Science and
Technology
Facilities Council

K. Long 1 June, 2023

Imperial College
London

LhARA
Laser-hybrid Accelerator for
Radiobiological Applications

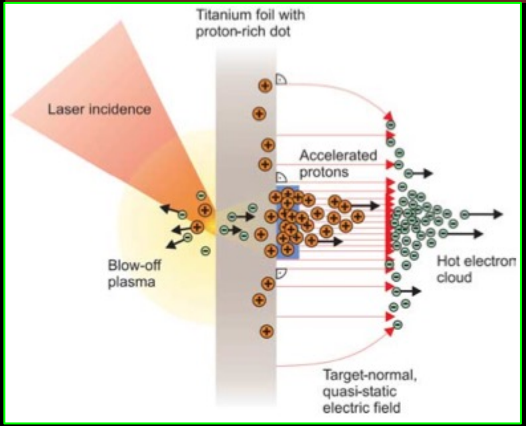
LhARA

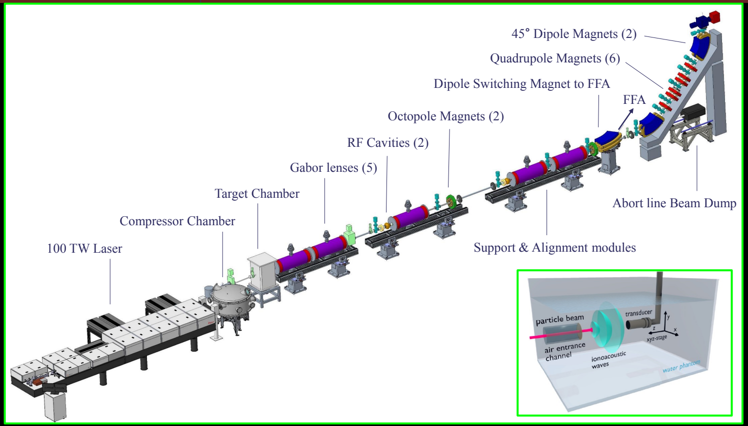
the Laser-hybrid Accelerator for Radiobiological Applications

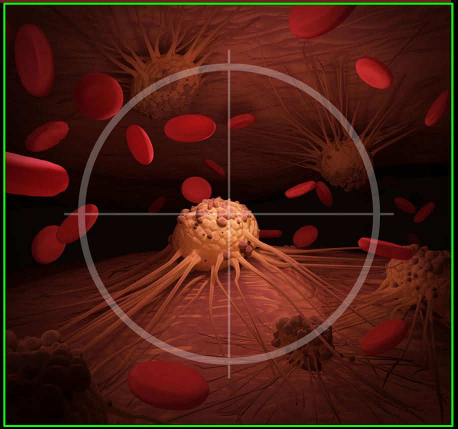
Our ambition is to:

- ***Deliver a systematic and definitive radiation biology programme***
- ***Prove the feasibility of laser-driven hybrid acceleration***
- ***Lay the technological foundations for the transformation of PBT***
  - automated, patient-specific proton and ion beam therapy

LhARA
Laser-hybrid Accelerator for
Radiobiological Applications







Radiotherapy; the challenge

- Cancer: second most common cause of death globally
  - Radiotherapy indicated in half of all cancer patients

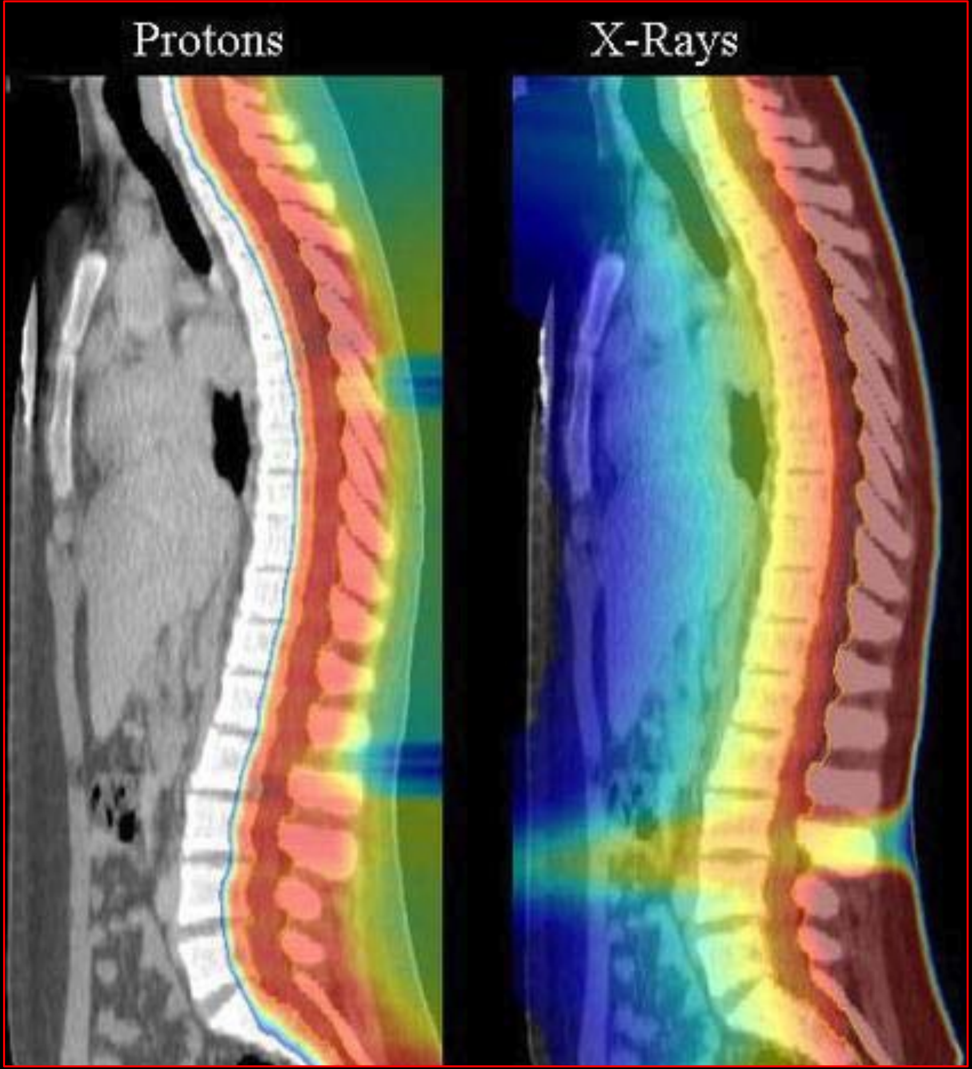
- Significant growth in global demand anticipated:
  - 14.1 million new cases in 2012 ⇢ 24.6 million by 2030
  - 8.2 million cancer deaths in 2012 ⇢ 13.0 million by 2030

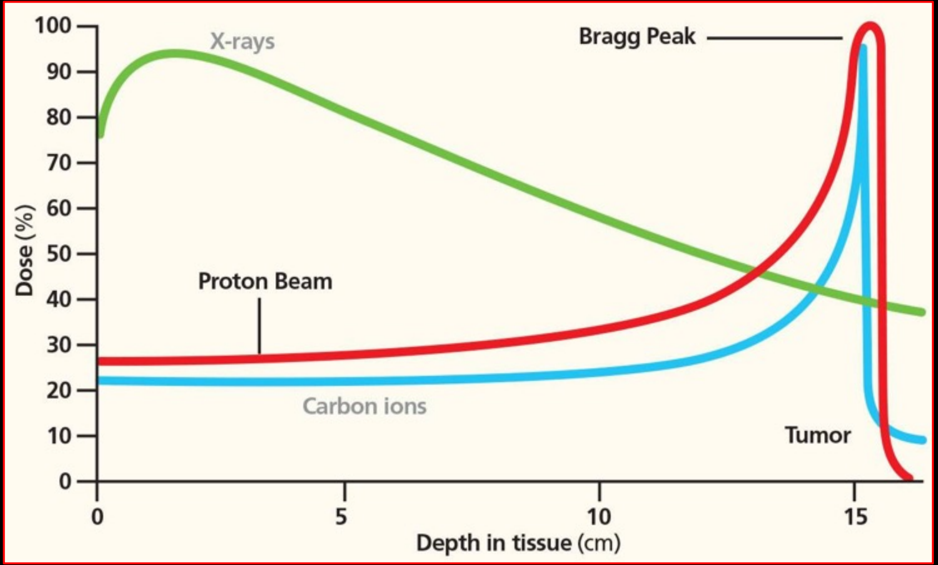
- Scale-up in provision essential:
  - Projections above based on reported cases (i.e. high-income countries)
  - Opportunity: save 26.9 million lives in low/middle income countries by 2035

- Provision on this scale requires:
  - Development of new and novel techniques … integrated in a
  - Cost-effective *system* to allow a distributed network of RT facilities

Atun, Lancet Oncol. 2015 Sep;16(10):1153-86

Particle-beam therapy





Proton and ion-beam therapy:

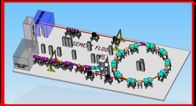
- Bulk of dose deposited in Bragg peak
- Significant normal-tissue sparing (entry)
- Almost no dose beyond the Bragg peak

Particle beam therapy today

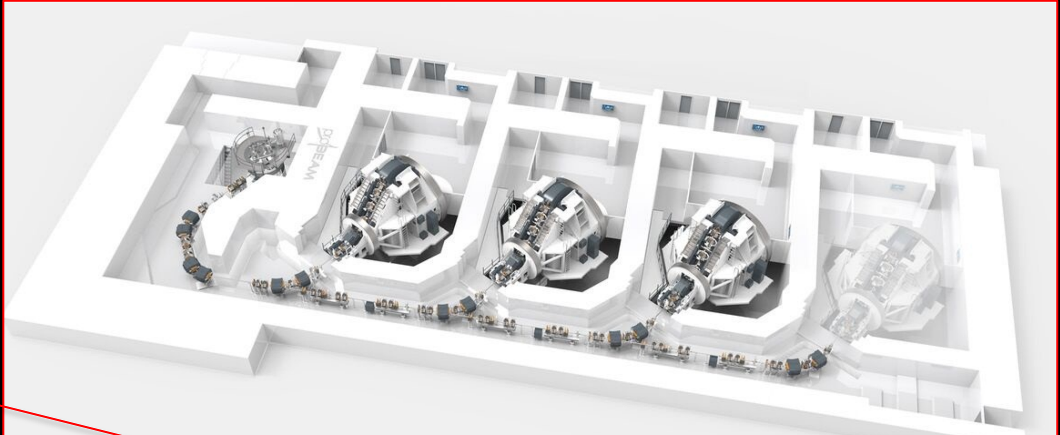
- **Cyclotron based:**
  - Limitations:
    - Energy modulation
    - Instantaneous dose rate

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

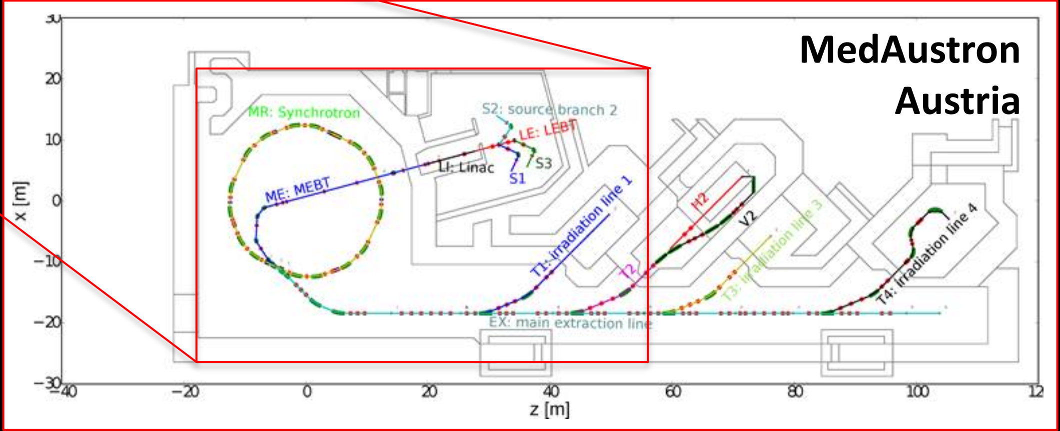
⇒ increase flexibility
optimize treatments



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

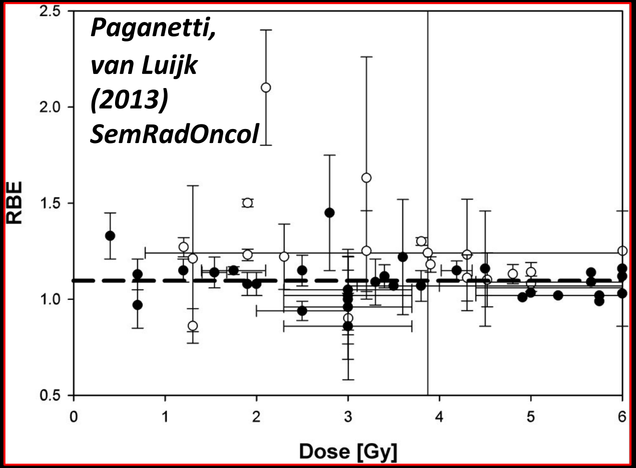


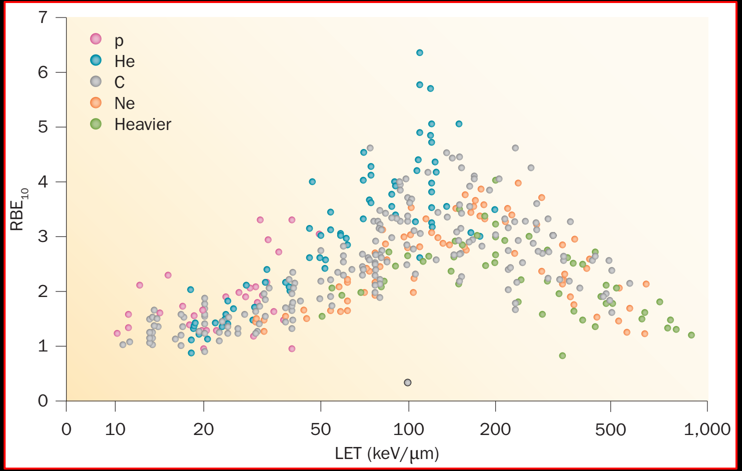
Christie Hospital Manchester



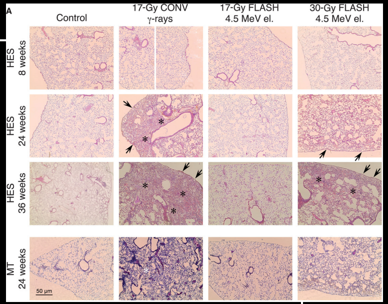
The case for fundamental radiobiology

- Relative biological effectiveness:
  - Defined relative to reference X-ray beam
  - Known to depend on:
    - Energy, ion species
    - Dose & dose rate
    - Tissue type
    - Biological endpoint
- Yet:
  - *p*-treatment planning uses 1.1
  - Effective values are used for C^{6+}
- Maximise the efficacy of PBT now & in the future:
  - Require systematic programme to develop full understanding of radiobiology





Radiobiology in new regimens



Worked example: FLASH

Conventional regime : ~2 Gy/min
FLASH regime : >40 Gy/s

Evidence of normal-tissue sparing while tumour-kill probability is maintained:
i.e. enhanced therapeutic window

Time line:

- Initial reports: 2014 (e.g. Flauvadon et al, STM Jul 2014)
- Confirmation in mini-pig & cat: 2018 (Clin. Cancer Research 2018)
- First treatment 2019 (Bourhis et al, Rad.Onc. Oct 2019)

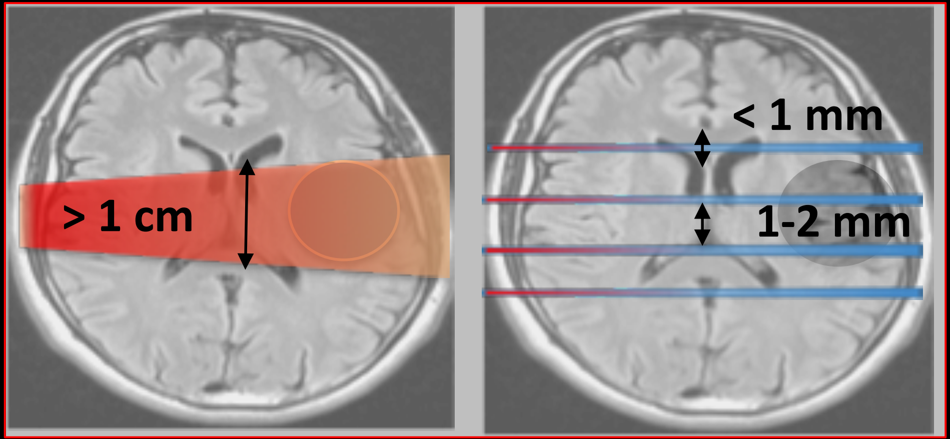
Radiobiology in new regimens

Prezado et al

Worked example: micro beams

Conventional regime: > 1 cm diameter; homogeous

Microbeam regime : < 1 mm diameter; no dose between 'doselets'

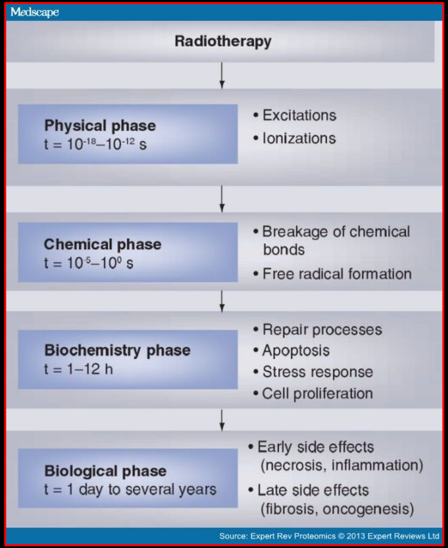


Remarkable increase of normal rat brain resistance.

[E.g. Dilmanian et al. 2006, Prezado et al., Rad. Research 2015]

Dose escalation in the tumour possible – larger tumor control prob.

Radiobiology in new regimens



Medscape

Radiotherapy

Physical phase
$t = 10^{-18}$–10^{-12} s

- Excitations
- Ionizations

Chemical phase
$t = 10^{-5}$–10^{0} s

- Breakage of chemical bonds
- Free radical formation

Biochemistry phase
t = 1–12 h

- Repair processes
- Apoptosis
- Stress response
- Cell proliferation

Biological phase
t = 1 day to several years

- Early side effects (necrosis, inflammation)
- Late side effects (fibrosis, oncogenesis)

Source: Expert Rev Proteomics © 2013 Expert Reviews Ltd

Time domain

Space domain

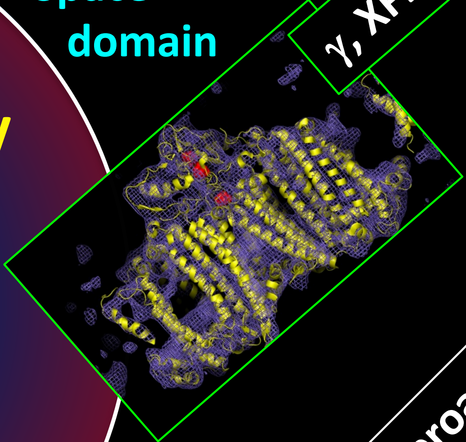
Energy

Ion species

The ideally flexible beam facility can deliver it all!

⇒ substantial opportunity for a step-change in understanding!

γ, XFEL, e^-



Multidisciplinary approach essential

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 Laboratory Industry Accelerator

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

central laser facility

ASTeC

Daresbury Laboratory

Particle Physics Department

ISIS Neutron and Muon Source

UNIVERSITY OF BIRMINGHAM | CYCLOTRON FACILITY | POSITRON IMAGING CENTRE

Corerain 鲲 云 科 技

INFN CATANIA

The Cockcroft Institute of Accelerator Science and Technology

CERN

LEO Cancer Care

MAXELER Technologies Maximum Performance Computing

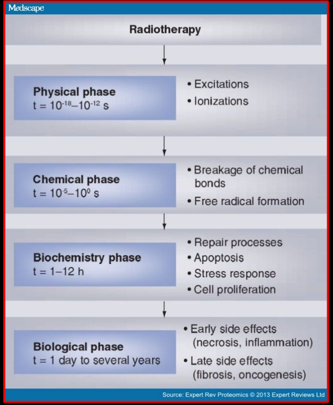
The Rosalind Franklin Institute

NPL National Physical Laboratory

Laser-hybrid Accelerator for Radiobiological Applications

A novel, hybrid, approach:

- Laser-driven, high-flux proton/ion source
  - Overcome instantaneous dose-rate limitation
    - Capture at >10 MeV
  - Delivers protons or ions in very short pulses
    - Bunches as short as 10—40 ns
  - Triggerable; arbitrary pulse structure
- Novel "electron-plasma-lens" capture & focusing
  - Strong focusing (short focal length) without the use of high-field solenoid
- Fast, flexible, fixed-field post acceleration
  - Variable energy
    - Protons: 15—127 MeV
    - Ions: 5—34 MeV/u



Radiotherapy

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- Stress response
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Biological phase
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- Early side effects (necrosis, inflammation)
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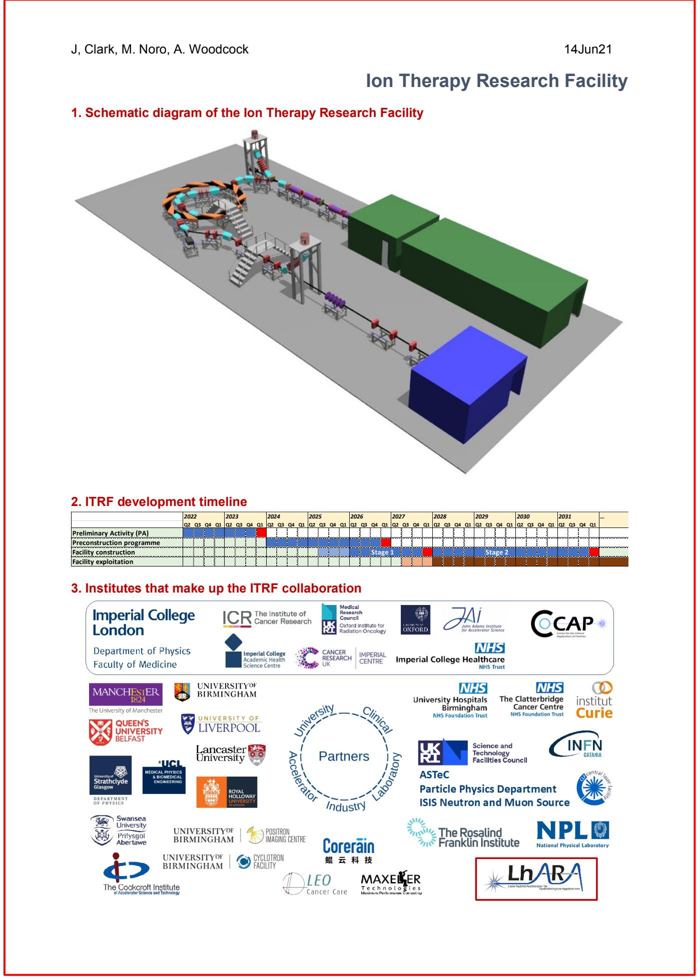
Source: Expert Rev Proteomics © 2013 Expert Reviews Ltd

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

Front. Phys., 29 September 2020; DOI: 10.3389/fphy.2020.567738



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

Imperial College London
Department of Physics
Faculty of Medicine
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
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
Queen's University Belfast
University of Liverpool
Lancaster University
University of Strathclyde Glasgow Department of Physics
UCL Medical Physics & Biomedical Engineering
Royal Holloway University of London
Swansea University Prifysgol Abertawe
University of Birmingham | Positron Imaging Centre
University of Birmingham | Cyclotron Facility
The Cockcroft Institute of Accelerator Science and Technology
LEO Cancer Care
Corerain 鲲云科技
Maxeler Technologies Maximum Performance Computing

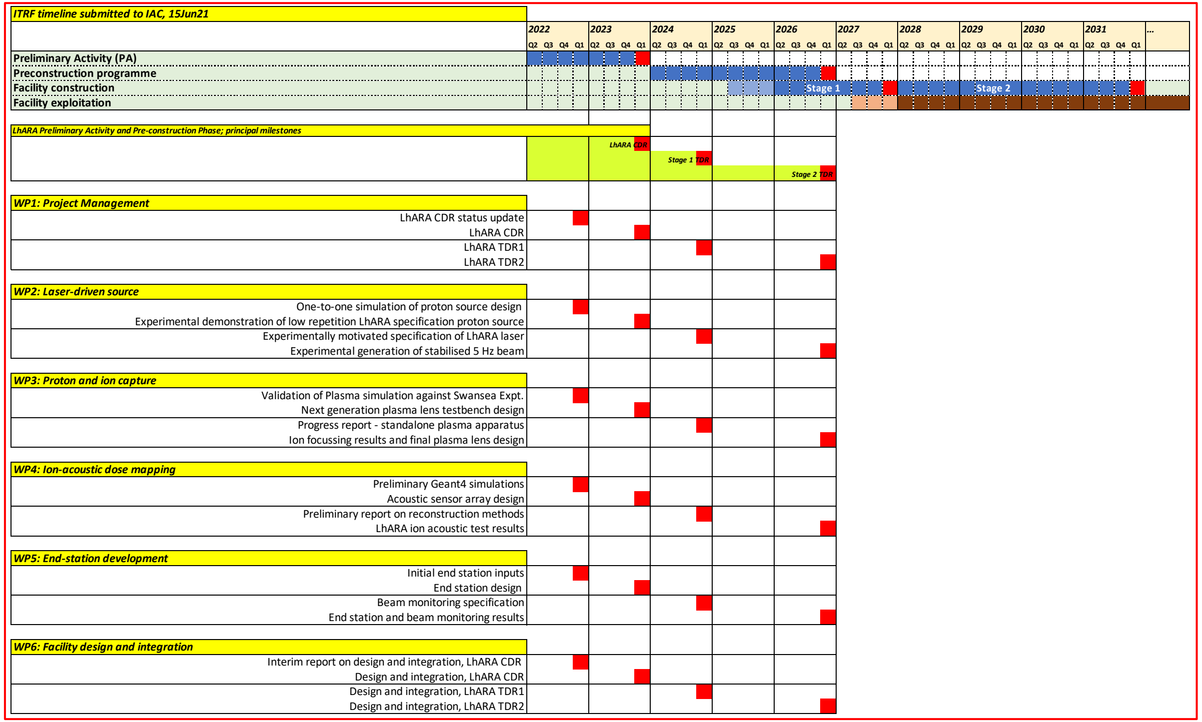
University
Clinical
Partners
Accelerator
Laboratory
Industry

NHS University Hospitals Birmingham NHS Foundation Trust
NHS The Clatterbridge Cancer Centre NHS Foundation Trust
institut Curie
UKRI Science and Technology Facilities Council
ASTeC
Particle Physics Department
ISIS Neutron and Muon Source
INFN Catania
CLF central laser facility
The Rosalind Franklin Institute
NPL National Physical Laboratory
LhARA Laser-hybrid Accelerator for Radiobiological Applications

LhARA to serve ITRF Preliminary Activity

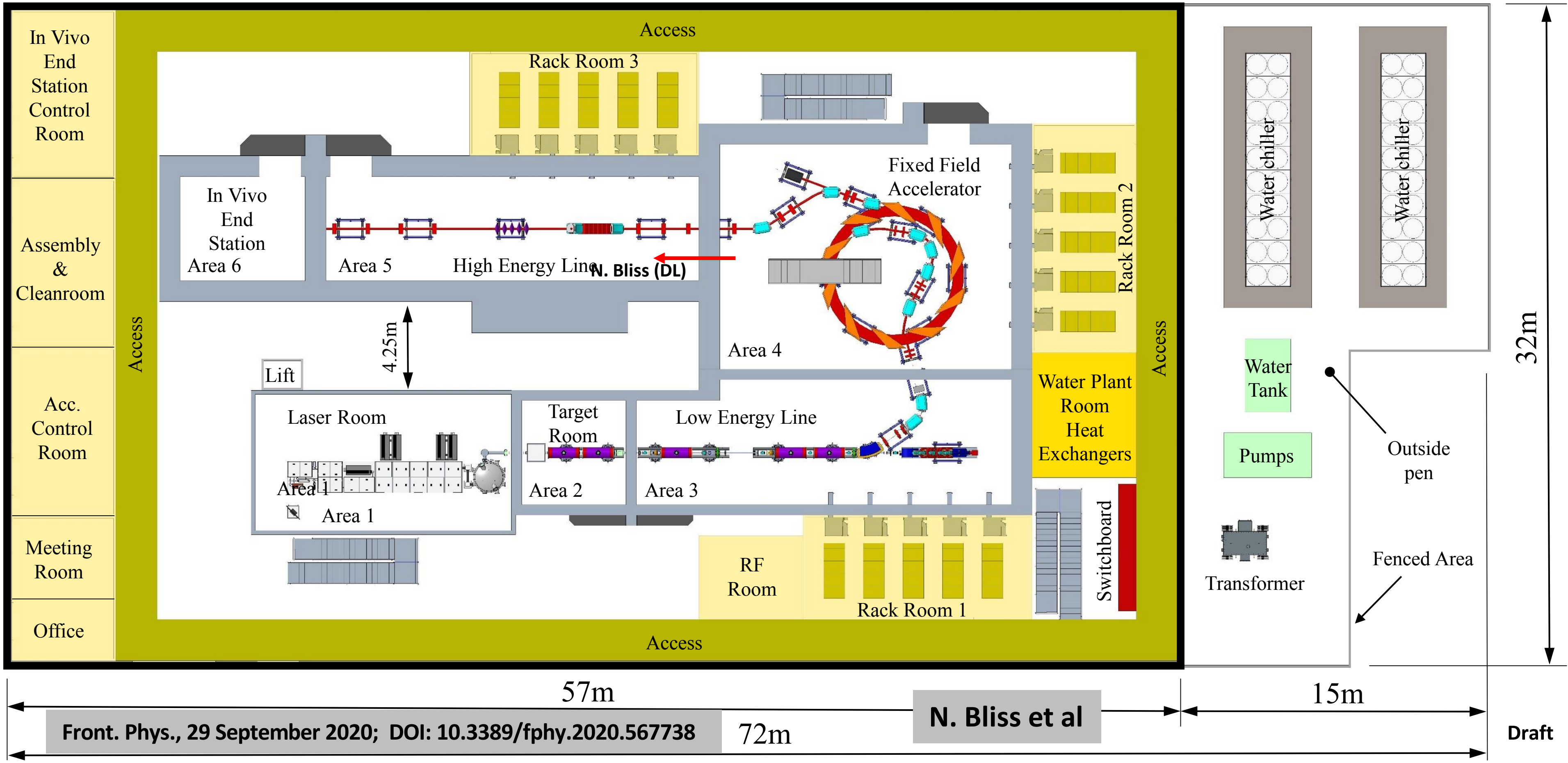
Preliminary Activity: £2M over 2 years

project start October 2022



ITRF timeline submitted to IAC, 15Jun21	*2022*				*2023*				*2024*				*2025*				*2026*				*2027*				*2028*				*2029*				*2030*				*2031*				…
	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	
Preliminary Activity (PA)	🟦	🟦	🟦	🟦	🟦	🟦	🟦	🟥																																	
Preconstruction programme									🟦	🟦	🟦	🟦	🟦	🟦	🟦	🟦	🟦	🟦	🟦	🟥																					
Facility construction														▨	▨	▨	🟦	🟦	🟦 Stage 1	🟦	🟦	🟦	🟦	🟥	🟦	🟦	🟦	🟦	🟦	🟦 Stage 2	🟦	🟦	🟦	🟦	🟦	🟦	🟦	🟦	🟦	🟥	
Facility exploitation																						🟧	🟧	🟧	🟫	🟫	🟫	🟫	🟫	🟫	🟫	🟫	🟫	🟫	🟫	🟫	🟫	🟫	🟫	🟫	🟫

LhARA Preliminary Activity and Pre-construction Phase; principal milestones					
		LhARA CDR 🟥			
			Stage 1 TDR 🟥		
					Stage 2 TDR 🟥
WP1: Project Management					
LhARA CDR status update	🟥				
LhARA CDR		🟥			
LhARA TDR1			🟥		
LhARA TDR2					🟥
WP2: Laser-driven source					
One-to-one simulation of proton source design	🟥				
Experimental demonstration of low repetition LhARA specification proton source		🟥			
Experimentally motivated specification of LhARA laser			🟥		
Experimental generation of stabilised 5 Hz beam					🟥
WP3: Proton and ion capture					
Validation of Plasma simulation against Swansea Expt.	🟥				
Next generation plasma lens testbench design		🟥			
Progress report - standalone plasma apparatus			🟥		
Ion focussing results and final plasma lens design					🟥
WP4: Ion-acoustic dose mapping					
Preliminary Geant4 simulations	🟥				
Acoustic sensor array design		🟥			
Preliminary report on reconstruction methods			🟥		
LhARA ion acoustic test results					🟥
WP5: End-station development					
Initial end station inputs	🟥				
End station design		🟥			
Beam monitoring specification			🟥		
End station and beam monitoring results					🟥
WP6: Facility design and integration					
Interim report on design and integration, LhARA CDR	🟥				
Design and integration, LhARA CDR		🟥			
Design and integration, LhARA TDR1			🟥		
Design and integration, LhARA TDR2					🟥



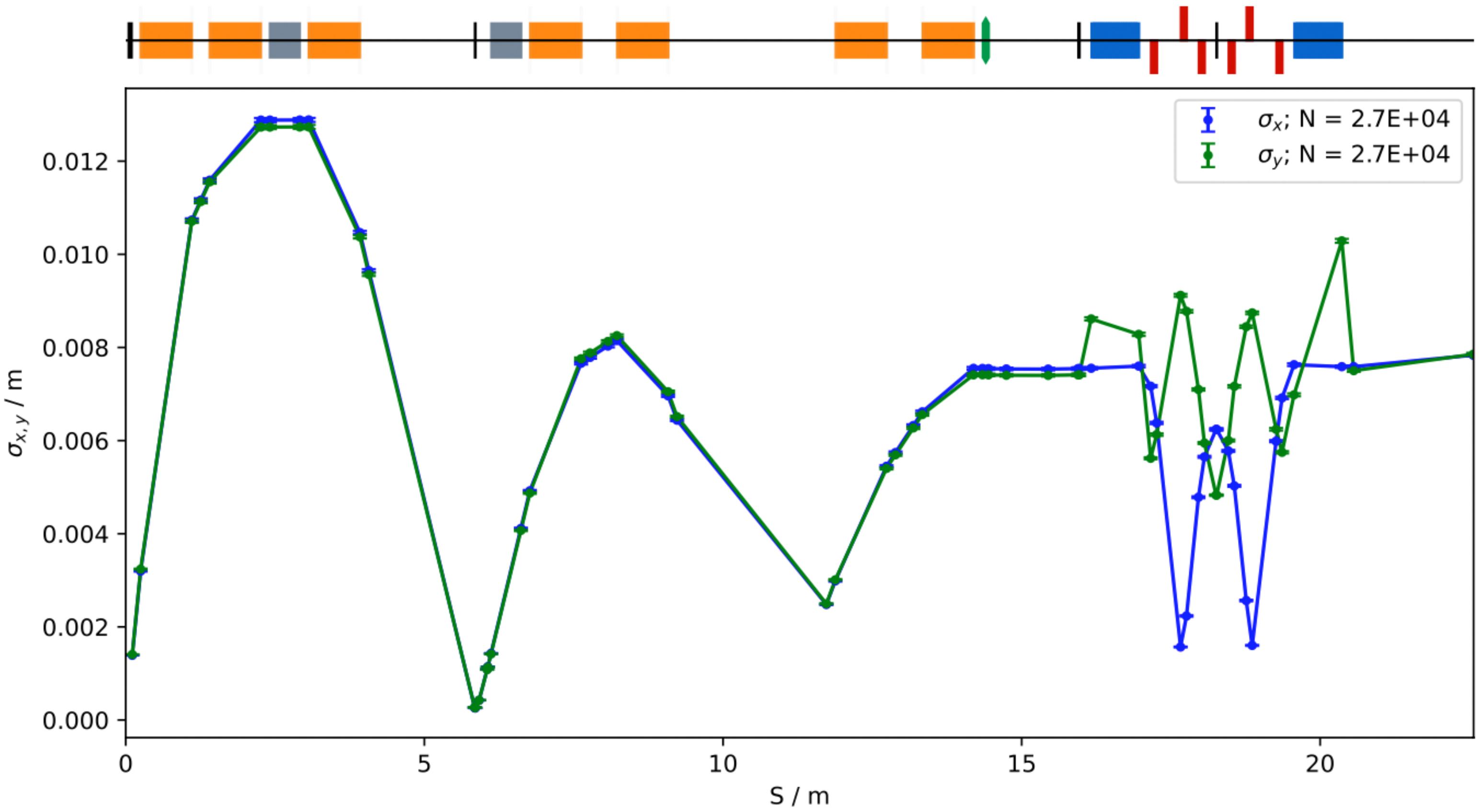
Front. Phys., 29 September 2020; DOI: 10.3389/fphy.2020.567738

N. Bliss et al

Draft

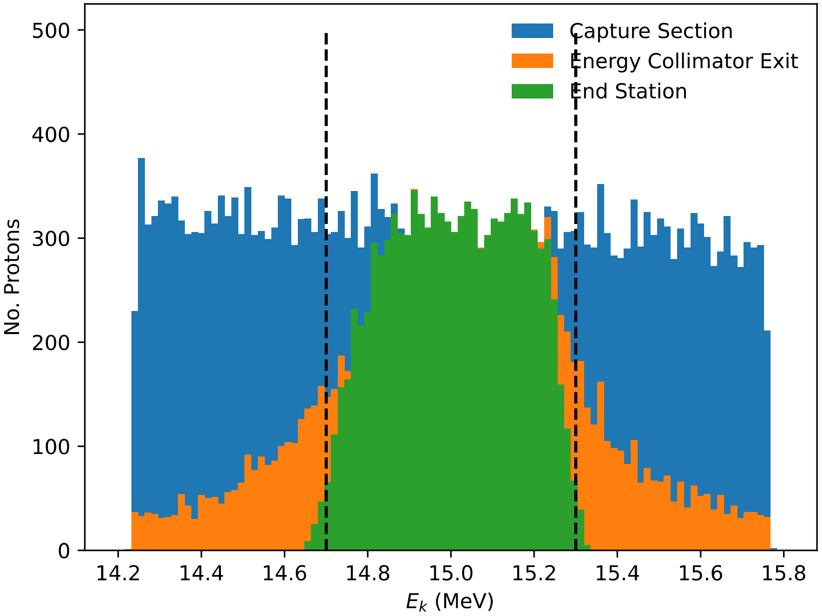
⇒ compact, uniquely flexible facility

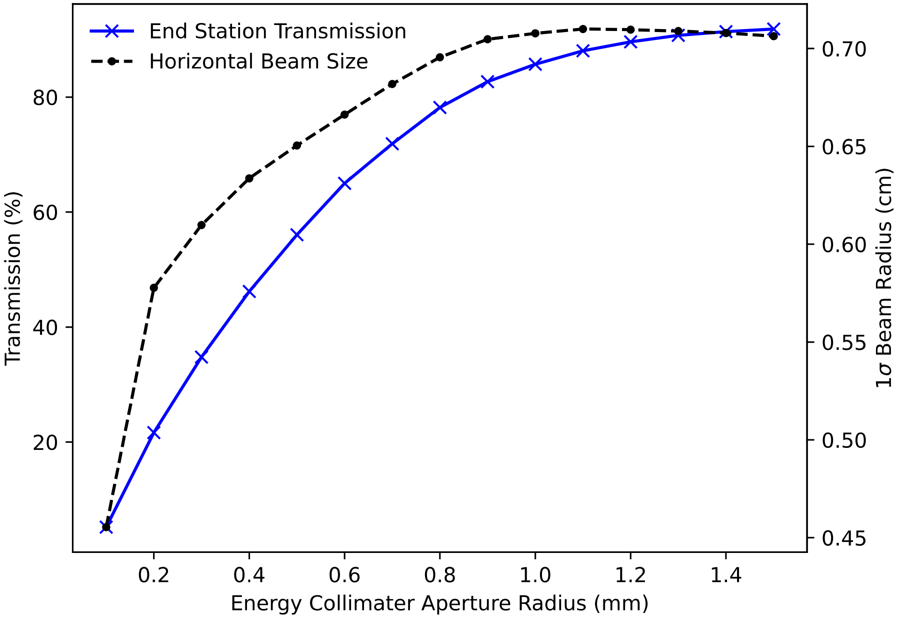
Matching Optimisation



- Optimised solutions for 7.5, 6.25, & 5.0 mm spot size with space charge
- Smaller beams remains focus of ongoing work.

Preliminary Collimator Investigation



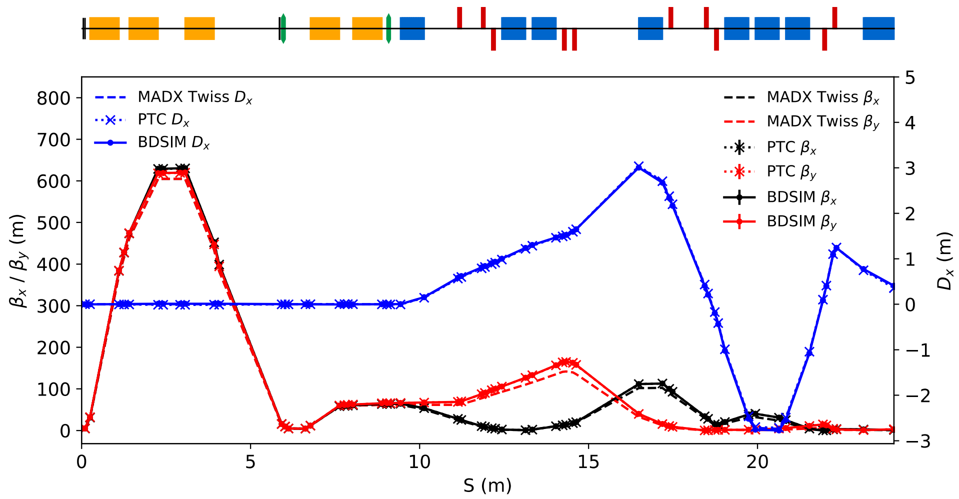


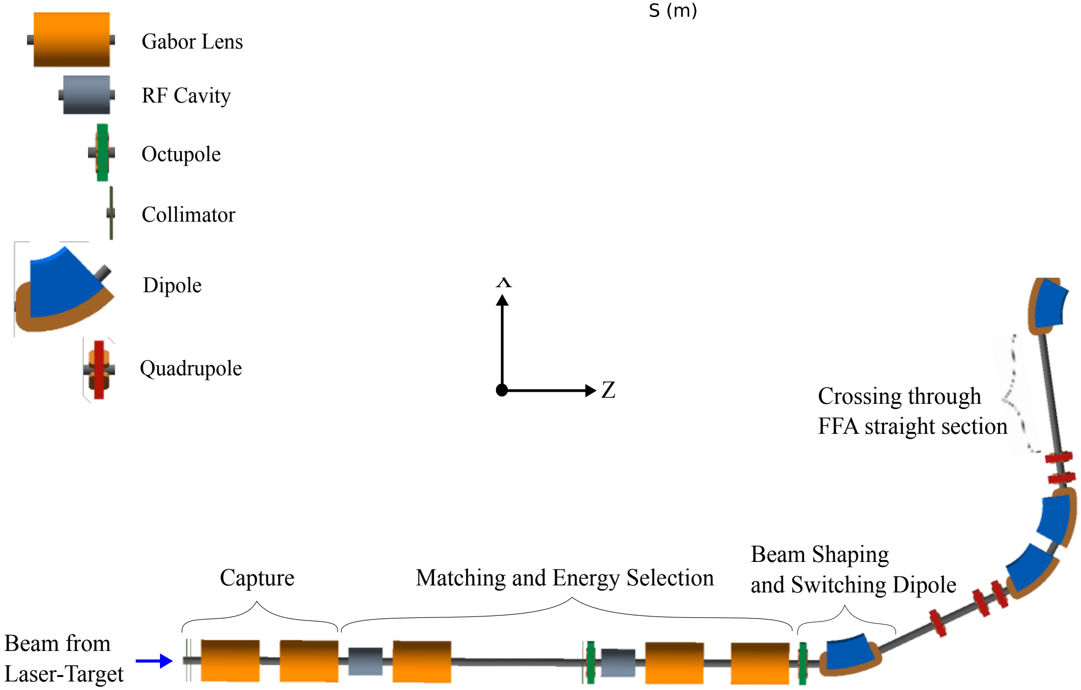
- Beam spectrum reduced to ± 2% spread at the end station

- Modest losses – transmission > ~ 80%

- Further optimisation required.

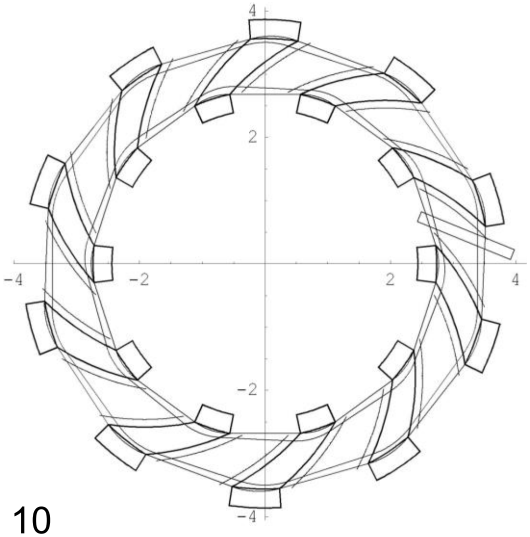
Stage 2: Injection line

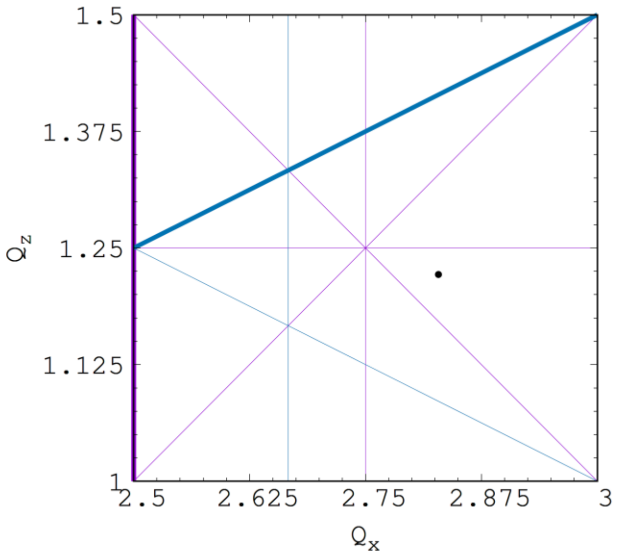


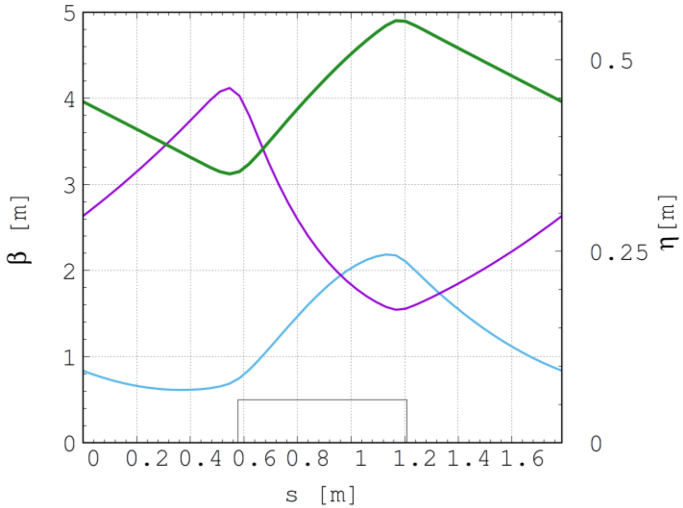


- Excellent agreement between BDSIM and PTC with idealised beam (10k primaries) for the baseline.
- Space charge optimisations required.
- Update needed to incorporate the shielding wall between the Stage 1 room and the FFA room.

LhARA baseline FFA ring parameters





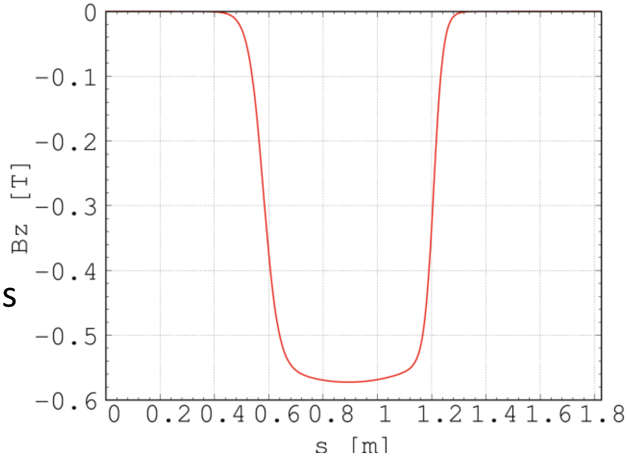


• N	10
• k	5.33
• Spiral angle	48.7°
• R_{max}	3.48 m
• R_{min}	2.92 m
• (Qx, Qy)	(2.83, 1.22)
• B_{max}	1.4 T
• p_f	0.34
• Max Proton injection energy	15 MeV
• Max Proton extraction energy	127.4 MeV
• h	1
• RF frequency for proton acceleration (15-127.4MeV)	2.89 – 6.48 MHz
• Bunch intensity	up to ~10^9 protons

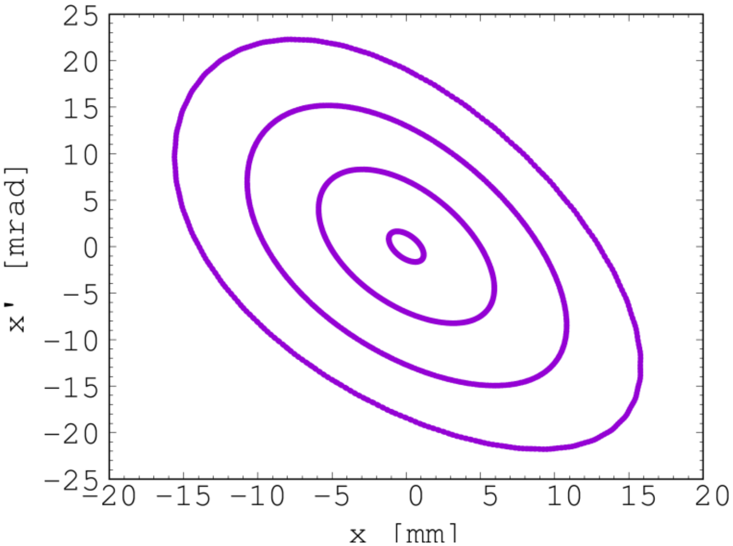
- Range of other extraction energies possible
- Other ions also possible

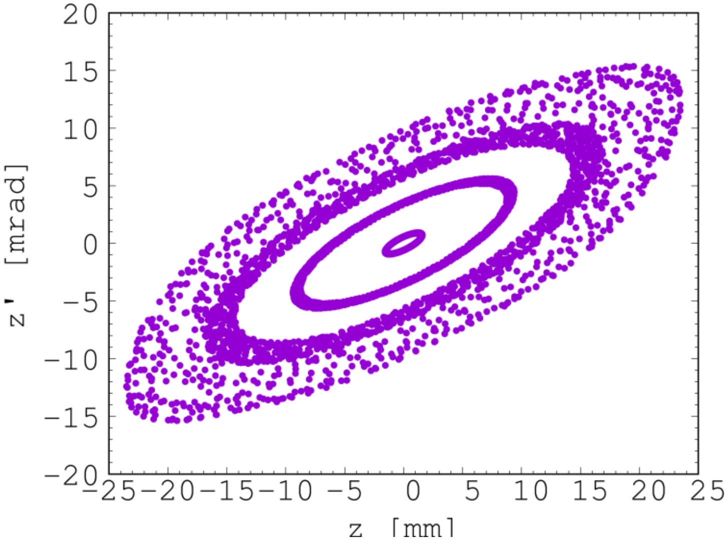
LhARA FFA ring tracking

LhARA Ring Tracking



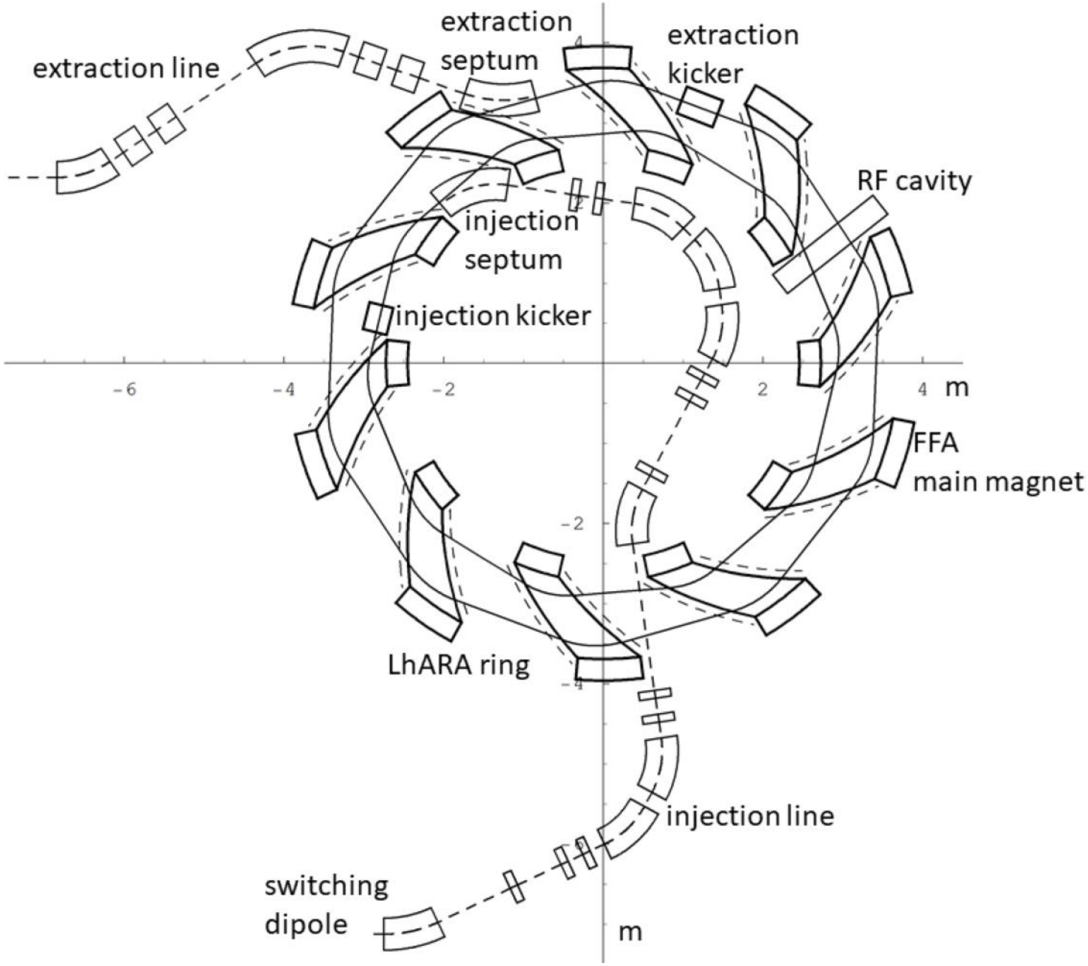
- Performed using proven stepwise tracking code
- It takes into account fringe fields and non-linear field components
- Results show dynamical acceptances are much larger than physical ones
- No space charge effects included yet
- Tracking performed using FixField code





FFA Ring subsystems

Parameter	unit	value
Injection septum:		
nominal magnetic field	T	0.53
magnetic length	m	0.9
deflection angle	degrees	48.7
thickness	cm	1
full gap	cm	3
pulsing rate	Hz	10
Extraction septum:		
nominal magnetic field	T	1.12
magnetic length	m	0.9
deflection angle	degrees	34.38
thickness	cm	1
full gap	cm	2
pulsing rate	Hz	10
Injection kicker:		
magnetic length	m	0.42
magnetic field at the flat top	T	0.05
deflection angle	mrad	37.4
fall time	ns	320
flat top duration	ns	25
full gap	cm	3
Extraction kicker:		
magnetic length	m	0.65
magnetic field at the flat top	T	0.05
deflection angle	mrad	19.3
rise time	ns	110
flat top duration	ns	40
full gap	cm	2



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

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