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ORIGINAL ARTICLE

Why did we encounter a pCRM-positive specimen whose preoperative MRI indicates negative mesorectal fascia involvement in middle to low rectal cancer?

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Abstract

Background This study aims to examine why we encounter a pathological circumferential resection margin (pCRM)-positive specimen whose preoperative MRI indicates negative mesorectal fascia involvement in middle to low rectal cancer.

Methods Forty-four consecutive patients included in this study had c(yc)T1–3 primary rectal adenocarcinoma without mesorectal fascia involvement and underwent laparoscopic total mesorectal excision (TME) with curative intent in the Department of Gastrointestinal Surgery of Kansai Medical University Hospital from January 2014 to April 2018. We adopted three checkpoints to investigate the misleading point causing positive pCRM (≤ 1 mm). (1) c(yc)CRM diagnosis by two radiologists with more than 20 and 15 years of experience in rectal cancer MRI diagnosis. (2) The specimen was assessed using the TME score presented by Nagtegaal. (3) We compared the standard sectioning according to UK guidelines (group A; $n=26$) with the specimen MRI image navigation-based section (group B; $n=18$) in terms of estimation of pCRM by c(yc)CRM.

Results We achieved a "complete" resection specimen in all cases. A simple correlation coefficient in group B revealed a significant correlation between c(yc)CRM and pCRM ($r=0.663$, $p=0.00513$); this correlation was not significant in group A ($r=0.261$, $p=0.19824$). However, tests for differences between linear regression coefficients in groups A and B showed no significant differences ($p=0.12596$). There were five cases of pCRM ≤ 1 mm: three in group A and two in group B. An anterior lesion caused pCRM ≤ 1 mm in three cases; the tumor deposits or extramural vascular invasion caused the other cases.

Conclusion The cause of misleading pCRM was the inaccurate preoperative MRI diagnosis of c(yc)CRM.

Keywords Rectal cancer · Circumferential resection margin · Mesorectal lymph nodes · Tumor deposits

Abbreviations

SMR	Specimen MRI
CRM	Circumferential resection margin
pCRM	Pathological circumferential resection margin
LAR	Low anterior resection
TME	Total mesorectal excision
EMVI	Extramural vascular invasion

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Background

According to Heald et al., total mesorectal excision (TME) [1] is effective in reducing the rate of local recurrence due to surgery, with a circumferential resection margin (CRM) ≤ 1 mm [2] being considered one of the most important prognostic markers for the local recurrence of rectal cancer [3–6]. The use of pathological circumferential resection margin (pCRM) as an endpoint for the superiority of transanal TME [7, 8] and robotic surgery [9] techniques over conventional laparoscopic surgery [10–13] is assessing the accuracy of the novel TME techniques.

The European Society of Gastrointestinal and Abdominal Radiology (ESGAR) has indicated that "the mesorectal fascia (MRF) is involved if the distance between the MRF and tumor is ≤ 1 mm", which can be determined by preoperative MRI [14, 15]. However, laparoscopic TME surgery based on preoperative diagnosis occasionally results in pCRM ≤ 1 mm. This can be attributed to either (1) inaccurate

preoperative diagnosis, (2) inaccurate surgical procedure, or (3) inaccurate pathological section for pCRM evaluation.

The quality of surgery in (2) is judged by looking at the specimen removed. Nagtegaal et al. classified the quality of excised mesorectum into three categories: complete, nearly complete, and incomplete. Complete was defined as an intact mesorectum with only minor irregularities of a smooth mesorectal surface. No defect is deeper than 5 mm, and there is no coning towards the distal margin of the specimen [16]. As shown by the Dutch trial, even in prospective clinical trials based on the principle of TME, only 56.6% of cases had a "complete" resection specimen [16, 17], and 43.3% were not curative as planned, putting patients at risk of local pelvic recurrence [18].

We have selected TME surgery since October 2013 according to MRI diagnosis of the negative MRF involvement. However, we encountered a case in which pCRM ≤ 1 mm was found even after surgery with a "complete" resection specimen. What kind of cases had a pCRM ≤ 1 mm but differed from the preoperative MRI diagnosis? Is there a method for improving the frequency of the pCRM-negative rate? Do new surgical techniques like robotic surgery and transanal TME improve TME quality and pCRM negative rates? In the present study, we aimed to investigate retrospectively why patients with negative MRF involvement on preoperative MRI had a pCRM ≤ 1 mm.

Methods

We adopted three checkpoints to minimize the human error that induces pCRM misdiagnosis.

1. The MRF involvement was diagnosed by two radiologists with more than 20 and 15 years of experience in rectal cancer MRI diagnosis in a joint conference with a rectal surgeon with more than 30 years of experience. The imaging conditions for T2W-MRI dedicated to the rectum are as follows: we used the same conditions for specimen MRI (SMR) (1.5–3.0 T: MRI T2, sequence TSE, TR 4000 ms, TE 96 ms, ETL16, BW 237 Hz/Px, average 6, concatenation 1, FOV 200 × 200 mm, phase oversampling 70, read matrix 320, phase matrix 320, slice thickness 3 mm, gap 0.3 mm, parallel imaging factor 2). We also referred to diffusion-weighted images [19–21].

   The MRI diagnosis and the procedure selection were performed according to our existing reports [22]. TME surgery was performed in patients with a c(yc)CRM ≥ 1 mm. A pathological CRM (> 1 mm) was defined as pCRM-negative. When it was difficult to measure the shortest distance from the tumor lesion to the mesorectal fascia, c(yc)CRM was determined using sagittal and 3D images and oblique images.

2. The dissection plane in laparoscopic TME surgery [23, 24] was as accurate as possible based on the anatomical schema of Sato [25]. TME was completed by dissecting up to the superior border of the anal canal using an electrocautery scalpel and, if a further distal margin was required, by dissecting between the internal and external sphincter muscles from the anal side [26].
3. In the sectioning of a specimen, the possibility of misleading pathology was verified by comparing the standard sectioning according to UK guidelines [27] with the SMR image navigation-based section.

Forty-four consecutive patients included in this study had c(yc)T1–3 primary rectal adenocarcinoma without mesorectal fascia involvement and underwent laparoscopic TME with curative intent in the Department of Gastrointestinal Surgery of Kansai Medical University Hospital from January 2014 to April 2018.

To verify the list of the three checkpoints, we compared two groups, group A, TME performed from January 2014 to February 2017 with standard sectioning ($n = 26$), and group B, TME performed from March 2017 to April 2018 with MRI image navigation-based sectioning using SMR after approval of our study "Comparative Analysis of the MRI to Pathological Findings in the Resected Specimen of Middle-Low Rectal Cancer" (CAMPaS RC Trial) by the Hospital Ethics Committee of the Kansai Medical University Hospital; reference no. 2017049) ($n = 18$).

For all cases in group A, we compare c(yc)CRM to pCRM, and the most crucial site of the c(yc)CRM was defined after obtaining 6-mm-thick sections; pictures of these sections were taken and documented. All patients in group B ($n = 18$) underwent SMR, which was used to measure the distance from the distal end of the specimen considered most plausible for CRM assessment, and a section was created. We used their CRM data as a pCRM.

Preparation of specimen for MRI of resected specimen (SMR) in group B

A surgical specimen of the rectum was inked on the TME dissection plane with a poster marker (Video 1B). We stuffed gauze into the specimen after inserting a plastic rod into its

lumen. The specimen was then placed in a semi-cylindrical tray made of moldable plastic. Three to four sutures were placed at each end and tied to the edges of the plastic tray to minimize shrinkage (Video 1C). The specimen in the plastic tray was subsequently inserted into a plastic tube before the MRI examination.

SMR and formalin fixation and slicing

Contiguous images (3 mm thick) of the specimen were obtained from the distal end along the length of the mesorectum. The specimens were then immersed in 10% neutral buffered formalin and fixed for at least 48 h. The most crucial site of the CRM to analyze was determined on the basis of the distance from the distal end of the specimen according to SMR findings and transverse specimen slicing to provide coronal sections through the rectum and mesorectum. After 6-mm-thick sections were obtained, pictures of these sections were taken and documented (Video 1D–G).

Diagnostic accuracy of MRI for mesorectal nodules

pCRM can be determined by the T and N factors or tumor deposits; we examined the diagnostic accuracy of nodules in the mesorectum. We also performed SMR in five rectal cancer surgery cases with beyond, extended TME during the CAMPaS RC Trial (two abdominoperineal excisions, one total pelvic exenteration, and two low anterior resection (LAR) cases that required combined resection of the adjacent organs due to cT4b). We examined the diagnostic accuracy of MRI for histopathologic findings in 96 mesorectal nodules of 23 patients who underwent SMR.

These nodules were indicated on the pictures of the sections of specimens (Video 1F) and assessed by two radiologists (Dr. 1 and 2) blinded to the pathological findings (Video 1A, D, G). According to the 2016 European Society of Gastrointestinal and Abdominal Radiology (ESGAR) diagnostic criteria [14, 28], nodules were diagnosed retrospectively as malignant or not with or without preoperative treatment. Irrespective of size, irregular nodule margins and morphological abnormality were classified as tumor deposits.

Correlation coefficient between c(yc)CRM and pCRM values

To determine the relationship between the c(yc)CRM and pCRM, we examined 44 cases of TME surgery in which the correlation between c(yc)CRM and pCRM was indicated by the simple correlation coefficient.

Validation of preoperative diagnosis and comparison with c(yc)CRM in cases with pCRM ≤ 1 mm

We validated the preoperative MRI diagnosis in cases with pCRM ≤ 1 mm and why the preoperative MRI diagnosed negative MRF (Table 2).

Pathological findings in Japanese classification of colorectal, appendiceal, and anal carcinoma

In the Japanese Classification of Colorectal Cancer, extramural cancer deposits without lymph node structure (EX) within the regional lymph node area should be recorded. EX includes localized lesions comprising lymphatic invasion, venous invasion, perineural invasion (vascular/perineural invasion lesions), and other lesions (tumor nodule: ND) [29]. We reported these pathological findings according to the Japanese Classification throughout the paper because the definition of pathological extramural vascular invasion (EMVI) and tumor deposits was not described in the Japanese Classification.

Statistical analysis

We used descriptive statistics to summarize the variables, and the differences between groups A and B were analyzed using univariate analysis. A simple correlation coefficient was used to determine the correlation between c(yc)CRM and pCRM. We also examined the correlation coefficient between the groups using tests to assess the differences between linear regression coefficients.

In MRI-based diagnostic accuracy tests of mesorectal nodules, we calculated the sensitivity, specificity, positive predictive value , negative predictive value and accuracy for MRI in predicting the histological presence or absence of tumor tissues in the nodules according to two radiologists (Dr. 1 and 2) independently and interobserver agreement was calculated.

All statistical analyses were performed with software (Statflex ver.7; Artec Co., Ltd. Osaka, Japan).

Results

Patient characteristics

The patient characteristics are summarized in Table 1. The staging followed the TNM 9th edition because the indication criteria for preoperative chemoradiotherapy (CRT) were determined concerning the European Society for Medical Oncology (ESMO) guidelines [30, 31] and the rectal cancer

Table 1 Patient characteristics

	Group	A	B	Total	*p*
Number		26	18	44	
Age (years of age)	Median (range)	66 (44–84)	67 (52–79)	66.5 (44–84)	NS
Gender	M/F	20/6	16/2	36/8	NS
BMI (kg/m^2)	Median (range)	23 (15.1–29.0)	22.7 (16.8–30.2)	23.0 (15.0–30.20)	NS
ASA-PS	1/2/3	11/13/2	2/16/0	13/29/2	NS
AV (cm)	Median (range)	5 (1–10)	8 (5–13)	6 (1–13)	0.00689
c(yc)T	1/2/3	0/7/19	1/5/12	1/12/31	NS
c(yc)N	0/1/2	4/9/13	6/7/5	10/16/18	NS
c(yc)M	0/1a/1b	18/7/1	15/3/0	33/10/1	NS
CRT	(−)/(+)	15/11	12/6	27/17	NS
Ope	LAR/ISR/Hartmann	22/3/1	18/0/0	40/3/1	NS
Max D (mm)	Median (range)	35 (0–70)	35 (0–105)	35 (0–105)	NS
Duration Ope (min)	Median (range)	348.5 (119–632)	260.5 (174–442)	308.5 (119–632)	NS
Bloos loss (ml)	Median (range)	38 (1–659)	31.5 (4–250)	37.5 (1–659)	NS
p(yp)T	0/1/2/3/4a	0/1/9/14/2	1/0/4/13/0	1/1/13/27/2	NS
p(yp)N	0/1a/1b/2a/2b/3	17/2/1/0/5/1	11/4/2/0/1/0	28/6/3/0/6/1	NS
p(yp)M	0/1a/1b	22/1/3	18/0/0	40/1/3	NS
Dissected LNs	Median (range)	19.5 (5–43)	15 (5–45)	17 (5–45)	NS
TME score	Completed	26	18	44	NS
c(yc)CRM	≤ 1 mm/> 1 mm	0/26	0/18	0/44	NS
pCRM	≤ 1 mm/> 1 mm	3/23	2/16	5/39	NS

M male, *F* female, BMI body mass index, *ASA–PS* American Society of Anesthesiologists physical status, *AV* tumor distance from the anal verge, *c(yc)T/N/M* TNM Stage (TNM 8th edition), *CRT* chemoradiotherapy, *Ope* operation, *LAR* low anterior resection, *ISR* intersphincteric resection, *Hartmann* Hartmann's operation, *Max D* maximum tumor diameter, *Duration Ope* duration of operation, *p(yp)T/N/M* TNM Stage (TNM 8th edition, p(yp)N3 was classified by the Japanese Classification of Colorectal Cancer), *Dissected LN* number of dissected lymph nodes, *CRM* circumferential resection margin, *NS* not significant

MRI diagnosis was made in compliance with the ESGAR consensus meeting results [14, 15].

In total, 44 patients were included. The median age was 67 years (44–84). The male-to-female ratio was 36:8. Median tumor distance from the anal verge was 6.0 cm (1–13). Initial T and N categories staging in all but two cases of cT2 in group B were diagnosed by 1.5–3.0 T MRI. These two cases of cT2 underwent only a CT scan preoperatively and were excluded from the examination of the correlation coefficient.

Twenty-seven cases with cT1–2, cT3 (cCRM ≥ 1 mm, cN0–1), and EMVI (−) and tumor deposits (−) underwent upfront surgery (laparoscopic TME), and 17 cases with cT4 or cT3 (cCRM < 1 mm, ≥ cN2, EMVI(+), tumor deposits (+)) underwent CRT (45–50.4 Gy; 1.8 Gy × 25–28 + TS1®: Taiho Pharmaceutical Co., Ltd. Tokyo, Japan) followed by laparoscopic TME after 6 weeks later. In CRT cases, the operative procedure was selected according to the status of post-CRT ycCRM following restaging with MRI. There were 11 cases of c(yc) M1 (10 cases in M1a, one in M1b). Seven cases of M1a were clinical lateral pelvic lymph node (LLN) metastasis, and only one had pathological metastasis of LLN. Apart from the distance from the anal verge to the tumor, there were no significant differences between groups A and B in the univariate analysis.

pCRM negative predictive value

pCRM negative (> 1 mm) predictive values of c(yc)CRM were 88.5(23/26) and 88.9(16/18) in groups A and B (Table 1).

Correlation coefficient between c(yc)CRM and pCRM values for TME surgery

The simple correlation coefficient revealed there was not a significant correlation between c(yc)CRM and pCRM in group A (r = 0.261, p = 0.19824) (Fig. 1). However, this correlation was significant (r = 0.663, p = 0.00513) in group B (Fig. 2). Tests for differences between linear regression coefficients in groups A and B showed no significant differences ($p = 0.12596$).

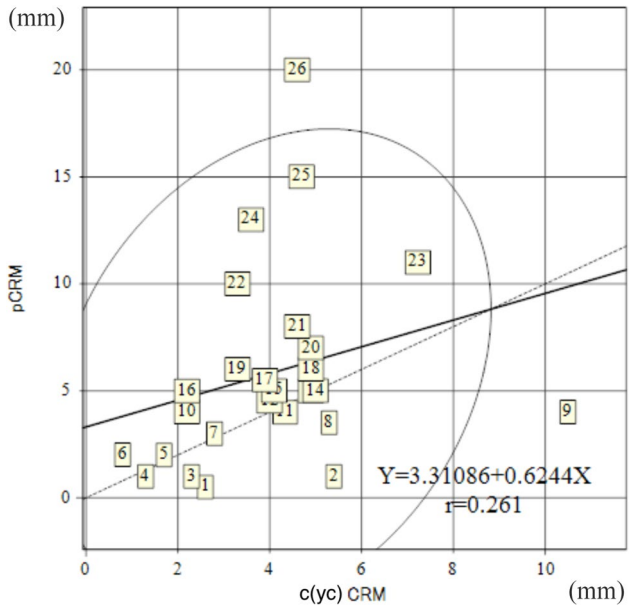

Fig. 1 Correlation coefficient between c(yc)CRM and pCRM values in 26 cases of the TME in group A. A simple correlation coefficient revealed there was not a significant correlation between c(yc)CRM and pCRM in group A ($r=0.261$, $p=0.19824$)

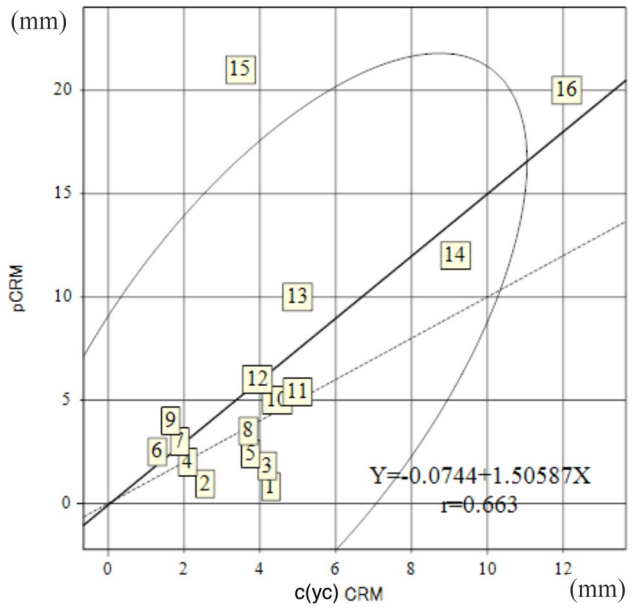

Fig. 2 Correlation coefficient between c(yc)CRM and pCRM values in 16 cases of the TME in group B. A simple correlation coefficient revealed a significant correlation between c(yc)CRM and pCRM ($r=0.663$, $p=0.00513$) in group B. Tests for differences between linear regression coefficients in group A and B showed no significant differences ($p=0.12596$)

Diagnostic accuracy of MRI for mesorectal nodules

Dr. 1 identified 91 among 96 nodules in the MRI corresponding to nodules in the sections and could not identify the other five nodules. Dr. 2 identified 95 of the 96 nodules in the MRI corresponding to the nodules in the sections but could not identify the other (Fig. 3).

Ninety-six mesorectal nodules included 77 pathological benign nodules (non-metastatic lymph nodes), and 19 pathological malignant nodules (10 metastatic lymph nodes , nine EX(+)). The two doctors performing evaluations demonstrated low agreement between the MRI and pathological findings: positive predictive value (PPV), 26.1% and 27.8%; negative predictive value (NPV), 84.4% and 84.7%; accuracy, 54.9% and 63.2%. The interobserver agreement was $k=0.204$.

Incidence of pCRM ≤ 1 mm

There were five cases of pCRM ≤ 1 mm: three in group A and two in group B. Three cases had a distance problem from the anterior wall dissection surface, of which two had a pCRM = 1 mm, and one had a pCRM = 0.95 mm (Fig. 4).

In contrast, in the other two cases, the distance was from the EX(ND)(+) (corresponding to a tumor deposit, or EMVI). One case was within 0.5 mm from the tumor deposit (Fig. 5), and the other was 0.8 mm, the distance from the EMVI of the posterior wall. The median observation period for the five patients was 4.9 years (1.2–5.7), without pelvic recurrences.

We had a case whose pCRM was the distance from the EX(ND) found at the time of sectioning in group A within 0.5 mm, which resulted in a pCRM(+), but the preoperative MRI could not diagnose a malignant nodule. If the EX(ND) had not been captured in this case, the pCRM could have been false negative (Fig. 5). The previous studies reported that the diagnostic accuracy was not sufficient to determine whether or not a nodule contains tumor cells [32, 33].

The EMVI was also sometimes difficult to recognize by the macroscopic examination of the section of the specimen, irrespective of its clear identification in the in vivo MRI (Table 2; Case 4). The tumor lesion along the vascular structure had shrunk after CRT, but the pathological diagnosis indicated neither venous nor lymphatic invasion.

Discussion

During the last three decades, several surgical techniques in rectal cancer have been developed to improve the outcomes, and the quality of these procedures has been compared in terms of pCRM [7–9, 33–35, 37]. Preoperative MRI should determine before registration whether curative TME surgery with negative CRM is possible [12]. However, the pCRM value is influenced not only by the operative quality [16]

Dr1		pathology malignant	benign	total	
MRI	malignant	12	34	46	PPV 26.1%
	benign	7	38	45	NPV 84.4 %
	total	19	72	91	
		sensitiviy 63.2%	specificity 52.8 %		accuracy 54.9 %

Dr2		pathology malignant	benign	total	
MRI	malignant	10	26	36	PPV 27.8 %
	benign	9	50	59	NPV 84.7 %
	total	19	76	95	
		sensitivity 52.6 %	specificity 65.8 %		accuracy 63.2 %

Inter-observer agreement : κ= 0.204

Fig. 3 Diagnostic accuracy of MRI for nodules in the mesorectum. MRI versus histopathologic assessment of 96 nodules in the mesorectum in 23 patients who underwent SMR. Malignant nodules (n=19) include metastatic lymph nodes (n=10) and EX(+) (n=9). Five nodules identified by Dr. 1 and one nodule identified by Dr. 2 could not be detected in MRI. The two radiologists' interobserver agreement (kappa coefficient) was $k = 0.204$

but also by the preoperative diagnosis and sectioning of the specimen [38, 39].

In this study, surgical factors did not affect the TME completeness. Other factors, such as inaccurate preoperative diagnosis or an inaccurate pathological section for pCRM evaluation, might affect the final pCRM status. The SMR was utilized because it was not always easy to detect tumor deposits, EMVI, and lymph nodes in the section when preparing sections from formalin-fixed specimens for pCRM assessment.

In our series, the negative predictive value of pCRM > 1 mm did not differ significantly between groups A and B. This may be because the number of cases affecting pCRM, whether intramural nodules or EMVI, is much smaller than that of T-factors, so it may not be sufficient to determine the effect of SMR. Although the results are from a single center with a small number of cases, the negative predictive value of c(yc)CRM for pCRM is considered high enough (88.5% and 88.9% in groups A and B) by conventional pathology searches.

On the other hand, in some cases, preoperative MRI negative MRF became pCRM ≤ 1 mm as a result of the limitations of the preoperative diagnosis of c(yc)CRM, which must always be evaluated in routine medical care.

In anterior wall lesions, the mesorectum is thin, and even if the c(yc)CRM > 1 mm, the shrinkage caused by formalin fixation is likely to affect the pCRM ≤ 1 mm. If the c(yc)CRM in case 5 was less than 1 mm, achieving a pCRM of 0.95 mm would be challenging, even if the TME was complete. Of course, there is a possibility that the section may have been prepared in the wrong part, so this study was designed to eliminate this as far as possible.

Case 3 is a patient with cT4a stage disease, which develops mainly on the anterior wall across the peritoneal reflection, and it was not easy to estimate the correct pCRM value from the estimated dissection plane on MRI imaging preoperatively.

Three of the five pCRM ≤ 1 mm cases (Case 1, 2, and 4) had EX(ND) (+ vascular invasion) that might be considered a tumor invasion corresponding to EMVI. Two patients were restaged after CRT to assess negative MRF involvement (cases 1 and 4). The three underwent TME surgery, but the tumor extension of EX(ND) (+ vascular invasion) resulted in a pCRM ≤ 1 mm in cases 1 and 2. It was not easy to diagnose the tumor extension, mainly if the deepest part of the tumor is located near the anterior wall, as is the case with tumor deposits and post-CRT EMVI.

The positive predictive value of tumor nodules by MRI is essential when tumor nodules such as tumor deposits and N factor determine pCRM. In the present study, the MRI diagnosis of two radiologists had a positive predictive value of 26.1% and 27.8%, with accuracy of 54.9% and 63.2%. The interobserver agreement was $k = 0.204$. Moreover, 19 of the 96 nodules were malignant, of which 9 were EX(+),

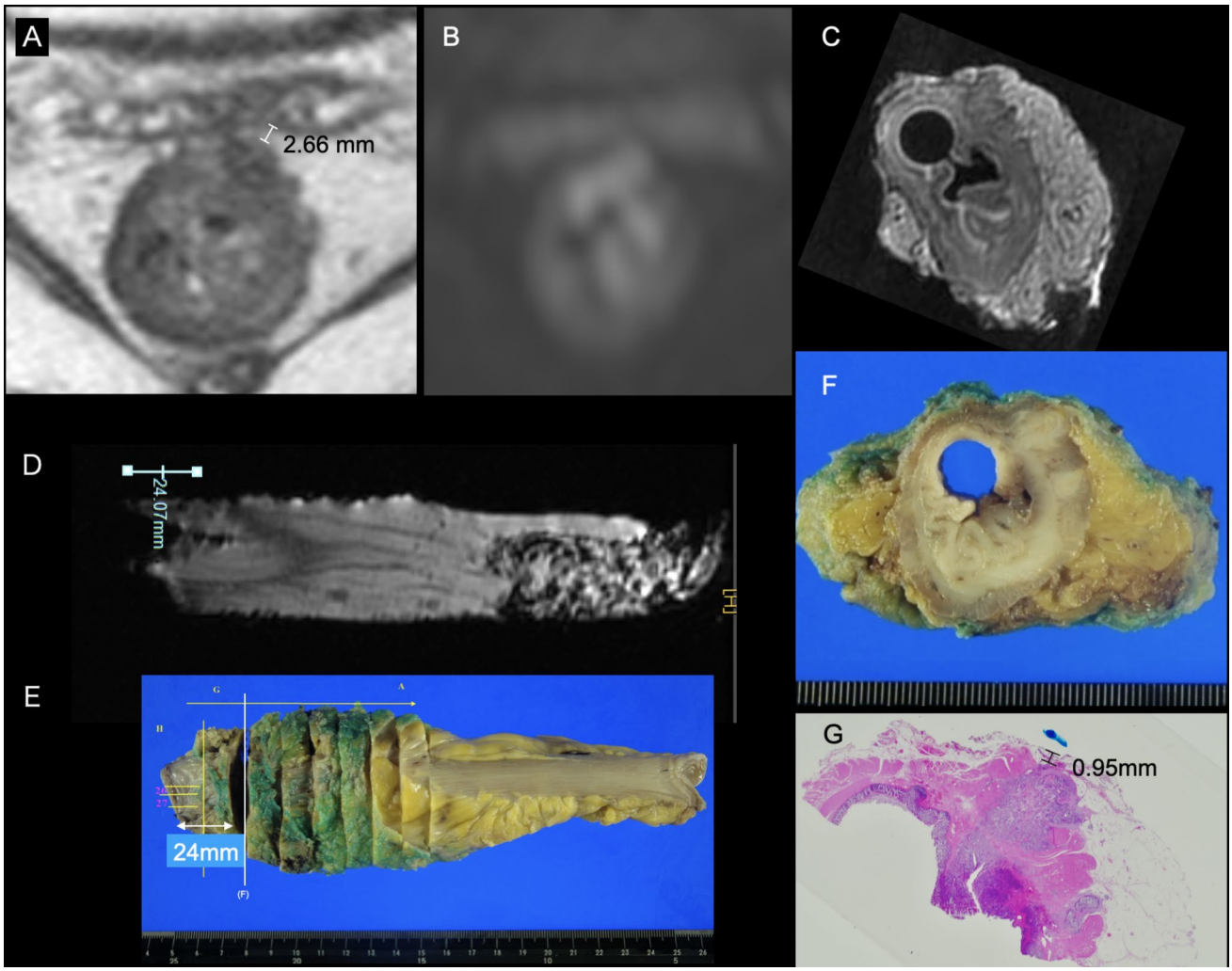

Fig. 4 Case 5, whose pCRM was 0.95 mm at the anterior side. **A** (T2W) and **B** (DWI) show a distance of 2.7 mm from the tumor to the mesorectal fascia. We selected low anterior resection for this patient. The specimen MRI (**C**, **D**) indicated that the deepest part of the tumor was located 24 mm from the distal end of the specimen. The section was made at 24 mm from the distal end of the specimen (**E**, **F**), which revealed 0.95 mm in pCRM (**G**)

corresponding to tumor deposits or EMVI. This shows that malignant nodules affecting the pCRM that are not correctly diagnosed by MRI can lead to misleading pCRM, as can MRI-diagnosed nodules that are not included in the sections.

The present study suggests that the discrepancy between c(yc)CRM and pCRM would not be corrected by improving TME quality to minimize the number of cases with pCRM ≤ 1 mm. On the other hand, improving the diagnostic performance of preoperative MRI would improve operative indications, including "beyond TME" surgery.

There were some limitations in our study. Firstly, only 44 cases were enrolled in this trial. As a result of the small number of cases, it is not possible in this retrospective study to statistically prove the effect of SMR on sectioning. However, this is an unprecedented study and can be used as primary data for calculating the planned number of cases and conducting a randomized controlled trial. Furthermore, the accumulation of 1000 cases in the "Japanese Prospect Multicenter Observational Study to Evaluate the Optimal Circumferential Resection Margin (CRM) and Distal Margin (DM) of Preoperative Magnetic Resonance Imaging in Rectal Cancer", which was conducted by the Japanese Society for Cancer of the Colon and Rectum, is scheduled to be completed in 2025. Although not all cases have been studied, more reliable data analysis will be possible on the sectioning problem and the limitations of MRI pCRM

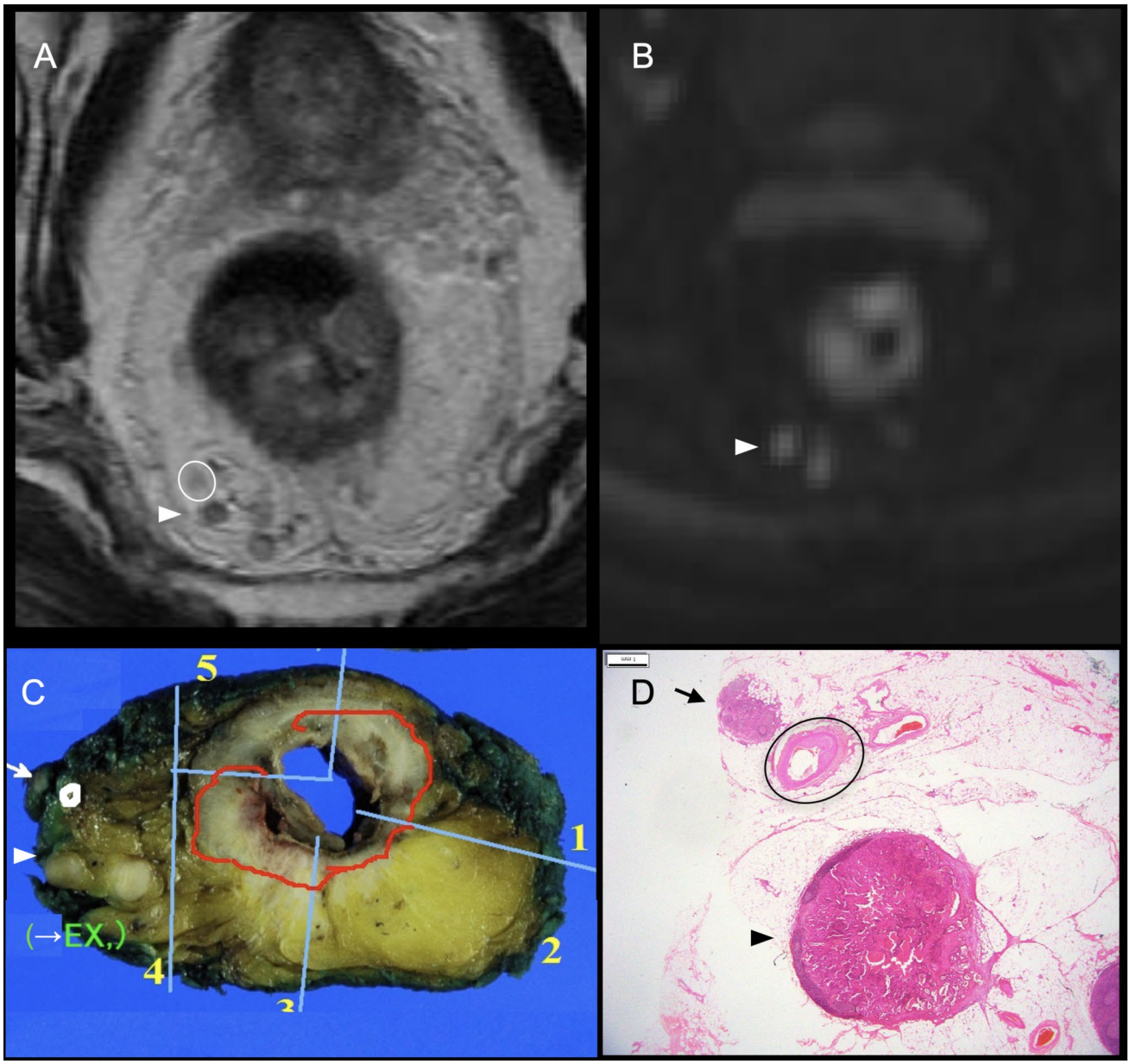

Fig. 5 Case 2, whose pCRM was within 0.5 mm because EX(ND) (tumor deposits) was not detected in the in vivo MRI. **A** (T2W) and **B** (DWI) show EX(ND) (suspected tumor deposits; arrowhead) and a vessel cross-section (white circle which is not detected in **B**), but no further tumor nodules close to the mesorectal fascia (MRF) can be noted. The microscopic image shows an EX(ND) (suspected tumor deposits; arrow) close to the MRF, reported and diagnosed as pCRM < 0.5 mm. The black circle in **D** indicates a vessel corresponding to the white circle in **C** and **A**. The black arrow in **D** shows the microscopic findings corresponding to the white arrow in **C**, in which the pCRM was measured. The cracks in the specimen below the arrowhead in **D** are those made during sectioning. The patient is alive at 7.5 postoperative years without recurrence

positive diagnostic rates, which are highlighted as causes of misleading pCRM in the study.

Second, various factors determining pCRM ≤ 1 mm other than lymph node, tumor deposit, EMVI, and malignant tumor tissue might not be delineated

Table 2 Cases of pCRM ≤ 1 mm

Case	Group	Age	Gender	BMI (kg/m^2)	AV(cm)	c(yc)T	c(yc)N	c(yc)M	NA	Ope	Max D (mm)	p(yp)T	p(yp)N	p(yp)M	TNMp(yp) Stage	c(yc)CRM (mm)	pCRM (mm)	TC	ply	pv	EX	OS(Y)	Outcomes
1	A	83	M	22.6	5	3	1	1b	CRT	LAR	55	3	1a	1a	IVA	1.8	1	A	1	2	ND(V+)	4.2	RA
2	A	81	M	26.4	8	2	1	0	(−)	LAR	50	3	2b	0	IIIC	2.4	< 0.5	RA	2	2	ND(V+)	7.5	A
3	A	67	M	23.3	10	3	2	0	(−)	LAR	70	4a	0	0	IIB	5	1	A	1	1	(−)	5.7	A
4	B	58	M	21.2	5	3	1	0	CRT	LAR	80	3	2b	0	IIIC	4.3	0.8	P	3	3	ND(V+), (Pn +)	1.2	A
5	B	66	M	24.5	5	3	1	0	(−)	LAR	20	3	0	0	IIA	2.66	0.95	A	1	2	(−)	4.9	RA

M male, *BMI* body mass index, *AV* tumor distance from the anal verge, *c(yc)T/N/M* TNM Stage (TNM 8th edition), *NA* neoadjuvant therapy, *CRT* chemoradiotherapy, *Ope* operation, *LAR* low anterior resection, *Max D* maximum tumor diameter, *p(yp)T N/N/M* TNM Stage (TNM 8th edition), *CRM* circumferential resection margin, *TC* tumor circumscribed location (*A* anterior, *RA* right-anterior, *P* posterior), *ply* pathological lymphatic invasion, *pv* pathological venous invasion, *EX* extramural cancer deposits without lymph node structure in Japanese Classification of Colorectal cancer, *EXND(V+)* tumor deposits other than vascular/perineural invasion with venous invasion, *EXND (Pn+)* tumor deposits other than vascular/perineural invasion with perineural invasion [29], *OS(Y)* overall survival (years), *RA* alive with recurrence, *A* alive without recurrence

by both preoperative MRI and SMR and could be noted on the first section on pathology.

Thirdly, although we used sagittal, 3D, and oblique images in CRM-threatening cases, as in case 5, we have to reevaluate whether our protocol enabled us to obtain T2W-MRI images correctly perpendicular to the most infiltrated margin of the tumor in the oblique images.

Finally, morphological changes of the tumor following neoadjuvant CRT and tumor progression from preoperative MRI to the operation were also challenging to interpret with MRI [40, 41]. We could also have considered modifying the SMR protocol, which was the same as the in vivo MRI protocol, which was initially not used to examine the specimen.

Conclusion

The present study shows that, at least at our institution, the discrepancy between c(yc)CRM and pCRM would not be corrected by improving TME quality to minimize the number of cases with pCRM ≤ 1 mm. On the other hand, improving the diagnostic performance of preoperative MRI would improve operative indications, including "beyond TME" surgery.

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Data availability The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Conflict of interest The authors declare no competing interests.

Ethical approval and consent to participate This study was approved by the Hospital Ethics Committee of Kansai Medical University (reference number #2017049: http://www.kmu.ac.jp/hirakata/hospital/2671t8000001356c.html).The consent form of all authors and the patient's written consent for the published photos were obtained. In addition, written consent was obtained from all registered patients to use the information for research and paper activities.

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