Project title: ***Advanced concepts and novel technologies for the study of the impact of ionising radiation on tissue***

Programme: ***Advanced technologies for radiobiology and clinical radiotherapy***

Project team: ***Ab initio a multi-disciplinary collaboration:***
Clinical oncology, biology/biophysics,
physics (laser, medical, accelerator, instrumentation),
computing, laboratory, industry

CCAP
Centre for the Clinical Application of Particles

University partners: University of Liverpool; Department of Physics; University of Strathclyde Science; Royal Holloway University of London; Queen's University Belfast

Accelerator institute partners:† John Adams Institute for Accelerator Science; The Cockcroft Institute of Accelerator Science and Technology

Laboratory partners:† Science & Technology Facilities Council Central Laser Facility; Science & Technology Facilities Council ISIS Neutron and Muon Source

Clinical partners:
Oncologists, medical/biophysics, providers
Imperial College Healthcare NHS Trust; NHS 70 Years of the NHS 1948–2018; The Clatterbridge Cancer Centre NHS Foundation Trust

Industrial partners: Maxeler Technologies Maximum Performance Computing; Corerain 鲲云科技; LEO Cancer Care

† ASTeC: support as project partner (post submission).

Aims and objectives:

- ***Outline CDR for the Laser-hybrid Accelerator for Radiobiological Applications:***
  - **Spring-board to bid successfully for significant resources to deliver the exciting programme.**
- ***Establish advanced-technology test-bed at the Clatterbridge Cancer Centre (CCC):***
  - **Early access to FLASH capability and essential test bed for development of LhARA.**
- ***Position UK as a force within International Biophysics Collaboration (IBC)***
  - **Optimise UK potential to contribute to – and to benefit from – the IBC.**

Workpackages, deliverables, and cost

1. **Preparation of initial CDR for LhARA:**
   - Deliverable: initial CDR for LhARA [milestone April 2020]
   - Resources:
     - Key enabling investment: *1.75 PDRAs for 6 months*
       - In place; can efficiently become core of effort to deliver initial CDR
     - Leverage support from participating institutes and project partners
     - Exploit strong synergy and close collaboration with ISIS Upgrade team
   - Request:
     - Staff: Imperial (Physics): £62.70k, Liverpool (Biology): £38.12k

2. **LhARA and radiobiology test facility:**
   - Deliverable: proton-FLASH dosimetry [milestone April 2020]
   - Resources:
     - Key enabling investment: *0.25 PDRA for 6 months*
       - In place; existing collaboration with Clatterbridge Cancer Centre (CCC)
     - Leverage support from CCC, participating institutes, and project partners
   - Request:
     - Staff: Liverpool (Biology): £17.24k

3. **UK and the International Biophysics Collaboration (IBC):**
   - Deliverables: Forge UK identity and define UK role in IBC [milestone September 2021]
   - Resources:
     - Key enabling investment: UK and European travel for effective networking activity
   - Request:
     - Staff: Liverpool (Biology): £6.30k
     - Travel: £15k

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DESIGN OF LhARA - LASER HYBRID ACCELERATOR FOR RADIOBIOLOGICAL APPLICATIONS

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J. Pasternak†, J. Pozimski, Imperial College London, London, UK
also at STFC/RAL, Didcot, UK

Abstract

Recent developments of using lasers interacting with targets for the creation of ion beams offer a possibility to provide beams for radiobiology research. This research aims to precisely study the radiobiological effectiveness of charged particles on various cultures of cells, which is essential to inform next generation hadron therapy treatment plans. The Laser hybrid Accelerator for Radiobiological Applications (LhARA) has been proposed to use a laser driven beam, which will be captured and focused using Gabor Lenses. The beam will be then energy and momentum selected to create a beam for in-vitro cells studies or sent to a post-accelerator ring to create beam for in-vivo studies. The optical design of LhARA is presented in this paper.

INTRODUCTION

Cancer is a major cause of death worldwide with a growing number of new cases each year. Its incidence rate is predicted to increase to 27.5 million new cases per year by 2040 [1]. Radiotherapy remains an important treatment option and may need to address the needs of low-income countries in the near future. The majority of the radiotherapy being delivered nowadays is based on X-rays, which, although well understood, still have some drawbacks. In particular, the dose delivery to sensitive organs in close proximity to tumours is an issue as the X-ray dose deposited decreases exponentially.

Hadrontherapy is able to address these issues by providing a very different dose distribution due to the Bragg peak, which means the dose is rapidly terminated beyond the tumour. However the radiobiological effectiveness of hadron beams remains to be fully characterised. Current treatment planning using proton beams assumes that the relative biological effectiveness (RBE) is 1.1 [2]. This is an average value, in fact RBE varies with several physical and biological parameters such as dose, dose rate, linear energy transfer and biological endpoint. A number of other studies have also shown there can be significant variation in the RBE, see [3], [4] and [5]. A detailed systematic study of the RBE for protons and especially heavier ions, under different physical conditions, with different tissue types would provide important information on RBE variation and could enable improved treatment planning protocols in hadrontherapy centres improving the prognosis for patients.

This motivates the need for a program of experiments dedicated to the study of radiobiology using a wide spectrum of ion species and beam conditions. Although such a program could, in principle, be realised in existing therapy facilities, in practice it is rather difficult as their primary goal is the delivery of treatment. In addition, there are several technical difficulties related with switching between ion types and dose profiles, when executed in conventional accelerator systems. Recent advances in using laser-driven particle beams o
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† j.pasternak@imperial.ac.uk

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where V is the cathode voltage in kV, R is the cathode radius in m, E is the proton beam kinetic energy in keV and γ is the beam relativistic factor. P_F represents an effective space-charge filling factor and is assumed to be ~0.5.

Figure 1: Gabor lens at the test stand at Imperial College.

LhARA Lattice Design

The LhARA Stage 1 lattice design consists of two Gabor lenses, which focus the beam from the laser target to provide initial capture. The beam is then focused in to a narrow collimator slit (typically 1mm in aperture) by the third Gabor lens. As this focusing is energy dependent, a strong dependence of the focus location on energy results, which enables the collimation in the subsequent drift to be an efficient energy selection system. Two more Gabor lenses are then used to provide flexible matching for the output beam size and divergence. The beam size assumed in the in-vitro end station is required to be flexibly varied in the range of 1-15 mm. Table 1 shows the principal parameters of the Gabor lenses assumed in the design of LhARA, which are carefully chosen to mitigate technical risks. The maximum achievable focusing strength of the Gabor lens with those parameters for a 15 MeV proton beam would be equivalent to 1.44 T solenoid. This would allow the use of normal-conducting solenoids in LhARA, however with a significantly higher cost.

Table 1: Parameters of Gabor Lenses Assumed in LhARA

Parameter	Value	Units
Total length	1.157	m
Effective focusing length	0.857	m
Max. Cathode voltage	65	kV
Cathode radius	0.0365	m

The beam is then bent vertically upwards by 90° arc consisting of four combined-function sector magnets into the end station, where the cells will be irradiated. Vertical delivery of the beam allows the use of conventional cell-culture plates, that provide breathable wells where the cell sample is grown on the bottom of a well filled with cell-nutrient liquid. This arrangement is preferred as it would facilitate the radiobiological experiments. The arc will also be used to perform momentum selection by collimation in the dispersive region which, in combination with preceding energy-selection, will allow particle-species selection. This is an important feature as typical target made of a plastic foil will emit both protons and carbon ions. In order to obtain a compact footprint an arc design consisting of identical magnets is foreseen. Figure 2 shows the layout of LhARA Stage 1 created using the BDSIM code [12].

Optics

The evolution of the optical functions in LhARA Stage 1, shown in Figure 3, reflects the characteristic properties of a lattice using Gabor lenses in a laser-driven accelerator. The initial beam parameters from the target result in a very large variation of betatron function over the initial capture

Figure 2: Layout of LhARA Stage 1 lattice. The laser target is located on the left. Four Gabor lenses (yellow boxes) are used to capture focus and transport the beam to the vertical arc, which bends the beam by 90° upwards towards the in-vitro end station.

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Total cost to STFC: £139.35k **In-kind income from project partners: £170.00k**