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## Launch of the National Rectal Cancer IMRT Guidance

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**Abstract:**

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**Key words:**

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Randomised trials have demonstrated that pre-operative radiotherapy in rectal cancer reduces the risk of locoregional recurrence when delivered either in the form of a one-week short course, or a long course of treatment combined with concurrent chemotherapy [1-6]. However, radiotherapy may also be associated with long-term, treatment-related toxicity [7-10]. Compared to 3D conformal radiotherapy (3D-CRT), intensity modulated radiotherapy (IMRT) has the potential to deliver superior target dose conformality and homogeneity and dose escalation including delivery of a Simultaneous Integrated Boost (SIB) whilst decreasing doses to organs at risk (OAR), especially small bowel, which might result in a reduction in early and late toxicities [11-20].

The majority of studies that have examined IMRT in rectal cancer have reported dosimetric endpoints or early toxicities [11-13, 15-17, 20, 21]. Early gastrointestinal toxicity has been shown to have a close dose-volume relationship with the volume of small bowel irradiated [22, 23]. However, no phase III studies directly comparing IMRT with 3D-CRT for either toxicity or efficacy outcomes have been reported. Despite this absence of high-level evidence, the uptake of IMRT in rectal cancer in the UK and internationally is increasing [24, 25].

As well as theoretical advantages and preliminary evidence of improved toxicity compared with 3D-CRT, IMRT or volumetric modulated arc therapy (VMAT) may deliver efficiencies in the radiotherapy workflow. Compared with 3D-CRT and delivery of a sequential boost, IMRT has potential resource/patient convenience benefits, including reduced planning time, shorter treatment delivery time and shorter overall treatment time. It may, however, be associated with an increased time for target and OAR definition [13, 14, 17-19].

The radiotherapy modernisation programme in the UK also played a major role in the increased use of IMRT [26-31]. Its overarching aims were to improve access to modern, advanced and innovative radiotherapy technologies including IMRT, to improve the patient experience/provision of holistic

care, to reduce variation in quality by adopting standardised best practice protocols, to increase participation in research and clinical trials and to undertake an equipment modernisation programme [31]. In 2012, the Department of Health in the UK recommended that IMRT should be offered to all patients where they could benefit from reduced treatment toxicities, stating a percentage of patients in any department who should be treated with IMRT [32]. This resulted in an increase in the uptake of IMRT in the UK. However the landscape of IMRT utilisation for rectal cancer and how it has been implemented has up to now been unknown. Data collected from the Radiotherapy Dataset and National Cancer Data Repository, in the era before IMRT was widely adopted in the UK, was recently examined [33]. The authors concluded that even without the additional complexity of IMRT, there was a wide variation in both the use and type of radiotherapy to treat rectal cancer.

This heterogeneity in UK practice demonstrates the need for a national strategy to harmonise implementation and delivery of IMRT for rectal cancer. An exemplar that informed the working group was the National Anal Cancer IMRT Guidance [34]. These recommendations for best practice have been widely adopted and have been successful in providing a national dataset for further research [35-37]. The harmonisation in practice has also helped establish a platform for current clinical trials [38]. It is known that the use of guidelines and protocols also correlates with improved radiotherapy delivery and patient outcomes including improved survival [39-45]. In summary, we consider the potential benefits for patient outcomes and the harmonisation of UK practice to be justification for development of robust and comprehensive rectal IMRT guidance.

Given the potential complexities associated with an IMRT workflow relating to rectal cancer treatment in the UK, a national multicentre, multidisciplinary working group was convened. The intention was to bring together clinicians, physicists and radiographers experienced in the treatment of rectal cancer using IMRT, to review and discuss the available evidence and to produce rectal cancer IMRT guidance. The overarching aim of the guidance was to encourage harmonisation of practice and to support the implementation of IMRT for the treatment of rectal cancer throughout the UK. The guidance was to provide specific recommendations regarding patient selection, pre-treatment investigations, target volume and OAR delineation, treatment planning, verification and IMRT delivery. It is hoped that this will increase adoption of IMRT and develop and standardise practice in those centres already using the technology leading to better outcomes for our patients. **Figure 1** illustrates the timeline and individual projects performed in the development of the guidance.

The National Rectal Cancer IMRT Guidance was developed by the working group through an iterative process which included face to face meetings at the Royal College of Radiologists (RCR) and, later, videoconference meetings. Throughout the process, in addition to synthesising the available evidence to inform our recommendations, we aimed to consider the views of the radiotherapy community in

the UK regarding what was practical and implementable in all centres. We reached out to all radiotherapy centres in the UK in the form of a survey of IMRT practice [XX]. We consider that a response rate of 70% represents a good return especially given the COVID-19 pandemic, although we remain mindful that this is not necessarily representative of the views and practice at all centres. The full results from the survey, including areas of consensus and heterogeneity in current UK practice, are outlined in an accompanying paper by XX and XX et al [XX]. These results informed multiple guidance recommendations and were especially useful where there were uncertainties within the working group concerning the feasibility of particular recommendations in UK clinical practice.

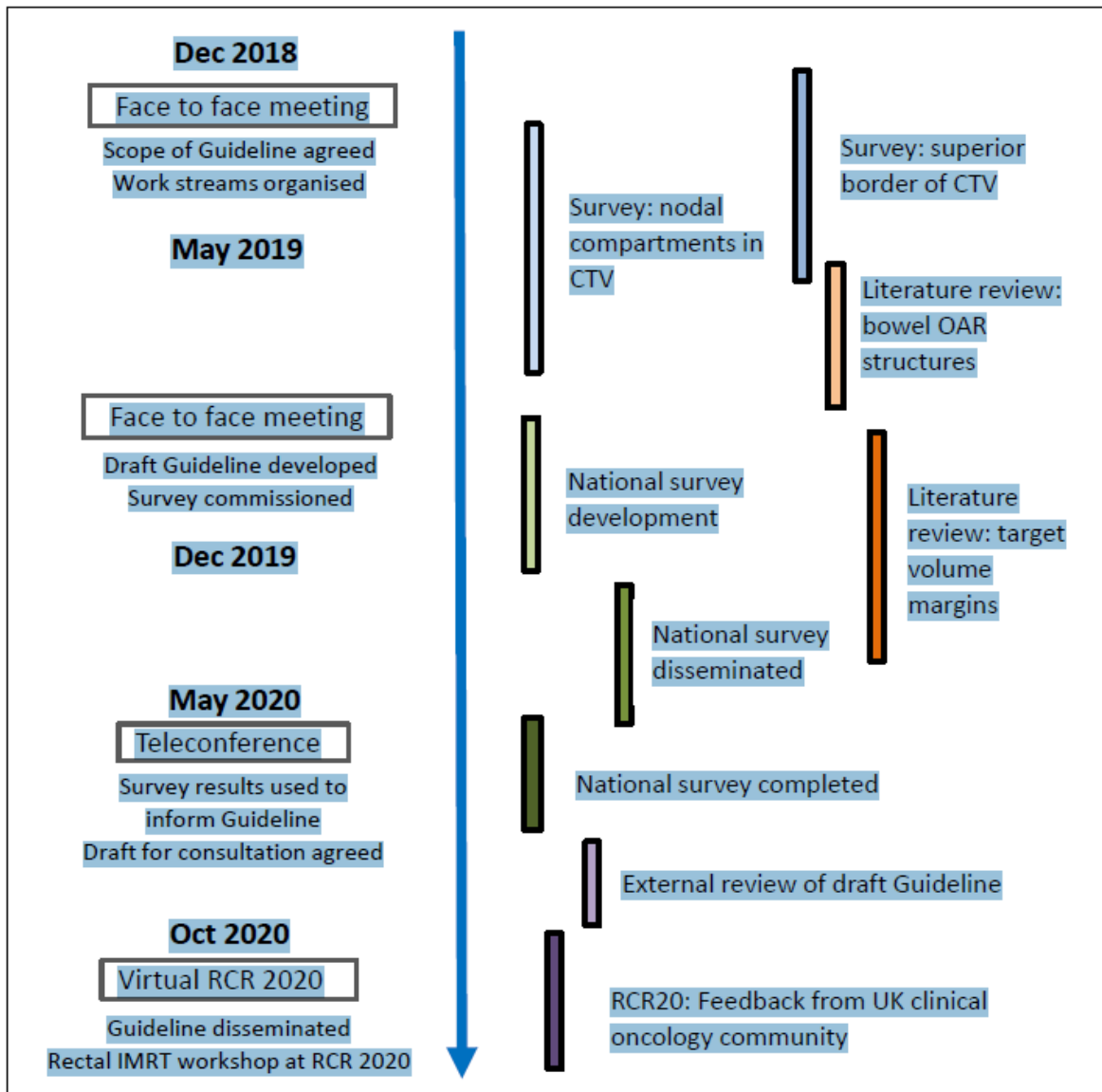
The working group also undertook several additional projects to inform specific aspects of the guidance. Our recommendations regarding target volume delineation depending on the extent of T and N staging was informed by a survey of 30 clinicians in 11 centres performed by O’Cathail et al [46]. A project was undertaken in several centres to identify the most reliable method of determining the superior border of the elective volume and this work helped inform our recommendation that the S1/2 vertebral interspace be taken as the superior border. Although this represents a departure from the superior border of S2/3 in ARISTOTLE, in this trial the superior border was deliberately lower than S1/2 because of concerns regarding excess toxicity with the addition of irinotecan [47]. Appelt et al performed a comprehensive literature review that informed our recommendations regarding target volume margins, considering published measurements of internal organ motion and whether image guidance is to be performed daily or via a ‘no action limit’ protocol [48]. Multiple test plans were delineated and planned in two centres to quality assure our recommendations regarding planning objectives and OAR constraints. Prior to publication of the guidance, we requested external moderation of the document by several reviewers and the group reflected on this feedback and further modified the guidance as a result.

There are likely to be contentious aspects of the guidance which were also encountered by the group during its development. These reflect areas of uncertainty in clinical practice and ongoing discussion within the wider community. As an example, the most obvious manifestation of this concerned the delineation of individual small bowel loops versus a peritoneal cavity/‘bowel space’ structure. As with all controversial areas within the guidance, we used the results of the survey to aid our decision making concerning the recommendations contained within the guidance. We do accept that there may be some recommendations that do not align completely with individual clinician or radiotherapy centre current preferences for practice. However, we do emphasise that we have made considerable efforts to obtain the input of the wider community and considered their feedback in the framing of our recommendations. We also sought the input of several external reviewers and further modification of the guidance was performed following this moderation. Many members of both the

development group and the wider review panel have accepted that the benefits of a national guidance that harmonises clinical practice across the UK are likely to outweigh firmly held individual views concerning particular aspects of practice where there exists limited high level evidence as to the optimum approach.

The guidance is now available on the RCR website at [\[insert guidance web address once available\]](#). The launch of the guidance was timed to coincide with the rectal IMRT workshop at RCR20 in October 2020 and was accompanied by the publication of the results of the survey [\[XX\]](#). We intend to publicise the guidance at the workshop, via RCR member e-mail and social media platforms. The success of the guidance will depend on its use by the radiotherapy community. We would consider the guidance to have been a success if it encourages further adoption of IMRT and development of practice within centres already using IMRT. We hope it will help establish a platform for the next generation of clinical trials in rectal cancer. We plan to repeat our survey in 1-2 years to investigate whether our recommendations have been adopted and seek specific feedback from centres. The guidance will be housed on the RCR website and should be seen as a work in progress.

In summary, we hope the National Rectal Cancer IMRT Guidance will improve the delivery of radiotherapy for patients with rectal cancer. We have aimed to make its development a collaborative effort with the whole UK radiotherapy community, especially with regards to the survey and external review of the guidance. Moving forward, we strongly encourage feedback from centres to inform subsequent versions. Specific comments can be addressed to: [publications@rcr.ac.uk](mailto:publications@rcr.ac.uk). By calling on all centres to embrace this guidance, the ambition is to harmonise and strengthen radiotherapy practice in the UK and to continue to lead on the international stage.



**Figure caption:**

**Figure 1:** A flow diagram illustrating the timeline for the National Rectal Cancer IMRT Guidance and the individual projects and milestones during its development

CTV, clinical target volume; OAR, Organs At Risk; RCR, Royal College of Radiologists; RCR20, Royal College of Radiologists annual conference 2020

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