Prognostic Staging of Rectal Cancer- Implications for Treatment

Dr Gina Brown MBBS MRCP FRCR MD
Royal Marsden Hospital
Sutton
Surrey
UK
gina.brown@rmh.nhs.uk

The role of the radiologist in the staging and assessment of rectal cancer has undergone a major reappraisal in recent years. The validation of imaging based prognostic factors has led to a paradigm shift in the treatment approaches offered to patients. The old paradigms were straightforward to apply and favoured a one size fits all approach of preoperative therapy to "locally advanced T3/T4 rectal cancers". This placed very little demand from the radiologist who had simply to identify T3/T4 tumours. Any such patient would receive preoperative radiotherapy prior to rectal cancer surgery.

With improved MRI staging and assessment of rectal cancers it has become important to question the logic of such a binary approach and several clinical trials are beginning to address this.

The widespread adoption and ongoing histopathological audit of the quality of surgical specimens have led to dramatic improvements in local recurrence rates which has reduced the need for routine preoperative radiotherapy that had previously been offered to >80% of all rectal cancer patients. However, improvements in the quality of surgery alone cannot improve the overall survival for patients with rectal cancer and the role of the radiologist has never been more important in providing the clinical team with the pertinent staging information to determine the optimum treatment choices that can be offered to the patient.

The overall aims of the multidisciplinary team managing patients with rectal cancer are:

- Reduce perioperative and longterm postoperative morbidity – preserve quality of life, this means the selective avoidance of radiotherapy in patients that can be cured by total mesorectal excision surgery alone
- Preserve the anal sphincter with good sphincter function
- Minimise/eliminate risk of local recurrence: through selective radiotherapy and audited surgery

The overall aims of the multidisciplinary team managing patients with rectal cancer are:
• Reduce the risk of death from distant failure: through imaging surveillance, prompt referral to hepatobiliary specialists for resection and modern chemotherapy

---

**MRI staging: new treatment possibilities**

![MRI staging diagram]

**Figure 1**
The approaches summarised in figure 1 – use an MRI based stratification that enable treatment to be tailored according to the risk of local failure / distant recurrence against the need to prevent overtreatment, reduce treatment related toxicity and morbidity and to preserve sphincter function, whilst intensifying therapy for patients that are at risk of local and/or distant failure.

### Management of early stage tumours.
The role of MRI in this setting, is to identify patients suitable for a less radical approach by confirming early stage polypoidal or sessile lesions which are infiltrating the submucosa and show preservation of the muscularis propria. Such patients can be readily identified using MRI and may well be less susceptible to overstaging when compared with endoluminal ultrasound, particularly when assessing the more bulky polypoidal lesions. Overstaging of such lesions by EUS is well documented and occurs in up to 18% of cancers by EUS[1-2].

### Local recurrence in rectal cancer.
In the past nodal status was one of the major factors governing the risk of pelvic recurrence in patients treated with rectal cancer. The published series giving rise to this evidence base were largely from the pre-TME era[3]. This was characterised by blunt resection of the mesorectum, resulting in nodal disease and tumour frequently being left behind within the pelvis and rates of circumferential resection margin involvement as frequent as 40%[4]. The outcomes analysis of patients treated by primary TME surgery without adjuvant radiotherapy has shown that local recurrence rates were less than 5% and nodal status no longer predicted for pelvic recurrence in tumours staged with MRI as early stage good prognosis primary rectal cancers[5]. For many centres treating rectal cancer with good quality audited total mesorectal excision surgery, this means that it is now possible to avoid excess toxicity and morbidity associated with the routine use of preoperative radiotherapy or chemoradiotherapy for MRI identified low risk patients.

### Patients at risk of distant failure.
As early as the 1950s Dukes and colleagues observed the strong positive relationship between the increasing depth of spread the millimetres of tumour beyond the muscularis...
propria and the prevalence of adverse features such as: nodal metastases and distant metastases[6]. Local tumour staging by MRI is not complete without also subclassifying patients according to depth of extramural spread. The patients’ risk of distant metastatic disease can be stratified much more precisely. The sub classification is as follows:

T3 a: tumours with extramural spread measures less than 1 mm beyond the muscularis propria. These patients have an excellent prognosis and survival outcomes. When tumour spread measured is less than 1 mm, this has been shown to be identical to tumours with no spread beyond the muscularis propria. This means that the prognostic distinction between T2 and T3 tumour with minimal spread is clinically irrelevant, as both categories would be defined as good prognosis.

T3b: tumours with extramural spread that measures between 1 and 5 mm beyond muscularis propria. Such tumours are also associated with good prognosis and have a low rate of metastatic disease.

T3d: these tumours with extramural spread that measures more than 5 mm but less than 15 mm beyond the muscularis propria. Such patients show significantly worse prognosis than T3a or T3b tumours and this prognosis worsens with each millimetre of tumour spread.

T3d: extensive extramural spread greater than 15 mm beyond muscularis propria. This finding carries the worst prognosis with only a 25% 5 year disease free survival. It is therefore far more clinically relevant to be able to categorise patients into the high or low risk categories by measuring the depth of tumour spread than simply to differentiate between T2 and T3 tumours[7].

MRI detected extramural venous invasion.
The detection of tumour signal intensity extending into the extramural vessels was first noted in a prospective trial conducted in rectal patients undergoing TME surgery and correlated with whole-mount histopathology examinations[8]. Its presence is associated with synchronous metastatic disease and is an independent prognostic predictor for poor disease-free survival. It is clear from outcome data analysis of the current treatment strategies of chemoradiotherapy followed by adjuvant chemotherapy are insufficient to improve survival in this group of patients[9-10]. Thus clinical trials are underway to evaluate the impact of neoadjuvant chemotherapy in this high-risk group of patients as well as surveillance strategies for synchronous and metachronous metastatic disease.

MR predictors for local recurrence.
One of the major advantages of MRI over alternative imaging modalities is the ability to depict the mesorectal fascia, which forms the radial margin. The total mesorectal excision in rectal cancer surgery. As a result of follow-up from patients in the Mercury study. It has been shown that the prediction of CRM involvement by MRI significantly increases the risk of local recurrence on follow-up[11]. Therefore the preoperative assessment of CRM is one of the crucial determinants for the decision to give local pelvic preoperative chemoradiotherapy aimed at eliminating or reducing the risk of pelvic recurrence. The risk is significantly reduced if tumour shrinkage away from the fascia can be achieved prior to surgery and reassessment following treatment is essential as a persisting potentially involved circumferential resection margin is defined by MRI remains a predictor for local recurrence even after chemoradiotherapy[12].

Low rectal cancers.
Tumours lying 6 cm from the anal verge have been shown to be at particular risk of local recurrence. On the other hand avoidance of permanent stoma and excision of the sphincter complex is often sought by the patient where possible. This poses a particular challenge to the multidisciplinary team managing such patients and the role of MRI in detecting the relationship of the tumour to the pelvic floor using high-resolution sequences is absolutely critical in enabling the team to optimise and tailor treatment to enable both the best
oncological outcome but also functional outcomes. Since the mesorectal fascia does not form the radial margins of excision and abdominoperineal surgery, it has become important to develop a classification system that enables the surgeon to select the plane of surgery that will achieve clear radial margins[13-14].

**Post treatment assessment**

Until recently, the precise role, importance and validity of staging rectal cancers after preoperative therapy has been uncertain [15]. The MERCURY study evaluated consecutive patients undergoing both primary surgery and preoperative therapy with histopathological correlation and analysis of survival outcomes [12]. This study showed that post chemoradiation MRI assessment of tumor regression grade (mrTRG) correlated with disease free survival and overall survival, and thus patient prognosis, before definitive surgery. Furthermore, post-treatment MRI prediction of circumferential resection margin involvement (mrCRM) also gave prognostic information regarding the risk of local recurrence.

**Summary**

The systematic assessment of the above known preoperative prognostic factors using high resolution MRI yields information that is crucial to the treatment and future improvements in patient survival.


