# Restaging magnetic resonance imaging of the rectum after neoadjuvant therapy: a practical guide

Ressonância magnética do reto no reestadiamento após terapia neoadjuvante: um guia prático

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Abstract Colorectal cancer is the third most common cancer and the second leading cause of cancer-related death. Rectal cancer accounts for approximately one-third of new colorectal cancer cases, with adenocarcinoma as the predominant subtype. Despite an overall decline in colorectal cancer incidence and mortality, due to advancements in screening, early diagnosis, and treatment options, there is a concerning increase in incidence rates among young patients. Recent significant advances in managing locally advanced rectal cancer, such as the establishment of different surgical approaches, neoadjuvant treatment using different protocols for high-risk cases, and the adoption of organ-preservation strategies, have increased the importance of the role played by radiologists in locoregional assessment on magnetic resonance imaging at baseline, at restaging, and during active surveillance of patients with rectal cancer. In this article, we review the role of restaging rectal magnetic resonance imaging after neoadjuvant therapy, providing radiologists with a practical, step-by-step guide for assessing treatment response.

Keywords: Rectal neoplasms; Neoadjuvant therapy; Magnetic resonance imaging; Treatment outcome.

**Resumo** O câncer colorretal é o terceiro câncer mais comum e a segunda principal causa de morte relacionada ao câncer. O câncer retal representa aproximadamente um terço dos novos casos de câncer colorretal, sendo o adenocarcinoma o subtipo predominante. Apesar de uma diminuição geral na incidência e mortalidade, impulsionada por avanços na prevenção do câncer, diagnóstico precoce e opções de tratamento aprimoradas, há uma preocupante elevação nas taxas entre os pacientes jovens. Avanços recentes significativos no manejo do câncer retal localmente avançado, como abordagens cirúrgicas, o uso de diferentes protocolos de tratamento neoadjuvante para casos de alto risco e a adoção de estratégias de preservação de órgãos, aumentaram o papel dos radiologistas na avaliação locorregional por meio da ressonância magnética na avaliação inicial, reestadiamento e vigilância ativa de pacientes com câncer retal. Este manuscrito tem como objetivo revisar o papel da ressonância magnética retal no reestadiamento após terapia neoadjuvante, fornecendo aos radiologistas um guia prático para revisar exames nesse contexto.

Unitermos: Neoplasias retais; Terapia neoadjuvante; Ressonância magnética; Resultado do tratamento.

# INTRODUCTION

Colorectal cancer is the third most commonly diagnosed cancer in men and women and the second leading cause of cancer-related death worldwide<sup>(1)</sup>. More than 150,000 new cases of colorectal cancer are expected to be diagnosed in the United States in 2024, positioning the disease as a major contributor to cancer-related death<sup>(2)</sup>. Because of advances in screening, early diagnosis, and treatment, colorectal cancer mortality rates have decreased from 29.2 deaths per 100,000 population in 1970 to 12.6 deaths per 100,000 population in 2020<sup>(3)</sup>. Nevertheless, there is a concerning rise in the proportion of individuals diagnosed with colorectal cancer, particularly rectal cancer, among individuals under 50 years of age<sup>(4,5)</sup>.

Currently, neoadjuvant therapy (NAT)—typically in the form of chemoradiation therapy (CRT)—followed by total mesorectal excision (TME) is considered the standard of care for locally advanced rectal cancer<sup>(6,7)</sup>. Depending on the histological findings after TME, some patients also undergo adjuvant systemic therapy. In recent years, nonoperative management (NOM) for selected patients with a complete response after NAT is an option that has increasingly been employed<sup>(8,9)</sup>. The aim of NOM is to avoid surgery (i.e., TME) while ensuring oncological safety and improving overall quality of life for patients.

It is possible to administer NAT in a different sequence, known as total neoadjuvant therapy (TNT), in which all systemic chemotherapy and CRT are administered before surgery. This newer approach is gaining prominence due to better rates of complete pathologic response (cPR) and patient outcomes, as shown in one meta-analysis<sup>(8,9)</sup>, and higher rates of nonsurgical cure-defined as a sustained complete clinical response (cCR)-as shown in the Organ Preservation in Patients With Rectal Adenocarcinoma (OPRA) trial<sup>(10)</sup>. Another new approach is programmed cell death 1 blockade immunotherapy in patients with locally advanced rectal cancer and mismatch repair deficiency; in an initial study, all patients who received this immunotherapy, with or without CRT, achieved a  $cCR^{(11)}$ . These newer approaches may further increase the number of patients eligible for NOM.

Restaging rectal magnetic resonance imaging (MRI) plays a critical role in defining the response to NAT and helps the multidisciplinary team define the best next step (i.e., involving or avoiding surgery). In the case of surgery, restaging rectal MRI also provides a roadmap to determine the best surgical approach for complete surgical resection of all tumor sites. The aim of this article is to review the role of restaging rectal MRI after NAT, providing radiologists with a practical step-by-step guide for assessing treatment response.

# **OVERVIEW OF NAT**

Conventional NAT for locally advanced rectal cancer involves the concurrent administration of radiation and radiosensitizing agents. Typically, patients receive radiation therapy to the pelvic area after administration of a radiosensitizer, typically fluorouracil or capecitabine<sup>(3)</sup>. Following the completion of neoadjuvant CRT, patients typically undergo TME to remove the remaining tumor. After TME, adjuvant systemic chemotherapy may also be recommended to target any remaining cancer cells and reduce the risk of recurrence. Conventional NAT is a longstanding, effective strategy for the comprehensive management of locally advanced rectal cancer. After neoadjuvant CRT followed by TME, 20% of patients achieve a cPR<sup>(12)</sup>.

Although conventional NAT continues to be widely used as the standard of care for locally advanced rectal cancer, TNT, which involves the integration of systemic chemotherapy with neoadjuvant CRT before any TME, has been increasingly adopted and is experiencing rapid growth. There are two main types of TNT, depending on whether systemic chemotherapy is added before or after neoadjuvant CRT: induction chemotherapy followed by CRT; and consolidation chemotherapy administered after CRT. The most common systemic chemotherapies are as follows: folinic acid, fluorouracil, and oxaliplatin; capecitabine and oxaliplatin; and folinic acid, fluoracil, irinotecan, and oxaliplatin. Patients undergoing TNT exhibit lower rates of distal recurrence, better 3-year disease-free survival, improved compliance with therapy, superior overall survival, and notably higher rates of cPR<sup>(13)</sup>.

# **ORGAN-PRESERVATION STRATEGY**

Organ preservation in the treatment of rectal cancer involves maintaining rectal integrity through the avoidance of radical surgery. In 2004, Habr-Gama et al.<sup>(14)</sup> devised an organ-preservation strategy for selected rectal cancer patients who achieved a cCR after NAT in Brazil. Since then, various studies have been published further exploring and validating their approach<sup>(8)</sup>. In rectal cancer, NOM is often referred to as a "watch-and-wait" approach or as active surveillance. Instead of undergoing TME immediately after NAT, patients undergoing NOM are monitored carefully through regular imaging and clinical assessments. Another organ-preservation approach involves local excision, utilizing either endoscopic microsurgery or transanal minimally invasive surgery, for selected patients with small viable lesions and an excellent response after NAT. The primary objective of organ-preservation strategies is to offer a individualized, minimally invasive alternative in the comprehensive management of rectal cancer. Such strategies emphasize effective disease control while minimizing the adverse effects associated with extensive surgery. This is especially significant in the case of low-rectal tumors, where abdominoperineal resection and permanent colostomy are conventionally indicated to provide an R0 resection (i.e., one in which the surgical margin is microscopically-negative for residual tumor). An organ-preservation approach seeks to tailor treatment to individual patient needs, thus optimizing outcomes and mitigating the impact of major surgical intervention<sup>(9,14,15)</sup>.

# ASSESSMENT OF THE RESPONSE TO NAT

Typically, the response to NAT is assessed 8–12 weeks after the initiation of the therapy, although the timing can vary depending on the treatment plan and trial<sup>(8)</sup>. Response is assessed through a multidisciplinary analysis incorporating endoscopy, digital rectal examination (DRE), and rectal MRI. The goal of a multidisciplinary response assessment is to classify the response as follows: complete clinical response (cCR), near-complete clinical response (nCR), or incomplete clinical response (iCR). The Memorial Sloan Kettering regression schema<sup>(15)</sup> used in the OPRA trial<sup>(16)</sup> continues to be employed in the ongoing Janus Rectal Cancer Trial; the category definitions can be summarized as follows:

- -cCR
  - DRE: normal, without palpable tumor
  - Endoscopy: flat, white scar with telangiectasia, no ulcer, and no nodularities
  - MRI: no evidence of viable disease at the tumor bed or

any sign of disease in general and no suspicious lymph nodes

– nCR

• DRE: smooth induration or minor mucosal changes

 Endoscopy: small mucosal nodules or minor mucosal abnormalities, superficial ulceration, mild persistent erythema, or scarring with telangiectasia

 MRI: evidence of a very small volume of viable disease at the tumor bed or partial regression of lymph nodes
 iCB

• DRE: palpable tumor

• Endoscopy: clear viable tumor

• MRI: clearly visible viable disease at the tumor bed or definitely suspicious lymph nodes

## **RESTAGING RECTAL MRI**

# **MRI** protocol

An optimal protocol should provide the necessary MRI sequences for response assessment while ensuring minimal acquisition time to prioritize patient comfort and ensure clinical efficiency.

#### Preparation

The use of an antispasmodic (e.g., glucagon or hyoscine butylbromide) shortly before the examination is beneficial to reduce motion artifacts (often observed in upper rectal tumors) caused by peristalsis. In addition, the use of a micro-enema (5 mL) can reduce susceptibility artifacts produced by rectal air<sup>(17,18)</sup>. Although the use of a microenema is controversial, it can easily be self-administered and can be particularly useful in the restaging setting, given that diffusion-weighted imaging (DWI) can be an important tool used as a complement to T2-weighted imaging (T2WI).

#### Protocol

The patient should be instructed to empty their bowels and bladder first and then lie comfortably in the supine position on the scanner bed. An MRI scanner with a field strength of 1.5 T or 3.0 T should be used and should be equipped with a phased-array surface coil that is adjusted to cover the region just below the pubic bone. Comparison with baseline scans is crucial for ensuring proper acquisition planning; it is especially important to select the axial oblique plane, which should be perpendicular to the tumor bed.

The main sequences to be acquired during restaging rectal MRI are two-dimensional fast spin-echo (FSE) T2WI without fat suppression and DWI (Table 1). In the restaging examination, as in the baseline examination, T2WI is fundamental and every effort should be made to ensure optimal T2WI quality. To assess the tumor bed<sup>(19)</sup>, extramural vascular invasion (EMVI), or tumor deposits, DWI is a valuable complement to T2WI<sup>(20)</sup>. Of note, the use of an endorectal coil, endorectal filling, sequences including T2WI with fat suppression, T1WI, and contrast-

#### Table 1-Restaging rectal MRI protocol.

Imaging technique	Details
Axial T2WI, large FOV	Whole pelvis, from the aortic bifurcation to the anal verge
Sagittal T2WI	Include both pelvic sidewalls
Axial oblique slice of the tumor bed	Perpendicular to the tumor bed, slice thickness of 3 mm
Coronal oblique slice of the tumor bed	Slice thickness of 3 mm
Coronal oblique slice of the anal canal	For lower rectal tumors, slice thickness of 3 mm
DWI*	With a b value $\geq$ 800 s/mm^2 and including ADC maps

FOV, field of view.

\* Two DWI sequences can be obtained: one with a large FOV of the pelvis and a low b value ( $\approx 800$  s/mm<sup>2</sup>); and one with a small FOV perpendicular to the tumor bed and a higher b value ( $\approx 1500$  s/mm<sup>2</sup>).

enhanced T1WI have not demonstrated added value in the local restaging of rectal cancer after NAT<sup>(21)</sup>.

# Stepwise approach to reviewing restaging rectal MRI Step 1 – Comprehensive review of the clinical history

The first step in reviewing a restaging rectal MRI examination is to perform a comprehensive review of the clinical history of the patient, including DRE findings, endoscopy findings, the type of NAT administered, and the time from the completion of NAT to the restaging rectal MRI<sup>(22)</sup>. Opinions vary regarding the optimal time from the completion of NAT to the first post-treatment restaging rectal MRI. The response assessment is typically performed 8–12 weeks after NAT completion, although the interval can be longer depending on the treatment approach; the optimal interval tends to be shorter after completion of CRT than after completion of TNT<sup>(8,23)</sup>.

#### Step 2 – Evaluation of the baseline MRI

Evaluation of the baseline MRI is important for radiologists to understand the precise location of the tumor bed and to identify any mucinous components, so as to avoid pitfalls (e.g., post-treatment changes that can mimic a viable tumor) and to identify extrarectal disease (e.g., extramural vascular invasion, tumor deposits, and lymph node invasion). For patients whose baseline MRI was performed at a different institution, it is highly recommended that patients and referring physicians be educated to provide the initial baseline rectal MRI in order to improve the interpretation of the restaging rectal MRI<sup>(24)</sup>.

#### Step 3 – Assessment of the treatment response

Assessment of the treatment response provides valuable data that correlate with patient outcomes and guides the next steps regarding disease management.

#### Treatment response and T2WI

Nonmucinous tumors will demonstrate a spectrum ranging from very low to intermediate signal intensity—

corresponding to fibrosis and viable tumor tissue, respectively<sup>(24)</sup>. Mucinous tumors (i.e., those with > 50% mucin at baseline), tumors with mucinous features (i.e., those with < 50% mucin at baseline), and tumors undergoing mucinous/colloid degeneration (i.e., those beginning to produce mucin after NAT) may demonstrate different degrees of mucin content, fibrosis, and viable tumor tissue<sup>(25)</sup>. The mucin component demonstrates very high signal intensity on T2WI and can be either cellular or acellular on histopathology. Currently, MRI cannot distinguish between cellular and acellular mucin<sup>(26)</sup>.

#### Treatment response and DWI

Serving as a complement to T2WI, DWI can detect viable tumor in nonmucinous tumors<sup>(27)</sup>. Hypercellular tissues, such as viable tumors, restrict the movement of water molecules because of their dense interstitial space, resulting in high signal intensity on DWI and low signal intensity on apparent diffusion coefficient (ADC) maps. In contrast, fibrotic tissues, with their looser, collagenous matrix, allow freer movement of water molecules, leading to lower signal intensity on DWI and higher signal intensity on ADC maps. In addition, the morphological characteristics of residual tumors on DWI often reflect the geometry of the original tumors, such that employing a pattern-based approach for identifying residual disease can improve the diagnostic performance in predicting a complete response.

Interpreting DWI requires expertise, as evidenced by the moderate inter-reader agreement reported in the literature for determining the response to neoadjuvant  $CRT^{(28)}$ , which improves slightly with the addition of T2WI (kappa = 0.402 vs. 0.51–0.688). Notably, the majority of positive DWI findings at restaging MRI align well with the endoscopic results, demonstrating a positive predictive value of 86%.

Viable non-mucinous tumor may appear as a focal wall thickening or nodules within the tumor bed, with high signal intensity on DWI and low signal intensity on ADC mapping. This differs from certain potential pitfalls, as outlined below.

Artifacts – False positives (high signal intensity on DWI and low signal intensity on an ADC map) may result from susceptibility artifacts caused by rectal air or other artifacts like metal artifacts (Figure 1). As previously mentioned, rectal air artifacts can be minimized by administering a micro-enema before the examination<sup>(17)</sup>. If artifacts significantly compromise image quality, it is crucial to acknowledge this in the radiology report, and DWI should not be the basis for final interpretation.

Lack of correspondence to the baseline tumor bed – For DWI to be considered positive, it is essential that the suspicious area corresponds to the designated tumor bed. If the suspicious area is outside the designated tumor bed, it should not be regarded as indicating suspicion of a viable tumor. T2 shine-through – The T2 shine-through effect occurs when there is high signal intensity on DWI and the ADC map, often representing fluid or mucin components. Intraluminal fluid typically shows T2 shine-through with a tri-radiate morphology ("Mercedes-Benz" sign), as depicted in Figure 1.

T2 blackout – The T2 blackout effect is identified by low signal intensity on DWI and the ADC map, representing fibrosis, and also shows markedly low signal intensity on T2WI<sup>(24)</sup>, as also depicted in Figure 1.

#### Treatment response classification

# Post-NAT MRI tumor regression grade

The post-NAT magnetic resonance tumor regression grade (mrTRG) system is employed at some institutions. The mrTRG system is an adaptation of the TRG system that is used in pathology<sup>(29)</sup>. The post-NAT mrTRG generates a score from 1 to 5, based on the degree of tumor remaining and the amount of fibrosis after NAT, as detailed in Table 2. The total mrTRG score has been associated with disease-free and overall survival<sup>(30)</sup>, as well as having shown moderate accuracy for detecting a cPR<sup>(31)</sup>. Specifically, a post-NAT mrTRG score of 1 or 2 (indicating complete or substantial radiological regression, respectively) has been shown to have a sensitivity of 70-71% and a specificity of 62-68% for a cPR<sup>(32,33)</sup>. Although the use of the mrTRG system has shown some benefits, it is crucial to acknowledge the limited correlation between the mrTRG and pathologic TRG scores. In addition, the consistency in reading mrTRG scores varies significantly among different reviewers, with kappa values ranging from 0.25 to  $0.80^{(34-36)}$ . Furthermore, it is important to note that even when incorporating DWI into the mrTRG classification, the area under the receiver operating characteristic curve increased from 0.69 to only  $0.74^{(37)}$ .

#### cCR, nCR, and iCR

The classification system used in the OPRA trial and recommended by some societies, such as the Society of Abdominal Radiology<sup>(21)</sup>, classifies treatment response into three groups (Figure 2): cCR, nCR, and iCR.

A cCR represents an extremely positive treatment response, defined as a significant reduction in tumor size, evidenced by marked disappearance of the intermediate signal

Table 2-Post-NAT mrTRG scoring.

Score	Description
mrTRG1	Minimal or no visible fibrosis (appearing as a thin linear scar), with low signal intensity on T2WI, and absence of tumor signal (intermediate signal intensity)
mrTRG2	Prominent fibrosis without tumor signal
mrTRG3	Mainly fibrotic but with noticeable, measurable areas of tumor signal
mrTRG4	Mostly tumor signal with negligible fibrosis
mrTRG5	Exclusive tumor presence or an increase in tumor size over baseline

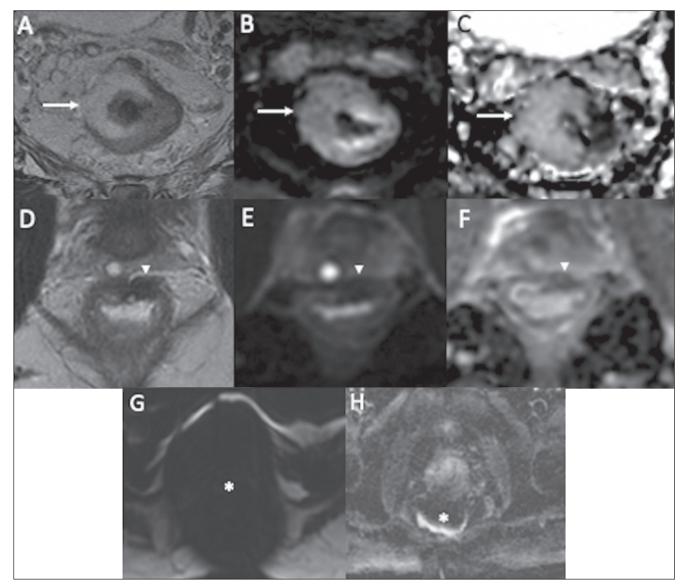


Figure 1. Examples of DWI artifacts. A–C: A T2 shine-through artifact (arrows) in a patient with a mucinous tumor showing high signal intensity on T2WI (A), DWI (B), and the ADC map (C). D–F: A T2 blackout artifact (arrowheads) identified by significant low signal intensity on T2WI (D), low signal intensity on DWI (E), and low signal intensity on the ADC map (F), representing fibrosis. G,H: Two additional examples of DWI artifacts (asterisks) due to surgical clips (G) and rectal air (H).

on T2 restaging rectal MRI. Specific changes on T2WI and DWI, as depicted in Figure 3, include the following:

T2WI – There can be a linear or crescent-shaped scar in the mucosal/submucosal layers, or even a return of the rectal wall to a normal appearance. It is noteworthy that rectal wall normalization, which indicates a complete response, occurs in about 5% of cases<sup>(38)</sup>.

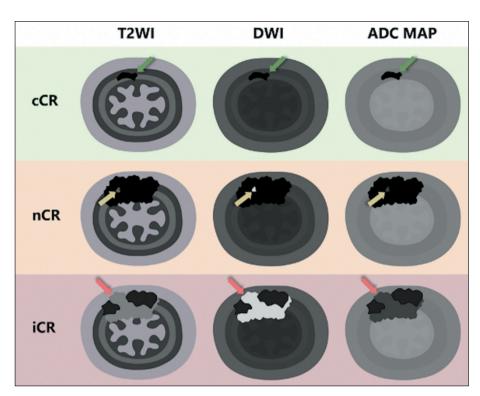
DWI – Absence of high signal intensity on images with a high b value<sup>(19,39–41)</sup>. Comparison with baseline images and referencing the normal rectum are crucial in this assessment. DWI is particularly useful for detecting cCR in small, subcircumferential scars<sup>(27)</sup>.

An nCR represents significant but not total regression. This category emerged from observations that many patients show a very good but not complete response and might achieve a cCR given more time between the completion of the NAT and the response assessment (Figure 4). With an nCR, there is a small area of intermediate signal intensity on T2WI or a small punctate area of restricted diffusion on DWI. An iCR represents significant residual tumor (Figure 5).

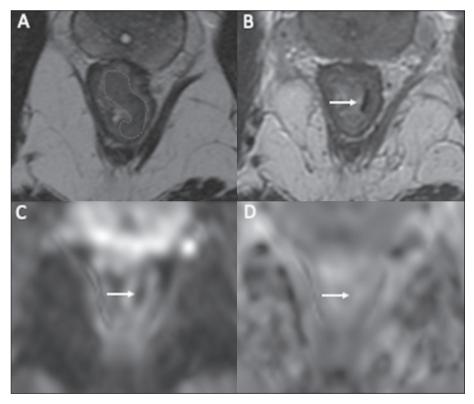
If the institution and multidisciplinary team are aiming at organ preservation, defining the initial post-NAT response (cCR, nCR, or iCR) is important (Figure 6). Most patients with an initial cCR or nCR will have a sustained cCR; these patients are candidates for watch-and-wait management, potentially avoiding surgery<sup>(42)</sup>. However, patients with an iCR are not suited for watch-and-wait management<sup>(15,16)</sup>.

# Step 4 – Evaluation of the relationship between the tumor and adjacent structures

In order to decide which surgical treatment is most appropriate for each patient, surgeons need to know whether Horvat N, et al. / Rectal MRI for restaging after neoadjuvant therapy



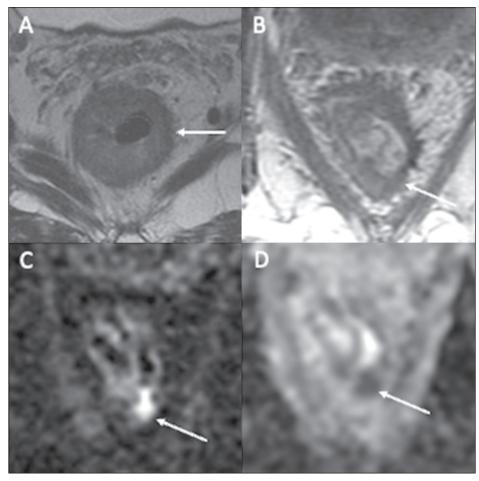
**Figure 2.** Illustration with examples of different clinical responses on restaging rectal MRI based on T2WI, DWI, and ADC mapping of the tumor bed. A cCR is characterized by markedly low signal intensity (SI) on T2WI and no restricted diffusion (low SI on DWI and the ADC map), indicated by green arrows. An nCR corresponds to marked fibrosis (low SI on T2WI, DWI, and the ADC map) with small areas of viable tumor, defined as intermediate SI on T2WI and restricted diffusion (high SI on DWI and low SI on the ADC map), indicated by yellow arrows. An iCR is defined as definite areas of viable tumor, indicated by red arrows.

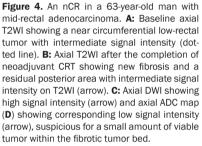


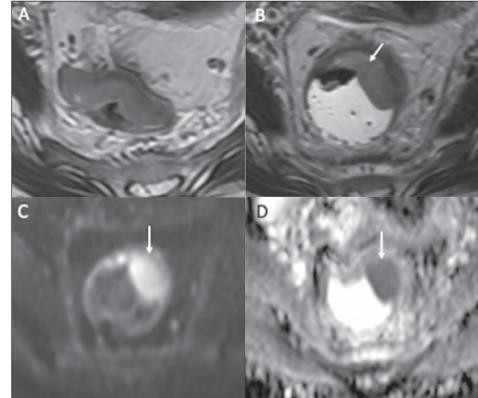
**Figure 3.** A cCR after NAT in a 41-year-old man with low-rectal adenocarcinoma. **A:** Baseline axial T2WI showing a low-rectal tumor (dotted line). **B:** Axial T2WI after the completion of NAT shows a thin hypointense scar at the site of the treated tumor (arrow). No diffusion restriction was present on DWI (**C**) or ADC mapping (**D**).

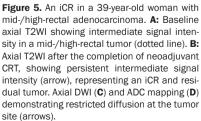
or not the tumor has invaded the adjacent structures. It is also important to describe potential fibrotic changes and whether they involve adjacent structures. The following structures should be included when assessing treatment response: the mesorectal fascia (MRF), peritoneum, pelvic viscera (bladder, ureters, urethra, prostate, seminal vesicles, uterus, and vagina), pelvic sidewalls, iliac vessels, sciatic nerve, sacral roots, lumbosacral trunk, levator ani muscles, puborectalis muscle, external sphincter, intersphincteric space, internal sphincter, and pelvic bones.

The status of the MRF in particular is a crucial element. A clear MRF on restaging MRI has a positive predictive value of up to 90% for clear margins upon pathological examination<sup>(43)</sup>. Involvement of the MRF is evaluated by









T2WI Assessment				
Complete Response	Near Complete Response	Incomplete / No Response		
<ul> <li>Normal appearing rectal wall</li> <li>OR</li> <li>Only fibrosis (low signal intensity) and no intermediate signal intensity at the site of tumor*</li> <li>AND</li> <li>No suspicious lymph nodes</li> </ul>	<ul> <li>Predominantly fibrosis at the site of tumor* with punctate areas of intermediate signal</li> <li>AND/OR</li> <li>No suspicious or borderline enlarged lymph nodes</li> </ul>	<ul> <li>Predominantly residual tumor (intermediate signal intensity) at the site of tumor*</li> <li>AND/OR</li> <li>Suspicious lymph nodes</li> <li>AND/OR</li> <li>Mucin at the site of tumor**</li> </ul>		
DWI Assessment				
Complete Response	Near Complete Response	Incomplete / No Response		
<ul> <li>No restricted diffusion at the site of tumor*</li> </ul>	<ul> <li>Punctate areas of restricted diffusion at the site of tumor*</li> </ul>	<ul> <li>Restricted diffusion at the site of tumor*</li> </ul>		
* Site of tumor: rectal wall, extramural vascular invasion and/or tumor deposit ** MRI is unable to differentiate cellular from acellular mucin				

Figure 6. Summary of the final assessment on restaging rectal MRI.

measuring the distance from the MRF to the nearest edge of the rectal tumor, taking into account the direct extent of the tumor, EMVI, tumor deposits, or lymph nodes with completely disrupted capsules<sup>(44)</sup>. Lymph nodes with intact capsules are not factored into the evaluation, because they do not typically increase the risk of local tumor recurrence. A distance of less than 0.1 cm is considered indicative of MRF involvement<sup>(21)</sup>. Although high-resolution T2WI plays a vital role in evaluating the involvement of the MRF, distinguishing between pure fibrosis and fibrotic tissue containing residual tumor cells can be challenging after NAT<sup>(45)</sup>.

# Step 5 – Evaluation of the lymph nodes

In most cases, restaging rectal MRI will depict a notable reduction in lymph node size or complete resolution of the lymph node enlargement. Notably, the effectiveness of rectal MRI for nodal staging is significantly higher at restaging than at baseline. Restaging rectal MRI can identify patients with no residual nodal disease, with negative predictive values as high as 95%<sup>(46)</sup>. Unlike at baseline, when morphology is the most reliable parameter for evaluating the lymph nodes, lymph node morphology is an unreliable parameter at restaging. In contrast, the imaging finding that best correlates with pathology at restaging is the short-axis diameter of the lymph node<sup>(21)</sup>. Size criteria to identify suspicious lymph nodes are detailed in Table 3. At restaging, it is particularly important to evaluate the lateral pelvic lymph nodes, given that they are not routinely resected.

 $\label{eq:constraint} \textbf{Table 3-} Criteria \ for \ suspicious \ lymph \ nodes \ on \ restaging \ rectal \ MRI.$ 

Location or aspect	Diameter (short axis)
Mesorectal, superior rectal	> 5 mm
Internal iliac	> 4 mm
Obturator	> 6 mm
M1 (inguinal, external iliac, common iliac, or retroperitoneal)	> 10 mm
Mucin within lymph nodes*	_

\* MRI is unable to differentiate cellular from acellular mucin.

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# Step 6 – Evaluation of EMVI and tumor deposits

Given their association with poor prognosis, EMVI and tumor deposits should be thoroughly evaluated. The resolution of EMVI after NAT correlates with improved survival. Although it can be challenging to distinguish viable from nonviable tumor within EMVI, DWI has high specificity and a high negative predictive value for predicting a complete response within EMVI or a tumor deposit<sup>(20)</sup>. In cases of uncertainty, particularly if watch-and-wait management is being considered, multidisciplinary discussion is suggested and close follow-up might be indicated.

# Step 7 – Providing a clinically meaningful conclusion

Lastly, providing a clinically meaningful conclusion is essential to guiding the multidisciplinary team in determining the optimal management plan after NAT. Figure 5 outlines the three common outcomes of restaging rectal MRI, considering T2WI and DWI. If the T2WI and DWI findings are discordant, it is recommended that the worse classification be considered. However, in such cases, the quality of the DWI should be taken into account.

#### CONCLUSION

Restaging rectal MRI plays an important role in assessing the treatment response after NAT, helping the multidisciplinary team define the optimal post-NAT treatment plan that is tailored to the needs of the patient and will achieve the best outcome. A review of the clinical history and baseline rectal MRI of the patient, together with the use of a rectal MRI protocol that prioritizes relevant sequences and ensures correct axial oblique planes, are essential to providing a high-quality restaging rectal MRI. The T2WI sequence remains fundamental for categorizing the treatment response and for local staging; DWI serves as a complementary tool to enhance the certainty of interpretation. Clear communication of the treatment response classification and detailed descriptions of the structures involved are crucial for guiding the multidisciplinary team in choosing the best course of action, whether it involves a watch-and-wait approach or surgical resection.

#### REFERENCES

- Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71:209–49.
- American Cancer Society. Key statistics for colorectal cancer. American Cancer Society; 2024. [cited 2024 April 2]. Available from: https://www.cancer.org/cancer/types/colon-rectal-cancer/about/keystatistics.html.
- Benson AB, Venook AP, Al-Hawary MM, et al. Rectal cancer, version 2.2022, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw. 2022;20:1139–67.
- Kasi PM, Shahjehan F, Cochuyt JJ, et al. Rising proportion of young individuals with rectal and colon cancer. Clin Colorectal Cancer. 2019;18:e87–e95.
- Araghi M, Soerjomataram I, Bardot A, et al. Changes in colorectal cancer incidence in seven high-income countries: a populationbased study. Lancet Gastroenterol Hepatol. 2019;4:511–8.
- 6. Heald RJ, Ryall RD. Recurrence and survival after total mesorectal excision for rectal cancer. Lancet. 1986;1:1479–82.
- Roodbeen SX, Penna M, van Dieren S, et al. Local recurrence and disease-free survival after transanal total mesorectal excision: results from the International TaTME Registry. J Natl Compr Canc Netw. 2021;19:1232–40.
- Fokas E, Appelt A, Glynne-Jones R, et al. International consensus recommendations on key outcome measures for organ preservation after (chemo)radiotherapy in patients with rectal cancer. Nat Rev Clin Oncol. 2021;18:805–16.
- Yuval JB, Garcia-Aguilar J. Watch-and-wait management for rectal cancer after clinical complete response to neoadjuvant therapy. Adv Surg. 2021;55:89–107.
- Verheij FS, Omer DM, Williams H, et al. Long-term results of organ preservation in patients with rectal adenocarcinoma treated with total neoadjuvant therapy: the randomized phase II OPRA trial. J Clin Oncol. 2024;42:500–6.
- Cercek A, Lumish M, Sinopoli J, et al. PD-1 blockade in mismatch repair-deficient, locally advanced rectal cancer. N Engl J Med. 2022; 386:2363–76.

- Maas M, Nelemans PJ, Valentini V, et al. Long-term outcome in patients with a pathological complete response after chemoradiation for rectal cancer: a pooled analysis of individual patient data. Lancet Oncol. 2010;11:835–44.
- Kasi A, Abbasi S, Handa S, et al. Total neoadjuvant therapy vs standard therapy in locally advanced rectal cancer: a systematic review and meta-analysis. JAMA Netw Open. 2020;3:e2030097.
- Habr-Gama A, Perez RO, Nadalin W, et al. Operative versus nonoperative treatment for stage 0 distal rectal cancer following chemoradiation therapy: long-term results. Ann Surg. 2004;240:711–7; discussion 717–8.
- 15. Smith JJ, Chow OS, Gollub MJ, et al. Organ preservation in rectal adenocarcinoma: a phase II randomized controlled trial evaluating 3-year disease-free survival in patients with locally advanced rectal cancer treated with chemoradiation plus induction or consolidation chemotherapy, and total mesorectal excision or nonoperative management. BMC Cancer. 2015;15:767.
- Garcia-Aguilar J, Patil S, Gollub MJ, et al. Organ preservation in patients with rectal adenocarcinoma treated with total neoadjuvant therapy. J Clin Oncol. 2022;40:2546–56.
- van Griethuysen JJM, Bus EM, Hauptmann M, et al. Gas-induced susceptibility artefacts on diffusion-weighted MRI of the rectum at 1.5 T – effect of applying a micro-enema to improve image quality. Eur J Radiol. 2018;99:131–7.
- Fraum TJ, Ma J, Jhaveri K, et al. The optimized rectal cancer MRI protocol: choosing the right sequences, sequence parameters, and preparatory strategies. Abdom Radiol (NY). 2023;48:2771–91.
- Kim SH, Lee JM, Hong SH, et al. Locally advanced rectal cancer: added value of diffusion-weighted MR imaging in the evaluation of tumor response to neoadjuvant chemo- and radiation therapy. Radiology. 2009;253:116–25.
- Kim TH, Firat C, Thompson HM, et al. Extramural venous invasion and tumor deposit at diffusion-weighted MRI in patients after neoadjuvant treatment for rectal cancer. Radiology. 2023;308:e230079.
- Lee S, Kassam Z, Baheti AD, et al. Rectal cancer lexicon 2023 revised and updated consensus statement from the Society of Abdominal Radiology Colorectal and Anal Cancer Disease-Focused Panel. Abdom Radiol (NY). 2023;48:2792–806.
- Horvat N, Rocha CCT, Oliveira BC, et al. MRI of rectal cancer: tumor staging, imaging techniques, and management. Radiographics. 2019;39:367–87.
- Beets-Tan RGH, Lambregts DMJ, Maas M, et al. Magnetic resonance imaging for clinical management of rectal cancer: updated recommendations from the 2016 European Society of Gastrointestinal and Abdominal Radiology (ESGAR) consensus meeting. Eur Radiol. 2018;28:1465–75.
- Horvat N, El Homsi M, Miranda J, et al. Rectal MRI interpretation after neoadjuvant therapy. J Magn Reson Imaging. 2023;57:353– 69.
- Miranda J, Pinto PVA, Kinochita F, et al. Mucinous degeneration on MRI after neoadjuvant therapy in patients with rectal adenocarcinoma: frequency and association with clinical outcomes. AJR Am J Roentgenol. 2023;221:206–16.
- Horvat N, Hope TA, Pickhardt PJ, et al. Mucinous rectal cancer: concepts and imaging challenges. Abdom Radiol (NY). 2019;44: 3569–80.
- Lambregts DMJ, Delli Pizzi A, Lahaye MJ, et al. A pattern-based approach combining tumor morphology on MRI with distinct signal patterns on diffusion-weighted imaging to assess response of rectal tumors after chemoradiotherapy. Dis Colon Rectum. 2018;61:328– 37.
- Chandramohan A, Siddiqi UM, Mittal R, et al. Diffusion weighted imaging improves diagnostic ability of MRI for determining complete response to neoadjuvant therapy in locally advanced rectal cancer. Eur J Radiol Open. 2020;7:100223.
- 29. Siddiqui MRS, Gormly KL, Bhoday J, et al. Interobserver agreement

of radiologists assessing the response of rectal cancers to preoperative chemoradiation using the MRI tumour regression grading (mrTRG). Clin Radiol. 2016;71:854–62.

- Patel UB, Taylor F, Blomqvist L, et al. Magnetic resonance imaging-detected tumor response for locally advanced rectal cancer predicts survival outcomes: MERCURY experience. J Clin Oncol. 2011;29:3753–60.
- Sclafani F, Brown G, Cunningham D, et al. Comparison between MRI and pathology in the assessment of tumour regression grade in rectal cancer. Br J Cancer. 2017;117:1478–85.
- 32. Jang JK, Choi SH, Park SH, et al. MR tumor regression grade for pathological complete response in rectal cancer post neoadjuvant chemoradiotherapy: a systematic review and meta-analysis for accuracy. Eur Radiol. 2020;30:2312–23.
- Miranda J, Horvat N, Assuncao AN Jr, et al. MRI-based radiomic score increased mrTRG accuracy in predicting rectal cancer response to neoadjuvant therapy. Abdom Radiol (NY). 2023;48:1911– 20.
- Patel UB, Brown G, Rutten H, et al. Comparison of magnetic resonance imaging and histopathological response to chemoradiotherapy in locally advanced rectal cancer. Ann Surg Oncol. 2012; 19:2842–52.
- Achilli P, Magistro C, Abd El Aziz MA, et al. Modest agreement between magnetic resonance and pathological tumor regression after neoadjuvant therapy for rectal cancer in the real world. Int J Cancer. 2022;151:120–7.
- van den Broek JJ, van der Wolf FS, Lahaye MJ, et al. Accuracy of MRI in restaging locally advanced rectal cancer after preoperative chemoradiation. Dis Colon Rectum. 2017;60:274–83.
- Hall WA, Li J, You YN, et al. Prospective correlation of magnetic resonance tumor regression grade with pathologic outcomes in total neoadjuvant therapy for rectal adenocarcinoma. J Clin Oncol. 2023;41:4643–51.
- 38. Dresen RC, Beets GL, Rutten HJT, et al. Locally advanced rectal cancer: MR imaging for restaging after neoadjuvant radiation ther-

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apy with concomitant chemotherapy. Part I. Are we able to predict tumor confined to the rectal wall? Radiology. 2009;252:71–80.

- 39. Song I, Kim SH, Lee SJ, et al. Value of diffusion-weighted imaging in the detection of viable tumour after neoadjuvant chemoradiation therapy in patients with locally advanced rectal cancer: comparison with T2 weighted and PET/CT imaging. Br J Radiol. 2012;85:577–86.
- 40. Sassen S, de Booij M, Sosef M, et al. Locally advanced rectal cancer: is diffusion weighted MRI helpful for the identification of complete responders (ypT0N0) after neoadjuvant chemoradiation therapy? Eur Radiol. 2013;23:3440–9.
- Lambregts DMJ, Vandecaveye V, Barbaro B, et al. Diffusion-weighted MRI for selection of complete responders after chemoradiation for locally advanced rectal cancer: a multicenter study. Ann Surg Oncol. 2011;18:2224–31.
- 42. Kang JH, Kim YC, Kim H, et al. Tumor volume changes assessed by three-dimensional magnetic resonance volumetry in rectal cancer patients after preoperative chemoradiation: the impact of the volume reduction ratio on the prediction of pathologic complete response. Int J Radiat Oncol Biol Phys. 2010;76:1018–25.
- 43. Fokas E, Liersch T, Fietkau R, et al. Tumor regression grading after preoperative chemoradiotherapy for locally advanced rectal carcinoma revisited: updated results of the CAO/ARO/AIO-94 trial. J Clin Oncol. 2014;32:1554–62.
- 44. Lambregts DMJ, Bogveradze N, Blomqvist LK, et al. Current controversies in TNM for the radiological staging of rectal cancer and how to deal with them: results of a global online survey and multidisciplinary expert consensus. Eur Radiol. 2022;32:4991–5003.
- 45. Park MJ, Kim SH, Lee SJ, et al. Locally advanced rectal cancer: added value of diffusion-weighted MR imaging for predicting tumor clearance of the mesorectal fascia after neoadjuvant chemotherapy and radiation therapy. Radiology. 2011;260:771–80.
- 46. Lahaye MJ, Beets GL, Engelen SME, et al. Locally advanced rectal cancer: MR imaging for restaging after neoadjuvant radiation therapy with concomitant chemotherapy. Part II. What are the criteria to predict involved lymph nodes? Radiology. 2009;252:81–91.