Imperial College London

MULTI-FACULTY CENTRE OF EXCELLENCE

ANNUAL REPORTING TEMPLATE - 2019

Purpose
The purpose of this report is to:

a) Provide the Vice-Provost's Advisory Group for Research with a progress report to assure that College approved Multi-Faculty Centres are meeting their planned objectives or provide explanation where there is variance;
b) Allow the Vice-Provost's Advisory Group for Research to review and where appropriate refresh the College's portfolio of Multi-Faculty research Centres and Networks;
c) Allow the Centre to highlight successes/achievements so that these may be further highlighted to stakeholders as appropriate;
d) Allow the Centre to highlight current or predicted barriers to progress so as to initiate further discussion as appropriate.

Review of Report
The report will be reviewed initially by the relevant Vice-Dean (Research) and subsequently by the Vice-Provost's Advisory Group for Research.

Submission of Report
Please submit your completed report and an updated membership list to researchoffice.fundingstrategy@imperial.ac.uk by 1st November 2019.

Reporting Period
Report since last review or since College approval, whichever is the most recent

Section 1: Multi-Faculty Centre Summary – please use Section 2 to provide explanation of any changes from the original information provided.	
Name of Director	Kenneth Long
Name(s) of co-Director(s) (if applicable)	
Name of Deputy Director(s) (if applicable)	
Name of Host Department	Physics
Title of Centre	Centre for the Clinical Application of Particles
Web address of Centre	https://www.imperial.ac.uk/clinical-application-of-particles/
Social media accounts	None
Start Date of Centre (dd/mm/yyyy)	01/10/2017
Number of FTE associated with the Centre	Membership: 77

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	FTE: 7.6 (FTE count from notional weighting of time spent on Centre activities
List of current Departments involved in the Centre	Imperial: Physics, Surgery and Cancer, Imperial Academic Health Science Centre Other: Institute for Cancer Research, John Adams Institute, Oxford Institute of Radiation Oncology
List of current Faculties involved in the Centre	Natural Sciences, Medicine

Section 2: Scope and Objectives

Please provide a summary of any changes to the purpose and scope of the Centre being sure to provide clarity where there may be perceived overlap between this Centre and other College entities. For the latest list of Multi-Faculty Centres and Networks see: https://www.imperial.ac.uk/multidisciplinary-research/

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The mission of the Centre for the Clinical Application of Particles (CCAP) remains to:

Develop the technologies, systems, techniques and capabilities necessary to deliver a paradigm shift in the clinical exploitation of particles.

The strategic themes in which the Centre's research programme is being developed are:

- The staged implementation of the 'Laser-hybrid Accelerator for Radiobiological Applications' (LhARA); a dedicated laser-driven accelerator dedicated to the systematic study of the micro-biophysical processes induced by proton and light-ion beams;
- The development of novel, real-time diagnostic, imaging, data-processing, and machine-learning techniques for clinical application;
- The delivery of a broad programme of measurement of the radiobiological effect of particle beams; and
- The establishment of the network of national and international collaborations necessary for the CCAP to initiate and then to sustain its radiobiological and technology-development programmes.

LhARA has the potential to be a world-leading facility in its own right and will also prove the Centre's novel accelerator, detector and data-processing technologies.

There are two multi-disciplinary networks and two multi-disciplinary centres at Imperial working in fields related to the activities of the CCAP. The goals of each of these networks and centres are complementary to, but do not overlap with, those of the CCAP. Links exist with both the Cancer Technology Network and the Physics of Life Network. It is our intention to strengthen these links as the CCAP programme develops. Prompted by the preparation of this annual report, contact will be made with the Centre for Mathematics of Precision Healthcare and the Centre for Integrative Biology and Bioinformatics with a view to collaboration in areas of mutual interest.

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Section 3a: Funding – P codes

Please provide a list of P codes representing the funding associated with the Centre since its inception discriminating any acquired after College recognition of Excellence. This will be used by the Research Office to summarise expenditure and the current budget available over the next three years.

P code	*Sponsor*	*Start*	*End*	*Value (1) £k*	*Scaled to Apr17 £k*	*Attribution to CCAP*	*Value (2) £k*
P54038	STFC	01Oct14	30Sep19	297.61	297.61	0.1	14.88
P63353	STFC	01Oct16	31Mar21	991.42	743.57	0.1	74.36
P28063	EPSRC	21May13	20May19	1,017.01	678.01	1.0	678.01
P66857	STFC	01Jan17	30Sep19	84.72	84.72	0.1	8.47
P63914	STFC	01Apr17	31Mar21	1,555.57	1555.57	0.2	311.11
P48107	STFC	01May13	30Apr23	390.06	78.01	0.8	62.41
P56866	STFC	01Jan15	31Dec19	191.30	114.78	0.8	91.82
P55678	STFC	01Oct15	30Sep19	147.55	73.78	0.2	14.76
PSF883	STFC	01Aug18	31Mar19	52.10	52.10	1.0	52.10
P65375	STFC	01Jan18	31Dec20	39.88	39.88	1.0	39.88
Successor to P54038	STFC	01Oct19	30Sep24	300.00	300.00	0.8	240.00
Successor to P55678	STFC	01Oct19	30Sep24	150.00	150.00	0.8	120.00
PSG954	STFC	01Jul19	31Mar20	37.66	37.66	1.0	37.66
P82401	STFC	01Oct19	30Sep21	78.53	78.53	1.0	78.53
						Total P codes	*1823.99*

The P codes representing the funding associated with the Centre are listed above[1]. The accounts listed in the first block (i.e. above the line) were in existence when the Centre was formed. For awards that were in place when the Centre was formed, the total value of each award (Value (1)) has been scaled to 01Apr17, the start of the financial year. The result is reported in the column headed 'Value (2)'. The accounts in the second block (below the line) have been won since the Centre was formed. Additional support for the Centre's programme is being provided by the Imperial CRUK Centre, by the Imperial/NIHR BRC, the ICR, the University of Liverpool and the STFC Particle Physics and ISIS Departments at RAL.

For each award an 'Attribution' has been estimated to reflect the fraction of the full award that is directly in support of the Centre's activities.

Section 3b: Funding – N codes

Please provide details of any other research income not on P codes associated with the Centre since its inception discriminating any acquired after College recognition of Excellence. This will be used by the Research Office to summarise expenditure and the current budget available over the next three years.

P code	*Sponsor*	*Start*	*End*	*Value (1) £k*	*Scaled to Apr18 £k*	*Attribution to CCAP*	*Value (2) £k*
Will be G account	STFC	01Oct18	30Sep22	87.56	88	0.1	8.76
G52142	FNAL	01Aug18	00Jan00	12.00	12	1.0	12.00
G53052	IC	01Oct18	31Mar20	5.00	5	1.0	5.00
F52281	IC	01Aug18	00Jan00	2.00	2	0.8	1.60
Louise will have	IC	01Aug18	00Jan00	2.00	2	1.0	2.00
Louise will have	IC	01Aug18	00Jan00	2.00	2	0.8	1.60
						Total N codes	*30.96*

The N codes associated with the Centre are listed above. Each account corresponds to resources won after the Centre was formed. The columns are as in section 3a.

[1] P-codes for two awards are unresolved. The 'Successor to P54038' is the STFC support for K. Long. The 'Successor to P55678' is the new STFC Consolidated Grant that supports the work of the HEP Group in the Physics Department.

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Section 3c: Funding – Core costs

Please provide a summary of any core costs required for the function of the Centre (e.g. admin, or director time) and how these are currently met.

There are two core posts associated with the Centre; the Director and the Manager. The Director is a permanent member of the academic staff in the Physics Department and is supported through STFC (successor grants to P54038 and P55678) and the Department. An agreement in principle to support the Centre Manager jointly by the Department of Physics and the Department of Surgery and Cancer is in place. To date it has not been possible to secure the resources necessary to support the Centre Manager. A. Kurup (Physics) is acting Centre Manager and is supported on a variety of grants. The present situation is not optimal as Kurup's other responsibilities mean that he is not able to dedicate his time to the management of the Centre.

Section 3d: Sustainability

Where £0.5M p.a. is not secured for the next 2 years or where funding ends in 2021, please list up to five funding schemes or other sources of income that the Centre can apply or explore to achieve the listed objectives. Please include any for which applications may have been submitted already.

A list of the applications made to support the Centre's activities is presented in the following table. Applications made in the current period are unshaded. Applications made before the Centre was formed are shaded dark grey. The rows shaded in a lighter grey are applications submitted in the 2018/19 reporting period.

Title	Funder	Lead	Value (£k)	Submission Date	Decision Date	Allocation (£k)	Allocation Start	Allocation End
STFC Earnest Rutherford Fellowship	STFC	CH	622.01	26-Jun-19				
Opportunities 2019	STFC	KL	139.35	13-Jun-19	Aug-19	139.35	01-Oct-19	30-Sep-21
Clinical Academic Research Partnerships March 2019	MRC	DG	188.78	17-Jun-19				
Contribution from HEP group for a high-spec server	HEP	AK	7.00			7.00		
Distributed, precise and personalised, particle-beam therapy for 2050	EPSRC	KL	6,983.30	02-May-19	15-Jun-19			
The SmartPhantom – A beam profile and dose measuring device	STFC/IAA	AK	35.00	09-May-19	05-Jun-19	37.66	Jul-19	31-Mar-20
Class of 64 Scholarship	Imperial	KL	63.81	04-Mar-19	03-Apr-19	63.81	Oct-19	Sep-22
Clinical Academic Research Partnerships March 2019	MRC	DG	142.91	09-Mar-19				
SoI to ASB	STFC	KL	302.35	25-Feb-19				
STFC Exploration award	STFC	KL	20.00	24-Jan-19				
STFC CG capital award	STFC	KL	18.73	Aug-18	23-Oct-18	18.73		
STFC CASE studentship CCAP/Maxeler	Imperial	DG/RMcC/KL	80.77	04-Oct-18	20-Dec-18			
Imperial College Research Fellowship	Imperial	CH	302.10	28-Aug-18	Oct-18			
STFC IAA	STFC/IAA	AK	20.00	29-Jun-18	Jan-18	52.14	Sep-18	Jan-19
STFC quota studentship via IC HEP	STFC	KL	70.00	Nov-17	Dec-18	70.00	01-Oct-18	Jun-22
Laser-driven ion beams for radiobiology and treatment	CRUK	KL, MW	498.35	24-Jan-18	25-Apr-18			
Building a European Network for the development of novel techniques for radiobiology and particle therapy	Imperial	VB	5.00	23-Jan-18	22-Feb-18	5.00	01-Mar-18	29-Feb-20
Laser-driven ion beams for radiobiology	RoseTrees Trust	KL, MW	251.46	01-Dec-17				
Ultra-fast prompt photon imaging for proton beam therapy	Imperial	KL, AK, DC, DG	250.00	24-Nov-17				
Opportunity: recruitment of PhD student to carry out research in accelerator-based radiobiology in collaboration with MedAustron	Imperial	KL	70.00	21-Nov-17				
Development of a programme for the measurement of the radio-biological effectiveness of charged particle beams	CRUK IC	KL/MW	70.00	19-Mar-17				
Development of a programme to investigate the biological foundations of charged-particle therapy	CRCE	KL/MW	29.83	31-Mar-17	05-May-17			

The success rate by reporting year is summarised in the following table. The shaded row refers to the year before the Centre was formed. In the current reporting period, a bid with a full-economic cost of £8.2M was submitted to the EPSRC against the 'Transformative Healthcare Technologies 2050' call. This proposal would have provided the resources to deliver the first stage of LhARA. While the proposal was declined, its preparation has proved valuable in the assembly of the wider

LhARA consortium. The column 'Corrected success rate' shows the rate of success excluding the single large proposal to the EPSRC. While the sums secured in new awards remain modest, the 'corrected success rate' shows a rising trend.

Period	Value (£k)	Award (£k)	Success rate	Corrected success rate
Oct16-Sep17:	99.83	0.00	0.00%	0.00%
Oct17-Sep18:	1,466.91	127.14	8.67%	8.67%
Oct18-Sep19:	7,882.50	247.81	3.14%	27.56%

Centre personnel remain energetic in seeking the resources necessary to execute the Centre's programme. The success in securing an STFC Opportunities 2019 award provides the resources to deliver a 'pre-CDR' for LhARA, to establish a FLASH-enabled test beam at the Clatterbridge Cancer Centre, and to form a UK consortium at the heart of the International Biophysics Collaboration. It is our intention to use the STFC Opportunities 2019 award as the vehicle by which to develop proposals to STFC, EPSRC and other research councils. Other opportunities to secure resources include the EPSRC Healthcare Technologies call, the MRC Multidisciplinary Project Award scheme and various CRUK collaborative awards.

Section 4: Leadership and Governance

Please provide a summary of any changes to the leadership and governance of the centre.

From its inception to 13th November 2018, the Centre Manager was V. Blackmore (Physics). Following Blackmore's departure from the College, A. Kurup (Physics) took on the role of acting Centre Manager pending a resolution of the financial arrangements for the support of the Centre Manager post between the Department of Physics and the Department of Surgery and Cancer.

No other changes have been made to the Centre's leadership or governance.

Section 5: Research Highlights

Please provide a brief lay summary of the research activity undertaken since the Centre's approval, taking the opportunity to highlight any particular successes/achievements so that these may be further highlighted to stakeholders as appropriate.
Separately, please link relevant publications in Symplectic to the Group for your Centre. For guidance on the creation of Groups speak to your Faculty Web Officer.
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Cancer is second most common cause of death globally. Radiotherapy is used alone or in combination with surgery, chemotherapy or other treatment modalities in more than half of patients. A significant growth in demand in first-world countries is anticipated. Moreover, in low- and middle-income countries it is estimated that 26.9 million life-years could be saved if radiotherapy capacity could be scaled up. The investment required to deliver this scale-up in capacity has the potential to generate substantial economic benefit.

Over the past year the Centre's research programme has developed to focus on the development of novel techniques to enhance the efficacy and practice of radiotherapy. Highlights of the programme are summarised below, further details may be found on the Centre's 'wiki'. The Centre has the ambition to: improve the efficacy of particle-beam therapy (PBT) by increasing our in-depth understanding of the biological effect of charged-particle beams; make 'best in class' treatments available to the many by reducing the footprint of future PBT systems such that a larger number of centres can be implemented across the country; and to contribute to the development of techniques by which incremental improvements in practice and efficacy can be delivered in the short term.

The Laser-hybrid Accelerator for Radiobiological Applications (LhARA)

The instantaneous dose rate that can be delivered by PBT facilities today is limited at the ion source by the space-charge effect. We propose to evade this limitation by developing a novel hybrid

accelerator in which laser interactions create a large flux of protons or light ions which are captured and formed into a beam in a series of strong-focusing plasma lenses. The hybrid approach harnesses the unique properties of the laser-driven approach: delivery of a range of ion species (proton to carbon) from a single source in ultra-short pulses that each deliver an enormous instantaneous dose. The successful demonstration of efficient capture and cylindrically symmetric electrostatic focusing will be an important step towards the exploitation of laser-driven beams.

A conceptual design for LhARA has been developed over the past year[2]. We propose that LhARA be implemented in two stages. In the first stage, the laser-driven beam, captured and transported using plasma lenses and bending magnets, will serve a programme of in-vitro experiments with proton beams of energy ~15 MeV. In stage two, the beam will be accelerated using a fixed-field accelerator (FFA) with large dynamic aperture. This will allow experiments to be carried out in vitro and in vivo with proton-beam energies of up to 125 MeV. Ion beams (including carbon) with energies up to 30MeV per nucleon will also be available. Our vision is that the integration of the techniques that we shall develop in this novel system for radiobiology will prove the feasibility of the laser-driven hybrid-accelerator approach, thereby laying the technological foundations of the programme required to transform the delivery of PBT while delivering a world-class radiobiology programme.

The progress made over the reporting period includes:

1. The revision of the outline conceptual design for the LhARA in-vitro facility. The present concept for the beam line is half the length of the initial concept;
2. The LhARA Stage 1 facility has been simulated to evaluate the capture efficiency, transmission, and impact of space charge;
3. A concept for the FFA post-accelerator has been developed;
4. A layout for the facility has been developed; and
5. The 'LhARA consortium' has been formed (see section 6). The consortium won an STFC Opportunities 2019 award to develop a 'pre-CDR' for LhARA.

The development of a systematic study of radiobiology

The efficacy of proton and ion beams is characterised by their 'relative biological effectiveness' (RBE) in comparison to reference photon beams. It is known that RBE depends strongly on many factors, including particle energy, dose, dose rate, and tissue type but the radiobiology that determines these dependencies is not fully understood. Over the reporting period a collaboration has been formed with the Biology Department at the University of Liverpool. Liverpool personnel have identified vital roles for specific proteins and mechanisms involved in the signaling and processing of DNA damage and repair as critical factors in the cellular response to protons. These results indicate that a systematic programme of radiobiology is vital for a full understanding of the bio-physical processes that are induced by ionising radiation to be developed. This understanding can then be exploited to maximise the efficacy of PBT now and in the future.

The development of the capability to contribute to a systematic study of radiobiology is central to the CCAP programme. Over the reporting period a graduate student recruited into the Centre's programme through the High-Energy Physics Group completed a long-term attachment at MedAustron (Wiener Neustadt, Austria). While resident at MedAustron the student contributed to the commissioning of the beamlines to the patient-treatment rooms as well as the research room. In addition, the student was able to bring Geant4-based simulation codes to MedAustron to allow multiple Coulomb scattering and energy-loss straggling to be simulated. The student has now returned to Imperial to develop a scintillating-fibre real-time dosimeter. This activity builds on the development of a novel low-energy ion-beam characterisation device developed by Centre personnel. It is planned that this device will be deployed in the radiobiology programme at

[2] A. Kurup et al., "Simulation of a Radiobiology Facility for the Centre for the Clinical Application of Particles,". Presented at the Third Geant4 International User Conference at the Physics-Medicine-Biology frontier, 29–31 October 2018, Bordeaux, France. C. Hunt et al., "Design of LhARA - Laser Hybrid Accelerator for Radiobiological Applications,". Presented at the 10th International Particle Accelerator Conference (IPAC'19), Melbourne, Australia, May 2019, paper THPGW001.

MedAustron early in 2020.

Incremental development of improved radiotherapy techniques

The majority of radiotherapy treatments are delivered using X-rays. Therefore, the development of techniques to provide incremental enhancements to X-ray-therapy practice today is a priority for the CCAP.

Variation of tumour position (due to breathing, peristalsis, etc.) is a major challenge in radiotherapy (RT), reducing the precision of the dose delivered to the tumour and increasing the risk to healthy tissue. Image-guided RT uses Cone beam CT (CBCT) to detect tumour position immediately prior to treatment, allowing adaptation of the RT if the target position differs from that assumed in planning. Present systems for image acquisition and matching of CBCT scans to reference baseline CT scans are manually operated, slow, have limited precision and suffer from 'artefacts' and 'noise'. These deficiencies limit the automated matching of CBCT to reference CT scans to bony matching.

Led by clinical oncologists and medical physicists, Centre personnel seek to establish a programme to enhance the processing of CBCT images to allow a soft tissue match to be performed automatically. Automation of the soft-tissue match has the potential to reduce the time spent by the patient 'on the couch' and to improve the accuracy of treatment delivery.

A team that includes clinical oncologists, medical physicists, academics from the Imperial Physics and Computing Departments, a company specialising in high through-put computing and a medical-equipment provider has been established to develop a proposal for submission to the EPSRC against its rolling Healthcare Technology call. In the mean-time, a start has been made on the investigation of the issues involved through an Erasmus-student project in the Department of Physics. Supervision is provided jointly by CCAP personnel from the Department of Physics at Imperial and the Radiation Physics and Radiobiology Department at the Charing Cross Hospital.

Section 6: Barriers to Success

Please describe any barriers or obstacles that the Centre has encountered that may prevent or slow progress of the Centre.

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As noted in the '*Barriers to Success*' section of last year's annual report, complementary lecturer-level appointments in the key areas of radiobiology and biophysics have been identified as a strategic priority by the Centre and by its principal stakeholders the Department of Physics and the Department of Surgery and Cancer. The fact that it has not yet been possible to make these appointments remains the principal barrier to the timely exploitation of the Centre's outstanding potential.

The complementary appointments appear in the strategic plans of the Departments of Physics and Surgery and Cancer as follows:

- *Lecturer in biophysics (FoNS/Physics)* with an interest in the measurement, characterisation and modelling of the biological impact of particle beams; and
- *Lecturer in novel particle radiobiology (FoM/Dept. of Surgery and Cancer)* with an interest in the development of a fundamental understanding of the radiobiology of novel particle beams and the application of this knowledge to improve clinical practice.

These lecturers will join the Centre's multidisciplinary team, including its collaborators in the UK and overseas and its industrial partners, from the outset contributing significantly to a large-scale, clinically focused project. These appointments will:

- Strengthen the effectiveness of the CCAP cross-faculty programme; each lecturer will bring expertise and 'cultural awareness' from 'the other side';

- In partnership, drive the development of: novel accelerator, detector and imaging technologies; a fundamental understanding of the radiobiology of ionising radiation; model systems and codes that can be used by the wider radiobiology community; and combined radiation, chemical and nano-particle modalities and automated treatment regimens.

The Gunnar Nilsson Trust has indicated its readiness to provide 50% of the funds required to support the two lecturer positions at least for an initial 5-year period. Failure to move forward on these essential recruitments puts the timely development of the Centre's strategic vision at risk.

The successful execution of the Centre's programme over the past year has strengthened the case for these strategic appointments and increased the likelihood of substantial return on the investment required. In particular, the Centre has:

- Won the resources to: deliver a pre-CDR for the Laser-hybrid Accelerator for Radiobiological Applications (LhARA); create a facility at which prototypes of the components of LhARA can be tested and an initial radiobiology programme can be carried out; and to create a UK consortium and forge a UK position within the International Biophysics Collaboration of which the CCAP became a founder member in May 2019;
- Established the LhARA consortium which is composed of: Academic institutions: *Imperial*: CCAP, Departments of Physics and Computing; *Liverpool*: Department of Physics, Institute of Translational Medicine (Department of Molecular and Clinical Cancer Medicine); *Belfast*: Centre for Plasma Physics (Department of Physics), Centre for Cancer Research and Cell Biology;*Manchester*: Division of Cancer Sciences; *Strathclyde*: Department of Physics; and *Royal Holloway University of London*: Department of Physics; Accelerator centres: John Adams Institute; and Cockcroft Institute; Laboratory Departments: *Accelerator Science and Technology Centre*; *Central Laser Facility*, *ISIS Department*, and *Particle Physics Department*; Clinical departments: *Department of Oncology*, *Radiotherapy Department* and Radiation Physics and Radiobiology Department, Imperial College Healthcare NHS Trust; *Clatterbridge Cancer Centre,* NHS Foundation Trust; and *Division of Cancer* Sciences, The Christie Hospital, Manchester; Industrial partners: Leo Cancer Care; Maxeler Technologies, Ltd.; and Corerain Technologies;
- Developed its collaboration with MedAustron, the Medical University of Vienna and the Technical University of Vienna such that the Centre's scintillating-fibre detector (SmartPhantom) will be deployed in the radiobiology programme at MedAustron early in 2020. This will allow the Centre to make its first radiobiological measurements with proton and carbon-ion beams; and
- Begun work on the development of algorithms to automate feature recognition to facilitate a soft-tissue match in Cone Beam CT images.

The proposed complementary recruitments are well aligned with the new Academic Strategy. The proposed recruitment will drive forward the strategic collaboration between the Faculty of Medicine and the Faculty of Natural Sciences and is essential to the timely realisation of the scientific potential of the Centre for the Clinical Application of Particles.