Status of preparation of …

White paper: *Ion therapy; the biological frontier*
LhARA proposal
STFC/CERN Framework Collaboration Agreement

K. Long
Imperial College London/STFC

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White paper:

- **Target journal:**
  - **Expert Reviews in Molecular Medicine**
    - **Special issue:**
      - **Editor: Jason Parsons**
      - **Special issue topic:**
        “Advancements in radiobiology”

Ion therapy; the biological frontier

White paper

Abstract

Lead authors: A. Giacca, K. Long, J. Parsons, P. Price

Review of current status of biological underpinning of radiotherapy and discussion of future requirement. Directions for future development are evaluated.

1. Introduction; particle beams for therapy

1.1 Development of particle beam therapy

Lead author: S. Green

History of PBT; from Wilson to present. Emphasis on last 20 years. Strengths, areas for development.

1.2 Overview of biological impact of ionising radiation on tissue

Lead author: A. Giacca, J. Parsons

Short historical review of biological foundations of PBT and present undertstanding of biological impact of ionising radiation on tissue. Areas of current research; discussion on of “terra incognita”.

1.3 Medical physics and delivery of beams for cancer therapy

Lead author: K. Kirkby

Present capability; foreseen developments; limitations. Draws on BJR paper.

1.4 Particle beams for biomedical application

Lead authors: K. Long, H. Owen, J. Pasternak [TBC], G. Schettino [TBC]

Short review of state of the art and both incremental and transformative developments.

1.5 Delivering the next generation particle-beam facility

Lead authors: A. Giacca, S. Green, K. Long

Opportunities for development, benefits of novel approaches, gap analysis.

2. Biomedical applications of ion beams

2.1 Ion beams for biological research

Lead author: Y. Prezado

Review of proton and ion beams available for biological research, their parameters, strengths, and weaknesses.

2.2 Ion beams for treatment

Lead author: TBC

Review of proton and ion beams available for treatment, their parameters, strengths, and weaknesses.

White paper:

- **Skeleton and lead authors defined:**
  - **Some lead author responses awaited [holiday season?]**
  - **One place where a lead is not yet defined**

3. Questions that must be addressed by a multidisciplinary research programme

3.1 Elucidating the biological impact of ion beams

Lead authors: A. Giacca, J. Parsons, Y. Prezado, K. Prise

Known unknowns and what is required to address them. Experiment (beams and instrumentation), theory and simulation.

3.2 Pre-clinical research programme

Lead authors: S. Green, K. Kirkby

Generating the evidence base to underpin ion-beam therapy, health economics, clinical sciences

3.3 Development of transformative technologies

Lead authors: J. Bamber (TBC), M. Borghesi, B. Cox (TBC), K. Long, H. Owen, P. McKenna, N. Dover, K. Prise, F. Romano, G. Schettino (TBC)

Scientific and technology-development issues to be addressed to deliver drive towards the next generation facility. Accelerator and instrumentation.

4. Ion beams for biomedical applications

4.1 Review of current and planned provision

Lead authors: S. Green

Present and planned (funded, i.e. developments to which there is commitment) ion-beam provision for research.

4.2 Next generation facilities

Lead authors: M. Vretenar, H. Owen, G. Schettino (TBC)

Developments using compact synchrotrons and linacs and superconducting cyclotrons.

4.3 The transformative potential of novel sources

Lead authors: M. Borghesi, K. Long, P. McKenna, N. Dover, F. Romano

The break-through potential of laser-driven sources; laser-hybrid, pure laser.

4.4 Potential for collaboration and the need for infrastructure

Lead authors: M. Noro, K. Long

Multidisciplinary, system-level approach.

5. Conclusions

Lead authors: A. Giacca, K. Long, J. Parsons P. Price

“Academic conclusion” and distillation of “recommendations” for taking the programme forward.

White paper:

- **Timetable:**
  - **Journal deadline Oct/Nov 2021**
  - **Preparation “milestones”:**
    - **“Copy deadline”: 24Sep21**
    - **Lead-author meeting week of 06Sep21**

A. Annex: Ion Therapy; the potential future for the UK

A.1 Introduction

Lead authors: A. Giacca, K. Long, J. Parsons, P. Price

UK has opportunity to take the lead in development and provision of novel beams etc. R&D programme such that incremental impact is realized along the way.

A.2 UK stakeholders and national collaboration

Lead authors: A. Giacca, K. Long, J. Parsons, P. Price

Universities, Research counsels, NHS, Department of innovation, Universities, skill, Department of Business and Enterprise, CTrad, RadNet; UK collaboration; industrial partners.

A.3

Lead authors: A. Giacca, K. Long, J. Parsons, P. Price

A.4 Government and industry support

Lead authors: A. Giacca, K. Long, P. Price

Industrial collaborations, skills and innovation, inward investment, wealth creation.

A.5 International interactions

Lead authors: A. Giacca, K. Long, P. Price

Collaboration CERN and others, lasers/accelerators, scientific collaborations

3

LhARA full Conceptual Design Report proposal

- **Proposal for 2—year programme; + 3 year forward look**
  [coincident with preliminary phase programme]
- **Scope:**
  - **2 year:**
    - **Complete Conceptual Design Report for LhARA**
    - **Key steps in the initial risk-mitigation programme:**
      - **Measurement of spectra produced at laser-driven ion source**
        - **And, benchmarking against simulation**
      - **Experimental programme leading to specification and manufacture of second plasma-lens prototype**
        - **Second prototype to demonstrate plasma dynamics has been understood and controlled; beam test "icing on cake"**
      - **Proof of principle of ion-acoustic imaging for in-vitro radiobiological experiments**
        - **Plan for next steps in the pre-construction phase R&D programme and considerations of what takes it to a clinical system**
      - **Complete design for vertical beam line for end-station system development**
        - **And, consultation to lead to specification of end-station developments required**
      - **Design and integration of LhARA facility required to:**
        - **Deliver completed LhARA CDR**
        - **Define next steps in the risk mitigation R&D programme to be carried out in the pre-construction phase (next 3 years)**
  - **5 year:**
    - **Full technical design report for Stage 1:**
      - **Supported by pre-construction phase risk-mitigation programme**
    - **Initial technical design for Stage 2:**
      - **Risk mitigation programme definition to be carried out in parallel to the Stage 1 build**
      - **Programme to deliver full TDR for stage 2**
    - **Initial ideas for "Stage 3":**
      - **Roll-out to enhance practice; elements of full system, system prototypes, …**

LhARA Conceptual Design Report proposal

LhARA "project organisation":

- Proposed for proposal and Preliminary phase
- Summarised below using "particle physics collaboration model"
- Co-spokes people:
  - Giacca (OIRO, Oxf), Long (ICL/STFC/JAI)
- Co-project-managers:
  - Parsons (Liv), Whyte (Str/CI)
- Work packages and work-package managers:
  1. Project Management: Parsons (Liv), Whyte (Str/CI)
     - Project Office: D. Kordopati (ICL)
  2. Laser-driven proton and ion source: Dover (ICL/JAI), + Gray (Str)
  3. Proton and ion capture: Charlton (Swn), Bertsche (Manch/CI)
  4. Real-time dose-deposition imaging: Bamber (ICR), Mattheson (STFC/PPD)
  5. Novel, automated end-station development: McLauchlan (ICL NHS), Price (Brm)
  6. Facility design and integration: Pasternak (ICL/JAI), + TBC

ccap-lhara-wpm <ccap-lhara-wpm@imperial.ac.uk>

Proposal timeline

- **Working backwards:**
  - **Monday 01Nov21:**
    - **Proposal complete (ink drying)**
  - **Monday 04Oct21:**
    - **First drafts of text of proposal and management annexes complete**
      - **Implies iteration of costs and time-line analysis**
  - **Monday 13Sep21:**
    - **Scope of proposal and w/s define:**
      - **Implies initial costing and initial time-line analysis**
  - **Tuesday 20Jul21:**
    - **Launch of proposal preparation**

STFC/CERN Framework Collaboration Agreement

- **Draft prepared:**
  - **Structure:**
    - Overarching agreement with Annexes

- **Shared with:**
  - **At STFC:**
    - Jim Clarke (Director ASTEC):
      - **JC has forwarded it to STFC Legal Department**
    - Dave Newbold (Director PPD)
  - **At CERN:**
    - Mike Lamont (Director Accel. and Tech.)
      - **M. Vretenar has sent it to CERN Legal Department**

European Organization for Nuclear Research
Organisation européenne pour la recherche nucléaire

FRAMEWORK COLLABORATION AGREEMENT
KNXXXX/ATS

between

The European Organization for Nuclear Research ("CERN")
and
The Science and Technology Facility Council ("STFC")

Concerning

The Development of Next Generation Ion Beams for Biomedical Applications

Framework Collaboration Agreement; Annex

- **Provides for 2 “work packages”:**

Work Package 1: The design of an advanced injector made of ion source, capture, and acceleration to 10-15 MeV, including:

- Contributions to beyond state-of-the-art multiple-ion sources of conventional or advanced design;
- High-gradient/high-frequency RFQ, laser-driven source characterisation, plasma-lens focusing;

Work Package 2: The design of a compact superconducting synchrotron for ion therapy, including development of compact lattice, study of alternating-gradient super-conducting magnets, and novel slow-extraction schemes.

ADDENDUM 1
KN XXXX/ATS
TO
FRAMEWORK COLLABORATION AGREEMENT
KN xXXX/ATS

BETWEEN

THE EUROPEAN ORGANIZATION FOR NUCLEAR RESEARCH (“CERN”), an Intergovernmental Organization having its seat at Geneva, Switzerland, duly represented by Michael Lamont, Director for Accelerators and Technology,

AND

THE SCIENCE AND TECHNOLOGY FACILITIES COUNCIL (“STFC”), a xxx, represented by its xxx, xxx.

Hereinafter each individually referred to as a “Party” and collectively as the “Parties”,

CONSIDERING THAT:

Framework Collaboration Agreement KNXXXX/ATS (the “Agreement”) concluded between the Parties defines the framework applicable to collaboration between them in designated domains;

Article 3.1 of the Agreement provides that the scope, each Party’s contributions and all other details of each specific Project shall be set out in Addenda to the Agreement;

The Parties have identified the collaborative project set out below, which shall be covered by the provisions of this Addendum No.1 KN XXXX/ATS (the “Addendum”),

AGREE AS FOLLOWS:

Article 1
Scope

1.1 Under the terms of this Addendum, the Parties shall collaborate on the development of specific accelerator elements for next generation of ion beams for biomedical applications (the “Project”). The currently envisaged conceptual design is based on an advanced superconducting synchrotron fed by a conventional linear accelerator as baseline design, with the option of using as alternative advanced injector concepts based on high-gradient laser-driven and/or plasma-based systems. .

In particular, the Parties shall collaborate on Project activities related to the design of the baseline accelerator, as follows:

Work Package 1: The design of an advanced injector made of ion source, capture, and acceleration to 10-15 MeV, including:

- Contributions to beyond state-of-the-art multiple-ion sources of conventional or advanced design;