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COVID RT - Assessing the Impact of COVID-19 on Radiotherapy in the UK

A National Cancer Research Institute
Clinical and Translational Radiotherapy Research working group (NCRI CTRad) Initiative in partnership with the Royal College of Radiologists (RCR), Society of Radiographers (SoR) and the Institute of Physics and Engineering in Medicine (IPEM).

Introduction

The World Health Organisation (WHO) declared a COVID-19 pandemic on 11th March 2020. Healthcare systems, including the NHS, had to adapt rapidly, focusing resources to support COVID-19 infected patients whilst continuing, where possible, to provide ongoing care for other illnesses. The pandemic created sudden and major challenges regarding the treatment of cancer patients. There were significant concerns that radiotherapy, systemic therapy and surgery could increase the risk of COVID-19 mortality for infected patients, and that there would be a dramatic loss of surgical HDU and ITU capacity for cancer surgery. Cancer centres across the UK were required to urgently review their policies for all cancer treatment modalities to try and balance the risk/benefit ratio for patients, and to continue to deliver a service where significant staff shortages due to self-isolation and COVID-19 infection were expected.

The COVIDSurg collaborative has studied the impact of COVID-19 on surgical practice. Cancer surgery cancellation rates from the UK are not currently available, but the group have estimated a likely 30% cancellation rate for cancer surgery across Europe over the 12-week pandemic peak (1). A further study led by the same group (2) demonstrated a 23.8% overall 30-day post-operative mortality rate in patients who developed peri-operative COVID-19 infection. The COVIDSurg initiative therefore currently recommends that consideration should be given to promoting non-operative treatment to delay or avoid the need for surgery where COVID-19 infection remains a threat.

The UK Coronavirus Cancer Monitoring project (UKCCMP) is addressing the impact of COVID-19 infection on cancer patients, predominantly focusing on systemic therapy. Their study showed that the risk of death from COVID-19 increased significantly with increasing age, male sex and comorbidity, but not when patients had received systemic anti-cancer therapy in the 4 weeks prior to testing positive for COVID-19 (3). Similarly, there was no increased risk of death in patients who had received treatment with immunotherapy, targeted therapy and radiotherapy within the same time period, but patient numbers in these groups were smaller, precluding definitive conclusions.

Both the COVIDSurg and UKCCMP initiatives have focused on mortality as a direct result of COVID-19 infection. Neither have addressed the impact of the COVID-19 pandemic on radiotherapy, a critical cancer treatment modality, or the indirect societal and health effects on cancer patient outcomes.

During the COVID-19 peak, radiotherapy services across the UK continued to treat cancer patients in often challenging circumstances. Significant changes were implemented (see Figure 1), based on rapid national and international clinical guidelines produced by NICE (4-5), tumour site-specific recommendations written by national experts and published by bodies including the RCR (6), and recently published clinical trial data (e.g. the FAST-FORWARD clinical trial in breast cancer) (7).

The scale of these changes in radiotherapy practice and their impact on cancer patients is unknown. It is important to understand them, in order to assess the true impact of COVID-19 on patient outcomes and, critically, to learn lessons for the reactivation phase of the pandemic and beyond, as recommencement of 'regular' cancer services occurs. Adopting lessons learnt and new models of care developed during the acute and recovery phases of the pandemic will equip radiotherapy providers with evidence-based recommendations, and improve preparedness for the impact of future

pandemics. There is also an opportunity to capture data from patients treated with novel fractionation schedules initiated in response to COVID-19, which may not have been used without further evidence in normal times. The evidence generated from these data will feed into recommendations for new models of care.

Additionally, it is important to understand the impact of radiotherapy on excess deaths projected to have arisen during the pandemic peak - the "untold toll" (8) of the pandemic. Modelling studies have predicted 6270 additional deaths in newly diagnosed cancer patients, and 17,915 additional deaths across prevalent cases of cancer with comorbidity in England and Northern Ireland (NI) at one year (9). Further modelling has highlighted the potential negative impact on cancer survival associated with a per-patient delay of 3 and 6 months in diagnosis and surgical intervention (>4,700 and 10,555 attributable deaths respectively), with dire predictions of a "public health crisis of avoidable cancer deaths" if diagnostic pathways and surgical interventions for cancer are not rapidly re-established (10). Such modelling studies, however, are inherently limited by their exclusion of any radiotherapy data. Radiotherapy contributes to the cure of approximately 40% of all cancers (11), yet has been excluded from the modelling studies conducted to date. The studies' usefulness to inform both clinical oncology practice and public health policy for cancer treatment is therefore restricted, highlighting the need to collect and analyse robust radiotherapy data from patients treated during the pandemic.

The National Cancer Research Institute Clinical and Translational Radiotherapy Research Working Group (NCRI CTRad) identified the urgent and unmet need to understand the impact of COVID-19 on both radiotherapy patients and the radiotherapy service at a national scale, leading to the COVID RT initiative. A COVID RT Steering Group, including representatives of the CTRad Executive, Radiotherapy Dataset (RTDS) and COVID RT partner organisations, was established in April 2020 to oversee project progress, and the initiative was launched via a series of webinars attracting >250 attendees from the multidisciplinary radiotherapy community.

COVID RT will complement and provide additional data to the standardised data submitted by NHS radiotherapy providers in England and Wales to the National RTDS. RTDS data can demonstrate when and how radiotherapy centres implemented changes in radiotherapy treatment schedules during the acute phase of the COVID-19 pandemic and whether they were temporarily or permanently adopted. COVID RT will also collect data from Scotland and NI, generating pan-UK data to demonstrate the scale of the changes seen in radiotherapy treatment provision across the whole country.

Project Aims

The aims of COVID-RT are to understand ***why*** changes in treatment schedules were implemented during the pandemic, and to explore the ***impact*** of these changes on patient outcomes. Specific aims related to ***why*** changes were made include:

- To identify patient cohorts in whom radiotherapy replaced surgery, or was used as a bridge to surgery
- To identify whether decisions to omit radiotherapy were made due to patient or clinician choice
- To identify changes in treatment which were underpinned by clinical trial evidence
- To understand clinical decision making related to concurrent chemotherapy prescriptions.

Linking the COVID RT data with national datasets aims to establish the *indirect* impact of COVID-19 on the outcomes of patients in whom radiotherapy was omitted, used to replace or as a bridge to surgery, and in whom concurrent chemo-radiotherapy regimens were altered. The impact of radiotherapy in reducing in excess cancer deaths can also be established using these data linkages. Additionally, the

direct impact of COVID-19 on the ability of infected patients to complete radiotherapy as planned can be assessed.

These data will help us understand the full impact of the pandemic on cancer patients and inform best practice recommendations for the ongoing reactivation phase of the COVID-19 pandemic and future pandemics. The data will also support future research and help underpin new clinical trials.

Progress to date

All UK radiotherapy centres were invited to take part in the COVID RT initiative and by July 2020, 84% (52 out of 62) had registered to participate [England: 45, Wales: 3, NI: 1, Scotland: 3].

A COVID RT Excel spreadsheet was developed and refined through discussion at webinars and with input from the RCR's data and audit team. It was circulated to participating sites on 11th May 2020. The spreadsheet is designed to collect data on adult cancer patients in whom radical radiotherapy is being considered. The data is initially stored locally following approvals by Trust Caldicott Guardians for local service evaluation. Sufficient data is included to enable future linkage with national databases (including RTDS and those in NHS Digital) following de-identification processes and appropriate Health Research Authority (HRA) approval.

Local data collection is currently ongoing at participating sites, starting from 1st March 2020 and the overall length of data collection will be based on interim results, community prevalence of COVID-19 infection and feedback from the radiotherapy community and partner professional organisations. Regular communication with sites is provided by a fortnightly COVID RT newsletter.

Future plan

Following HRA approval, central data collection, scientific analysis and data linkage will be undertaken by Professor Eva Morris and her team at the Nuffield Department of Population Health at the University of Oxford, working in conjunction with CTRad and Cancer Research UK (CRUK). A COVID RT Advisory Group will oversee the research priorities, and interim analyses are anticipated in the Autumn of 2020. Data on the impact of COVID-19 on radiotherapy patient outcomes are expected in 2021.

Summary

Radiotherapy providers across the UK have continued to give safe, effective treatment for cancer throughout the COVID-19 pandemic. Whilst it has been said that a "deluge of poor-quality research is sabotaging an effective evidence-based response" (12) to COVID-19, the response of the radiotherapy community was considered and very collaborative, utilising best evidence and maintaining patient and staff safety as a priority.

COVID RT will provide valuable data from centres across the UK to determine the impact of COVID-19 on radiotherapy services, and on outcomes for radiotherapy patients. It will also yield important insights into the lessons that can be learnt from the first wave of COVID-19, to inform how radiotherapy services can be utilised most effectively during future pandemics.

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