

# The role of the pathologist

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## Introduction

The opening years of the 21st century are seeing a revolution in the management of rectal cancer. The disease has changed from a surgically managed disease with contributions from other colleagues to the requirement for management by a highly skilled truly multidisciplinary team. Discussion now needs to occur between all team members and the opportunity for multidisciplinary learning is unrivalled in any other cancer.

What is the role of the pathologist in this condition? Firstly it must be said that good pathology can directly save lives and improve management. Pathologists contribute to the prognosis given to the patient, the audit and learning processes of surgeons and radiologists, and the postoperative treatment plan of the oncologists. They are also critical to driving our understanding of the biology of the disease and possibly the prediction of the types of therapy that the patient might respond to. This article will concentrate on the function and role of the pathologist in the multidisciplinary team (MDT) namely improving routine pathology, the importance of the circumferential margin, the assessment of the quality of surgery, new insights into the resection of low rectal cancer and the abdomino-perineal resection. It will also contain a discussion of the assessment of the rectal cancer post chemoradiotherapy and will also touch on the need for an effective method of developing new international staging methods.

## Improving routine pathology

A number of audits have demonstrated the poor quality of routine pathology in day to day practice [1–3]. The Welsh CROPS study [2,3] revealed that only 78% of colonic cancer reports and 46.6% of rectal cancer reports included all of the data required to manage the patient.

A regional audit performed in Trent that is unpublished also showed poor reporting of this disease.

Reports from other European countries such as Sweden and Belgium also suggest that the standard of pathology could be improved. The importance of the circumferential margin and local recurrence was first reported in 1986 but in 1997 was only reported in 51.5% of cases in the CROPS study [3]. Extramural vascular invasion and peritoneal involvement are also frequently under-reported yet directly contribute to the adjuvant treatment of colorectal cancer. With increasing benefits and the costs of newer adjuvant regimens the indications for treatment need to be refined and made increasingly robust.

How can this be done? Firstly education programmes are important. These can occur through new trials and the education processes that are put in place to set the standards within these trials. Whilst these initiatives have a positive effect they are not guaranteed to permeate through the whole system. Guidelines are important and there should be national or preferably international guidelines for the dissection and reporting of colorectal cancer. These need to be ‘minimum’ in that they only require the essential information for the management of patients. They need to be widely owned and require widespread consultation in their drafting and in their acceptance and, most importantly, they need an excellent evidence base and a clear policy for their content. In recognition of the importance of standards in this area the Royal College of Pathologists in the United Kingdom have created minimum datasets that have undergone widespread consultation with colleagues and professional bodies. In 1998 dissection guidelines and a colorectal minimum dataset for colorectal cancer were produced and this has gained widespread acceptance as the minimum standard for reporting this disease. It is available on the web at <http://www.rcpath.org/resources/pdf/colorectalcancer.pdf> [4]. This is currently in the process of being updated and will appear on this website when approved. Minimum datasets act as *aide memoirs* to pathologists as well as recording the absence of features that might otherwise not be recorded. They act as an excellent summary and can be used in conjunction with free text reports.

Most importantly they can be used as an audit tool and allow monitoring of standards of reporting. Using this method in Yorkshire we have been able to demonstrate a year-on-year improvement in the quality of reporting in over 5500 colorectal cancer patients [5]. Major improvements in the frequency of recording information, the number of lymph nodes found, extramural vascular invasion and peritoneal involvement have all been found. In the Welsh CROPS study 1044 reports were analysed in the study arm using proforma reporting and 998 in the control arm of free text reports. Use of pre-defined forms led to a 28.4% increase in complete reporting of the minimum dataset required for cancer registration and a 24.5% increase in complete reporting of minimum data required for patient management [3]. Form-based reporting was acceptable to pathologists and preferred by clinicians. This has also been seen by others [6]. In conclusion, guidelines and computerised forms significantly improve the quality of histopathology reporting. This form of dataset is in use for surgeons and pathologists but the adoption of such strategies into radiology and oncology would be very welcome, building up a picture of the quality of all arms of the multidisciplinary team. It is better to consider team performance when assessing patient outcome as no one specialty can function in isolation.

Improving the dissection of rectal cancer is important. It is essential that senior pathologists are involved in the day-to-day activity in the cut up room, teaching trainees and raising standards amongst their colleagues. In the United Kingdom each Hospital has a lead pathologist who is responsible for the performance of their colleagues in their day-to-day practice in colorectal cancer and regular audits must be undertaken to provide evidence of the quality of their practice. This may sound like a police state but poor practice loses opportunities to reduce the morbidity and mortality from this condition. If we do not monitor our own performance then others will demand to do so.

The macroscopic examination of the specimen is critical. From this an understanding of the anatomy and its variability can be obtained. The size and shape of the mesorectum are different between patients. In some individuals the mesorectum is small, increasing the risk of surgical CRM involvement by smaller tumours whereas in others tumours can be quite advanced before they encroach on the margin. Figure 1



Fig. 1. Difference between the volumes of the mesorectum in two different individuals. Both were dissected and photographed at the same time and to the same 1-cm scale. The specimen on the left is much smaller and a lesser degree of tumour spread would be needed to generate an involved margin.

shows an example of a small and large mesorectum with the associated cross sections. It should be noted that the mesorectum is thinnest anteriorly between 15:00 and 21:00 hours and it is here surgeons must operate most carefully. The size of the mesorectum can be identified on MRI as can the shape of the pelvis. Attempts are currently being made to develop markers of the difficulty of surgery from anatomical structures on an MRI scan [7].

### Dissection of the specimen

On receipt the anterior and posterior surfaces should be photographed to record any perforation and the plane of the surgical dissection. The specimen is opened except for the area of the tumour to preserve assessment of the anterior aspect of the rectum where CRM involvement or peritoneal involvement may be seen most frequently. The surgically-created margin surfaces are painted with ink. The surgically-created surface of the mesorectum is larger posteriorly and extends up to a higher level than it does anteriorly. The specimen should be fixed in formalin for 72 hours or longer. It should then be described and the tumour thinly sliced (3–5 mm) transversely to a minimum of 2 cm below to 2 cm above the tumour. Good fixation allows thinner slices to be taken and thus a better assessment of tumour spread. There is usually no hurry to make a decision about further therapy and adequate time to examine the specimen should be repaid by a better, more detailed report. The slices should also be photographed as a valuable demonstration of the quality of the surgery and for comparison with the transverse MRI images. An assessment of the quality of surgery of the mesorectum should be made by

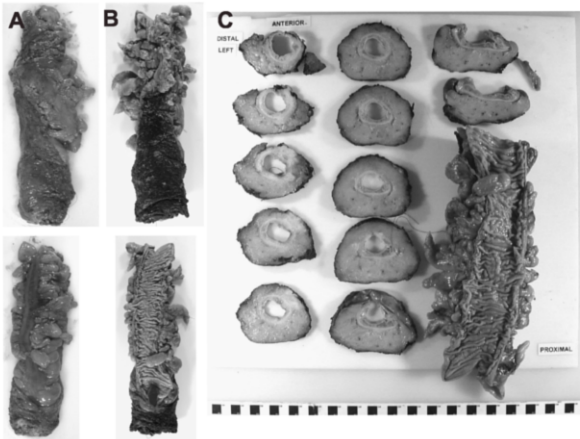


Fig. 2. Dissection method. (A) the fresh, opened, uninked surgical resections; (B) the same after fixation and inking; and (C) after creating the cross sections of the rectum.

the reporting pathologist and in abdomino-perineal excisions of the tissue anal canal and levators if present (Fig. 2).

The distance of direct tumour spread outside the muscularis propria should be recorded and the area in which tumour spreads closest to the CRM should be macroscopically identified. Blocks should be taken from the area closest to the circumferential margin and any area where the tumour extends to within less than 3 mm from the margin. Any area identified as interesting by the radiologist should also be sampled. Other blocks should be taken to allow at least 5 blocks of tumour to confirm presence or absence of extramural venous invasion. It is preferable to use large whole mount sections but if the resources are not available then standard blocks can be used. Preparing large whole mount blocks facilitates comparison with the MRI image and also allows a larger volume of tissue to be easily examined. The number of large blocks containing tumour can be subtracted from the minimum of 5 tumour blocks. Likewise the peritoneal surface should be sampled by a minimum of 2 blocks if the tumour impinges on it and levels cut if required.

The circumferential margin is considered involved if the tumour extends to within 1 mm of the circumferential excision margin. No distinction is currently made between the various modes of involvement, e.g. direct spread, lymph node spread, vascular, etc. as all have shown an increased local recurrence rate [8]. Involvement by tumour within a lymph node does have a lower rate of recurrence but this has not been studied widely enough at present to provide adequate data; thus, it should be considered as margin involvement. A measurement at 1 mm or less is considered incompletely excised.

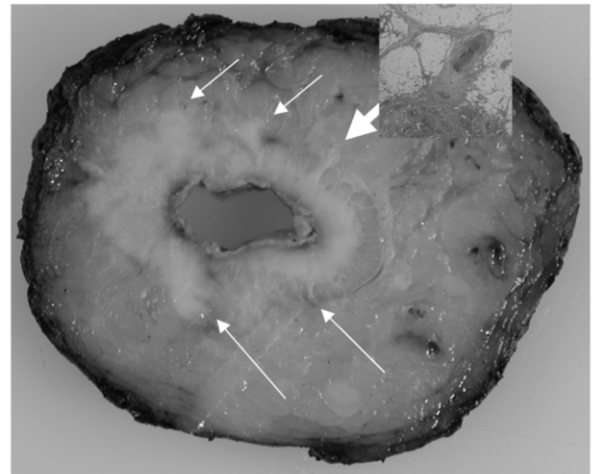


Fig. 3. Arrows showing areas of confirmed extramural vascular invasion in a cross section of a rectal carcinoma.

The assessment of the completeness of excision and the planes of the surgical approach are important. The fine cross slicing of a well fixed specimen will repay close examination. It is possible to macroscopically recognise intramural and extramural vascular invasion and to identify areas at high risk of extramural vascular invasion (EMVI) and peritoneal involvement (PI) by taking into account the anatomy of the colon and rectum. In Fig. 3 the arrows show tumour extending along the sites of exit of the large intramural veins from the rectum.

The comparison of MRI images with the macroscopic and whole mount microscopic blocks will improve preoperative staging and thus the management of patients. This is an important role of the pathologist and is facilitated by having the photographs available for display at the MDT meeting. To facilitate radiological learning we are involved in a study to allow the creation of a teaching set of MRI images that have high resolution digital images of the whole mount pathology embedded in them. These will then be ultimately presented over the web. A development site can be seen at <http://www.virtualpathology.leeds.ac.uk> [9]. It will also be possible to develop histopathological training packages using virtual slides to provide feedback to colleagues over their ability to recognise important features such as extramural vascular invasion or peritoneal involvement. Figure 4 shows one way of presenting virtual slides on the web. These can be opened up to give full histopathological resolution up to a magnification of  $\times 800$ .

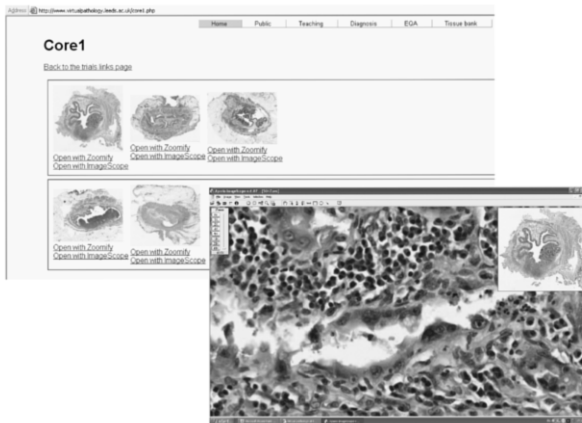


Fig. 4. A virtual slide of one of a set of whole mount sections of rectal cancer. The image has been opened via the internet from a remote site showing the level of resolution available by this new technology.

### *The importance of the surgical circumferential margin*

Surgeons create margins that can be involved by tumour spread at a variety of sites. The most well known are of course the proximal and distal margins of a resection. However surgeons are taught to avoid involvement of these margins and only 1–2% of cases in randomised trials show involvement. A further margin is the mesenteric margin where the surgeon devascularises the bowel. This is infrequently examined but we know that tumour is close to it in 8% of cases as involvement of the highest lymph

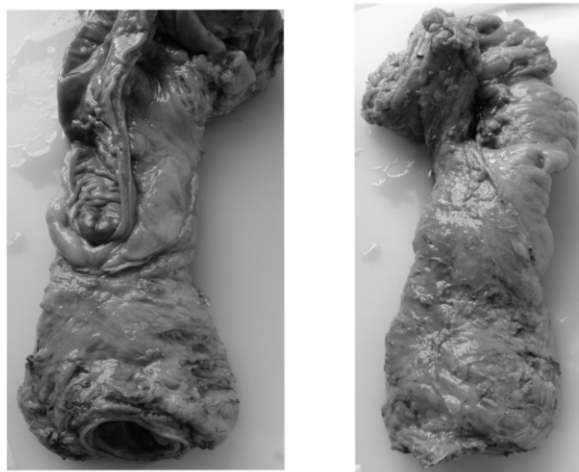


Fig. 5. The large surgical CRM created at operation on an anterior resection with a full total mesorectal excision. Anteriorly the surgical CRM lies below the peritoneal reflection but posteriorly it has a much larger surface area and can be involved by tumour spread high in the rectum.

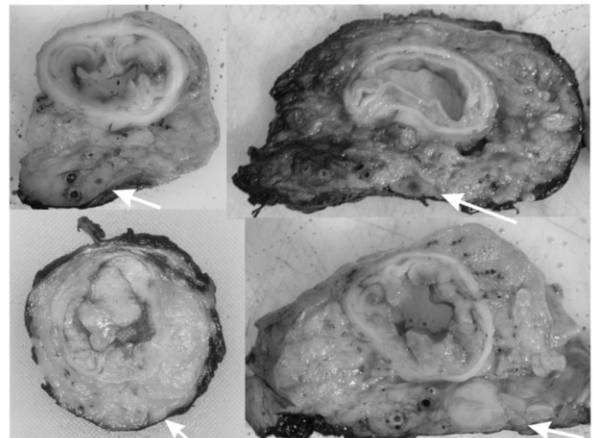


Fig. 6. Lymph nodes lie against the posterior and sometimes the anterior CRM and care needs to be taken to remove the whole of the mesorectum otherwise there is an increased risk of leaving tumour behind. In node positive cases extranodal spread can occur resulting in involvement.

node (stage Dukes C2) is recorded when reporting according to Dukes [5].

By far the most important margin is that created along the rectum or colon. The surgical circumferential margin is largest in the rectum but also occurs elsewhere notably the ascending colon and caecum. Figure 5 shows the anterior and posterior surfaces of the rectum. This margin is under threat by direct involvement but also by the incomplete removal of lymph nodes that lie just under the mesorectal fusion. Four examples of this are shown in Fig. 6. All of these lymph nodes are very very close to the mesorectal fusion and any small deviation from the correct surgical plane could enter them, potentially compromising cure.

### *Involvement of the circumferential margin*

In 1986 we were able to demonstrate the relationship of tumour involvement of this margin with local recurrence and survival [10]. Subsequent studies by us and others [11–17] have shown that local recurrence is greatly increased and survival halved when tumour can be demonstrated within 1 mm of the surgical plane of resection. Knowledge of the importance of this margin and its status in any individual is critical to the management of rectal cancer patients. For the radiologist they must predict whether surgical clearance is possible, the surgeon must follow the correct mesorectal planes and, if necessary, extend their operation outside the plane. Also, the pathologist needs to judge the success of prediction and the subsequent operation. Unfortunately we still do not know whether long-course radiation or radiochemotherapy

benefits patients with involved margins. The recent Dutch study suggests that short course radiotherapy is an inadequate treatment [18].

The evidence base for the importance of the surgical CRM is now established. Over 4,000 patients have been reported in a range of studies from audits [5,10,12,16,17], prospective interventions [14], and a randomised clinical trial [15]. Two further randomised clinical trials are either in follow-up MRC CLASICC [19,20] or still open (MRC CR07) [21] and MERCURY [22], which compares MRI prediction to gold standard histopathology is in follow-up. All report higher local recurrences when clearance is less than 1 mm and lower survivals. Only the Dutch study suggests the limit should be 2 mm [15] but this is a small group of 54 patients and is not confirmed in other studies [5,10–14,16,17].

The recording of the frequency of involvement of the surgical CRM is important for feedback to radiologists for accuracy of prediction as well as to the surgeon and patient as an indicator of the quality of surgery. We have produced evidence that reducing the frequency of CRM involvement by improving surgical technique improves survival for a single surgeon [9]. What is an acceptable frequency of margin involvement? This depends on the group of patients included in the study. In a population-based study in Yorkshire the rate is 27% in 1200 rectal cancers of all stages. With modern radiology and the appropriate use of radiochemotherapy this appears to be able to be halved [22]. In 400 patients in the MRC CLASICC study it was 14% [20]. If curative studies are investigated then in 656 patients treated by total mesorectal excision (TME) alone the rate is 18.3% [15], in the first 900 patients in the current MRC CR07 study [21] is 13% and 9.4% in 686 patients undergoing curative TME operations in the Norwegian prospective audit [14]. In this latter study, those undergoing conventional operations i.e. non-TME, were excluded. What is certain is that the rate of involvement must be reduced and that it is possible to do so with good MRI, optimal surgery and excellent pathology and this is a good tool to gauge the quality of surgery within a large population-based study or trial.

### Quality of surgery

We first introduced the concept of pathological audit of the quality of surgery in the MRC CLASICC [19] and MRC CR07 [21] studies. These have recruited slowly but the concept was adopted in the Dutch

TME trial [18] and we have early evidence of its value [23]. In spite of extensive surgical training only 57% of cases were judged to be good/complete excisions with nearly one quarter of all cases (24%) assessed as a poor/incomplete excision. In CRM-positive patients, this assessment did not add to the prediction of local recurrence above CRM involvement alone. However, in patients with a negative CRM the overall recurrence rate was doubled from 15% to 29% and survival was decreased from 91% to 77% ( $p < 0.05$ ) in incomplete resections (Grade 1) (data not shown). This small study shows that good or average resections conferred a better outcome on patients and that there was a significant relationship between the quality of the resection and the amount of clearance of the tumour. An increased frequency of margin involvement was seen in tumours ‘incompletely’ removed by poor surgery with 44% of incomplete resections having CRM involvement as opposed to 27% of complete resections. In MRC CR07 and Mercury this data is being collected prospectively and over 1000 assessments have been recorded. We await the closure of CR07 and follow-up of both trials. Since first developing this audit tool we have performed further work on low rectal cancer and refined the assessments. This will be described below after a discussion of low rectal cancer.

### Low rectal cancer

We reviewed the outcomes of the abdominoperineal resections (AP) and anterior resections (AR) performed in Leeds [17] showing that over a 12-year period APs had a much higher frequency of involvement of the CRM than ARs (36.5% vs 22.3%). When other series are investigated this is also seen in the MRC CLASICC series 21% vs 10% [20], Norwegian audit (12% vs 5%) [24] and the Dutch RT study (29% vs 13%) [25]. Recent data from the Mercury study also shows that tumours below 6 cm show a much higher frequency of involvement of the surgical CRM in APs than ARs at the same length (33% vs 13%) [26]. This is in the context of higher quality surgery performed by functioning multidisciplinary teams in this study. The frequency of involvement of this margin has not decreased with the increasing frequency of TME. In the Leeds study [17], a Norwegian audit (local recurrence: APs 15% vs ARs 10% and survival APs 55% vs ARs 68%) [24] and a Yorkshire audit where local recurrence was higher and survival poorer in APs vs ARs (6.7% poorer survival) [27].

What are the causes of this increased frequency of margin involvement in low rectal cancer? Firstly we

believe it is due to the anatomy of the low rectum. The mesorectum terminates abruptly between 2 and 6 cm from the anal verge. It thins and disappears. The rectum is then bounded by the levators, sphincters and associated ischiorectal fat. It is these structures that need to be considered to reduce the rate of margin involvement in low rectal cancer.

With upper and mid-third cancers surgeons performed a variety of operations that were called by them TME or an anterior resection. The same situation is seen when considering AP operations. An abdominoperineal excision can be performed predominantly from above or from below and can entail the removal of the tumour by the surgeon following one of a number of surgical planes. Progress can only be made in understanding the issues by defining the operative types and the planes they use for removal and then comparing their effectiveness at ensuring a tumour free margin and ultimately local recurrence, improved survival and morbidity.

The classical AP entails removal of the mesorectum and the area of the tumour from above. The planes followed are the mesorectal fascia and coning in onto the surface of the sphincters. The anus is then removed from below. This operation means that the most difficult part of the operation, the removal of the area of tumour and its local tissue is performed from above. Thus the surgeon has poor vision of the area of removal and the surgery is taking place right at the bottom of the pelvis often in difficult circumstances. This leads to the creation of irregular surgical planes and an increased risk of perforation. The alternative approach and that followed by Mr T Holm and shown elsewhere [17] at the Karolinska is to dissect to the level of the seminal vesicles or an equivalent height in the female and to then stop. The main dissection and especially the area around the tumour is dissected from below. Thus there is good surgical access with optimum vision and the planes are easier to identify. It is possible to extend the operation to remove the coccyx if necessary and thus a more regular and cylindrical specimen is produced. The two surgical approaches also differ for one good reason. From below the levators are removed wide and left attached to the specimen forming increased protection for the CRM whereas from above the levators are incised on the sphincter muscle reducing the surgical clearance at this level. The perineal approach should reduce margin involvement and local recurrence. The effect of removal of more perineal tissue can be solved by the swinging of gluteal flaps or, if necessary, anterior abdominal flaps [28].

We have audited the type of AP performed in both the Dutch [25] and Mercury studies and these confirm the most frequently performed operation is the abdominal approach leading to waisted specimens with the CRM on the sphincter muscle. With this approach the CRM is frequently involved, perforation is far too frequent and the CRM is at the level of the muscle or worse in 1/3 of all cases. The avoidance of CRM positivity and perforation in APs should improve outcome. Review of the Norwegian experience of rectal cancer from 1993 to 1999 showed perforation in 16% of APs vs 4% of ARs in 2873 patients [29]. In a multivariate analysis, the risk of perforation was significantly greater in patients undergoing AP (odds ratio, 5.6) and in those aged 80 years or more (odds ratio, 2.0). The 5-year local recurrence rate and survival were 28.8% and 41.5% following perforation, compared with 9.9% and 67.1% in patients with no perforation.

#### *Assessment of the quality of surgery (Fig. 7)*

The mesorectum and the levator area and anal canal should be graded separately. Thus for an anterior resection there will only be one grade – the grade for the mesorectum. For APs there will be a grade for the mesorectum and a further grade for the levator canal area below the mesorectum.

#### *Quality of resection of the mesorectum*

The quality of a mesorectal resection can be easily assessed. The best description is that of the plane of surgery which for the mesorectum can be one of three. Dissection either taking place in the plane of the mesorectal fascia, within the mesorectum itself or entering onto the muscularis propria:

- (1) Mesorectal fascial plane: the mesorectum should be smooth with no violation of the fat, good bulk to the mesorectum anteriorly and posteriorly and the distal margin should appear adequate with no coning near the tumour. No defect should be more than superficial or 5 mm deep.
- (2) Intramesorectal plane: moderate bulk to mesorectum but irregularity of the mesorectal surface. Moderate coning of the specimen towards the distal margin. At no site is the muscularis propria visible with the exception of the area of insertion of levator muscles. Moderate irregularity of the CRM.
- (3) Muscularis propria plane: there will be areas of substantial loss of mesorectal tissue. Deep cuts and tears down onto the muscularis propria will be present. On cross section there will be a very

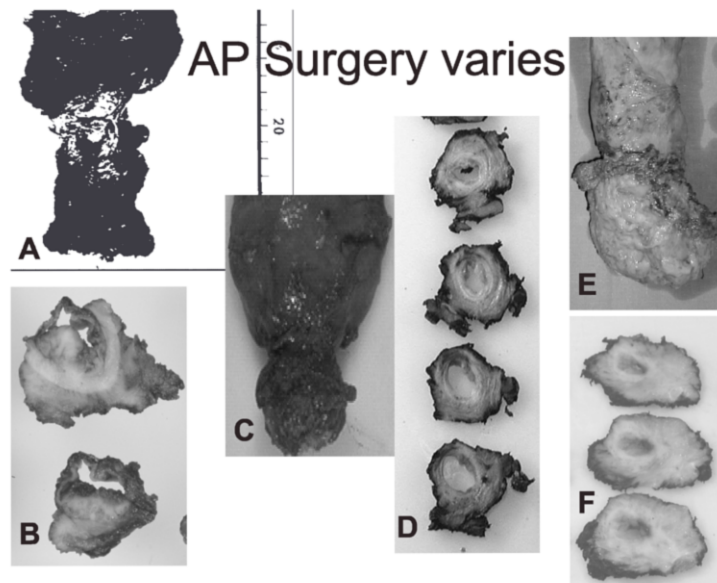


Fig. 7. Variation in the quality of surgery in low rectal cancer: (A) a perforation through a tumour in the anal canal; (B) a cross section of the anal canal where the surgical resection margin lies in the submucosa; (C) a typical operation with a waist in the area of the anal canal and only a small area of levator attached; (D) typical cross sections of a low rectal tumour with the CRM on the muscular wall; (E) a cylindrical specimen created by Dr T. Holm of the Karolinska Hospital, Stockholm; (F) the cross sections of this specimen revealing the greater bulk of this type of approach.

irregular CRM with little bulk to the mesorectal fat and the muscularis propria will form the CRM in places.

Although also called either a grade from 1 to 3 or complete-partially complete-incomplete this classification has been used in CR07 [21] and CLASICC [19] trials and shown to predict a higher risk of local recurrence in the Dutch TME trial [23]. The frequency of CRM involvement can also be determined for surgeons and it is likely that this is a good early determinant of the quality of surgery and subsequent risk of local recurrence [8].

#### *Assessment of the levator/anal canal area*

The quality of surgery of the levator/anal canal area below the mesorectum can also be assessed by a description of the plane of surgery:

**Levator plane:** the surgical plane lies external to the levators with them being removed en-bloc with the specimen. This creates a cylindrical specimen with the levators forming an extra protective layer on the sphincters.

**Sphincteric plane:** either there are no levator muscles attached to the specimen or only a very small cuff and the resection margin is on the surface of the sphincters. The specimen has a waisted/apple core appearance

**Intrasphincteric/submucosal plane:** the surgeon has inadvertently entered the sphincters or even deeper

into the submucosa or perforated the specimen at any point.

Thus for an AR there will be a single mesorectal grade and for an AP there will be two grades one for the mesorectum and one for the anal canal as summarised in Table 1.

Table 1  
Grading of rectal cancer specimens. One grade for TME and two grades for APs

Mesorectal Excision	Abdomino-Perineal Excision
	(Mesorectal plus anal canal grade)
<b>Mesorectum</b>	<b>Anal canal</b>
Mesorectal plane (smooth surface)	Levator plane/cylindrical
Intramesorectal plane (irregular surface)	Sphincteric plane/waisted
Muscularis propria	Intrasphincteric/submucosa/perforation

#### **Preoperative chemo-radiotherapy**

There is now good evidence that preoperative chemo-radiotherapy is able to downstage rectal tumours. In around 8–30% of cases this can lead to complete destruction of tumour cells. Early data suggests that local control can be greatly improved and this may translate into improved long-term survival. There are



a number of suggested methods for assessing such regression [30,31] which are modifications of the scoring system developed by Mandard et al. [32] for oesophageal carcinoma. The Dworak system was assessed in a preoperative 5FU plus radiotherapy study by Rodel et al. [33] with complete loss of tumour cells and the presence of very few tumour cells (defined as difficult to find microscopically), leading to a 72% relapse free survival vs 28% in the tumours showing less regression. In an accelerated radiotherapy schedule Bouzourene et al. [31] showed that the presence of rare tumour cells was associated with a similar disease free survival of 75% vs 25–50% for the other groups. They had no cases of complete regression but surgery was performed rapidly after therapy. Thus, using similar grading systems the presence of very few or no tumour cells was associated with a much better outcome after therapy. It may be possible to simplify this into tumours that show an *excellent response*, i.e. no residual tumour cells or tumour cells that are difficult to find microscopically (Dworak 4 and 5 or Bouzourene/Mandard 1 and 2) vs those with a *poor response* with easily identifiable tumour cells or no response at all (Dworak 0, 1 and 2 or Bouzourene/Mandard 3, 4 and 5). The importance of this approach has been recently confirmed in an excellent study of preoperative radiochemotherapy vs postoperative radiochemotherapy [34]. Using 5FU plus radiotherapy they obtained an 8% complete response rate but more importantly they demonstrated a significant relationship between the degree of regression and survival in the context of a prospective randomised trial (German Rectal Cancer Study Group, pers. Commun.). No regression was seen in 7%, minimal regression in 19%, moderate regression in 15% and good regression in 51%. Complete regression had the best 5-year survival followed by good regression but no separation of the curves occurred for the other groups. From recent unpublished data it appears likely that achieving a clear margin is an important predictor of outcome and may be more important than a complete response. In 112 patients local and distant recurrence occurred in 7% and 22% of CRM negative patients and 43% and 57% of CRM positive patients after chemoradiotherapy [35].

Complete response is increasingly being used as an end-point in studies of radiotherapy and radiochemotherapy. At a meeting of European pathologists for the recent phase II CORE study [36] we have defined a pathological protocol for the trial to be followed before classifying a tumour as having undergone a complete response. It was agreed that where tumour cells cannot be found anywhere in

the specimen on the first assessment that the whole area of the tumour will be embedded. Should no further tumour cells be seen then three levels will be taken and examined from each tumour block. If after these assessments no tumour cells are identified then the tumour should be considered to have undergone a complete response. Further levels should not be taken as it is important to standardise the degree of effort made to find the presence of tumour. All future protocols need to accurately define the pathology protocol as this has the potential to greatly change the frequency of complete response. It is very tempting for pharmaceutical companies to use an inferior pathology protocol to inflate their complete response rate compared to others.

In conclusion we would agree wholeheartedly with the recent statement of Madoff [37] that the best outcomes can only be achieved when the interlocking care of multiple specialists is routinely provided. One of these key specialists is the pathologist and every team must have a knowledgeable individual providing high quality opinions.

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