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Review Article

Pitfalls and Challenges in the Interpretation of Rectal Cancer Magnetic Resonance Imaging

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Abstract

Magnetic resonance imaging (MRI) has taken a center stage in the imaging armamentarium of rectal cancer evaluation. Rectal cancer staging has undergone a paradigm shift from a surgico-pathological approach to a chemo-radiological one, helping effectively stratify patients for appropriate management. Primary lesion characterization, its morphology and internal characteristics, proximity of tumor to the mesorectal fascia, presence of extramural venous invasion, presence of extra mesorectal pelvic lymph nodes, and involvement of peritoneum and distant metastases are critical findings that impact patient management for which MRI is the preoperative gold standard. However, there are pitfalls, challenges, and misinterpretations related to technique, image quality, and knowledge gaps among the radiologists. These have major implications for patient management and their outcomes. In this article, we highlight the pitfalls and challenges in rectal cancer MRI and present practical solutions to circumvent these.

Keywords
- rectal cancer staging
- MRI protocol
- diffusion weighted imaging
- pitfalls and challenges

Introduction

Colorectal cancer is the third most commonly diagnosed cancer and the second most common cause of death due to cancer worldwide. Magnetic resonance imaging (MRI) has taken center stage in the imaging armamentarium of rectal cancer evaluation.[1] Rectal cancer staging has undergone a paradigm shift from a surgico-pathological approach to a chemo-radiological one, helping effectively stratify patients for appropriate management.[2] MRI is sine qua non for treatment planning as it evaluates many critical findings that impact patient management. However, there can be pitfalls, challenges, and misinterpretations related to technique, image quality, and knowledge gaps among the reporting radiologists. There is a wide spectrum of interobserver variability depending upon the utilization of structured reporting. Good interobserver agreement has been reported for dichotomous classification as high- versus low-risk T staging and N0 versus N-positive staging, tumor deposits, and involvement of the mesorectal fascia (MRF). However, poor agreement has been reported in multicategorical T and N staging and extramural venous invasion (EMVI) assessment.[3] Specialized and individualized training of the radiologists as well as the technical staff is imperative and an integral part of the whole process, which will ensure better MR interpretation in light of better MR acquisition.[4] The main purpose of this article is to simplify and lucidly present a practical view point while approaching rectal MRI in rectal cancer staging and categorize the main pitfalls and challenges with their redressal mechanisms wherever feasible. We have subcategorized the pitfalls and challenges with respect to patient preparation, MRI technique, MRI interpretation, histological types, and restaging MRI.

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Patient Preparation–Related Pitfalls

The latest Society of Abdominal Radiology (SAR) guidelines are followed in this discussion.[5] An endorectal coil is neither necessary nor recommended. Fasting 3 to 6 hours prior to a procedure decreases small gut movement. Spasmolytic agent administration (intravenous hyoscine butyl-bromide 20-mg injection) to prevent artifacts caused by small bowel motion is an area of disagreement. It might prove helpful if rectal gel is used, which can increase peristalsis, especially while imaging high rectal cancers. Administration of rectal gel/contrast remains a gray-zone area. Proponents cite benefits including a possibly improved ability to localize small tumors, clearance of pseudo-thickening of nondistended rectal wall, clear identification of tumor edges, and better appreciation of tumor spread beyond the muscularis propria.[6,7] Opponents raise concern about rectal distension causing artifactual decrease in the MRF distance and subsequent incorrect interpretation. The same holds true for rectal overloading. The other significant pitfall is high T2 signal of rectal gel may cause T2 shine-through effects on diffusion weighted imaging (DWI), leading to difficult evaluation of DWI, especially at 3 T and after chemoradiotherapy (CRT). Given the lack of consensus, use of intrarectal gel remains institution and protocol specific. Similar artifactual decrease in the MRF distance is noted when the urinary bladder is overdistended[7] (►**Fig. 1**).

MRI Technique–Related Pitfalls

High-resolution T2-weighted (T2W) 2D fast-spin echo sequences in sagittal, axial, and coronal planes are the essential sequences providing detailed anatomical and pathological information. Fat suppression is not required. 3D T2W sequences are not recommended due to associated motion artifacts and lower in-plane resolution.[7] In low rectal cancers, high-resolution T2 coronal sequence angled parallel to the anal canal is a mandatory addition to image the levator ani, sphincters, intersphincteric plane, and relationship to the rectal wall. For T2W axial images, slice thickness of $\leq$3 mm is recommended with in-plane resolution between 0.35×0.35 and 0.94×0.94 mm[1,7] (►**Fig. 2**). The axial sequence must be angled orthogonal to the tumor. Poor plane acquisition might lead to blurred margin of the muscularis propria leading to false T staging[3] (►**Fig. 3a**). The part of tumor projecting maximally into the mesorectal fat is detected on the sagittal plane. It is at this level that the axial sequence is planned perpendicular to the tumor (►**Fig. 3b**). In large tumors, more than one axial sequence angulation may be needed. DWI is a recommended component of the standard protocol as it might improve tumor and node detection.[8] However, echo planar DWI sequences are prone to susceptibility artifacts at the interface of gas and soft tissues. These artifacts can be prevented by administration of enema prior to the procedure.[9] DWI is performed at high *b*-values in rectal cancers as lower *b*-values cause water to appear brighter affecting the apparent diffusion coefficient (ADC) maps and lead to incomplete bladder fluid suppression[10] (►**Fig. 4**). A large field of view noncontrast T1W sequence is usually added to identify bone marrow abnormalities and nonregional enlarged lymph nodes.[2] Intravenous contrast medium administration is not mandatory, and the general consensus is that it does not improve staging of rectal cancer by MRI.[2,8]

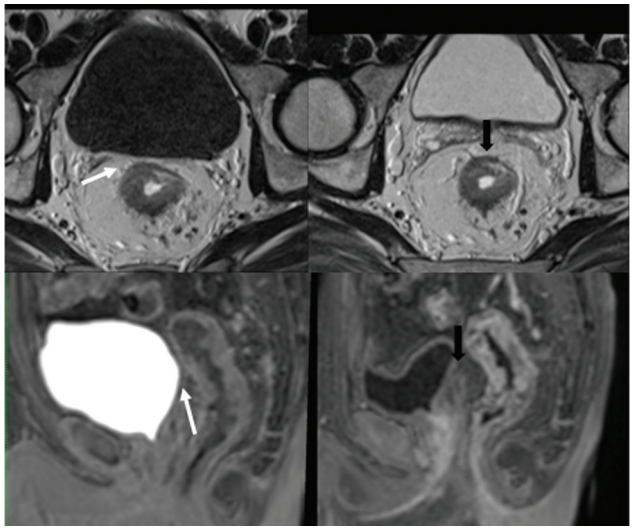

Fig. 1 Over-distended bladder leading to an apparent decrease in the distance between the mesorectal fascia (MRF; *white arrow*) and the anterior rectum, which may lead to erroneous upstaging of the tumor. The corresponding axial and sagittal images with adequately filled bladder after voiding show the actual position of the tumor with respect to the MRF (*black arrow*).

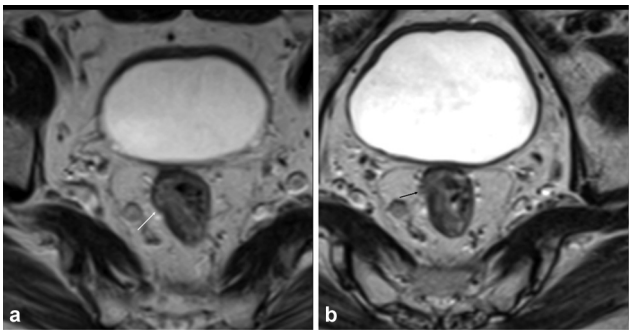

Fig. 2 Axial T2-weighted images at the level of the mid-rectum (**a**) with slice thickness of 5 mm, showing an eccentric thickening in the rectal wall (*white arrow*) confined to the serosa, (**b**) at slice thickness of 2.5 mm, showing the thickening infiltrating into the mesorectal fat (*black arrow*).

MRI Interpretation–Related Pitfalls and Challenges

Structured MRI reporting is a sine qua non in rectal cancer management. We discuss the MRI interpretation–related pitfalls and challenges in the following subsections.

Primary Tumor Morphology

The primary rectal tumor can be polypoidal (►**Fig. 5**), semi-annular, or circumferential in shape.[11] The site of attachment of the lesion to the rectal wall, also known as the invasive margin, needs to be focused when assessing the T stage and extramural invasion. The degree of attachment to the rectal wall called tumor circumference is described from one o'clock position to other o'clock position.[12] The tumors are

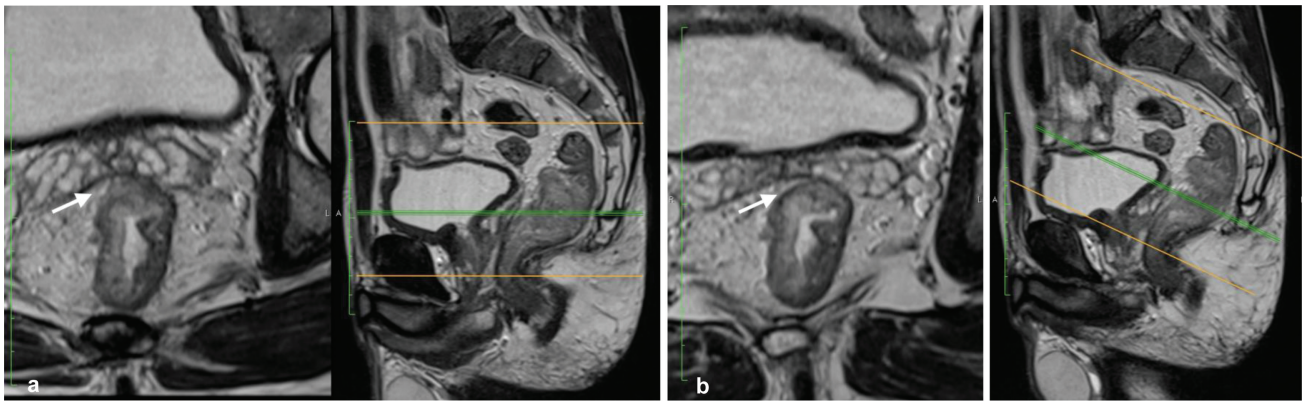

Fig. 3 (**a**) Axial T2-weighted (T2W) image shows loss of plane between the tumor margin and the seminal vesicle (*white arrow*) anteriorly staging the tumor as T4b. The corresponding sagittal image shows that the axial image was planned nonorthogonal to the primary tumor. (**b**) Axial T2W image in the same patient shows clear demarcation between the tumor and the seminal vesicles, downstaging the tumor to T3. The corresponding sagittal image shows the localizer plane is orthogonal to the tumor.

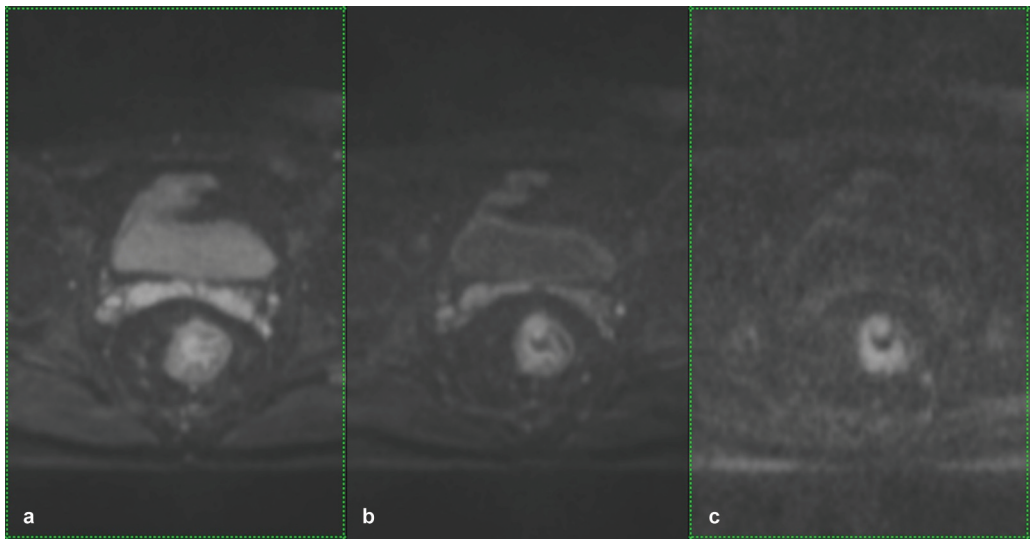

Fig. 4 Diffusion weighted imaging at *b*-values of (**a**) 500 s/mm^2, (**b**) 800 s/mm^2, and (**c**) 1,200 s/mm^2 showing incomplete bladder fluid suppression at low *b*-values. The tumor definition is increased on high *b*-values, while becoming less conspicuous on low *b*-values.

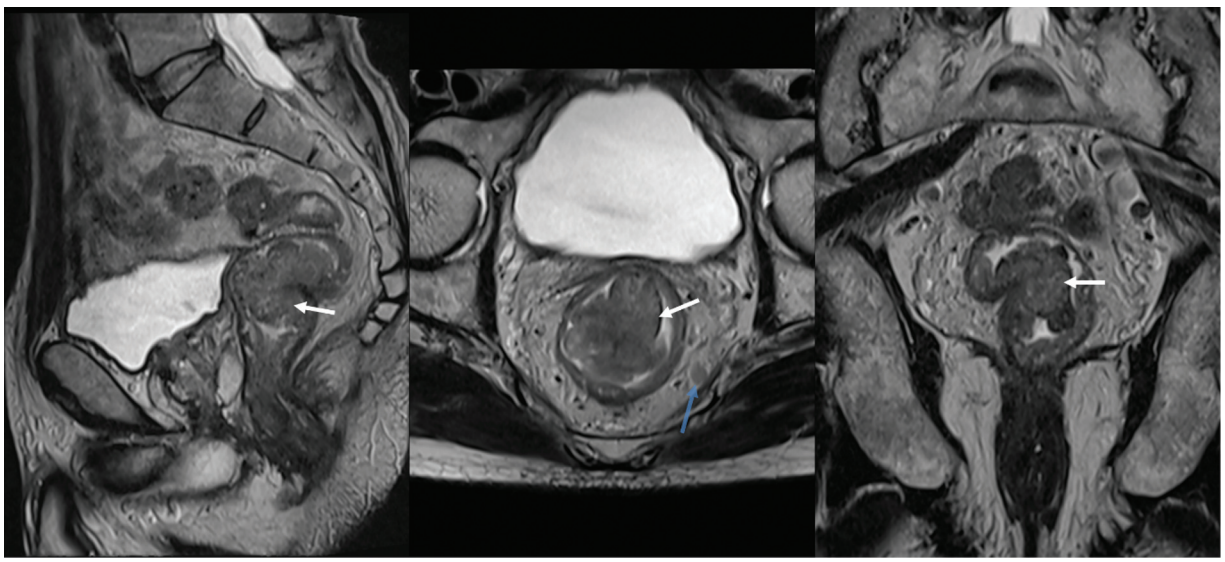

Fig. 5 Sagittal, axial, and coronal T2-weighted images depicting a polypoidal mass (*white arrows*) filling up the rectal lumen, with a nodal deposit (*blue arrow*) abutting the circumferential resection margin.

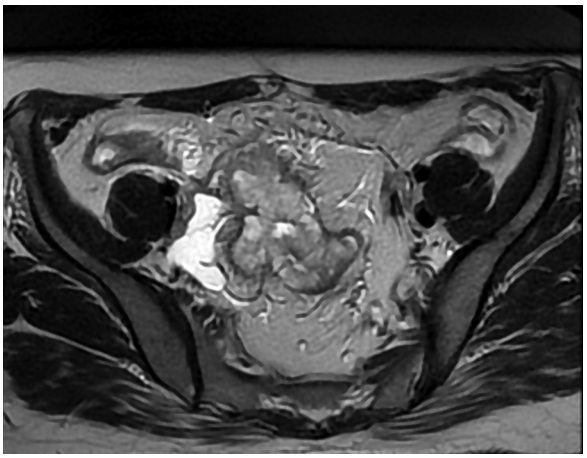

Fig. 6 Axial T2-weighted image showing bulky circumferential tumor in the upper rectum with T2-hyperintense signal. Histopathology revealed the mucinous nature of the tumor.

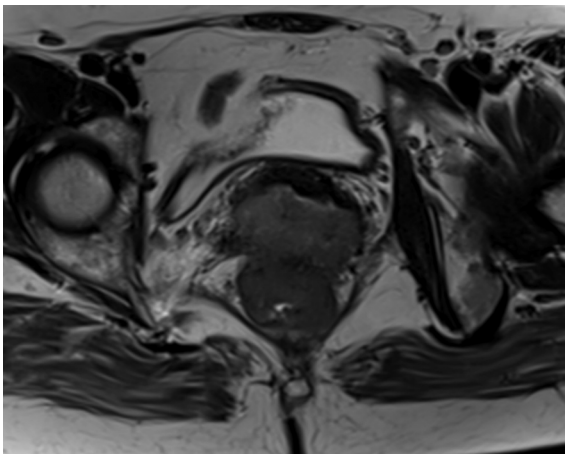

Fig. 8 Axial T2-weighted images demonstrating a T2-intermediate signal lesion infiltrating into the vagina anteriorly (T4b).

intermediate in signal on T2W images and higher in signal intensity than the muscularis propria (►**Fig. 6**). If the tumor contains a high proportion of mucin, it appears T2 hyperintense in signal.[2] There is considerable interobserver variability in discerning polypoidal tumors from semi-annular tumors since the former have a better prognosis, while the latter have an invasive/infiltrative margin.[3] Polypoidal tumors have been defined as those with less than equal to one-fourth the circumferential wall attachment and with a pedicle.[13]

T Staging

It is based on TNM staging. T1 tumors involve the mucosa and the submucosa with no extension into the muscularis propria. T2 shows invasion into the muscularis propria (►**Fig. 7**). T3 disease extends through the muscularis propria into perirectal tissues.[14] T3 is further subcategorized into a, b, c, and d on the basis of the depth of extramural invasion as the following: T3a <1 mm; T3b 1 to 5 mm; T3c >5 to 15 mm, and T3d >15 mm.[15] Subcategorization is important as studies show T3c patients have a 5-year survival rate of 54%, whereas T3b or less patients have 5-year survival rates of more than 85%.[16] T4 disease is staged as T4a if the disease involves the visceral peritoneum or anterior peritoneal reflection and T4b if the tumor invades organs or structures outside the mesorectum. Involvement of the pelvic organs (►**Fig. 8**), bones, striated/skeletal muscles (external anal sphincter, puborectalis, levator ani, obturator, piriformis, and ischiococcygeus), sciatic or sacral nerves, sacrospinous ligaments, any vessel outside the mesorectal compartments, or any loop of small or large bowel in the pelvis is considered T4b disease.[17]

T staging must be assessed on planes strictly perpendicular to the tumor. Involvement of perirectal fat differentiates T2 from T3 tumors. The T2 low signal intensity of the muscularis propria is completely obliterated and cannot be clearly distinguished from perirectal fat. Extension of the extramural spread is measured in millimeters beyond the extrapolated outer edge of the muscularis layer (►**Fig. 9**). Sometimes the outer edge of the muscularis propria is focally disrupted by small vessels penetrating the wall; this may not necessarily indicate tumor invasion.[18] Extramural tumor spread is sometimes difficult to distinguish from desmoplastic reactions resulting in staging failures between T2 and T3a. It can be frequently attributed to use of increased slice thickness and lower-resolution sequences. Ulcerative tumors are frequently associated with desmoplasia at the outer edge —it is typically seen as fine spicules that are nonrestrictive on diffusion and low signal intensity on T2W imaging (T2WI).

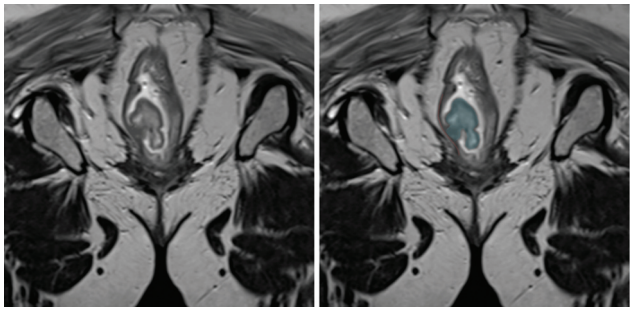

Fig. 7 Axial T2-weighted images demonstrating a polypoidal growth extending into the muscularis (*green*), without breaching the serosa (*red*)—T2 tumor.

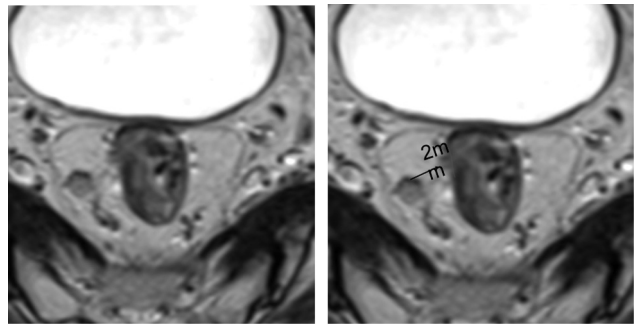

Fig. 9 Axial T2-weighted images showing an eccentric rectal thickening causing breach (*green line*) in the muscularis, extending into the surrounding mesorectal fat (*black arrow*) with a 2-mm-deep extramural invasion (T3b).

Extramural tumor spread, on the other hand, appears as nodular bands, which are restrictive on DWI and have an intermediate signal intensity on T2WI with disruption of the muscularis propria.[19]

Extramural Venous Invasion

Direct tumoral invasion of venous structures beyond the muscularis propria defines EMVI. Preoperatively EMVI is estimated on MRI (mrEMVI) and postoperatively by histopathology (pEMVI).[20,21] It is an independent prognostic predictor of adverse outcomes like local recurrence, distant metastasis, and overall prognosis. Detection before any intervention becomes an indication for neoadjuvant CRT. If detected on follow-up scan after CRT, further intensified CRT is indicated. Positive EMVI is denoted by obvious irregular vessel contour or nodular expansion of a vessel by definite tumor signal (►**Fig. 10**). EMVI is associated with tumors that are at least stage T3; T1 and T2 tumors do not invade extramural venous structures. EMVI can be contiguous and noncontiguous (separate from tumor). Positive/threatened circumferential resection margin (CRM) is also applied to EMVI in the same manner as for the main tumor.[22] MRI has limited sensitivity in the detection of EMVI in vessels less than 3 mm. It stems from the fact that these small vessels lack the normal signal void appearance as seen in large vessels. EMVI in these vessels can only be detected in the presence of vessel expansion, nodularity, or irregularity.[20] Misinterpretation of EMVI as a pathological lymph node, extramural spread, and desmoplastic reaction can be a source of error. However, the suspicious finding can be closely followed in multiple planes, helping in better differentiation.[23]

Circumferential Resection Margin

An independent prognostic marker for local recurrence and distant metastasis, CRM represented by the MRF is assessed in patients undergoing total mesorectal excision. Positive CRM is defined as lesion lying within 1 mm of the MRF. The lesion can be the main tumor, tumor deposit(s), or EMVI. CRM involvement cannot be discussed in tumors lying above the peritoneal reflection as there is no mesorectum above this level. Anteriorly the mesorectal fat is very thin and CRM involvement assessment is difficult as the rectum is very close to the CRM.[19] Anterior invasion of the peritoneum above the level of peritoneal reflection should never be mistaken as MRF invasion. Several T4a cases with simultaneous MRF involvement are under-staged as T3 MRF positive, choosing either MRF or peritoneal invasion (T4a) rather than acknowledging that the two may occur simultaneously.[3]

Lymph Node Staging

Locoregional lymph nodes include mesorectal, superior rectal, internal iliac, and obturator nodes.[24] Superficial inguinal nodes are considered locoregional only when the tumor is extending below the dentate line. Nodes elsewhere are considered distant metastasis. Therefore, there needs to be a basic understanding of the lymphatic drainage of the rectum.[25] The specificity of MRI for detection of nodal metastasis is only moderate, while its sensitivity depends on the criteria used. The most well-known features used include the size and morphology criteria. Promising results have been obtained with novel nodal contrast agents, nodal perfusion, diffusion and dynamic contrast-enhanced fat-suppressed high-resolution 3D gradient echo sequence (GRE) T1W sequences especially in less than 5 mm nodes; however, no standard consensus statement exists regarding their applicability.[26] TNM staging has recently subcategorized the N1 and N2 stages as different studies have shown significant differences in overall survival when patients were stratified by the extent of nodal metastasis. N1 is further substratified into N1a: metastasis in one regional node; N1b: metastasis in two to three regional nodes; and N1c: no regional lymph node is positive, instead tumor

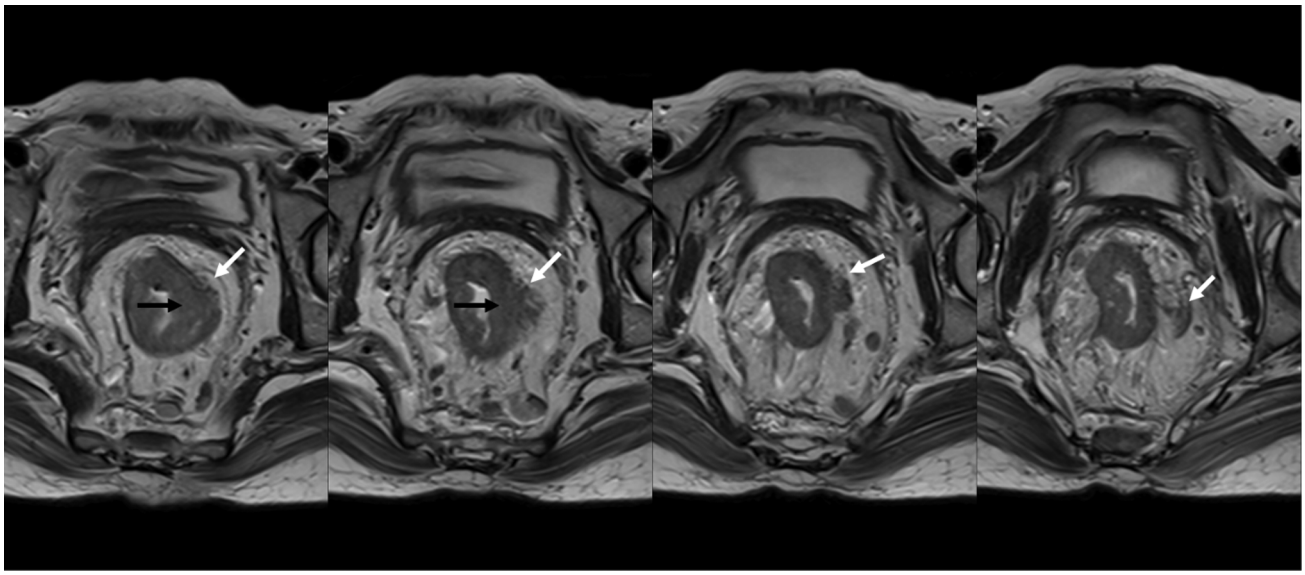

Fig. 10 Consecutive axial T2-weighted images showing extension of the rectal thickening (*black arrows*) causing nodular enlargement of an adjacent vessel (*white arrows*), which shows signal intensity similar to the primary tumor, representing extramural venous invasion.

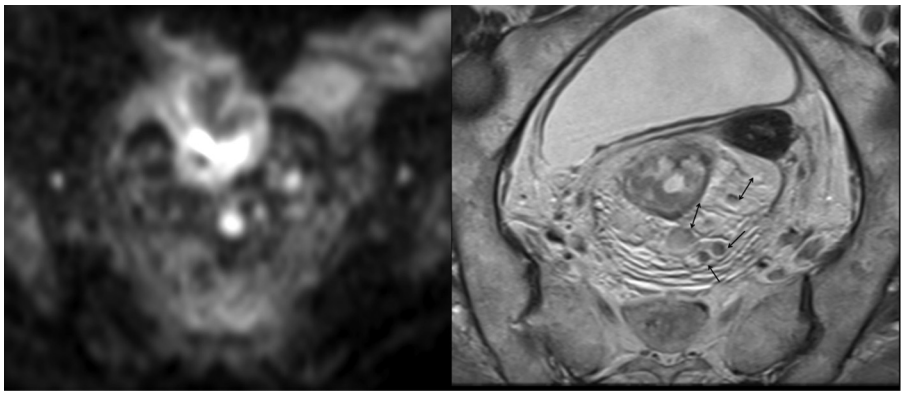

Fig. 11 Axial T2-weighted (T2W) images in a patient after chemoradiotherapy demonstrating hyperintense mesorectal nodes with restricted diffusion on diffusion weighted imaging, which appear T2 hyperintense on axial T2W image (*double headed arrows*) suggesting no response. However, the hypointense nodes (*black arrows*) show no diffusion restriction, suggestive of treatment response on restaging MRI.

deposits are seen in the subserosa, mesentery, or nonperitonealized, pericolic, or perirectal/mesorectal tissues. N2 is subcategorized into N2a (4–6 lymph node metastasis) and N2b (involvement of $\geq$7 regional lymph nodes).[27]

Mesorectal nodes are noted within the MRF, and rectal tumors located between the dentate line and the rectosigmoid junction can spread to these nodes.[28] Restaging of mesorectal nodes is more precise than staging since the absence of nodes on DWI rules out any residual nodal involvement; however, when present, size in combination with diffusion restriction is a more reliable indicator than the malignant morphologic criteria[29] (►**Fig. 11**). Although a cutoff of 5 mm has been set in discerning malignant from reactive mesorectal nodes, there is a frequent overlap between the two.[24,25] More than 50% of metastatic lymph nodes are less than 5 mm in diameter. Additional features like spiculation and heterogeneous contrast enhancement hardly increase the sensitivity of MRI in nodal metastasis detection. This leads to nodal under-staging with consequent prognostic implications like withholding of CRT in patients who can benefit from it.[30] DWI is considered a highly sensitive technique for lymph node detection in rectal cancer. However, DWI is not able to characterize lymph nodes as benign or malignant. Inflammatory nodes can also show diffusion restriction. Using diffusion as a lone criterion can lead to over-staging and unnecessary administration of adjuvant CRT.[26,31]

Lateral pelvic lymph nodes receive supply from tumors located at or beyond the anterior peritoneal reflection.[32] According to the Lateral Node Consortium Study group, patients with baseline pelvic nodes $\geq$7 mm at staging are considered suspicious and those with lateral pelvic nodes greater than 4 mm but less than 6 mm are also considered part of residual disease and warrant pelvic node dissection.[25] Superior rectal and inferior mesenteric lymph nodes may be erroneously labeled as common iliac nodes due to their close proximity to these vessels, leading to incorrect upstaging of the tumor.[33] Ovoid anterior obturator nodes are often reactive and should not be included as part of the disease.[25]

Histological Types

More than 90% of rectal carcinomas are adenocarcinomas.[34] Rectal adenocarcinomas are classified as nonmucinous and mucinous. Mucin containing carcinomas are further classified into mucinous and signet ring cell carcinomas containing greater than 50% of extracellular and intracellular mucin, respectively. They are associated with worst prognosis. MRI is more accurate than biopsy in diagnosing mucinous adenocarcinomas, which have a characteristic T2 hyperintense signal intensity with T2 hyperintense nodes. Signet ring cell carcinomas are characterized by a submucosal growth pattern and a linitis plastica appearance. Mucinous carcinomas show a T2 shine-through effect and hence may not be distinguishable on DWI. Persistence of T2 hyperintense signal intensity on restaging MRI may lead to an erroneous misdiagnosis of residual tumor. Signet ring cell carcinomas may be misdiagnosed as inflammatory thickening of the bowel.[35]

Restaging Magnetic Resonance Imaging

It helps in assessing response to treatment, progressive disease, and planning further management. Complete response is seen as a fibrotic scar with low T2 signal intensity of the submucosa, intermediate signal intensity of the muscularis propria, and low signal intensity of the serosa of the rectal wall (►**Fig. 12**). This split scar sign is highly specific and moderately sensitive in determining complete response. Following chemoradiotherapy, submucosal edema may be mistaken for residual tumor.[29] DWI with corresponding ADC is imperative in distinguishing between the two and would depict a T2 shine-through effect in the former (►**Fig. 13**). Submucosal edema can also be noted in the uninvolved rectal wall post-CRT mimicking tumor. Comparison with pretreatment MRI can help solve this discrepancy. T2 blackout effect can be seen at the site of posttreatment fibrosis, making it all the more imperative to assess DWI in the light of the corresponding ADC maps.[25]

In conclusion, the various pitfalls and challenges in rectal cancer MRI interpretation can be better addressed through specialized and individualized training of the radiologists as well as the technical staff. Errors in interpretation of primary

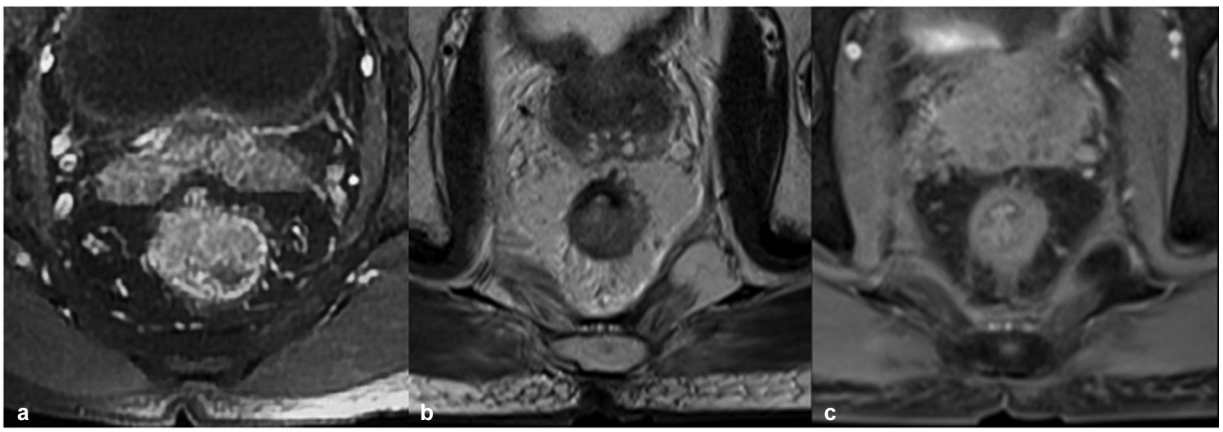

Fig. 12 Axial postcontrast T1 weighted (T1W) axial image showing enhancing semi-annular thickening along the (**a**) anterior wall of rectum, (**b**) posttreatment T2W image showing T2W hypointensity anteriorly at the previous site of tumor, (**c**) with no enhancement on the corresponding postcontrast magnetic resonance imaging, suggestive of a complete treatment response.

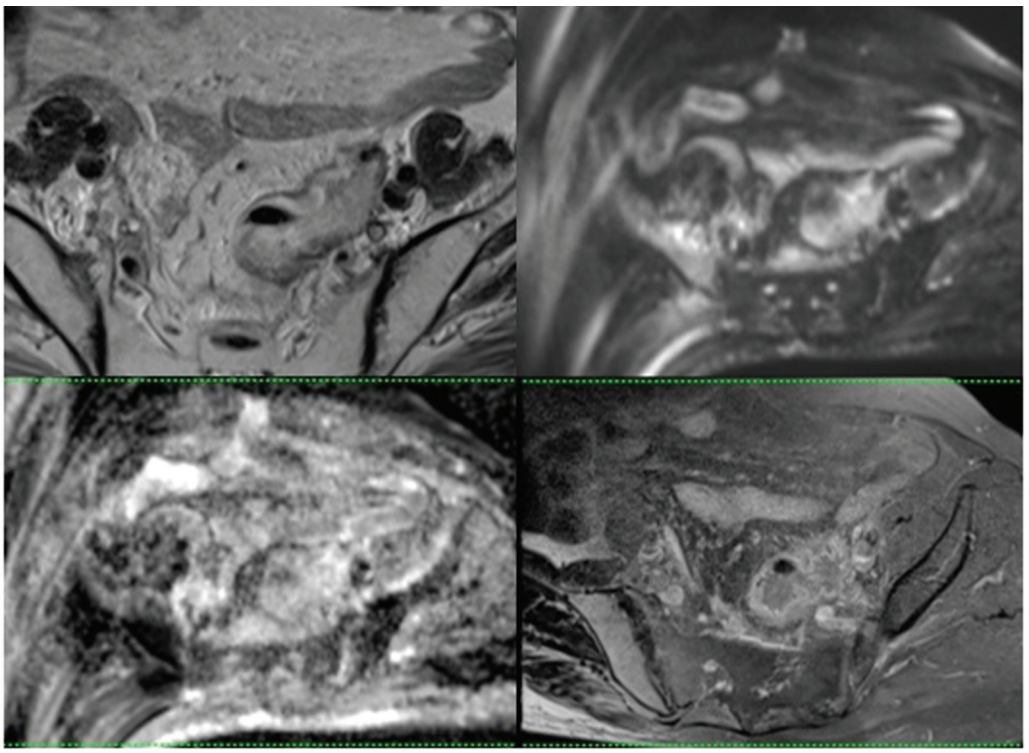

Fig. 13 Axial T2-weighted (T2W) image showing hyperintense thickening in the extensive rectosigmoid carcinoma, which appears bright on the corresponding diffusion weighted imaging and apparent diffusion coefficient map, suggestive of a T2 shine-through effect. Postcontrast magnetic resonance imaging shows no enhancement suggestive of submucosal edema after chemoradiotherapy.

staging and restaging rectal cancer MRI can be mitigated to a significant extent by proper technique, protocol optimization, and structured and sequential reporting. The accuracy of MRI in T staging is high, but the nodal staging still lacks specificity and standardization.

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Conflict of Interest
None declared.

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