LOREC: the English Low Rectal Cancer National Development Programme

Low rectal cancer is a challenging disease. Recent evidence has shown that the treatment of low rectal cancer can be optimized. The purpose of the English Low Rectal Cancer National Development Programme is to enhance multidisciplinary colorectal cancer team knowledge and skill to improve outcomes of this complex condition.

Rectal cancer is common in the UK with approximately 14 000 cases diagnosed every year (Morris et al, 2011). Surgical resection is the mainstay of treatment and surgery for rectal cancer can be broadly divided into restorative procedures that preserve the sphincter and abdomino-perineal excision where the sphincter is excised with the specimen. Low rectal cancers are more challenging to treat because of a conflict between wide excision and conservative approaches that preserve the sphincter, in an attempt to maintain function and quality of life.

Although surgery is the mainstay in achieving cure, attention has focused on the variability in outcomes between centres, with large variations in the proportion of patients who undergo restorative procedures between centres (Morris et al, 2008). Additionally there have been reports of poor outcomes in patients who had complete rectal resection by abdomino-perineal excision compared with those who could have a restorative procedure (Wibe et al, 2004). While the main reason for this is undoubtedly more advanced and lower tumours in patients who require abdomino-perineal excision, the operation of abdomino-perineal excision may be suboptimal in many cases and could be optimized.

The lower rectal anatomy is complex. The rectum, levators and anal canal have been described as a 'tube within a funnel'; the funnel being the levators, the stem of the funnel being the sphincter complex and the tube within, the rectum (Shihab et al, 2009). The mesorectum, the embryological lymphovascular package surrounding the rectum (Heald, 1988), tapers in its lower part resulting in a 'waist' (described in the following article) around this level (Salerno et al, 2008). This potentially predisposes a tumour in the region of the waist (3–4 cm from the anal verge) to be exposed during excision leading to suboptimal surgery (Salerno et al, 2006) with increased rates of local recurrence and poor survival (Wibe et al, 2004; Nagtegaal et al, 2005).

Some patients with low rectal cancer (at the upper end of the extent of the low rectum) can have a restorative procedure in the form of an anterior resection. Heald and colleagues (1997) reported that in anterior resection, keeping the mesorectal fascia intact, which is the fascial envelope covering the mesorectum, was associated with significantly improved disease control and overall survival. While some patients most certainly require an abdomino-perineal excision because of proximity of the tumour to the anal verge, in a significant proportion of patients either operation might be feasible (Morris et al, 2008). Morris et al (2008) found significant variation in the abdomino-perineal excision rates in England and fears were raised that some surgeons could be overusing this procedure resulting in some patients needlessly receiving a stoma and, potentially, a poorer quality of life (Pachler and Wille-Jorgensen, 2005).

The English Low Rectal Cancer National Development Programme (LOREC; www.lorec.nhs.uk) was launched partly in response to this and also in recognition that abdomino-perineal excision outcomes were sub-optimal (Morris et al, 2008). The focus of the programme is to promote awareness and self-development of multidisciplinary teams, facilitate the decision-making process towards the right operation for the patient, and to support surgeons to perform surgery based on oncologically safe principles where restorative surgery is not possible in advanced low rectal cancer. The key components are precise staging, appropriate selective neo-adjuvant (preoperative) therapy, optimal surgical decision making and technique with maximal input from nurse specialists, pathologists and other members of the multidisciplinary team.

Staging low rectal cancer

Radiological imaging is central to both the local and systemic staging of rectal cancer. Endorectal ultrasound and high resolution magnetic resonance imaging are the two main modalities used for staging the local extent of the tumour and *Table 1* (Kosinski et al, 2012) enumerates their staging parameters. It is pertinent to be aware that both compliment careful per rectal palpation by an experienced surgeon able to perform the range of operations now appropriate in the optimal management of low rectal cancer.

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Table 1. Staging of rectal cancer

	Endorectal ultrasound	Magnetic resonance imaging
Rectal wall invasion	T1: Break in mucosa	T1: Smooth muscularis propria margin
	T2: Penetration through mucosa, thickening of muscularis propria	T2: Tumour penetrates muscularis propria; spiculation in mesorectal fat can be fibrosis, not tumour
	T3: Extension into perirectal fat	
	T4: Penetration into adjacent structure	T4: Abnormal signal extends into adjacent organ (loss of flat plane not sufficient) or into peritoneal space
Lymph node involvement	Round shape, irregular contour, proximity to primary tumour, size >5 mm	Findings of irregular contour and heterogeneous signal intensity are more accurate than size
Circumferential margin	Cannot be determined on endorectal ultrasound	Threatened circumferential margin if tumour or suspicious lymph node <1 mm from mesorectal fascia

From Kosinski et al (2012)

Endorectal ultrasound offers the convenience of being possible as an outpatient examination at the time of initial consultation but is technically difficult if the tumour is very low, very high or near obstructing (Kosinski et al, 2012). A meta-analysis showed endorectal ultrasound had similar sensitivity but higher specificity when compared with magnetic resonance imaging and computed tomography for detecting muscularis propria invasion (T1 *vs* T2). The authors found that magnetic resonance imaging tended to overstage T1 and understage T3 tumours and argued that when feasible endorectal ultrasound more accurately distinguished T1 from T2 and T2 from T3 tumours (Muthusamy and Chang, 2007). Other authors, however, believe that magnetic resonance imaging performed with high resolution can be equally useful and more beneficial in facilitating decision making because of its superior ability to assess abnormal nodes higher up and because it is more discriminating for defining pelvic anatomy (Brown et al, 2003a; MERCURY Study Group, 2006).

Lymph node involvement has been described as decreased echogenicity and round rather than oval shape on endorectal ultrasound, and increased signal intensity or inhomogeneity on magnetic resonance imaging (Brown et al, 2003b; Kim et al, 2004). Both endorectal ultrasound and magnetic resonance imaging share the risk of understaging small nodes. With 25% of positive lymph nodes measuring 3 mm or less, this can be problematic (Kosinski et al, 2012). In addition, endorectal ultrasound can fail to detect upper mesorectal lymph nodes in patients with obstructing lesions.

Close proximity or involvement of the mesorectal fascia by the cancer increases the risk of a positive circumferential resection margin (Kosinski et al, 2012). In low rectal cancer below the insertion of the levator, the mesorectum has tapered out and the margins are formed by the external sphincter which is one of the challenges of low rectal cancers at this level.

An involved circumferential resection margin is an independent adverse predictor of both local recurrence and survival (Quirke et al, 2009). High resolution magnetic resonance imaging can determine the mesorectal fascia with high accuracy (MERCURY Study Group, 2006). If the tumour is in close proximity to the mesorectal fascia (<1 mm), there is an increased risk of a positive circumferential resection margin and the margin is said to be threatened on magnetic resonance imaging (Brown et al, 2003a; Taylor et al, 2011a). The mesorectal fascia cannot be imaged by endorectal ultrasound. In addition, magnetic resonance imaging can detect vascular invasion which is a crucial prognostic factor for systemic recurrence (Smith et al, 2008a,b).

Taylor et al (2011b) found that high resolution magnetic resonance imaging could accurately and safely identify patients with rectal cancer who have a favourable prognosis and can be managed by surgery alone. Their definition of such a rectal cancer was one that had a clear circumferential resection margin on preoperative magnetic resonance imaging (tumour >1 mm to the mesorectal fascia), no evidence of extra-mural vascular invasion, and early T stage (spread less than 5 mm from bowel wall), regardless of N stage disease. A further refinement was to evaluate low rectal cancers by magnetic resonance imaging and categorize good prognosis rectal cancers as magnetic resonance imaging stage 1 or 2 (a tumour that was not encroaching into the intersphincteric plane or levators) which had very good outcomes compared with more advanced magnetic resonance imaging stage 3 and 4 (Shihab et al, 2011).

For systemic staging, a computed tomography scan of the chest, abdomen and pelvis is usually sufficient, although additional magnetic resonance imaging or in some cases functional imaging such as positive emission tomography computed tomography may be performed.

Preoperative (neoadjuvant) therapy in rectal cancer

Preoperative treatment, in the form of preoperative radiotherapy or radio-chemotherapy, is now alluded to as neoadjuvant therapy to distinguish from postoperative or 'adjuvant' therapy. There is ongoing debate as to the precise role of neoadjuvant therapy but increasingly complete agreement that not all patients will benefit, some may have serious harm, and therefore a selective approach is crucial. Part of the ongoing debate is that much of the evidence base for neoadjuvant therapy is based on experiences before the total mesorectal excision era where surgery was often suboptimal and local recurrence after rectal cancer surgery was common. It is important to note that there are no specific trials on low rectal cancer and any information on low rectal cancer is based on subset analysis of trials with cancers at all levels in the rectum. With this caveat the results can give some applicable information which may help in managing tumours of the low rectum.

The National Surgical Adjuvant Breast and Bowel Project R-01 and R-02 trials elucidated the role of radio-

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therapy in minimizing local recurrence in those patients with T3/T4 or N+ disease (Wolmark et al, 1988, 2000). However, these studies were performed before the recognized benefits of a total mesorectal excision surgical approach. Further high quality Swedish randomized trials (Pahlman and Glimelius, 1990; Cedermark et al, 1995; Swedish Rectal Cancer Trial, 1997; Martling et al, 2001) confirmed the benefits of a 5-day short course preoperative radiotherapy schedule. These studies were planned and recruited as total mesorectal excision was being embraced but was not a prerequisite for patient enrolment. The results showed a significant reduction in local recurrence with a smaller effect on overall survival but not when patients over 80 years old were treated. As might be expected there was no benefit in terms of controlling distant disease as radiotherapy is a loco-regional treatment.

Once it was appreciated that total mesorectal excision alone could decrease local recurrence to the same degree as neoadjuvant radiotherapy in the Swedish trials (Kosinski et al, 2012), the next major contribution was the Dutch total mesorectal excision trial whereby patients with 'operable' rectal cancer were randomized to either total mesorectal excision surgery alone or preoperative short course radiotherapy and subsequent total mesorectal excision surgery within a week (Kapiteijn et al, 2001). The Dutch total mesorectal excision trial demonstrated a treatment benefit in local recurrence reduction with neoadjuvant radiotherapy compared with total mesorectal excision surgery. Local recurrence rates were reduced from 11% in the total mesorectal excision alone group to 6% in the neoadjuvant treatment group with no benefit in overall survival.

This was further confirmed by the Medical Research Council CR07 trial. Patients were randomized to total mesorectal excision surgery or short course radiotherapy followed by total mesorectal excision. Patients in the surgery alone arm were allocated postoperative radiotherapy if the circumferential resection margin was involved. Again neoadjuvant radiotherapy significantly reduced local cancer recurrence (4.4% *vs* 10.6% at 3 years) (Sebag-Montefiore et al, 2009), but there was no difference in overall survival between the two groups, and the Cochrane review of relevant international trials came to similar conclusions (Fleming et al, 2011).

The Polish rectal cancer trial (Bujko et al, 2006) compared short course radiotherapy with long course preoperative chemo-radiotherapy and concluded that although long course treatment was associated with improved downstaging this was at the expense of greater toxicity, with no improvement in survival or local control. The side effects of radiotherapy can be significant and are both acute in impairing wound healing and long-term such as chronic diarrhoea, incontinence, infertility, sexual dysfunction, bowel obstruction, anastomotic stricture and second cancers (Ooi et al, 1999; Kosinski et al, 2012). It is therefore crucial to select patients appropriately for this treatment to avoid expense, treatment delay and associated toxicity (Birgisson et al, 2005).

There is considerable variation between and within countries in the proportion of patients receiving neoadjuvant treatment (Mathis et al, 2012). Most clinicians agree that neoadjuvant treatment is beneficial for margin threatened or positive disease and usually unnecessary for early T1 and T2 cancers. However, there are a large proportion of patients in between, who have intermediate risk tumours with good prognosis, who may not require neoadjuvant treatment and can be managed by surgery alone, and magnetic resonance imaging has been helpful in defining this group (Taylor et al, 2011b). Precise assessment of these patients before surgery may allow omission of preoperative radiotherapy, thus avoiding the its side effects.

With regard to low rectal cancer Mathis et al (2012) reported results in 655 patients who underwent curative surgery for rectal cancer without radiotherapy. Their study included 133 patients with stage III lymph node positive disease and 246 who had an abdomino-perineal excision. They found that the local recurrence rate for patients who had restorative surgery was 3.6%, not significantly different from the 5.5% in patients who had an abdomino-perineal excision. The study supports the concept that the use of radiotherapy should be selective and substantiates the argument that if low rectal cancer is completely excised with negative margins, the majority of patients will be cured by this treatment alone (Moore and Moran, 2012).

Surgical treatment of low rectal cancer

Curative surgery for rectal cancer may involve a dreaded aspect of colorectal surgery from a patient's perspective, namely formation of a stoma. Also, even if the sphincters are preserved, the combination of neoadjuvant therapy and a subsequently low anastomosis may result in suboptimal anal function and incontinence with a major impact on the quality of life. It is therefore crucial to choose the right operation for the right patient. The following article in this issue elaborates on ELAPE (extralevator abdomino-perineal excision) and its concept in low rectal cancer. This procedure has been found to be superior to the standard abdomino-perineal excision (West et al, 2008) as it removes more tissue at the level of the sphincter and decreases the chances of positive resection margins in low rectal cancer. ELAPE in itself, however, is not without risks of perineal wound morbidity; the best technique to minimize this is still under debate.

LOREC: The English Low Rectal Cancer National Development Programme

The English Low Rectal Cancer National Development Programme was initiated by the combined efforts of the UK Department of Health and the Association of Coloproctology of Great Britain and Ireland. The programme is organized and delivered by a group of national experts in colorectal surgery, oncology, pathology and radiology. The focus is to improve awareness in personnel treating patients with rectal cancer by improving multidisciplinary team cooperation in recognizing the com-

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plexity of low rectal cancer, optimizing maximum information from high resolution imaging to help with preoperative and operative decision making, selecting appropriate patients who will benefit from ELAPE, and focussing on management of resultant pelvic floor defects (Moore and Moran, 2012). The main aims of LOREC are to improve patient oncological outcomes and quality of life by appropriate choice of treatment and precise surgery by ELAPE performed by appropriately trained surgeons where indicated (Finan and Haboubi, 2012). The project also aims to reduce the use of neoadjuvant radiotherapy through better prediction of the local extent of disease using high resolution magnetic resonance imaging (Taylor et al, 2011b). **BJHM**

Conflict of interest: none.

Birgisson H, Pahlman L, Gunnarsson U, Glimelius B (2005) Adverse effects of preoperative radiation therapy for rectal cancer: long-term follow-up of the Swedish Rectal Cancer Trial. *J Clin Oncol* **23**: 8697–705

Brown G, Radcliffe AG, Newcombe RG et al (2003a) Preoperative assessment of prognostic factors in rectal cancer using high-resolution magnetic resonance imaging. *Br J Surg* **90**: 355–64

Brown G, Richards CJ, Bourne MW et al (2003b) Morphologic predictors of lymph node status in rectal cancer with use of high-spatial-resolution MR imaging with histopathologic comparison. *Radiology* **227**: 371–7

Bujko K, Nowacki MP, Nasierowska-Guttmejer A et al (2006) Long-term results of a randomized trial comparing preoperative short-course radiotherapy with preoperative conventionally fractionated chemoradiation for rectal cancer. *Br J Surg* **93**: 1215–23

Cedermark B, Johansson H, Rutqvist LE, Wilking N (1995) The Stockholm I trial of preoperative short term radiotherapy in operable rectal carcinoma. A prospective randomized trial. Stockholm Colorectal Cancer Study Group. *Cancer* **75**: 2269–75

Finan P, Haboubi N (2012) The Miles operation--extralevator abdominoperineal excision. *Colorectal Dis* **14**: 1171–2

Fleming FJ, Pahlman L, Monson JRT (2011) Neoadjuvant therapy in rectal cancer. *Dis Colon Rectum* **54**: 901–12

Heald RJ (1988) The 'Holy Plane' of rectal surgery. *J R Soc Med* **81**: 503–8

Heald RJ, Smedh RK, Kald A, Sexton R, Moran BJ (1997) Abdominoperineal excision of the rectum--an endangered operation. Norman Nigro Lectureship. *Dis Colon Rectum* **40**: 747–51

Kapiteijn E, Marijnen CA, Nagtegaal ID et al (2001) Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer. *N Engl J Med* **345**: 638–46

Kim JH, Beets GL, Kim M-J, Kessels AGH, Beets-Tan RGH (2004) High-resolution MR imaging for nodal staging in rectal cancer: are there any criteria in addition to the size? *Eur J Radiol* **52**: 78–83

Kosinski L, Habr-Gama A, Ludwig K, Perez R (2012) Shifting concepts in rectal cancer management: a review of contemporary primary rectal cancer treatment strategies. *Cancer J Clin* **62**: 173–202

Martling A, Holm T, Johansson H et al (2001) The Stockholm II trial on preoperative radiotherapy in rectal carcinoma: long-term follow-up of a population-based study. *Cancer* **92**: 896–902

Mathis KL, Larson DW, Dozois EJ et al (2012) Outcomes following surgery without radiotherapy for rectal cancer. *Br J Surg* **99**: 137–43

MERCURY Study Group (2006) Diagnostic accuracy of preoperative magnetic resonance imaging in predicting curative resection of rectal cancer: prospective observational study. *BMJ* **333**: 779

Moore TJ, Moran BJ (2012) Precision surgery, precision terminology: the origins and meaning of ELAPE. *Colorectal Dis* **14**: 1173–4

Morris E, Quirke P, Thomas JD et al (2008) Unacceptable variation in abdominoperineal excision rates for rectal cancer: time to intervene? *Gut* **57**: 1690–7

Morris EJA, Birch R, West NP et al (2011) Low abdominoperineal excision rates are associated with high-workload surgeons and lower tumour height. Is further specialization needed? *Colorectal Dis* **13**: 755–61

Muthusamy VR, Chang KJ (2007) Optimal methods for staging rectal cancer. *Clin Cancer Res* **13**: 6877s–6884s

Ooi BS, Tjandra JJ, Green MD (1999) Morbidities of adjuvant chemotherapy and radiotherapy for resectable rectal cancer: an overview. *Dis Colon Rectum* **42**: 403–18

Pachler J, Wille-Jorgensen P (2005) Quality of life after rectal resection for cancer, with or without permanent colostomy. *Cochrane Database Syst Rev* **2**: CD004323

Pahlman L, Glimelius B (1990) Pre- or postoperative radiotherapy in rectal and rectosigmoid carcinoma. Report from a randomized multicenter trial. *Ann Surg* **211**: 187–95

Quirke P, Steele R, Monson J et al (2009) Effect of the plane of surgery achieved on local recurrence in patients with operable rectal cancer: a prospective study using data from the MRC CR07 and NCIC-CTG CO16 randomised clinical trial. *Lancet* **373**: 821–8

Salerno G, Daniels IR, Moran BJ, Wotherspoon A, Brown G (2006) Clarifying margins in the multidisciplinary management of rectal cancer: the MERCURY experience. *Clin Radiol* **61**: 916–23

Salerno G, Chandler I, Wotherspoon A et al (2008) Sites of surgical wasting in the abdominoperineal specimen. *Br J Surg* **95**: 1147–54

Sebag-Montefiore D, Stephens RJ, Steele R et al (2009) Preoperative radiotherapy versus selective postoperative chemoradiotherapy in patients with rectal cancer (MRC CR07 and NCIC-CTG C016): a multicentre, randomised trial. *Lancet* **373**: 811–20

Shihab OC, Heald RJ, Rullier E et al (2009) Defining the surgical planes on MRI improves surgery for cancer of the low rectum. *Lancet Oncol* **10**: 1207–11

Shihab OC, Taylor F, Salerno G et al (2011) MRI predictive factors for long-term outcomes of low rectal tumours. *Ann Surg Oncol* **18**: 3278–84

Smith NJ, Barbachano Y, Norman AR et al (2008a) Prognostic significance of magnetic resonance imaging-detected extramural vascular invasion in rectal cancer. *Br J Surg* **95**: 229–36

Smith NJ, Shihab O, Arnaout A, Swift RI, Brown G (2008b) MRI for detection of extramural vascular invasion in rectal cancer. *Am J Roentgenol* **191**: 1517–22

Swedish Rectal Cancer Trial (1997) Improved survival with preoperative radiotherapy in resectable rectal cancer. *N Engl J Med* **336**: 980–7

Taylor FGM, Quirke P, Heald RJ et al (2011a) One millimetre is the safe cut-off for magnetic resonance imaging prediction of surgical margin status in rectal cancer. *Br J Surg* **98**: 872–9

Taylor FGM, Quirke P, Heald RJ et al (2011b) Preoperative high-resolution magnetic resonance imaging can identify good prognosis stage I, II, and III rectal cancer best managed by surgery alone: a prospective, multicenter, European study. *Ann Surg* **253**: 711–19

West NP, Finan PJ, Anderin C et al (2008) Evidence of the oncologic superiority of cylindrical abdominoperineal excision for low rectal cancer. *J Clin Oncol* **26**: 3517–22

Wibe A, Syse A, Andersen E et al (2004) Oncological outcomes after total mesorectal excision for cure for cancer of the lower rectum: anterior vs. abdominoperineal resection. *Dis Colon Rectum* **47**: 48–58

Wolmark N, Fisher B, Rockette H et al (1988) Postoperative adjuvant chemotherapy or BCG for colon cancer: results from NSABP protocol C-01. *J Natl Cancer Inst* **80**: 30–6

Wolmark N, Wieand HS, Hyams DM et al (2000) Randomized trial of postoperative adjuvant chemotherapy with or without radiotherapy for carcinoma of the rectum: National Surgical Adjuvant Breast and Bowel Project Protocol R-02. *J Natl Cancer Inst* **92**: 388–96

KEY POINTS

- Multimodal treatment of rectal cancer has improved outcomes for this complex but eminently curable disease.
- High resolution magnetic resonance imaging plays an important role in the accurate staging and preoperative planning of neoadjuvant treatment.
- In selected patients extra-levator abdomino-perineal excision is the surgical procedure of choice.
- The objectives of the English Low Rectal Cancer National Development Programme are based on principles that revolve around enhancing patient-centred multidisciplinary team decision making, optimizing operative technique, minimizing postoperative complications and improving quality of life and oncological outcomes.

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