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EPSRC Outline PROPOSAL

Document Status: With Owner
EPSRC Reference:

Transformative Healthcare Technologies 2.0 - Outlines

Organisation where the Grant would be held (mandatory)

Organisation	Imperial College London	Research Organisation Reference:	TBA
Division or Department	Physics		

Project Title (mandatory) [up to 150 chars]

Transformative personalised, precision particle-beam therapy for 2050

Start Date and Duration (mandatory)

a. Proposed start date	01 September 2021	b. Duration of the grant (months)	15

Applicants (mandatory)

Role	Name	Organisation	Division or Department
Principal Investigator	Professor Kenneth Long	Imperial College London	Physics

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Objectives (mandatory)

List the main objectives of the proposed research in order of priority [up to 4000 chars]

We propose to lay the technological foundations for a step-change in the clinical of particle beam therapy. The principal objectives of our proposed research is to:

* Create the capability to deliver particle-beam therapy in completely new regimens
  by combining a variety of ion species in a single treatment fraction and exploiting ultra-high dose rates and novel spatial- and spectral-fractionation schemes; and
* Make "best in class" treatments available to the many
  by demonstrating in operation a highly flexible system that incorporates dose-deposition imaging in a fast feedback-and-control system thereby removing the requirement for a large gantry.

Our approach is to prove the principle of the laser-hybrid acceleration technique and the technologies necessary to automate the delivery of dose in a system dedicated to the study of radiobiology. We have developed the concept of a proof-of-principle system in which novel strong-focusing electron-plasma (Gabor) lenses capture and focus the large flux of protons or ions which is created when a short pulse, high-power laser strikes a target. The development and operation of the proof-of-principle system will lay the technological foundations for the paradigm shift in the clinical exploitation of proton and ion beams.

We have created a multidisciplinary collaboration of clinical oncologists, medical, particle, plasma and laser physicists, accelerator and instrumentation scientists, radiobiologists, industrialists, and patient representatives that has the ambition to:

* Improve the efficacy of PBT now and in the future
  by increasing our in-depth understanding of the biological effect of charged-particle beams; and
* Enhance the clinical practice of particle beam therapy
  by integrating imaging, real-time-treatment-planning, and fast feedback-and-control systems incrementally to automate the delivery of optimised, adaptive, multi-species particle-beam therapy.

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 with confidence. Such a programme will enhance the clinical effectiveness of proton therapy and is essential for a robust case for ion-beam therapy to be made. The laser-hybrid facility we propose to develop will serve ground-breaking in-vitro and in-vivo radiobiology programmes, thereby demonstrating that the feasibility of the laser-hybrid technique and providing the foundations on which a future clinical system can be built.

The clinical benefits of automated, adaptive, multi-species PBT can only be delivered once the full system is integrated. We have therefore adopted a holistic 'system approach' from the outset. With this Phase 1 propose we therefore seek the resources required to:

* Develop the elements of an integrated system in which movements of patient, organs-at-risk, and tumour are measured and used in conjunction with real-time dose-deposition imaging to adjust the dose delivered shot-by-shot; and
* Exploit novel computing techniques to allow real-time updates to the treatment plan to be made using algorithms based on detailed and precise measurements of the radiobiological impact of ion beams.

Our research programme will lay the technological foundations upon the proof-of-principle laser-hybrid system for radiobiology can be developed to demonstrate the feasibility of the technique.

The resources requested here will allow us to initiate a programme that has the potential drive a paradigm shift in the provision of PBT. A well-coordinated staff development programme is an essential to ensure that the team effort can be sustained to take the programme forward to deliver a clinical system for 2050.

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Summary (mandatory)

In simple terms please describe your proposed research in a way that it could be publicised to a general audience [up to 4000 characters].

The long-term objective of the research programme is to transform the delivery of proton- and ion-beam therapy using a system that is:

* Automated and is capable of adjusting the dose delivered in real time based on measurements of the position of patient, tumour, organs at risk, and the dose-deposition profile;
* Capable of delivering a range of ion species from proton to carbon over a wide variety of dose rates, up to and including those required for FlASH radiotherapy, in the same treatment session; and
* Has a footprint small enough that provision of the therapy can be distributed across the country.

The societal benefits of the substantial increase in access to advanced proton- and ion-beam therapy that would result from the successful execution of this programme is clear.

To lay the foundations of the technological programme required to deliver the programme outlined above we have formed an multidisciplinary collaboration composed of clinical oncologists, medical and academic physicists, biologists, engineers, and industrialists. We propose to take a holisitic `system' approach to the delivery of the programme. This requires that various technological developments required to implement a full system are brought forward in parallel.

Individual elements of the full system will mature at different times. Therefore we have adopted a project structure that will allow the `asynchronous exploitation' of the technologies that we shall develop. For example, the expoitation of novel high-throughput computing running novel feature-recognition algorithms to automate the adjustment of the position of the target volume is likely to be an early opportuntiy to generate impact. The development and explotation of such a system is aligned with the business plans of the industrial project partners. The identification of such opportunities is one of the responsibilities of the 'Co-creation of impact' workpackage, the leader of which is a consultant medical physicist. The identification of opportunities for spin out will be a continuing focus of the project leadership team throughout the project.

The creation of a project team that has the diverse skill set and motivation to take the project forward to deliver the long-term goal is a clear priority. Further, the sustainable development of the programme from proof of concept to spin out will require staff with a breadth of experience across the disciplines. We shall implement a staff-development programme in which early career researchers, and more established staff, recruited into one of the partner organisations are seconded for significant periods to other members of the collaboration. Resources to support the staff exchanges outlined above have been included in the costing prepared for this outline proposal and will be justified in the Pathways to Impact section of the full proposal.

Overall, our programme seeks to improve the delivery of particle-beam therapy. It is important to understand how these developments might be viewed by patients, staff and carers. Members of the team have previously developed and run a program of "Clinical implications of AI" funded by the Imperial College Patient Experience Research Centre (PERC). We propose to build on this experience to develop a Patient and Public Involvement (PPI) activity in years four and five of our programme. In this way patient-input will help us frame our bids for the continued support for our programme. Although this is earlier than is usual in the development pipeline, there is increasing emphasis on the involvement of patients early in the technology-development process. Engaging with patients from the outset will also give us experience in presenting and explaining concepts in novel particle therapy to patients and carers, which will be of longterm value in itself.

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Summary of Resources Required for Project

Summary fund heading	Full Economic Cost £	EPSRC contribution £	% EPSRC contribution
Directly Incurred			
Directly Allocated			
Indirect Costs			
Exceptions			
Total requested from EPSRC			

Total Cash Contribution from Project Partners			
Total In-Kind Contribution from Project Partners			

Project Partners: details of partners in the project and their contributions to the research. These contributions are in addition to resources identified above.

	Name of partner organisation	Division or Department	Name of contact