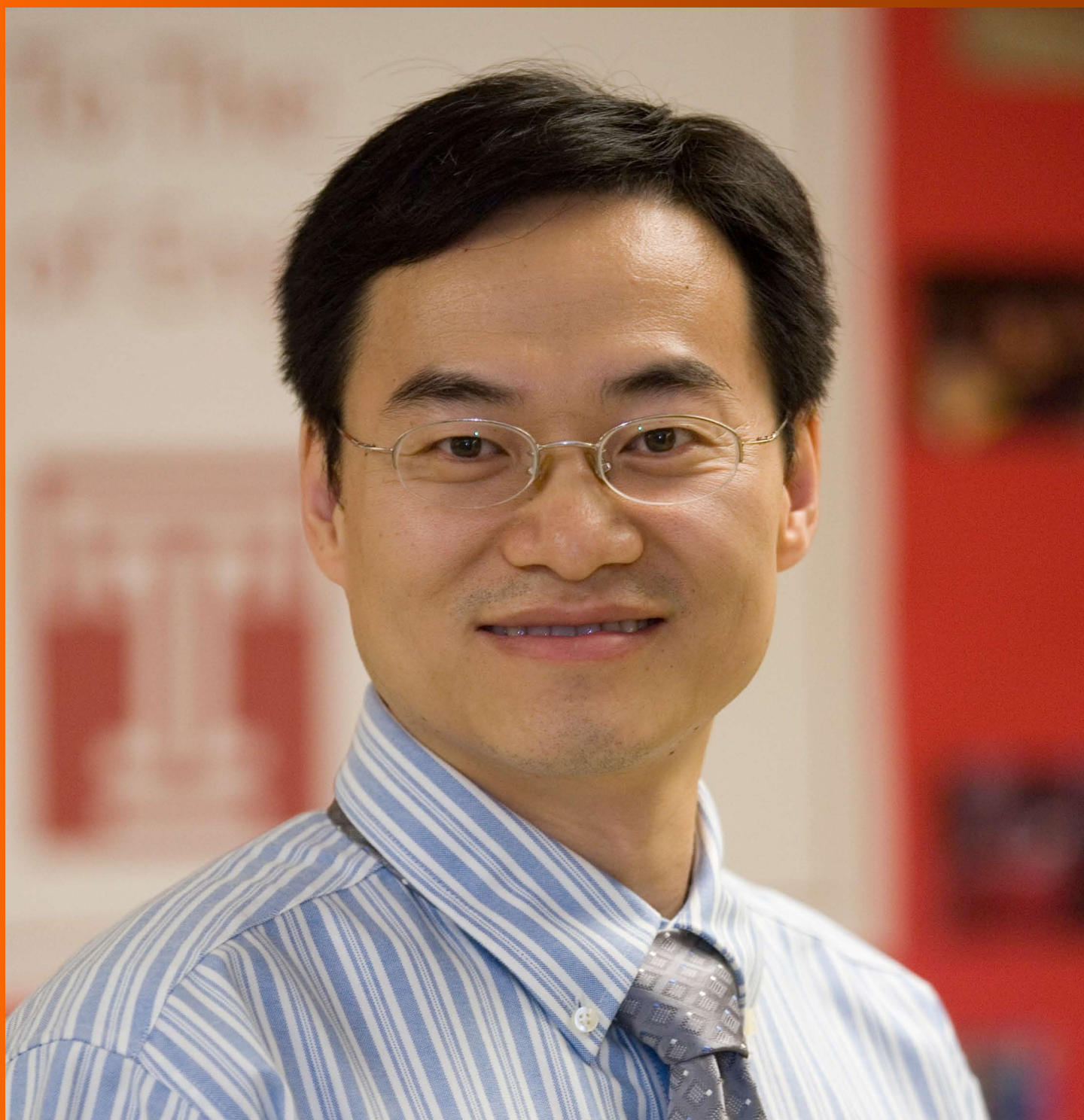


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World Journal of Clinical Oncology (*World J Clin Oncol*, *WJCO*, online ISSN 2218-4333, DOI: 10.5306) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

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Magnetic resonance imaging for diagnosis and neoadjuvant treatment evaluation in locally advanced rectal cancer: A pictorial review

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(MRI) is the primary method for staging rectal cancer. MRI is highly accurate in the primary staging of rectal cancer; however, it has not proven to be effective in re-staging, especially in complete response evaluation after neoadjuvant therapy. Neoadjuvant chemoradiotherapy produces many changes in rectal tumors and on adjacent area, as a result, local tumor extent may not be accurately determined. However, adding diffusion-weighted sequences to the standard approach can improve diagnostic accuracy. In this pictorial review, an overview of the situation of MRI in the staging and re-staging of rectal cancer is exhibited as a pictorial assay. An experience- and literature-based discussion of limitations and difficulties in interpretation are also presented.

Key words: Rectal cancer; Locally advanced; Magnetic resonance imaging; Staging; Neoadjuvant treatment

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Core tip: Accurate staging and circumferential resection margin evaluation significantly impacts determining optimal treatment scheme. Preoperative magnetic resonance imaging (MRI) is highly accurate; however, it has yet to be proved as effective in re-staging. The adding of diffusion-weighted sequences to standard T2-weighted MRI can positively affect its diagnostic accuracy.

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Abstract

High-resolution pelvic magnetic resonance imaging

INTRODUCTION

Multimodal treatment of rectal cancer, with the combination

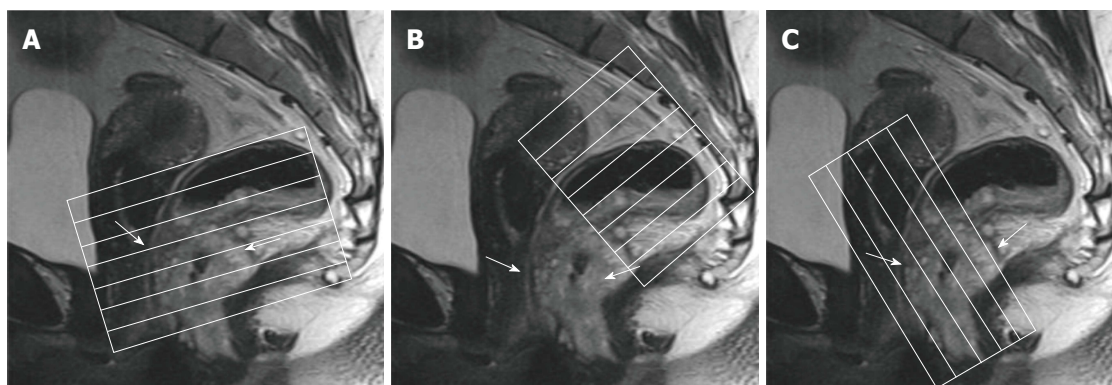


Figure 1 Magnetic resonance imaging planes. T2-weighted sagittal images are used to determine the longitudinal tumor axis in order to angle the axial and coronal planes. A: Oblique axial plane is obtained perpendicular to the rectal wall at the level of the rectal mass; B: Oblique axial plane is angled perpendicular to the pelvic floor, used to cover lymph node drainage territory; C: Coronal plane is angled parallel to the anal canal for imaging of low rectal tumors. Rectal tumor is indicated by arrows.

of preoperative (neoadjuvant) chemoradiotherapy (CRT) followed by surgery increases local control in locally advanced cancers and has become the standard approach to such rectal cancers^[1-5].

High-resolution pelvic magnetic resonance imaging (MRI) is the primary method for evaluation in rectal cancer^[6-10]. When applied according to the optimal protocols, high-resolution MRI accurately determining patients regarding neoadjuvant CRT requirement^[11]. Moreover, assessing treatment response in tumors using MRI also predicts probable survival outcomes, and could be used in the future to further adjust treatment according to the patients' response^[12]. In recurrent rectal cancer, MRI enables the depiction of the extent of tumor growth, and can establish the resectability of disease^[13,14].

MRI has not met expectations in re-staging, especially in complete response evaluation after neoadjuvant CRT because of post-therapeutic fibrosis and inflammation^[15-19]. However, adding functional MR sequences such as dynamic contrast-enhanced and diffusion-weighted sequences to the standard approach can improve diagnostic accuracy of MRI^[20-23].

In this pictorial review, we present a synopsis of the current standing of MRI in the staging and re-staging of rectal cancer. We also present an experience- and literature-based discussion of limitations and difficulties in interpretation.

MRI TECHNIQUE

Rectal MRI should be performed with pelvic phased-array coils. Rectal MRI using this technique provides overall assessment of the rectal wall layers with high-spatial-resolution and benefits from a large field of view^[15,24].

PATIENT PREPARATION

Routine rectal filling using endoluminal contrast agents such as ultrasonography gel is discouraged^[24] because this can distend of the rectum and compress the mesorectal fat, which may result in overestimation of

fascial involvement and interfere with assessment of mesorectal nodes^[25].

Bowel preparation is generally not necessary before the examination, but spasmolytics can be used when excessive fecal matter is visible on the planning images^[15,24]. For this purpose, a dose of 40 mg butylscopolamine is used intramuscularly unless contraindicated, immediately prior to placing the patient on the MRI table.

IMAGING PROTOCOL

Standard MR rectal protocols must at least include 2D T2-weighted sequences in sagittal, axial, and oblique coronal planes with 1-3 mm slice thicknesses. Sagittal sequences are used to identify the longitudinal tumor axis such that axial and coronal planes may be angled as perpendicular and parallel to the tumor axis as possible, respectively. Coronal planes must be angled in line with the anal canal for low tumors in order to evaluate the relation to the anal complex and pelvic floor muscles^[15,24,26] (Figure 1). Axial images are useful for evaluation of the tumor and its relationship with the intestinal wall, mesorectal fascia (MRF), and the adjacent pelvic tissue. Sagittal images are useful for the assessment of the tumor height and length and its relationship with peritoneum and other adjacent tissue.

In addition to T2-weighted sequences, diffusion-weighted imaging (DWI) sequences are recommended for inclusion in restaging protocols. DWI provides no additional benefit in primary staging; however, evidence is accumulating suggesting that it increases the diagnostic capability of MRI in the assessment of therapy response (yT-stage) after CRT^[24]. DWI also helps T2-weighted fast-spinecho (FSE) sequences to distinguish patients having good vs poor response^[20-23]. However, there is not adequate proof for supporting the usage of DWI for primary T-staging and lymph node assessment^[27].

ANATOMIC LANDMARKS

The rectum is approximately 15 cm in length from the anal verge, which is the lowest part of the anal canal.

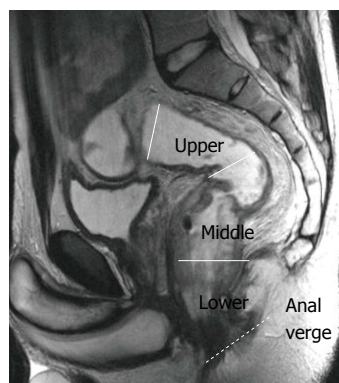


Figure 2 Rectal segments. T2-weighted sagittal image shows rectal segments: Lower, < 5 cm; middle, 5-10 cm; upper, > 10 cm from the anal verge.

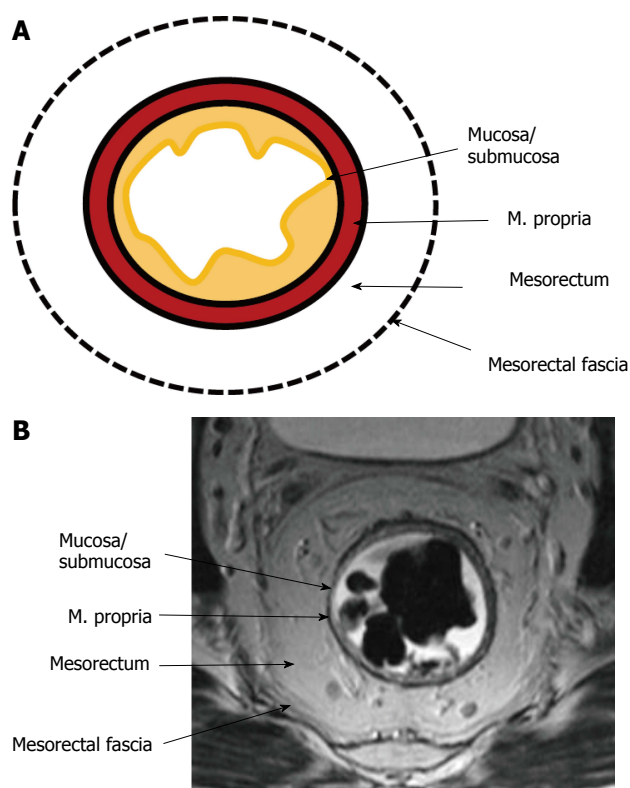


Figure 3 Normal rectal wall anatomy of higher and middle rectum. Schematic (A) and T2-weighted axial magnetic resonance imaging (B) presentation. The internal hyperintense layer represents the mucosa and submucosa (no distinction is possible between in two layers); the medial hypointense layer and external hyperintense area represent the muscularis propria and the mesorectum, respectively. Mesorectal fascia is seen thin hypointense layer enveloping the mesorectum (arrows).

The rectum has traditionally been divided into three segments according to the distance from the anal verge: Upper (> 10 cm), middle (5-10 cm), and lower (< 5 cm)^[27,28] (Figure 2).

The upper and middle rectal walls consist of three separate layers that can be distinguished in MRI. T2-weighted MRI sequences are the best for visualizing rectal wall anatomy. The internal hyperintense layer represents the mucosa and submucosa (no distinction is possible between in two layers); the medial hypointense

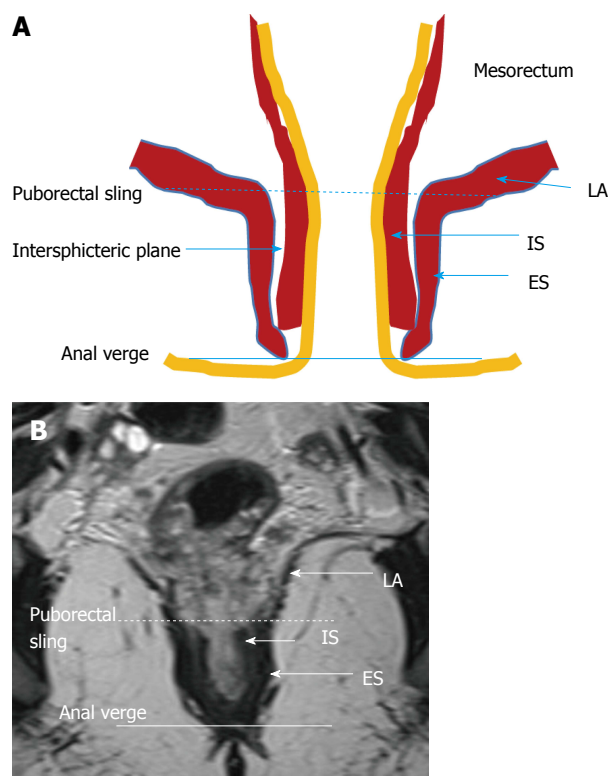


Figure 4 Normal anatomy of lower rectum. Schematic (A) and coronal plane T2-weighted (B) magnetic resonance imaging presentation. Puborectal sling, the upper portion of the puborectal muscle displaying the uppermost portion of the anal canal (intermittent line). Anal verge is the lowermost portion of the anal canal (line). LA: Levator ani muscle; IS: Internal sphincter; ES: External sphincter.

layer and external hyperintense area represent the muscularis propria and the mesorectum, respectively^[15,29] (Figure 3).

The puborectal sling constitutes the upper limit of the anal canal. The inner muscular wall of the anal canal comprises the internal sphincter, which is the direct continuation of the circular layer of the muscularis propria of the rectum. The outer muscular wall of the anal canal is cranially composed of the puborectal muscle and caudally of the external sphincter^[15,26] (Figure 4).

The puborectal sling constitutes the upper limit of the anal canal. The internal sphincter (the internal muscular wall) of the anal canal is consisted of the direct continuity of the muscularis propria circular layer of the rectum. The external muscular wall of the anal canal is formed by the puborectal muscle in cranially and the external sphincter in caudally^[15,26] (Figure 4).

The peritoneal reflection covers the anterior wall of the upper rectum; the risk of peritoneal perforation in upper rectal tumors is high^[27]. The peritoneal reflection can be easily displayed on sagittal and axial high-resolution T2-weighted images. In sagittal images, it can be depicted whereon upper pole of the seminal vesicles in men and at the uterocervical angle in women^[15]. The evaluation of the peritoneal invasion is very important in staging, because rectal tumor is staged as T4a in the presence of peritoneal invasion (Figure 5).

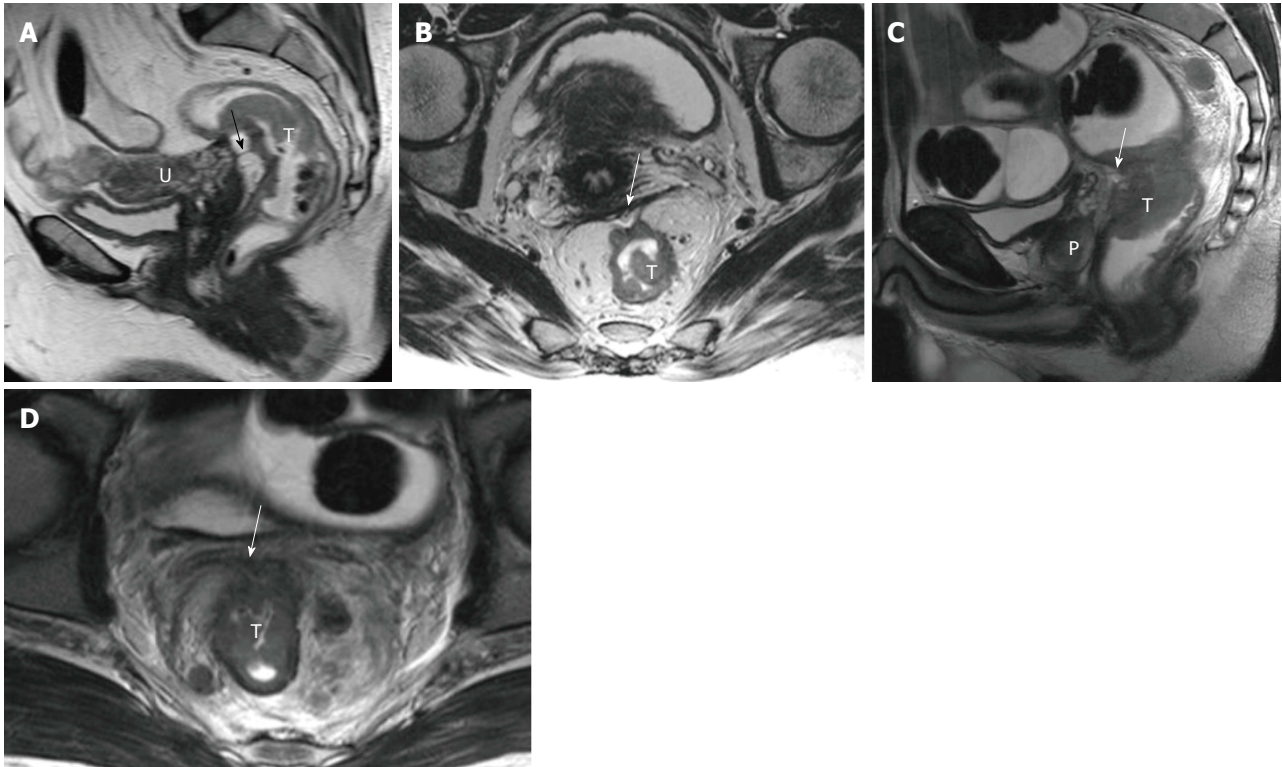


Figure 5 Periton invasion in female (A and B) and male (C and D) patients with T4a rectal tumors. On sagittal T2-weighted images, periton is seen as a hypointense linear structure in front of the tumor (arrows in A, C). On axial T2-weighted images, the peritoneum has a V shape and attaches onto the anterior aspect of the rectal cancer (arrows in B and D). T: Tumor; U: Uterus; P: Prostate.

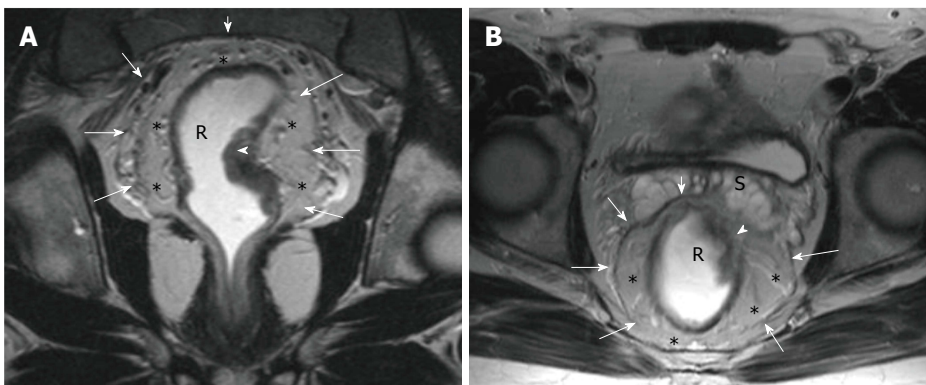


Figure 6 Magnetic resonance imaging anatomy of mesorectum and mesorectal fascia. On T2-weighted (A) axial and (B) coronal plane magnetic resonance images, mesorectal fascia (arrows) is seen as a thin, low-signal intensity layer enveloping the mesorectal fatty tissue (*) and rectum in a male patient with rectal carcinoma.

The middle rectum, which lies below the peritoneal reflection, is completely surrounded by mesorectal fatty tissue which is called the mesorectum. Mesorectum is encircled by the MRF which constitutes the circumferential resection margin (CRM)^[26-29]. The MRF can be seen as a thin, low-signal intensity envelop which surrounds the rectum and mesorectum (Figure 6). MRF tapers downward at the lower rectal level^[26]. The MRF is easily seen in posterolateral views, although it is difficult to distinguish it from Denonvilliers' fascia in the anterior wall^[30].

PRIMARY STAGING OF RECTAL CANCER

Tumor height and length

Tumor height and length should be routinely reported because outcomes and surgical management are affected by the location of the tumor^[24].

The distance and length are measured on a line drawn on the sagittal MR images. For tumor localization, the distance of the lowest portion of the tumor from the anal verge is measured. Rectal tumors are classified as high, middle or low when their most caudal border

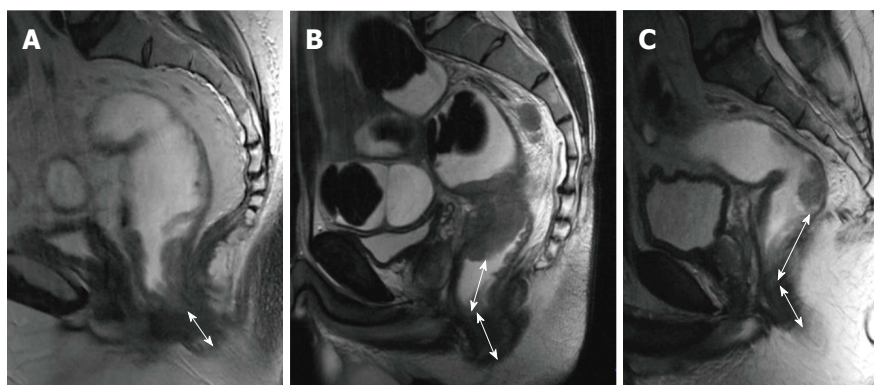


Figure 7 Rectal tumor levels. T2-weighted sagittal images in different patients with rectal carcinoma show distance from the anal verge (double-headed arrows) in (A) low rectal, (B) midrectal, and (C) upper rectal tumors (low rectal tumor, < 5 cm; midrectal, 5-10 cm; upper rectal, > 10 cm).

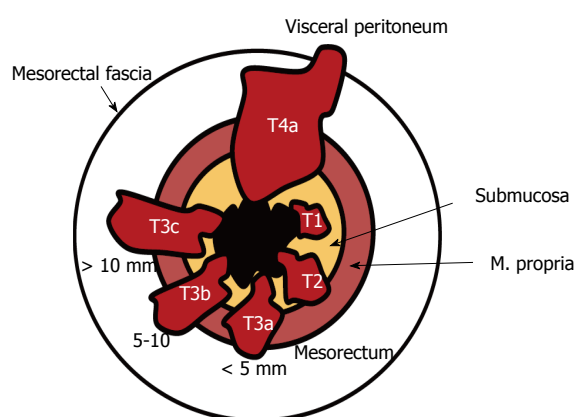


Figure 8 Rectal tumor T staging. The American Joint Committee on Cancer suggested an optional stratification of T3 tumors based on the extramural depth of invasion: Less than 5 mm, T3a; 5-10 mm, T3b; and more than 10 mm, T3c (adapted from ref. [27]: Nougaret S, Reinhold C, Mikhael HW, Rouanet P, Bibeau F, Brown G. The use of MR imaging in treatment planning for patients with rectal carcinoma: have you checked the "DISTANCE"? *Radiology* 2013; **268**: 330-344).

is > 10 cm, 5-10 cm, or < 5 cm from the anal verge, respectively^[15] (Figure 7).

T staging for middle and high tumors

On T2-weighted imaging, the muscularis propria is seen as a hypointense line between the hyperintense mesorectal fat and the inner submucosa and mucosa, which show intermediate to mild hyperintensity. The signal intensity of a rectal tumor on T2-weighted images is typically intermediate between the signal intensity of the muscularis propria and mucosa (Figure 8).

T1 tumors are confined to the submucosa; T2 tumors extend into, but not beyond, the muscularis propria. The differentiation of T1 tumors from T2 tumors on MRI is usually not reliable without an endorectal coil or endorectal ultrasound, and tumors should generally be staged as T1/T2^[15]. A tumor is staged as T3 when it extends beyond the muscularis propria and strands the mesorectal fat. Disruption of the muscularis propria because of penetrating vessels should not be overstaged as T3 (Figures 8 and 9).

The extramural depth of invasion refers to extension

of tumor beyond the muscularis propria^[31]. The American Joint Committee on Cancer suggested an optional stratification of T3 tumors based on the extramural depth of invasion: Less than 5 mm, T3a; 5-10 mm, T3b; and more than 10 mm, T3c^[32]. An extramural depth of invasion of less than 5 mm presents a significantly higher survival rate, and these early T3 tumors may be adequately managed with surgery alone and have a prognosis comparable to that of tumors characterized as T1/T2^[33]. T4 tumors extend onto the surface of the visceral peritoneum or an adjacent structure (Table 1, Figures 8 and 10).

Distance to the mesorectal fascia

For T3 tumors, the shortest distance between the most penetrating parts of the tumor and the MRF should be measured^[34,35]. The distance to the MRF is a critical local prognostic factor for rectal cancer^[36,37]. A tumor-MRF distance of more than 1 mm is a reliable predictor for negative margins after TME^[38]. In the presence of satellite nodules such as tumor deposits, lymph nodes or extramural vascular invasion (EMVI), the shortest distance between the nodules and the MRF should also be reported^[15] (Figures 11 and 12).

EMVI

EMVI is associated with local and distant recurrence and poor survival^[39]. It is defined as the presence of malignant cells within blood vessels located beyond the muscularis propria in the mesorectal fat. EMVI is suggested when vessels close to the tumor are obviously irregular or expanded by tumoral signal intensity^[39] (Figure 13).

The assessment of EMVI is a routine component of MR evaluation for primary staging; however, for restaging, there is no agreement as to whether evaluation of EMVI remains beneficial^[24].

T staging for low tumors

A specific T staging system is used to identify tumors and its circumferential resection margin (CRM)^[40] (Table 1, Figures 14 and 15).

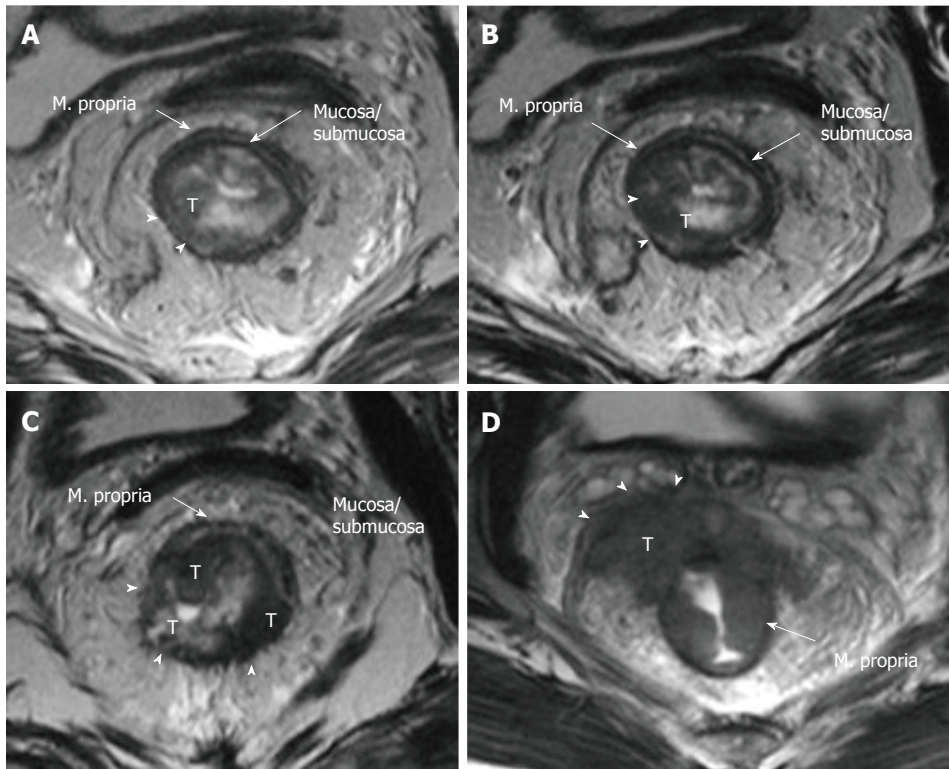


Figure 9 Rectal cancer T staging on magnetic resonance imaging. T2-weighted axial images showing rectal carcinomas with different T stages. A: T1 tumor is confined to the submucosa, has not entered the muscularis propria (arrowheads); B: T2 tumor extends into, but not beyond, the muscularis propria (arrowheads); C: T3 tumor extends beyond the muscularis propria and strands into mesorectal fat (arrowheads); D: T4a tumor invades the visceral peritoneum (arrowheads). T: Tumor.

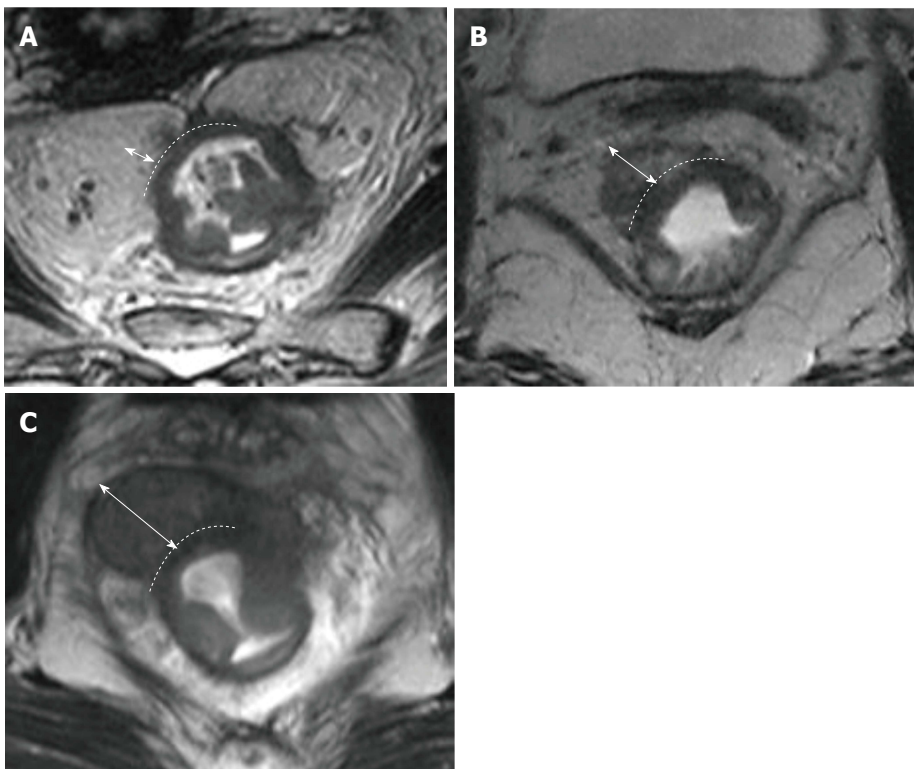


Figure 10 Stratification of T3 tumors on magnetic resonance imaging. T2-weighted axial magnetic resonance images in different patients with T3 rectal carcinoma showing extension of the tumor beyond the muscularis propria (double-headed arrows). The distance A: Less than 5 mm, T3a; B: 5-10 mm, T3b; and C: More than 10 mm, T3c.

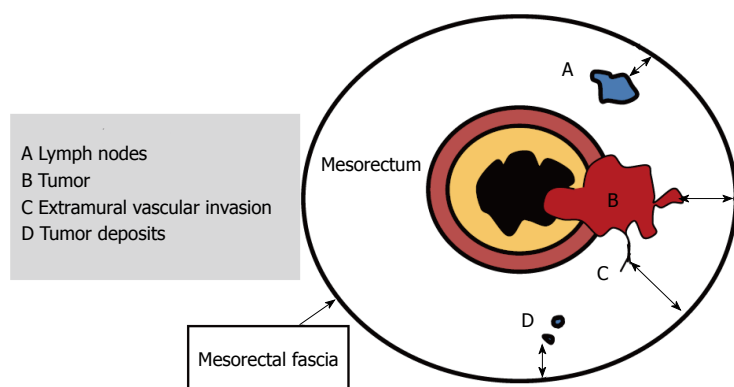


Figure 11 Schematic representation of positive resection margin. For T3 tumors, the shortest distance between the most penetrating parts of the tumor and the MRF is measured (double-headed arrows). A tumor mesorectal fascia distance of more than 1 mm is a reliable predictor for negative margins. In the presence of satellite nodules such as tumor deposits, lymph nodes or EMVI the shortest distance between the nodules and the MRF should also be reported (Adapted from ref. [27]: Nougaret S, Reinhold C, Mikhael HW, Rouanet P, Bibeau F, Brown G. The use of MR imaging in treatment planning for patients with rectal carcinoma: have you checked the "DISTANCE"? *Radiology* 2013; **268**: 330-344). EMVI: Extramural vascular invasion; MRF: Mesorectal fascia.

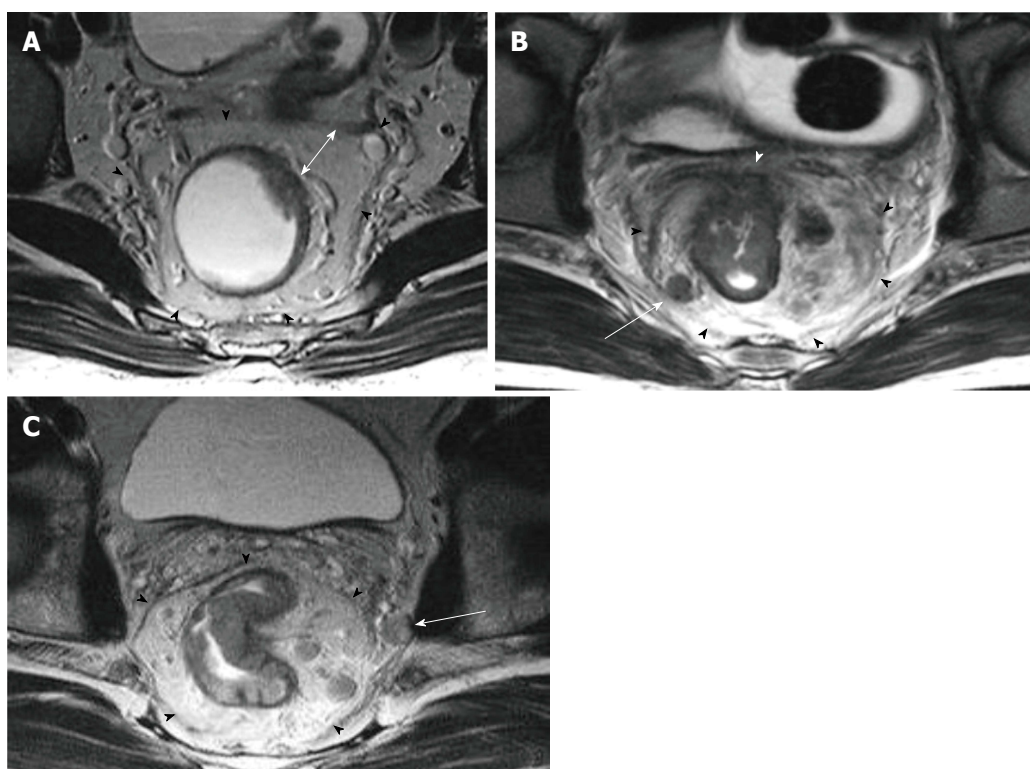


Figure 12 Distance to mesorectal fascia and mesorectal fascia invasion in different patients on T2-weighted axial images. A: T3a tumor is far away from the mesorectal fascia (double-headed arrow); B: T4a tumor (white arrowhead) and a suspicious mesorectal lymph node (arrow) are abutting the mesorectal fascia; C: Rectal tumor is lying > 1 mm from the mesorectal fascia; however, a suspicious lymph node, located out of the mesorectal fascia, is lying within < 1 mm of the mesorectal fascia (arrow). Mesorectal fascia is indicated with black arrowheads.

N-staging

Staging of nodes is very important for planning preoperative treatment^[41]. In the TNM system, disease involving only the regional nodes, including the mesorectal and internal iliac nodes, accounts for the N stage (Table 1); involvement of other nodes is regarded as metastasis^[38].

Mesorectal nodes are often the first and the most commonly involved group of nodes. Nodal metastases are usually within the proximal 5 cm of the tumor^[41].

Extramural nodes (iliac, superior rectal or inferior mesenteric nodes) are generally involved in locally advanced cancers^[42]. Low rectal tumors can also spread superficial inguinal nodes and imply poor prognosis^[43].

Node size is the usual criterion in nodal staging using MRI. Lymph nodes are usually considered pathologic when their short axis is longer than 0.5 cm; however, no

optimal cut-off threshold exists for involved nodes^[24]. The inclusion of morphologic features such as round shape, irregular contour, and nonhomogeneous signal intensity to a size cutoff increases the accuracy of MR^[44]. Although DW MRI is not accurate enough for characterizing nodes, it may be useful for locating them^[45] (Figure 16).

RESTAGING AFTER NEOADJUVANT TREATMENT

Neoadjuvant CRT provides downstaging and downsizing along with improvement in less extensive surgery, decreased local recurrence, and general survival^[12,46]. Tumor restaging involves correlating the posttreatment images with the pretreatment images with respect to

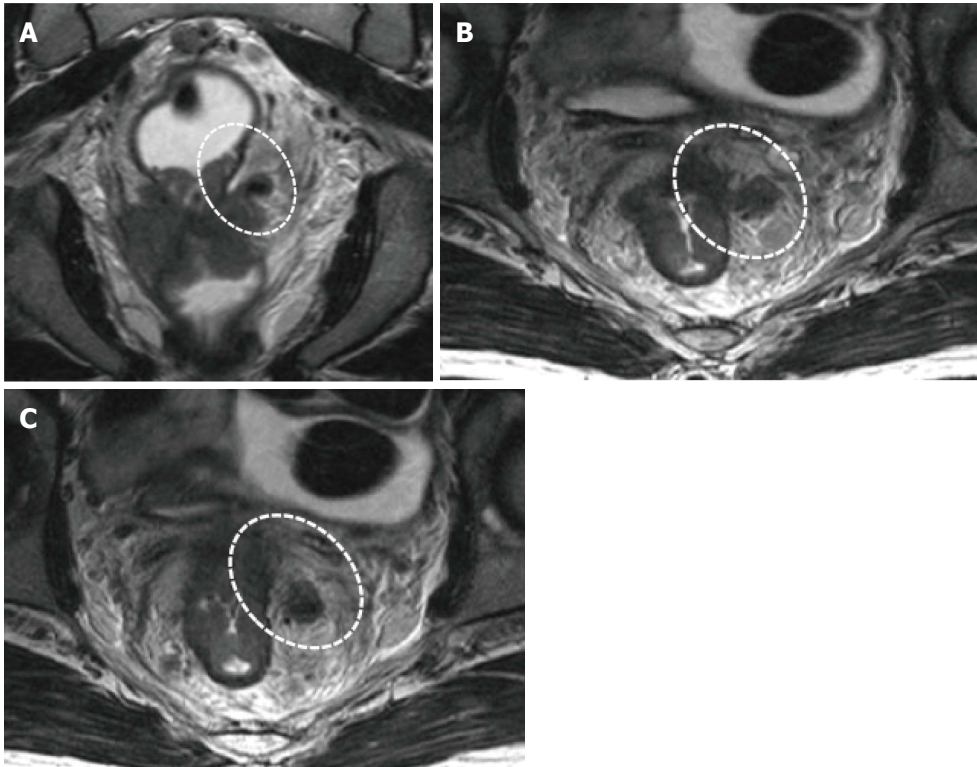


Figure 13 Extramural vascular invasion. T2-weighted (A) coronal and (B and C) serial axial magnetic resonance images in the same patient with T4a rectal cancer showing an irregular and expanded vessel insert to the tumor with tumoral signal intensity (circles).

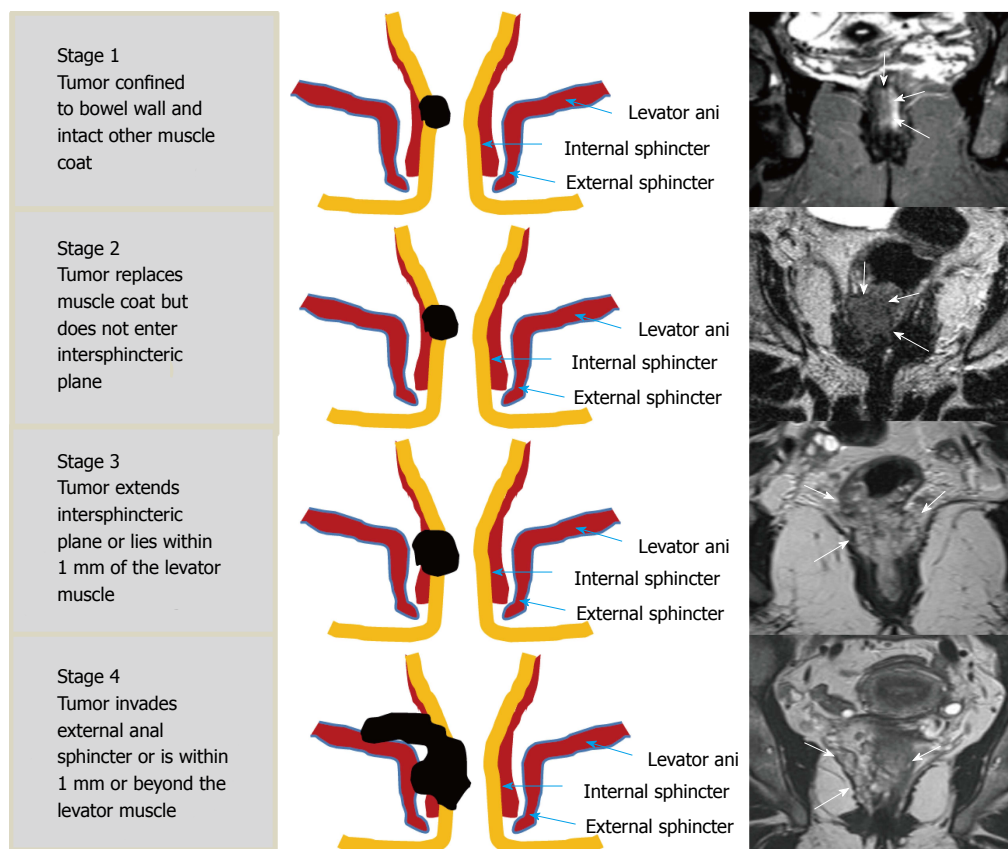


Figure 14 Schematic and high-spatial-resolution coronal T2-weighted magnetic resonance images for each stage according to the low rectal cancer. Rectal tumors in different patients are indicated with arrows on magnetic resonance images (Adapted from ref. [27]: Nougaret S, Reinhold C, Mikhael HW, Rouanet P, Bibeau F, Brown G. The use of MR imaging in treatment planning for patients with rectal carcinoma: have you checked the “DISTANCE”? *Radiology* 2013; **268**: 330-344).

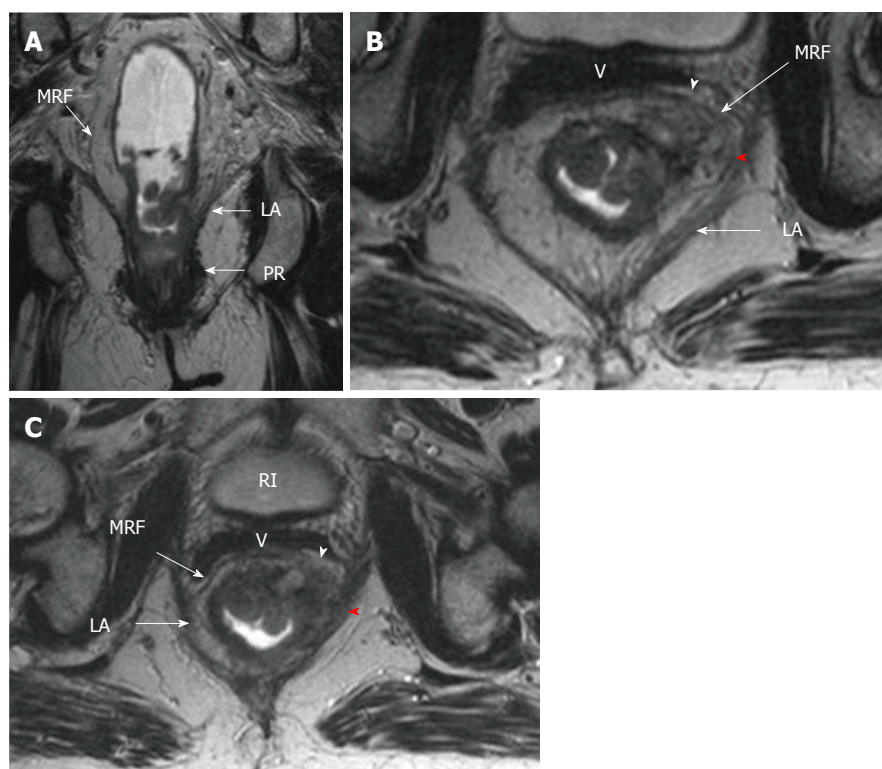


Figure 15 Stage 4 low rectal cancer. On T2-weighted (A) coronal (B, C) serial axial magnetic resonance images, rectal cancer showing invasion of levator ani (red arrowheads) and mesorectal fascia (white arrowhead). LA: Levator ani; PR: Puborectal; MRF: Mesorectal fascia; BL: Bladder; V: Vagina.

Table 1 Staging systems for rectal cancer

Stage	MRI findings
T stage for middle and high tumors ¹	
T1	Tumor signal intensity is confined to the submucosal layer
T2	Tumor signal intensity extends into the muscle layer, with loss of the interface between the submucosa and circular muscle layer
T3	Tumor signal intensity extends through the muscle layer into the perirectal fat, with obliteration of the interface between muscle and perirectal fat
T3a	Tumor < 5 mm into the perirectal fat
T3b	Tumor 5-10 mm into the perirectal fat
T3c	Tumor > 10 mm into the perirectal fat
T4a	Tumor signal intensity extends to surface of visceral peritoneum
T4b	Tumor signal intensity extends into an adjacent structure or viscus
T stage for low tumors ²	
T1	Tumor signal intensity confined to bowel wall, outer muscle coat intact
T2	Tumor signal intensity replaces muscle coat but does not enter intersphincteric plane
T3	Tumor signal intensity extends intersphincteric plane or lies within 1 mm of levator muscle
T4	Tumor signal intensity extends external anal sphincter or is within 1 mm or beyond levator muscle with/without adjacent organ invasion
N stage	
Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in 1-3 regional lymph nodes
N2	Metastasis in > 3 regional lymph nodes

¹Adapted from ref. [32]: Edge SB, Byrd DR, Compton CC. AJCC cancer staging handbook: from the AJCC cancer staging manual, 7th ed. New York, NY: Springer, 2010: 718; ²Adapted from ref. [40]: Taylor FG, Swift RI, Blomqvist L, Brown G. A systematic approach to the interpretation of preoperative staging MRI for rectal cancer. *AJR* 2008; **191**: 1827-1835. MRI: Magnetic resonance imaging.

all the elements assessed in the initial staging, and necessitates image acquisition with almost the same protocol and on the same planes.

T staging

Post-CRT restaging using conventional MR sequences is less accurate than primary staging, especially when

confirming complete response (yT0), mostly because it is difficult to distinguish fibrosis, edema and normal mucosa from small foci of residual tumor^[46-48]. As such, a normal, two-layered rectal wall after CRT is indicative of complete response, whereas residual fibrosis indicates either residual tumor or complete response (Figure 17). In practice, areas of fibrosis have very low signal intensity

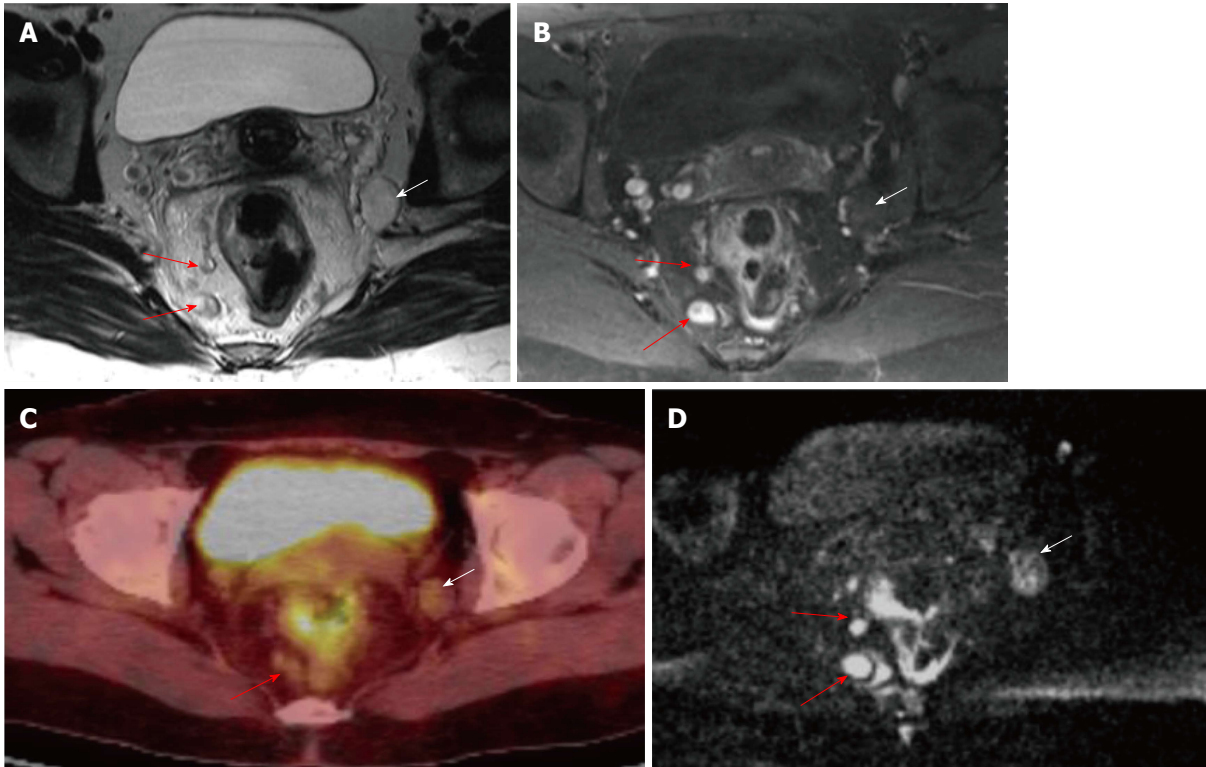


Figure 16 Mesorectal and extramesorectal lymph node involvement in rectal cancer. A: T2-weighted; B: T1-weighted contrast-enhanced axial MR images; C: ^{18}F -FDG PET-CT; D: DWI showing suspicious lymph nodes in mesorectal (red arrows) and extramesorectal areas (white areas). On DWI, extramesorectal lymph node is more remarkable than T2W and contrast-enhanced T1W sequences. DWI: Diffusion-weighted imaging; ^{18}F -FDG PET-CT: ^{18}F -fluorodeoxyglucose positron emission tomography-computed tomography.

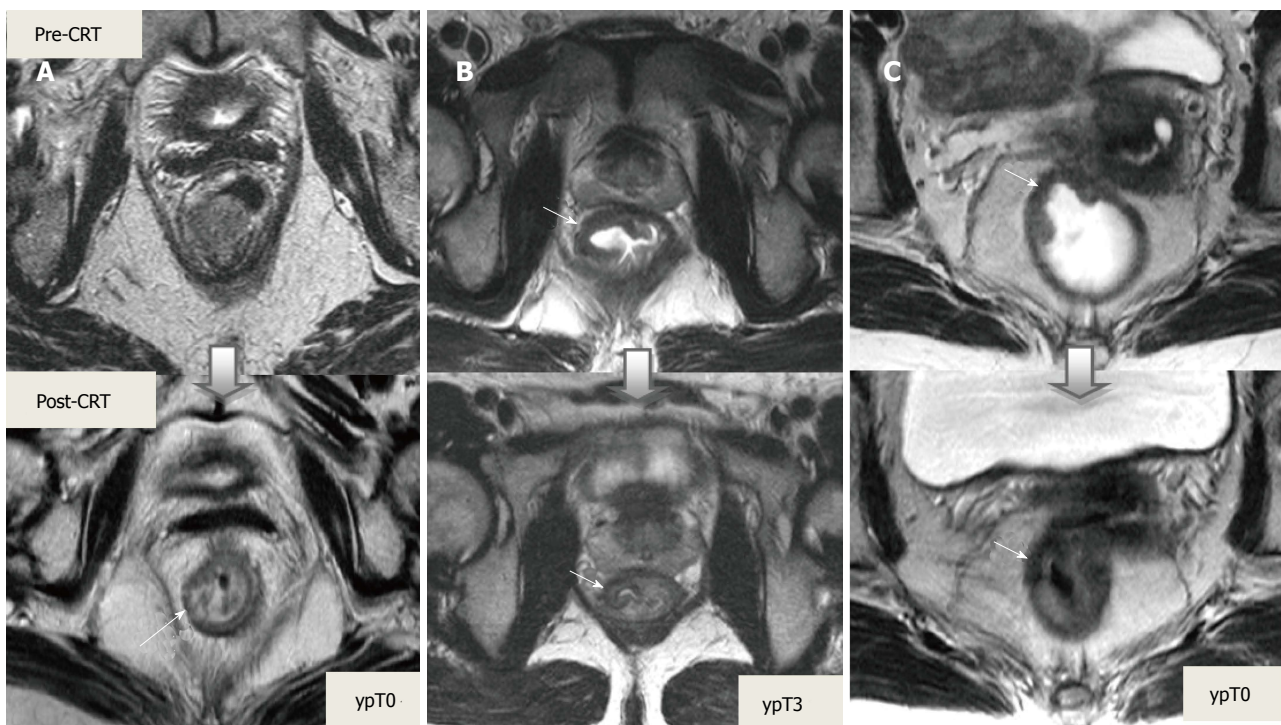


Figure 17 Tumor restaging after neoadjuvant chemoradiotherapy. On T2-weighted MR images in different patients showing baseline and post-CRT images on upper and lower series, respectively. A: In ypT0 rectal tumor, posttreatment axial image shows a normal, two-layered rectal wall (arrow), corresponding to complete response; B: In ypT3 rectal tumor, posttreatment axial image shows normal, two-layered rectal wall (arrow). This is an example for false-negative MR assessment of complete tumor regression; C: In ypT0 rectal tumor, posttreatment axial image shows thick, fibrotic low signal intensity scar (arrow) in pretreatment T3 tumor area. CRT: Chemoradiotherapy.

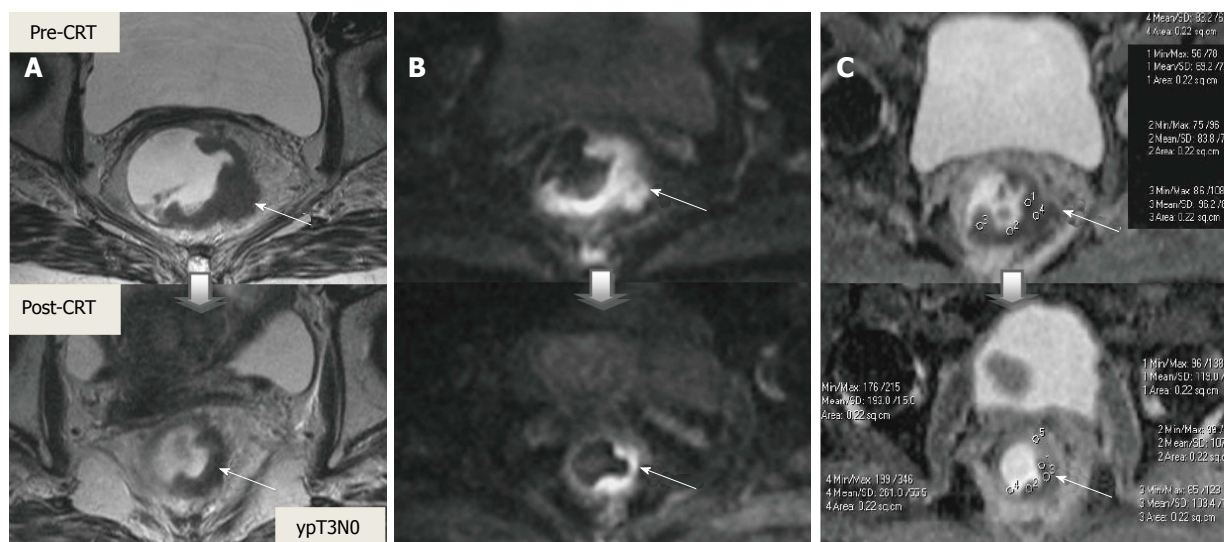


Figure 18 Post-chemoradiotherapy restaging using diffusion-weighted imaging in ypT3 rectal tumor. On T2-weighted (A), DW (B) and ADC (C) images in the same patient, baseline and post-CRT images are shown on upper and lower series, respectively. A: Posttreatment T2-weighted axial image shows semiannular infiltrating tumor, compatible with a residual T3 tumor (arrow); B: Posttreatment DW; C: ADC images delineate high and low signal-intensity corresponding to the tumor, respectively (arrow). Pre- and post-treatment mean ADC values are $0.68\text{--}0.72$, $1.22\text{--}1.44 \times 10^{-3} \text{ mm}^2/\text{s}$, respectively, in the tumor area. Post-therapy ADC increase is compatible with therapy response. CRT: Chemoradiotherapy.

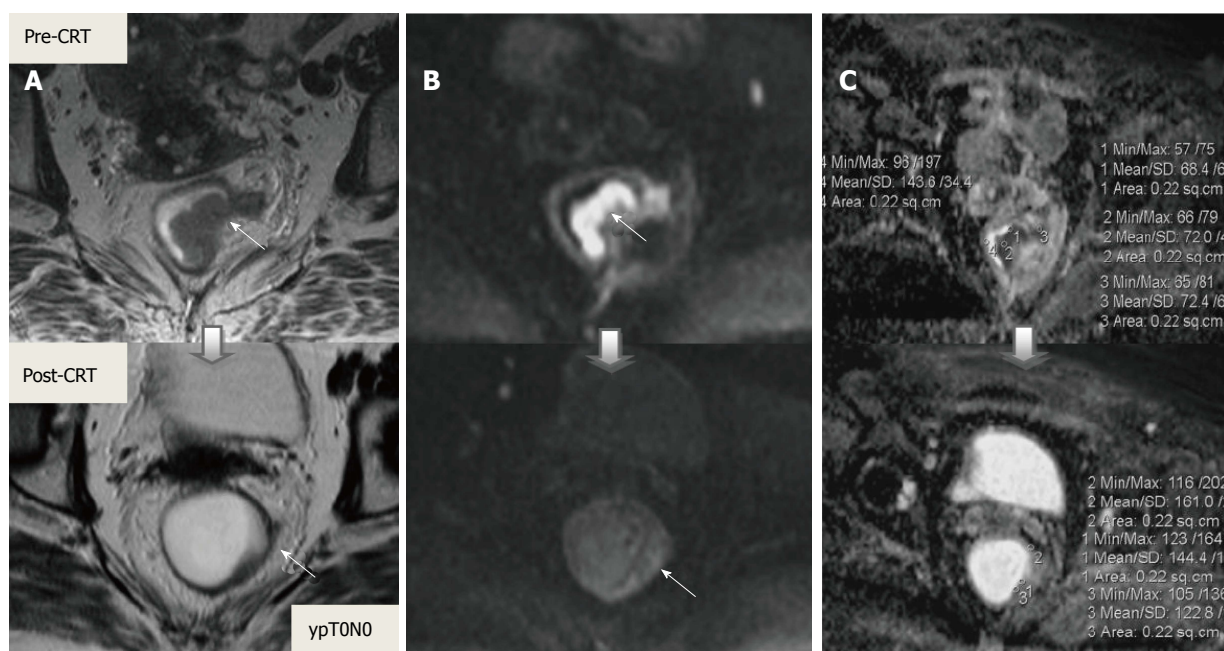


Figure 19 Post-chemoradiotherapy restaging using diffusion-weighted imaging in ypT0 rectal tumor. On T2-weighted (A), DW (B) and ADC (C) images in the same patient, baseline and post-CRT images are shown on upper and lower series, respectively. A: Posttreatment T2-weighted axial image shows a thick wall of low-signal-intensity fibrosis in the previous rectal tumor area (arrow). It is difficult to determine whether this area contains tumor cells or completely devoid of tumor cells (complete response); B: On posttreatment DW image (B-800), there is no diffusion signal in previous tumor area (arrows), compatible with complete response. In this case, DWI allows the correct differentiation of viable tumor from fibrosis; C: ADC images show post-therapy mean ADC increase ($0.70 \times 10^{-3} \text{ mm}^2/\text{s}$ vs $1.40 \times 10^{-3} \text{ mm}^2/\text{s}$) compatible with therapy response, but does not allow prediction of complete response. DWI: Diffusion-weighted imaging; CRT: Chemoradiotherapy.

on post-CRT T2-weighted MRI, in contrast, areas of residual tumor have intermediate signal-intensity^[46]. Careful review of high-resolution images and DWI can enable distinction of small residual tumor within fibrosis (Figure 18).

In addition to morphologic findings, DWI can provide

functional information that can be correlated with changes at the cellular level in response to treatment. After CRT, the decrease in cellularity and development of fibrosis or necrosis in responders results in an increase in diffusion, which decreases diffusion signal intensity in diffusion-weighted images and increases ADC values

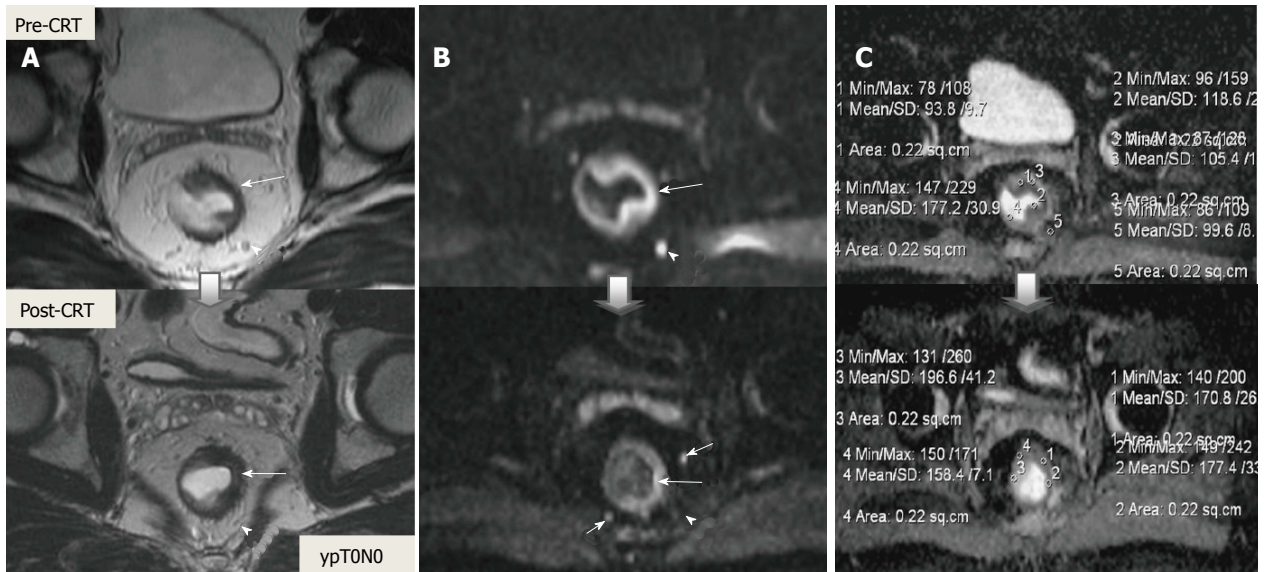


Figure 20 Post-chemoradiotherapy restaging using diffusion-weighted imaging in ypT0 rectal tumor. On T2-weighted (A), DW (B) and ADC (C) images in the same patient, baseline and post-CRT images are shown on upper and lower series, respectively. A: Posttreatment T2-weighted axial image shows a thick wall of low-signal-intensity fibrosis and areas suspicious for residual tumor have intermediate signal-intensity in the previous rectal tumor area (long arrow); B: Posttreatment DW images delineate a small foci of intermediate and low signal-intensity, respectively, compatible with residual tumor (long arrow); C: ADC images show post-therapy mean ADC increase ($1.05 \times 10^{-3} \text{ mm}^2/\text{s}$ vs $1.80 \times 10^{-3} \text{ mm}^2/\text{s}$), compatible with therapy response, but not with complete response. The suspicious mesorectal lymph node (arrowheads) is invisible on T2 and DWI after CRT, but the other two are still visible (short arrows). This case is an example for false-positive tumor and lymph node response evaluation of DWI. DWI: Diffusion-weighted imaging; CRT: Chemoradiotherapy.

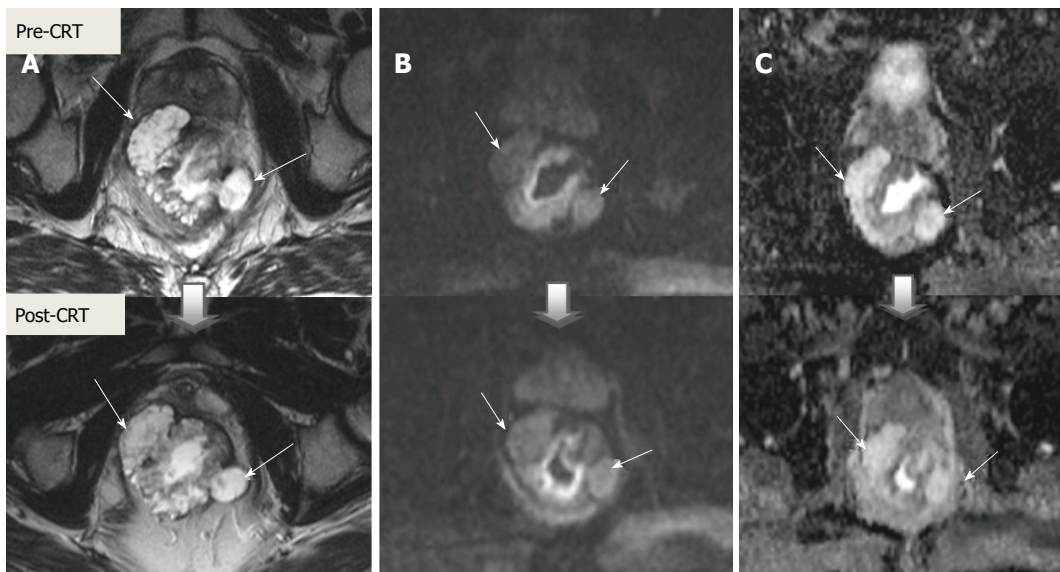


Figure 21 Mucinous adenocarcinoma. A: T2; B: Diffusion-weighted; C: ADC images in the same patient, baseline and post-CRT images are shown on upper and lower series, respectively. The mucinous tumor exhibits hyperintensity on T2, diffusion, and ADC images before and after treatment regardless of their response to treatment. Pre- and post-treatment ADC values are $1.70 \times 10^{-3} \text{ mm}^2/\text{s}$ and $2.10 \times 10^{-3} \text{ mm}^2/\text{s}$, respectively. Their response to CRT cannot be assessed using diffusion-weighted imaging. CRT: Chemoradiotherapy.

and ADC signal intensity in ADC images^[20,23] (Figures 18 and 19). Although DWI can differentiate viable tumor from fibrosis and good and bad response, it does not allow for predicting complete response^[19] (Figure 20). Moreover, the response of mucinous tumors to CRT cannot be assessed using DWI because they exhibit ADC hyperintensity even before treatment (Figure 21).

DISTANCE TO THE MESORECTAL FASCIA

CRM is considered uninvolved if a tumor free margin is seen at least 1 mm from MRF after CRT. This finding has strong negative predictive value (98%) of MR imaging for CRM involvement, whereas it has low positive

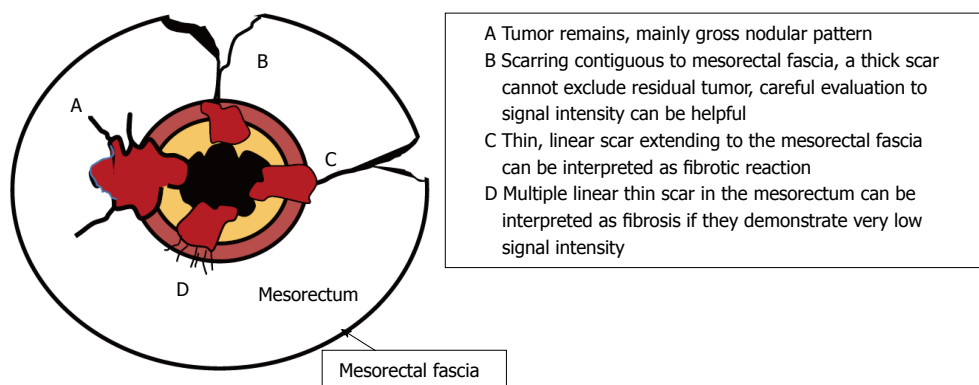


Figure 22 Schematic representation of effects of chemoradiotherapy on a rectal tumor and circumferential resection margins. Adapted from ref. [27]: Nougaret S, Reinhold C, Mikhael HW, Rouanet P, Bibeau F, Brown G. The use of MR imaging in treatment planning for patients with rectal carcinoma: have you checked the "DISTANCE"? *Radiology* 2013; **268**: 330-344.

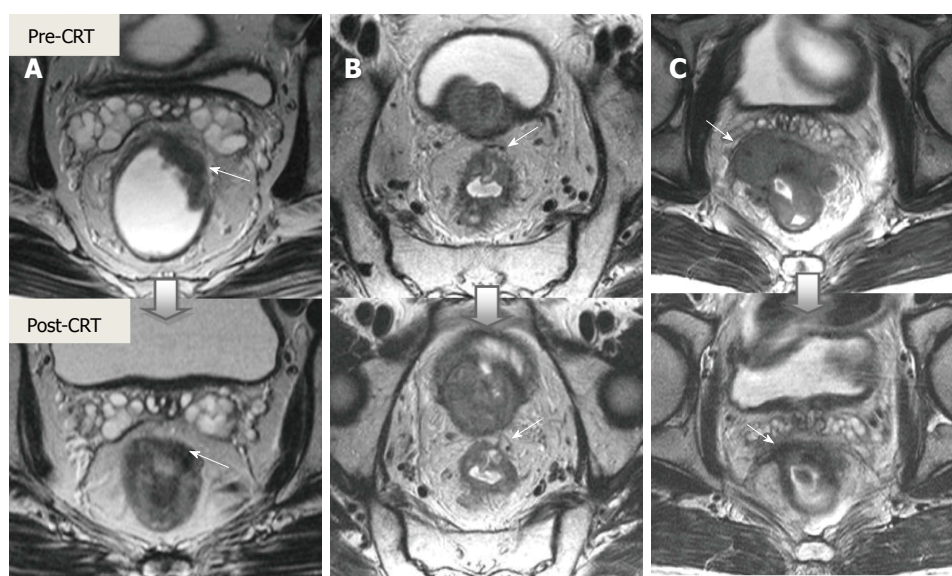


Figure 23 The effects of chemoradiotherapy on a rectal tumor and circumferential resection margins. T2-weighted axial magnetic resonance images in different patients show baseline and post-CRT images on upper and lower series, respectively. A: Overstaging due to thick, hypointense tissue infiltration at the mesorectal fascia (arrow) in ypT2 rectal tumor with no MRF invasion; B: In ypT3 rectal tumor with no MRF invasion, thick fibrous retractions of the tumor, suspicious for CRM positivity (arrow); C: Rectal mass is markedly shrunk with low-signal-intensity tissue infiltration at the mesorectal fascia (arrow). At surgery, there was tumor invasion of the mesorectal fascia. CRM: Circumferential resection margins; MRF: Mesorectal fascia; CRT: Chemoradiotherapy.

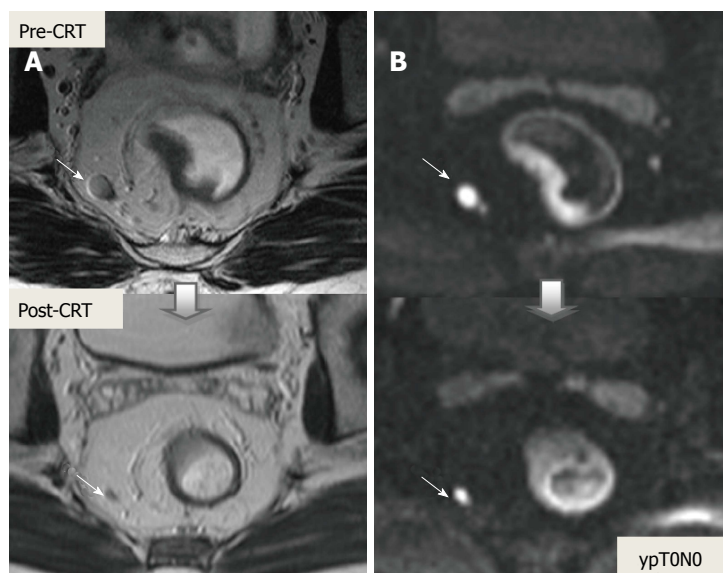


Figure 24 On diffusion-weighted imaging, false-positive mesorectal lymph node evaluation after chemoradiotherapy in ypT0N0 rectal cancer. A: T2-weighted axial magnetic resonance images show significant diminution in nodal size after chemoradiotherapy, compatible with negative lymph node (arrows); B: Diffusion-weighted images, high diffusion signal continues after treatment in the perirectal lymph node, compatible with positive lymph node (arrows). CRT: Chemoradiotherapy.

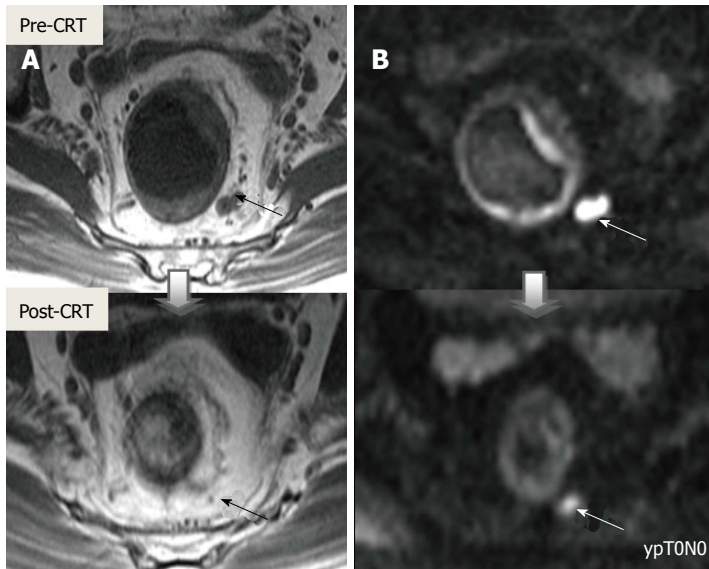


Figure 25 On diffusion-weighted imaging, false-positive mesorectal lymph node after chemoradiotherapy in ypT0N0 rectal cancer. A: T2-weighted axial images show significant diminution in nodal size, compatible with complete response; B: The continuation of high diffusion signal intensity on residual fibrotic lymph node incorrectly corresponds to a metastatic lymph node (arrows). CRT: Chemoradiotherapy.

predictive value^[49]. In some rectal tumor, however, CRT results in a markedly reduction tumor volume, but also in retraction of pre-existing contacts with MRF. It is difficult to determine whether this area contains tumor cells or completely devoid of tumor cells^[50] (Figures 22 and 23).

N-staging

After CRT, nodal size (short axis diameter) is more reliable for nodal re-staging. It is difficult to differentiate a metastatic lymph node from a healthy lymph node with irradiation changes using morphologic criteria or DWI; therefore, lymph node restaging often results in overstaging^[27,50] (Figures 24 and 25).

The accuracy of MRI for restaging is generally lower than the accuracy of MRI for initial staging, mainly owing to overstaging of nodal disease, failure to differentiate tumoral infiltration or residual tumor from desmoplastic reaction or radiation fibrosis^[50]. According to recent meta-analysis results, MRI accuracy was variable for restaging rectal cancer after neoadjuvant treatment; however, significantly better results were achieved when DWI was used or with experienced observers. The authors also reported that MRI could be used for evaluating CRM staging, but nodal staging remained a challenge^[51].

CONCLUSION

Using high-resolution MRI, standardizing image acquisition techniques and interpretation of images, comparative evaluation of pre- and post-CRT MR images, adding DWI to the standard approach, and importantly, experience and awareness of the limitations can improve diagnostic accuracy of MRI for re-staging.

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