

ACTA ONCOLOGICA LECTURE

Preoperative staging of rectal cancer

NEIL SMITH¹ & GINA BROWN²

¹Royal Marsden Hospital Colorectal Cancer Network, Department of Colorectal Surgery, Mayday University Hospital, Croydon, Surrey, UK and ²Department of Academic Radiology, Royal Marsden Hospital NHS Trust, Downs Road, Sutton, Surrey, UK

Abstract

Detailed preoperative staging using high resolution magnetic resonance imaging (MRI) enables the selection of patients that require preoperative therapy for tumour regression. This information can be used to instigate neoadjuvant therapy in those patients with poor prognostic features prior to disturbing the tumour bed and potentially disseminating disease. The design of trials incorporating MR assessment of prognostic factors prior to therapy has been found to be of value in assessing treatment modalities and outcomes that are targeted to these preoperative prognostic subgroups and in providing a quantifiable assessment of the efficacy of particular chemoradiation treatment protocols by comparing pre-treatment MR staging with post therapy histology assessment. At present, we are focused on achieving clear surgical margins of excision (CRM) to avoid local recurrence. We recommend that all patients with rectal cancer should undergo pre-operative MRI staging. Of these, about half will have good prognosis features (T1–T3b, N0, EMVI negative, CRM clear) and may safely undergo primary total mesorectal excision. Of the remainder, those with threatened or involved margins will certainly benefit from pre-operative chemoradiotherapy with the aim of downstaging to permit safe surgical excision. In the future, our ability to recognise features predicting distant failure, such as extramural vascular invasion (EMVI) may be used to stratify patients for neo-adjuvant systemic chemotherapy in an effort to prevent distant relapse. The optimal pre-operative treatment regimes for these patients (radiotherapy alone, systemic chemotherapy alone or combination chemo-radiotherapy) is the subject of current and future trials.

Staging is the method of summarising the anatomical extent of a malignant tumour, thereby communicating information regarding prognosis. Historically, the development of cancer staging has its origins in the descriptive studies of Dukes in the field of rectal cancer [1]. The pathological staging of tumours into distinct prognostic groups relies exclusively on static morphologic features seen in the resected surgical specimen. Prognostic factors that predict for risk of disease failure from either local recurrence, distant metastases or both were identified from careful analysis of clinico-pathological data [1–4]. However, it was not possible to improve patient outcomes from that predicted by histological staging because at the time that many of these landmark studies were being carried out, surgery remained the only treatment for rectal cancer.

Over time, the efficacy and safety of other anti-cancer treatments, including chemotherapy and

radiotherapy has been evaluated and these have become available as adjuvant treatments for patients with rectal cancer. Overall survival was shown to be significantly improved in those patients with pathologically demonstrated lymph node metastases if they were given postoperative 5-FU chemotherapy [5]. When radiotherapy was given postoperatively to all patients with rectal cancer a significant reduction in local recurrence rates was observed [6], and when radiotherapy was combined with chemotherapy, local control was better [7]. For the first time, the clinical outcome could be improved from the prognosis offered by post-operative pathological staging. However, clinical decision-making still relied on the histopathological staging, to determine which patients might gain the most benefit from receiving these potentially harmful treatments. Any pre-operative imaging performed was essentially carried out to diagnose or exclude the presence of visible

Correspondence : Gina Brown, Department of Academic Radiology, Royal Marsden Hospital NHS Trust, Downs Road, Sutton, Surrey SM2 5PT, UK. Tel: +44 2086613964. E-mail: gina.brown@rmh.nhs.uk

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metastases (usually hepatic or pulmonary). Patients found to have synchronous metastatic disease could be diverted into either a non-surgical palliative treatment plan, or referred for specialist assessment for metastasectomy.

The importance of pre-operative staging for rectal cancer

The identification of prognostic factors by standard pathological assessment is of great importance, but for the postoperative patient, the primary therapy (i.e. surgery) has already been delivered. Useful prognostic information about likelihood of survival may be obtained, but it may be too late to influence survival substantially since the opportunity to downstage and produce tumour regression prior to surgery has been lost. With advances in oncology and widening of therapeutic options, primary surgery is no longer the only treatment, or necessarily the most appropriate treatment for rectal cancer. Adjuvant radiotherapy reduces rates of local recurrence [8], with the greatest benefits seen in patients receiving radiotherapy pre-operatively. The Swedish Rectal Cancer Trial demonstrated a survival benefit in patients undergoing pre-operative radiotherapy+surgery versus surgery alone [9], although this observation has not been repeated in other studies. The potential advantages of pre-operative versus post-operative treatments means that a technique which identifies poor prognostic factors preoperatively could be applied to select patients for neoadjuvant therapy prior to disturbing the tumour bed and potentially disseminating the disease. Furthermore, the intensity of preoperative therapy may be modified according to prognosis. Efficacy in terms of local control and reduced toxicity are both improved when chemoradiation is used before rather than after surgery [10].

MRI staging of rectal cancer

An optimal pre-operative staging technique would accurately identify prognostic factors preoperatively, enabling the selection of patients into appropriate treatment groups. High-resolution MRI has been shown to be superior to clinical examination (digital rectal examination), computed tomography, and endoluminal ultrasound (EUS) for staging of rectal tumours. Tumours of the distal sigmoid, rectosigmoid, and upper rectum can all be staged accurately using MRI [11]

Since the late 1990s, sophisticated multiple element coil arrays have been developed. These coils were designed to have the advantages of the surface coil by obtaining higher signal but with greater coverage and improved homogeneity. This was

achieved by combining surface coils in to an array of four (or more) coils, which are connected to amplifiers and multiple receiver channels. The signals undergo mathematical post processing to produce a single image from the information received by each coil. Thin (3 mm) sections with the pelvic phased-array coil give similar in-plane resolution as that obtained with the endorectal coil, but with much wider coverage. Using a high-resolution protocol [12] (Figure 1), MRI can not only distinguish tumour from rectal wall (Figure 2), but also consistently depict the mesorectal fascia [13] (Figure 3) and anatomical structures that relate to the optimal surgical technique for rectal cancer [14]. In addition, we use a standardised reporting proforma (Figure 4).

We will now discuss the main prognostic factors that have been identified by clinico-pathological studies, and see how MRI can be used to stage each of these factors pre-operatively.

Pre-operative identification of prognostic factors in rectal cancer

The TNM system

The TNM system uses the principle that the anatomical extent of the disease may be based on

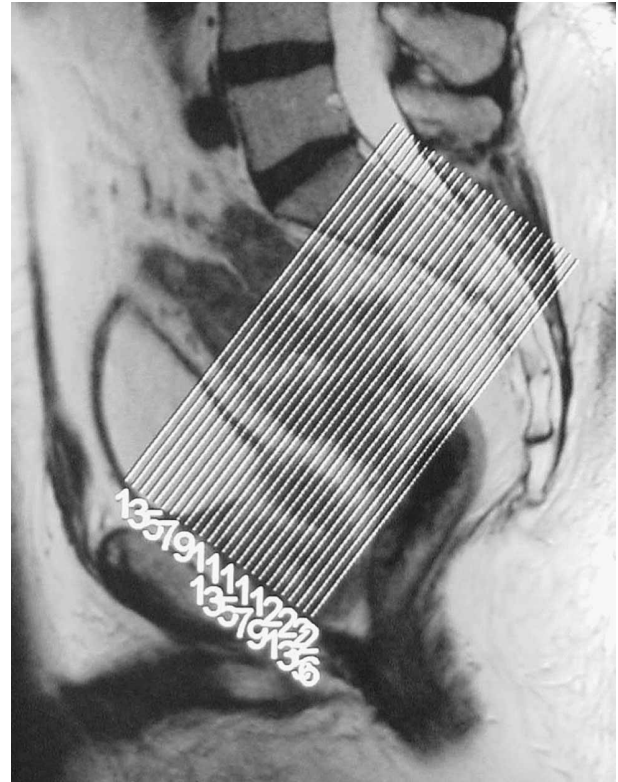


Figure 1. Sagittal scout image using standard high resolution protocol: 3 mm slice interval, 16–18 cm FOV, 4–6 NSA, 256 × 256 matrix, TR >3,000, TE 80–100, ETL 16. In plane resolution 0.6 × 0.6 mm.

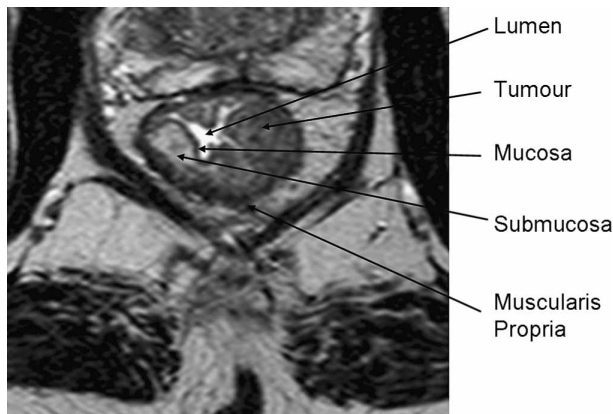


Figure 2. Detailed anatomy of bowel wall and tumour seen on high-resolution MRI.

the size and extent of the primary tumour (T), the absence or extent of regional lymph node metastasis (N) and the presence or absence of distant metastasis (M). The greater the extent of the cancer in each of the TNM categories, the higher the numerical modifier (ranging between 0 and up to 4). TNM is versatile in that it allows for both clinical and pathological assessment of stage. The various combinations of T-stage, N-stage and M-stage are clustered into stage groupings (Stage I to IV) based on prognosis. The TNM system for staging cancer of the colon and rectum was originally devised to correspond directly with the original Dukes system [1]: Stage I, Dukes A; Stage II, Dukes B; Stage III, Dukes C. Stage IV corresponds to the presence of distant metastases. The prognostic accuracy of the TNM system is ensured by its periodic revision, taking into account data from outcome studies. This process of continuous improvement, together with

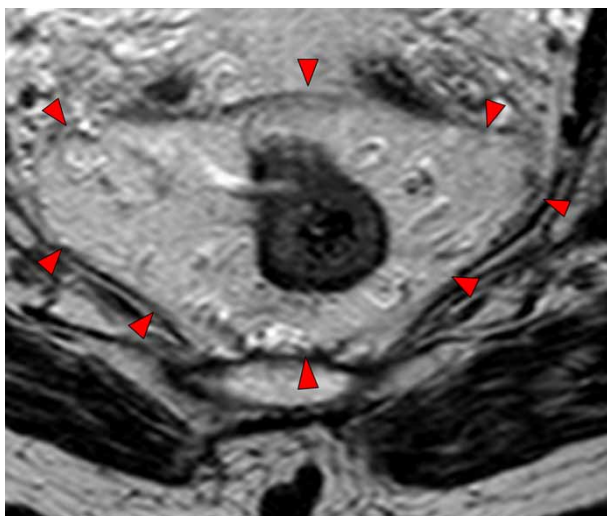


Figure 3. High resolution T2-weighted axial MRI through rectal tumour showing the fascia propria of the mesorectum (red arrowheads) which corresponds to the surgical circumferential resection margin.

its comprehensive set of definitions and rules of application and its multidisciplinary design are cited as key advantages over other staging systems [15]. Consequently, this system is the standard for colorectal cancer staging, recommended by international bodies including the Royal College of Pathologists of England and the College of American Pathologists. The latest (sixth) revision was published in 2002 [16].

Within each T stage there is a heterogeneous survival range and there has been much interest in identifying poor prognostic groups within each stage. Both T1 and T2 tumours have high 5 year survival but the widest range in survival is demonstrated in patients with T3 tumours, which make up 80% of rectal tumours seen in clinical practice. A number of authors have shown a relationship between survival and the depth of extramural spread that is independent of other prognostic factors including the circumferential margin status [17,18]. With respect to depth of tumour invasion, the sixth edition of the TNM classification suggests an optional expansion of the classification of pT3 tumours according to measured extramural invasion (<1 mm; 1–5 mm; >5–15 mm; >15 mm). This represents the most precise subdivision yet to be proposed and reflects the accumulated body of evidence, which can be traced right back to 1932 and Dukes' original observations.

1. MRI prediction of extramural spread/T-Stage

Thin-slice high resolution MRI can be used to accurately measure the depth of extramural spread. A prospective series of 28 patients undergoing pre-operative MRI using a four-element surface coil was the first study to show good correlation with histology [13]. In that study 21/24 (88%) of patients with tumour infiltrating 5 mm or over in to perirectal fat were correctly identified. In most cases, extramural depth, as measured using MRI, showed direct agreement with corresponding histopathological measurements. Cases of discordance between MRI and histology measurement of extramural depth occurred in ulcerating tumours that produced erosion of the muscularis propria. This was because of difficulty in identifying the muscularis propria and thus measuring distance from the outer muscle coat when an eroding ulcer was present. We were also able to show good agreement between pathology and MRI assessment of T-stage in a larger prospective study of 98 patients (weighted $\kappa = 0.67$) [19].

The Sharp Memorial Hospital in San Diego, Californian published a retrospective evaluation of their use of MRI to stage both rectal and colonic cancers in a series of 48 patients [20]. They reported

Code No:	MRI Reporting Proforma	Addressograph
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Radiologist.....

Patient Name:	Date: / / 200
Date of Birth: / /	Hosp. No.
Exam performed elsewhere	Yes No If yes, where
Exam technically satisfactory (3mm)	Yes No
Image quality	Optimal Sub-Optimal
Pathology identified	Yes No
Has the patient received Radiotherapy	Yes No
Has the patient had a previous rectal MRI	Yes No
If Yes, date of previous examination /...../.....	

Gross Morphology

Polypoidal ☐ Annular ulcerating ☐ Annular non ulcerating ☐

Infiltrating margin of extramural spread

Eroding ☐ Pushing ☐ Infiltrating ☐ No Extramural spread ☐

Mucinous Tumour Yes ☐ No ☐

Metastatic spread

Nodes demonstrated not suspicious Yes ☐ No ☐

Nodes demonstrated suspicious Yes ☐ No ☐

Extramural venous invasion Yes ☐ No ☐

Tumour deposits / satellites present Yes ☐ No ☐

Local invasion

Submucosa (T1) ☐ Muscularis (T2) ☐

Beyond Muscularis <1.00 mm (T3a) ☐ Beyond Muscularis 1.01-5.00 mm (T3b) ☐

Beyond Muscularis 5.01-15.00mm (T3c) ☐ Beyond muscularis >15.01mm (T3d) ☐

Into adjacent organs (T4a) ☐ Perforation of visceral peritoneum (T4b) ☐

Margins

Distance to mesorectal fascia <1.00 mm **Me1** ☐ Distance to mesorectal fascia >1.01 mm **Me0** ☐

Low tumour (below levator) >T2 **MeLev** ☐

Measurements

Maximum extramural spread of tumour mm

Min distance to mesorectal fascia/potential CRM from outer edge of tumour mm

Please state distance to CRM for:

a. Main tumour mm

b. Suspicious lymph node mm

c. Extramural venous invasion mm

d. Tumour satellite/deposit mm

Distance to sphincter (Low tumours only) mm

Figure 4. Standardised proforma for reporting of rectal MRI.

84% agreement between pre-operative MR and final pathological T-stage in 19 rectal tumours and overall TNM stage was correctly predicted in 95%. In another series of 40 patients, T-staging was correctly predicted in only 20 (12 under-staged, 8 over-staged) although a clear learning curve was evident as MRI prediction became more accurate over the course of the prospective study [21]. A recent study from Tokyo demonstrated good correlation between MRI and depth of invasion, with at least 82% accuracy for T-stage prediction ($\kappa=0.82$) [22].

The largest study to date looking at the accuracy of MRI staging of rectal cancer has been the MERCURY study, a multicentre prospective trial which recruited 679 consecutive patients with rectal cancer in 11 centres in Britain, Germany, Norway and Sweden [23]. After exclusions for missing data, direct comparison of the extramural depth of invasion measured by MRI and histology was made in 295 (94.9%) of 311 patients undergoing primary surgery. The mean difference between MRI and histopathology was -0.046 mm (SD = 3.85 mm, 95% confidence interval -0.487 to 0.395 mm). Thus MRI has been shown to be equivalent to within 0.5 mm for prediction of local tumour spread.

2. *Lymph node involvement*

Preoperative assessment of lymph node status in rectal cancer is of importance for a number of reasons. Firstly, the number of involved nodes has an influence on prognosis [3,5]. Second, the presence of tumour-containing lymph nodes close to the mesorectal fascia (which forms the conventional surgical circumferential resection margin) increases the risk of recurrence [24] unless the standard excision plane is altered. Nodes lying outside the mesorectal fascia may require extended lymphadenectomy in order to achieve clearance of tumour [25,26]; those that remain unresected may be responsible for local recurrence despite apparently clear surgical resection margins [27]. The use of neoadjuvant preoperative therapy may be influenced by the presence of nodes containing tumor close to the potential resection plane. Finally, the ability to determine reliably node-negative status preoperatively could result in less aggressive surgery and preoperative therapy in some patients.

A major challenge for any cross-sectional imaging modality lies in the ability to predict lymph node status prior to surgery, not least because involved nodes may contain only microscopic tumour foci, and therefore be normal-sized. Inability to predict nodal status in patients with rectal cancer is viewed as an important limitation of pre-operative staging techniques. An analysis of 437 lymph nodes har-

vested from 42 Total Mesorectal Excision specimens, with careful comparison of the axial pre-operative MRI images and the matched transversely-sectioned histopathology specimens showed that the diameters of benign and malignant nodes were similar [28]. The finding that no particular size cut-off is useful in predicting nodal status is supported by a histological survey of over 12 000 lymph nodes in rectal cancer [29] that showed considerable size overlap between normal or reactive nodes and those containing metastases.

Studies using endoluminal ultrasound found that the internal texture of an imaged node may correlate better with the presence of metastasis than nodal size [30–32]. We applied these observations to high resolution MR evaluation of lymph node status, and demonstrated that intranodal signal heterogeneity (i.e. a mixed signal) was a highly specific discriminant. When lymph nodes were defined as suspicious based on having an irregular border, or mixed signal intensity, greater accuracy was achieved, with sensitivity of 85% and specificity of 97%. In another study, we demonstrated 85% accuracy ($\kappa=0.68$) comparing MRI prediction of lymph node status with histology in a prospective series of 98 patients [19]. In both series, prediction of lymph node status showed good reproducibility between observers and was independent of, and greatly superior to, lymph node size.

Fifteen to 42% of small (<5 mm) mesorectal lymph nodes in rectal cancer patients may contain metastases [28,29,33]. In the Cardiff study, 23% of all the nodes harvested from resection specimens were missed by MRI, but these were all <3 mm and only two of the 102 contained metastases [28]. On the other hand, this technique did correctly identify many nodes measuring 2–5 mm, and correctly predicted the presence of metastases in some based on irregular contour. Whilst its power to resolve such small nodes is clearly suboptimal, it would seem that MR evaluation of nodes using border/signal criteria will result in understaging of few patients. Nevertheless, the inability to detect microscopic metastases in all lymph nodes suggests that a negative MR examination should not be used to select patients for local excision surgery.

Work in our department using ultra-small particles of iron oxide (USPIO) has shown promising results in terms of identifying very small (>1 mm) foci of tumour within mesorectal nodes [34]. Malignant nodes (confirmed by histological correlation) have been shown to have a characteristic appearance on T2-weighted high-resolution MRI following administration of USPIO which is different to the appearance of reactive or non-malignant nodes.

MRI cannot necessarily distinguish between a lymph node replaced by tumour and a separate extramural tumour deposit in the mesorectum. Nevertheless since patients with discontinuous tumour deposits have a much worse prognosis [35,36], it is another advantage of the technique that such deposits can be detected pre-operatively.

3. Tumour involvement of the Circumferential Resection Margin

The association between local recurrence after surgery for rectal cancer and tumour involvement of the lateral (now called 'Circumferential') resection margin was first demonstrated in 1986 by Professor Quirke's group in Leeds [37]. They examined operative specimens from 52 patients with rectal cancer, and found that in 14 (27%) tumour had spread to the lateral margin of resection, and that 12 of these patients went on to develop pelvic recurrence. They concluded that incomplete surgical excision was therefore the cause for most local recurrences in rectal cancer. Two larger studies by the Leeds group revealed that not only did CRM involvement by tumour increase the risk of local recurrence, but that it also predicted poor survival. Patients with CRM involvement (defined as tumour within 1 mm of the resection margin [38]) were reported to have 3.5 times the risk of local recurrence and double the risk of death [24,39].

Total mesorectal excision

The risk of local recurrence after surgical resection of rectal cancer is much lower when the mesorectum is excised intact [40,41]. The mesorectum is a distinct anatomical unit comprising the rectum, perirectal fat, blood vessels, nerves and lymphatic vessels. It is surrounded by a layer of fibroareolar tissue called the mesorectal fascia. The detailed anatomy of the mesorectal fascia was described only relatively recently by Bissett et al. [42], who dissected the fascia propria off the mesorectum and showed that the fascia was a continuous structure that encircled the rectum and mesorectum, fusing with the peritoneum as it reflected off the rectum. At the level of the anorectal junction, the mesorectum thins out.

Total mesorectal excision (TME) is performed by sharp dissection along the plane that separates the visceral from the parietal layers of the perirectal pelvic fascia thus enabling the radical removal of the rectum within its surrounding mesorectum [43]. The principle rationale for this method of surgery is the total removal of rectum and its draining lymph nodes en bloc, preserving the anal sphincter and

autonomic nerves. Most rectal tumours are confined to within the mesorectal 'packet', and the results of Professor Heald [44] and others [45] lend support to Quirke's observation that incomplete surgical excision is largely responsible for local recurrences. Initial concerns that the results of TME surgery were not reproducible [46] were refuted by subsequent studies. For example Dixon et al. demonstrated a 5 year survival of 64% after TME surgery [47]. Similar results have been corroborated at other centres with local recurrence rates falling from 30% with conventional surgery to under 10% following TME [48,49].

The widespread acceptance of TME surgery as the gold standard operative procedure for patients with rectal cancer promises to be one of the single most important factors in reducing local recurrence [41,45,50,51]. Nevertheless, the CRM may still be positive if the tumour extends up to or through the mesorectal fascia. A national audit of rectal cancers in Norway confirmed that even after TME surgery, 9% of patients had a positive CRM, and the local recurrence rate in this group was 22% compared to 5% for those with negative CRM [52]. The importance of CRM status as a prognostic factor is not therefore diminished by TME, although the incidence of CRM positivity is much lower when TME is performed.

MRI assessment of potential resection margins (CRM)

Curative sphincter-preserving surgical resection of rectal cancer is dependent on the complete removal of all macroscopic and microscopic tumour in the pelvis. The tumour must be clear of adjacent anatomical structures, the mesorectal fascia and the sphincter complex. The MRI appearances of the anatomical structures relevant to TME, including the peritoneal reflection, Denonvilliers' fascia, the pelvic nerve plexuses, mesorectal fascia and mesorectum itself have all been described [14]. The mesorectal fascia represents the potential CRM in patients undergoing TME surgery. Bissett et al. conclusively demonstrated by using markers that the mesorectal fascial plane seen with MRI [42] corresponds to the fascia propria encasing the mesorectum and excised by TME. MRI can therefore be used to assess the distance from the tumour edge to the potential circumferential margin and thereby predict the final CRM status in patients undergoing TME surgery.

Studies have used different cut-off values of the measured distance to the mesorectal fascia to predict CRM status. The authors of one study concluded that CRM status could be predicted with a high degree of accuracy and consistency [53] when a

cut-off of 5 mm MRI measured distance to the CRM was used. Other authors have been able to use more precise MRI measurements to predict CRM status. Our own prospective study involving 98 patients undergoing pre-operative MRI staging, predicted the CRM status to be positive when tumour was identified by MRI within 1 mm of the mesorectal fascia. Comparison with histology showed very good (92%, $\kappa=0.81$) agreement [19] (Figure 5). In a different British study, high-resolution pre-operative MRI correctly predicted the CRM status (the cut-off value was not reported) in 39/40 cases [21].

A recently published meta-analysis which compared MRI against histology after total mesorectal excision included data from nine studies (which did not include MERCURY) involving 529 patients. This confirmed that high-resolution MRI accurately predicts tumour involvement of the CRM with a sensitivity and specificity of 94% and 85% respectively [54]. The multi-centre MERCURY study itself demonstrated accurate prediction of CRM status throughout the 11 participating hospitals. Of 408 consecutive patients undergoing surgery after MRI staging, 354 had clear CRM on histology. Three hundred and twenty seven of three hundred and fifty four of these were correctly predicted by the pre-operative MRI giving a specificity of 92.4%. The negative (clear margin) predictive value was 94% [55]. Overall accuracy for prediction of a clear margin was higher for the 311 patients undergoing primary surgery (91%) than for those 97 who completed pre-operative chemo-radiotherapy or long-course radiotherapy (77%).

Abdomino-Perineal excision rates have declined in specialist colorectal centres as evidence accumulates for the oncological safety of sphincter-saving procedures [43].

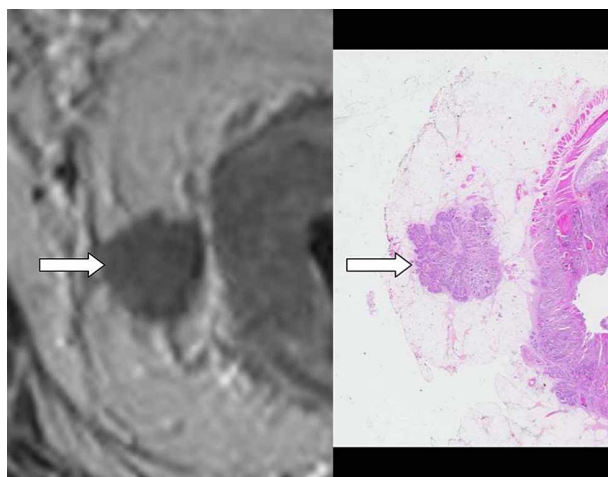


Figure 5. CRM is safe if distance of tumour to mesorectal fascia is >1 mm.

4. Extramural Vascular Invasion (EMVI)

The landmark pathological studies into vascular invasion were published in the early 1980s by Professor Ian Talbot [56–58], and the body of evidence in the literature suggesting that vascular invasion is of prognostic significance continues to grow. Amongst these histological studies, the rate of detection of vascular invasion is variable with incidences ranging from 17 to 70% reported [56,59–65]. Even in patients undergoing careful radical excision of the rectum and mesorectum, venous invasion remains an important independent prognostic factor [40,66] EMVI is associated with higher risk of local recurrence [64], distant metastases [29,62,67–69] and death [4,62,64,70–74].

The typical appearance on MRI, which is the only imaging modality that has been shown to demonstrate extramural vascular invasion in rectal cancer [19] is that of discrete serpiginous or tubular projections of intermediate signal intensity into perirectal fat, following the course of a visible perirectal vessel (usually a vein). We have previously reported that extramural vascular invasion was correctly identified on 15 of 18 patients with rectal cancer [19]. More recently, we have devised an MRI-EMVI grading score to evaluate the presence or absence of radiological features indicative of EMVI (Table I). In a recent study carried out in our own unit [75] we found that the proportion of patients with MRI-detected EMVI in 94 rectal and rectosigmoid cancers undergoing primary surgery was 26%, which was similar to the histologically-proven proportion (28%). The sensitivity and specificity of MRI for detecting EMVI in this series was 62% and 88% respectively. Some patients with microscopic vascular invasion could not be resolved on MRI, while others with very obvious EMVI on the pre-operative images had false-negative histopathology due to obliteration of normal venous architecture which makes it difficult for the pathologist to recognise that a tumour deposit lies within the course of a vessel, something which may be more readily appreciated on serial MR images (Figure 6).

In the same paper, we were able to show that MRI-detected EMVI is associated with poor clinical outcome. Despite MDT-directed pre-operative and post-operative therapy, the presence of EMVI on a pre-operative MRI scan was associated with a four-fold higher risk of distant metastasis (52% versus 12%), and a reduction in relapse-free survival at 3 years to only 35% versus 74% for patients with no EMVI (Figure 7).

Table I. Summary of MRI-EMVI scoring system.

MRI-EMVI score	Radiological Feature			
	Tumour Margin	Tumour Location	Vessel calibre	Vessel Border
0	Smooth	Away from vessels	Normal	Normal
1	Nodular			
2		Near vessels		
3		Within Vessel	Slightly expanded	
4			Grossly expanded	Irregular

5. Peritoneal involvement

Locally-advanced upper rectal tumours may perforate through the peritoneum. In one prospective study of 412 colon cancers, local peritoneal involvement was found to be an independent risk factor for intraperitoneal recurrence after surgery. Similarly in rectal cancer, peritoneal involvement predicts for local recurrence.

The typical appearance seen on rectal MRI is one of nodular extension of intermediate signal intensity through the fine low-signal-intensity peritoneal reflection at or above the level of its attachment to the anterior surface of the rectum: this is best demonstrated on axial high resolution images. The Cardiff series included 11 patients with pT4 tumours, nine of whom had histological evidence of perforation with tumour cells seen on the peritoneal surface. This was correctly identified in 7/9 cases. In two other cases, MRI suggested nodular tumour infiltration through the peritoneum, and while histology confirmed that the tumour was close to the peritoneal surface, there was actually no perforation [19]. Although cases of peritoneal perforation were undoubtedly identified using preoperative MRI, many cases will be missed by MRI due to failure to resolve microscopic infiltration of peritoneal lined clefts. The accuracy of MRI in correctly identifying peritoneal involvement at this site is therefore less reliable than detection of other prognostic factors [76]. However, knowledge of the relationship of

tumour to the peritoneal reflection anteriorly should prompt a careful search for subtle peritoneal infiltration.

Pre-operative therapy and the multi-disciplinary team approach to the management of patients with rectal cancer

We recommend a selective approach to pre-operative therapy in rectal cancer, with selection based on MRI-identified features occurring in the context of the multi-disciplinary team (MDT). This team of surgeons, radiologists, oncologists, pathologists and associated clinical nurse specialists is now established as the optimum approach to the management of patients with rectal cancer. We have shown that rectal cancer patients discussed in the MDT meeting pre-operatively had lower rates of histological CRM involvement (2% versus 26%), and that patients with irresectable disease could be identified and offered alternative treatment [77]. Detailed pre-operative MDT discussion based on MRI staging is therefore essential to the aim of achieving resection with clear margins.

The benefits of a selective approach using MRI based selection criteria are self evident. Approximately 40 – 50% of patients can be treated successfully with primary surgery without significant risk of local recurrence or systemic failure. Of the remainder, potentially dramatic improvements may be achieved through the use of intensive and targeted

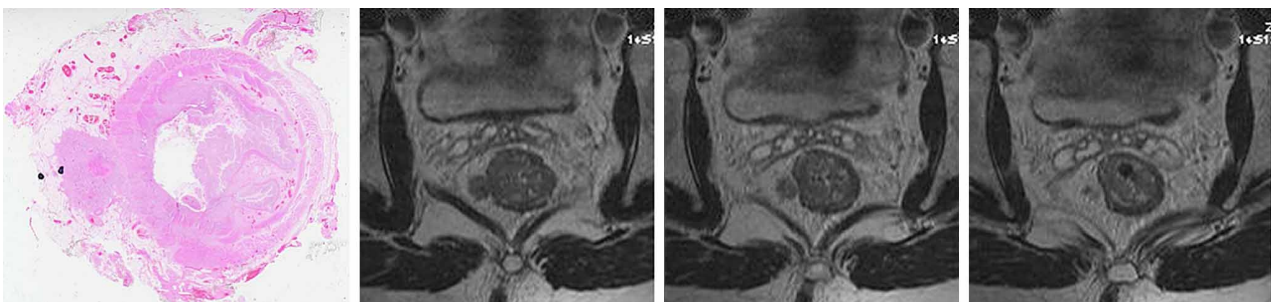


Figure 6. A tumour nodule is seen apparently extending laterally from the right side of the primary tumour. There is no histological evidence that this nodule is associated with any vascular structure on this slide. Serial ascending axial MRI slices through the same tumour suggest that the nodule lies within a tubular structure running parallel to the bowel wall, and the upper-most image shows signal void indicating that this is likely to be a vein.

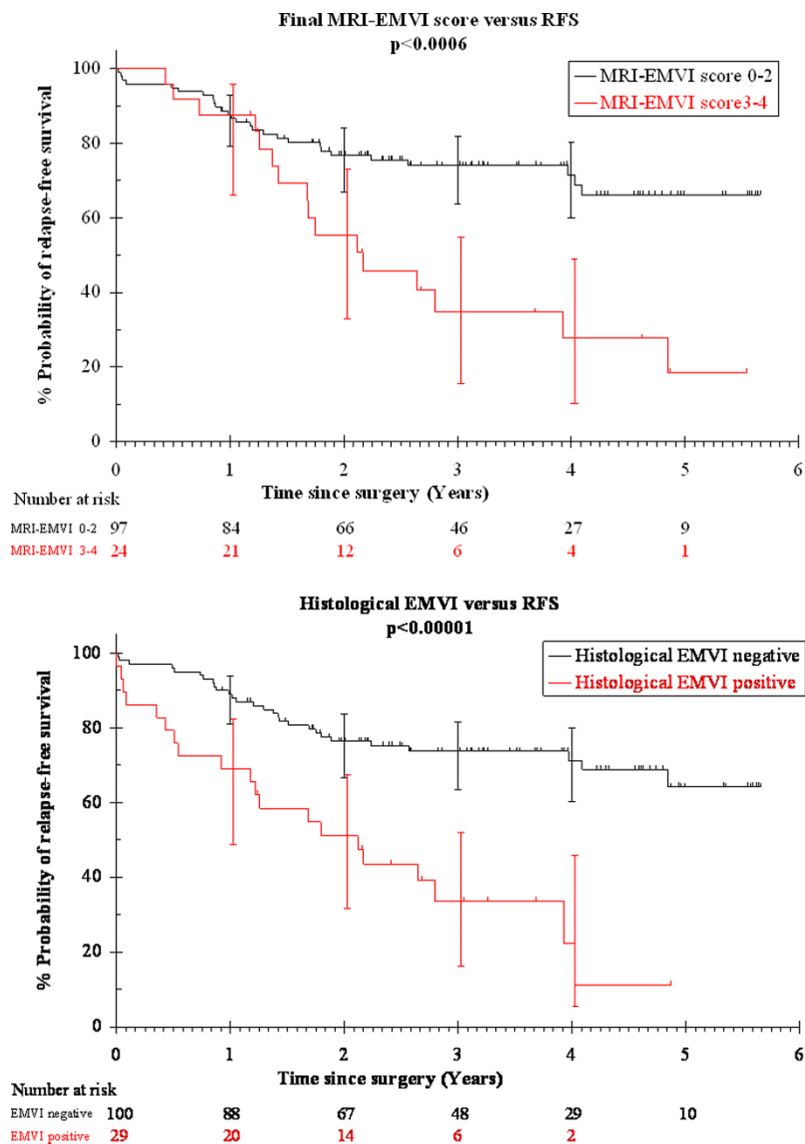


Figure 7. The presence of EMVI is associated with a significant reduction in relapse-free survival whether it is identified pre-operatively (upper graph) or histologically (lower graph).

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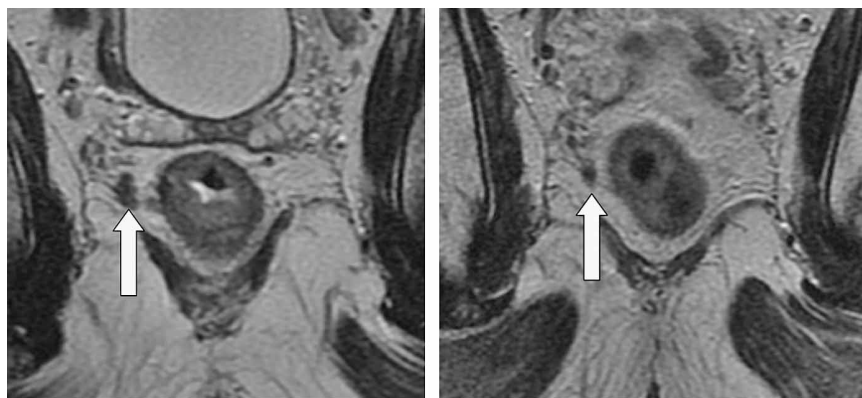


Figure 8. Extramural venous invasion lying close to the mesorectal resection margin. The image on the right shows the same level after chemoradiotherapy with some downstaging evident.

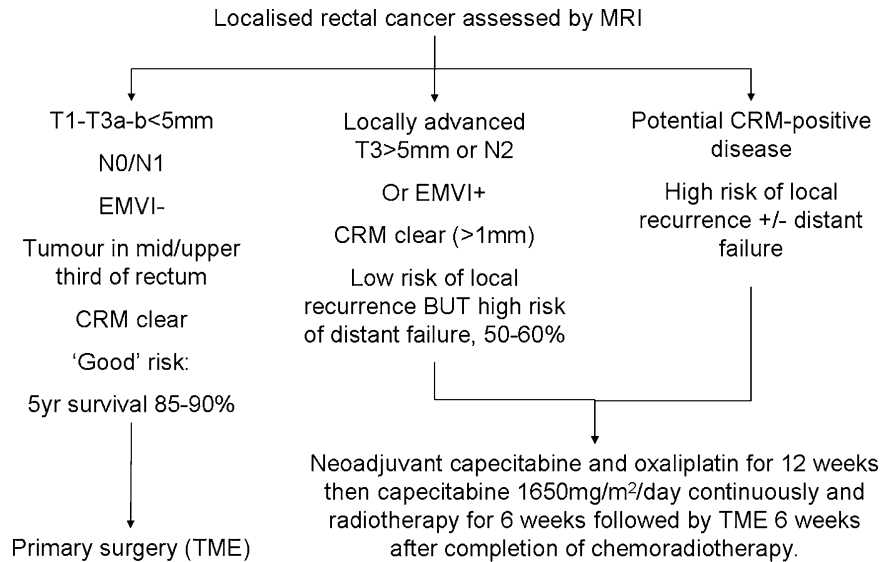


Figure 9. MRI-directed pre-operative treatment stratification as used in the EXPERT study.

preoperative therapy aimed not only at reducing the size of the primary tumour and rendering potentially irresectable tumour resectable with tumour free circumferential margins but also to enable patients at high risk of systemic failure to benefit from intensive combined modality therapy aimed at eliminating micrometastatic disease (Figure 8). The characterisation of a patient's tumour as either "good" (no adverse features), "bad" (features suggesting increased risk of systemic relapse, although surgical margins clear and therefore resectable) or "ugly" (surgical margins involved) may suggest three possible pre-operative therapeutic strategies. However, the optimal strategy for each is still under investigation [78].

We routinely use high spatial resolution MRI to select patients with poor risk tumours for intensive pre-operative therapy. This approach has been tested prospectively in a phase II trial (Figure 9) which showed an objective tumour response to systemic chemotherapy followed by combination chemo-radiotherapy in 88% of patients. Sixty-six of 67 (99%) patients with originally-threatened or involved margins who underwent surgery had R0 resections [79].

Conclusions

Detailed preoperative staging using high resolution MRI enables the selection of patients that require preoperative therapy for tumour regression. This information can be used to instigate neoadjuvant therapy in those patients with poor prognostic features prior to disturbing the tumour bed and potentially disseminating disease. An MRI-directed multidisciplinary team approach to the identification

of patients at high risk for local and/or distant failure is recommended. The optimal pre-operative treatment regimes for these patients (radiotherapy alone, systemic chemotherapy alone or combination chemo-radiotherapy) is the subject of current and future trials.

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