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A qualitative study of the development of a multidisciplinary case conference review methodology to reduce involved margins in pelvic exenteration surgery for recurrent rectal cancer

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Abstract

Aim Pelvic exenteration surgery remains the only curative option for recurrent rectal cancer. Microscopically involved surgical margins (R1) are associated with a higher risk of local recurrence and decreased survival. Our study aimed to develop a *post hoc* multidisciplinary case conference review and investigate its potential for identifying areas for improvement.

Method Patients who underwent pelvic exenteration surgery for recurrent rectal cancer with R1 resections at a tertiary referral centre between April 2014 and January 2016 were retrospectively reviewed from a prospectively maintained database. Patients with non-rectal cancers or who underwent palliative surgery were excluded. Cases, imaging and histopathology were evaluated by a dedicated panel including colorectal surgeons, an abdominal radiologist and a gastrointestinal pathologist.

Results R1 resections were reported in 32 of 110 pelvic exenterations. Patients with other tumours were excluded and one patient had a palliative resection. Nine male patients with 11 exenterations were included with a median age of 56 years. All patients had positive soft tissue margins, and one patient also had an involved bony margin. Failures were due to (interdisciplinary) communication problems, specific management of tumour biology (multifocality, spiculated tumours), which can lead to radiological under-calling, and inadequate surgical technical planning. In hindsight, surgery would have been withheld from one patient.

Conclusion A retrospective multidisciplinary case evaluation of pelvic exenteration patients with involved surgical margins led to a list of recommendations which included the need to plan for wider surgical soft tissue resections and improvement in interdisciplinary communication. Lessons learned may increase clear margin rates in future resections.

Keywords Pelvic exenteration, recurrent rectal cancer, surgical margin, involved margin, histopathology, imaging

What does this paper add to the literature?
This study shows that a retrospective multidisciplinary case conference for patients with rectal cancer who underwent pelvic exenteration with involved margins results in practical recommendations. Our format can be used to identify general or local areas for improvement and may help to increase clear margin rates and thereby survival.

Introduction

Patients with recurrent rectal cancer may be suitable to undergo pelvic exenteration surgery with curative intent. Previous results showed that clear operative

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margin rates of up to 74% are feasible for patients who undergo pelvic exenteration combined with sacral resection for recurrent rectal cancer [1]. Achieving clear margins has significant benefit for patients in terms of local control and survival compared to patients with microscopically (R1) and macroscopically (R2) involved margins, with median survival rates of 45 months *vs* 19 and 8 months, respectively [1]. Similar outcomes were recently reported by an international collaborative group, showing median survival rates of 43 months *vs* 21 and 10 months, respectively [2].

Factors influencing the extent of surgical resection, and thereby the chances of achieving clear margins, include preoperative radiological imaging, surgical technical planning and intra-operative pathological results (i.e. frozen section margin assessment).

Our study aimed to develop the methodology of a *post hoc* multidisciplinary case conference review of patients who underwent pelvic exenteration with microscopically involved margins. Furthermore, we investigated its potential for identifying potential areas for improvement for all disciplines involved in the perioperative process.

Method

Patients who underwent pelvic exenteration surgery with microscopically involved surgical margins at a tertiary level exenteration unit between April 2014 and January 2016 were retrospectively reviewed from a prospectively maintained database. All patients consented to the use of their data. The study was exempted from Institutional Review Board review. This period was chosen because all multidisciplinary team meeting correspondence was electronically available from April 2014 onwards. Exenterations performed for recurrences during follow-up of these patients after January 2016 were also included in the analyses. Microscopically involved margins were defined as evidence of tumour cells within 1 mm of the resection margins. Patients with non-rectal cancers or patients who were planned for palliative resectional surgery, including those with macroscopically involved margins, were excluded.

Development process

The predefined list of the potentially important factors was qualitatively canvassed from all specialty groups and then with sequential iterations was included into the following phases in the perioperative process: preoperative, intra-operative and postoperative. For all patients, relevant medical and surgical history as well as dates and results of radiological imaging, surgical resections and histopathology were prepared in digital presentations (Microsoft® PowerPoint; GHvR). All available radiological imaging, macroscopic and microscopic images were reviewed by the dedicated radiologist and gastrointestinal pathologist, respectively. The radiologist was advised to focus the evaluation of the preoperative imaging on the area of resection which would prove later to contain the involved surgical margin. Relevant images were added to the digital presentations.

After these preparations, all cases were discussed by a multidisciplinary panel consisting of dedicated colorectal surgeons, dedicated radiologist and pathologist, and specialized pelvic exenteration nurses. Up to date information on patient outcomes (e.g. death/recurrence/distant metastases) were retrieved by one of the specialized nurses and presented at the conference (S.S.). After each case, potential areas of failure or explanations for involved margins were discussed using predefined headings (Table 1), and these outcomes were recorded on paper (S.S.).

Also, the role of communication and the judgements and/or choices made by the radiologist, surgeon and pathologist were included under these headings.

Two weeks after the original meeting, a summary of findings and missing information was presented to the expert panel and recommendations for improvement were discussed. Following this second meeting, missing information, e.g. bone margin status, was supplied to the group by the relevant team member.

Results

Between April 2014 and January 2016, a total number of 110 patients underwent pelvic exenteration surgery at our tertiary referral hospital, 33 of whom were for recurrent rectal cancer. Thirty-two out of 110 operated patients had microscopically involved surgical margins. None of the patients with recurrent rectal cancer who underwent surgery with curative intent had macroscopically involved surgical margins on final histopathology. Patients with other cancers were excluded and one patient had a palliative resection (Fig. 1). In the case of one patient with multiple recurrences, only the most recent recurrence was included as no older reports and/or imaging were available at our hospital. In one patient details were available for three recurrences. This left nine male patients with 11 exenterations who were included in the study with a median age of 56 years (range 35–68) (Table 2). In the cohort of 110 patients, radical resections were obtained in 39/68 men and 28/42 women; R1 resections in 21/68 men and 11/42 women; R2 resections in 5/68 men and 2/42 women ($P = 0.662$). For three men and one woman, margin status was unknown.

Table 1 Predefined potential factors of influence on resections with involved margins.

	Radiologist	Surgeon	Pathologist
Preoperative	Non-accurate prediction of tumour* based on study type, study quality or interval tumour growth		
Intra-operative		No frozen section of relevant area Involved margins for technical/ morbidity reasons	Frozen section false negative/ positive
Postoperative			Involved margins false negative/ positive
Communication		Plan for resection inadequately recorded: multidisciplinary team letter, surgeon's letter, informed consent	

*Involvement of vessels, bone, nerves, soft tissue, other (adjacent) organs.

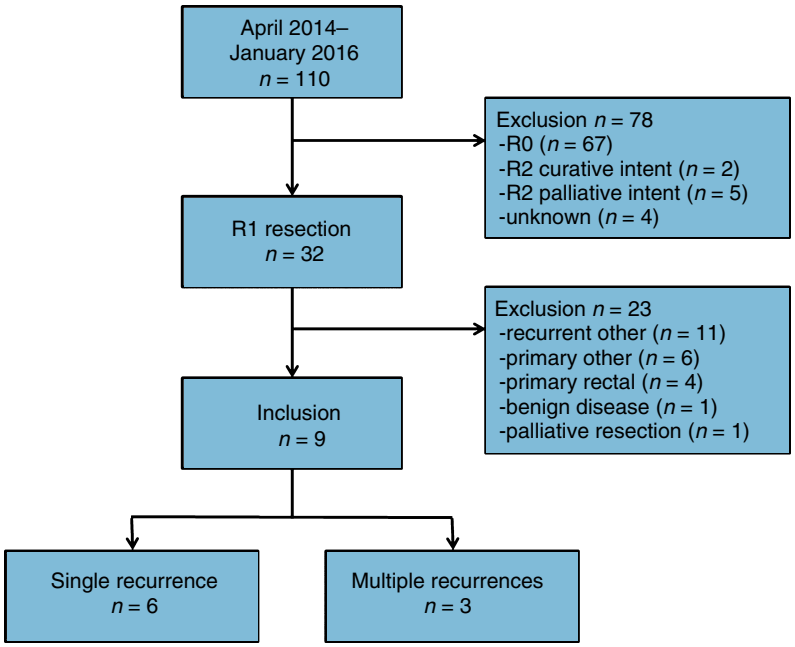

Figure 1 Flow chart.

All patients were discussed during a 3-h meeting. All patients had positive soft tissue margins, and one patient also has an involved bony margin; most involved margins were situated at the right posterior or left lateral side (Fig. 2).

For each patient, areas of failure were recorded. This required expansion of our original headings with the addition of 'communication' and 'biology' (Table 3).

Interdisciplinary communication

In one patient, the wrong nerve root level for resection was recorded in the preoperative multidisciplinary team meeting. At the time of surgery, the patient was operated at the correct nerve root level and this was not a cause for the involved margin. Also, there was found to be a lack of communication within the Anatomical Pathology Department with regard to the final reports for bone margins and decalcified specimens of two patients, so these results were not subsequently discussed at the regular multidisciplinary meetings.

Pathology

In one case of human error, slides were incorrectly labelled and the opposite side of the specimen was

Table 2 Patient characteristics, treatments and outcomes.

Patient	Age (years)	Recurrence	Previous (neo-) adjuvant treatment	Operation	Adjuvant treatment	Long-term outcome	Follow-up (months)
1	51	2008 anterior resection (T3N1 (1/16)M1) 2015 presacral recurrence adjacent to anastomosis, invading into sacrum at level of S1/2 on left side	2008 CT 2015 LCCRT	2015 posterior and left lateral PE with partial S1/S2 sacrectomy, division of the left internal iliac vessels, abdominal perineal resection with end colostomy	CT	2016 recurrence, distant metastases	12
2	68	2012 anterior resection (Dukes Bx) 2014 tumour 12 cm from anal verge fixed to the posterior sacrum	2014 LCCRT	2015 PE with S1 sacrectomy, cystoprostatectomy, APR, aortoiliac lymphadenectomy, ileal conduit, end colostomy	CT	2016 recurrence	27
3	64	2012 anterior resection (T4N2) 2014 isolated recurrence left pelvic nodal disease	2012 CRT	2014 left lateral and posterior PE, excision of presacral mass and soft tissue mass involving obturator internus and aortoiliac retroperitoneal node dissection, pelvic lymphadenectomy, left ureterolysis	CRT	2015 recurrence	31
4	35	2014 APR (T4N2) 2015 local recurrence	2014 LCCRT	Complete PE with *en bloc* S1/S2 sacrectomy, excision of presacral tumour, bilateral obturator internus muscle, right iliac inner crest and ischium bone, internal iliac vessels, pelvic lymphadenectomy, small bowel resection, repair entero-urinary cutaneous fistula, bilateral ureterolysis, ileal conduit, reconstruction with vertical rectus abdominis muscle flap, mesh hernioplasty (pelvis, abdominal wall)	Nil	2016 deceased without evidence of recurrence	10
5	62	2004 ultralow anterior resection (T3N0, earlier tumour perforation) 2006 APR for recurrence 2015 PE for recurrence involving presacral region and coccyx	2005 CT 2014/2015 LCCRT	2015 PE with S3 sacrectomy, excision of ischial spine and tuberosity, excision of presacral tumour, internal iliac vessels, pelvic lymphadenectomy, obturator internus muscle. Division of left S3–5 nerve roots, right sciatic nerve, ileal conduit	Nil	2016 recurrence, deceased	20
6	63	2010 ultralow anterior resection (T3N0) 2014 recurrence right pelvic side wall	2014 LCCRT	2014 right lateral PE, excision of mass of obturator internus muscle, pelvic bone, right internal iliac vessels, pelvic lymphadenectomy, re-implantation of right ureter	CT	2017 recurrence	26
7	67	2013 low anterior resection (T3N0) 2015 recurrence at anastomosis	2015 LCCRT	2015 PE with abdominal perineal resection, high sacrectomy, excision of presacral mass, right internal iliac vessels, right seminal vesicles and vas deferens, Boari flap	CT	2016 recurrence, deceased	12

Table 2 (Continued).

Patient	Age (years)	Recurrence	Previous (neo-) adjuvant treatment	Operation	Adjuvant treatment	Long-term outcome	Follow-up (months)
8*	53	2006 APR (T4N1) 2007 PE for first recurrence 2009 PE for second recurrence 2015 third recurrence pelvic side wall	2006 LCCRT	2015 left lateral PE with *en bloc* resection of internal iliac vessels, obturator internus and piriformis muscle, ischial spine, S1/S2 nerve roots, small bowel resection	CT	2015 recurrence, deceased in 2016	11
9-1	53	2013 PE for T4 rectal cancer	2013 LCCRT	2014 posterior, central and right lateral PE, APR, resection of presacral mass, S2/S3 sacrectomy, omental interpositioning	Nil	2015 recurrence	31
9-2	54	2015 sacral bone recurrence at S3/4, sacral nerve roots	See above	2015 posterior PE, resection presacral mass, prone sacrectomy through S2/S3, gluteus flap	Nil	2016 recurrence	See above
9-3	56	2016 recurrence in nodule at left S2 vertebral level, left S1 foramen	See above	2016 complete PE with cystoprostatectomy, resection of left sacroiliac joint, ilial bone, S1, lateral pelvic side wall, internal iliac vessels, presacral mass, piriformis and gluteus muscles, ileal conduit, pelvic mesh, titanium implant	Nil	No evidence of recurrence	See above

APR, abdominoperineal resection; CRT, chemoradiotherapy; CT, chemotherapy; LCCRT, long-course chemoradiotherapy; PE, pelvic exenteration.
*Multiple recurrences, most recent included in analyses.

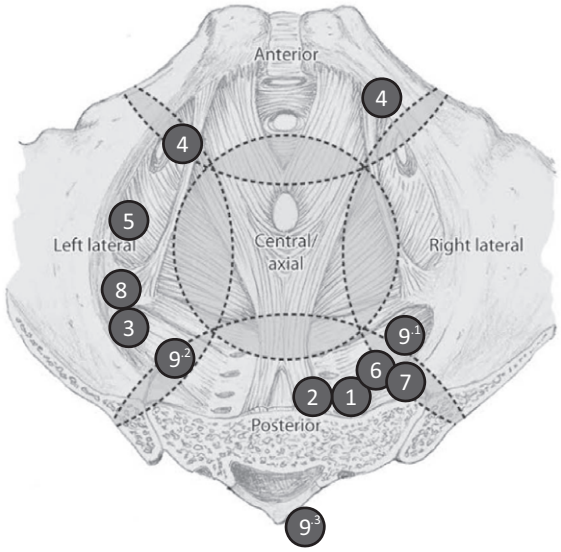

Figure 2 Sites of involved margins. Case 4 had two positive soft tissue margins; case 6 had a positive bone and positive soft tissue margin in the same vicinity (shown once).

declared as having an involved margin in the final histopathological report. In general, it was noted that no protocol existed for standardized inking of the specimen margins, resulting in different use of inking colours, e.g. for bone, soft tissue, true and false margins. For one patient, review of microscopy showed that only one margin was actually involved instead of two (as originally reported), because a false margin (created by pathological specimen dissection) had originally been mistaken for a true margin.

Two weeks after the original meeting, a list of recommendations based on the previously discussed findings was made and these are summarized in Table 4. For the Anatomical Pathology Department, introduction of a standardized specimen inking protocol and improvement of (interdisciplinary) communication were advised.

Review of the histology allowed the group to identify patterns of tumour growth which were considered important factors for failure in five patients: three with spiculated growth patterns, one with perineural invasion, and two patients with multifocal growth.

Radiology

Radiological undercalling of tumour extent was identified as a possible area of failure in two patients. One

Table 3 Areas of failure.

Patient	Pathology	Radiology	Surgery	Communication	Biology
1	Incorrect labelling of slides No follow-up report after decalcification			Lack of interdisciplinary communication concerning follow-up histopathology Error in multidisciplinary team letter concerning level of nerve involvement	
2		No T1 sequence available for MRI studies	No frozen section taken from tumour margin, wider resection needed		Spiculated tumour
3					Perineural tumour
4			Surgical technical planning inadequate, need for pubic bone resection		
5	Only one positive margin instead of two		Nerves not resected in view of morbidity		
6			Wider resection of soft tissue needed		
7				Preoperatively underestimated high extent of tumour	
8		Radiological undercalling of tumour extent	No frozen section taken, wider resection was needed		Spiculated tumour
9.1			Wider resection was needed		
9.2		Radiological undercalling of tumour extent due to oedema	Wider resection was needed		Multifocal
9.3	Bony margins not reported, after review margin proved clear		Wider resection was needed Multifocal recurrence	No interdisciplinary communication concerning follow-up histopathology	Multifocal

patient with multifocal growth on histology and who had a positive soft tissue margin exhibited asymmetric oedema and enhancement in the region of the positive soft tissue margin. It was postulated that in this case the oedema was indicative of tumour rather than reactive change. In the other patient, growth on MRI and confirmed on histology was via multiple radiating spicules. This pattern of growth should be discussed and documented at the multidisciplinary team meeting preoperatively.

The team recommendations for the Department of Radiology included specifically mentioning ill-defined or spiculated (soft tissue) tumour borders and identifying asymmetric oedema at a tumour margin as this may indicate tumour spread rather than reactive change. Tumour evaluation by MRI using both T1 and T2 weighted images was also recommended.

Surgery

Surgical resections were considered inadequately performed in seven patients, mostly due to not obtaining wide enough resections for patients with the aforementioned spiculated tumour biology or tumour growth. Figure 3 shows the MRI image (left) of a recurrent mass at the level of the upper sacrum with

Table 4 Summary of recommendations for improvement.

Radiology	MRI: T1 and T2 sequences
	Report specifically if soft tissue tumour borders are ill-defined
	Describe perilesional oedema and note if asymmetric – may indicate tumour spread rather than reactive change
Surgery	Planning wide soft tissue margins, especially for spiculated tumours
	Consider taking frozen section of margins in case of spiculated tumours
	Morbidity and radicality of resection to be balanced with patient
Pathology	Standardized specimen inking protocol
	Avoid incorrect labelling/changing of slides
	Follow-up and communication of additional histopathological reports both internally and interdisciplinary
	Evaluation of true *vs* false margins
Multidisciplinary communication	Re-evaluation in case of recurrence (multifocality, tumour biology)

involvement of the left S1 and S2 nerve roots, with the positive left-sided soft tissue margin indicated by an arrow. On the right, a postoperative CT scan shows the bony resection cavity, which should have been wider on the right of the cavity to obtain a radical resection. Figure 4 shows T2 (left) and T1 (right) weighted images of a large mass involving the anterior, right lateral, central and posterior compartments. The right soft tissue margin, indicated by an arrow, was one of the involved margins in this patient. The two images are complementary. Figure 5 shows MRI images: axial (left) and coronal (right) of a right posterior anastomotic recurrence with spread into the right S3 nerve sacral foramen and invasion of the right piriformis muscle. The site of the positive anterior soft tissue margin is indicated by an arrow.

In some patients, no frozen sections were taken from tumour margins. In hindsight, one patient would have benefited from pubic bone resection in order to obtain a clear margin. In another patient, resection of additional nerve roots should have been performed but was omitted to avoid patient morbidity.

One patient had developed multifocal recurrences and subsequently had two further pelvic exenteration operations. In our multidisciplinary review, the multifocal nature of this tumour growth was highlighted. In hindsight, the team decided that surgery would have been withheld if the multifocal nature of his disease had been more clearly appreciated in view of the morbidity associated with the operations.

Team recommendations included planning for wider soft tissue margins and consideration of taking frozen sections of soft tissue margins in the case of spiculated tumours, as 'branch pattern' extensions can easily be missed macroscopically.

Discussion and conclusions

Recurrent rectal cancer can be difficult to manage when anatomical borders are crossed by the tumour, invading adjacent organs and anatomical structures. Whereas radical resections (R0) after pelvic exenteration surgery can increase 3-year survival rates to 56.4%, survival rates drop significantly to 29.6% and 8.1% for microscopically and macroscopically involved surgical margins, respectively [2]. Achieving clear operative margins has proven to be the key to survival. As in all operations for malignancy, however, a balance needs to be found between the radicality of resection and the resultant expected morbidity.

To our knowledge, no studies as yet have retrospectively investigated the value of a multidisciplinary case conference review to identify potential areas for improvement in this patient group. The preparation of the multidisciplinary conference was the key step to this

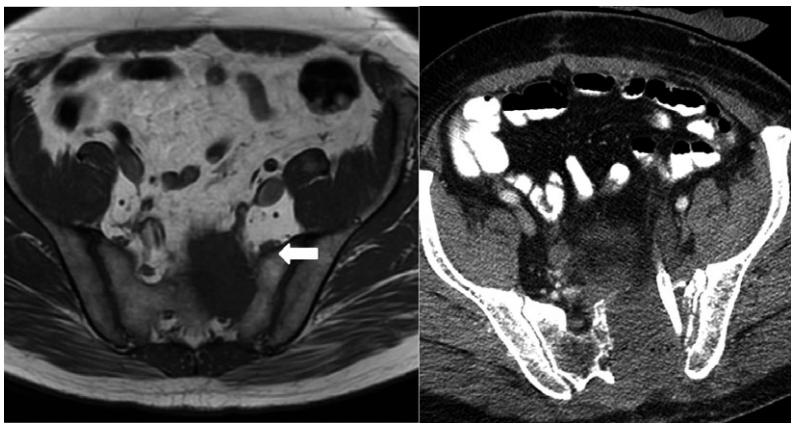

Figure 3 Patient 1. An axial T1 weighted image shows a recurrent mass at the rectal anastomosis with posterior invasion of the upper sacrum and involvement of the left S1 and S2 nerve roots, with the left L5 nerve root uninvolved. Surgery took place 3.5 months following the MRI and the axial postoperative CT shows the bony resection cavity. The site of the positive left-sided soft tissue margin is shown by the arrow.

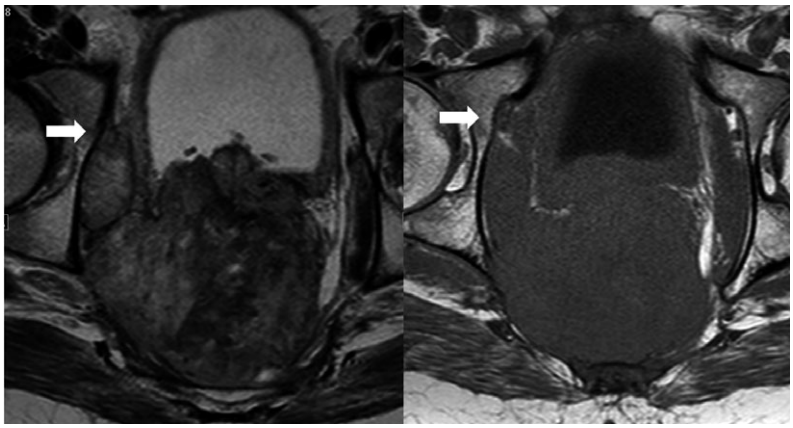

Figure 4 Patient 4. Axial T2 (left) and T1 (right) weighted images of the pelvis at the level of the obturator internus muscles show a large mass which involves the anterior, right lateral, central and posterior compartments. The axial T2 weighted image shows involvement of the right obturator internus muscle and the obturator nerve and vessels are encased and effaced, one of the positive soft tissue margin sites (as shown by the arrow). The axial T1 weighted image taken slightly more inferiorly shows the thickened obturator nerve and vessels surrounded by fat as they exit the pelvis via the obturator foramen. Note also the bony involvement of the right ischial spine and coccyx.

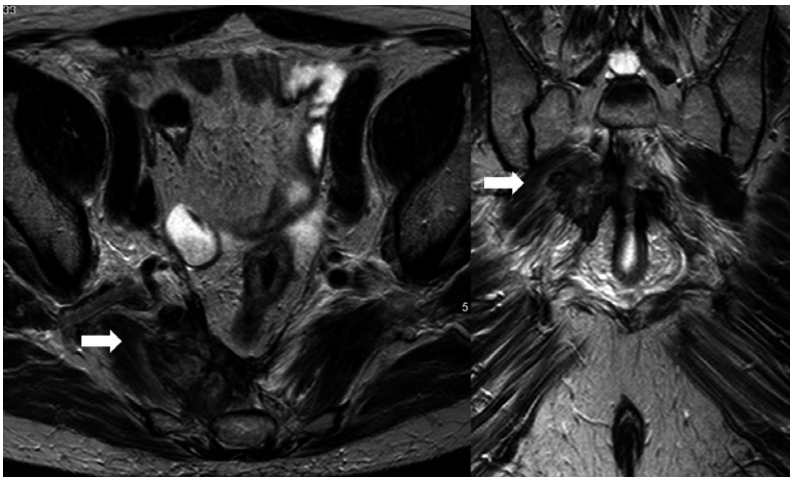

Figure 5 Patient 7. Axial and coronal T2 weighted images of the pelvis show a right posterior anastomotic recurrence with spread into the right S3 nerve sacral foramen and invasion of the right piriformis muscle (the arrow shows the site of the positive anterior soft tissue margin on the right). Tumour encases the right S2 and S3 nerves and there is thrombosis of a right internal iliac vein branch.

process, with high levels of engagement of our radiologist and pathologist. The preparation of individual cases was labour intensive and required detailed knowledge of surgical procedures and anatomy. Ideally, this preparation phase should be led or overseen by a surgeon. In our preliminary work, it was hypothesized that areas of failure might have occurred due to decisions taken at different stages in the perioperative process with involvement of any of the medical specialists of the multidisciplinary team. Our study showed that two important additional factors, (interdisciplinary) communication and tumour biology, were important in the resultant R1 resections. The follow-up meeting was considered by the team to be of positive value to present the findings, to highlight missing information and to reach a consensus on recommendations.

Our retrospective multidisciplinary evaluation of pelvic exenteration patients with microscopically involved surgical margins resulted in practical recommendations. The study results highlighted the need for improvement of the logistic and (interdisciplinary) communication process for the specimen margin inking and follow-up

of histopathological specimens after bone decalcification. As a result, we have standardized the use of different inking colours in the manual for dissection as well as educating the pathology registrars who are responsible for the dissection and sampling of these specimens. Also, pathologists reporting these cases have been advised to order a supplementary report in the laboratory information system for the bone findings at time of verification of the initial report of the soft tissue results. This means that the case will remain on pending lists until the bone pathology is formally reported.

Tumour biology, including multifocal growth and tumour progression patterns, which was not included in the predefined headings, proved to be an important factor. With regard to histopathological findings, Uemura *et al.* [3] described three types of tumour progression patterns in 21 cases of local re-recurrence after complete resection (R0) of local recurrence of rectal cancer. Type A was described as the expanding type, where the tumour edge could be traced by a smooth curve, type B the infiltrating type, with an irregular and invasive tumour edge, and type C an intermediate variant. It seems that there is an overlap between type B as described by Uemura *et al.* and the patients with a spiculated tumour edge in our series. Resection of tumours with a spiculated edge on radiological imaging is difficult as 'branches' of tumour cells reach surgical margins that macroscopically appear clear. Also, repeated extensive pelvic surgery appears less favourable in patients with tumours with multifocal tumour recurrence or spiculated growth patterns. It would be of interest to know if growth of the primary tumour was of the same pattern which would mean that knowledge of the histology of the initial tumour may be of value when selecting patients and planning surgery.

We have previously investigated the role of MRI to predict resection margin in 62 patients with locally recurrent rectal cancer and found that involvement of the upper sacrum, nerves and structures in the pelvic side wall (lateral compartment) were risk factors for achieving an involved operative resection margin [4]. All patients in the current study had involvement of the pelvic side wall, sacrum or both, which had the potential to predispose to a positive margin and agreed with the earlier results. Evaluation of undercalling of the tumour extent on MRI is limited by the retrospective nature of the research. Further, it is difficult to decide where to perform the surgical resection intra-operatively based on the preoperative radiological imaging.. Radiological interpretation of the tumour extent did not hinder excision of central, anterior and low posterior tumours, and a negative resection margin was consistently seen for these tumours during the study period. In part, this is explained by the lateral and posterior location of neurovascular structures. Standardized MRI sequences and imaging planes may aid interpretation of tumour extent as well as create an awareness of the need for a wider surgical plane.

Before this multidisciplinary case review, the assumption by the surgeons in our group was that involvement of the bony resection margin would be one of the major reasons for an R1 resection in our patient population. However, our analysis showed that patients were more prone to have tumour involvement at the soft tissue resection margins. As for surgical technical planning, this study has shown that the soft tissue resections need to be planned to be even wider, especially in patients with spiculated tumours showing infiltrating growth patterns. Also, we feel the need to improve the preparation of our preoperative multidisciplinary team review of patients with recurrent rectal cancer. In addition, we need to improve the interdisciplinary communication with the gastrointestinal pathologists regarding the final histopathology report, to better define the location of margins in the specimen for more accurate audit.

Intra-operative imaging has been proved feasible in a small clinical study by Handgraaf *et al.* [5]. In this study, intra-operative tumour and sentinel lymph node localization using near-infrared fluorescence imaging was performed in five patients after endoscopic tattooing with indocyanine green/nanocolloid solution. In the future, the introduction of new tumour detection technology, such as diffuse reflectance spectroscopy and mass spectrometry, may help to detect the presence of tumour cells intra-operatively, ultimately to replace intra-operative frozen sections [6,7].

The limitations of our study include the low number of patients and recurrences. In one patient, information was only available for one of the recurrences. Also, this is a single centre study with one radiologist and one pathologist. In addition, we have not reviewed those who were successfully resected to assess reasons for that outcome, nor compared the similarities and differences between the R0 and R1 groups.

As the knowledge in this field is limited, it would be interesting to compare our results with those of other high-volume pelvic exenteration centres and to compare expert opinions of surgeons, pathologists and radiologists in those centres. Based on our results, we are planning multidisciplinary case evaluations every 3–6 months. We hope that new tumour detection technology and our recommendations from this study will result in optimization of the perioperative process, higher clear margin rates and improved overall survival for patients with recurrent rectal cancers who need to undergo pelvic exenteration surgery.

Acknowledgements

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Conflicts of interest

None.

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