Imperial College London

UKRI Science and Technology Facilities Council

Pre-publication review of the LhARA pre-CDR

Introduction

K. Long, 27 March, 2020

CCAP Centre for the Clinical Application of Particles

Background

- **Centre for the Clinical Application of Particles:**
  - **Imperial centre of excellence; established October 2017**
  - **Mission:**

    Develop the technologies, systems, techniques and capabilities necessary to deliver a paradigm shift in the clinical exploitation of particles.

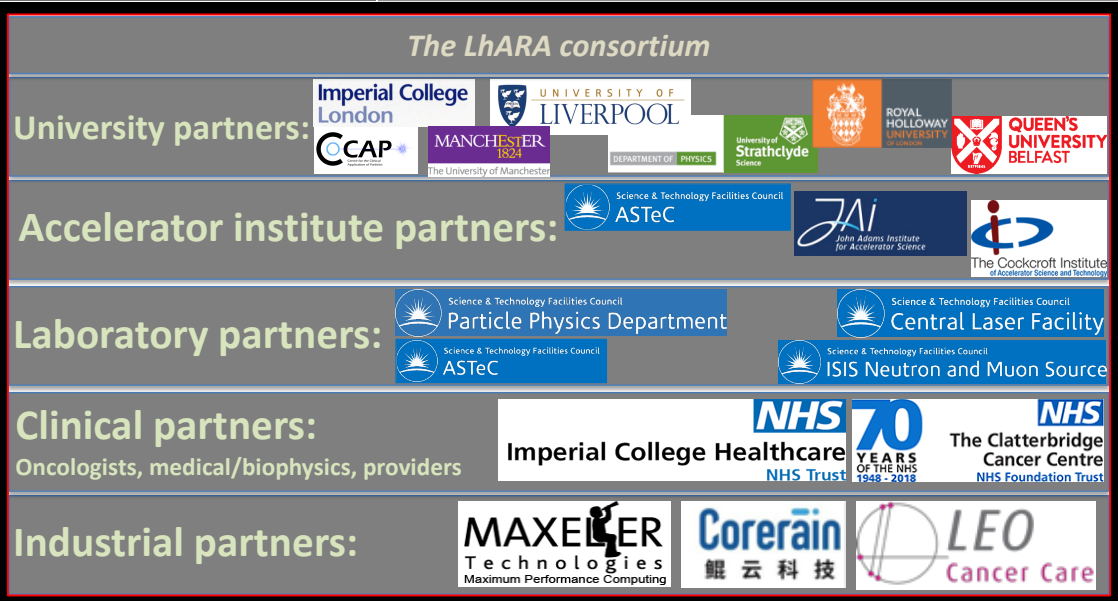
  - **Key objectives:**
    - **Develop novel, compact, laser-driven accelerator systems for clinical applications;**
    - **Deliver the capability to assess the biological and therapeutic efficacy of different ion species; and**
    - **Develop improved diagnostic, dose-measurement, imaging, treatment-planning, data-processing, andmachine-learning techniques.**

- **LhARA, the Laser-hybrid Accelerator for Radiobiological Applications:**
  - **Central to the CCAP's research and development programme**

Multidisciplinary collaboration

CCAP
Centre for the Clinical Application of Particles

Imperial: Academic Health Science Centre, Faculty of Medicine, Department of Physics, CRUK Cancer Centre
Imperial College NHS Healthcare Trust
Institute of Cancer Research
John Adams Institute
Oxford Institute for Radiation Oncology

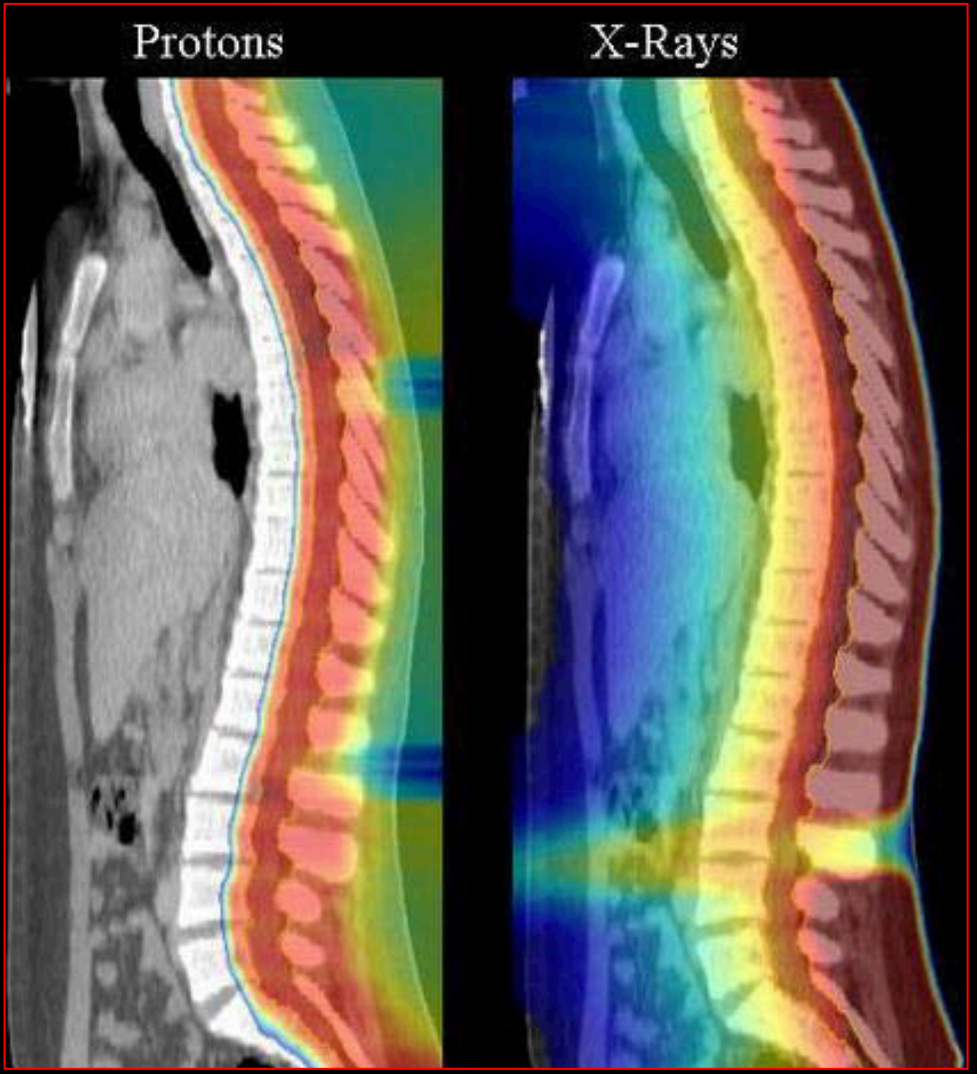


Further interest from:

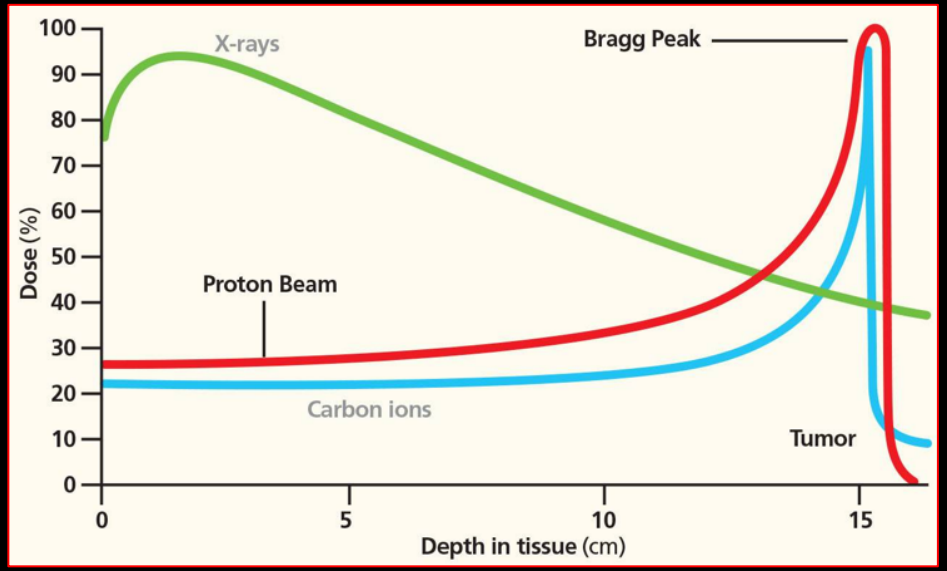
- **Groups in the UK and overseas**

Radiotherapy; the challenge

- Cancer: second most common cause of death globally
  - Radiotherapy indicated in half of all cancer patients
- Significant growth in global demand anticipated
- Today, most radiotherapy delivered with X-rays
  - But, interest in proton and ion beam therapy is increasing



Particle-beam therapy



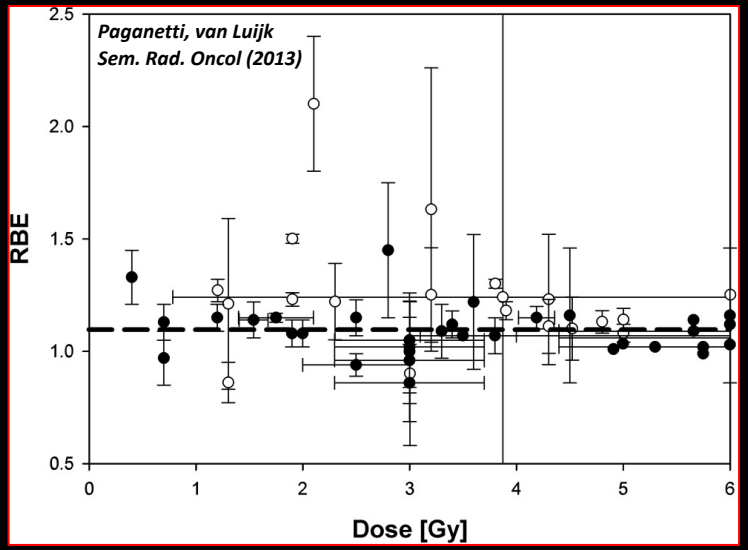
Proton and ion-beam therapy:

- Bulk of dose deposited in Bragg peak
- Significant normal-tissue sparing (entry)
- Almost no dose beyond the Bragg peak

The radiobiology needs to be understood

- **Treatment planning:**
  - **Based on 'Relative Biological Effectiveness (RBE)**
    - **Proton-treatment planning uses RBE = 1.1**
    - **Effective values are used for C^{6+}**

RBE:
Ratio of dose required to gain same biological response as reference photon beam



RBE known to depend on:

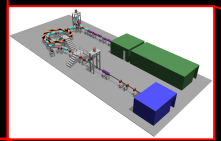
- Energy, ion species
- Dose & dose rate
- Tissue type
- Biological endpoint

Essential: improved, fundamental, understanding of radiobiology

Particle beam therapy today

- **Cyclotron based:**
  - **Limitations:**
    - **Energy modulation**
    - **Instantaneous dose rate**

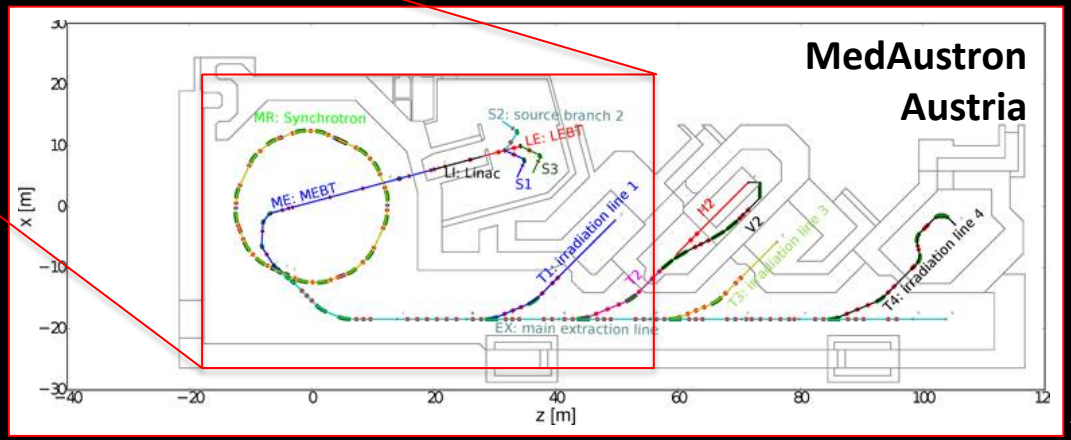
⇒ reduce footprint, cost and complexity
'PBT for the many'



⇒ increase flexibility
optimize treatments

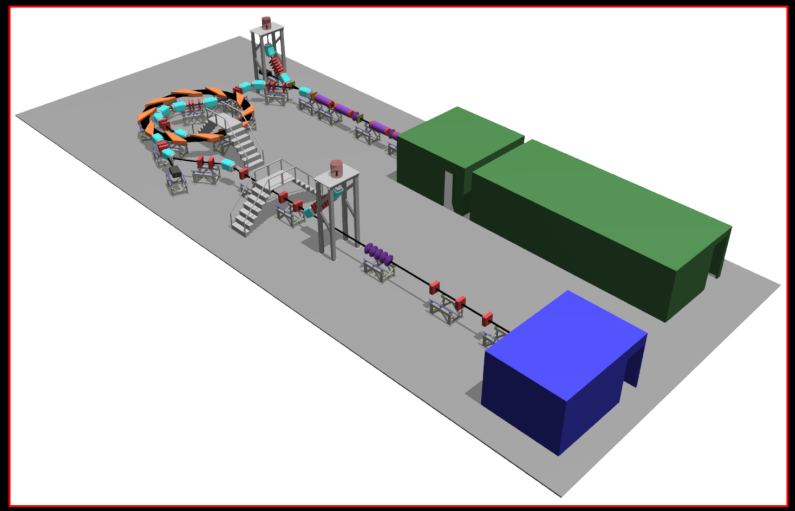
Christie Hospital Manchester

- **Synchrotron based:**
  - **Limitiations:**
    - **Complexity**
    - **Instantaneous dose rate**



Laser-hybrid Accelerator for Radiobiological Applications

- LhARA; a novel, hybrid, approach:
  - High-flux, laser-driven proton/ion source:
    - Overcome instantaneous dose-rate limitation
    - Delivers protons or ions in very short pulses:
      - Pulse length 10 – 40 ns
    - Can provide arbitrary pulse structure
  - Novel plasma-lens capture & focusing
  - Fast, fixed-field post acceleration



⇒ *compact, uniquely flexible facility*

LhARA consortium

CCAP Centre for the Clinical Application of Particles

Radiobiology in new regimens

Our vision and our ambition

- **Vision:**

  LhARA will be a uniquely-flexible, novel system that will:

  - ***Deliver a systematic and definitive radiobiology programme***
  - ***Prove the feasibility of the laser-driven hybrid-accelerator approach***
  - ***Lay the technological foundations for the transformation of PBT***
    - **automated, patient-specific: implies online imaging & fast feedback and control**

- **Ambition:**
  - **Develop:**
    necessary techniques, technologies, and *systems*
  - **Exploit:**
    ***system* approach to bring novel techniques into clinical practice as they mature**
  - **Integrate:**
    production prototypes in a production *system* for radiobiological research
  - **Engage:**
    industry and clinical PBT centres
    ***during development* of techniques, technologies, and systems**

Laser-hybrid Accelerator for Radiobiological Applications (LhARA)

Conceptual Design Report

G. Aymar[1], T. Becker[2], S. Boogert[3], M. Borghesi[4], R. Bingham[5a], C. Brenner[1], P. Burrows[6], O.C. Ettlinger[7], T. Dascalu[7], S. Gibson[3], T. Greenshaw[8], S. Gruber[9], D. Gujral[10], C. Hardiman[10], J. Hughes[8], K. Kirkby[11], A. Kurup[7†], J-B. Lagrange[1], K. Long[7a], W. Luk[7], J. Matheson[1], P. Mckenna[5], R. Mclauchlan[10], Z. Najmudin[7], H.T. Lau[7], J. Parsons[8], J. Pasternak[7a], J. Pozimski[7a], K. Prise[4], P. Ratoff[12], W. Shields[3], S. Smith[13], J. Thomason[1], S. Towe[14], P. Weightman[8], C. Whyte[5], R. Xiao[15]

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14. *Leo Cancer Care, Broadview, Windmill Hill, Hailsham, East Sussex, BN27 4RY, UK*
15. *Cororain, 14F, Changfu Jinmao Building(CFC), Trade-free Zone, Futian District, Shenzhen, Guangdong, China*

a. *Also at STFC Rutherford Appleton Laboratory, Harwell Oxford, Didcot, OX11 0QX, UK*

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Pre-publication review

LhARA pre-CDR review: terms of reference

Background

LhARA, the Laser-hybrid Accelerator for Radiobiological Applications, 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 modulated by the physical characteristics of the beam. The laser-driven source allows protons and ions to be captured at energies significantly above those that pertain in conventional facilities, thus evading the current space-charge limit on the instantaneous dose rate that can be delivered. This makes it possible to consider dose rates up to and potentially significantly beyond the current ultra-high dose-rate, "FLASH", regime. Rapid acceleration will be performed using a fixed-field accelerator (FFA) thereby preserving the unique flexibility in the time and spatial structure of the beam afforded by the laser-driven source.

It is proposed that LhARA be developed in two stages. In the first stage, 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 up to 15 MeV. In stage two, the beam will be accelerated to allow in-vitro and in-vivo experiments to be carried out with proton-beam energies of up to 125 MeV. Ion beams (including C^{6+}) with energies up to 30 MeV per nucleon will also be available. The rapid acceleration provided by the FFA preserves the unique flexibility in the time-structure of the beam provided by the laser-driven source.

Since October 2019 work on the LhARA pre-CDR has been funded by an STFC Opportunities 2019 award. This modest award supports 6-months' full-time effort of a post-doc at Imperial, who is coordinating the work and contributing to the accelerator design, and a post-doc in Liverpool who is contributing to the radiobiological aspects of the work. The STFC investment has leveraged additional support from across the consortium.

The pre-CDR will define the scope of the LhARA project, present an indicative costing for the facility, and an initial evaluation of the "technology-limited schedule". The pre-CDR also defines the R&D programme required to take the project forward. The pre-CDR will be submitted for publication in Applied Nuclear Physics at Accelerators. The LhARA consortium will use the pre-CDR as the springboard from which to launch the next round of bids for funding.

Terms of reference

The review panel will consider the pre-CDR document and a series of short presentations which will summarise its content to:

- Review the objectives of the LhARA consortium and comment on their scientific merit and timeliness;
- Review the scope of the programme and comment on its potential to deliver the consortium's objectives; and to
- Review and comment on the cost and schedule evaluation paying particular attention to the pre-construction R&D programme.

At the end of the review meeting the panel will prepare a short report summarising its findings and recommendations for transmission to the LhARA Steering Group.

Membership

Paul Bolton; Munich
Mike Lamont; CERN
Yolanda Prezado; Curie Institute, Paris
Francesco Romano; INFN

Timetable

25th *March 2020*: Y. Prezado will meet with the project team to review the radiobiological aspects of the programme. A report will be provided to inform the review of the technological aspects of the programme.
31st *March 2020*: The review panel will meet to consider the technological aspects of the programme.
3rd *April 2020*: The panel's report will be finalised and sent to K. Long for transmission to the LhARA Steering Group.

In conclusion

- Many thanks for taking part in the review
- Many thanks too for your patience and flexibility in the light of the pressures imposed by the Covid-19 pandemic

Agenda for 31Mar20 session of the review:

Agenda 31st March 2020

Time*	Speaker	Title
12:00—12:30	Reviewers and PIs	Clarifications, administrative issues, and organisation
12:30—12:45	All	Assemble and contingency
12:45—13:00	K. Long (ICL)	Welcome and introduction
13:00—13:25	J. Parsons(Liverpool)	Radiobiological motivation and feedback from Y. Prezado
13:35—13:55	A. Kurup, pre-CDR PM (ICL)	LhARA pre-CDR overview
13:55—14:00	All	Contingency
14:00—14:20	Z. Najmudin (ICL)	Laser driven proton and ion source
14:20—14:40	C. Whyte (Strathclyde)	Proton and ion capture
14:40—15:00	J. Pasternak (ICL)	Design of the LhARA accelerator facility
15:00—15:20	W. Shields (RHUL)	Simulation of LhARA
15:20—15:40	J. Matheson (STFC RAL, PPD)	Instrumentation
15:40—16:00	J. Hughes (Liverpool)	Biological end stations
16:00—16:20	G. Aymar (STFC RAL, ISIS)	Infrastructure considerations
16:20—16:30	All	Contingency
16:30—17:00	Reviewers	Discussion
17:00—17:30	All	Feedback and close-out

* Times are to be understood to include 5 minutes for questions.