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Radiotherapy Related Research in **Manchester**

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www.mcrc.manchester.ac.uk



Welcome

The Manchester Cancer Research Centre (MCRC) was established in 2006 by three founding partners: The University of Manchester, Cancer Research UK and The Christie NHS Foundation Trust.

Our vision is to be a world-leading comprehensive centre for translational cancer research – transforming the clinical care of cancer patients by developing and implementing an integrated personalised medicine strategy.

We have a strong and enviable heritage in radiation research. The Manchester and District Radium Institute was founded in 1914, and from the 1930s was linked to the Christie Hospital on its current site. Dr Ralston Paterson built a team of physicists and clinicians who turned the hospital into a world-recognised centre for radiotherapy, setting the first international standards and developing the 'Manchester Method'. Manchester was also the setting for Ernest Rutherford's discovery of the proton in 1917, which we now harness 100 years later in the treatment of cancer.



Size and Scope

The Christie is one of the world's largest radiotherapy centres.

- 14 linear accelerators networked across three clinical sites.
- In 2018, we provided over 103,000 fractions to more than 7000 patients.

Internationally peer reviewed through CTRad as the only UK centre to have both breadth and depth in all 4 radiotherapy capabilities: physics, technology, biology and clinical.

We take a Team Science approach and have strong links between the laboratory and the clinic. Our multi-disciplinary research expertise spans biology, clinical oncology, physics, computing, engineering and imaging.

Recognised Excellence & Leadership

Radiotherapy research is uplifted by a large grant within the CRUK Manchester Centre. The research programme leverages other resources including the National Institute for Health Research (NIHR) Manchester Biomedical Research Centre (BRC), as well as:

- Cancer Research UK Lung Cancer Centre of Excellence
- Prostate Cancer UK Movember Centre of Excellence

We lead two UK networks: Global Challenge Network+ in Advanced Radiotherapy and the Engineering and Physical Sciences Research Council (EPSRC) proton therapy network.

Strategic Relationships

We have a track record in developing partnerships with industry:

- Formal agreements with Varian for proton therapy and Elekta for MR-guided radiotherapy.
- A strategic alliance with AstraZeneca and interaction with other pharmaceutical companies.

Collaboration

Within Manchester, we can exploit local complementary expertise in various disciplines across the MCRC partners.

- The Cancer Research UK Manchester Institute is home to world-leading cancer biology, drug discovery and translational research.
- The Cockcroft Institute is an international centre for accelerator science and technology.
- Dalton Nuclear Institute supports research across the field of nuclear science and technology.



Themes

In Manchester, our radiotherapy-related research predominantly fits within one of five research themes.

- Advanced/adaptive radiotherapy
- Biomarkers
- Clinical trials
- Immunotherapy
- Proton beam therapy

Advanced/ Adaptive Radiotherapy

We have long contributed to the implementation of developments in image-guided radiotherapy. We explore this in our Advanced Radiotherapy theme, alongside other approaches to improving accuracy, including target volume definition, treatment planning and follow-up, in order to increase survival and reduce toxicity.

- Patient-reported outcome measurements
- Improving delineation
- Improving image guidance
- Treatment personalisation
- Clinical validation and implementation

Biomarkers

The challenge for radiotherapy-related research is to find ways of giving as much radiation as possible to kill cancer cells while minimising the doses received by surrounding healthy tissue. Our researchers are developing tissue and imaging biomarkers for patient stratification.

- Radiogenomics
- Hypoxia
- Biobanking
- Radiosensitivity





Clinical Trials

Proton beam therapy

With the arrival of high-energy proton beam therapy in the UK, we are now leading clinical evaluation in order to determine its exact role and value. Our first trial – TORPEdO - is exploring the relative quality of life benefits and toxicities of PBT versus photon radiotherapy in head and neck cancer patients. The design of this trial has been shaped by patients and carers, and the research team conducted focus groups to understand the acceptability of randomisation, willingness to travel and choice of outcome measures.

Combination therapies

We carry out a range of trials exploring the combination of radiotherapy with other treatments. This includes the BCON trial, which investigated hypoxia modification in bladder cancer, a variety of immunotherapy studies and investigation of novel targeted agents.

Phase II/III

Our researchers lead large national and international phase II/III trials. The results of these are impacting on standard of care and changing treatment guidelines.

Immunotherapy Proton Beam Therapy

In order to further improve cancer outcomes using radiotherapy, an increased understanding of what determines effective radiation-induced anti-tumour responses and how best to combine radiotherapy with others treatments is required. Our research programme evaluates various aspects relating to the combination of radiation and immunotherapy, in both pre-clinical and clinical studies.

- Immune response to radiotherapy
- Integrating radiotherapy with immunomodulatory agents
- Monoclonal antibodies in the treatment of lymphoma

The Christie was chosen to be the location for one of two UK National Health Service's high-energy proton beam therapy centres, alongside UCL in London. Our clinical facility opened and treated its first patient in December 2018. Through the clinical facility and dedicated research room, our PRECISE group carries out a variety of research into the modality.

- Biological optimisation
- Range verification
- Computational oncology
- New accelerator developments
- Proton imaging
- Translational technical radiotherapy
- Clinical trials

www.bmh.manchester.ac.uk/research/domains/cancer/proton

Big Data & Machine Learning

Much of our research creates or deals with large datasets. We aim to combine information from genomics, imaging, and other sources in order to truly personalise radiation therapy. This approach includes data relating to outcomes, both clinical and patient-reported measures of quality of life.

Increasingly, we are looking to harness artificial intelligence in order to make predictions and decisions without the need for human input.

People

Robert Bristow



Robert Bristow is Director of the Manchester Cancer Research Centre, University Professor of Cancer Studies in the Division of Cancer Sciences and Chief Academic Officer at The Christie NHS Foundation Trust. He came to Manchester in 2017 from Toronto, Canada. As a Senior Scientist at the Princess Margaret Cancer Centre he treated genitourinary cancers. His primary research interests are in tumour hypoxia, DNA damage signalling and DNA repair in tumours, and the genomics of prostate cancer progression and cancer treatment response. He is particularly interested in novel clinical trials that intensify cancer therapy to prostate cancer patients whose tumours harbour aggressive genetic changes and hypoxic sub-regions.

Neil Burnet



Neil Burnet is Chair in Academic Proton Clinical Oncology at The University of Manchester. He started his consultant career at Velindre Hospital in Cardiff, where he initiated CT planning for patients with brain tumours. He then worked at Addenbrooke's Hospital in Cambridge for a little over 20 years, latterly as Professor of Radiation Oncology, and moved to Manchester in February 2018. He is especially interested in how to reduce the adverse effects that both tumour and treatment cause to patients with brain tumours, and how proton beam therapy might contribute to this. He is also interested in radiotherapy for chordoma of the skull base and spine and pituitary tumours, the optimisation of treatment with image-guided IMRT, and multi-scale mathematical modelling of cancer treatments.

Ananya Choudhury



Ananya Choudhury is Chair and Honorary Consultant in Clinical Oncology. She graduated from Trinity College, Cambridge, and then undertook her Clinical Oncology training at the Yorkshire Deanery from 2000-2008. Between 2005 and 2007, she was a Cancer Research UK Clinical Training Research Fellow and she undertook her PhD at the University of Leeds and Princess Margaret Hospital in Toronto, Canada. Ananya joined The Christie in 2008 specialising in urology and sarcoma. Her work aims to optimise and personalise radiotherapy using new techniques or imaging technology to deliver high doses of radiotherapy while minimising side effects, and develop predictive biomarkers to determine which patients benefit from different treatments.

Corinne Faivre-Finn



Corinne Faivre-Finn is a Professor of Thoracic Radiation Oncology at The University of Manchester and Honorary Consultant Clinical Oncologist at The Christie NHS Foundation Trust, with a specialist interest in lung cancer. Professor Faivre-Finn trained in Paris until 1998 and accepted a consultant post at The Christie in 2001. Her interests lie in the development of advanced radiotherapy techniques and combined modality treatments for stage III non-small-cell lung cancer and limited disease small-cell lung cancer.

Peter Hoskin



Peter Hoskin is Chair in Clinical Oncology at The University of Manchester. Having trained at the Royal Marsden Hospital, he was appointed to the Royal London Hospital in 1991 and subsequently in 1992 to Mount Vernon Cancer Centre, where he also held an academic post at University College London. He moved to Manchester in 2018. His areas of clinical interest include pelvic cancers and lymphoma, and he specialises in advanced radiotherapy techniques, translational radiobiology and imaging.

Tim Illidge



Tim Illidge is Professor of Targeted Therapy and Oncology at The University of Manchester and Honorary Consultant in Clinical Oncology at The Christie NHS Foundation Trust. He completed an undergraduate degree in Biochemistry before his medical degree from Guy's Hospital, London. His PhD at the University of Southampton was in antibodies and radiotherapy combinations. In 1994 he was appointed a Cancer Research UK clinical fellow and in 1999 a CRUK senior clinical fellow / senior lecturer at the University of Southampton. His translational research programme is based around radiotherapy and immunotherapy combinations.

People

Karen Kirkby

Karen Kirkby is Richard Rose Chair in Proton Therapy Physics at The University of Manchester. She studied for a PhD in the optical properties of ore minerals at the Natural History Museum, London. Her focus on ion beams and their applications developed from an interest in radiation damage in materials into the field of radiation damage in living cells and tissues and its application to advanced radiotherapy. At the University of Surrey, she worked with colleagues to develop the Ion Beam Centre into an internationally recognised centre of excellence in the applications of ion beams. Her current research aims to address the key scientific and technological challenges for proton therapy. These involve developing models that enable the proton dose to be biologically optimised to the tumour and its microenvironment, and also looks at options for proton range verification and determination of stopping powers.



Norman Kirkby

Norman Kirkby spent 33 years at the University of Surrey where he became professor in the Department of Chemical & Process Engineering, before gaining an interest in cell cycle modelling and radiotherapy. Norman moved to Manchester in January 2015 when the PRECISE group was established where he has been working in Mathematical Oncology, especially in support of the Proton Beam Therapy Service. The mathematical models he is developing describe the interactions between protons and DNA as well as the molecular biology of DNA damage detection and repair. One model, Malthus, models the National demand for radiotherapy. Norman has a special interest in the interactions between reactions and mass transfer, and population balance models of the cell cycle, including the varying sensitivity to radiotherapy with cell cycle phase and oxygen status.



Ranald Mackay

Ranald Mackay is Director of Medical Physics at the Christie NHS Foundation Trust and Co-Chair of Workstream 4 of CTRad (New Technologies), which has been instrumental in changing the perception of funding bodies to radiotherapy. He leads the Christie for proton therapy projects and was instrumental in gaining the funding to bring MR-linac technology to the Christie NHS Foundation Trust.



Marcel van Herk

Marcel van Herk is Professor of Radiotherapy Physics at The University of Manchester and The Christie NHS Foundation Trust. He moved to Manchester in 2015 after 32 years at the Netherlands Cancer Institute (NKI). Marcel undertook a PhD at the NKI and then spent time at Harvard Medical School as a post-doctoral researcher. He also held a part-time teaching role as a Professor at the University of Amsterdam for ten years. The main focus of his research is on accuracy of radiotherapy including target volume definition, treatment planning, image guidance and treatment follow-up.



Kaye Williams

Kaye Williams is the Leader of the Hypoxia and Therapeutics Group within the Manchester Pharmacy School. Kaye joined the Experimental Oncology division in November 1996 upon completion of PhD studies. Following back-to-back Research Associate and Research Fellow positions funded by the Medical Research Council, she gained a tenured Senior Lecturer position in January 2006, was promoted to Reader in July 2010 and Chair in Experimental Therapeutics and Imaging in August 2012. Her group currently focuses upon the tumour microenvironment, investigating therapeutic targets, vascular biology and molecular interactions.



Catharine West

Catharine West is Professor of Radiation Biology at The University of Manchester. She studied biology at York University and radiobiology at the Institute of Cancer Research, Sutton. After postdoctoral work at the University of Rochester Cancer Centre in upstate New York, she moved to Manchester in 1986. In 2002, she established the Translational Radiobiology Group. Her research focuses on trying to predict how cancer patients respond to radiotherapy with a particular interest in measuring radiosensitivity and hypoxia.



Facilities

Proton Beam Therapy Centre

The Christie is home to the first high-energy NHS proton beam therapy centre in the UK. The centre offers three clinical treatment rooms alongside a room dedicated to research.



Research room

The research room is located within The Christie Proton Therapy Beam Centre. It has been developed in parallel with the clinical treatment facility and is a unique research resource. It will be available to national and EU users through the EPSRC Network grant and EU grant INSPIRE.

The room features a pencil beam scanning nozzle to match that used in the clinical facilities. This ensures our experiments can emulate the beam delivery in the gantry treatment rooms in the clinical centre.

The research room has two horizontal beam lines that transport the beam to the scanning nozzle and then to modular experimental end-stations. These end-stations are interchangeable to allow the maximum flexibility in the design of experiments and optimum use of the beam time available for research.

Adjoining the research room is a biological preparation room, with tissue culture facilities and access to hypoxia cabinets. There is also a control room for remotely controlling the beam and experimental end-stations.

MR-linac

In 2014, The Christie joined a worldwide research consortium, led by Elekta and Philips, with a mission to develop an integrated magnetic resonance imaging (MRI) guided radiotherapy system.

The Elekta Unity MR-linac combines high field-strength MR imaging with a linear accelerator in a single system. Installation of our MR-linac began in 2016 and we are expecting to treat our first patients later in 2019.

In order to unlock the true potential of this novel technology, researchers are undertaking clinical and translational research studies in the prostate, cervical, lung and hepatobiliary-pancreatic cancers

SABR

Stereotactic ablative body radiotherapy (SABR) is the use of multiple small radiation beams to deliver high dose radiotherapy. The Christie has a number of linear accelerators capable of providing SABR at its main site.



Training and Development

We are committed to training the next generation and there are numerous opportunities provided by our partner organisations.

Postgraduate Study

The University of Manchester offers Master's and doctoral degrees.

Our MSc in **Cancer Biology and Radiotherapy Physics** is suitable for those with a first degree in biology or physics, and aimed at those who wish to pursue a career in cancer research and/or cancer therapy involving ionising radiation. Students will develop as

multidisciplinary scientists and have access to our MR-guided radiotherapy linear accelerator and proton therapy centre for their research project.

PhD projects are available through a range of schemes.

Higher Specialist Scientist Training

The Christie provides NHS Higher Specialist Scientist Training in Medical Physics. This is a five-year programme available to registered and experienced clinical scientists in preparation to become a consultant clinical scientist.



Advanced Radiotherapy Summer School

The Christie's Advanced Radiotherapy Summer School is an opportunity to learn about recent advances in radiotherapy from leading practitioners in the field. It features lectures, workshops, panel discussions and debates, as well as social events and the chance to visit our facilities.

Contact

Please contact us to find out more about any of the research programmes and opportunities listed here. We are always keen to hear from you:

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