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Overview

Imaging for Target Volume Delineation in Rectal Cancer Radiotherapy — A Systematic Review

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Abstract

The global move towards more conformal radiotherapy for rectal cancer requires better imaging modalities that both visualise the disease accurately and are reproducible; to reduce interobserver variation. This review explores the advances in imaging modalities used in target volume delineation, with a view to make recommendations for current clinical practice and to propose future directions for research. A systematic review was conducted using MEDLINE and EMBASE. Articles considered relevant by the authors were included. Planning with orthogonal films is being replaced by computed tomography (CT) simulation. This is now considered the 'gold standard' and allows conformal three-dimensional planning. Magnetic resonance imaging (MRI) has been shown to overcome some of the limitations of CT and can be used either as a diagnostic image to visually aid planning, or as a 'planning' MRI carried out in the treatment position and co-registered with the planning CT. The latter approach has been shown to change the treated volumes compared with CT and in prostate cancer patients has been shown to reduce interobserver variation. There are remaining issues with four-dimensional motion that are yet to be fully appreciated or overcome. 2-[18F] fluoro-2-deoxy-D-glucose positron emission tomography/CT co-registered with planning CT results in smaller volumes than CT alone and also reduces interobserver variation, but requires further validation before routine implementation. Experimental work utilising novel positron emission tomography tracers and diffusion-weighted MRI shows promise and requires further evaluation. Rigorous quality assurance is important with processing of newer imaging modalities. Further work needs to be conducted into both interobserver variation and the formal evaluation of the clinical benefits of newer imaging modalities. Developments in image-guided radiotherapy are also required to ensure that improvements in target definition at the planning stage are reproducible throughout treatment.

Key words: CT simulation; interobserver variation; MR–CT co-registration; MRI planning; PET/CT; radiotherapy planning; rectal cancer

Statement of Search Strategies Used and Sources of Information

A review of published studies and conference abstracts was conducted using MEDLINE and EMBASE databases based on the terms 'rectal cancer, radiotherapy planning, CT simulation, CT planning, MRI planning, PET-CT, MR-CT co-registration, interobserver variation' up to August 2010. The search was limited to human subjects and English language, but no date limits were applied. This was supplemented by hand searching of conference abstracts from ESTRO and ASTRO 2008 and 2009. These were then assessed for relevance by two authors (SG and SM). Studies were only included if they examined advanced imaging modalities to define radiotherapy target volumes for preoperative radiotherapy of rectal cancer.

Introduction

Rectal cancer affects over 14,000 people a year in the UK [1]. The last two decades have seen significant advances in the radiological staging [2], pathological staging [3] and surgical management of rectal cancer [4,5], but the 5 year survival is still only 45% [6]. The radiotherapy process has also changed, with an increased use of conformal radiotherapy to reduce toxicity. Imaging modalities that clearly and

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accurately visualise the disease, improved understanding of organ motion and a better process of quality assurance should minimise the risk of geographical miss. The aim of this review is to look at the advanced imaging modalities that have been used for target volume delineation (TVD) in rectal cancer to make recommendations for current clinical practice and to propose future directions for research.

Role of Radiotherapy in Rectal Cancer

Three radiotherapy approaches are commonly in use for rectal cancer in the UK: short-course preoperative radiotherapy (SCPRT) (25 Gy in five fractions over 5 days followed by surgery within 1 week) has been shown to reduce pelvic recurrences in resectable rectal cancer [7,8]; long-course preoperative chemoradiotherapy (45–50.4 Gy in 25–28 fractions) has been shown to downstage tumours when the circumferential resection margin is threatened, improve margin negative (R0) resection rates and reduce local recurrence rates [9,10]. Preoperative treatment is recommended where possible [11] and postoperative chemoradiotherapy after R1 resection, which has become less frequent as preoperative staging has improved [9].

What should be the Optimal Target Volume?

There is an increasing consensus on the structures that should be included in the target volume, mainly guided by recurrence data [12–14] and recent Radiation Therapy Oncology Group guidelines have been published [15]. Current practice is to include the same structures for both SCPRT and LCPRT. Roels *et al.* [12] conducted a systematic review to determine what should be included in the clinical target volume (CTV) based on published recurrence data and concluded that the tumour, mesorectum, presacral region and internal iliac lymph nodes should be included, an approach broadly adopted by the National Cancer Research Institute-approved ARISTOTLE trial for rectal cancer. Within ARISTOTLE, the gross tumour volume (GTV) is defined as all gross sites of disease, and would include the whole rectal wall at the level of the tumour with a 1 cm margin to create CTV A. This would then be added to CTV B, which includes the whole mesorectum and nodes to create a final CTV, which is then grown by 1 cm to create the planning target volume (PTV). Although the recurrence data used to define these volumes is based on patients planned conventionally, locoregional control seems favourable with more conformal methods, albeit with limited follow-up [15]. This evolution towards conformal radiotherapy has also demanded improved methods to accurately assess the spatial relationship between target volumes and surrounding tissues [16].

Orthogonal Films (Conventional Planning) and Computed Tomography Planning

Traditionally, radiotherapy planning for rectal cancer has been based on two-dimensional radiological anatomy. Rectal contrast (with or without oral contrast) and bony landmarks were used to delineate the treatment volumes [17–19], supplemented by clinical examination to aid definition of the inferior extent of the tumour. This should be considered outdated, having been replaced by computed tomography (CT) planning with all available diagnostic imaging as a minimum, as there are major limitations affecting the ability to accurately define the tumour itself [17,20] and any local extension into the mesorectum or surrounding structures [21]. Studies have shown that CT planning has advantages over orthogonal films in terms of better definition of anterior and superior borders and reduced toxicity compared with historical controls [17–19,22–24]. 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 [21]. Some improvement in the CT image for contouring can be achieved by changing the grey scale 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 and Drzymala [25] recommend a level of about −60 Hounsfield units and a somewhat larger than usual window of about 600 Hounsfield units to help better identify both loops of bowel and perirectal soft tissue densities.

Advances in Radiotherapy Planning

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is generally considered the gold standard for staging rectal cancer [2] and in the era of conformal radiotherapy most UK radiation oncologists would have MRI images available at the time of planning to aid the delineation of the target volume, a fact confirmed by recent pan-UK audit data (Katharine Parker, personal communication). MRI addresses many of the limitations of CT, such as definition of depth of invasion through the rectal wall into local structures [21] and extension into presacral space and mesorectal circumference [12,21], which are high-risk areas for recurrence [12]. The visual transfer of data from MRI to CT is susceptible to errors in interpretation and transfer [26]. 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. This is now considered the gold standard in prostate cancer radiotherapy planning [27] and is recommended in a 2004 Royal College of Radiologists' document [28]. The images can be co-registered either manually or automatically using the planning software. The former can be inefficient and error prone [29], whereas automated approaches reduce interoperator variability and allow more accurate registration between multimodality imaging systems [29,30].

Diffusion-weighted Magnetic Resonance Imaging

Diffusion-weighted MRI evaluates the diffusion capacity of water molecules and obtains information about