DEPARTMENT OF ONCOLOGY
Medical Sciences Division

A. Giacca, K. Long, 21 April, 2023

Imperial College London
UKRI Science and Technology Facilities Council

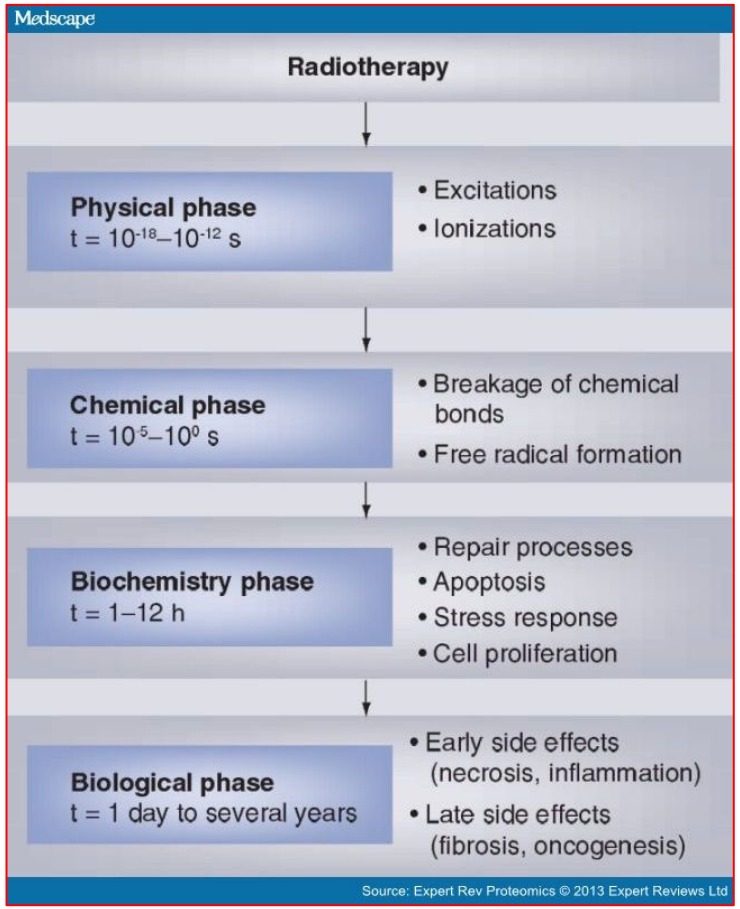
LhARA (ITRF WP 1) update

Since last presentation to ITRF AC (03Nov22)

LhARA Laser-hybrid Accelerator for Radiobiological Applications

CCAP Centre for the Clinical Application of Particles

Radiobiology in new regimens



Time domain

Space domain

The ideally flexible beam facility can deliver it all!

⇒ substantial opportunity for a step-change in understanding!

Energy

Ion species

In combination

and with chemo/immuno therapies


Imperial College London
ICR The Institute of Cancer Research
Medical Research Council
UKRI
Oxford Institute for Radiation Oncology
University of Oxford
JAI John Adams Institute for Accelerator Science
LhARA Laser-hybrid Accelerator for Radiobiological Applications
CCAP Centre for the Clinical Application of Particles
Imperial College Academic Health Science Centre
Cancer Research UK Imperial Centre
NHS Imperial College Healthcare NHS Trust
Manchester 1824 The University of Manchester
University of Birmingham
University of Liverpool
NHS University Hospitals Birmingham NHS Foundation Trust
NHS The Clatterbridge Cancer Centre NHS Foundation Trust
NHS The Christie NHS Foundation Trust
institut Curie
Queen's University Belfast
Swansea University Prifysgol Abertawe
UCL Medical Physics & Biomedical Engineering
University
Clinical
Accelerator
Laboratory
Industry
Partners
Netherlands Cancer Institute Antoni van Leeuwenhoek
Hampton University Proton Therapy Institute Fighting Cancer, Saving Lives
University of Strathclyde Glasgow Department of Physics
Royal Holloway University of London
Lancaster University
UKRI Science and Technology Facilities Council
ASTeC
Daresbury Laboratory
Particle Physics Department
ISIS Neutron and Muon Source
CLF central laser facility
University of Birmingham | Cyclotron Facility | Positron Imaging Centre
INFN Catania
The Cockcroft Institute of Accelerator Science and Technology
CERN
Corerain 鲲云科技
LEO Cancer Care
MAXELER Technologies Maximum Performance Computing
The Rosalind Franklin Institute
NPL National Physical Laboratory

LhARA collaboration

LhARA Memorandum of Understanding

Draft; 31Jan23

Preamble

The objective of the Laser-hybrid Accelerator for Radiobiological Applications (LhARA) Collaboration is to:

- Design, build and operate a laser-driven proton and ion accelerator for the study of the radiobiology relevant to the treatment of cancer. The LhARA facility is described in detail in the document *The Laser-hybrid Accelerator for Radiobiological Applications*[1];
- Pursue a cutting-edge radiobiology research programme in which the novel techniques developed by the collaboration play an ever increasing role and which culminates in the exploitation of the uniquely flexible LhARA facility; and
- Generate clinical and other impact through incremental deployment of the novel techniques and technologies developed by the collaboration.

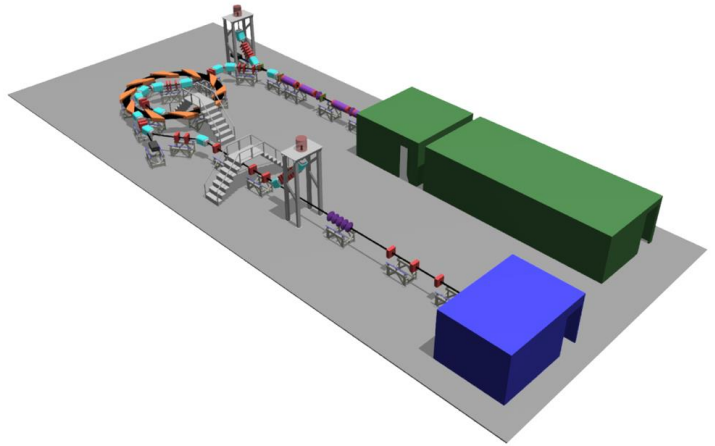
LhARA collaboration Programme Organisational Breakdown Structure

LhARA project within ITRF

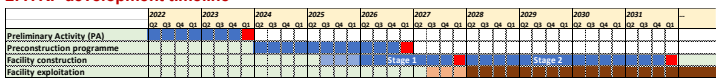
J, Clark, M. Noro, A. Woodcock 14Jun21

Ion Therapy Research Facility

1. Schematic diagram of the Ion Therapy Research Facility

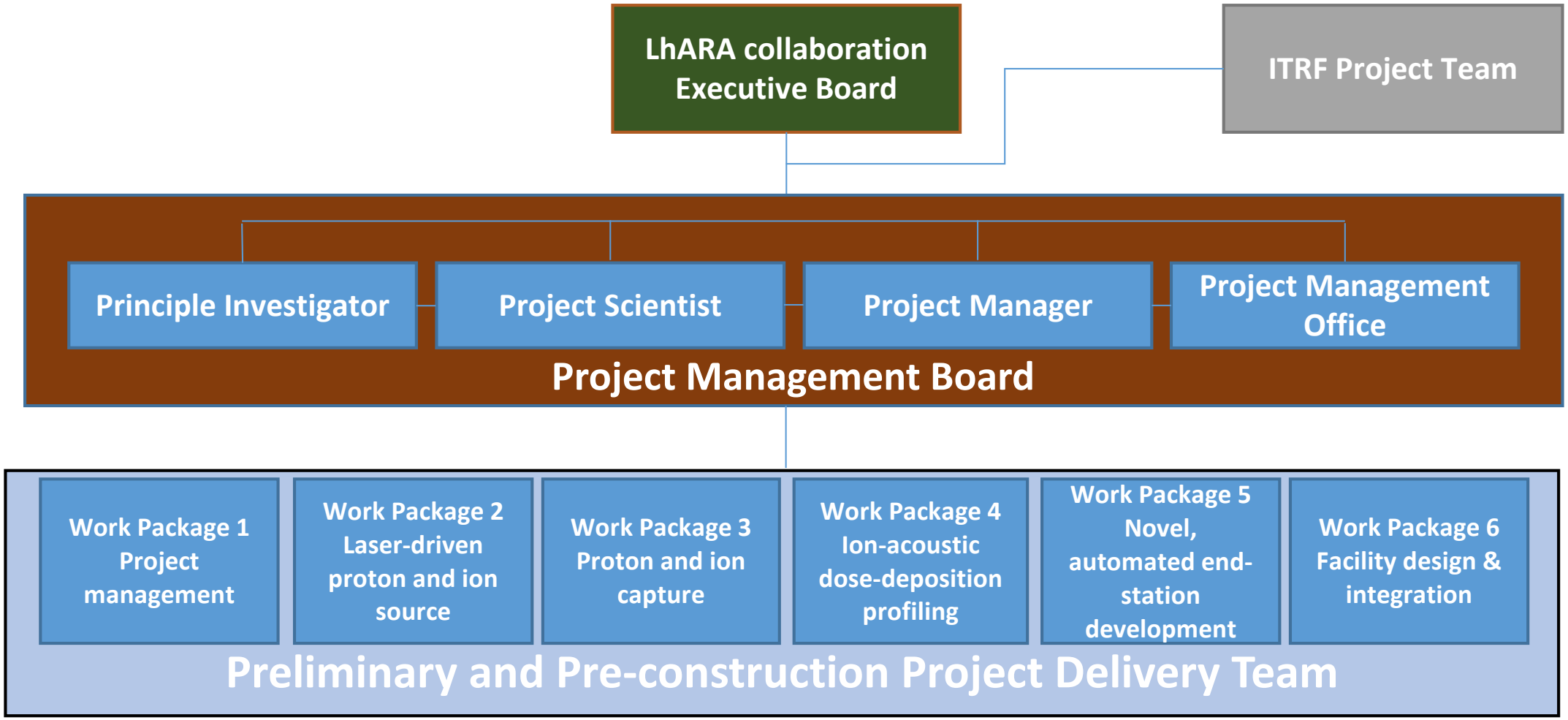


2. ITRF development timeline



3. Institutes that make up the ITRF collaboration

LhARA Project
Organisational Breakdown Structure



Material taken from … and …

LhARA collaboration meeting, 08Feb23:

LhARA Collaboration Meeting

https://indico.stfc.ac.uk/event/685/

Wednesday 8 Feb 2023, 10:00 → 18:30 Europe/London

Physics West

Amato Giacca (Oxford/Stanford) , Jason Parsons (Birmingham) , Jason Parsons (Liverpool) , Tony Price (Birmingham)

Description This, the third, LhARA collaboration meeting will be held in the Vinen Room in Physics West, School of Physics and Astronomy, Birmingham, B15 2TT

The meeting will be held in "mixed mode" but if you are able to attend "in person" that would be excellent.

Zoom: https://bham-ac-uk.zoom.us/j/86538837135?pwd=M3dqMHZ3MGo5dUdnMHlTVDBCWjZqUT09

Science and Technology Facilities Council

ITRF Project

LhARA

LhARA-Gov-PMB-2023-03 Final
1272-pa1-pm-rpt-0005-1.0-six-month-design-review-report

April 19, 2023

LhARA/ITRF: six month progress report

C. Baker [1], J. Bamber [2], W. Bertsche [13,5], N. Bliss [3], E. Boella [4,5], N. Dover [6], R. Gray [7,5], E. Harris [2], M. Johnson [3,5], K. Kirkby [12,13,5], A. Kurup [6,8], K.R. Long [6,8], R. Mclauchlan [9], H. Owen [3,5], J.L. Parsons [10], J. Pasternak [6,8], T. Price [11], C. Whyte [7,5],

1. *Department of Physics, Faculty of Science and Engineering, Swansea University, Singleton Park, Swansea, SA2 8PP*
2. *Institute of Cancer Research, UK*
3. *UKRI-STFC Daresbury Laboratory, Sci-Tech Daresbury, Daresbury, Warrington, WA4 4AD, UK*
4. *Lancaster University, UK*
5. *Cockcroft Institute, Sci-Tech Daresbury, Daresbury, Warrington, WA4 4AD, UK*
6. *John Adams Institute, Imperial College London, Exhibition Road, London, SW7 2AZ, UK*
7. *Department of Physics, SUPA, University of Strathclyde, 16 Richmond Street, Glasgow, G1 1XQ, UK*
8. *UKRI-STFC Rutherford Appleton Laboratory, Didcot, OX11 0QX, UK*
9. *Imperial College NHS Healthcare Trust, The Bays, South Wharf Road, St Mary's Hospital, London W2 1NY, UK*
10. *Institute of Cancer and Genomic Sciences, University of Birmingham, Edgbaston, Birmingham, B15 2TT, UK*
11. *School of Physics and Astronomy, University of Birmingham, Edgbaston, Birmingham, B15 2TT, UK*
12. *Division of Cancer Sciences, Faculty of Biology, Medicine and Health, The University of Manchester, The Christie Proton Therapy Centre, The Cristie NHS Foundation Trust, Wimslow Rd, Manchester M20 4BX*
13. *Department of Physics and Astronomy, The University of Manchester, Oxford Rd, Manchester, M13 9PL, UK*

Contents

Six-month progress report

… and, 6-month design review

Meeting included Giacca/Parsons:

"LhARA Science Consultation Plan"

ITRF & LhARA Project 6 Month Design Review Meeting

Tuesday 21 Mar 2023, 12:30 → 17:10 Europe/London

Daresbury Laboratory

https://indico.stfc.ac.uk/event/722/

Colin Whyte (University of Strathclyde), Hywel Owen (STFC), Neil Bliss (STFC)

Description https://ukri.zoom.us/j/98759354257

Contact Hywel Owen, Neil Bliss hywel.owen@stfc.ac.uk neil.bliss@stfc.ac.uk

Radiobiological Research Directions for LhARA

- Characterising the key biophysical characteristics of laser-driven ions compared to conventional ions by interrogating the response of different models. Specially those enriched in stem-cell populations.
- Assessing the impact of oxygenation levels on DNA damage and immune responses in response to different temporal and spatial patterns.
- Identify the impact of genetic mutations where ion beams would be effective.
- Test the impact ultra-high dose-rate and spatially delivered ions on cell killing using in vivo mouse models and probe the impact of clinically relevant fractionation schedules.

Summary

Technical advantages of the LhARA facility

- Provides a reproducible, stable and reliable beam critical for acquiring accurate radiobiological data, and for performing systematic evaluations of the biological response.
- Beam which is flexible, easily accessible, and potentially high throughput (unlike clinical facilities).
- Ions can be delivered in very short pulses (10-40 ns) and high repetition rates.
- Ability to deliver particle ions at different energies/LET (protons at 15 and 125 MeV; carbon ions at 30 MeV) and at different dose rates (e.g. FLASH).
- *In vitro* and *in vivo* end-stations both for routine cell culture experiments (with automated handling in controlled environments), but also animal irradiations.
- Stimulate the analysis of more complex biological end-points.
- Potential for live cell imaging, rather than single end-point measurements.

Science consultation:

- **Being developed in parallel with end-station peer group consultation**

LhARA Science Board:

Just getting going

- **Co-chairs: Bob Bingham, Kevin Prise;**
  Remit: publication, conference talks, outreach

Laser-driven, high-flux proton/ion source

- Overcome instantaneous dose-rate limitation
- Can deliver protons or ions in 10-40 ns bunch
- Triggerable; arbitrary pulse structure

- Novel “electron-plasma-lens” capture & focusing
  - Strong focusing without high power, high-field solenoid
- Fast, flexible, fixed-field post acceleration
  - Protons: 15—127 MeV Ions: 5—34 MeV/u

LhARA performance summary arXiv:2006.00493

	12 MeV Protons	15 MeV Protons	127 MeV Protons	33.4 MeV/u Carbon
Dose per pulse	7.1 Gy	12.8 Gy	15.6 Gy	73.0 Gy
Instantaneous dose rate	1.0×10^9 Gy/s	1.8×10^9 Gy/s	3.8×10^8 Gy/s	9.7×10^8 Gy/s
Average dose rate	71 Gy/s	128 Gy/s	156 Gy/s	730 Gy/s

C. Whyte

Updates by WP: WP1 Management (ITRF WP 1.1)

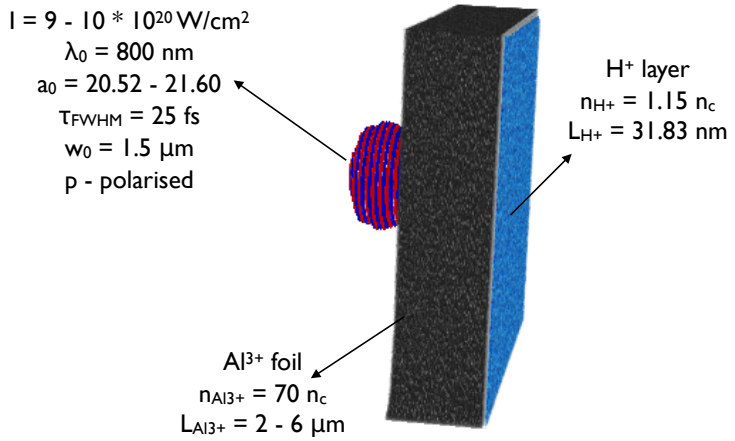
M5.1. Initial report on the user requirements for the in-vitro and in-vivo end stations.	WP5	Fri 31/03/23	Fri 31/03/23	
M3.1 Validate plasma simulations with existing Swansea experimental set-up	WP3	Mon 03/04/23	Mon 03/04/23	
M6.1: Early review of R&D work towards LhARA CDR (6 months)	WP6	Mon 03/04/23	Mon 03/04/23	
M5.2. Report on the beam-monitoring technology for LhARA.	WP5	Fri 29/09/23	Fri 29/09/23	
M2.1: Prediction of optimised proton source parameters for 100+ TW laser systems based on hydrodynamic and kinetic simulations	WP2	Sun 01/10/23	Sun 01/10/23	
M6.2: Interim review of R&D work towards LhARA CDR (12 months)	WP6	Mon 02/10/23	Mon 02/10/23	
M2.2: First SCAPA ion source simulations and experiment completed.	WP2	Mon 01/04/24	Mon 01/04/24	
M5.3. Second report on the user requirements for the in-vitro and in-vivo end stations.	WP5	Sat 30/03/24	Sat 30/03/24	
M3.2 Progress report of large diameter plasma experiments and simulations	WP3	Mon 01/04/24	Mon 01/04/24	
M6.3: Final review of R&D work towards LhARA CDR (18 months)	WP6	Tue 02/04/24	Tue 02/04/24	
M4.1 Geant4 simulations of beam energy deposition profile	WP4	Mon 01/04/24	Mon 01/04/24	
M3.3 Next generation plasma lens testbench design	WP3	Mon 30/09/24	Mon 30/09/24	
M4.2 Acoustic sensor array design	WP4	Mon 30/09/24	Mon 30/09/24	

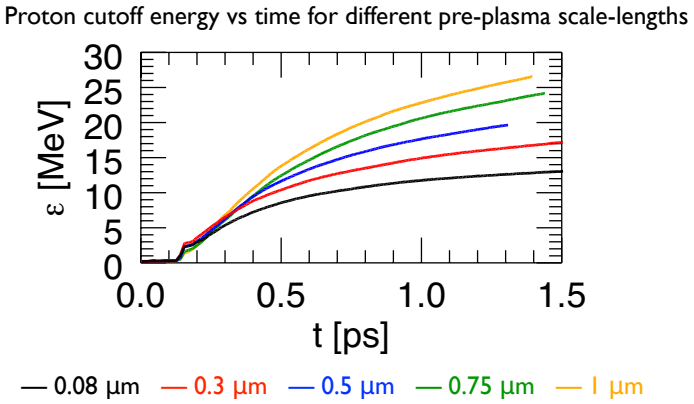
E. Boella, R. Gray, N. Dover

Proton and ion source (ITRF WP 1.2)

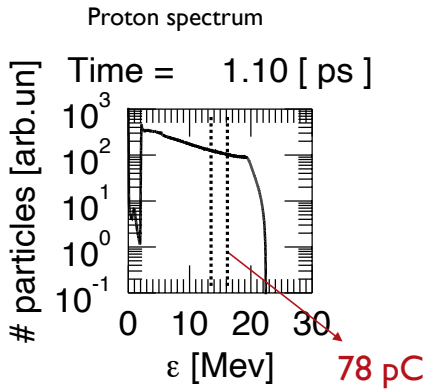
Progress on full 3D PIC simulations

Simulations and analysis performed by E. Boella (Lancaster)





- 3D simulations predict generation of ion beam parameters similar to LhARA baseline
- Optimal density profile will boost ion energies
- Currently developing workflow for modelling of effect of laser temporal pulse structure



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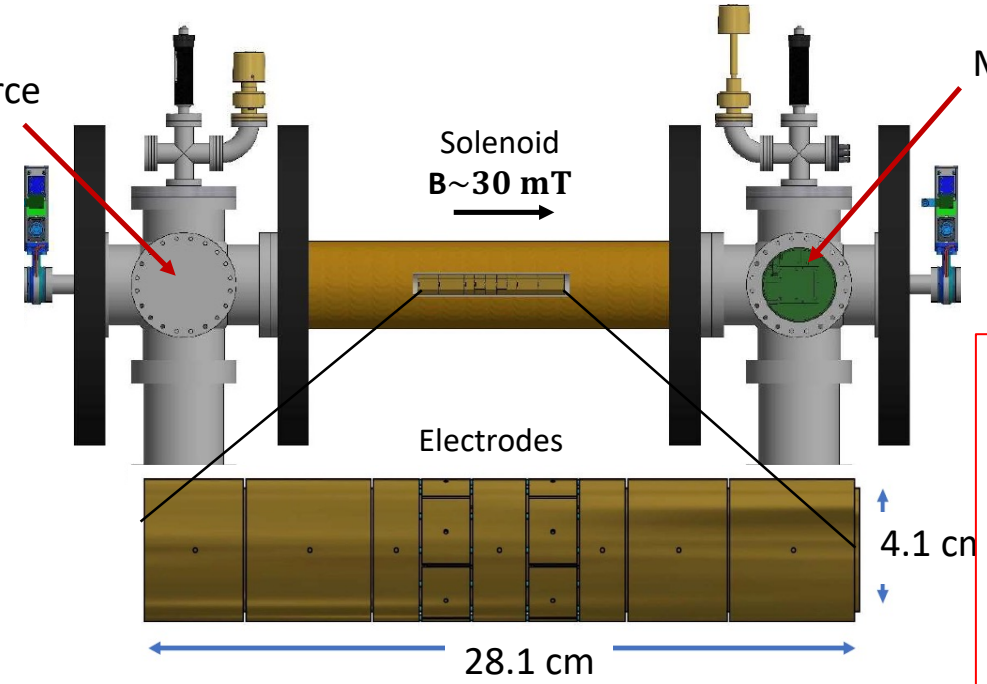
Progress by milestone:

1. **Prediction of optimised proton source (Sep23)**
   - Initial 3D simulations completed
2. **First SCAPA simulations and experiment (Mar24)**
   - First beam time Jul23
   - Expt. area commissioned

C. Baker, W. Bertsche

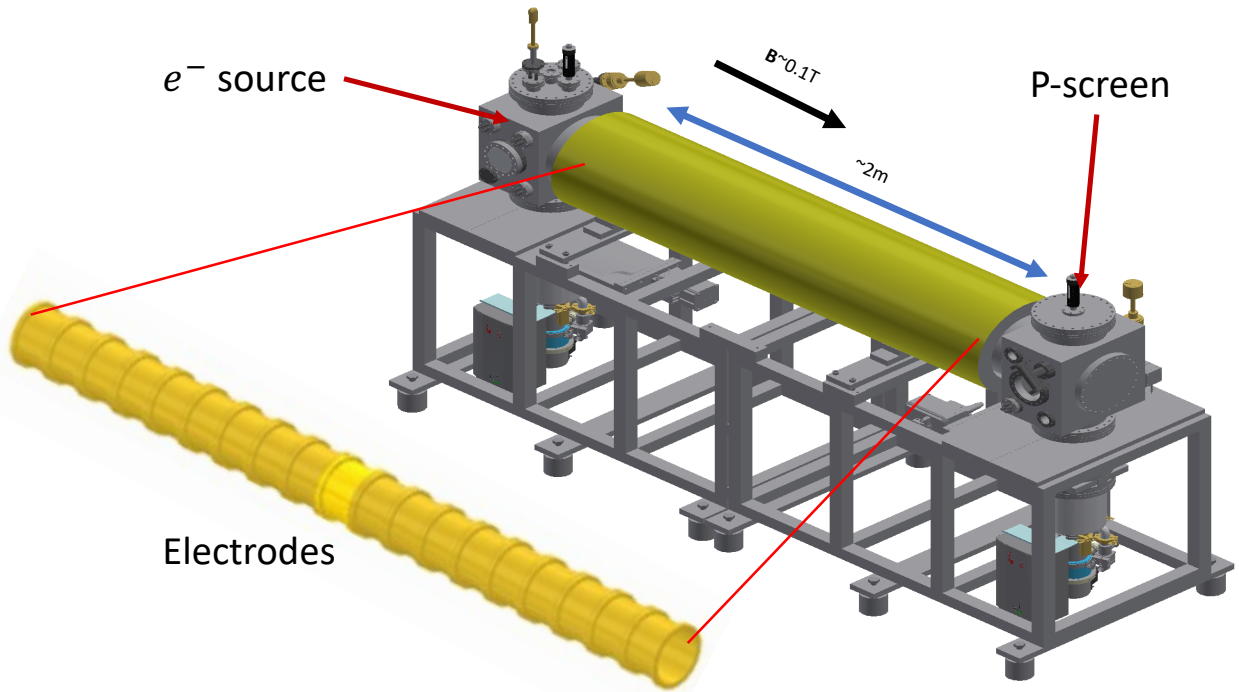
Proton and ion capture (ITRF WP 1.3)

Current Apparatus (preliminary activity)



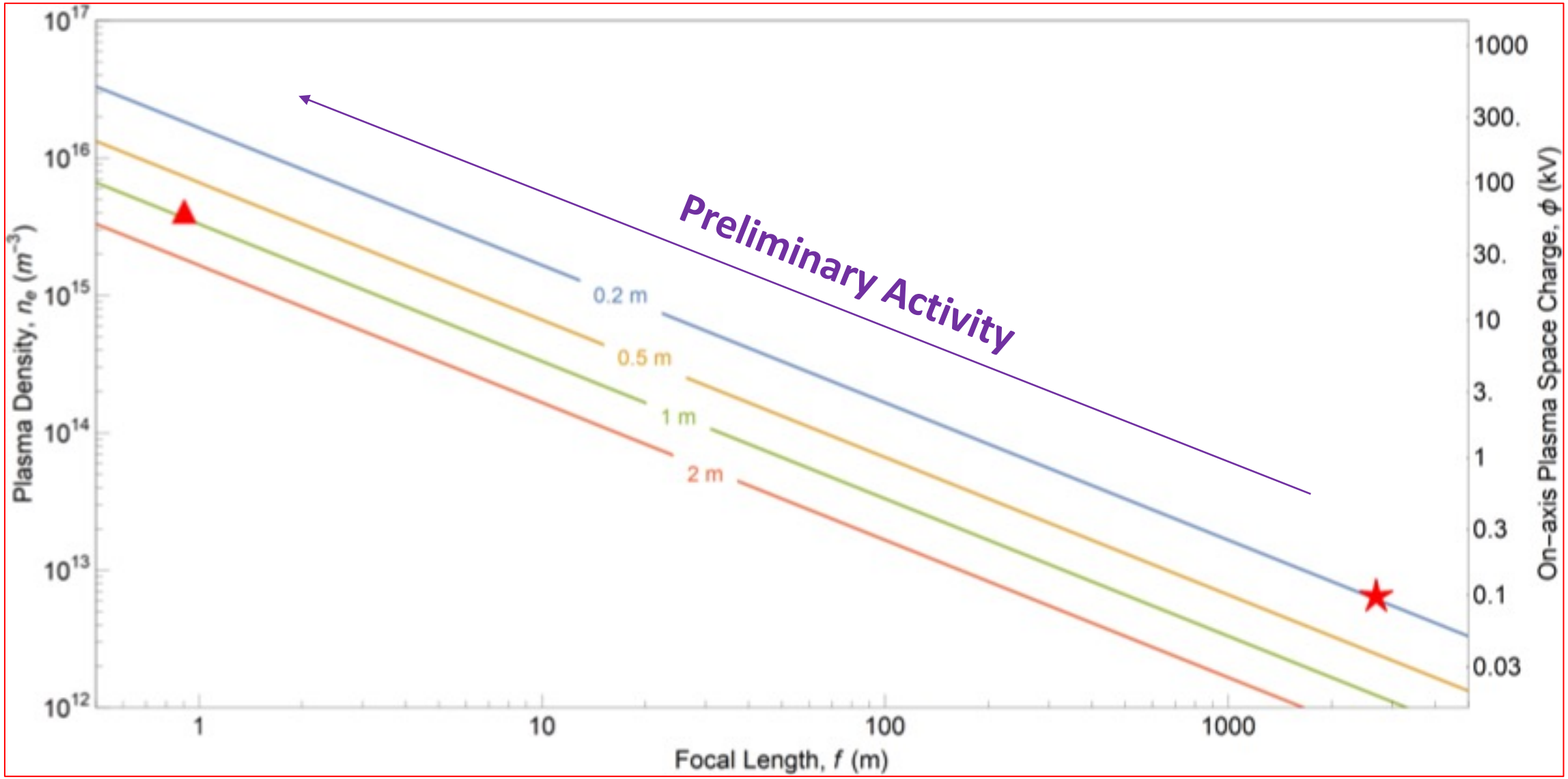
Full design by end of Preliminary Activity

Proposed Apparatus (preconstruction phase)



C. Baker, W. Bertsche

WP3 Proton and ion apture (ITRF WP 1.3)

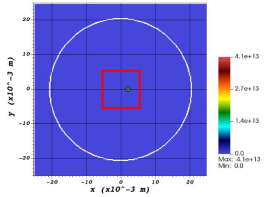


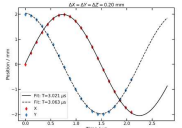
C. Baker, W. Bertsche

WP3 Proton and ion apture (ITRF WP 1.3)

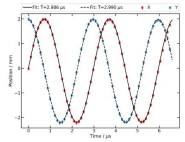
Simulation data

Speed up single simulation

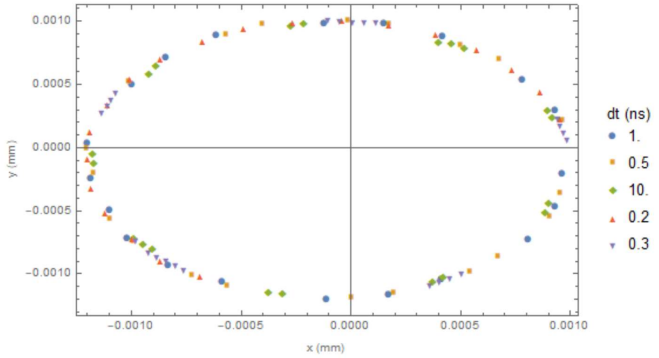




~48 hours
(16 CPUs)



~24 hours
(16 CPUs)

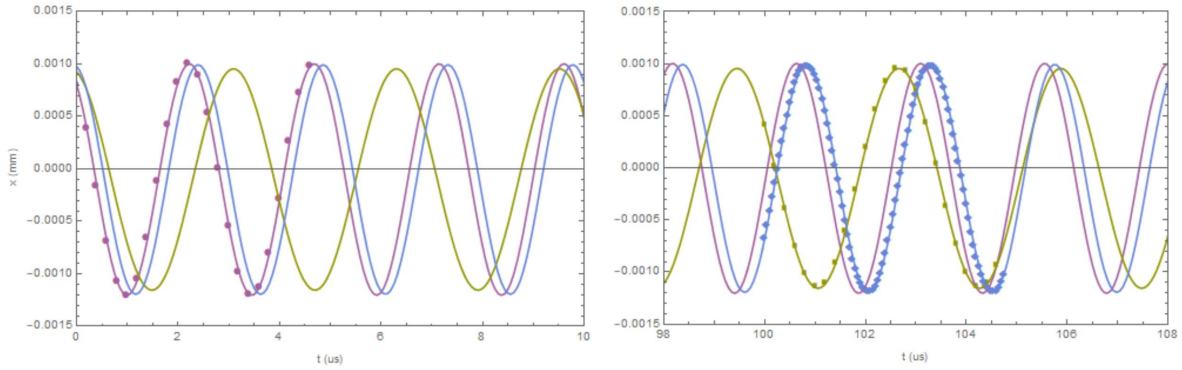


- Fields are kept constant throughout the simulation (no effect of the charges induced in anode wall, ~1 kHz for rigid plasma column)

0 - 5 us, dt = 0.2ns –
f=406.47(3) kHz

0 – 100 us, dt = 0.2ns ->
100 – 105 us, dt = 0.2ns –
f=406.4(1) kHz

0 – 100 us, dt = 10ns ->
100 – 105 us, dt = 0.2ns –
f=311.34(2) kHz



2023 LhARA ITRF 6 month review 12

Progress:

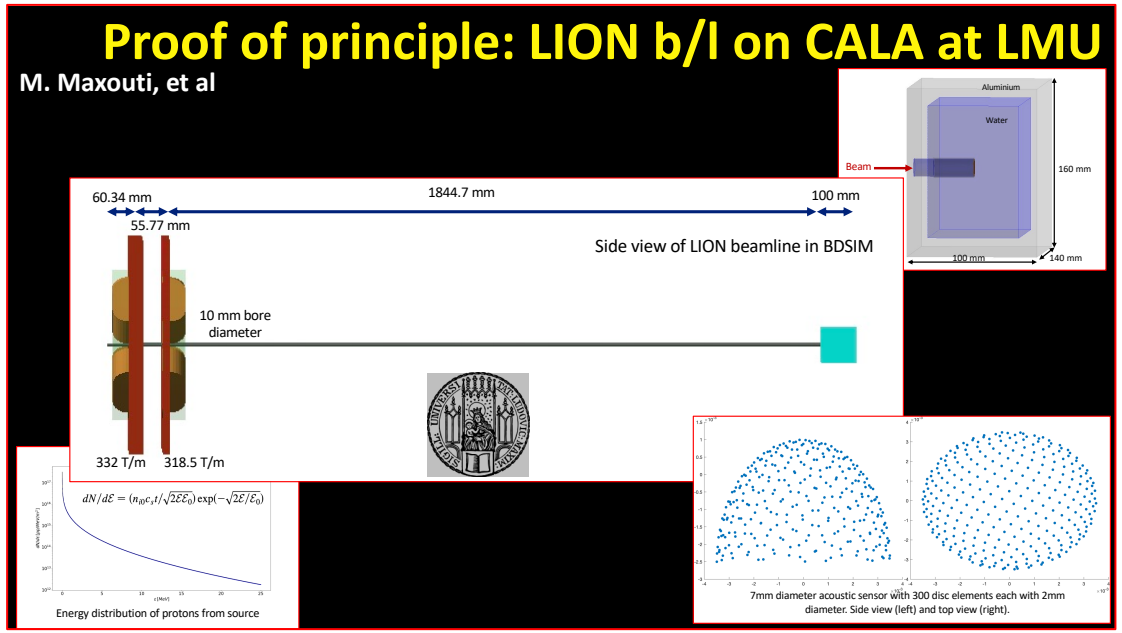
- **PDRA recruitment delay:**
  - Swansea/STFC admin issue (now resolved)
  - Expert person to be in post early summer
- **Benchmarking PIC codes:**
  - Essential preparation for start of simulation programme
- **Impressive support from:**
  - Swansea University
  - Supercomputing Wales

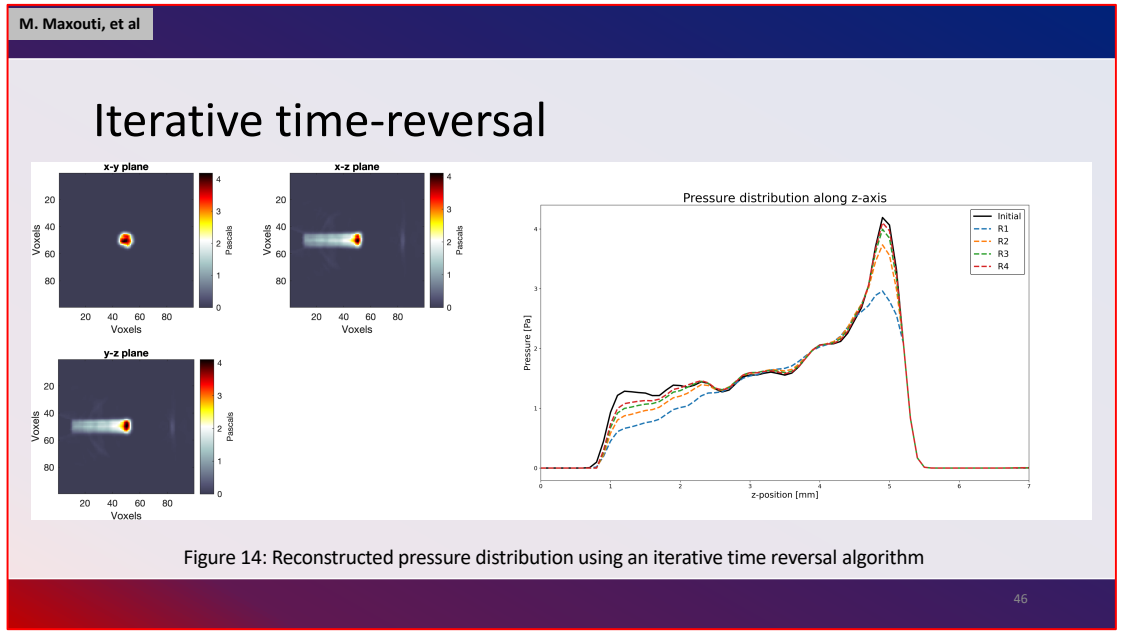
J. Bamber, E. Harris

WP4 Ion-acoustic dose mapping (ITRF WP 1.4)

Principal goal: proof of principle experiment

Current status: simulation to specify design of test vessel





Continued development of collaboration with LMU on design and simulation

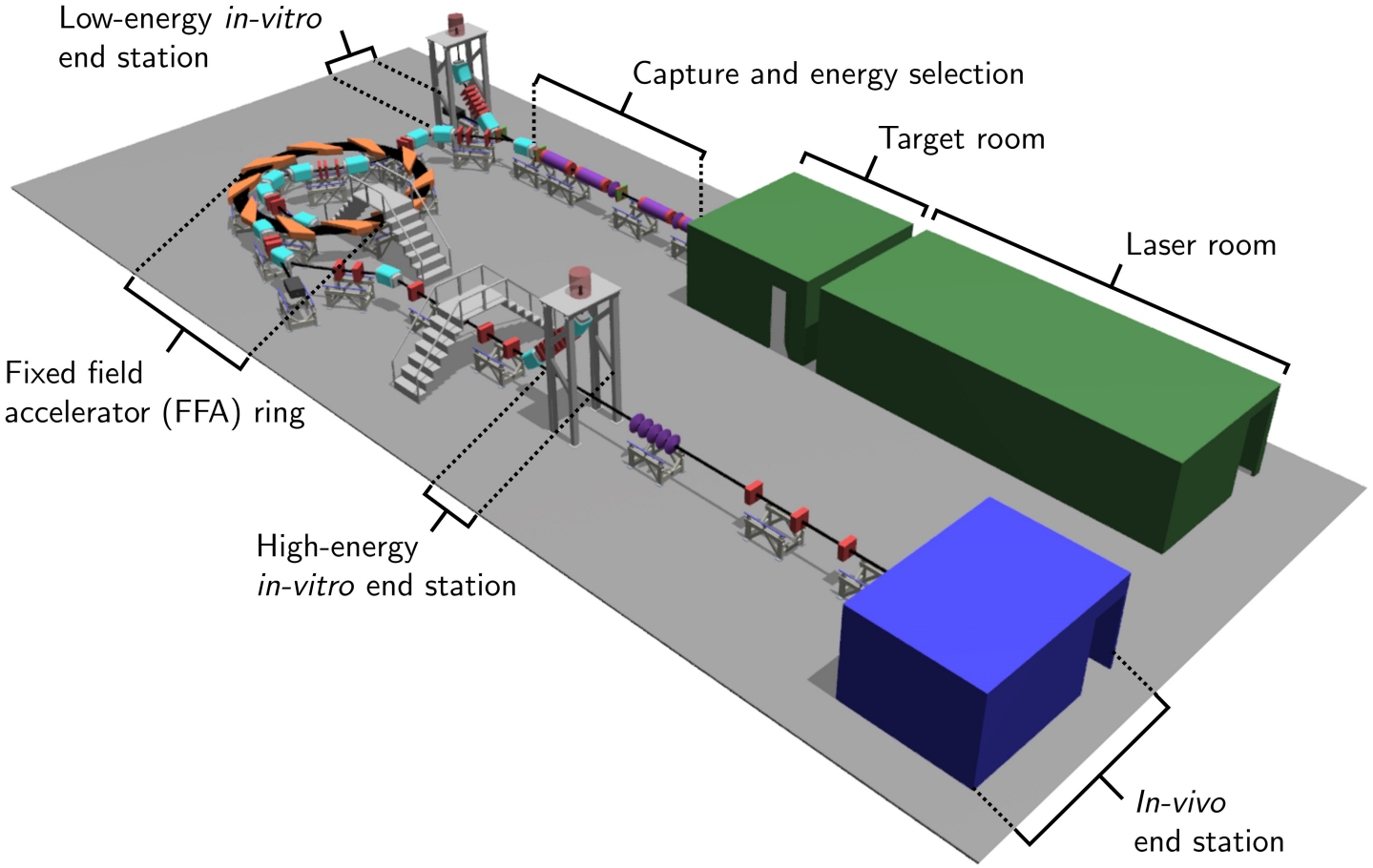
Opportunity to make tests on CALA laser at LMU

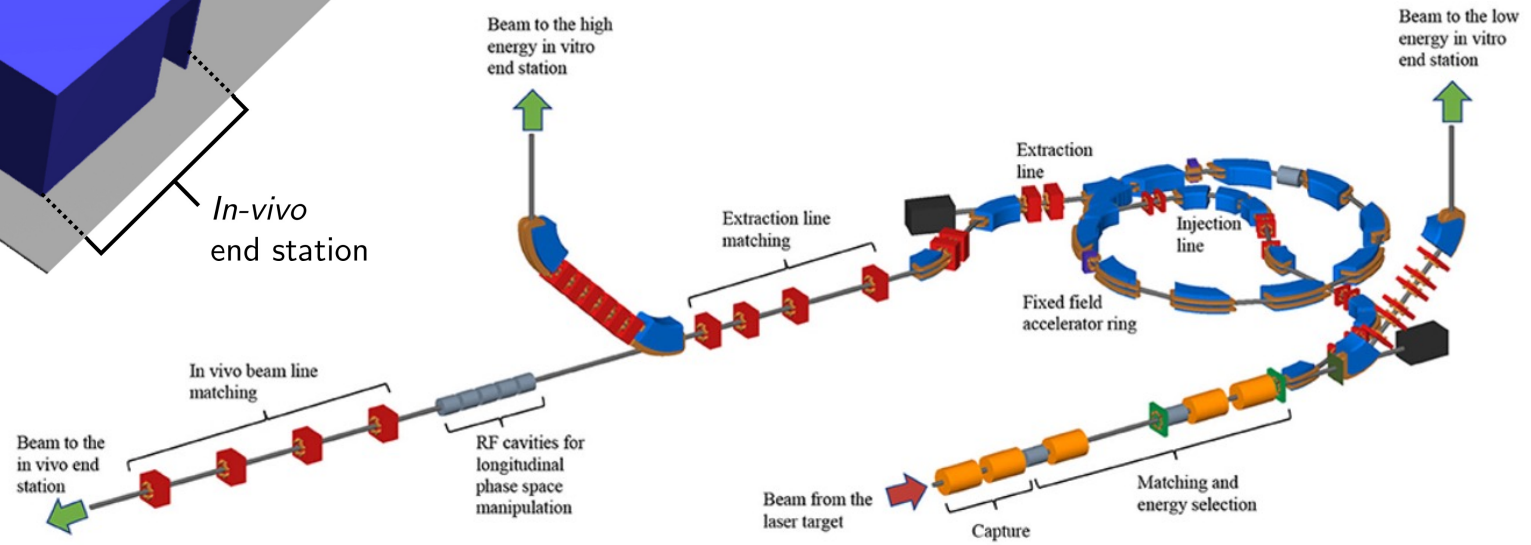
New opportunity: thermoacoustic validation experiment

Create gel mould to excite with IR laser

Novel end-station development (ITRF WP 1.5)

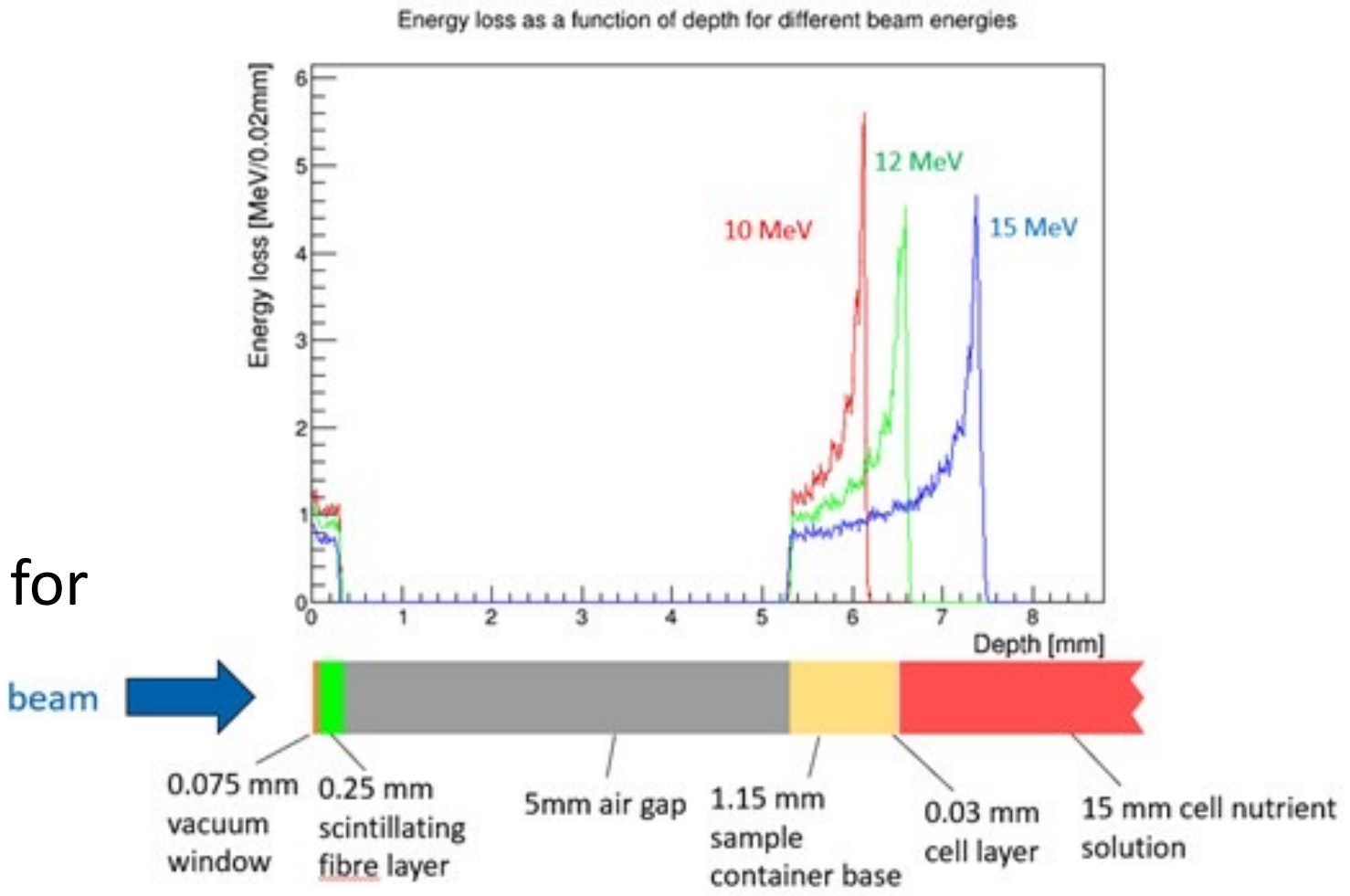
R. McLauchlan, T. Price et al





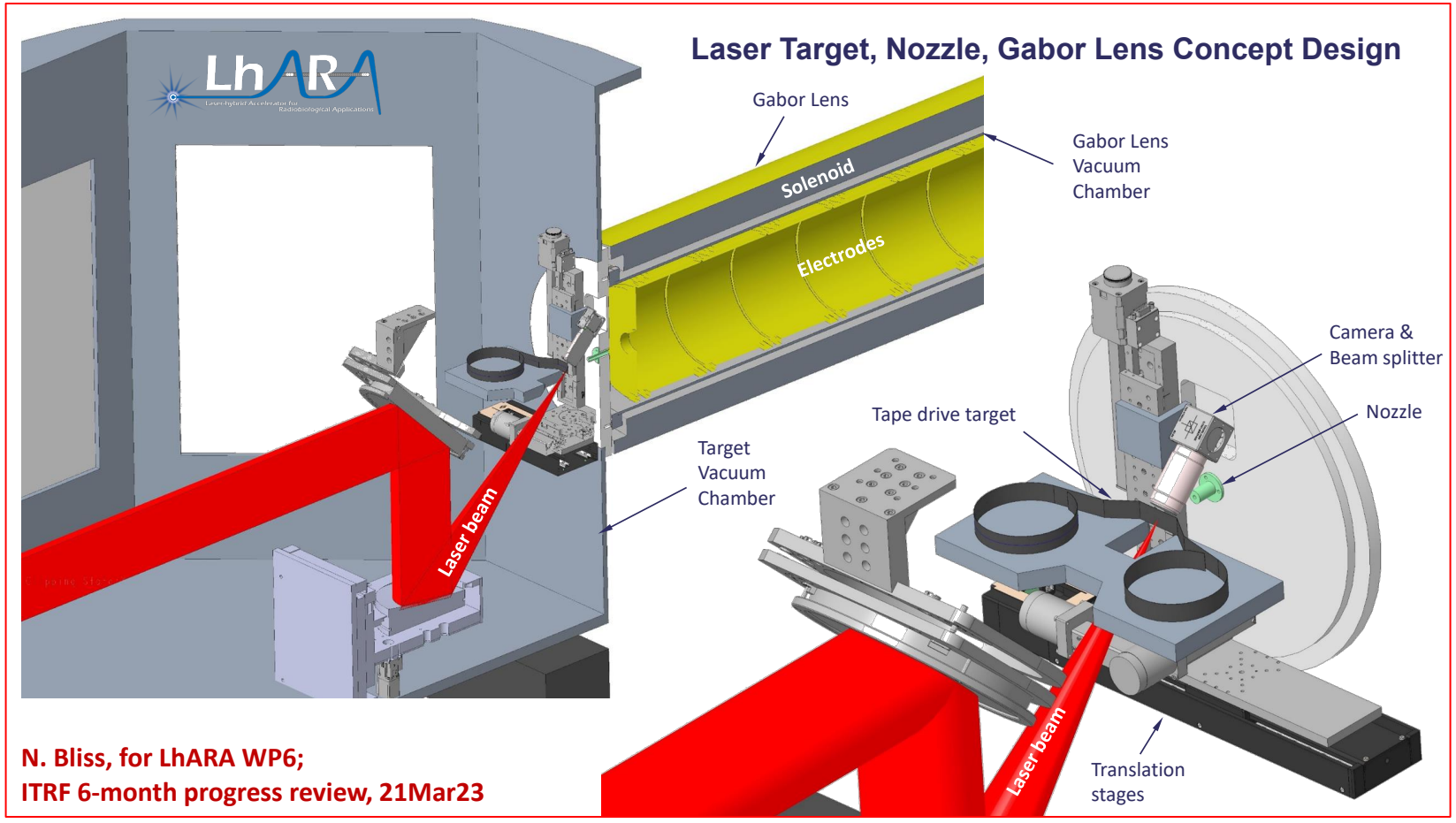
R. McLauchlan, T. Price et al

- User engagement – Peer group consultation.
- Automated Handling
- Controlled atmosphere
- Acoustic Imaging
- Cellular imaging
- In-vivo irradiation
- Brm MC40 cyclotron operation for testing and de-risking.
- Beamline instrumentation
- Gas jet beam profiler.
- Dosimetry verification



N. Bliss, J. Pasternak

Design & integration (ITRF WP 1.6)



Facility integration:

- Significant progress on layout
- Beginning to look at critical areas:
  - E.g. target/capture integration
- Much more detail in 6-month progress report

N. Bliss, J. Pasternak

Design & integration (ITRF WP 1.6)

Ongoing & Next Steps

- Vlasov solver for co-propagating beams
- Continued optimisation for spot size flexibility
- Collimator & octupole settings
- RF cavity performance
- Wien filter for particle selection
- Alternative lattices (quadrupoles)
- FFA tunability
- Injection line redesign
- Stage 2 beam transport optimisation
- RF & FFA magnet conceptual designs

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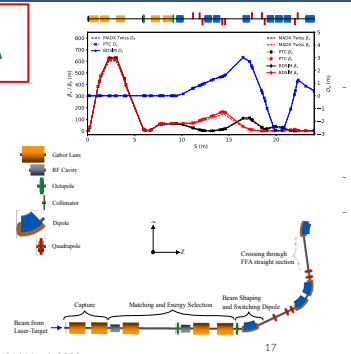
Revision of injection line to FFA

Stage 2: Injection line



- Excellent agreement between BDSIM and PTC with idealised beam (10k primaries) for the baseline.
- Space charge optimisations required.
- Update needed to incorporate the shielding wall between the Stage 1 room and the FFA room.

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Preliminary Collimator Investigation

- Beam spectrum reduced to ± 2% spread at the end station
- Modest losses – transmission > ~ 80%
- Further optimisation required.

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Working towards improved baseline for Stage 1

Design & integration (ITRF WP 1.6)

Summary

- Last 6 months saw a very significant progress in Stage 1 studies
  - Development of the components naming scheme and BDSIM/CAD interface
  - In understanding the input beam properties
    - Still more studies needed, especially to include effects from the electron distribution
  - Space charge optimisation with GPT
    - Verification with a different code in progress
  - Development of the flexible optics with a new baseline candidate
- Stage 2 has a solid baseline, but further updates are required
  - Foundations for the FFA magnet and RF cavity conceptual designs has been established

Collaboration building

- **Discussions initiated with:**
  - **CERN Accelerator Beam Physics Group:**
    - **Mutual interest in plasma lens, space charge/collective effects, FFA …**
  - **ISIS Intense Beams Group:**
    - **Mutual interest in space charge/collective effects, FFA …**

- **Seeking to continue and enhance communication with:**
  - **Institut Curie; perhaps CNRS more broadly**
  - **HZDR, LMU**

Conclusions

- **Excellent progress to date**
  - **Project largely on track**
    - **Stage 1 baseline lattice update moved to May23; preparation advanced**
  - **Issues:**
    - **PDRA recruitment in Swansea; now "unlocked", some mitigation from the rest of the WP1.3 team**
  - **Evaluation, review and articulation of science programme underway**

- **National and international interest in our programme:**
  - **Mini beam Radiotherapy Conference, Paris, March 2023:**
    - **LhARA discussed; attendees wished to be included in the ongoing consultations**
  - **IoP meeting being prepared by Biophysics, Medical Physics, PAB, and HEPP Groups**

- **Good foundations are being laid!**

Acknowledgements


Imperial College London
ICR The Institute of Cancer Research
Medical Research Council
UKRI
Oxford Institute for Radiation Oncology
University of Oxford
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Manchester 1824 The University of Manchester
University of Birmingham
University of Liverpool
NHS University Hospitals Birmingham NHS Foundation Trust
NHS The Clatterbridge Cancer Centre NHS Foundation Trust
NHS The Christie NHS Foundation Trust
institut Curie
Queen's University Belfast
Swansea University Prifysgol Abertawe
UCL Medical Physics & Biomedical Engineering
University
Clinical
Accelerator
Laboratory
Industry
Partners
Netherlands Cancer Institute Antoni van Leeuwenhoek
Hampton University Proton Therapy Institute Fighting Cancer, Saving Lives
University of Strathclyde Glasgow Department of Physics
Royal Holloway University of London
Lancaster University
UKRI Science and Technology Facilities Council
ASTeC
Daresbury Laboratory
Particle Physics Department
ISIS Neutron and Muon Source
CLF central laser facility
University of Birmingham | Cyclotron Facility | Positron Imaging Centre
INFN Catania
The Cockcroft Institute of Accelerator Science and Technology
CERN
Corerain 鲲云科技
LEO Cancer Care
MAXELER Technologies Maximum Performance Computing
The Rosalind Franklin Institute
NPL National Physical Laboratory