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Standard PROPOSAL

Document Status: With Owner
STFC Reference:

Open (none)

Organisation where the Grant would be held (mandatory)

Organisation	Imperial College London	Research Organisation Reference:	PA4725
Division or Department	Physics		

Project Title (mandatory) [up to 150 chars]

ITRF

Start Date and Duration (mandatory)

a. Proposed start date	01 October 2022	b. Duration of the grant (months)	24

Applicants (mandatory)

Role	Name	Organisation	Division or Department	How many hours a week will the investigator work on the project?
Principal Investigator	Professor Kenneth Long	Imperial College London	Physics	0.01
Co-Investigator	Dr Jaroslaw Pasternak	Imperial College London	Physics	3.75
Co-Investigator	Professor Zulfikar Najmudin	Imperial College London	Physics	0.01

Proposal Classifications

Classification Areas:

Research Areas are the subject areas in which the research proposal may fall and you should select at least one of these with a maximum of five allowed. You will need to assign the relative percentage totaling 100% across all areas selected. To add or remove Research Areas use the relevant link below. To set a primary area, click in the corresponding checkbox and then the Set Primary Area button that will appear.

Subject	Topic	Indicator %	Keyword
Facility Development	Accelerator R&D	20	
Instrumentation, sensors and detectors	Instrumentation Engineering and Development	20	

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Tools, technologies and methods	Development (Biosciences)	20	
Tools, technologies and methods	Intelligent Measurement Systems	20	
Tools, technologies and methods	Medical Instrumentation, Devices and Equipment	20	

Qualifiers:

Qualifiers are terms that further describe the area of your research and cover aspects such as approach, time period, and geographical focus. Please ensure you complete this section if relevant. To add or remove Qualifiers use the links below.

Keywords:

Free-text keywords may be used to describe the subject area of the proposal in more detail. To add or remove those previously added use the links below.

Objectives (mandatory)

List the main objectives of the proposed research in order of priority [up to 4000 chars]

The LhARA collaboration's proposal for an initial five-year R&D programme [1] was designeded to deliver the essential work to mitigated the technical risks contingent on the implementation of the Laser hybrid Accelerator for Radiobiological Applications and to establish the technical design for the LhARA facility. The proposal was aligned to the timescale defined in the proposal to the UKRI Infrastructure Fund for the establishment of the Ion Therapy Research Facility (ITRF) [2]. LhARA formed the basis of the ITRF proposal.

The ITRF proposal was for resources to support a two-year "Preliminary Activity". The principal deliverable of the two-year Preliminary Activity is a complete Conceptual Design Report for the facility. The ITRF proposal identified a subsequent, three-year, "Preconstruction Phase". Resources for the Preconstruction Phase will be sought during the Preliminary Activity. The first two years of the LhARA proposal was designed to coincide with the Preliminary Activity defined in the ITRF proposal, while years three to five are designed to coincide with the Preconstruction Phase.

In June 2022 UKRI announced £2M over two years for the ITRF as one of the projects supported by the Infrastructure Fund in 2022. The ITRF project will be carried out through four Work Packages [3]:

0. Management and CDR;
1. LhARA;
2. ITRF Facilities and Costing; and
3. Conventional Technology.

It is anticipated that the ITRF Preliminary Activity funding line will provide a total of £1.81M to support the development of LhARA to serve the ITRF [3]. This total is broken down as follows:

* ITRF Work Package 1: £1.49M to support LhARA technical-risk mitigation and preparation of the CDR; and
* Work Package 2: £0.32M to support the evaluation of the conventional technical facilities and to produce a cost estimate of the LhARA facility for inclusion in the CDR.

It is anticipated that resources will be made available to allow the ITRF project, and therefore the LhARA project, to start in October 2022.

This document defines the cost and scope of ITRF Work Package 1. The scientific justification, organisational and managerial structures, and the reporting arrangements are as described in [1,3]. The work supported by the resources provided by ITRF Work Package 1 will be carried out in six sub work packages:

1. Project management;
2. Laser-driven proton and ion source;
3. Proton and ion capture;
4. Ion-acoustic dose mapping;
5. Novel automated end-station development; and
6. Design and integration.

The principal objectives of the work to be carried out supported by the resources requested here are:

* WP1: coordination of LhARA contributions to the ITRF CDR;
* WP2: initial design for a stable laser-driven high-flux proton and ion source capable operating at 10 Hz;
* WP3: initial experimental evaluation of electron trapping at Swansea and initial evaluation of design of second Gabor lens prototype;
* WP4: initial simulation study of an experiment to prove the principle of the ion-acoustic dose mapping technique;
* WP5: through consultation of the potential user community complete specification and CDR of in-vitro and in-vivo end-stations for LhARA; and
* WP6: development of conceptual design and beam-transport simulation for LhARA stages 1 and 2.

1. https://ccap.hep.ph.ic.ac.uk/trac/raw-attachment/wiki/Communication/Notes/CCAP-TN-10.pdf
2. STFC ASTeC/TD document 1272-pm-pmp-0003
3. https://ccap.hep.ph.ic.ac.uk/trac/raw-attachment/wiki/Communication/Notes/CCAP-TN-11.pdf

Summary (mandatory)

Describe the proposed research in simple terms in a way that could be publicised to a general audience [up to 4000 chars]. Note that this summary will be automatically published on STFC's website in the event that a grant is awarded.

The Laser-hybrid Accelerator for Radiobiological Applications (LhARA) formed the basis of the proposal to the UK Research and Innovation (UKRI) Infrastructure Advisory Committee (IAC) to create an ``Ion Therapy Research Facility'' (ITRF) in the UK. 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 ITRF proposal to the UKRI IAC requested funding for a "Preliminary Phase" activity "... to develop over 2 years the specification, design, and cost of the ITRF and present these in a full Conceptual Design Report (CDR).

We propose to develop LhARA to serve the ITRF. 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, 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 electron plasma lenses. The triggerable, laser-driven source allows protons and ions to be captured at energies significantly above the capture energies of conventional facilities, circumventing the current space-charge limit on the instantaneous dose rate that can be delivered. 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 LhARA collaboration's long-term vision 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 delivering a variety of ion species, 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.

With this proposal, the multidisciplinary LhARA collaboration seeks the resources to:

* Deliver the Conceptual Design Report for LhARA to serve the Ion Therapy Research Facility;
* Initiate the R&D programme necessary to demonstrate the feasibility of the laser-driven creation of the requisite proton and ion fluxes through measurement and simulation;
* Create the detailed specification of a second Gabor-lens prototype through an initial programme of experiment, simulation, and design;
* Develop the design of an experiment to 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 proposed two-year programme will lay the foundations for the pre-construction phase identified in the ITRF proposal. Serving the ITRF, LhARA will be a unique, compact, research infrastructure. Fundamentally new biological mechanisms in radiation treatment and immune response which underpin the clinical efficacy of proton- and ion-beam therapy will be elucidated. Exploitation of LhARA at the ITRF will promote the disruptive technologies required to pave the way for a radical transformation of clinical practice.

Academic Beneficiaries (mandatory)

Describe who will benefit from the research [up to 4000 chars]

The LhARA collaboration seeks to establish an entirely new technique for the automated delivery of personalised, precision, multi-ion beam therapy (IBT). The present proposal is a step on the way and will bring together novel technologies, each developed for, or demonstrated in, unrelated fields. This programme carries significant technical risk. The high-risk approach is justified by the high level of reward and will place the UK at the forefront of the IBT field, establish UK industry as a key player in the delivery of novel clinical equipment, and allow significantly enhanced access to state-of-the-art IBT across the UK.

The direct academic beneficiaries of this proposal (Birmingham, the ICR, Imperial College, Lancaster, Liverpool, Manchester, Queen's Belfast, Royal Holloway, and STFC) will carry out the Preliminary Activity on behalf of, and in collaboration with, the Laser-hybrid Accelerator for Radiobiological Applications (LhARA) collaboration. Therefore, the members of the 40-institute strong, international LhARA collaboration will be among the academic beneficiaries of the proposed investment.

The LhARA collaboration are actively engaged in establishing collaborations and partnerships with others in the UK and overseas to enhance the coalition of clinical oncologists, medical, particle, plasma and laser physicists, accelerator and instrumentation scientists, and radiobiologists who seek to contribute to, and to benefit from, the development of novel beams for biological and therapeutic application. This is a substantial opportunity and will be of benefit to physicists and clinicians with an interest in the interactions of PBT with molecules and cells, linked to a specific biological end-point (e.g. DNA damage, cell death), as well as those with an interest in clinical oncology in general.

Working within the framework of the Ion Therapy Research Facility (ITRF) Preliminary Activity, the collaboration will ensure that the results of the research are made available to the academic community at large through open-access peer-reviewed publications and presentations at national and international scientific conferences. In this way, all academic beneficiaries will have access to the outcomes of the proposed research programme. This will enhance the potential for the collaboration to secure further collaborative research income. Given the significant increase in PBT centres worldwide, and particularly in the UK, the work proposed here is vital as the radiobiology of PBT must be more fully understood to deliver optimal strategies for effective treatment of specific cancers.

This proposal involves and is supported by a multidisciplinary collaboration of clinical oncologists, medical, particle, plasma and laser physicists, accelerator and instrumentation scientists, radiobiologists, and industrialists. While executing the Preliminary Activity the collaboration will work to deliver an outreach programme that will disseminate the collaboration's vision, the results of the programme as it develops, and the plans for the future to the relevant international peer groups and to the wider community.