Image guided radiotherapy for rectal cancer

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Introduction

Three radiotherapy (RT) approaches are commonly in use for rectal cancer in the UK: short course preoperative RT (SCPRT), long course preoperative chemoradiotherapy (LCPCRT) and postoperative chemoradiotherapy (CRT). SCPRT (25 Gy in five fractions over five days followed by surgery within a week) has been shown to reduce pelvic recurrences in resectable rectal cancer.\(^1\) LCPCRT (45-50.4 Gy in 25-28 fractions) has been shown to downstage tumours when the circumferential resection margin (CRM) is threatened and to improve margin negative (R0) resection and local recurrence rates.\(^2\) Post-operative CRT, used in cases of incomplete resection, is being used less frequently as better pre-operative staging improves the identification of those who would benefit from pre-operative RT.

RT for rectal cancer has evolved from the traditional two dimensional (2D) approach, based on orthogonal films and bony landmarks, to conformal three dimensional (3D) planned volumes and intensity modulated radiotherapy (IMRT) and these have only been possible by the corresponding improvements in imaging. ‘Image guided’ radiotherapy can refer to two separate aspects of radiotherapy – target volume delineation and ensuring accurate delivery of the RT, both of which are discussed in this article.

Imaging for target volume delineation

Traditionally RT planning for rectal cancer has been based upon two-dimensional radiological anatomy. Rectal contrast (with or without oral contrast) and bony landmarks were used to delineate the treatment volumes,\(^3\) supplemented by clinical examination to aid definition of the inferior extent of the tumour. This is now considered to be outdated, having been replaced by CT planning utilising information from all available diagnostic imaging as a minimum. Studies have shown that CT planning has advantages over orthogonal films in terms of better definition of anterior and superior borders of the radiotherapy field and reduced toxicity compared to historical controls.\(^4,5\) However, CT simulation has its limitations because of poor contrast between faeces and tumour, partial volume effects due to the curves/valves of Houston and imaging of the horizontal sigmoid.\(^6\) Some improvement in the CT image for contouring can be achieved by changing the greyscale to maximise the contrast between the soft tissue infiltration and normal fat. The routine window for abdominal CT is not optimal for this purpose and Myerson has recommended a level of ~60 Hounsfield units and a somewhat larger than usual window of ~600 Hounsfield units to help better identify both loops of bowel and perirectal soft tissue densities.\(^7\)

MRI is generally considered the gold standard for staging rectal cancer\(^8\) and in the era of conformal RT most UK radiation oncologists would have MRI images available at the time of planning to aid the delineation of the target volume. MRI addresses many of the limitations of CT such as definition of depth of invasion through the rectal wall into local structures and extension into presacral space and mesorectal circumference, which are high risk areas for recurrence. However, the visual transfer of data from MRI to CT is susceptible to errors in interpretation and transfer method and one method to overcome this is co-registration of the images, where MR images are used for optimal outlining while retaining the CT data for dose calculations.

CT has a relatively high spatial resolution but is limited in respect of specificity. In contrast, 2-[18F] fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) can better define macroscopic colorectal cancer tissue and improves staging accuracy before surgery or at restaging.\(^9\) There is no standardised technique for the use of PET in RT planning.\(^10\)

It can be useful for delineating GTV but will not help with delineation of CTV (figure 1). Areas of further research are using more tumour specific tracers such as fluorothymidine\(^11\) F-FLT(FLT) and fluoromisonidazole \(^12\) F-FMISO(FMISO), the former a measure of cell proliferation, the latter of hypoxia.\(^13\)

Recommendations for the use of these modalities based on a recent systematic review are detailed in box 1 below. The review is included in the further reading section.

Imaging for radiotherapy delivery

Both the rectum and mesorectum are mobile structures and without accurate target volume delineation, immobilisation and the addition of appropriate geometrical margins, the benefits of advanced RT techniques may be lost, or even become detrimental. Image guided radiotherapy (IGRT) techniques aim to reduce geometrical uncertainty by imaging the patient’s anatomy at several time points before and during RT and either altering the patient position or adapting...
Orthogonal films are outdated and should be replaced with CT planned conformal techniques.  
(Level 3 evidence – Grade B recommendation)

Diagnostic MRI scans should be available at the time of planning.  
(Level 5 evidence – Grade D recommendation)

Interobserver variation is an important issue in the era of conformal RT and an increased emphasis on training is needed.  
(Level 1 evidence – Grade A recommendation)

There is currently insufficient data to support the use of clips and gold markers for TVD.  
(Level 4 evidence)

Fusion of diagnostic MRI with planning CT should be performed with caution, taking into consideration the possible issues with organ motion.  
(Level 4 evidence – Grade C recommendation)

Fusion of PET scans with the planning CT should only be undertaken in a research setting.  
(Level 5 evidence – Grade D recommendation)

**BOX 1**

**Recommendations for the use of imaging in rectal radiotherapy planning.**

The treatment plan with respect to the anatomical changes that occur during the RT treatment course. This may improve local control by minimising geographic miss, reduce radiation damage to organs at risk (OAR) or enable margin reduction that may allow dose escalation, but these have not been studied extensively in rectal cancer. There are several available methods to reduce image the patient during a course of rectal cancer RT and these are detailed in *table 1*. Electronic portal imaging devices (EPIDs) can minimise set up errors by using skeletal anatomy to verify the edges of treatment fields. A limitation of this technique is the inability to account for changes in soft tissue anatomy. CBCT (figure 2) or tomotherapy based kilovoltage (kV) or megavoltage (MV) CT scans (figure 3) provide more detailed information on internal anatomy and allow assessment of shape, volume and motion of target organs. There is a cost of additional radiation, however. The dose-length product (DLP), a product of the computed tomography dose index (CTDI) (dose to tissue) and scan length, is approximately 450mGy/cm for a planning CT scan and 300mGy/cm for a CBCT image.

With the increasing trend towards conformal RT the assessment of internal motion will become more important. It has not yet been, and may not be possible to show, that rectal motion is associated with risk of recurrence from geographical miss. From the available data EPIDs should continue to be used to match for bony anatomy. Additional information on internal motion can be obtained by CBCT or tomotherapy and if available its use should be considered. Further information can be obtained from a recently published systematic review (Gwynne, Webster et al 2011).

**Conclusions**

There have been considerable advances in imaging for rectal cancer that have changed the way we plan and deliver radiotherapy for this condition. Much is already known but further studies are required to establish the optimal role for these imaging modalities in the future of rectal cancer radiotherapy.

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<thead>
<tr>
<th>Method</th>
<th>Pros</th>
<th>Cons</th>
<th>Potential use</th>
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<tbody>
<tr>
<td><strong>EPIDs</strong></td>
<td>Widely available</td>
<td>Soft tissue structures cannot be visualised</td>
<td>Inter-fractional motion</td>
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<td></td>
<td>Bony anatomy visualised</td>
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<td></td>
<td>No additional radiation compared to CT scanning</td>
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<td><strong>Cone Beam CT (CBCT)</strong></td>
<td>Some soft tissue structures can be visualised</td>
<td>Mesorectum is hard to visualise difficult due to poor contrast</td>
<td>Inter- and intra-fraction motion</td>
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<tr>
<td></td>
<td>Imaging in radiotherapy treatment room same time and position</td>
<td>Additional radiation – 300mGy/cm per fraction</td>
<td>Adaptive re-planning possible</td>
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<td><strong>Serial diagnostic quality CT scans</strong></td>
<td>Soft tissue structures can be visualised</td>
<td>Imaging outside radiotherapy treatment room</td>
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<td></td>
<td>Hounsfield units available for adaptive re-planning</td>
<td>Additional radiation – 300mGy/cm per fraction</td>
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<td></td>
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<td>Additional time on set for online IGRT</td>
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<td></td>
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<td>Hounsfield unit for adaptive re-planning not automatic for all manufacturers</td>
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<tr>
<td><strong>Helical tomotherapy</strong></td>
<td>Soft tissue structures can be visualised</td>
<td>Not widely available</td>
<td>Inter and intrafraction re-planning</td>
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<td></td>
<td>Imaging in radiotherapy treatment room same time and position</td>
<td>Radiation dose – 2.5% of prescribed dose up to 10cm from target</td>
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<td>Hounsfield units available for adaptive re-planning</td>
<td>Additional time on set for online IGRT</td>
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<tr>
<td><strong>Cine MRI</strong></td>
<td>Soft tissue structures can be visualised and MRI is imaging of choice for rectal cancer No additional radiation</td>
<td>No studies reported in rectal cancer</td>
<td>Intrafraction</td>
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<td></td>
<td></td>
<td>Imaging outside radiotherapy treatment room</td>
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<td></td>
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<td>?Availability, distortion MRI to CT?</td>
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<td><strong>Clips</strong></td>
<td>Well tolerated and no evidence of displacement during radiotherapy</td>
<td>Invasive technique</td>
<td>Interfraction if fluoroscopy or tracking system used</td>
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<td>Better definition of inferior end of PTV (No additional radiation)</td>
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TABLE 1
Pros and cons of methods used to define motion in rectal cancer.
Key: EPID – electronic portal imaging device; CBCT – cone beam CT; PTV – planning target volume.

<table>
<thead>
<tr>
<th>Method</th>
<th>Pros</th>
<th>Cons</th>
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<tr>
<td>EPID</td>
<td>Provides real-time feedback of radiation</td>
<td>Limited field of view; requires shielding</td>
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<tr>
<td>CBCT</td>
<td>High spatial resolution; accurate tracking</td>
<td>Requires additional equipment; time-consuming</td>
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<tr>
<td>PET CT</td>
<td>Sensitivity to metabolic changes; accurate</td>
<td>Requires radioactive tracer; expensive</td>
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References

Further reading