CTRad Ten Years On: from Ten Point Plan to Top Ten Achievements

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The UK Clinical and Translational Radiotherapy Research Working Group (CTRad) was established in 2009 by The National Cancer Research Institute (NCRI) and its funding partners, in response to reviews of the radiotherapy research landscape in 2003[1] and 2008[2], which had identified radiation biology and oncology as areas of unmet need. At the launch, CTRad's inaugural chair, Professor Tim Maughan, announced a 10-point plan to tackle the challenges identified in the reviews while capitalising on opportunities for progress.[2]

In 2019 we celebrate CTRad's 10th anniversary and illustrate the progress made by the UK radiotherapy research community by describing CTRad's 'Top 10' achievements.[3]

1. Development of a broad portfolio of radiotherapy trials

Developing innovative, impactful radiotherapy clinical trials has always been CTRad's primary function. We have overseen the development of a broad portfolio of radiotherapy-focused trials, including early and late phase studies evaluating intensity modulated (IMRT), stereotactic ablative (SABR) and molecular radiotherapy (MRT). To achieve this, CTRad

created a pipeline that features Clinical Trials Workshops, aimed at junior researchers, Trials Sandpit Events and biannual Clinical Trials Proposals Guidance Meetings that are attended by most CTRad members. These meetings have educated, challenged and supported research teams progressing from concept through development to funding and recruitment. Between 2009 and 2018, 231 study proposals have been presented, of which 71 have been funded.

2. Spearheading innovative clinical trial design

Responding to the increasingly competitive funding environment and recognising the limitations of traditional clinical trial designs, CTRad has encouraged researchers to develop more innovative and collaborative approaches. A prime example is the recently funded CONCORDE trial[4]: a randomised, phase I platform study evaluating five different inhibitors of the DNA damage response in combination with radical radiotherapy for non-small cell lung cancer (NSCLC). As well as bringing together researchers from multiple UK centres, CONCORDE represents effective partnership with the pharmaceutical industry. Other innovative trials include PATHOS[i] (de-intensification of treatment for human papillomavirus driven head and neck cancer), PLATO [ii] (phase II-III platform study in anal cancer), PIVOTALboost [iii] (pelvic node and prostate boost radiotherapy in prostate cancer) and PARADIGM[iv] (radiotherapy plus the PARP inhibitor olaparib in glioblastoma). CTRad convenes trial-specific workshops at which researchers from diverse disciplines and NCRI Consumers refine study concepts and maximise translational content.

3. Benchmarking radiotherapy research excellence

[i] https://clinicaltrials.gov/ct2/show/NCT02215265
[ii] http://www.isrctn.com/ISRCTN88455282
[iii] http://www.isrctn.com/ISRCTN80146950
[iv] http://www.isrctn.com/ISRCTN52658296

Prior to CTRad, radiotherapy research had a low profile within the higher education and research funding communities and information about research activity in UK centres was lacking. To address this, CTRad undertook a world-leading 'Centres of Excellence in Academic Radiation Oncology' benchmarking exercise, which established categories of research activity and criteria of success then evaluated eighteen UK centres. Completed in 2016,[5] the exercise received international attention and has profoundly influenced the aspirations and activities of researchers and funders. More recently, CTRad undertook a survey of UK Academic Medical Physics activity, identifying key strengths and weaknesses that will inform future work in this area.[6]

4. Excellence in patient and public involvement (PPI)

In keeping with NCRI policy placing patients at the heart of its activities, CTRad's NCRI Consumers have provided innovative, high quality contributions at all stages of our strategic development, and in the development of individual studies. This engagement has helped the radiotherapy research community to maximise the quality and impact of its clinical trials. For example, CTRad's NCRI Consumers have developed a range of resources for researchers, including guidance on writing a good lay summary, which is available online.[7]

5. Engagement with funders and influencing policy

An important barrier to the development of world class radiotherapy research programmes in the UK has been the relative paucity of funding. Although radiotherapy is received by approximately half of cancer patients, only 5% of cancer research funding has been directed at radiotherapy related projects. This can be attributed to the absence of specific funding schemes, poor representation of radiation researchers on funding committees, and lack of investment in infrastructure. To address this imbalance, CTRad has facilitated and influenced new funding schemes, notably the CRUK Radiation Research Network (RadNet) initiative,[8] and

supported successful collaborative networks including CRUK ART-NET,[9] STFC Global Challenge Network+,[v] EPSRC Grand Challenge Network[vi] and EU INSPIRE.[vii] CTRad also worked with CRUK and NHS England to secure NHS support for radiotherapy costs for SABR trials.

6. National and international leadership on radiotherapy-drug combinations

Having identified a dearth of clinical trials evaluating novel radiotherapy-drug combinations, CTRad convened a multidisciplinary panel to identify causes and potential solutions, with particular emphasis on the route to registration for novel drugs in combination with radiotherapy. This work was captured in a 'Consensus Statement' published in *Nature Reviews Clinical Oncology* in 2016[10], which inspired an FDA sponsored workshop in Bethesda, USA that generated further published guidelines in 2018.[11] This initiative has leveraged unprecedented international engagement, with input from the US Food and Drug Administration (FDA), European Medicines Agency (EMA), UK Medicines and Healthcare products Regulatory Authority (MHRA), US National Cancer Institute (NCI), American Association for Cancer Research (AACR) and American Society of Radiation Oncology (ASTRO). In the UK, CTRad created and leads the Radiotherapy-Drug Combinations Consortium (RaDCom) and established the UK NSCLC Radiotherapy-Drug Consortium, which has developed the CONCORDE and SPITFIRE studies.

7. Building a multidisciplinary radiotherapy research workforce

CTRad has worked with multiple stakeholders to support the establishment of a sustainable community of researchers that includes clinical oncologists, radiographers, medical physicists, statisticians, radiologists, laboratory scientists, medical oncologists, nuclear medicine physicians and consumers. Many of these disciplines lack established research communities

[v] https://www.advanced-radiotherapy.ac.uk
[vi] http://protontherapynetwork.com
[vii] https://protonsinspire.eu

or academic career pathways so we have engaged with relevant colleges and higher education institutes to support the evolution of successful research leaders and academic cohorts. In parallel, 'Academic Think Tank' events have been organised for clinicians, physicists and radiographers. Trainees are regularly involved in projects, making important contributions to our work investigating delays in opening trials. We encourage all individuals working within, or connected to, the UK radiotherapy community to become CTRad members; details are available on our website: http://ctrad.ncri.org.uk

8. Supporting quality assurance for radiotherapy clinical trials

Quality assurance is a fundamental component of radiotherapy research, particularly when new and complex technologies are being evaluated. In the UK, all National Institute for Health Research (NIHR) portfolio radiotherapy trials have access to the unique expertise and resources of the Radiotherapy Trials Quality Assurance (RTTQA) group, which receives core funding from the NIHR. CTRad has worked closely with RTTQA since its inception in 2010, playing important roles in governance and the development and delivery of scientific outputs. CTRad also undertook a comprehensive review of the national MRT landscape, its 2016 report[12] on which led to implementation of QA programmes creating a unique network of centres capable of standardised dosimetry for current and future MRT trials.

9. Coordinating a national approach to proton beam therapy (PBT) trial development

The CTRad PBT Strategy Group is a multidisciplinary, UK-wide group currently co-ordinating the development of PBT clinical trials in partnership with ART-NET.[13] The opening of NHS England proton beam facilities in Manchester (2018) and London (2020) provided a unique opportunity to design and deliver high quality clinical trials that will determine the benefits to patients of PBT compared with photon-based treatments, across a range of adult tumour sites. This initiative convenes relevant disciplines to accelerate funding of the best clinical studies;

to date, three workshops have reviewed 10 PBT trials proposals, providing investigators with expert feedback. CRUK has funded the UK's first PBT trial, the TORPEdO study in head and neck cancer, which was developed with CTRad's guidance and strategic oversight.

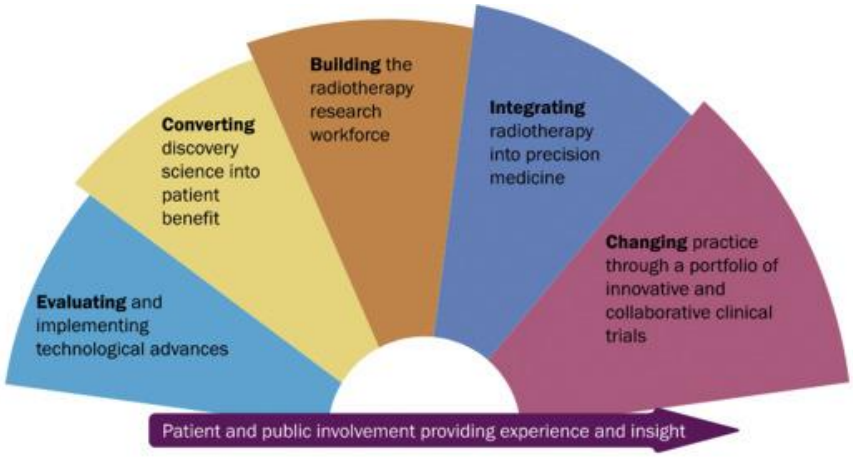
10. CTRad identified as NCRI's flagship initiative

Having been supported by multiple NCRI partners since its launch in 2009, CTRad was delighted to be described as the NCRI's "flagship radiotherapy initiative" in its 2017-18 annual review. Illustrating this, CTRad has inspired the creation and design of new initiatives including the Cellular Molecular Pathology (CM-Path) programme that was launched in 2016.

Summary

Since 2009, CTRad has dramatically influenced the UK radiotherapy research landscape by championing multi-disciplinary radiotherapy research on a national scale. Significant challenges remain, however, including delivering the five pillars of CTRad's new research strategy (Figure 1) and addressing the key scientific and clinical research questions identified in CRUK's recent Strategic Review of radiotherapy research. [14]

While CRUK's investment in RadNet is an important step forward, substantial further work is required to address underfunding of radiotherapy research across the UK as a whole. CTRad will play a pivotal role in addressing this issue, aiming to leverage investment across the full spectrum of funders while uniting the UK research community to improve outcomes for cancer patients.



CTRad is funded by the following Partners

Figure 1 CTRad's strategic vision, 2018–2021.

Appendix 1. CTRad Executive Group members (June 2019)

David Sebag-Montefiore (Chair)

Mererid Evans (Deputy Chair)

Anthony Chalmers (Ex-officio)

Gillies McKenna (Ex-officio)

Elizabeth Miles (Ex-officio)

Jonathan Wadsley (Ex-officio)

Kaye Williams (Ex-officio)

Richard Stephens (Consumer member)

Nicola Curtin (Workstream 1)

Ricky Sharma (Workstream 1)

Richard Adams (Workstream 2)

Ananya Choudhury (Workstream 2)

Emma Hall (Workstream 3)

Robert Huddart (Workstream 3)

Karen Kirkby (Workstream 4)

Maria Hawkins (Workstream 4)

Carolyn Chan (NCRI)

For more information and a list of members, please see the CTRad webpage (https://ctrad.ncri.org.uk).

Appendix 2. CTRad's funding partners

CTRad is funded by Cancer Research UK, the Medical Research Council, Chief Scientist Office Scotland, Health and Care Research Wales, HSC Public Health Agency Northern Ireland, Breast Cancer Now and Prostate Cancer UK.

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