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# ITRF / LhARA conceptual design report: executive summary

H Ahmed, M Alderton, RA Amos, et.al.

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# ITRF/LhARA

## Conceptual Design Report: Executive Summary

# UKRI Science and Technology Facilities Council

## The LhARA collaboration

H. Ahmed[1], M. Alderton[2], R.A. Amos[3], D.O. Ariyanto[4], C.J. Baker[5], J. Bamber[6], J. Bebbington[7], W. Bertsche[8,9], R. Bingham[2,1], N. Bliss[10], E. Boella[11,9], S. Boogert[8,9], M. Borghesi[12], R. Buckley[7], P.N. Burrows[13,14], G. Casati[15,16], M. Charlton[5], X. Chen[17], J. Clarke[7], B.T. Cox[3], G. Cox[10], T.S. Dascalu[11,9], E. Dolier[2], M. Dosanjh[13,14], N.P. Dover[15,16], C. Dyson[15,16], S. Eriksson[5], A. Fernandez-Rodriguez[18,19], S. Gerlach[20], A. Giaccia[21,22], S. Gibson[23,24], A. Goulden[7], R. Gray[2,9], S. Green[25], T. Greenshaw[26], S. Griffiths[10], D. Gujral[27], H.C. Hall[28], C. Hardiman[29], E.J. Harris[6], C. Hill[10], P.R. Hobson[30], R.P. Hugtenburg[31], A. Isaac[5], M. Johnson[7], W.G. Jones[15,28], P.J. Jurj[15,16], A. Knoll[32], N. Kumar[26,9], T.J. Kuo[15,16,33], A. Kurup[15,16], J.B. Lagrange[33], J. Lascaud[20], A.M. Lombardi[34], K.R. Long[15,16,35], W.G. Luk[36], S. Lyu[17], T.A.M. Masilela[37], P. Matthews[38,39], M. Maxouti[15,16,35], J.M. McGarrigle[15], P. McKenna[2,9], R. McLauchlan[29,40], I. McNeish[4], E. Melia[41], K. Middleman[7], Z. Najmudin[15,16], M. Noro[42], S.R. O'Neill[11,9], L. Obst-Huebl[43], U. Oelfke[6], H. Owen[7], C. Palmer[12], F. Parambil[26], K. Parodi[20], J.L. Parsons[41], J. Pasternak[15,16,33], M. Patel[26,9], R. Pattathil[1], M. Pereira[23,24], H. Poptani[26], Y. Prezado[44,19], P. Price[4], T. Price[45], K.M. Prise[46], C. Pugh[7], P. Ratoff[11,9], R. Razak[15,16], F. Romano[47], P. Ruksasakchai[5], M. Sabate-Gilarte[48], Z. Sadur[15], A. Sandhu[49], G. Schettino[50], J. Schreiber[20], W. Shields[23,24], B. Smart[48], R.A. Smith[15], A.M. Snijders[43], D. Spiers[2,9], S. Tantawi[49], J.W.G. Thomason[33], S. Towe[51], T. Underwood[51,3], A. Vick[7], A. Vikhoreva[10], P. Weightman[26], C.P. Welsch[26,9], C. Whyte[2,9], R. Wilson[2], N. Zakhir[15], D.P. van der Werf[5]

**UK Research and Innovation**
Polaris House
Swindon
SN2 1FL
www.ukri.org
www.lhara.org

1 Central Laser Facility, STFC Rutherford Appleton Laboratory, Harwell Oxford, Didcot OX11 0QX, UK
2 Department of Physics, SUPA, University of Strathclyde, Glasgow G4 0NG, UK
3 Dept of Medical Physics and Biomedical Engineering, University College London, WC1E 6BT
4 Department of Surgery and Cancer, Imperial College, Hammersmith Hospital London, W12 0NN, UK
5 Department of Physics, Faculty of Science and Engineering, Swansea University, Singleton Park, Swansea, SA2 8PP, UK
6 Joint Department of Physics, Institute of Cancer Research and Royal Marsden NHS Foundation Trust, Sir Richard Doll Building, 28 Oakleaf Avenue, Sutton, London, SM2 5GP
7 Accelerator Science and Technology Centre, STFC Daresbury Laboratory, Daresbury, Cheshire, WA4 4AD, UK
8 Department of Physics and Astronomy, The University of Manchester, Oxford Rd, Manchester, M13 9PL, UK
9 Cockcroft Institiute for Accelerator Science, Keckwick Ln, Daresbury, Warrington WA4 4AD
10 Technology Department, STFC Daresbury Laboratory, Daresbury, Cheshire, WA4 4AD, UK
11 Department of Physics, Lancaster University, Bailrigg, Lancaster, LA1 4YW, UK
12 School of Mathematics and Physics, Queen's University Belfast, University Road, Belfast, BT7 1NN, Northern Ireland, UK
13 Particle Physics, Denys Wilkinson Building, Keble Rd, Oxford, OX1 3RH
14 The John Adams Institute for Accelerator Science, University of Oxford, Keble Rd, Oxford, OX1 3RH
15 Department of Physics, Imperial College London, Exhibition Road, London, SW7 2AZ, UK
16 The John Adams Institute for Accelerator Science, Department of Physics, Imperial College London, Exhibition Road, London SW7 2AZ, UK
17 Department of Bioengineering, Imperial College London, Exhibition Road, London, SW7 2AZ, UK
18 Institut des Sciences Moléculaires d'Orsay, Rue André Rivière, Bâtiment 520, 91400 Orsay, France
19 Institut Curie, Universit PSL, CNRS UMR3347, Inserm U1021, Signalisation Radiobiologie et Cancer, 91400 Orsay, France
20 Fakultät für Physik, Lehrstuhl für Medizinische Physik, Ludwig-Maximilians-Universität Münich, Am Coulombwall 1, D-85748 Garching, Germany
21 Department of Oncology, University of Oxford, Old Road Campus Research Building, Roosevelt Drive, Oxford, OX3 7DQ, UK
22 Department of Radiation Oncology, Stanford University, Stanford, CA 94305, USA
23 Department of Physics, Royal Holloway University of London, Egham, Surrey, TW20 0EX, UK
24 The John Adams Institute for Accelerator Science, Royal Holloway University of London
25 Department of Medical Physics, University Hospital Birmingham Foundation NHS Trust, Edgbaston, Birmingham, B15 2TH, UK
26 Department of Physics, University of Liverpool, Liverpool, L69 7ZE, UK
27 Imperial College NHS Healthcare Trust, Department of Clinical Oncology, Charing Cross Hospital, London W6 8RF, UK
28 CRUK PPI group, Charing Cross Hospital, London, W6 8RF, UK
29 Dept. Radiation Physics and Radiobiology, Imperial College Healthcare NHS Trust, London, W2 1NY, UK
30 School of Physical and Chemical Sciences, Queen Mary University of London, Mile End Road, London, E1 4NS, UK
31 Department of Biomedical Sciences, Faculty of Science and Engineering, Swansea University, Singleton Park, Swansea, SA2 8PP, UK
32 Department of Aeronautics, Imperial College London, Exhibition Road, London, SW7 2AZ, UK
33 ISIS Neutron and Muon Source, STFC Rutherford Appleton Laboratory, Harwell Oxford, Didcot OX11 0QX, UK
34 CERN, CH-1211 Genève 23, Switzerland
35 Particle Physics Department, STFC Rutherford Appleton Laboratory, Harwell Oxford, Didcot OX11 0QX, UK
36 Department of Computing, Imperial College London, Exhibition Road, London, SW7 2AZ, UK
37 Department of Radiation Oncology, University of California San Francisco, San Francisco, CA, 94115, USA
38 Rosalind Franklin Institute, Harwell Campus, Didcot, OX11 0QX, UK
39 Department of Brain Sciences,Faculty of Medicine, Imperial College London, Exhibition Road, London SW7 2AZ, UK
40 Department of Physics, Imperial College London, Exhibition Road, London SW7 2AZ, UK
41 Department of Cancer and Genomic Sciences, College of Medicine and Health, University of Birmingham, Edgbaston, Birmingham, B15 2TT, UK
42 Business Innovation Department, STFC Daresbury Laboratory, Daresbury, Cheshire, WA4 4AD, UK
43 Lawrence Berkeley National Laboratory, 1 Cyclotron Road, Berkeley, CA 94720, USA
44 University of Santiago de Compostela, Center for Research in Molecular Medicine and Chronic Diseases, 15782, Santiago de Compostela, Spain

45 *School of Physics and Astronomy, University of Birmingham, Edgbaston, Birmingham, B15 2TT, UK*
46 *Patrick G Johnston Centre for Cancer Research, Queens University Belfast, 97 Lisburn Road, Belfast, BT9 7AE, UK*
47 *INFN Catania, Via Santa Sofia,64 - 95123 Catania - Italy*
48 *Particle Physics Department, STFC Rutherford Appleton Laboratory, Harwell Oxford, Didcot, OX11 0QX, UK*
49 *Arizona State University: Tempe, Arizona, US*
50 *National Physical Laboratory, Hampton Road, Teddington, TW11 0LW, UK*
51 *Leo Cancer Care, Broadview, Windmill Hill, Hailsham, East Sussex, BN27 4RY, UK*

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# Executive Summary

## Motivation

In 2022, the UK Research and Innovation (UKRI) Infrastructure Fund established a two-year Preliminary Activity to develop the conceptual design of the Ion Therapy Research Facility (ITRF) [1]. The ITRF is conceived as a unique, single-site research infrastructure delivering high-dose-rate ions at energies sufficient for the study both *in vitro* and *in vivo* of the fundamental biology that underpins the efficacy of proton and ion beam therapy [2, 3]. The Preliminary Activity was extended for 10 months through a Bridging Award to allow the completion of the approved programme [4].

Cancer is the second most common cause of death globally [5]. Radiation therapy (RT), a cornerstone of cancer treatment, is required in over 50% of cancer patients [6] and is a contributor to ∼40% of cancer cures in England [7], according to England's national cancer registry and oncology treatment datasets [7]. Global utilisation varies due to differences in access [8].

Radiotherapy is most frequently delivered using X-ray photon beams with MeV-scale energies. The energy deposited by X-ray beams rises rapidly as the beam enters the tissue, reaching a maximum at a depth of $\sim 10\,\text{mm}$; it then falls exponentially. The therapeutic dose is proportional to the energy deposited. Modern X-ray-therapy systems maximise the dose delivered to the tumour while minimising dose to healthy tissue by irradiating the patient from a variety of directions with beams of appropriately modulated intensity.

Proton and ion beams offer substantial advantages over X-rays because the dose deposited close to the surface of the tissue is low and remains low until the beam comes to rest when the bulk of the beam energy is deposited in the Bragg peak. Modulating the energy of the proton or ion beam allows the Bragg peak to be localised at the site of the tumour and the therapeutic dose to be conformed to the tumour volume. The dose delivered to healthy tissue in the path of the beam leading up to the Bragg peak is significantly lower than that which an equivalent dose of X-rays would deliver. The sharp fall-off of the energy deposition after the Bragg peak means that almost no damage is done to tissues that lie beyond the Bragg peak.

Proton and ion beam therapy is usually delivered over a period of several weeks in a series of daily sessions. Each session consists of the delivery of a single fraction of $\sim 2\,\text{Gy}$ delivered at a rate of $\leq 5\,\text{Gy/minute}$. The dose in each fraction is usually distributed uniformly over an area of several square centimetres. Exciting evidence of therapeutic benefit has recently been reported when dose is delivered at ultra-high dose-rate, $> 40\,\text{Gy/s}$ ("FLASH" radiotherapy) [9], or provided in multiple mini-beams with diameters of less than $1\,\text{mm}$ distributed over a grid with inter-beam spacing of $\sim 3\,\text{mm}$ [10].

To allow systematic and definitive studies to be made of the radiation biology relevant for the development of new treatment regimens and the elucidation of fundamentally new biological mechanisms, the ITRF is required to:

- Be capable of delivering a variety of ion species from proton to carbon, exploiting ultra-high dose rates and novel temporal-, spatial- and spectral-fractionation schemes;
- Have automated, *in-vitro* end stations in which high-resolution, real-time imaging is able to resolve the time-evolution of the biological impact of the beams on the samples; and to

- Have automated *in-vivo* end stations which incorporate real-time imaging of the subject and its tissues, and in which the dose profile is measured shot-by-shot.

## ITRF Preliminary Activity

When the ITRF Preliminary Activity was initiated, it was recognised that the laser-hybrid proton/ion source proposed by the international LhARA collaboration could meet the needs of the ITRF [2]. LhARA, the Laser-hybrid Accelerator for Radiobiological Applications [11], exploits a high-power pulsed laser to drive the creation of a large flux of protons or light ions, which are captured and formed into a beam by strong-focusing plasma lenses [12, 13]. The proton/ion beams are then accelerated using a fixed field alternating gradient accelerator (FFA) that preserves the unique flexibility in the time, energy, and spatial structure of the beam afforded by the laser-driven source. The Preliminary Activity was therefore structured to advance the design of LhARA and to tension the laser-hybrid technique with more conventional synchrotron- or linac-based approaches [14].

## ITRF/LhARA Conceptual Design Report

This document, the principal deliverable of the Preliminary Activity, presents the conceptual design for LhARA to serve the ITRF. The conceptual design of the accelerator facility is presented in Chapter 2. Comparison of the laser-hybrid solution with the conventional alternatives has allowed the LhARA approach to be confirmed as the baseline design [15]. The conceptual design for the facility is shown in figure 1.

The Preliminary Activity allowed substantial progress to be made on the development of key techniques and prototype systems. In addition to the conceptual design of the accelerator facility, the principal achievements over the Preliminary Activity period are:

- *Implementation of the initial configuration of the PoPLaR, Proof of Principle LhARA Radiobiology, platform on the SCAPA facility at Strathclyde.*
  A permanent-magnet-quadrupole beam line was designed to serve a series of experiments by which to demonstrate capability and establish a track record in the systematic study of radiobiology using laser-driven beams [16]. The delivery of protons with energies in excess of 10 MeV was demonstrated in August 2025 [17]. Bespoke, thin-bottomed, cell dishes were developed and tested at the Birmingham MC40 cyclotron by personnel from the Universities of Birmingham and Oxford [18]. Bespoke diagnostics is also being developed. First biological exposures took place on November 19$^{\text{th}}$ 2025.

- *A detailed specification of the high-power pulsed laser and target system has been developed.*
  Simulation, design and experimental work have been carried out to develop the specification of the laser-driven source for LhARA (see chapter 3). The specification of the LhARA source has been validated through experiments at the University of Strathclyde, Imperial College London, and Queen's University Belfast.

- *The principle of the ion-acoustic dose-profile measurement technique was demonstrated in an exposure on the LION beam line at Ludwig Maximilians Universität, Munich*
  A volume of liquid scintillator was exposed to the laser-driven proton beam on the LION beam line (see chapter 4) [19]. The optical and acoustic signals were detected simultaneously in order to calibrate the acoustic response using the scintillation light. The results are now being prepared for publication, and a follow-up experimental campaign is being discussed.

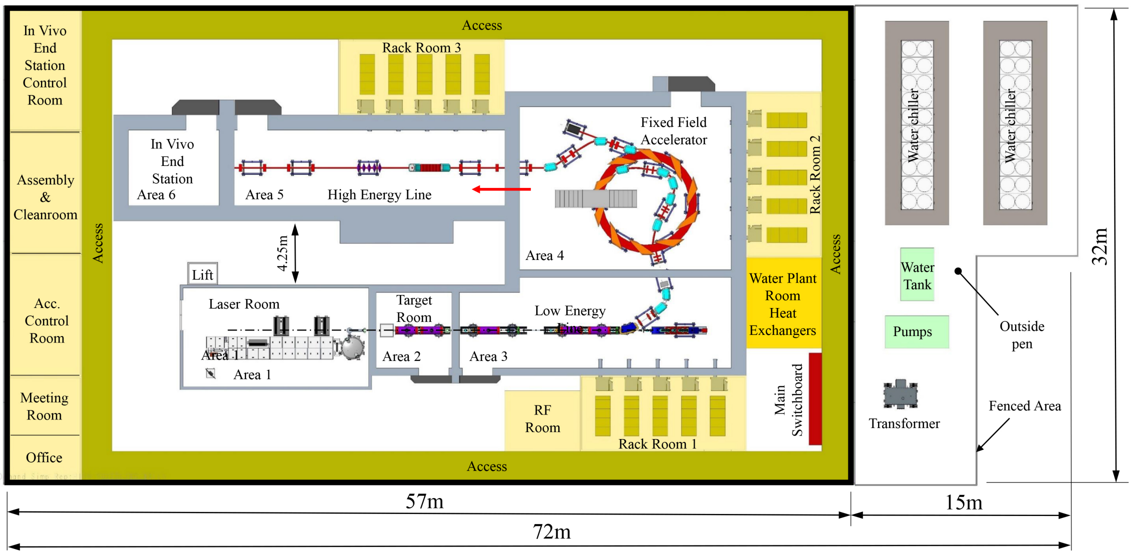

**Figure 1:** Schematic representation (top view) of the Laser-hybrid Accelerator for Radiobiological Applications (LhARA) integrated within the Ion Therapy Research Facility (ITRF). The figure depicts the accelerator facility, located on the ground floor, which is split into six main areas, each performing distinct functions. In Area 1 (Laser Room), a laser beam is generated and focused onto the proton and ion target located in Area 2 (Target Room). Protons or ions are captured by two electron-plasma lenses before being transported to Area 3 (Low Energy). The beam is then directed to one of two paths: either to the Fixed Field Accelerator (FFA) in Area 4, or to a low-energy *in-vitro* end-station (not shown), situated on the first floor. Beam extracted from the FFA is routed via the High Energy Line (Area 5) to either a high-energy *in-vitro* end-station (not shown, located on the first floor), or to the *in-vivo* End Station (Area 6).

- *The Penning-Malmberg trap on the positron beam line at the University of Swansea has been used to investigate and develop the electron trapping procedure.*
  Trapped-electron densities in excess of $10^{15}\,\mathrm{m}^{-3}$ in small volumes have been obtained and held for periods of 10s of seconds (see chapter 5). The electron density required for the LhARA plasma lenses has therefore been demonstrated. Future experimental and numerical development will focus on extending the volume of the high-density plasma whilst maintaining and extending the excellent plasma stability.

- *An initial specification for the* in-vitro *end stations and the* in-vivo *end station has been drawn up following an international peer-group consultation exercise.*
  The end-station specification is documented in a series of technical notes that define many of the requirements for the end stations and are the basis of future developments (see chapter 6) [15, 20, 21].

The work reported here was carried out by staff at the STFC national laboratories and the collaborating institutes. Much of the simulation and experimental work was carried out by excellent early-career researchers. To date, 4 PhD theses have been defended in the UK on the LhARA programme [19, 22–24] with more in the pipeline. Two theses from Institüt Curie have analysed aspects of the LhARA programme (beam delivery and TOPAS-based evaluation of the beam delivered to the *in-vitro* end station) [25, 26] and a third will be delivered next year. Interest in our programme is growing in France, Spain, the US, and Asia.

The legacy of the UKRI Infrastructure Fund ITRF Preliminary Activity is substantial; not only does this document provide the “blueprint” for the future development of the initiative, but a new experimental radiobiology programme has been initiated at SCAPA. The technical progress made during the Preliminary Activity has been presented widely at conferences and in seminars at national and international institutes. The collaboration has also been active in making the case for a vibrant programme of R&D aimed at advancing radiotherapy in general and identifying the unique potential of the laser-hybrid approach in this context. Supported enthusiastically by Radiotherapy UK and the Global Coalition for Radiotherapy, the collaboration has engaged with:

- Decision makers, taking part in a number of events organised by Radiotherapy UK in the House of Commons;
- Patient groups, for example presenting the initiative to the Northern Ireland Research Consumer Forum when the collaboration met at Queen's University Belfast [27]; and with the
- Public, presenting LhARA at the 2025 Great Exhibition Road Festival, which was attended by more than 40,000 members of the public, influencers and decision makers. The LhARA presentation at this event was prepared in collaboration with Leo Cancer Care. The collaboration's engagement with the Great Exhibition Road Festival led directly to the opportunity to present the LhARA initiative to President Macron and the French and UK scientific delegations on the occasion of the President's state visit in July 2025.

Over the period of the Preliminary Activity, the collaboration has developed a communication strategy and is now working to communicate its ambitious programme to all its stakeholders.

## Taking the LhARA initiative forward

The ITRF Preliminary Activity selected the LhARA technology to serve the facility as it is capable of providing the requisite variety of ion species over the required range of dose rates and temporal-, spatial- and spectral-fractionation schemes [28]. It is proposed that the facility be implemented in two Stages: Stage 1 based on laser-plasma acceleration; and Stage 2 in which the Stage 1 beam line is used as an injector to the FFA. Stage 1 delivers initial capability for *in vitro* research at low energy, followed in Stage 2 by a higher-energy *in vitro* and *in vivo* provision.

The LhARA collaboration now seeks to build on the foundations laid during the ITRF Preliminary Activity to:

- Deliver a systematic and definitive radiation biology programme;
- Prove the feasibility of laser-driven hybrid acceleration; and thereby
- Lay the foundations for the transformation of ion beam therapy.

The efforts of the collaboration will focus on the creation of a self-sustaining, multidisciplinary R&D programme alongside science-delivery and impact-generation programmes that maximise the benefits of the LhARA initiative, with the ultimate goal of building LhARA as an international research facility and developing a clinical particle-beam therapy system with industry.

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