

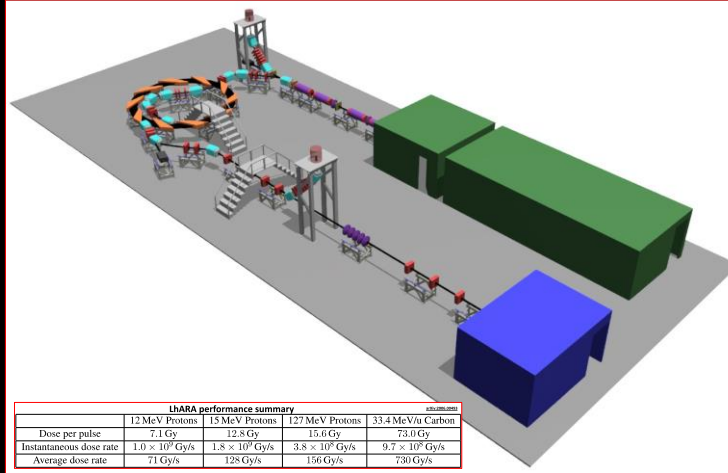
Introduction

Impact:
clinical & industrial

LhARA Project

Biological Science

MRes activity with
Leo Cancer Care
Ideas; still need to
develop



08Feb23

Making a start on developing the biological pillar:

- MRC “Developmental Pathway Funding Scheme”:
 - <https://www.ukri.org/opportunity/developmental-pathway-funding-scheme/>
 - A.Giacca, J.Parsons developing outline proposal
- Need Biological Science CM ...

Impact:
clinical & industrial

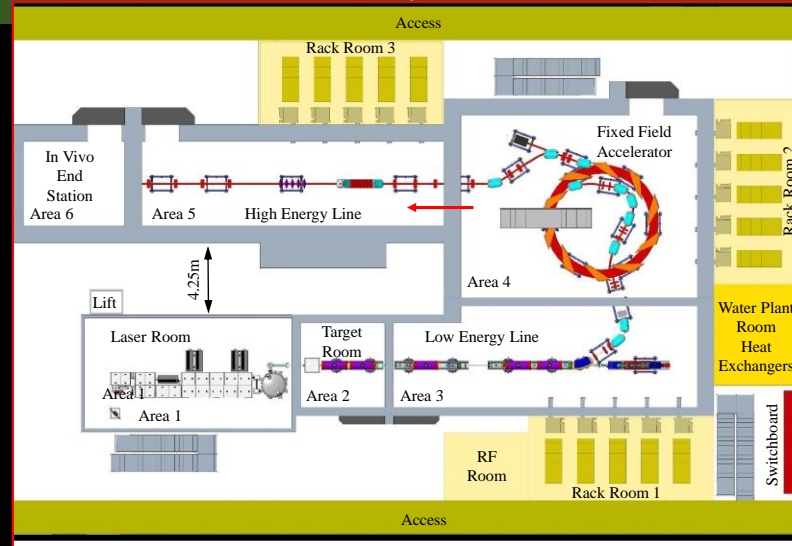
LhARA Project

Biological Science

Pat Price

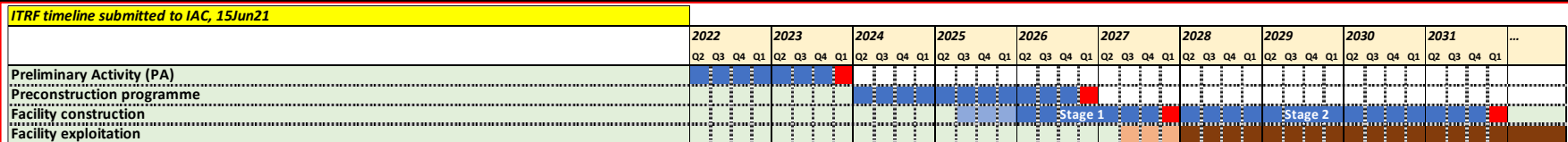
developing stakeholder,
comms, outreach and
impact plans for PA2

MRes activity with
Leo Cancer Care
successful



Vision firming up:

- Proof-of-principle experiment proposed for PA2
 - Discussion this afternoon
- Concept for a parallel programme of experiments @ other sources



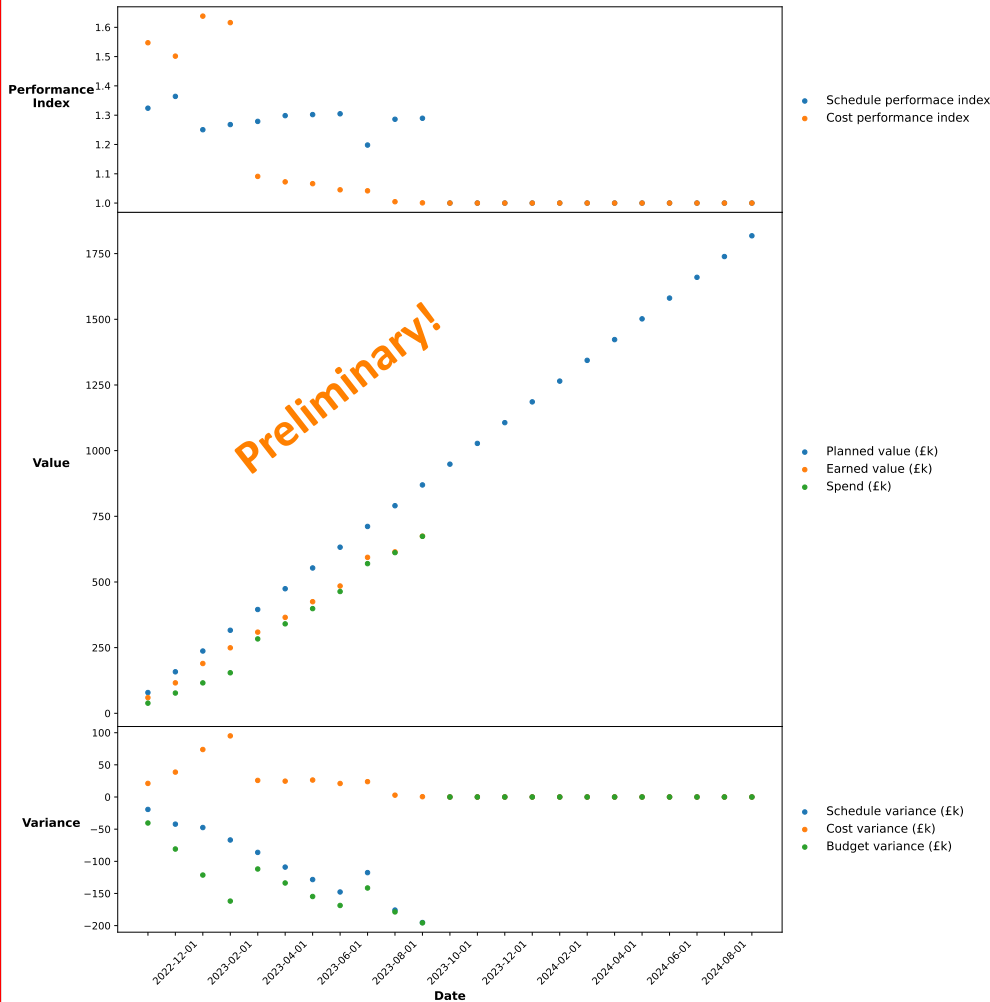
LhARA Preliminary Activity and Pre-construction Phase; principal milestones	
	LhARA CDR
	Stage 1 TDR
	Stage 2 TDR
WP1: Project Management	
LhARA CDR status update	12-month report
LhARA CDR	
LhARA TDR1	
LhARA TDR2	
WP2: Laser-driven source	
One-to-one simulation of proton source design	
Experimental demonstration 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	12-month report
Design and integration, LhARA CDR	
Design and integration, LhARA TDR1	
Design and integration, LhARA TDR2	

Waterfall chart from PA1 proposal ...
 → CM/12-month review to take stock of progress
 → Formal element: check against milestones

PA1 progress

- **Earned value:**
 - **Arcane but useful ...**
- **In general:**
 - **Tracking well:**
 - **Comments:**
 - **WP1: PMO**
 - “All” staff (OK)
 - **WP2: Source**
 - No spend reported first 4 months
 - Recovering well
 - **WP3: Capture**
 - Recruitment issues
 - Known problem, some of delays down to Home Office
 - **WP4: Ionacoustic**
 - Tracking well
 - Some equipment spend to come
 - **WP5: End-station**
 - Tracking well
 - **WP6: Design & integration**
 - Tracking well

Project: LhARA





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Creating world-class research and innovation infrastructure

Visions Panel feedback

...

Proposal Feedback: Ion Therapy Research Facility (ITRF)

The Visions Panel found the ITRF proposal to provide evidence of the project's potential to deliver of a step-change in capability and understood that such a facility would allow experimentation that does not currently exist elsewhere.

In terms of strategic drivers and the timeliness of the proposal within the current strategic landscape, the panel considered the proposal to be **timely but felt that the proposal may benefit from clarifying the existing level of community support for the proposal**. It was also noted that as the collaboration involved in the proposal is wide-reaching **the proposal may benefit from including further information on the level of engagement from all members of the collaboration**.

Please let us know if you have any queries.

Kind regards,
STFC Visions Team

... also discussing whether to revise the "total infrastructure cost".

Details and descriptions

Key Information	
1. Name of project (and acronym or short name if relevant)	Ion Therapy Research Facility (ITRF) Preliminary Activity 2
2. (a) Lead contact	Amato Giaccia (amato.giaccia@oncology.ox.ac.uk) Kenneth Long (k.long@imperial.ac.uk)
(b) STFC contact	Massimo Noro (massimo.noro@stfc.ac.uk)
3. Which submission route are you using (Advisory Panel, internal, resubmission) etc.?	Internal
4. One-line description of the Preliminary Activity (22 words)	

The ITRF will be a unique radiobiological research facility exploiting technologies that can transform ion-beam and the treatment of "hard-to-treat" cancer.

Project description

5. Summary of the Preliminary Activity (800 words) – please note this box expands as you type.

Background:

Conventional X-ray therapy (RT) is needed in 40% of cancer cures but some tumours are radioresistant and treat and cure. In Ion Beam Therapy (IBT), X-rays are replaced by energetic particles such as carbon ions. IBT allows the dose to be more precisely localised in the tumour and IBT causes significantly more direct, repair, DNA damage and stimulates a robust immune response. As a result, more tumours will be cured and side effects. However, IBT has yet to reach its full potential.

Globally, there is no facility that can be used to explore the fundamental biological processes underlying which can be used to optimise radiation delivery in time, space, ion species, and energy spectrum, also combination with new drugs. The project proposed here will create a facility to explore advanced radiotherapy new cancer treatments fit for 2050 and beyond, and make the UK a leader in the global fight against cancer.

Objectives:

The Preliminary Activity (ITRF PA2) proposed here will complete the design and planning of the ITRF construction to create the world-leading, compact, single-site research infrastructure that will deliver the multidisciplinary programme necessary to:

- Elucidate radiobiological mechanisms that underpin the clinical efficacy of particle therapy;
- Generate the accelerator, diagnostic, imaging, and computing technologies required to transform the clinical practice of IBT; and
- Deliver the capability to provide IBT in completely new regimens by combining ion species from protons to carbon exploiting ultra-high dose rates and novel spectral-, spatial- and temporal-fractionation schemes.

The design, specification and planning carried out within ITRF PA2 will build on the complete Conceptual Design Report that is the principal deliverable of the current ITRF Preliminary Activity (ITRF PA1).

Engagement:

To ensure direct engagement of the target user community, members of the leadership team are drawn equally from the biomedical and natural science communities. On the biomedical side, key leadership positions include LhARA/ITRF collaboration Co-Spokesman, A. Giacca (Director Oxford Institute of Radiation Oncology), Institute Board Co-Chair, Y. Prezado (CNRS Institute Curie), Biological Science Programme Manager, J. Parsons (Birmingham, Vice-Chair of the Association for Radiation Research), and Impact; Clinical and Industrial Programme Manager, P. Price (Imperial, Chair Radiotherapy UK). The biological and medical communities are also strongly represented on the PA1 oversight and advisory bodies.

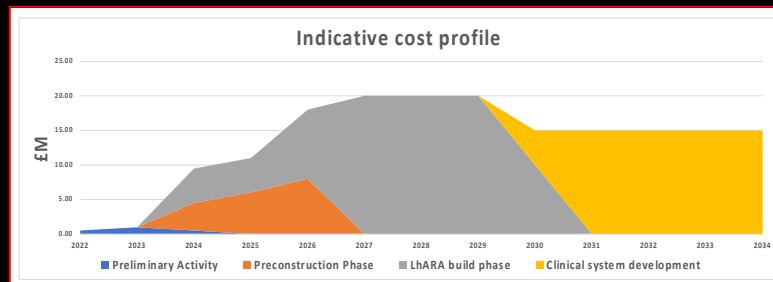
The pressing research need for an ion-therapy research platform was established through peer-group consultation (BJR 93 (11.16) 20200247). The LhARA/ITRF initiative now has significant momentum and breadth of engagement, e.g.:

- CLF, CI, JAI, QUB, and Strathclyde collaborate on the laser-driven ion source;
- The UK groups responsible for the ALPHA positron trap (Swansea, CI/Manchester) lead the plasma-lens development;
- The FFA team now encompasses ASTEC, ISIS, JAI; and
- Well-attended peer-group consultation meetings have attracted more than 50 researchers from the UK, Europe, and elsewhere.

The LhARA/ITRF initiative now has significant international visibility, allowing the collaboration to discuss collaboration with key contributors to the field (e.g., HZDR, LMU, BELLA@Berkeley, and CERN).

23. a. Complete the following table for UKRI Infrastructure Fund requirements, noting that costs are only approximations at this stage.

Infrastructure Fund requirement (£m) Point estimates.	Year												Total	
	Y1	Y2	Y3	Y4	Y5	Y6	Y7	Y8	Y9	Y10	Y11	Y12		
Project costs	22	50	81	50	22									225
TOTAL	22	50	81	50	22									225



Activity	Preliminary Activities
Deadline for proposal submission to STFC by Advisory Panels	July 21st 2023
Visions Panel	Late August 2023
Deadline for proposal submission to STFC after the Visions Panel	September 14th 2023
Review of proposals by Board members (SB, TAAB) Target for full programme definition	Late September – Mid November 2023
Executive Board/Council meeting	Early-Mid November 2023
Outcomes/feedback to proposal authors mid Oct23	Mid November 2023
Final proposal drafting/iteration with infrastructure team	Late November – Early December 2023
Proposal submission for IAC	Early December 2023

Process document and progress

August 10, 2023

PA2 programme definition process

Draft 1

Process for the preparation of the project specification for ITRF Preliminary Activity 2

This document sets out the process, steps and timeline for the preparation of the detailed project plan to be carried out under ITRF Preliminary Activity 2 (PA2). Throughout the process the key stakeholders, including STFC Department Directors, the LhARA collaboration management, the collaborating institutes, and the ITRF Project Board and Advisory Committee, will be kept informed. The stakeholders will be able to monitor progress against the timeline agreed for the preparation of the PA2 project plan. This document will be updated as necessary as the process progresses.

Background

The proposal for a second Preliminary Activity (PA2) in Infrastructure Fund Wave 4, "Ion Therapy Research Facility (ITRF) Preliminary Activity 2", was submitted to STFC on the 21st July 2023 [1]. If successful, this proposal will define an envelope of £21.5M for the execution of a four-calendar-year project, funded over five financial years, to prepare for the construction of the Laser-hybrid Accelerator for Radiobiological Applications (LhARA) to serve the ITRF. The present Preliminary Activity (PA1) will end in September 2024 and PA2 is scheduled to start in October 2024 and complete at the end of September 2028.

The programme to be executed in PA2 is based on years 3–5 of "The Laser-hybrid Accelerator for Radiobiological Applications R&D proposal for the preliminary, pre-construction phases" [2] [3]. In addition to the programme for years 3–5 of [2] [3], the PA2 proposal includes provision for a programme of radiation biology, targeted at preparing the collaboration for scientific exploitation of the facility, and modest provision for essential clinical engagement and outreach.

In parallel to the STFC Visions process, through which the PA2 proposal is being considered for submission to the UKRI Infrastructure Fund, it is essential to develop a detailed project plan for the execution of PA2. The PA2 project must address the principal risks to the successful construction of LhARA to serve the ITRF. A bid to the UKRI Infrastructure Fund for the funds to carry out the construction project will be made as part of the PA2 project.

Formal steps that the PA2 project-development programme must satisfy

The steps in the STFC Visions process that culminate in submission of the PA2 proposal by STFC to the UKRI Infrastructure Advisory Committee are [4] [5]:

21Jul23	Deadline for submission to STFC
Late Aug23	Visions Panel meets
14Sep23	Deadline for submission to STFC after the Visions Panel
Late Sep23 – mid Nov23	Review of proposals by STFC Science Board and Technology and Accelerator Advisory Board
Mid Nov23	Outcomes/feedback to proposal authors
Late Nov23 – early Dec23	Final proposal drafting/iteration with STFC infrastructure team
Early Dec23	Proposal submission to UKRI Infrastructure Advisory Committee

- Updated following EB comments, shared with WPMs and LhARA collaboration, no further comments
- Still awaiting comments from ITRF management
- Shared with attendees at STFC Bid Review: 04Sep23

Timeline

The Visions Process culminates in the submission by STFC of selected proposals to the UKRI Infrastructure Advisory Committee in December 2023. The preparation of the detailed PA2 project plan must therefore complete by the end of October 2023. To meet this requirement, the process defined above will be executed in line with the following timeline:

1. 31 August 2023: initial review of risk register complete;
2. 15 September 2023: initial, fully costed work-package programmes complete;
3. 20 September 2023: presentation of the full programme at the LhARA collaboration meeting and ITRF 12 Month Design Review; and
4. 30 October 2023: documentation of full PA2 programme complete and ready for independent review.

Review of the collaboration's "R&D proposal for the preliminary and pre-construction phases"

Feedback

The [Laser-hybrid Accelerator for Radiobiological Applications](#) (LhARA) formed the basis of the [STFC proposal to the UKRI Infrastructure Advisory Committee](#) to establish the Ion Therapy Research Facility (ITRF). This document presents the feedback from the [review](#) of the LhARA collaboration's [proposal for a five-year programme of R&D](#) that is designed to be carried out during the Preliminary Activity and Preconstruction phases of the development of the ITRF. A [page on the LhARA collaboration's wiki](#) has been prepared to record the terms of reference, review panel, documentation, presentations, and feedback.

The review was carried out between August and October 2022, with formal meetings held on the [30th August](#)¹ and the [26th and 27th October](#). The review panel was presented with a top-level description of the LhARA initiative and the LhARA project on the 30th August. A more detailed review of the radiation biology programme took place on the 26th October. The accelerator-science aspects of the LhARA project was carried out on the 27th October. The accelerator-science review focused principally on the [two-years of the programme proposed for the Preliminary Activity](#).

Review panel

International Advisory Board of the Centre for the Clinical Application of Particles:

- Mile Lamont (CERN) (Chair);
- Michael Baumann (DKFZ);
- Paul Bolton (LMU); and
- Brita Singers Sørensen (Aarhus)

Expert reviewers:

- Gianluigi Arduini (CERN)
- Christian Carli (CERN)
- Malek Haj-Tahar (PSI)

1. Review of radiobiology input for LHARA

Brita Singers Sørensen

Quality of the science and technology:

The radiobiology program encompasses a panel of the currently hot topics both within radiobiology as such, and more specifically within particle radiobiology. The research areas are focusing on tumor radiobiology as well as on radiation modalities which can potential spare normal tissue.

¹This link is to an Indico page for which the pass phrase is CCAP3008.

Review of the collaboration's "R & D proposal for the preliminary and pre-construction phases"

Response to feedback

The LhARA Project Management Board

On behalf of the LhARA collaboration, the Project Management Board welcomes the feedback [\[1\]](#) of the reviewers following the review meetings held on the [30th August 2022](#)¹ and [26th and 27th October 2022](#). This document provides the project team's response to each of the panel's recommendations.

1 Response to feedback

1.1 Review of radiobiology input for LHARA

Recommendations

1. Ensure possibilities for *in vivo* research. This includes nearby animal facilities and possibility for small animal imaging thought into the facility.

The project team agrees that providing the capability to carry out *in-vivo* studies is an important element of the LhARA project. Efficient exploitation of the *in-vivo* end station will require appropriate access to animal facilities. To maximise the scientific programme that can be supported by the facility will require an appropriately high level of automated remote handling. This implies the need for in-situ imaging to ensure the correct positioning and exposure of the animal. These ideas will be developed through the peer-group consultation being carried out in work package 5.

2. Ensure access to experimental reference beams (e.g. conventional proton beams and photon beams).

The project team agrees that comparison of the results obtained with the novel beams that LhARA will provide with those of conventional sources will be an essential part of the programme. Work has started on the preparation of a proposal to the Medical Research Council under the [Developmental Pathway Funding Scheme](#) for an initial programme of experimentation on conventional and laser-driven proton and ion beams. Our objective is to begin to investigate the radiobiology themes to which LhARA will provide access and to develop the techniques required to maximise the scientific potential of the LhARA facility. The "sister review to look at the instrumentation, diagnostics, novel end-station development, and radiobiological topics" identified in [\[2\]](#) will be scheduled taking into account the timescale of the review of the collaboration's proposal to the MRC DFPS scheme and the ongoing peer-group consultation being carried out by WPS.

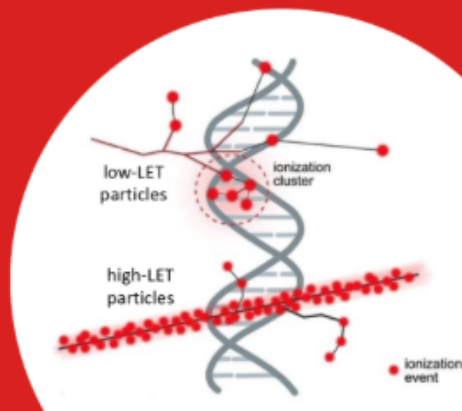
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PA2 detailed project plan

- **Rolling and formal reviews:**
 - **Chris Townsley; STFC, RAL (PPD) Proj. Man. Off. has agreed to provide “rolling independent review” as we prepare the PA2 project plan**
 - **On board; conversation with CT, Monday 18Sep23**
 - **Mike Lamon (CERN Dir Acc. + Tech.) has agreed to organize second independent international review of PA2 programme:**
 - **Will have greater focus on biomedical parts of programme than first review**
 - **Will discuss with ML early October**
 - **Target date for review Feb/Mar 2024**

Advancing Radiobiology Technology

24 October 2023
Institute of Physics, London, UK



Home

The Biological Physics, Medical Physics, High Energy Particle Physics, and Particle and Beams Groups of the Institute of Physics have come together to organise a meeting to discuss the novel techniques required to elucidate the mechanisms that determine the impact of ionising radiation on tissue. Such techniques have the potential to significantly impact clinical practice in particle beam therapy.

For example, proton beam therapy shows significant promise in tackling a range of cancers, traditionally using a Penning Ionization Gauge (PIG) ion source coupled to cyclotron technology, with recent developments using laser-based systems for particle generation showing huge potential—UKRI have provided seed-corn funding for the development of LhARA, a Laser-hybrid Accelerator for Radiobiological Applications, to serve the Ion Therapy Research Facility (ITRF) with a long-term vision is to transform the clinical practice of proton- and ion-beam therapy (IBT) by creating a fully automated, highly flexible system to harness the unique properties of laser-driven ion beams. However, full exploitation of particle generation facilities requires a range of developments from automated sample handling to fast feedback from the experimental end stations to the accelerator. This requires that advances in a variety of branches of physics be harnessed.

The joint meeting will be held at the Institute of Physics in London and will receive presentations on and promote discussion of the challenges in advancing radiobiology technology, including the underlying biology and biophysics, new accelerator systems, detector instrumentation and computing, and moving forwards into transforming biomedicine and clinical impact.