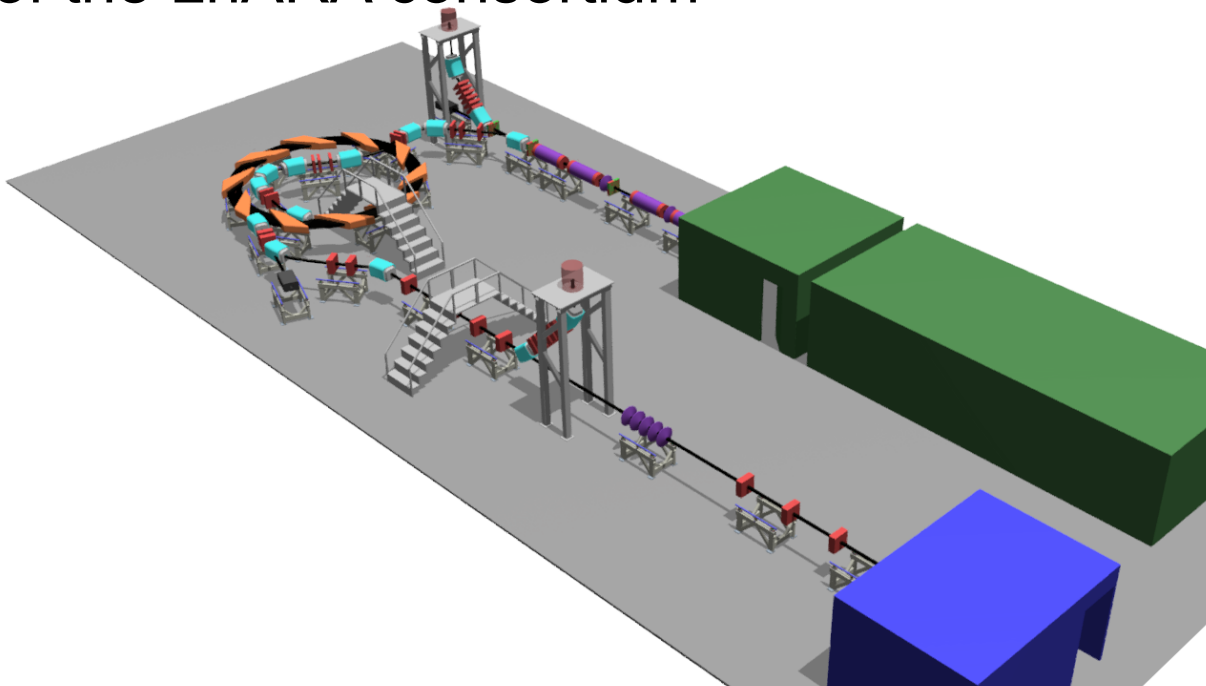
Laser-hybrid Accelerator for Radiobiological Applications (LhARA)

N. P. Dover (ICL) on behalf of the LhARA consortium

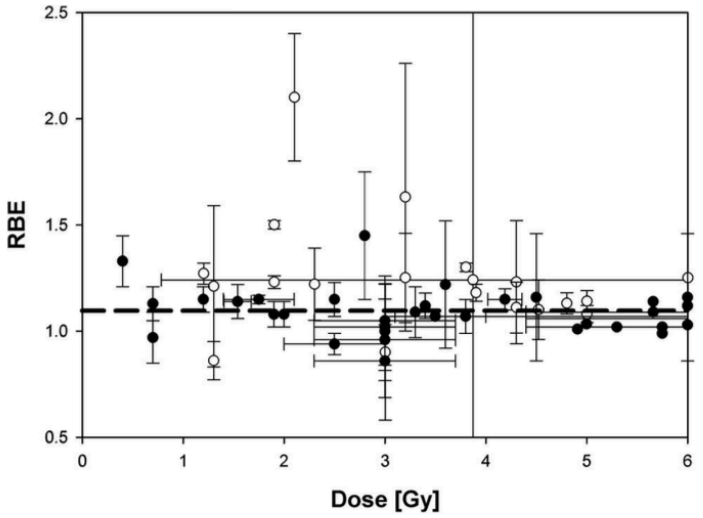
JAI Advisory Board Meeting
7th April 2022



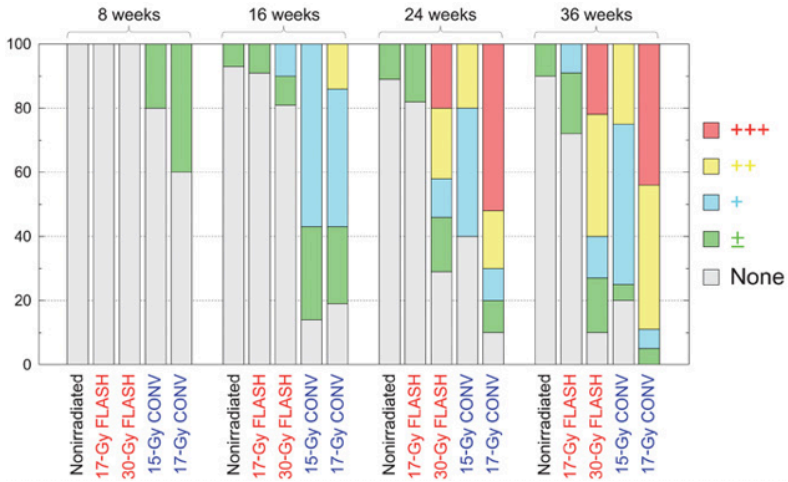
The case for LhARA

- **Growing global requirement for RT**
  - Scale up in provision is essential
  - Development of new technologies and cost effective systems
- **Systematic study of the radiobiology of ion beams**
  - Accurate treatment planning relies on RBE
  - For ions, uncertainty due to many factors:
    - Energy, dose, dose rate, dose spatial distribution, ion species…
- **Novel beams for radiobiology**
  - Therapeutic benefits for ultrahigh dose rates (“FLASH” RT) and microbeam threrapy
  - Requires extensive further study both *in vitro* and *in vivo*

Paganetti and van Luijk, Sem. Rad. Oncol. 23, 77 (2013)

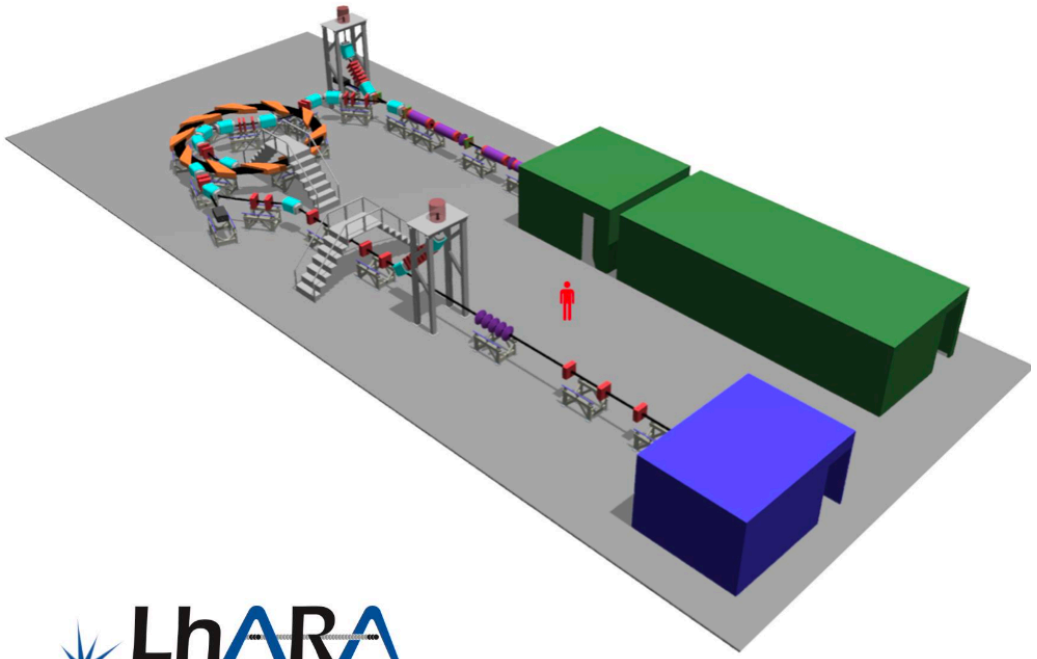


Favaudon et al., Sci. Transl. Med. 6, 245 (2014)



The LhARA consortium

The LhARA approach



LhARA
Laser-hybrid Accelerator for Radiobiological Applications

arXiv:2006.00493

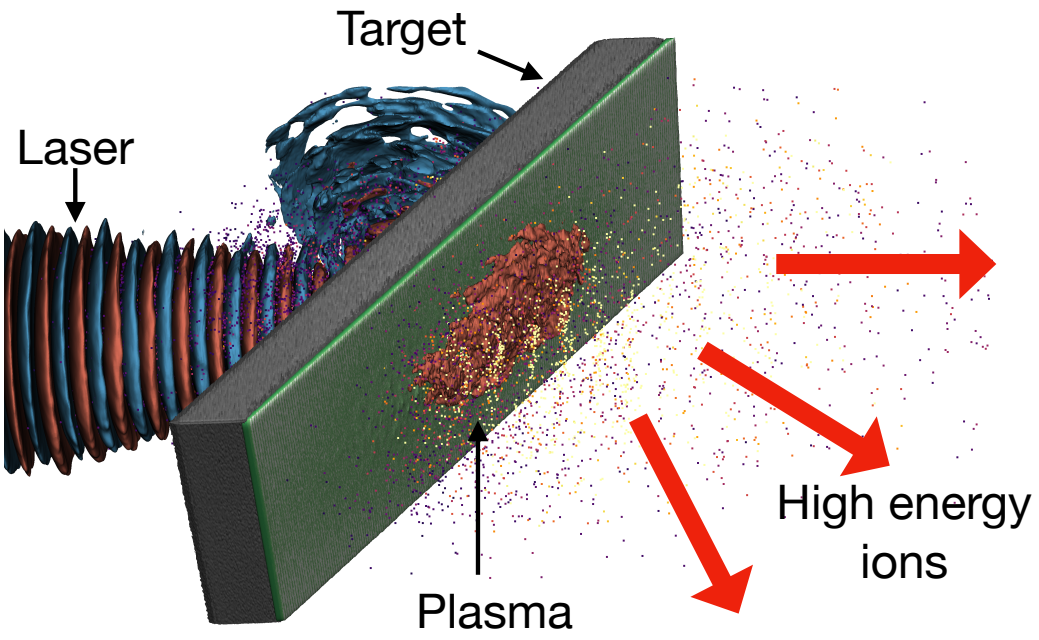
A novel laser-hybrid approach

- **Laser-driven high-flux proton/ion source**
  - Overcome instantaneous dose-rate limitations
  - Proton/ion bunches as short as 10-40 ns
  - Triggerable
- **Electron-plasma lenses for capture and beam focusing**
  - Short focal length without the use of high field solenoids
- **Fast post acceleration with an FFA**
  - Variable energy:
    - ➡Protons 15-127 MeV
    - ➡Ions 5-34 MeV/u

Conceptual design for LhARA: Aymar et al. Frontiers in Physics **8**, 567738 (2020)

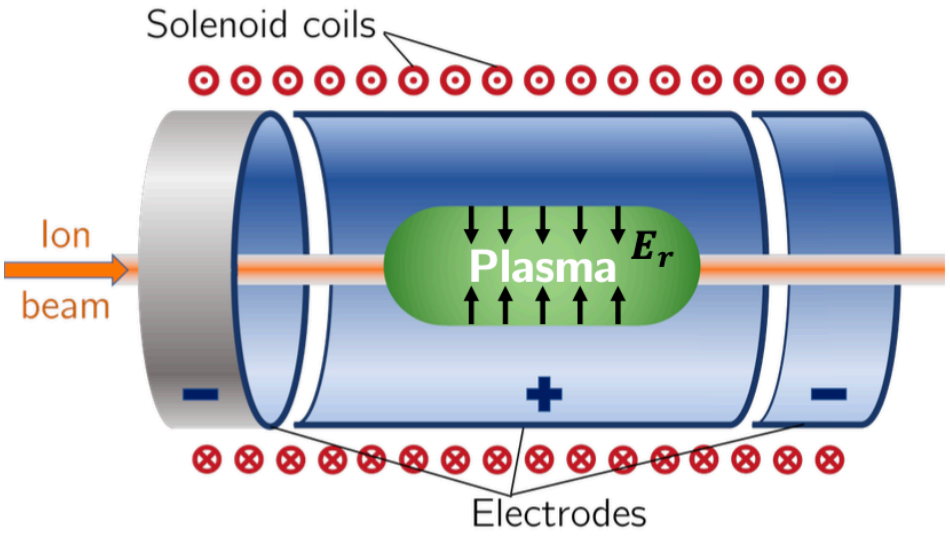
Basis of the laser-hybrid approach

Laser Ion Source



- High energy (e.g. ~15 MeV p+, 4 MeV/u C6+) *from source*
- Minimised space charge issues, enabling high flux
- Divergent broadband beams

Gabor plasma lens



- Focus in both planes simultaneously
- Energy-dependent focusing strength
- Cost effective solenoid alternative

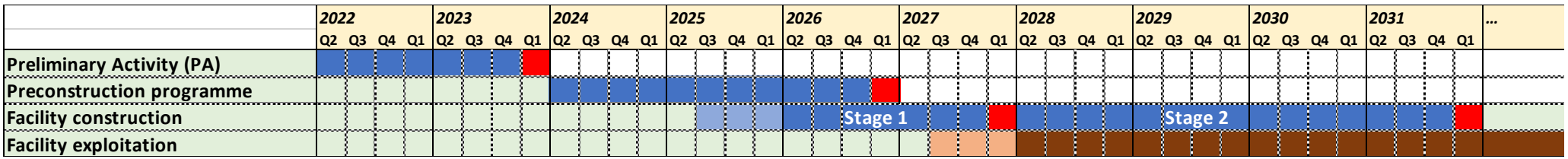
ITRF: Ion Therapy Research Facility

Ion therapy research facility:

- Compact, single-site national research infrastructure delivering ions (protons through oxygen and beyond) at high dose rates (FLASH)
- Energies sufficient for both in-vitro and in-vivo studies
- Facility will answer cancer biology questions for better clinical care

Proposal to UKRI Infrastructure Advisory Committee

- Proposal for 2 year preliminary activity, which will then require a three-year pre-construction phase
- LhARA formed the basis of this proposal, and alignment between ITRF and LhARA is now being developed



Mapping of LhARA to the ITRF proposal

From ITRF proposal to UKRI:

Transformative, multidisciplinary approach:
Very high dose rate FLASH therapy may transform radiotherapy; new modalities in spatially-fractionated therapy could be disruptive in ion-beam therapy. A laser-hybrid proton/ion source, as proposed by the existing, UK-led, international LhARA collaboration (see figure 3), can deliver this and meet the needs of the ITRF. LhARA (see figure 1) is a hybrid system coupling a laser-driven proton/ion source to a novel, rapid-acceleration system. The delivery of the ITRF will require a multidisciplinary approach that includes oncologists, radiobiologists, accelerator, and instrumentation scientists; this expertise is present in the ITRF collaboration and its Advisory Board.

The Preliminary Activity (PA):
The PA will develop over 2 years the specification, design, and cost of the ITRF and present these in a full Conceptual Design Report (CDR), leading to a 2-year pre-construction TDR phase and the construction phase (see figure 2). The PA will be performed via two main work streams:

1. End-station specification and design:
Learning from previous and planned ion-research infrastructures, we will develop an end-station design and associated beam specification to support a definitive biomedical research programme. This activity will benefit from significant expertise at: MRC Oxford Institute of Radiation Oncology; Liverpool University's Institute of Systems, Molecular and Integrative Biology; Christie Hospital/Manchester University PRECISE proton therapy research group and research beamline. We envisage a staged plan first for high-throughput *in-vitro* and then small-animal *in-vivo* research to improve understanding of biological effectiveness and biologically-augmented treatment planning with AI/ML as part of a wider UK plan towards eventual clinical ion treatment. The potential and need for both transmission and Bragg-peak FLASH will also be assessed.

2. Conceptual Design Report, technology choice, technical-risk management:
A conceptual design study will be conducted to produce a full project plan including operating modality for national/international users, and a scientific, technological, economic, and societal impact assessment. This will feed into subsequent development of an Outline Business Case.

We will build upon UK expertise in the relevant accelerator technologies. Laser-source design will be led by Belfast/CLF/Imperial/Strathclyde; conventional acceleration by Cockcroft/JAI/STFC; novel dosimetry and instrumentation by Birmingham/ICR/Liverpool/Manchester/NPL/STFC/UCL; infrastructure and engineering integration by STFC. We recognise the significant challenges of our transformative technical approach, which will be managed as described later; our modular design allows the research end-station to be compatible with several accelerator source options.

Effective tensioning of the benefits and costs of parameter trade-offs, technology choices, and implementation strategies will be carried out through 6-monthly reviews via our Advisory Group. Technology choices will be supported by appropriate prototyping building on existing test infrastructures and instrumentation at Belfast/Birmingham/Christie/Imperial/Strathclyde and elsewhere.

Multidisciplinary collaboration:
- Labs (ASTeC, CLF, PPD, TD)
- HEIs from all 4 nations
- JAI/CI
- International partners

CDR/TDR development - **WP6**

End-station specification and design - **WP5**
- Exploit Birmingham ambition to create a vertical beamline
- Scientific measurement/ prototype/comissining

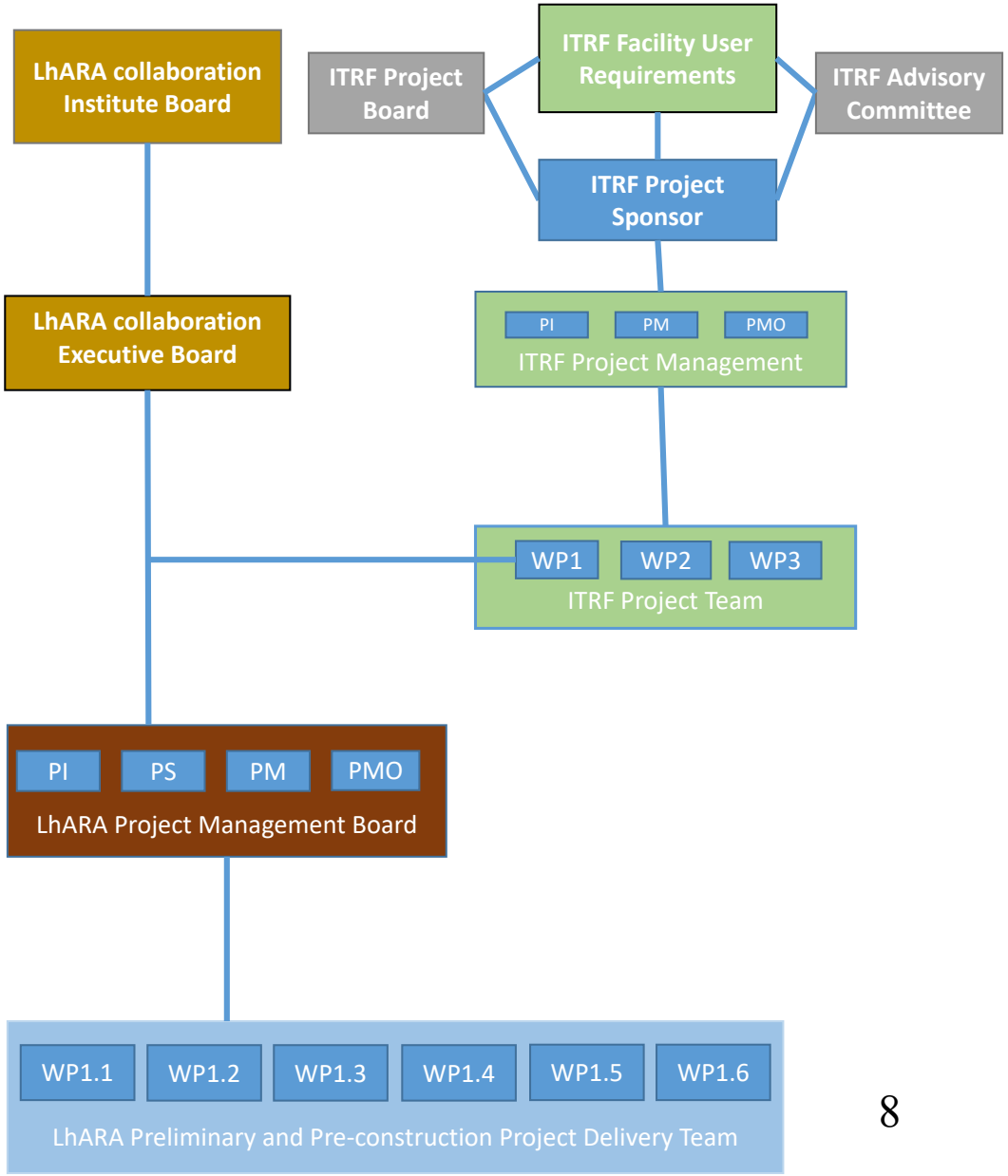
Programme to address key technical risks:
- **WP2-4** on ion source, capture, and realtime shot-by-shot non destructive dose mapping

Integration of LhARA into ITRF management structure

- LhARA has been adapted into ITRF framework
- Discussions ongoing, but majority of proposed funding will be used for LhARA preliminary activity

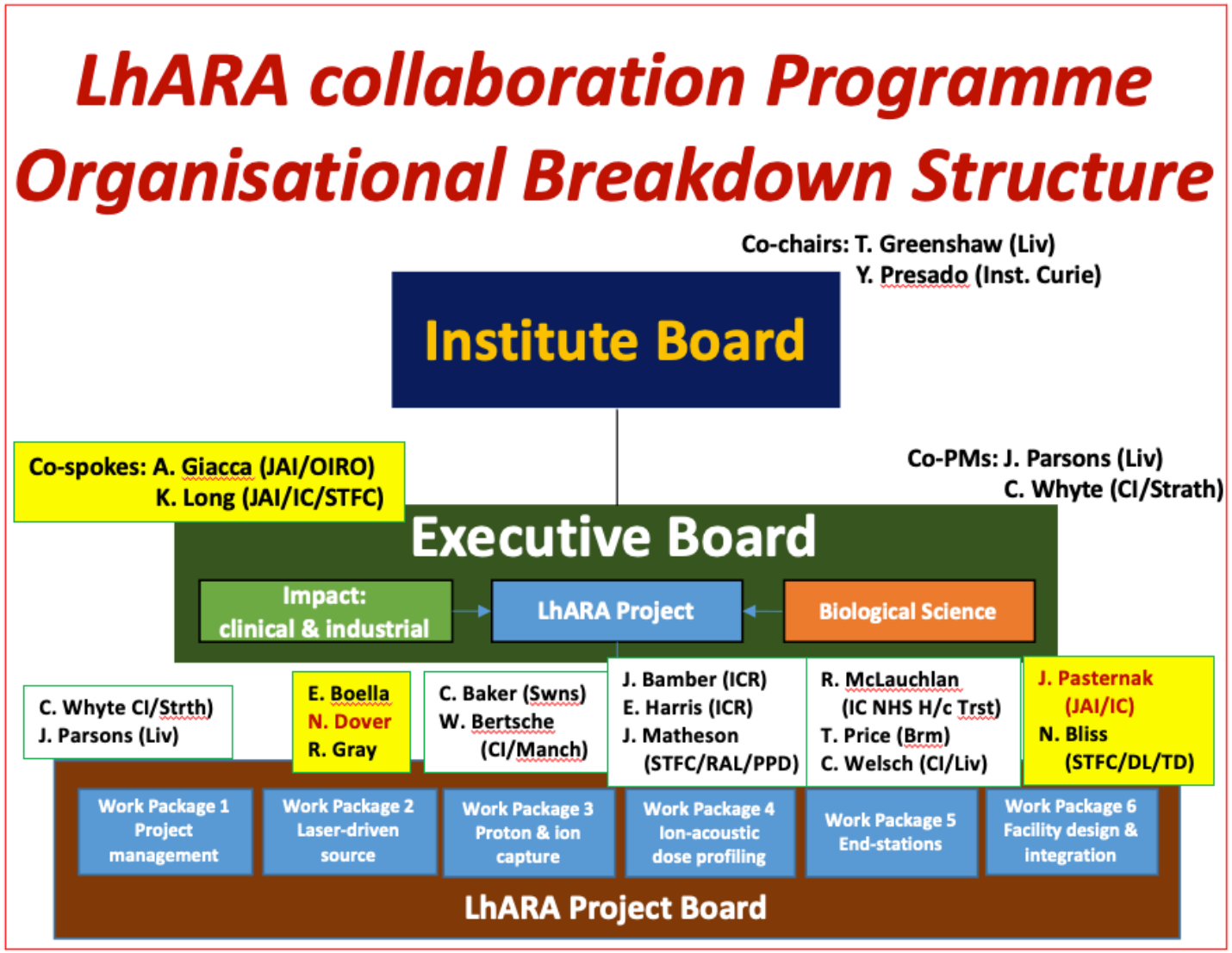
LhARA preliminary and pre-construction activity:

- WP1.1: project management
- WP1.2: laser-driven source
- WP1.3: beam capture
- WP1.4: Ion acoustic diagnostics
- WP1.5: Novel End Station
- WP1.6: Design & Integration



JAI contribution to LhARA & ITRF

- JAI providing leadership at different levels in LhARA management



JAI contribution to LhARA & ITRF

- JAI involved in various roles throughout all technical work packages

WP2: Source
Work package management, experimental R&D and development of ion source, utilising in-house laser systems, numerical simulations

- Zulfikar Najmudin, Nick Dover, Ollie Ettlinger, George Hicks, Nuo Xu, HT Lau (JAI-ICL)

WP3: Capture
Experiments and simulations of Gabor lens

- Titus-Stefan Dascalu, HT Lau, Ken Long (JAI-ICL)

WP4: Ion Acoustic
Simulation of ion-acoustic system

- Maria Maxouti, Ken Long (JAI-ICL)

WP5: End station
End station development

- *Amato Giaccia (JAI/OIRO)*

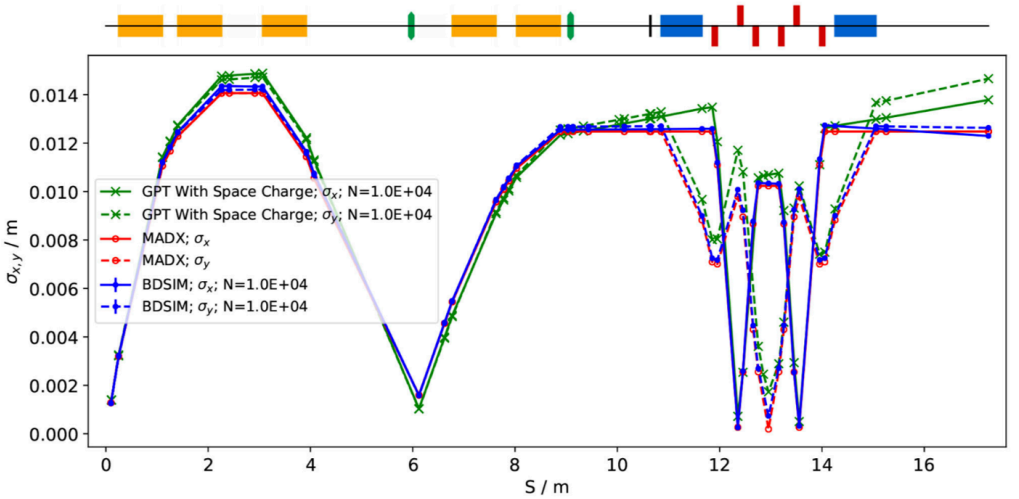
WP6: Design and integration
WP6 management, beamline design

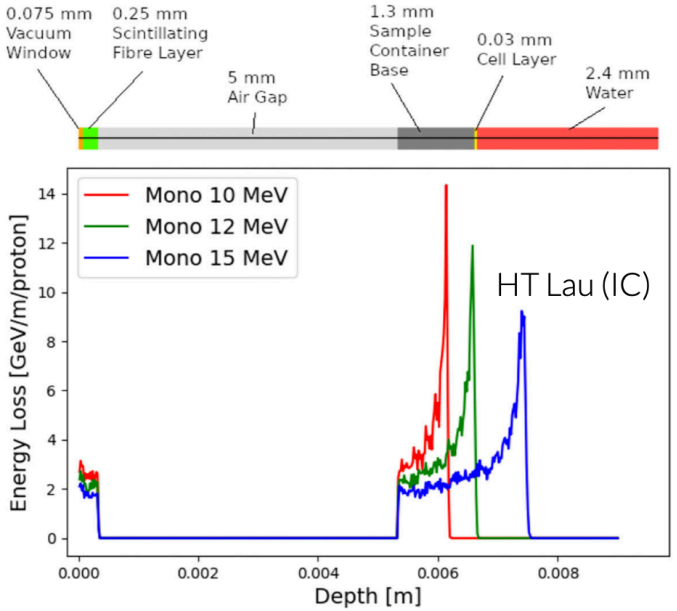
- Jaroslaw Pasternak (JAI-ICL)
- Will Shields (JAI-RHUL)

JAI-RHUL contribution to start-to-end MC modelling

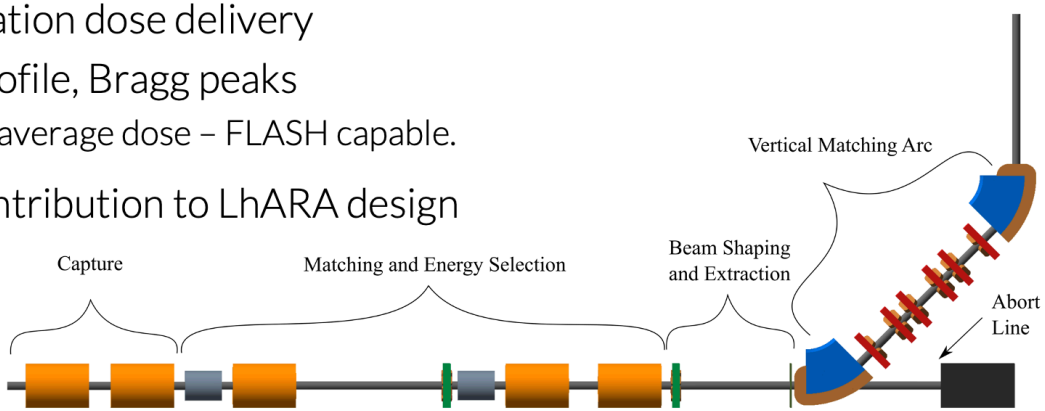
LhARA Performance Evaluation

- Start-to-end Monte Carlo modelling for performance evaluation:
  - BDSIM (Geant4) 3D accelerator model: tracking, losses, particle-matter interactions, energy deposition
  - GPT: Space charge effects





- Good optical agreement, minor impact from space charge forces,
  - Stage 1, stage 2 injection line, & stage 2 post FFA.
- Stage 1 end station dose delivery
  - Beam profile, Bragg peaks
  - 128 Gy/s average dose – FLASH capable.
- Continuing contribution to LhARA design



Courtesy of W. Shields (JAI-RHUL)

Current state-of-play

- R&D proposal for preliminary, preconstruction phases will be completed this month
- Collaboration getting ready to begin preliminary activity if proposal successful
- Upcoming meetings at RAL:
  - 27th April: LhARA collaboration meeting
  - 28th April: workshop on Disruptive technologies for proton/ion oncology

Contents

Proposal to be reviewed by international advisory board

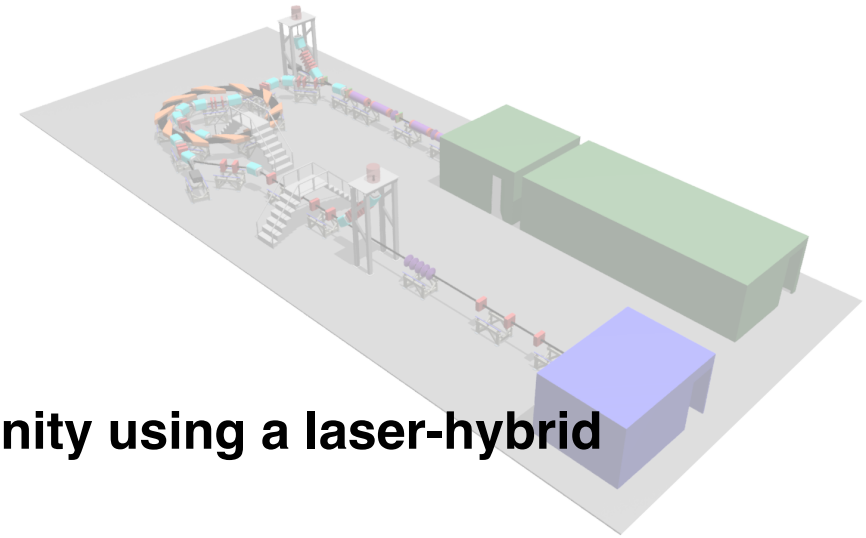
The IAB from the CCAP (Centre for Clinical Application of Particles) have agreed to review the LhARA proposal

- **CCAP IAB:**
  - M. Lamont (CERN, Chair)
  - P. Bolton (LMU, retired)
  - M. Baumann (DKFZ)
  - B. Sorensen (Aarhus)
- **For review of proposal (i.e. co-opted)**
  - I. Robson (STFC, retired)

Review strategy discussed with IAB chair:

- **Co-opt expertise on e.g. source, FFA, etc.**
- **Proposed to do review in two parts:**
  - Biomedical science
  - Technological and Project aspects
- **Timeline to be announced, but likely May/June**

Summary



- **LhARA will serve the radiobiology community using a laser-hybrid approach**
  - Overcome dose-rate limitations of present and ion beam therapy sources
  - Deliver a range of ion species, energies, dose, dose-rate and time and spatial distribution
  - Used in an automated, triggerable system
- **The LhARA collaboration aligning with the ITRF to develop a "Preliminary Phase" programme**
  - Prove the novel laser-hybrid system in operation
  - Provide facility capable of delivering broad radiation biology programme
  - Create the novel capabilities required to transform proton and ion therapy

LhARA
Laser-hybrid Accelerator for Radiobiological Applications

JAi
John Adams Institute for Accelerator Science