step-change in clinical practice. The laser-hybrid accelerator proof-of-principle system combines a state-of-the-art laser-driven proton-production target with a capture and focusing system based on novel strong-focusing Gabor lenses. I propose to characterise the proof-of-principle system using state-of-the-art silicon-pixel sensors. To prove the principle of the laser-hybrid technique in operation my programme will culminate with the test irradiation of *in vitro* biological samples.

#### *Challenges addressed:*

Cancer is the second most common cause of death globally [3]. 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 [4,5]. It is estimated that 26.9 million life-years could be saved in low- and middle-income countries if radiotherapy (RT) capacity could be scaled up [6].

Radiation therapy, a cornerstone of cancer treatment, is used in over 50% of cancer patients [7]. The most frequently used types of radiotherapy employ photon or electron beams. Proton and ion beams offer substantial advantages over photon and electron beams because the bulk of the beam energy is deposited in the Bragg peak that occurs as the beam comes to rest [8]. 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. The Particle Therapy Co-Operative Group (PTCOG) [9] currently lists 90 proton therapy facilities and 12 carbon-ion-therapy facilities [10]. These facilities are located predominantly in high-income countries [11]. Low and middle-income countries (LMIC) are poorly served, indeed nearly 70% of cancer patients globally do not have access to RT [12].

The beam characteristics that can be exploited in PBT facilities today are restricted to low dose rates ( $< 10$  Gy/min), a small number of temporal schemes (typically 2 Gy per day over several weeks) and a small number of spatial distributions (predominantly large beams delivering a homogeneous dose over several square centimetres). Conventional proton or ion sources produce relatively long pulses at low energy ( $\sim 60$  keV). At such a low energy the maximum flux that can be captured is limited by the mutual repulsion of the ions. Recent studies have shown that the efficacy of PBT can be improved substantially if the dose is delivered at ultra-high rate,  $> 40$  Gy/s in “FLASH” RT [13,14], or provided in multiple “microbeams” with diameter less than 1 mm distributed over a grid with inter-beam spacing of  $\sim 3$  mm [15]. These results indicate that a new, highly flexible, multiple-ion source is required for the full potential of particle-beam therapy to be realised.

The laser-hybrid technique I propose is capable of delivering a wide variety of ion species in almost arbitrary time, spatial, and spectral structures. Further, the laser-hybrid system allows protons and ions to be captured at high energy (15 MeV for protons). At this high energy, 250 times that of current sources, the effect of the mutual repulsion is suppressed, evading the instantaneous dose-rate limitation of current sources. My vision is that by proving the principle of the laser-hybrid technique I will:

1. Create the highly flexible proton and ion source required for particle-beam therapy to realise its full potential; and
2. Lay the technological foundations for the development of a fully automated PBT system that incorporates time-resolved tissue and dose-deposition imaging to harness the unique features of the laser-hybrid technique to remove the requirement for a large gantry and so reduce the footprint of the facility and make “best in class” treatments available to the many.

#### *Deliverables:*

With this proposal I seek the resources to:

1. Demonstrate the laser-driven injection of a large instantaneous flux of high-energy protons into a Gabor lens;
2. Demonstrate the efficient capture and transport of the laser-created proton beam; and
3. Carry out initial *in-vitro* radiobiological measurements using the laser-hybrid technique.

### **a:2 Ground-breaking enabling technologies and challenges**

Recent advances in the laser-driven acceleration of particles at Imperial [16], Strathclyde [17], and elsewhere [18], 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 are captured and formed into a beam. 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 laser-accelerator, Gabor lens, instrumentation, and dose-measurement systems.

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. Three novel, strong-focusing Gabor lenses will be used to capture and focus the 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.

The beam emerging from the Gabor-lens capture system will be characterised using state-of-the art silicon-pixel sensors. In collaboration with the National Physical Laboratory, the dose delivered to the samples will be determined through a combination of passive (alanine and Gafchromic films) and active detectors (ionization chambers and calorimeters) appropriately calibrated for the high-dose regimen. An automated, computer-controlled system with remote monitoring will be implemented to allow samples to be irradiated without the need for operator intervention. This will maximise the flexibility of the system in operation and minimise the beam-time lost in sample manipulation.

### **a:3 Awareness and context**

Laser-driven ions have been posited as a source for radiobiological studies for a number of years [19]. A number of radiobiology experiments have been conducted with laser-accelerated ions [20]. 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) [21], the Technical University of Munich [22], and Gesellschaft für Schwerionenforschung (GSI) Helmholtzzentrum für Schwerionenforschung [23]. Primary experiments are also beginning at the ELIMAIA-ELIMED facility in the Czech Republic [24]. The ELIMED project has a dedicated programme for radiobiology research based on a laser-accelerated source [25]. At the J-KAREN-P facility in Japan the focus is on developing carbon ions for particle treatment [26]. In the UK Queens University Belfast, Imperial College London, and the Scottish Centre for the Application of Plasma-based Accelerators (SCAPA) collaborate through the A-SAIL project [27] to deliver high-repetition ion beams at the energies necessary for deep-seated tumour treatments at about 200 MeV/nucleon.

The initiatives outlined above exploit conventional magnetic quadrupole or solenoid focusing to capture and transport the laser-generated beam. The approach I propose distinguishes itself from these alternative approaches by:

1. Shifting the focus away from attaining high energies from the laser source and focussing instead on the delivery of a stable and high ion flux; and
2. Integrating the Gabor lens with the laser-driven source to maximise the capture efficiency.

By emphasising flux stability at production and highly-efficient capture I seek to deliver beams with a stable and high instantaneous dose rate.

### **a:4 Laser-hybrid ion-capture proof-of-principle system**

To prove the principle of the laser-hybrid ion-capture scheme requires the successful integration of the laser-driven proton source with the Gabor-lens based capture-and-focusing system to produce a beam that can be

precisely characterised and exploited for the exposure of biological samples *in vitro*. The programme I propose will address the key challenges required to meet each of the three deliverables defined above:

- Stable operation of an electron-plasma (Gabor) lens system;
- Integration of the first Gabor lens with the laser-target chamber;
- Implementation of the full three-Gabor-lens system; and
- Measurement of the beam parameters at appropriate points along the beamline.

My design for the proof-of-principle system will exploit the ZHI laser at Imperial College London. I will design and build a vacuum vessel in which the short, intense laser pulse will be focused onto a foil, impinging at an angle of 45° so that protons will be accelerated through the “target-normal sheath acceleration” (TNSA) mechanism [28]. The intense electric field generated on the front surface of the target accelerates the surface electrons, driving them into the material. Electrons which gain sufficient energy will traverse the target, ionising the material as they go. A strong space-charge electric field, the “sheath”, is created as the accelerated electrons exit the rear surface of the target. This field in turn accelerates protons from the surface of the target. Sheath-acceleration has been shown to produce ion energies greater than 40 MeV/u at the relevant laser intensities [29]. In my design the first Gabor lens is integrated with the target vessel. Since the interaction of the laser with the target will create debris and cause out-gassing the vacuum in the target vessel will not be as good as that required for the operation of the Gabor lens. Therefore, my design incorporates a re-entrant cone pointing back to the laser-target interaction point such that the aperture that connects the target vessel to the plasma lens is as small as possible to allow the vacuum pressure in the target to be different to that in the plasma lens. An energy-selected beam will be produced using a further two Gabor lenses and a collimator. The beam will be sampled between each beam-line element with a silicon-pixel detector placed on a retractable mount. The total dose delivered to the sample position will be determined using a silicon microstrip dosimeter.

## a:5 Programme of work

I propose to prove the principle of the laser-hybrid technique by using laser acceleration to inject protons at high energy into a capture and beam-transport system based on novel strong-focusing Gabor lenses. The principle technical risks that must be addressed to deliver the proof-of-principle system are:

- Reproducible production of a large proton flux at 15 MeV using the TNSA technique; and
- Production of a stable non-neutral (electron) plasma confined within the Gabor lens.

The integration of the laser-target vessel with the first Gabor lens and the instrumentation required to monitor and characterise the beam presents significant engineering challenges. I have extensive experience of the management of risk in the successful execution of a large scientific project through my leadership of the international Muon Ionization Cooling Experiment (MICE). The programme of work outlined below will address *ab initio* the principle risks to the successful demonstration of the laser-hybrid technique.

### a:5.1 Workpackages

I propose to divide the work necessary to meet the deliverables defined above into the four work packages. The project timeline and milestones are summarised in section a:5.2.

#### a:5.1.1 Physics simulation

*I will exploit state of the art particle-in-cell codes to demonstrate that the strong-focusing plasma-lens system proposed here is capable of delivering proton and ion beams of large instantaneous flux.*

Existing particle-in-cell codes will be used to evaluate the particle production from the laser-driven source and for the dynamic simulation of the electron-plasma lens. The results will be used to develop a detailed simulation of the proton beam from the production point through the beam line. This simulation will include consideration of the laser- and particle-beam diagnostics and the effect of space charge.

#### a:5.1.2 Gabor lens design, build, and validation

*I will design and build three plasma-lenses and characterise their performance in stand-alone tests.*

I will lead the design of the novel Gabor lens system, exploiting where possible the experience gained using the existing Gabor-lens prototype at Imperial [30]. I will expedite the manufacture and commissioning of the first Gabor lens. Once the performance of the first Gabor-lens system has been validated, I will lead the project team in the construction of the remaining lenses and their validation.

### *a:5.1.3 Target vessel integration; design, build, and validation*

*I will deliver the integrated laser-target vessel and first Gabor lens capture and transport system on the ZHI laser at Imperial College London.*

The critical engineering challenge is the integration of the first plasma lens with the laser-target vessel. I will lead the design team in the completion of a comprehensive design report in which the integrated system is detailed. I will then oversee the manufacture of the components of the system and their installation on the laser.

### *a:5.1.4 Commissioning, characterisation, and exploitation*

*I will characterise the beam by measuring the evolution of the energy and spatial distributions of the particle flux along the beamline. I will measure the dose delivered at the end of the beam line and thereby to determine the dose delivered to the cell cultures in the irradiation of biological samples.*

The construction of the laser-target vessel will start as soon as the integrated design is complete. The target drive and the target vessel will be expedited so that the first tests with the laser can begin. The characterisation of the beam will begin with measurements of the spectra produced close to the foil. Measurements will be made to characterise the evolution of the beam along the beam line as components are added. The measurements will culminate with the irradiation of cells *in vitro*.

## *a:5.2 Timeline and milestones*

I propose to execute the project in four overlapping phases. The key milestones through which progress will be measured have been defined in relation to the delivery of the four phases as follows:

***Phase 1: Concept validation and detailed design (months 1 to 15):*** a detailed end-to-end simulation of the proof-of-principle system will be developed using particle-in-cell and particle-tracking codes. These codes will be used to support and evaluate the detailed design of the laser-target vessel, the Gabor lens, and the full proof-of-principle system.

Critical analysis of the results of the end-to-end simulation is the immediate first step in the mitigation of the particle-production and plasma-stability risks identified above.

Milestones:

M1: month 12: Time-resolved, 2D & 3D simulations of particle production spectra

M2: month 15: Report presenting detailed design of laser-target vessel and Gabor lens

***Phase 2: Prototype construction, evaluation, and refinement of design (months 9 to 32):*** as detailed designs for the laser-target vessel and the Gabor lens mature, the construction of appropriate prototype components will be expedited. Detailed evaluation of the first Gabor lens will be used to drive a revision of the lens design. The evaluation of the laser-target vessel will include tests of the tape-drive target system in air and under vacuum and exposure of the target to the laser. The evaluation process will culminate with the characterisation of the particle spectra produced. Comparison of the simulations developed in phase 1 with the measured performance of the Gabor lens and the measured particle-production rates will be used to inform revisions of the system design.

Simulations of the measured performance will be used to continue the design-revision process and further mitigate the particle-production and plasma-stability risks identified above.

Milestones:

M3: month 30: Laser-target and Gabor lens performance evaluation and design revision complete

M4: month 36: Report presenting revision of detailed design of laser-target vessel and Gabor lens

***Phase 3: Component construction, quality assurance, and characterisation (months 28 to 54):*** the integration of the functional sections of the proof-of-principle system will begin at month 30 when the design revision of the laser-target vessel and the Gabor lens is complete. Component characterisation and particle-flux measurements will be made at each stage of the assembly of the full system.

The incremental characterisation of the beam line will allow decisions to be made to reduce the risk that the proof-of-principle system will not perform to specification.

Milestones:

M5: month 54: Beam line complete, characterisation of beam at point of use complete

**Phase 4: System integration, qualification, characterisation, and exploitation (months 42 to 60):** A thorough and systematic investigation of the particle flux, optical properties of the beam line, as well as the properties of the beam delivered to the point of use, will be carried out. This process will culminate in the first irradiation of biological samples *in vitro*.

The full characterisation of the beam line will culminate in the measurements required to prove the principle of the laser-hybrid technique and the first irradiation of biological samples.

Milestones:

M6: month 60: Final report on activities and achievements ready

### 5.3 The project team

As Principal Investigator and Project Leader I will direct the execution of the project through the four work-packages outlined above. I propose to recruit three early-career researchers: the first will take charge of the simulation suite in work package 1, the second will take charge of the development and characterisation of the Gabor lens in work package 2, and the third will take charge of the development and characterisation of the laser-target. I place particular importance on the creation of an excellent research environment and have therefore recruited internationally recognised experts who will, under my direction, provide advice to and mentor the early career researchers in the development of the programme.

The key personnel and the roles they play in the project team are:

- *PI and project leader:* Prof. Kenneth Long (Imperial)
- *Physics simulation:* Prof. Robert Bingham (Strathclyde)
- *Gabor lens design, build, and validation:* Dr. Colin Whyte (Strathclyde)
- *Laser-target vessel design, build, and validation:* Prof. Zulfikar Najmudin (Imperial)
- *Commissioning, characterisation, and exploitation:* Dr. Jaroslaw Pasternak (Imperial)

Professors Bingham and Najmudin and Dr. Pasternak will provide the required assistance at no cost to the project. Oversight of system integration will be provided by Dr. Ajit Kurup, Senior Accelerator Project Leader at Imperial. Dr. Alexander Howard (Imperial) will take charge of the instrumentation. All the individuals listed above (whether at Imperial or elsewhere) are either world or leading experts in their field and will work under my guidance.

### 5.3 Justification of resources

The resources requested will support the three early-career researchers (two at Imperial College London and one at the University of Strathclyde) and the engineering effort at Imperial and Strathclyde necessary to deliver the proof-of-principle system. Resources to procure the target vessel, the Gabor lenses, and the associated power supplies, vacuum systems, instrumentation and diagnostics are also requested.

Dr. C. Whyte is a leading expert in the design, implementation, and characterisation of plasma systems. He and the Strathclyde group have an established track record of delivery in this field. I appointed Dr. White as MICE Project Manager when I became international spokesperson of the MICE collaboration. Dr. Whyte and I worked effectively to deliver the MICE project and I am confident that the working relationship with Dr. Whyte and the Strathclyde group will be excellent.

Prof. R. Bingham is an internationally renowned expert in laser-plasma acceleration, intense laser-matter interactions, inertial and magnetic confinement approaches and fundamental plasma physics. His insight into the TNSA mechanism and the dynamics of non-neutral electron-plasma physics will be essential in the development of laser-hybrid proof-of-principle system.

## 7. Summary

By proving the principle of the laser-hybrid accelerator technique I will:

- Establish a new technique for the creation of high-flux proton and ion beams for a wide variety of applications;
- Create the capability to deliver particle-beam therapy in completely new regimens, combining a variety of ion species in a single treatment fraction and exploiting ultra-high dose rates; and
- Pave the way for the footprint of PBT facilities to be reduced by exploiting the unique flexibility of the laser-hybrid source in a fully automated system removing the requirement for a large gantry.

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