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Overview

Rectal Cancer Magnetic Resonance Imaging: Imaging Beyond Morphology

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Abstract

Magnetic resonance imaging (MRI) has in recent years progressively established itself as one of the most valuable modalities for the diagnosis, staging and response assessment of rectal cancer and its use has largely focused on accurate morphological assessment.
The potential of MRI, however, extends beyond detailed anatomical depiction: aspects of tissue physiology, such as perfusion, oxygenation and water molecule diffusivity, can be assessed indirectly. Functional MRI is rapidly evolving as a promising non-invasive assessment tool for tumour phenotyping and assessment of response to new therapeutic agents. In spite of promising experimental data, the evidence base for the application of functional MRI techniques in rectal cancer remains modest, reflecting the relatively poor agreement on technical protocols, image processing techniques and quantitative methodology to date, hampering routine integration into clinical management. This overview outlines the established strengths and the critical limitations of anatomical MRI in rectal cancer; it then introduces some of the functional MRI techniques and quantitative analysis methods that are currently available, describing their applicability in rectal cancer and reviewing the relevant literature; finally, it introduces the concept of a multi-parametric quantitative approach to rectal cancer.

Key words: Diffusion MRI; functional imaging; magnetic resonance imaging; multi-parametric MRI; rectal cancer; whole-body MRI

Statement of Search Strategies Used and Sources of Information

Data for this review were identified by searches of PUBMED using the search terms 'rectal MRI', 'rectal cancer', 'colorectal cancer', 'magnetic resonance imaging', 'diffusion MRI', 'perfusion MRI', 'BOLD MRI', 'DCE MRI', 'functional MRI', 'PET MRI', 'MRI spectroscopy', 'multi-parametric MRI', 'susceptibility MRI', 'whole body MRI', 'tumor volumetry', 'feature analysis', 'texture analysis'. Only papers published in English between 1990 and 2015, including review articles in some instances, were considered. Decisions on materials to be included were based on personal experience.

Introduction

The past 15 years have witnessed a progressive affirmation of magnetic resonance imaging (MRI) as a valuable imaging modality for rectal cancer. Specialist and multidisciplinary international guidelines now recommend MRI as the technique of choice for primary staging (with the exception of T1 tumours) and for restaging after neoadjuvant chemoradiotherapy [1–3].

The fundamental strength of MRI, most evident since the use of thin-section high-resolution imaging sequences, has been the ability to depict in great detail the anatomy of the rectal wall, perirectal tissues and pelvic organs, thanks to its excellent high-contrast soft-tissue resolution.

The potential of MRI, however, extends beyond detailed anatomical depiction: aspects of tissue physiology, such as perfusion, oxygenation and water molecule diffusivity, can be indirectly assessed; metabolic information can also be derived by means of MRI alone or by the acquisition of

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simultaneous positron emission tomography (PET) data on state-of-the-art PET/MRI scanners.

The additional value of functional and metabolic MRI techniques in the clinical contexts of rectal cancer staging, tumour phenotyping and therapy response assessment is only partly understood and remains the focus of current research.

This overview outlines the established strengths and the critical limitations of anatomical MRI in rectal cancer; it then illustrates some of the currently available functional MRI techniques and quantitative imaging methods applicable to MRI, summarising the salient research findings that foreshadow their potential role in rectal cancer; finally, it introduces the concept of an integrated, multi-modality and multi-sequence quantitative imaging approach (multiparametric), made practicable in rectal cancer by recent technological advances and already in use for other pelvic malignancies.

Strengths and Limitations of Anatomical Magnetic Resonance Imaging

Primary Tumour Staging

Seminal studies published at the turn of this century have shown how MRI is a reliable technique for measuring the extent of mural and extramural tumour penetration, key for T (tumour) staging, and for determining the tumour distance from the mesorectal fascia, or circumferential resection margin (CRM), thus identifying patients who are likely to have a clear CRM and those who may benefit from preoperative (chemo)radiotherapy to increase the likelihood of a R0 resection (clear surgical margin) subsequently [4,5].

Since then, multicentre prospective research has reinforced these findings, by showing that CRM status assessed preoperatively by MRI is a significant predictor of overall survival, disease-free survival and local recurrence and that it is possible to predict negative pathological CRM using a 1 mm cut-off on MRI [6,7].

The international MERCURY II study has recently investigated MRI in the assessment of low rectal tumours and their relationship with the anal sphincter complex, crucial to determining the feasibility of a restorative surgical resection: primary surgical management with intersphincteric resection in patients deemed to have a 'safe' low rectal plane assessed by MRI led to a clear pathological CRM margin in 98% of cases [8].

Important local features such as the tumour relationship to the peritoneal reflection and the presence of extramural macroscopic venous invasion can be identified with accuracy on high-resolution MRI and are prognostically significant [9–11].

Nodal Staging

Accurate nodal staging remains problematic with standard anatomical sequences. State-of-the-art high-resolution T2 sequences allow the assessment of nodal morphological features such as shape, border irregularity and signal heterogeneity in addition to size, increasing the accuracy of MRI over size criteria alone [12,13]. These morphological features, however, are challenging or impossible to assess in small nodes (typically <5 mm), which have been shown to represent over half the nodal metastases in rectal cancer [14]. Currently, cases where no nodes are visible on MRI are considered N0; mesorectal nodes ≥ 8 mm showing two or more of the mentioned morphological features are considered N+; nodes ≤ 7 mm should be viewed with uncertainty and only be called positive when their features are strongly suggestive of malignancy [15].

Restaging after Preoperative Chemoradiotherapy

Anatomical MRI assessment of tumour regression grade (TRG), carried out 6–8 weeks after the completion of neoadjuvant chemoradiotherapy, has been shown to correlate with disease-free survival and overall survival in the MERCURY study [16]. MRI can accurately assess clearance from an initially threatened or invaded mesorectal fascia, with negative predictive values for involvement up to 90% [17,18], and potentially justify an alteration to the initial management plan in good responders.

The main limitation of anatomical MRI in the restaging setting is its inability to distinguish between small remaining tumour foci and post-treatment fibrosis; this impacts negatively on its sensitivity for ypT stage (tumour pathological staging following neoadjuvant therapy), as low as 50% [19].

In contrast to primary staging, restaging MRI performs well in the assessment of nodal disease, showing a negative predictive value of around 95%; this means that ypN0 patients can be accurately identified [20,21].

Detection of Local Relapse

MRI has been shown to be more accurate than computed tomography for the detection of local relapse and is certainly valuable in assessing whether a local relapse is surgically resectable [22,23]. The requirement to exclude distant metastases favours whole-body imaging techniques in this setting, such as computed tomography and PET/computed tomography. Technological advances, however, allow the use of MRI for whole-body imaging in clinically acceptable times (<60 min); the performance of whole-body MRI for colorectal cancer staging is currently under investigation in the National Health Service (Figure 1). Staging with hybrid PET/MRI with 18F-fluorodeoxyglucose (18F-FDG) is also being explored, combining the sensitivity of FDG with the high contrast and spatial resolution of MRI.

Functional Magnetic Resonance Imaging Techniques

A number of 'functional' MRI techniques are now available to assess several aspects of tumour physiology in

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