Imperial College London

CCAP Centre for the Clinical Application of Particles

Accelerator applications for medicine

M.Dosanjh[1], I.Konoplev[2], K.Long[3], S.Sheehy[4]

[1]. CERN, *recently appointed Visiting Professor in Oxford*
[2]. JAI, Oxford
[3]. Imperial
[4]. JAI, Oxford

Science & Technology Facilities Council

07 March 2019

Medical accelerators; the challenge

- Cancer:
  - 2nd most common cause of death globally
  - Radiotherapy is indicated in half of all cancer patients
- Anticipated growth in demand:
  - 14.1×10^6 new cases in 2012 ⇢ 24.6×10^6 by 2030
  - 8.2×10^6 cancer deaths in 2012 ⇢ 13.0×10^6 by 2030
- Demographic:
  - Projections above based on reported cases (i.e. HIC)
  - Opportunity to save 26.9×10^6 lives in LMIC by 2035

- Scale-up in provision:
  - Requires development of new and novel techniques

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

Medical accelerators; the *opportunity*

- **Scale-up in provision:** Atun, Lancet Oncol. 2015 Sep;16(10):1153-86
  - Requires development of new and novel techniques
    - Investment required will generate substantial economic gains
- **R&D programme:**
  - Incremental development of current practice:
    - Instrumentation, imaging/image-processing, f/b and control
  - System approach to robust, flexible next-generation facilities:
    - Multi-species, combined therapies, integrated imaging
    - Resilient to e.g. environment, component failure, …
  - Collaborative R&D to harness novel techniques:
    - Multi-species, combined therapies, UHDR/FLASH, integrated imaging
    - Laser-driven, hybrid, novel (e.g. FFA) approaches
- **Opportunity to contribute to underpinning science and R&D:**
  - Radiobiology: especially charged particle (*p*, ion)
  - In-situ dose-deposition imaging: especially *p*, ion
  - Integration of planning, on-treatment, imaging, simulation, feedback and control

Accelerator applications for medicine

Electron linacs for X-ray/*e* therapy

Medical linac

- Electrons accelerated to 5—10 MeV:
  - 3 GHz cavity
- Delivers *e* and X-rays:
  - X-rays created on internal target
  - Intensity-modulated therapy delivered using sophisticated collimation & gantry systems

- Substantial initiative:
  - "Medical linacs for challenging environments"
    - CERN, ICEC, JAI, STFC, …
  - Target proposal to GCRF

- Investigation of UHDR (FLASH) RT:
  - Feasibility of use/modification of linac at CXH for research
    - CXH, ICL, ICR, RMH

Medical LINACs for challenging environments

M. Dosanhj

- Design Characteristics of a Novel Linear Accelerator for Challenging Environments, November 2016, CERN
- Bridging the Gap Workshop, October 2017, CERN
  - Understanding the problem
  - Oncologists, medical physicists, accelerator physicists
  - Outcome – 5 seed-corn projects

- Burying the Complexity Workshop, March 2018, Manchester
- Next Workshop in Botswana planned for March 2019

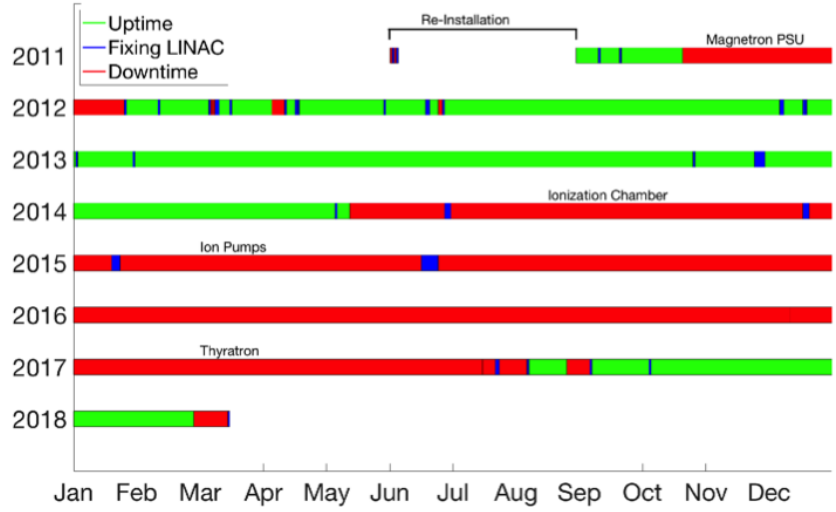
CERN

International Cancer Expert Corps
Partnering to transform global cancer care

Science & Technology Facilities Council | UK Research and Innovation

Towards an understanding of the issues

Abuja, Nigeria

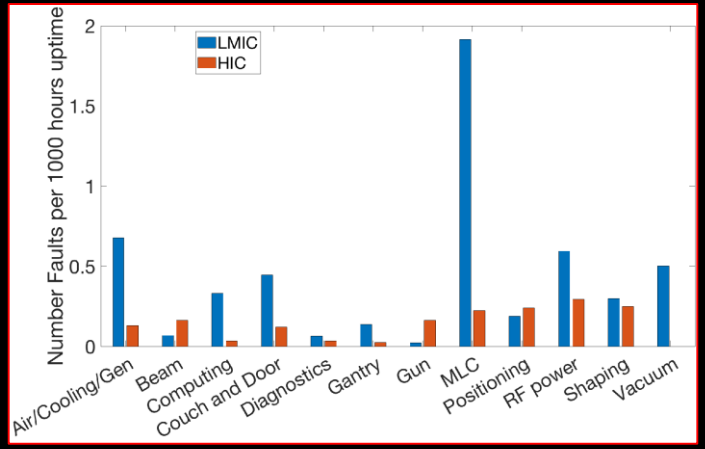


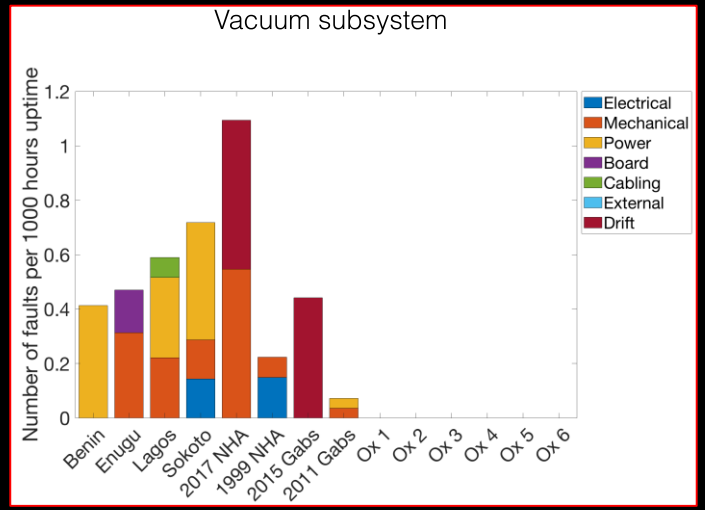
Comparative analysis of radiotherapy LINAC downtime and failure modes in the UK, Nigeria and Botswana

L. M. Wroe[a], C. S. Chinedu, T. A. Ige[b], S. Grover, R. Makufa[c], S. L. Sheehy[a], on behalf of the CERN-ICEC-STFC Medical LINAC collaboration

[a]Department of Physics, University of Oxford
[b]National Hospital Abuja (NHA), Nigeria
[c]Life Gaborone Private Hospital (GPH), Botswana

In preparation





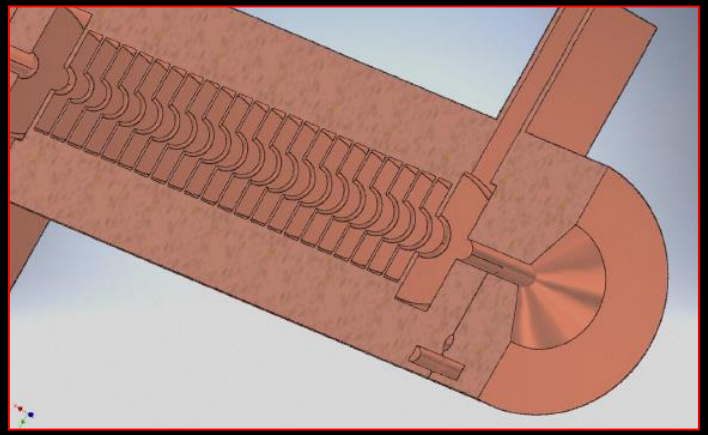
S. Sheehy

Medical LINAC: accelerating structure

I. Konoplev

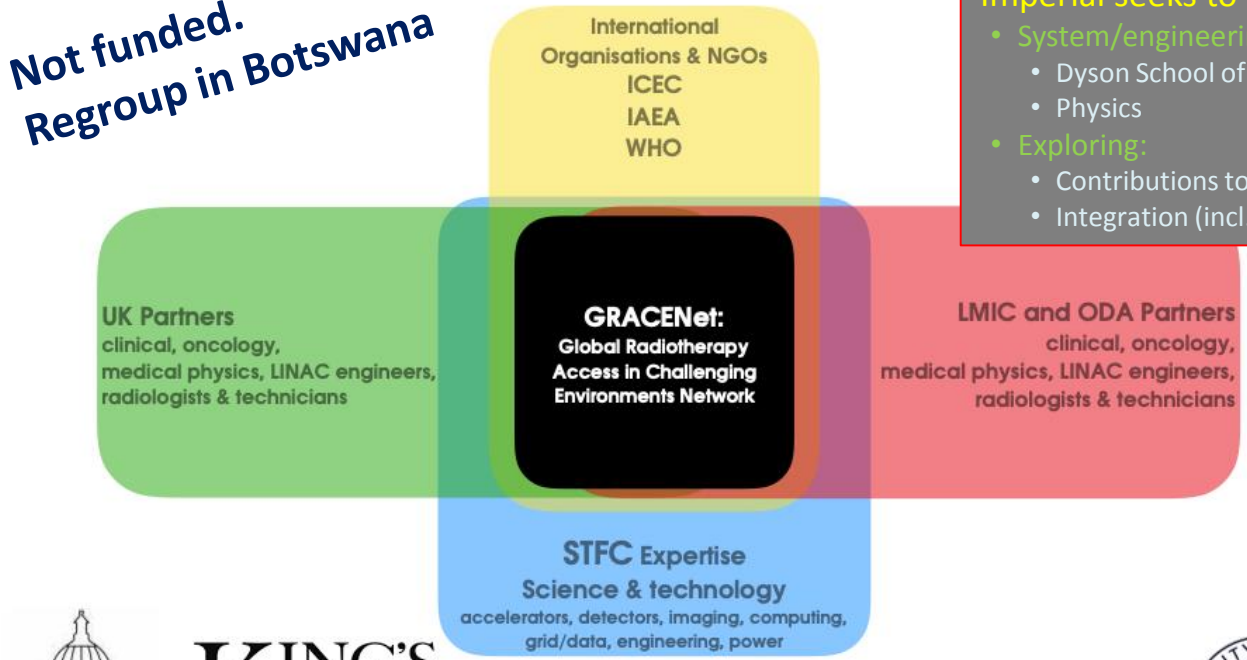
- **Objectives:**
  - **Design and build TW 12GHz accelerating structure that is:**
    - **Vacuum sealed, has cathode included**
    - **From 50keV to 8MeV (x-ray bulb)**
  - **Minimise the construction and running cost**
  - **Compatible with permanent magnets**

Preliminary numerical studies have been carried out.



Technical drawing of the prototype

Prototype of the TW accelerating structure



Not funded.
Regroup in Botswana

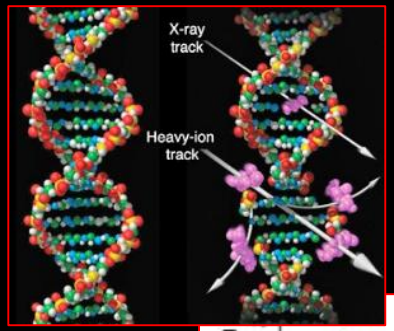
Imperial seeks to contribute too!

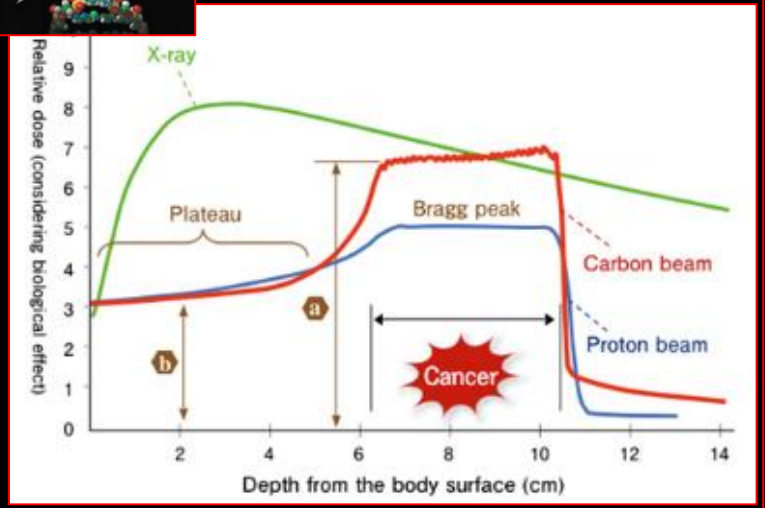
- System/engineering aspects:
  - Dyson School of Engineering Design
  - Physics
- Exploring:
  - Contributions to system-engineering; &
  - Integration (incl. imaging 'n' control)

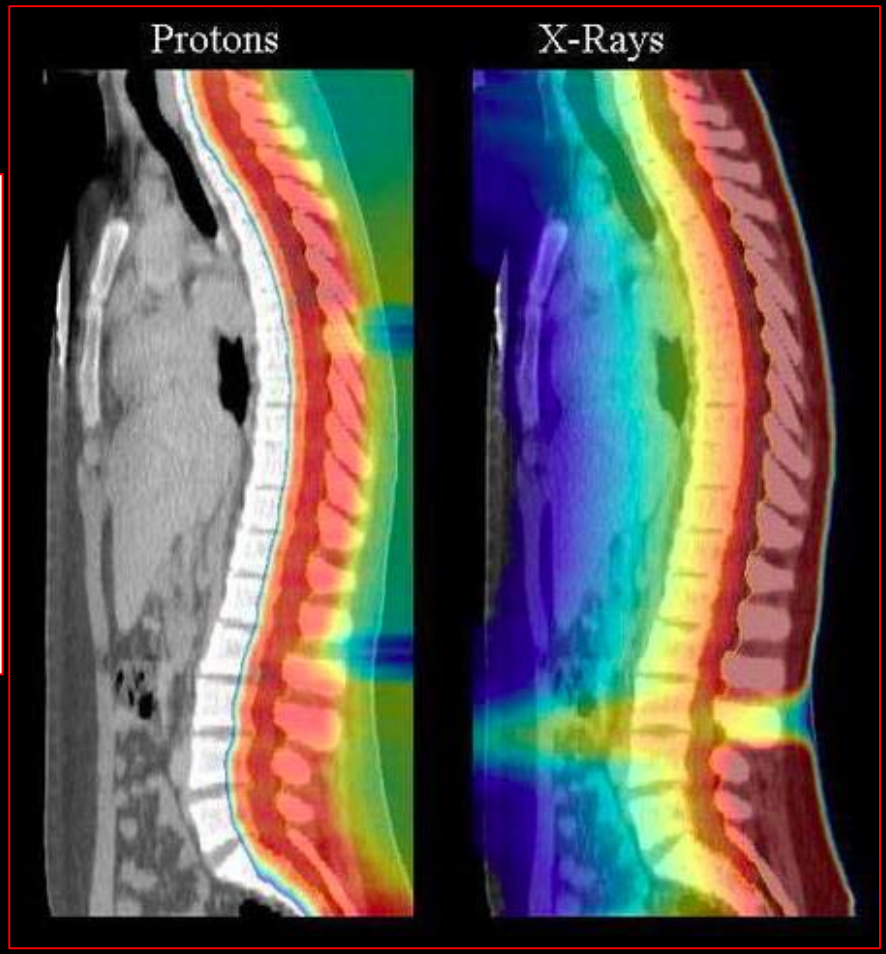
Accelerator applications for medicine

Hadron-beam therapy

The benefit of hadron beams



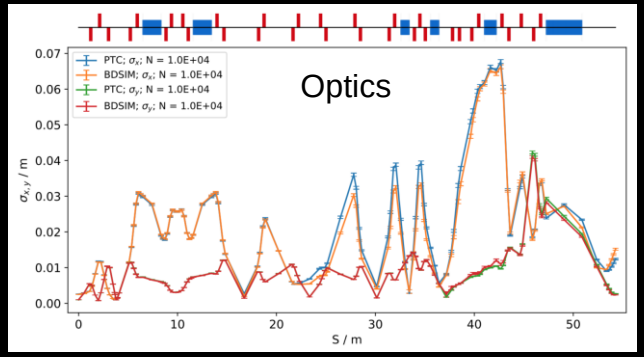


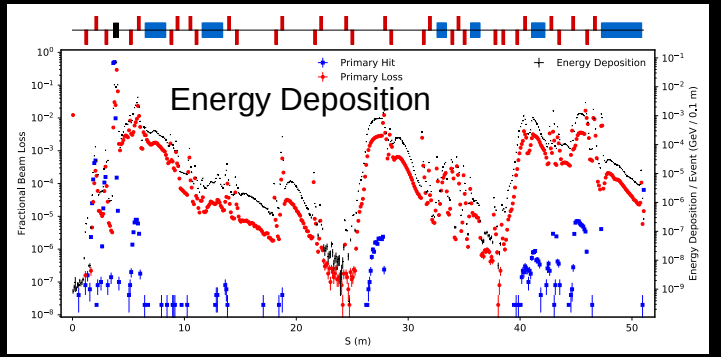


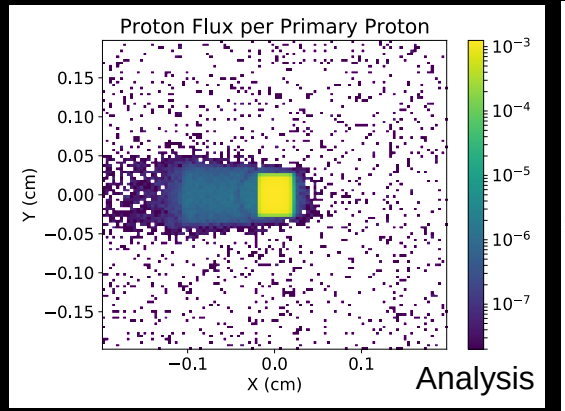
- **Relative Biological Effectiveness (RBE):**
  - **Dose required to generate particular biological effect relative to reference radiation**

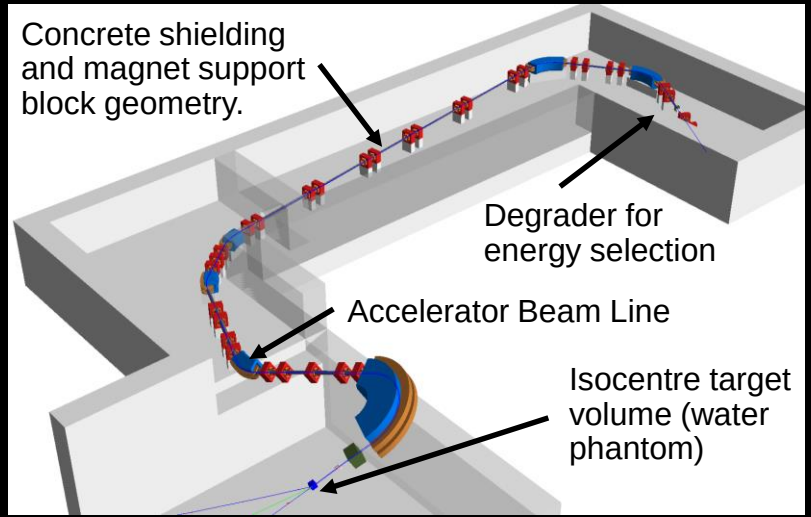
Medical Beam Line Simulations with BDSIM

- **Tracking & Optics:**
  - Particle tracking though Geant4 models of beam lines
    - Excellent agreement with accelerator tracking codes
    - Beam line optics calculations with full statistical uncertainties
- **Dosimetry:**
  - Record particle-matter interactions and energy deposition:
    - Energy deposition in beam line, shielding, isocentre target…
    - Full tracking of secondary particles
- **Flexibility:**
  - User customization
    - External geometry and field maps
    - Separate tool for user-defined analyses.
- **Impact:**
  - Ongoing simulation studies:
    - CCAP – LhARA
    - CCAP – MedAustron
    - IBA
    - In-house model (based on PSI Gantry 2)









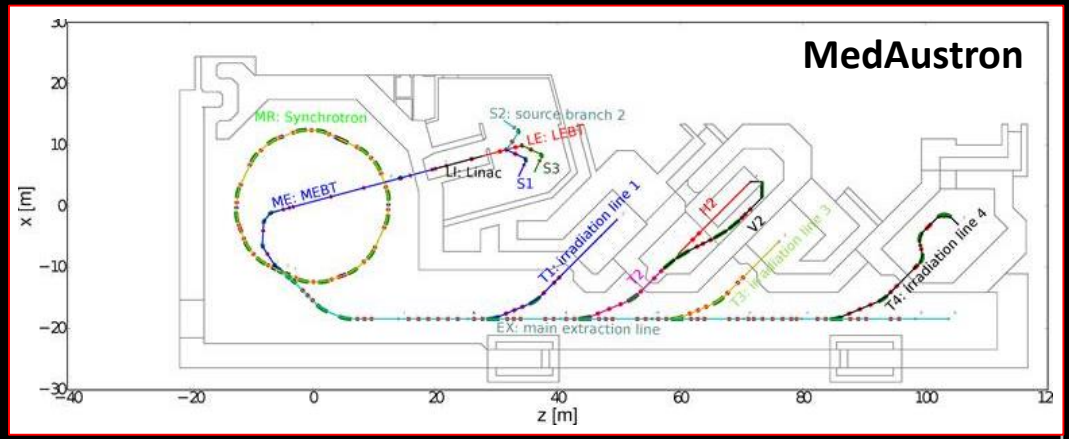
W. Shields, L. Nevay,
S. Boogert, et al. (RHUL)

Contact: william.shields@rhul.ac.uk

Particle beam therapy

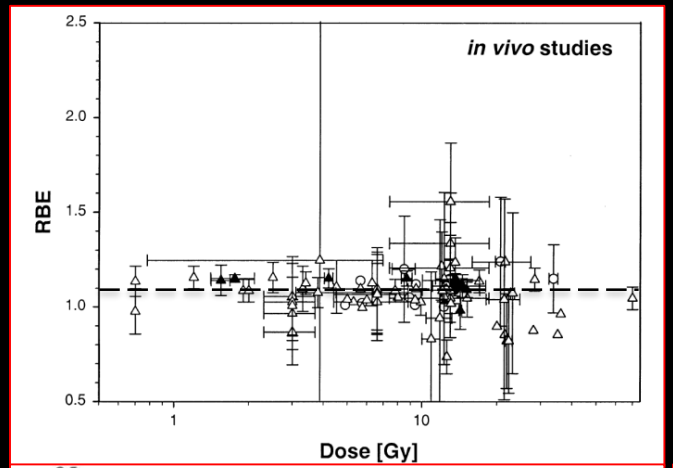
- Proton:
  - Mostly cyclotron-based
    - Issues:
      - Energy modulation;
      - Shielding
- Proton & ion (carbon):
  - Synchrotron based:
    - Issues:
      - Energy modulation
      - Source:
        - » Injector per ion species
        - » Limit to dose rate
- Many initiatives!
  - PIMMS2
  - LhARA

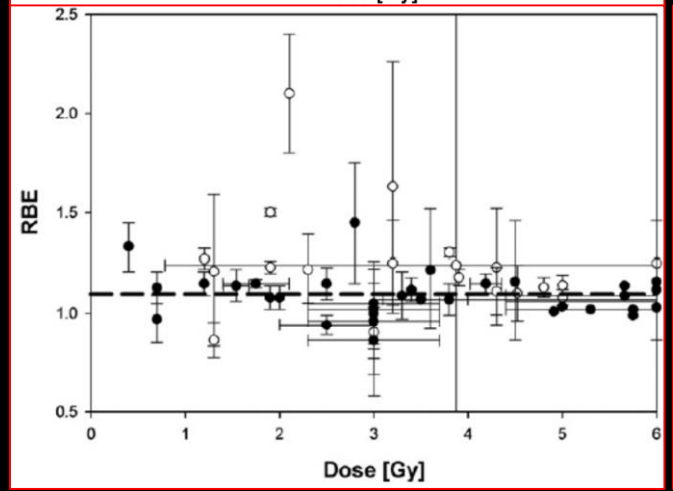
Christie

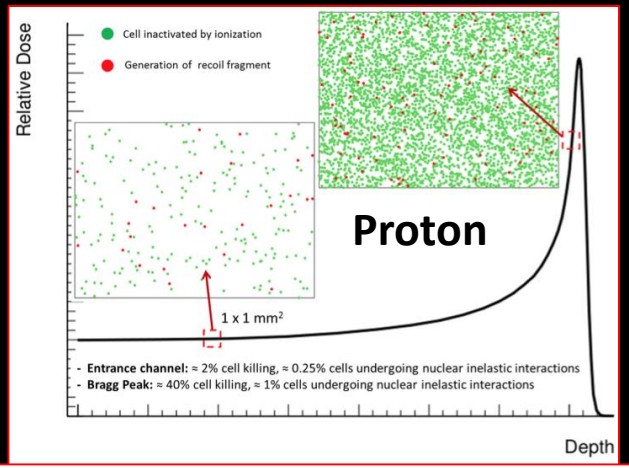


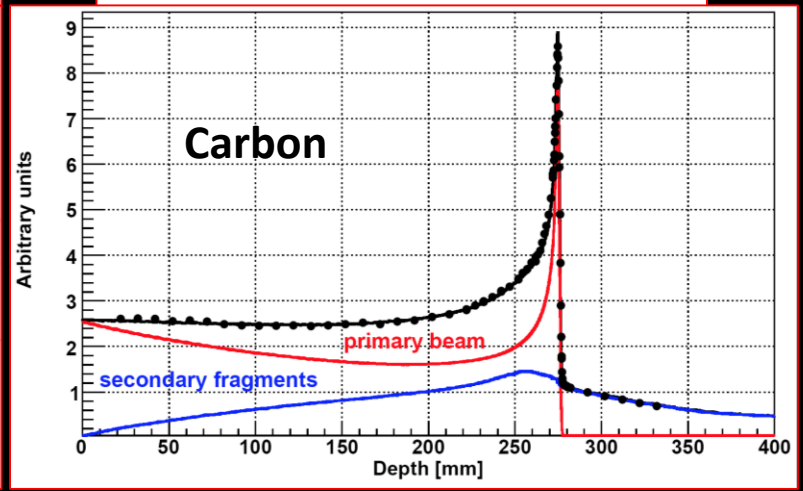
Hadron therapy; the issue of precision

- **RBE:**
  - Known to depend on, e.g.:
    - Tissue type, energy, dose, dose-rate, ion species …
  - Yet:
    - For *p*, RBE=1.1 is used
    - For *C*, less information available
- **Target (i.e. tissue) fragmentation:**
  - Protons:
    - Delivers radiation distant from beam
  - Carbon:
    - Substantial & distant contributions *and* strong tail beyond Bragg Peak
- **Opportunity!**
  - Prove new techniques while contributing to basic radibiology









Laser-hybrid Accelerator for Radiobiological Applications

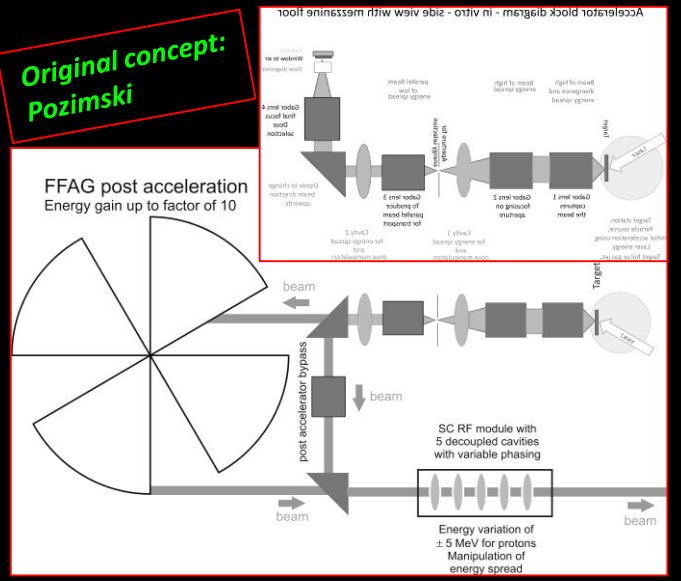
- **LhARA; a novel, hybrid, approach:**
  - High-flux, laser-driven proton/ion source;
  - Novel plasma (Gabor) lens capture & focusing
  - Post-acceleration with large-dynamic aperture FFA

- **Unique features:**
  - Very large flux of *p* or ions in very short pulses:
    - Enormous instantaneous dose
  - Inject at ~15 MeV into first accelerating structure
    - Overcomes space-charge limit of today's ion sources

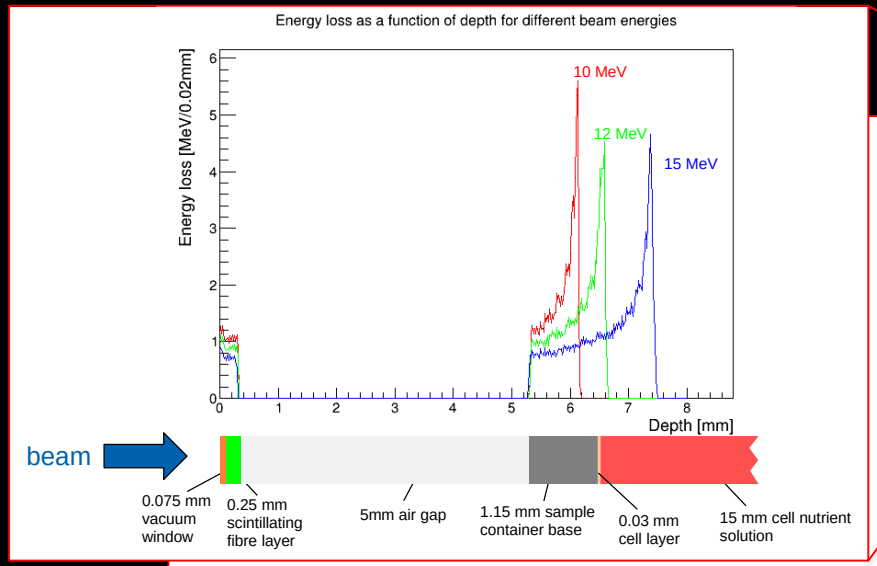
  - Staged implementation:
    - In-vitro studies permitted at 15 MeV:
      - Source, capture, transport
    - In-vivo studies using post-accelerator (75 MeV *p*; ~20 MeV/u)

- **Uniquely flexible radiobiology facility:**
  - Many ions, proton to carbon, in single facility
  - Wide range of energy and dose rate, allows UHDR/FLASH radiotherapy

- **Technologies can be developed to create uniquely flexible therapy facility**



LhARA; stage 1



END STATION
Where the cells will be irradiated. The beam will be delivered vertically from below the cell sample container.

DOWNSTREAM MATCHING
Quadrupole focussing channel to match the beam to the end station

LASER TARGET
Laser used to generate intense ions beams and beams of different types of ions, e.g. protons and carbon ions.

CAPTURE SECTION
Gabor lenses used for compact focussing to capture the large divergence and energy spread of the laser driven ion beam.

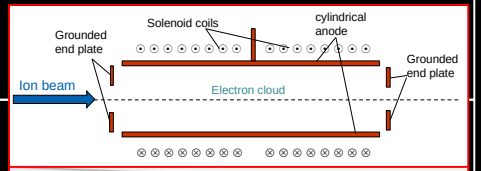
UPSTREAM MATCHING
Quadrupole focussing channel to match the beam from the Gabor lenses to the dipole.

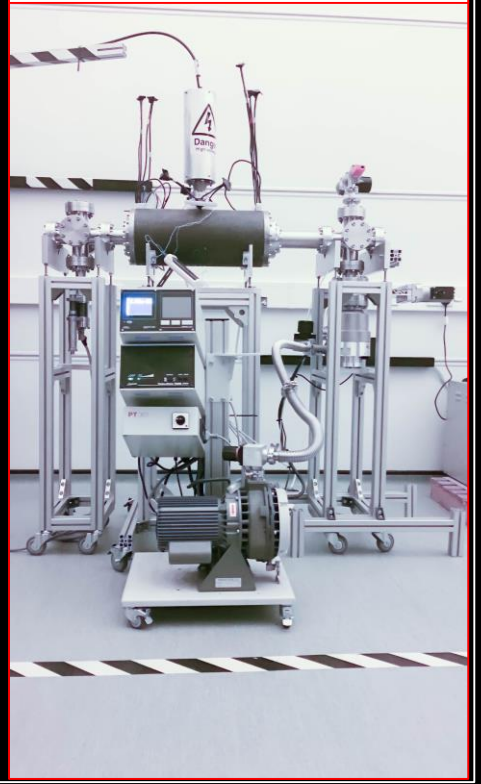
ENERGY AND ION SELECTION
Dipole bending and collimator system to select particles based on momentum.

LhARA work in progress

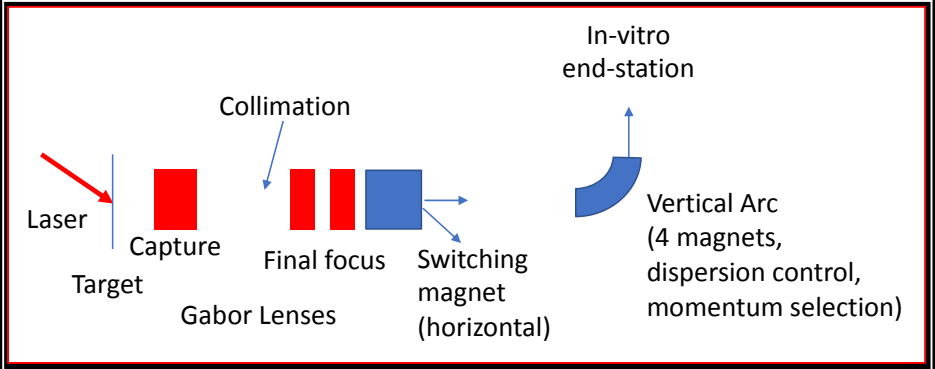
Capture

- Electron plasma:
  - Strong focusing of +ve ions
- 1st prototype:
  - 1 MeV protons Surrey Ion Beam Centre
  - Aberrations observed
- Upgraded prototype:
  - Under test in 022





Towards compact design



- Capture and transport using Gabor lenses:
  - Normal conducting solenoids alternative/risk mitigation
- Energy selection based on collimation
- Momentum selection in the arc
- Switching magnet:
  - Select in-vitro or to send beam to post-accelerator

Laser-hybrid Accelerator for Radiobiological Applications

Conceptual Design Report — Statement of Interest

The 'Laser-hybrid Accelerator for Radiobiological Applications', LhARA, is a novel hybrid accelerator in which laser interactions create a large flux of protons or light ions which are captured, formed into a beam and accelerated. The hybrid approach harnesses the unique properties of the laser-driven source: delivery of a range of ion species (p to C^{6+}) from a single source in ultra-short pulses that each deliver an enormous instantaneous dose. LhARA will be a uniquely flexible radiobiology facility serving experiments over a broad range of beam momentum and dose rate. By removing the dose-rate limitation of conventional ion-beam sources, LhARA will allow detailed investigation of FLASH (ultra-high dose-rate) radiobiology. The technologies demonstrated in LhARA may be developed for use in a new generation of similarly flexible hadron-therapy facilities.

The 'Centre for the Clinical Application of Particles' (CCAP) has recently been established at Imperial. The CCAP is ab initio a multidisciplinary collaboration between Imperial's Department of Physics, Faculty of Medicine, Academic Health Science Centre, the Imperial CRUK Cancer Centre, the Institute of Cancer Research, the John Adams Institute and the Oxford Institute for Radiation Oncology. The development of the Centre is a strategic priority for Imperial and the development of LhARA is central to the CCAP's programme.

With this Statement of Interest (SoI) we seek the resources to recruit a post-doctoral researcher for two years and a post-graduate student. Together, the two early-career researchers dedicated full time to the development of LhARA will leverage the effort of experienced personnel from the participating institutes to deliver a CDR for LhARA which will be presented in a refereed journal. During the preparation of the CDR we shall engage with stakeholders from the clinical, radiobiological, academic, and industrial communities so that when the CDR is published it will be possible to propose the staged development of the facility.

Motivation

In the UK, Europe, Asia, and the Americas, interest in proton- and ion-beam therapy is growing and a significant growth in demand is anticipated[1]. Analysis of the trends in cancer diagnosis and treatment indicates that, by 2035, 26.9 million life-years in low- and middle-income countries could be saved if the radiotherapy capacity could be scaled up[1]. There is powerful evidence that the investment required for this expansion would generate substantial economic gains as well as reduce the global cancer burden[1]. Novel techniques such as those proposed here are required if the necessary increase in capacity is to be delivered and the footprint and cost of particle-beam therapy is to be reduced.

Relative biological effectiveness (RBE) is the ratio of the dose of a reference radiation (X-rays) to the dose that must be delivered using proton or ion beams to achieve the same biological effect. RBE is known to depend on a variety of factors including energy, dose, dose-rate, tissue type, and ion species[2]. However, today a representative RBE value of 1.1 is used in proton-beam treatment-planning systems, for carbon, an RBE-weighted dose is used. This is sub-optimal and a systematic programme of radiobiology is required to underpin the development of a micro-biophysical understanding of proton- and ion-tissue interactions with precision sufficient for their biological effectiveness to be simulated and used with confidence to enhance hadron-beam therapy.

The hybrid, laser-driven approach that we propose is uniquely well suited to the radiobiology programme because it allows: a wide variety of ion species to be delivered using a single source; a very large instantaneous dose to be delivered because of the high capture-efficiency of the strong-focusing plasma (Gabor) lenses; a wide range of energy to be delivered using a single post-accelerator with large dynamic aperture based on the fixed-field accelerator (FFA) principle.

Context and opportunity

Laser-driven ions have been posited as a source for radiobiological studies for a number of years[3]. However, to date the ion energies, energy spread, and shot-to-shot variability of the flux produced has meant that such sources were not suitable to serve a radiobiology laboratory. A number of radiobiology experiments have been conducted with laser-accelerated ions, but these

LhARA SoI to ASB

- **Modest request; goal:**
  - **CDR in two years**
- **Build case and 'coalition':**
  - **Already broad national *and* international participation**

Principal partners/collaborators (and level of commitment)

The two early career researchers that will be recruited through the present proposal will join the CCAP LhARA design team to leverage the work of the experienced researchers at Imperial and within the CCAP. Personnel from the 'proto-coalition' support the work proposed here. The early career researchers will be able to call on advice from personnel within the institutes that form the proto-coalition.

CCAP LhARA design team D. Colling[1a], O. Ettlinger[1b], S. Gruber[2], C. Hunt[1a], A. Kurup[1a], H.T. Lau[1a], Z. Najmudin[1b], J. Pasternak[1a], J. Pozimski[1a]

[1] Dept. of Physics, Imperial College London

[2] Christian Doppler Laboratory for Medical Radiation Research for Radiation Oncology, Medical University of Vienna

Proto-coalition: M. Borghesi[1], B. Bingham[2], C. Brenner[3], P. Burrows[4], T. Greenshaw[5], D. Georg[6], D. Gujral[7], C. Hardiman[8], K. Kirkby[9], R. McLauchlan[8], P. McKenna[2], J. Parsons[10], K. Prise[11], P. Ratoff[12], S. Smith[13], J. Thomason[14], P. Weightman[5]

1. Centre for Plasma Physics, Centre for Advanced and Interdisciplinary Radiation Research, School of Mathematics and Physics, Queen's University, Belfast
2. Department of Physics, University of Strathclyde, Glasgow
3. Central Laser Facility, STFC Rutherford Appleton Laboratory, Harwell
4. John Adams Institute, Department of Physics, the University of Oxford, Oxford
5. Department of Physics, University of Liverpool, Liverpool
6. Christian Doppler Laboratory for Medical Radiation Research for Radiation Oncology, Medical University of Vienna
7. Department of Oncology, Imperial College Healthcare NHS Trust, Charing Cross Hospital, London
8. Radiotherapy Department, Imperial College Healthcare NHS Trust, Charing Cross Hospital, London
9. Division of Cancer Sciences, University of Manchester and The Christie Hospital, Manchester
10. Institute of Translational Medicine, University of Liverpool, Liverpool
11. Centre for Cancer Research and Cell Biology, Institute for Health Sciences, School of Medicine, Dentistry and Biomedical Sciences, Queen's University, Belfast
12. Cockcroft Institute, SciTech Daresbury, Daresbury
13. Accelerator Science and Technology Centre and STFC Daresbury Laboratory, Warrington
14. ISIS Department, STFC Rutherford Laboratory, Harwell

Accelerator applications for medicine

Conclusions

Conclusions

- JAI has exciting programme in medical accelerators:
  - Electron linacs for X-ray/*e* therapy:
    - Medical Linac for Challenging Environments;
    - Modification of ‘production’ machine for UHDR/FLASH studies
  - Hadron-beam therapy:
    - Engagement with PIMMS2 in collaboration with CERN
    - Development of unique facility, LhARA

- Emerging collaborations JAI ⇠⇢ CCAP/Imperial:
  - A growing strength!

Proton and Ion Medical Machine Study 2

Requirements for the future of ion therapy

Key messages from the International Workshop organized at Archamps in June 2018

Delivery:

- Fast dose delivery (possibly with 3D feedback for moving organs);
- Some range calibration online (e.g. proton or helium radiography);
- The rotating gantry is mandatory (possibly coupled to on-line MRI);
- Using multiple ions might be an asset.

Accelerator:

- Lower cost, compared to present (120 M€ for HIT and CNAO);
- Higher beam intensities than present (e.g. 10 times HIT);
- Reduced footprint from present (to about 1'000 m2);
- Lower running costs;
- Smaller facilities with less treatment rooms, distributed on the territory.

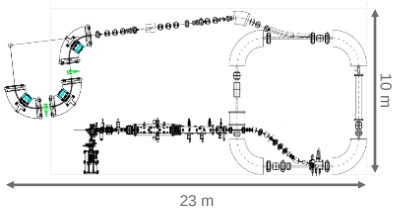
M. Vretenar (CERN)

M. Vretenar (CERN)

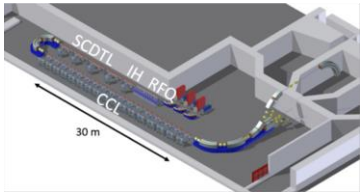
Guidelines for PIMMS2

The new PIMMS2 should **concentrate on ions** (we leave proton therapy to industry that is already well advanced) and be based on:

- Novel accelerator designs (compactness, cost, simple operation)
- Fast delivery scheme;
- Multiple ion capability;
- Equipped with a rotating gantry.



1. Superconducting synchrotron (90º magnets)



2. Bent linear accelerator

Alternative options (cyclotrons, FFAG) are technically complex and far from the CERN expertise

35

- **PIMMS2 study start 2019**
  - **Open collaboration with: CERN and SEEIIST**
  - **Resources through EU accession / structural funds**

- **Opportunities:**
  - **Ion source / LEBT;**
  - **Linac/ring**
  - **Gantry, imaging/feedback/control**