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Recommendations/*Gastrointestinal imaging*

MRI restaging of rectal cancer: The RAC (Response–Anal canal–CRM) analysis joint consensus guidelines of the GRERCAR and GRECCAR groups

Stephanie Nougaret[a,b,*], Pascal Rousset[c], Doenja M.J. Lambregts[d], Monique Maas[d], Kirsten Gormly[e,f], Oliver Lucidarme[g,h], Serge Brunelle[i], Laurent Milot[j], Lionel Arrivé[k,l], Celine Salut[m], Franck Pilleul[n], Constance Hordonneau[o], Guillaume Baudin[p], Philippe Soyer[q,r], Vanessa Brun[s], Valérie Laurent[t], Celine Savoye-Collet[u], Iva Petkovska[v], Jean-Pierre Gerard[w], Eddy Cotte[x,y], Philippe Rouanet[z], Onofrio Catalano[aa,bb], Quentin Denost[cc], Regina Beets Tan[d], Nora Frulio[m], Christine Hoeffel[dd]

[a] *Department of Radiology IRCM, Montpellier Cancer Research Institute, 34000 Montpellier, France*
[b] *INSERM, U1194, University of Montpellier, 34295, Montpellier, France*
[c] *Department of Radiology, CHU Lyon-Sud, EMR 3738 CICLY, Université Claude-Bernard Lyon 1, 69495 Pierre-Benite, France*
[d] *Department of Radiology, The Netherlands Cancer Institute, 1006 BE, Amsterdam, the Netherlands*
[e] *Jones Radiology, Kurralta Park, 5037, Australia*
[f] *University of Adelaide, North Terrace, Adelaide, South Australia 5000, Australia*
[g] *Department of Radiology, Pitié-Salpêtrière Hospital, AP-HP, 75013 Paris, France*
[h] *LIB, INSERM, CNRS, UMR7371-U1146, Sorbonne Université, 75013 Paris, France*
[i] *Department of Radiology, Institut Paoli-Calmettes, 13009 Marseille, France*
[j] *Department of Diagnostic and Interventional Radiology, Hôpital Edouard Herriot, Hospices Civils de Lyon, University of Lyon, 69003 Lyon, France*
[k] *Department of Radiology, Hôpital Saint-Antoine, AP-HP, 75012 Paris, France*
[l] *Sorbonne Université, 75013 Paris, France*
[m] *CHU de Bordeaux, Department of Radiology, Université de Bordeaux, 33000 Bordeaux, France*
[n] *Department of Radiology, Centre Léon Bérard, Lyon, France Univ Lyon, INSA-Lyon, Université Claude Bernard Lyon 1, UJM-Saint Etienne, CNRS, Inserm, CREATIS UMR 5220, U1206, 69621, Lyon, France*
[o] *Department of Radiology, CHU Estaing, 63000 Clermont-Ferrand, Cedex, France*
[p] *Department of Radiology, Centre Antoine Lacassagne, 06100 Nice, France*
[q] *Department of Radiology, Hôpital Cochin, AP-HP, 75014 Paris, France*
[r] *Université Paris Cité, 75006 Paris, France*
[s] *Department of Radiology, CHU Hôpital Pontchaillou, 35000 Rennes, France*
[t] *Department of Radiology, Nancy University Hospital, Université de Lorraine, 54500 Vandoeuvre-lès-Nancy, France*
[u] *Department of Radiology, Rouen University Hospital, 76000 Rouen, France*
[v] *Department of Radiology, Memorial Sloan Kettering Cancer Center, New York, NY 10065, USA*
[w] *Department of Radiotherapy, Centre Antoine Lacassagne, 06000 Nice, France*
[x] *Department of Digestive Surgery, Hospices Civils de Lyon, Lyon Sud University Hospital, 69310 Pierre Bénite, France*
[y] *Lyon 1 Claude Bernard University, 69100 Villeurbanne, France*
[z] *Department of Surgery, Institut Régional du Cancer de Montpellier, Montpellier Cancer Research Institute, INSERM U1194, University of Montpellier, 34295, Montpellier, France*
[aa] *Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, USA*
[bb] *Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Harvard Medical School, Charlestown, MA 02129, USA*
[cc] *Department of Digestive Surgery, Hôpital Haut-Lévèque, Université de Bordeaux, 33000 Bordeaux, France*
[dd] *Department of Radiology, Hôpital Robert Debré & CRESTIC, URCA, 51092 Reims, France*

Abbreviations: ADC, apparent diffusion coefficient; CRM, circumferential resection margin; ECRT, external chemoradiotherapy; DWI, diffusion-weighted imaging; EMVI, extramural vascular invasion; ESGAR, European society of gastrointestinal and abdominal radiology; FOV, field of view; GRERCAR group, Groupe de REcherche en Radiologie sur le CAncer du Rectum; GRECCAR group, Groupe de REcherche en Chirurgie sur le CAncer du Rectum; LARC, locally advanced rectal cancer; MRF, mesorectal fascia; MRI, magnetic resonance imaging; NAT, neoadjuvant therapy; T2W, T2-weighted; TME, total mesorectal excision; TNM, classification of malignant tumor (tumor, nodes, metastasis); mrTRG, mr tumor regression grade

* Corresponding author.
E-mail address: stephanienougaret@free.fr (S. Nougaret).

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ABSTRACT

Purpose: To develop guidelines by international experts to standardize data acquisition, image interpretation, and reporting in rectal cancer restaging with magnetic resonance imaging (MRI).
Materials and methods: Evidence-based data and experts' opinions were combined using the RAND-UCLA Appropriateness Method to attain consensus guidelines. Experts provided recommendations for reporting template and protocol for data acquisition were collected; responses were analysed and classified as "RECOMMENDED" versus "NOT RECOMMENDED" (if ≥ 80% consensus among experts) or uncertain (if < 80% consensus among experts).
Results: Consensus regarding patient preparation, MRI sequences, staging and reporting was attained using the RAND-UCLA Appropriateness Method. A consensus was reached for each reporting template item among the experts. Tailored MRI protocol and standardized report were proposed.
Conclusion: These consensus recommendations should be used as a guide for rectal cancer restaging with MRI.

1. Introduction

For a long time, surgical strategies for locally advanced rectal cancers (LARCs) were mainly determined on the basis of findings at baseline staging magnetic resonance imaging (MRI) examination [1]. However, after external chemoradiotherapy (ECRT), most patients demonstrate variable degrees of tumor response, including complete response in 4–31% of them [2,3]. MRI excels, in conjunction with endoscopy, in identifying poor responder who may be referred to consolidation therapy and complete responders who can potentially undergo organ sparing treatment [4,5]. In addition, MRI helps redefine surgical strategy as downstaging and retraction from previous involved structures such as mesorectal fascia (MRF) or sphincter involvement, may alter the initial surgical plan. As such, MRI restaging after neoadjuvant therapy (NAT) has become a critical issue to define tailored therapies and propose a more personalized approach [6–8]. However, the evaluation of the tumor response after NAT is challenging to assess, especially for non-expert radiologists [9]. Interpretation of MRI examination after ECRT is well-known to be hampered by difficulties in discerning fibrosis from residual disease. Different MRI interpretation and classification systems have been suggested focusing on specific morphological patterns on T2-weighted (T2W) images (including MR tumor regression grade [mrTRG]) and/or signal patterns on diffusion-weighted imaging (DWI) to assess response after ECRT. In order to improve accuracy of radiology reports, the European Society of Gastrointestinal Abdominal Radiology (ESGAR) and the Society of Abdominal Radiology have published/updated guidelines regarding rectal MRI staging and restaging [10,11]. However, both guidelines lack practical tumor response descriptions and assessments. Particularly, the recent concept of "near-complete response" driven by the observation that a significant proportion of patients with a very good but incomplete response at first assessment (*i.e.*, six to eight weeks after ERCT) may convert into a complete response if given a longer interval and that re-assessment should be more detailed [12]. It was recently pointed out that the terminology, criteria and features used to describe a near CR present wide variations [13]. As such, the aim of this joint paper was to propose recommendations for rectal cancer MRI restaging in line with clinical requirements. Our intent was first to present a practical resource for radiologists with some tips for high quality interpretation at MRI restaging and second improve reproducibility in reporting among radiologists for / or 'involved in' GRECCAR multicenter clinical trials.

2. Methods

Over the past year and similarly to the first guidelines, members of the GRERCAR group (Groupe de REcherche en Radiologie sur le CAncer du Rectum) associated with lead experts of the GRECCAR group (Groupe de REcherche en Chirurgie sur le CAncer du Rectum) and an expert radiation oncologist have re-examined the current literature regarding MRI to evaluate tumor response in rectal cancer.

The RAND-UCLA Appropriateness Method was used previously to develop the European Society of Gastrointestinal and Abdominal Radiology (ESGAR) consensus guidelines for MRI assessment of rectal cancer and our first staging guidelines [11,14]. This method was also chosen for the present statement paper because of its strength in combining evidence-based data and experts' opinions to attain consensus regarding a variety of clinically relevant questions. The method used included the following seven steps:

- Step 1: Literature review: Medline (Ovid), EMBRASE (embrace.com), and Cochrane Library were searched for the original manuscripts published between January 2007 and January 2022 that pertained to MRI and restaging of rectal cancer including the word: "complete response, response, after treatment, restaging".
- Step 2: Template development: A restaging reporting template based on GRERCAR initial staging, ESGAR and Society of Abdominal Radiology template was proposed and adjusted based on more recent clinical developments. An MRI protocol table and response classification system was developed as well. Discussion regarding time interval between the end of the NAT and MRI was also included. The draft was developed by SN and later refined with the input from three advising members (D. L., M. M., I. P.).
- Step 3: Panel selection: The panel comprised all members of the GRERCAR group.
- Step 4: Survey prior to the first meeting of the panel.
- The restaging template, MRI protocol table and response classification system was distributed to all members of the panel via electronic mail in November 2021 and responses were recorded.
- Step 5: Data extraction and analysis

The answers to the restaging template, MRI protocol table and response classification were collected in January 2022 and analysed. Based on the answers to the survey, each item was classified as follows: (*i*), "RECOMMENDED" (if ≥ 80% agreement in favor); (*ii*), "NOT RECOMMENDED" (≥ 80% agreement in opposition); or (*iii*), "UNCERTAIN" (*i.e.*, consensus was not reached, with < 80% agreement). The results were presented and discussed during a virtual GRERCAR group meeting in January 2022.

- Step 6: Second survey: A new version 1.1 of the restaging template, MRI protocol table and response classification was distributed to all members via electronic mail to clarify any potentially conflicting answers that arose during the first survey round and the first meeting.
- Step 7: Second and final meetings of the panel: The members of the GRERCAR group met again in March 2022 to expedite

remaining issues regarding restaging template, MRI protocol table and response classification. The focus was on the questions without consensus among the experts.
- Step 8: Data reporting: The final version 1.2 of the restaging template, MRI protocol table and response classification system was proposed and approved by all of the panellists.

3. Results

The panel comprised 15 radiologists from 15 different institutions, three surgeons from the GRECCAR group (E. C., P. R., Q. D.), a radiation oncologist (J.-P.G.) and six international moderators (D. L., M. N., R. B.-T., K. G., I. P., O. C.).

Regarding MRI protocol, results are summarized in Table 1. Consensus was not reached for the use of enema, intravenous administration of a gadolinium-based contrast agent and reduced field-of-view (FOV) DWI despite two meeting sessions, and as such, those protocol techniques were left as optional (Table 1).

Regarding reporting template, a consensus was reached for the use of each of the 50 discussed reporting template items (100%) among the experts at first round of discussion. All experts agree to follow the same structure as the initial GRERCAR staging template and add the morphological evaluation based on mrTRG (Fig. 1) and functional evaluation based on DWI.

Regarding MRI response classification, a consensus was reached after second round of discussion using a combined evaluation integrating mrTRG and DWI (Fig. 2). A consensus was not reached regarding the use of volumetric analysis and apparent diffusion coefficient (ADC) measurements.

Table 1
Protocol for rectal cancer restaging MRI examination.

Protocol detail	Application
Patient preparation	
Endorectal coil	No
Use of spasmolytic agents	Yes
Use of rectal filling (small amount < 30 mL)	Yes
Use of a cleansing enema	Optional
Sequence parameters	
Sagittal high resolution T2W (3-mm slice thickness, 0.6 × 0.6 mm^2 in-plane resolution)	Yes
Straight axial T2W	Yes
High resolution axial oblique FSE T2W perpendicular to the tumor	Yes
High resolution coronal oblique FSE T2 parallel to the tumor (particularly important for low lying tumor)	Yes
Use of three-dimensional imaging with intravenous GBCA	Optional
Use of DWI	Yes
DWI with small, tumor-centered FOV	Optional
DWI with standard FOV	Yes

FSE indicates fast spin-echo; FOV indicates field of view; DWI indicates diffusion-weighted imaging; GBCA indicates gadolinium-based contrast agent; T2W indicates T2-weighted image.

4. Discussion

4.1. MRI protocol and timing

4.1.1. MRI protocol

The restaging protocol is similar to the primary staging protocol with a few exceptions. The high-resolution T2-weighted technique is again recommended for optimal visualization of rectal and mesorectal anatomy and for characterization of mesorectal lymph nodes. The recommended slice thickness is 3 mm with an in-plane resolution of 0.6 × 0.6 mm^2. A strict axial T2W sequence is also recommended to obtain a large FOV and cover all compartments relevant for nodal staging. In addition, it has been recently shown that axial plane helps in the assessment of the sigmoid take off [15].

Comparison of post-treatment MRI with pretreatment MRI is essential. Ideally both pre and post NAT images should be acquired using the same angles. Pretreatment images are used to help locate the treated tumor, which may be difficult to visualize in patients who have had a good response to NAT. It helps evaluate tumor shrinkage and change of tumor SI related to NAT response. As such, it's critical to read post treatment image always in conjunction with the primary staging images.

In this setting of tumor visualization after NAT, the GRERCAR group obtained a consensus regarding the use of endoluminal gel for restaging rectal cancer (note, no consensus was obtained at primary staging). The GRERCAR group felt that the benefit of using a small amount of rectal gel (< 30 mL) was superior to its non-use. The benefits of rectal filling with gel are a potential improved ability to localize and delineate the primary rectal tumor, particularly for small cancers [16]. On the other hand, concerns that rectal distension could artificially decrease the distance to the mesorectal fascia, and lead to overstaging of the circumferential resection margin status have been reported [17]. However, a recent study has shown that although the distance between normal rectum and the mesorectal fascia can be decreased with rectal distention, there is no significant change at the level of the

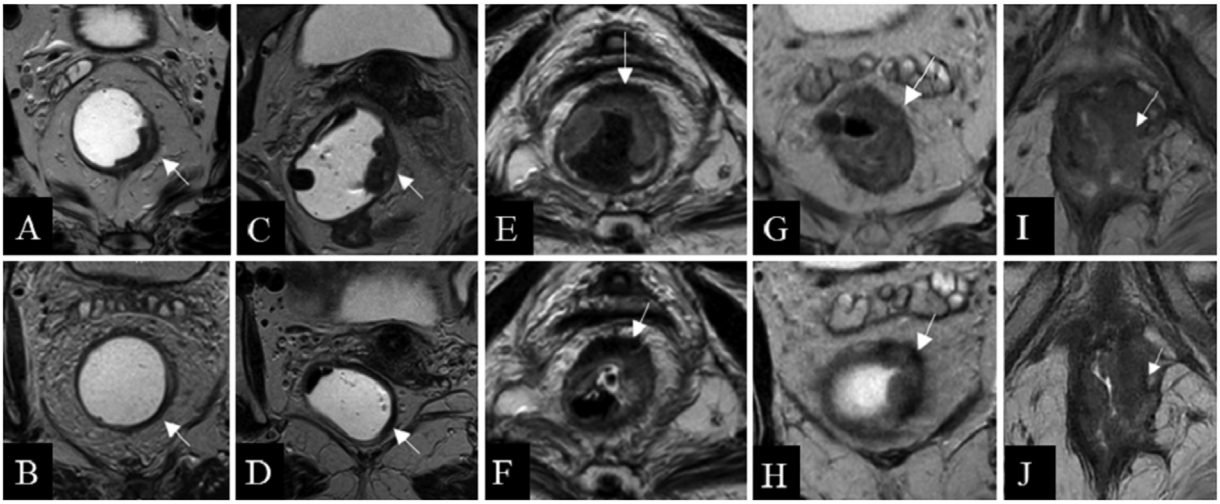

Fig. 1. In line with Table 3 lexicon. MR images illustrate the different MR tumor regression grade (mrTRG) categories. A, B, mrTRG1; C, D, mrTRG2; E, F, mrTRG3; G, H, mrTRG4; I, J, mrTRG5.

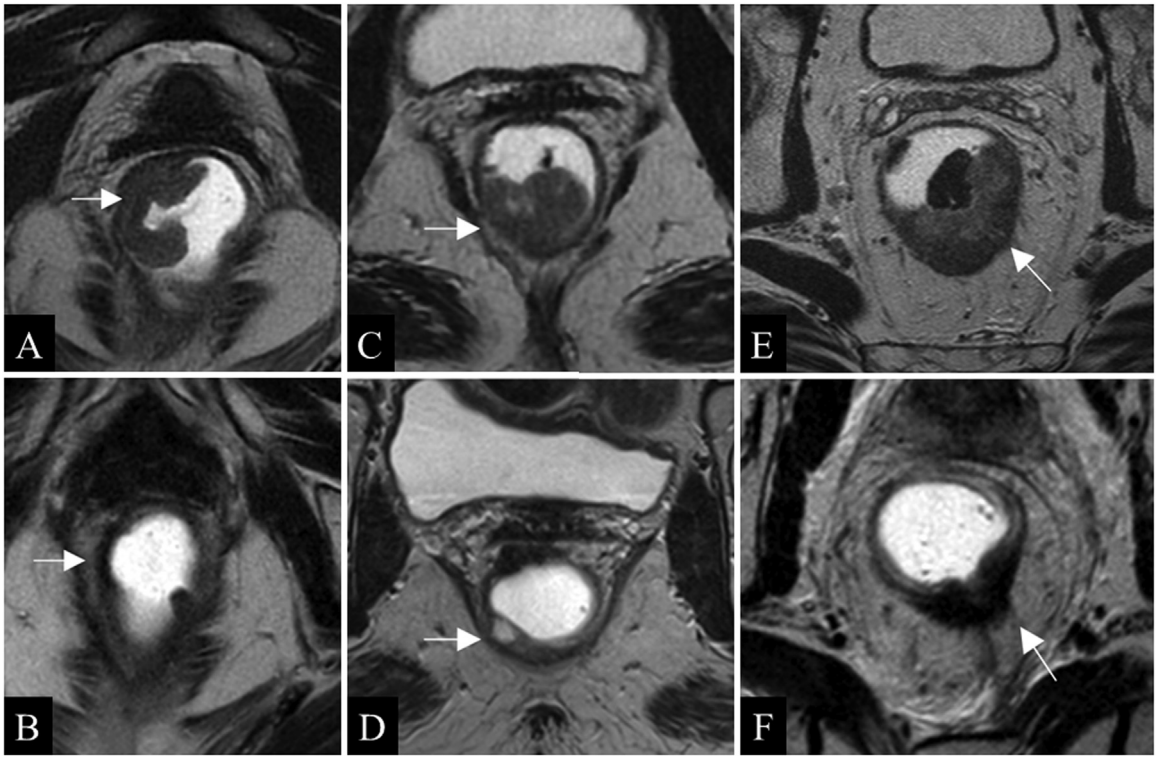

Fig. 2. In line with Table 3 lexicon. A, C, E are baseline axial oblique T2-weighted images. B, D, F are post neoadjuvant evaluation MR images. After external chemoradiotherapy, a dense fibrotic scar is shown as hypointense on T2-weighted image in B. D, shows mucinous changes with hyperintense foci on T2-weighted image, F, shows thin spicules within the mesorectal fat indicating desmoplastic reaction.

cancer where the rectal wall is more fixed [18]. In addition, it should be noted that ultrasound gel may cause T2-shine through artifact, which may obscure small residual tumor. Of note, this recommendation was solely based on GRERCAR expert panelist experience but not on published evidence and was not validated by the external reviewer panel. Thus, ultrasound gel should be used at the radiologist discretion.

In contrast with initial rectal tumor staging, where enema was not recommended, use of enema alone or with rectal gel was considered as a strong option for restaging. Since DWI is critical to assess for tumor restaging, methods to improve DWI quality should be proposed. In a recent study, Van Griethysen et al. found the enema to be useful in reducing gas-artifacts [24.3% for no micro-enema *vs.* 3.7% for micro-enema) [19].

A DWI sequence in the axial oblique plane is recommended. No consensus was obtained regarding the use of reduced FOV DWI sequence, sometimes referred to as 'Zoom' DWI. DWI technique is mostly based on single shot echo-planar imaging DWI sequences. These sequences are highly sensitive to *b*0-field inhomogeneities, particularly in the rectum where air-fluid-tissue interfaces pose a challenge and may result in limited image quality including geometric distortion, ghosting and blurring. The reduced FOV DWI sequence is performed using a two-dimensional spatially selective echo planar radiofrequency pulse in the phase-encoding direction. By reducing the FOV in the phase-encoding direction of the echo-planar imaging readout, the two-dimensional echo planar radiofrequency pulse theoretically reduces the number of k-spacing lines with increased spatial resolution, while reducing off resonance-induced artifacts. While some authors [20,21] report increased resolution with diminished susceptibility artifacts and distortion using reduced FOV DWI as compared to full FOV DWI, others [22] did not find significant differences in terms of image quality between the two types of DWI, even with longer acquisition times and higher number of averages for zoom echo-planar imaging. Moreover, results concerning ADC values are also controversial, as Attenberger et al. reported lower ADC values using reduced FOV DWI [22] while Peng et al. showed no significant differences between the two sequences [20]. Yet, results of the different studies are difficult to compare as vendors differ, along with the parameters used to acquire the images and to calculate the ADC values. As such and due to the paucity of data and the increased magnet time, the use of reduced FOV was considered as optional.

Regarding intravenous administration of gadolinium-based contrast agents, studies have shown that their use do not improve staging of rectal cancer with MRI and as such is not recommended [23,24]. However, it potentially may be helpful in specific situations. The use of intravenous administration of gadolinium-based contrast agents has been shown to improve the evaluation of extra-mural vascular invasion (EMVI) [25–27]. The use of dynamic contrast-enhanced MRI has been recently evaluated to predict tumor response [28–35]. However, this is still in the research domain and as such not recommended in routine evaluations. Administration of intravenous gadolinium-based contrast agents requires additional scanning time for post contrast images to be acquired. Given the lack of consensus in the literature and expert opinion, the GRERCAR position is that the use of intravenous gadolinium-based contrast agents is optional. Conversely, the additional time needed to acquire a post contrast sequence should not deter from performing mandatory high resolution T2W sequences.

4.1.2. MRI timing

The issue of when to assess tumor response is still debated. While the rate of pathologic complete response may increase after 12 weeks post-radiotherapy [36], some surgeons are reluctant to operate beyond eight weeks due to concerns about radiation-induced pelvic fibrosis and related surgical complications. In addition, a substantial number of patients will always remain "poor responders" and will never be candidate for organ preservation. In contrast, studies have found that delaying surgery to 15 or 16 weeks after the start of ECRT (10–11 weeks from the end of ECRT) seemed to result in the highest chance of a pathologic complete response [37–39]. A study found

Table 2
Template for rectal cancer restaging MRI report

RECTAL CANCER RESTAGING TEMPLATE			
Distance to the anal verge: [ ] cm Distance to the anorectal junction: [ ] cm Anal canal length: [ ] cm Maximal tumor length on T2 including fibrotic changes: [ ] cm Circumferential location (o'clock position  :) [ ] [ ] to [ ] o'clock % circumference: [ ].			
Response evaluation: MRI reading evaluation in conjunction with staging MRI and clinical evaluations (clinical examination and endoscopy)			
Tumor	Poor response Mucinous tumor mrTRG3 (with obvious residual tumor) – mrTRG 4 – mrTRG5 Residual high SI on DWI	Near complete response (NCR) Non mucinous tumor mrTRG2 – thick fibrosis (transmural) – no obvious residual tumor or tiny focus of residual tumor (< 5 mm) Negative DWI Or A punctiform focus of high SI on DWI Or Small linear focus of high SI on DWI in the inner part of the tumor Further summarized as: • NCR = Only fibrotic changes with negative DWI • Equivocal NCR= TRG2 like with a tiny focus of residual tumor on T2W or DWI	Complete response Non mucinous tumor mrTRG1- normal rectal wall/ thin hypo SI scar on T2W within the mucosa and submucosa less than 2 mm No diffusion restriction
Mesorectal nodes	Mucinous nodes ≥ 5 mm and/or Persistent tumor signal And/or Heterogeneous	Non mucinous nodes < 5 mm or Disappearance	Non mucinous nodes < 5 mm or Disappearance
Latero pelvic nodes (internal iliac, obturator)	Mucinous nodes >4 mm* and/or Persistent tumor signal And/or Heterogeneous	Non mucinous nodes ≤ 4 mm* for internal iliac ≤ 0.6* for obturator or Disappearance	Non mucinous nodes ≤ 4 mm* for internal iliac ≤ 0.6* for obturator or Disappearance
EMVI/TD	Mucinous content Residual T2 tumor signal intensity Residual high SI on DWI	Non mucinous content No obvious residual tumor but residual thick fibrotic changes Negative DWI or A tiny focus of high SI on DWI is possible	Non mucinous content Disappearance, normalization of vessel or thin fibrotic scar No high SI on DWI
Anal canal: (possibility of sphincter sparing surgery) Invasion of anal sphincter complex: ☐Absent ☐Invades internal sphincter ☐Invades intersphincteric space ☐Invades external sphincter ☐Invades puborectalis muscle Length of internal sphincter invasion: (mm)			
CRM: yes/no involved Shortest distance of tumor/TD/EMVI to MRF: [ ] mm and clockwise location: (For low lying tumor consider the shortest distance to levator ani muscle) → CRM involvement as - Residual tumor/EMVI/TD SI on T2W sequence lying ≤ 1 mm to the MRF - Dense and thick fibrotic changes lying ≤ 1 mm to the MRF - High SI on high DWI b value lying ≤ 1 mm to the MRF → No CRM involvement as - Residual tumor/EMVI/TD SI on T2W sequence > 1 mm to the MRF - Thin fibrotic changes lying ≤ 1 mm to the MRF - High SI on high DWI b value lying > 1 mm to the MRF			

* Please refer to the comment regarding lymph node size cut off in the main text.

that MRI restaging at ten weeks rather than the standard six weeks was associated with higher complete response rates, higher concordance with pathological specimens and higher inter-reader agreements [8]. Similarly, Hupkens et al. found that in near-CR patients up to 90% proceed to CR after additional 6–12 weeks [12]. As such, the GRERCAR group recommends a minimum restaging time not less than eight weeks. In patients with a near complete response and possible enrolment in an organ sparing management, another MRI should be performed at six to ten weeks later. This later follow up is supported by recent data which advocates for a response surveillance program [40,41].

4.2. Reporting

A template to be used in routine reporting is proposed as part of restaging (Table 2). A lexicon is proposed as part of a didactic summary of all terms used in rectal cancer restaging with MRI (Table 3, Fig. 2). The GRERCAR group recommends a response assessment based on the "RAC assessment: Response – Anal canal – CRM".

4.2.1. Response

The authors reviewed the extensive literature regarding tumor response assessment. It is well known that the accuracy of MRI in the assessment of treatment response using only T2W images is about 50% and it is even lower regarding the detection of complete responders [8,42,43]. Interpretation of MRIs after ECRT is well-known to be hampered by difficulties in discerning fibrosis from residual disease. The addition of DWI has shown significantly improved diagnostic performance of MRI for restaging after ECRT (77% sensitivity, 86% specificity, 63% positive predictive value, and 93%negative predictive value as shown in a recent meta-analysis including data from 19 individual studies) [44]. The T2W high resolution MRI could help locate the site of lesions of the rectal wall, and DWI could help differentiate residual tumor from fibrosis. However, it must be noted that DWI tends to overestimate presence of tumor in patients with complete response which would result in unnecessary resections. This is why it is critical to combine findings of MRI with endoscopy when aiming to select patients for organ preservation [6].

Table 3
Terms used in rectal cancer restaging with MRI.

TERM	DEFINITION
Tumor changes	
Fibrosis	On T2W images, fibrosis demonstrates a very low SI similar to that of the normal *muscularis propria*, and residual tumor will demonstrate a more intermediate SI similar to that of tumor on pretreatment MR images. Fibrosis also tends to demonstrate irregular, somewhat linear margins, whereas a tumor will exhibit a more nodular morphologic structure. Careful review of high-resolution T2W images will enable delineation of small foci of intermediate-SI tumor with- in areas of low-SI fibrosis.
Mucin	Mucinous and non-mucinous tumors can present with the production of pools or lakes of acellular mucin which is considered as a type of tumor response. Mucinous changes are shown as an increase in SI on T2WI in areas previously showing intermediate signal intensity.
Desmoplastic reaction (reactive fibrosis)	On histopathology, it corresponds to the deposition of collagen as a stromal response. Desmoplastic reaction does not contain tumor. On T2W images, desmoplastic reaction is depicted as linear hypointense spiculations radiating into the mesorectal fat from the residual tumor. To avoid overstaging, desmoplastic reaction should be differentiated from tumor, which is usually more nodular and demonstrates more intermediate SI.
Diffusion	
Pearls and pitfalls	On T2WI, edema appears hyperintense and may not be distinguishable from residual tumor. High b values DWI and ADC maps may be helpful to distinguish edema (high ADC) from residual viable tissue (reduced ADC). Low signal portions on ADC map may correspond to high fibrous content. It is important to always read ADC map and DWI together. In case of fibrosis no high SI on DWI is seen. Owing to its long T2-relaxation time, intraluminal rectal fluid/gel can remain bright on high b value images (T2 shine-through effect). Again, correlation with the ADC map is necessary to distinguish between T2 shine through (high ADC) and residual tumor (low ADC). Moreover, luminal shine-through is typically star-shaped, while a high signal caused by a tumor is typically more nodular or tubular/U-shaped. The use of fused imaging helps as well to locate the lumen. Susceptibility artifacts caused by air in the rectal lumen may determine high signal on DWI: the reader has to verify if hyperintense areas on DWI are located at the same site of the tumor bed or not. Comparison with the pretreatment scan is essential to avoid calling suspicious areas which are not at the site of the original tumor. Collapsed rectal wall may show high SI on DWI caused by superposition of the two sides of the rectal wall. High DWI signal may not be found despite obvious remaining tumor on T2W images. Always evaluate T2W images as they will weigh more in the assessment compared to DWI.
TRG	mrTRG is determined by the proportion of presumed residual tumor and fibrotic change on T2W images. On post- CRT T2-weighted imaging, the fibrotic portion shows dark SI similar to that of the *muscularis propria*, whereas the portion of the residual tumor shows intermediate SI similar to that of baseline tumor. The balance between tumor and fibrosis includes all disease remaining in the mesorectum, including EMVI, lymph nodes and extra nodal tumor deposits (TD).
TRG 1	mrTRG scoring system and the definition of TRG 1–2 have been changed between 2012 and 2016. It now indicates linear/crescentic 1–2 mm scar in mucosa or submucosa only
TRG 2	Dense fibrotic transmural mass without intermediate tumor SI (arrow) which also corresponds to ESGAR-based fibrotic wall thickening without clear mass. No obvious residual tumor, signifying minimal residual disease or no tumor
TRG 3	Mostly fibrosis, with <50% visible tumor with intermediate SI.
TRG 4	Mostly tumor with fibrosis < 50%
TRG 5	Intermediate SI, same appearances as original tumor/tumor regrowth

ADC indicates apparent diffusion coefficient; CRT indicates chemoradiotherapy; DWI indicates diffusion-weighted imaging; EMVI indicates extramural vascular invasion; SI indicates signal intensity; T2W indicates T2-weighted; TRG indicates tumor regression grade.

The use of volumetry has been proposed to predict tumor response with relatively high accuracy, high specificity, and good reproducibility [45–49]. However, volumetry analysis is time-consuming, which limits its application in clinical practice. The development of automated segmentation techniques may contribute to more efficient tumor analysis for better clinical application, but it still needs further research. In this setting, the GRERCAR group does not advocate the use of volumetry to predict tumor response.

Several studies have demonstrated the potential of tumor ADC in distinguishing good responders from poor responders and complete responders from non-complete responders [50–52]. However, the results remain very inconsistent and contradictory. In this setting, the GRERCAR group does not advocate the use of ADC value to evaluate tumor response.

Different MRI interpretation and classification systems have been suggested focusing on specific morphological T2W MRI patterns (including mrTRG) and/or DWI signal patterns to assess response after ECRT. Among them, the mrTRG is the most widely used [53–55]. The mrTRG is determined by the proportion of presumed residual tumor and fibrotic change on T2W images. On post-ECRT T2W images, the fibrotic portion shows dark SI similar to that of the muscularis propria, whereas the portion of the residual tumor shows intermediate SI similar to that of baseline tumor (Fig. 2). The mrTRG score is intended to include all residual local disease and not just the rectal wall. Residual positive lymph nodes, tumor deposits and EMVI count towards residual tumor, even if there has been a complete luminal response. Siddiqui et al. showed that this metric has a good interobserver agreement and in 90% the radiologists correctly identified poor responders [53]. Lambregts et al. proposed a method to qualitatively assess the fibrotic pattern that appears after ECRT and combine it with distinct corresponding signal patterns on DWI [56]. They showed that the exact type of fibrotic pattern on restaging T2W-MRI helps evaluate the response after ECRT [56]. For example, a polypoid, or (semi)circular tumor shows a sharply demarcated semicircular fibrotic wall after ECRT, and an irregular or spiculated tumor often shows irregular fibrotic thickening of the wall on restaging MRI. They found out that detecting macroscopic tumor remnants in focal patterns of disease was easier than detecting more diffuse/scattered tumor remnants in cases with large fibrotic changes [56]. More recently, Haak et al. described an MRI 3 points scale (poor, intermediate and good responders taking into account the findings of both T2W MRI and DWI) associated with pathologic evaluation and reproducible among radiologists with different levels of expertise [57].

The GRERCAR group recommends the imaging stratification in three response groups based on a combination of morphological (mrTRG) and functional findings (DWI) derived from Haak et al. [58]. In addition, the GRERCAR recognises the combination of data from the baseline staging MRI, the clinical evaluation and endoscopy results critical to assess the post NAT response on MRI as it has been shown that the clinical and endoscopy evaluation improve the accuracy of MRI response evaluation [7,58–60] (Fig. 3).

Regarding patient treatment management related to tumor response, no guidelines have been proposed and large variations

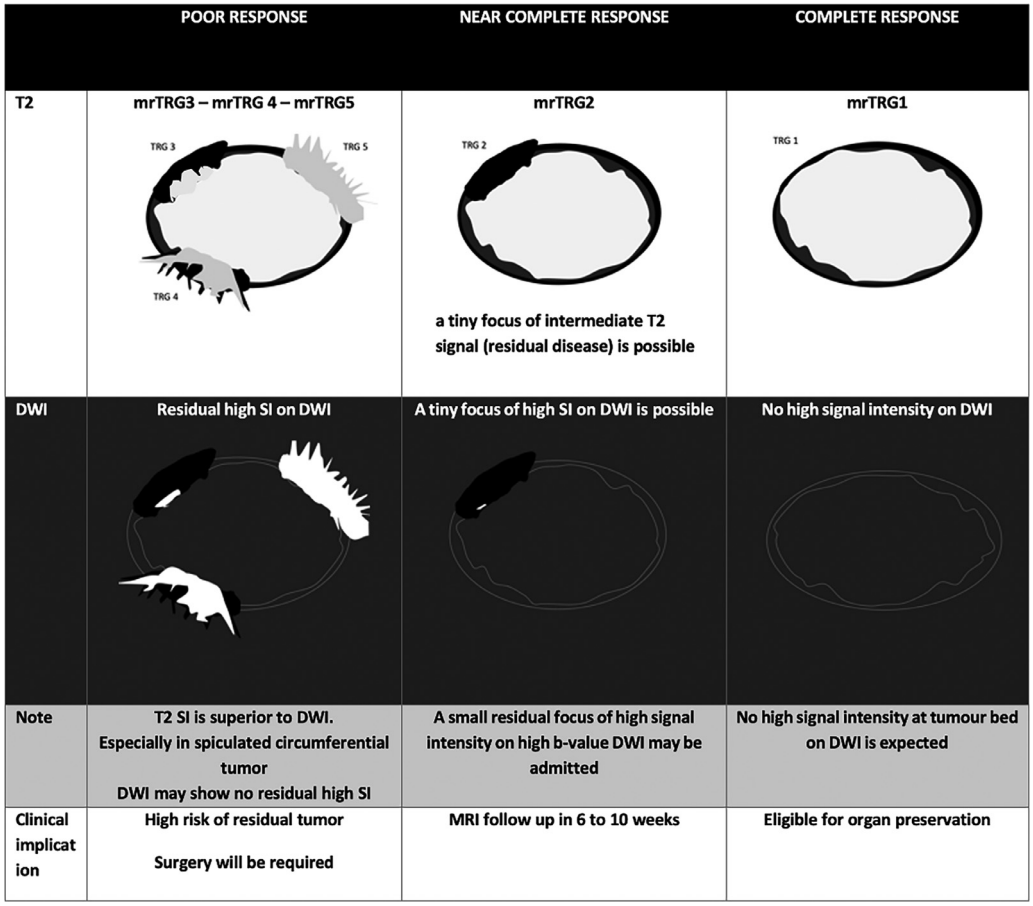

Fig. 3. Three-category schematic forms to differentiate poor, complete and near complete response based on MRI findings. The response categories take into account the morphology on T2-weighted MR images and diffusion-weighted images.

exist among centers. Total mesorectal excision (TME) is the standard treatment for the majority of patients who undergo NAT. However, organ-sparing strategies have also been proposed to avoid TME in patients in whom complete tumor shrinkage without residual tumor tissue has been identified after neoadjuvant ECRT. These strategies are divided into local excision and watch-and-wait strategy. Table 4 details the different surgical strategies.

4.2.1.1. Incomplete/poor responders. Approximately 20% of locally advanced rectal cancer patients show a poor or incomplete response to neoadjuvant therapy [37,59].

4.2.1.1.1. Tumor level. Regarding MR tumor regression grades (mrTRG) 3–5, the GRERCAR group decided to include mrTRG 3 in this group. Despite published data which have shown good long-term outcome of mrTRG3, the likelihood of complete response in this group is low and it is therefore considered a sign of an incomplete response (Fig. 4) [60,61].

Persistence of restriction on DWI indicates viable tumor whereas its absence suggests a complete response [62–65]. Note, that restriction may be absent in incomplete responses, particularly in cases with extensive fibrosis containing small tumor nests that are scattered throughout the fibrosis [56]. These scattered tumor patterns will be more difficult to detect on imaging than more focal, macroscopic tumor remnants. The GRERCAR group agrees to consider T2 signal superiority over DWI. When there is a residual intermediate tumor signal on T2W images or when the fibrosis is very extensive, irregular (e.g., "ugly fibrosis"), irrespective of DWI findings, the likelihood of viable tumor is very high (≥ 80%) and as such it should be considered as incomplete response [56]) (Fig. 4).

Regarding the particular settings of mucinous tumors, they present with a greater frequency of residual viable tumor after NAT and as such are not usually referred to organ sparing surgery [66]. In addition, the evaluation of residual tumor on MRI for such tumors is very difficult as our subjective assessment cannot identify small residual tumors cells within mucin lakes and as such those patients should always be considered as poor responders.

Following treatment, the local tumor is traditionally restaged to give a ymrTstage. Panel experience and recent literature have highlighted the poor accuracy of tumor T restaging. In this setting, the GRERCAR group does not advocate for including the ymrTstage in the imaging report.

4.2.1.1.2. Mesorectal level and EMVI. The GRERCAR group agrees to the following statements: Persistent lymph node with a short axis ≥ 5 mm is associated with a likelihood of residual disease up to 63%. Persistent "tumor" signal or heterogeneous T2W SI within the node is associated with residual macroscopic tumor [67]. Mucinous nodes (*i.e.,* those with residual high signal intensity) are considered suspicious for residual tumor.

Regarding response of EMVI to neoadjuvant therapy, a specific TRG for EMVI (mr-vTRG) has been proposed, similar to mrTRG with grades 4 (< 25% fibrosis) and 5 (minimal fibrosis) associated with higher local recurrence rates (44%) and lower disease-free survival (46%) compared to grades 1–3 (50% fibrosis or more)— 9% local recurrence and 88% 3-year disease-free survival [68]. However, the GRERCAR group considers it might be difficult in routine practice to evaluate the percentage of residual fibrosis. As such, the use of mr-vTRG did not obtain a consensus. The GRERCAR group agrees to consider incomplete response in EMVI or tumor deposit when persistent "tumor" signal or

Table 4
Type of surgical approaches proposed for rectal cancer.

Surgery type	Definition	MRI requirements
Organ sparing surgery*		
TAE, TEM, or TAMIS	Transanal excision (TAE) is possible for low rectal tumors (within 5 cm from the verge) and is performed by gaining exposure to the tumor via an anoscope or re- tractor. The tumor along with a full thickness resection of rectum with a margin of normal colonic mucosa is typically resected with electrocautery.	Low lying tumor
	Transanal endoscopic microsurgery (TEM), and transanal minimally invasive surgery (TAMIS) are used to remove superficial tumors located higher in the rectum being able to reach as high as 15 cm. During TEM or TAMIS, the rectum inflated with carbon dioxide, and the tumor is removed with instruments similar to those used for laparoscopic surgery. TEM requires specialized training and equipment and is not available at all centers. These full thickness resections include all layers of the rectum and frequently the adjacent mesorectal fat. Lymph nodes are often present in the specimen, but a complete lymph node dissection cannot be performed using these minimally invasive endoluminal techniques. Therefore, accurate interpretation of lymph node status at MR is critical.	Low, mid and high lying tumor
TME	Total mesorectal (TME) includes removal of the tumor, rectum, and mesorectal fat. TME is performed for T2 and higher lesions because of the likelihood of positive lymph nodes.	Patient with ymrT2 or higher stage tumor
LAR	Low anterior resection (LAR) is performed for tumors that are distant from the anal sphincter	Distal margin of treated tumor 1 cm above the anorectal junction Intact anal sphincter complex
ISR	Intersphincteric resection (ISR) is performed for tumor lying within the canal anal and consist with partial or complete removal of the internal sphincter	Distal margin of treated tumor 1 cm below anorectal junction Internal sphincter invasion
More extensive approach		
Extra levator APR	Unlike traditional APR, because ELAPE includes the en-bloc removal of the levator muscles, ELAPE is considered to be a more radical approach and thus increases CRM clearance, particularly in patients whose levator plane is still threatened on post-CRT MRI.	Intersphincteric space, levator ani invasion, external sphincter involvement
Pelvic exenteration	Pelvic exenteration is performed for T4 tumors that have invaded other organs	Adjacent organ invasion

* Patient with tumor downstaging to ymrT0-1/n0 on MRI.
TAE indicates transanal excision; TEM indicates transanal endoscopic microsurgery; TAMIS indicates transanal minimally invasive surgery; TME indicates total mesorectal excision; LAR indicates low anterior resection; ISR indicates intersphincteric resection; APR indicates abdominoperineal resection; ELAPE indicates extralevator abdominoperineal excision; CRM indicates circumferential resection margin, post CRT indicates post chemoradiotherapy.

heterogeneous T2W SI is visible within an EMVI or tumor deposit or persistent diffusion restriction within an EMVI or tumor deposit.

4.2.1.1.3. Lateral pelvic sidewall. The GRERCAR group agrees to the following regarding lymph node criteria associated with residual lymph node involvement. Short axis >4 mm for internal iliac node and short axis > 6 mm for obturator on post-neoadjuvant therapy MRI are associated with residual lymph node involvement [69]. However, it should be noted that this cut off is mostly based on extensive Japanese literature where lymphadenectomy is commonly performed in contrast to European approach with ongoing debate between East and West approaches [70,71]. As such, in a setting of suspicious residual lateral pelvic lymph node, the GRERCAR group advocates for a lengthy discussion during tumor board meeting. Future international guidelines on this subject may propose another insight in term of location and size after neoadjuvant therapy.

4.2.1.2. Complete responders. Approximately 10–25% of patients will show a pathologic complete response after neoadjuvant treatment. We evaluated the extensive literature regarding the complete response on T2W MRI and/or DWI and recent meta-analyses (Fig. 4) [6–8,29,33,34,42,43,72–86].

4.2.1.2.1. Tumor level. The GRERCAR group agrees that the presence of a linear/crescentic, 1–2 mm scar in the mucosa or submucosa or normalization of the rectal is highly specific for complete response, in the range of 92–98% [87]. Note that, the mrTRG scoring system and the definition of TRG 1–2 have been changed between 2012 and 2016. Grade 1 now indicates a complete radiologic response with a linear/crescentic 1–2 mm scar in the mucosa or submucosa on MRI.

Complete response on DWI is supported by the absence of high signal intensity at high b-value DWI (using normal rectum as reference) [64,88] and it may be particularly valuable in small, sub circumferential scars.

4.2.1.2.2. Mesorectum level. A short axis reduction ≥ 70% or disappearance of the lymph node on T2W images may indicate ypN0 status in 100% of tumors [69] and according to ESGAR guidelines, lymph node < 5 mm after neoadjuvant therapy should be assumed as negative for tumor involvement [11].

Absence of visible lymph nodes in high b value DWI may be a reliable predictor of ypN0 status [89]. In this role DWI is particularly interesting as the absence of nodal signal intensity at DWI is suggestive of lymph node negative status.

There is paucity of data regarding complete response and EMVI/TD. Without concrete data on the subject, the GERCAR group agrees to consider that normalization of vessels or conversion to hypointense thin “fibrotic” scar on T2WI without high signal intensity on DWI would favor a complete response of extramural venous invasion, the same applying to tumor deposits.

4.2.1.2.3. Pelvic side wall level. Lateral pelvic sidewall lymph nodes that shrink to ≤ 0.4 cm for internal iliac nodes, and to ≤ 0.6 cm for obturator nodes in short axis after NAT present no risk of local recurrence at three years according to Ogura et al. [88]. The GRERCAR group endorses those findings. Again, these thresholds may change in the coming years thanks to upcoming clinical trials.

4.2.1.3. Near complete response (NCR). The concept of a “near-complete response” was introduced more recently, driven by the observation that a significant proportion of patients presenting with a very good but incomplete response at first assessment (6–8 weeks) may convert into a complete response if given a longer interval and re-assessment [12].

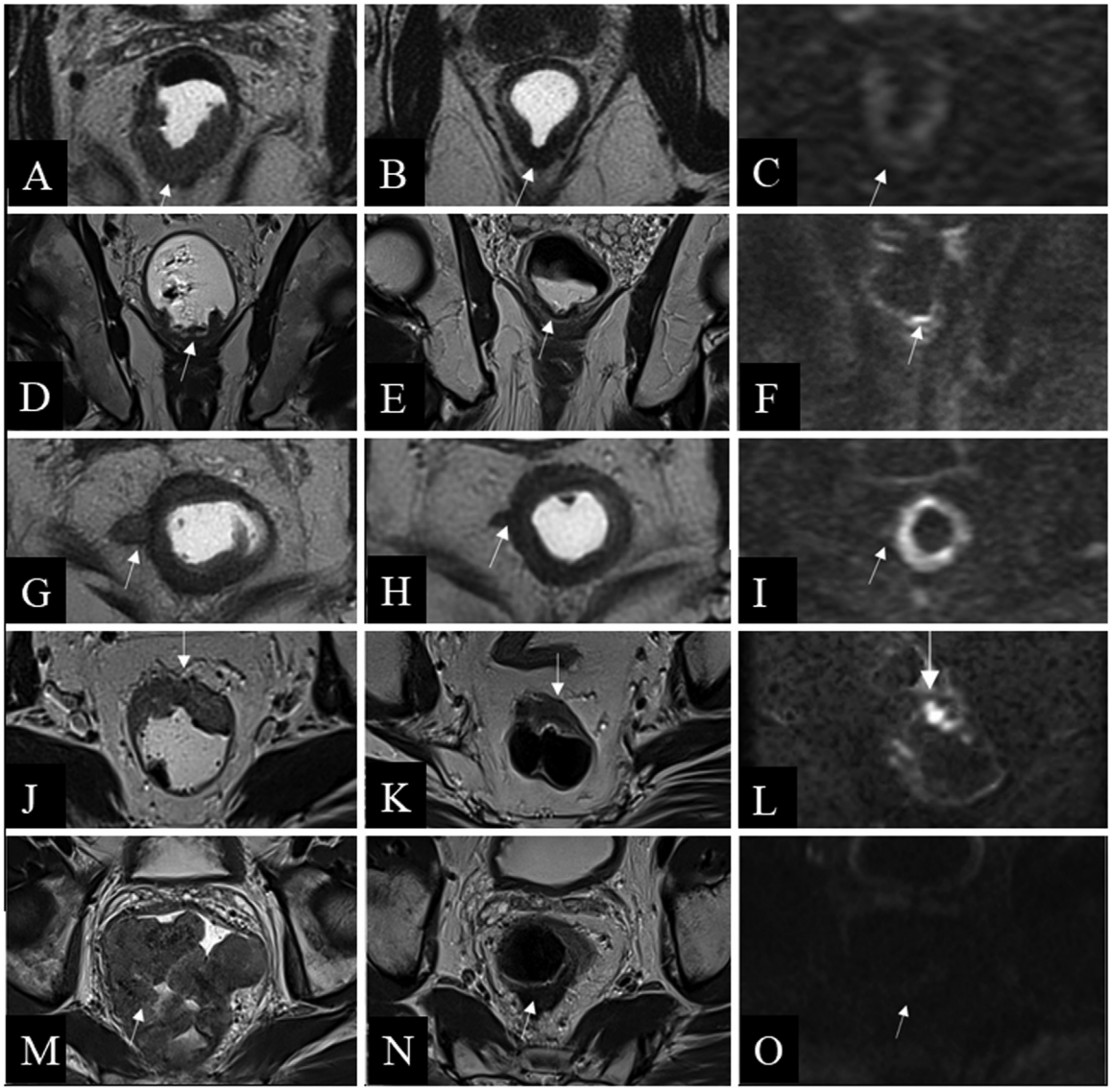

Fig. 4. Examples of tumor response. A, D, G, J, M are baseline T2-weighted images in the axial oblique plane. B, E, H, K, N are T2-weighted images in the axial plane obtained after chemoradiotherapy. C, F, I, L, O are diffusion-weighted (DWI) images in the axial plane obtained after chemoradiotherapy. B, demonstrates dense fibrotic change within T2 intermediate tumor signal in keeping with mr tumor regression grade (mrTRG) 2 without residual hyperintensity on DWI (C). This is consistent with a near complete response. Figure E shows a thin fibrotic scar again compatible with a mrTRG 2. A small rim of submucosal line is seen on DWI (F) in keeping with a near complete response (equivocal NCR). Figure H shows residual tumor with intermediate signal on T2-weighted image associated with concordant hyperintense signal on DWI (I) consistent with poor response. Figure K, shows obvious residual tumor displaying intermediate signal on T2-weighted image with a small focus of hyperintense signal on DWI (L) consistent with poor response (note the discordance between the T2WI and DWI in this case, the DWI is similar to that Figure F however, the T2 signal is totally different. As such, evaluation of response must be always assessed by reading T2 weighted images and DWI in conjunction). Figure N, shows large decrease in size of the initial tumor with residual T2 tumor intermediate signal without any abnormal DWI signal (O). In that case of "ugly tumor", a poor response should always be considered.

4.2.1.3.1. Tumor level. Patients with dense/thick fibrosis > 2 mm or with dense fibrosis and a very minimal residual intermediate signal (not considered as TRG 3 because very inferior to 50% of the tumor, almost mrTRG2) may be considered near-complete responders [12,90] (Fig. 4). This may be associated with a small focal area of high SI on high b value DWI or the absence of high SI on high b value DWI (Fig. 4).

The panel decided to further summarize these patterns as NCR = Only fibrotic changes with negative DWI and equivocal NCR= TRG2 like with a punctiform focus of residual tumor on T2W images or on DWI.

4.2.1.3.2. Mesorectum level. Regarding lymph node involvement, the only study on near-complete response mentioning lymph nodes con- siders that “suspicious” lymph nodes, whether mesorectal or sidewall, should not be present on re-staging MRI [90]. As such, the same criteria as for complete responders should be applied. Although again no data was found on the matter, the same may work for EMVI and extranodal tumor deposits.

Patient presenting with a near complete response and candidate for an organ sparing strategy should be imaged again at 16–20 weeks to confirm/infirm a complete response.

4.2.2. Anal canal

After NAT, the relationship between the tumor and anal sphincter complex is critical to assess when deciding whether sphincter-saving surgery is possible or not. ECRT increases the tumor distance to the anorectal junction, leading to an increase of sphincter-preserving surgery in up to 21–25% of patients [91].

When measuring the distance from anal canal to the tumor, it’s important to measure the distance to the fibrotic remnant (as it might contain tumor) and measure the entire fibrotic remnant instead of the residual tumor as the whole scar will be taken out completely when deciding to perform a TME. The GRERCAR group recommends the description of: *i*), Distal margin of the tumor

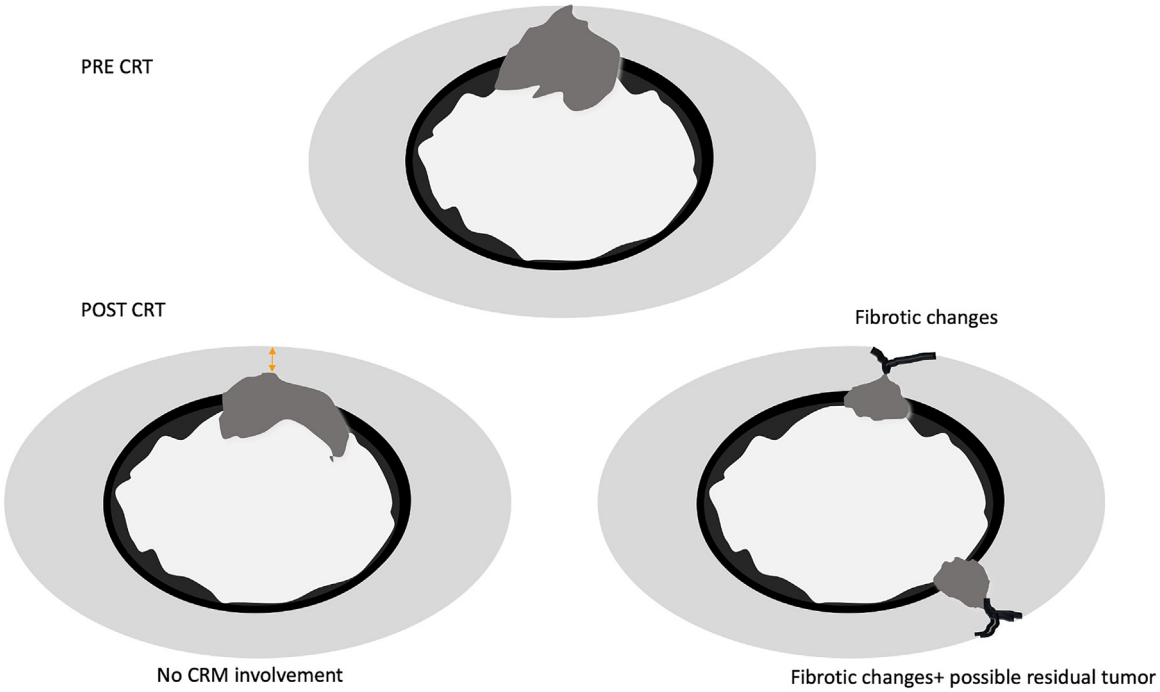

Fig. 5. Different aspects of circumferential resection margin (CRM) involvement post chemoradiotherapy (CRT). Drawing on the left shows decrease in tumor size compared to upper drawing with a clear fat plane >1 mm to the mesorectal fascia (MRF). Post CRT drawing on the right shows two frequent situations. Thin fibrotic spiculation attached to the MRF and in keeping with no CRM involvement and thick fibrotic changes post CRT which may be associated with residual tumor.

whether it is located at/ above / below a 1 cm line above the anorectal junction; *ii*), Tumor extension to the internal sphincter; and *iii*), Tumor extension to the intersphincteric fat plane/external sphincter muscle/levator ani muscle.

Low anterior resection is possible when the inferior pole of the tumor (or fibrosis) lies above a line located one centimetre up from the anorectal junction. When the tumor extends to the internal sphincter only, and if the CRM with regards to the levator ani is not threatened, an intersphincteric resection is possible. For lower rectal cancers that threaten the levator ani muscle or involve the intersphincteric plane/external sphincter muscle, sphincter saving surgery is not feasible and an extralevator abdominoperineal resection is recommended.

4.2.3. CRM

Prospective trials have reported a local recurrence rate of 25–26% after NAT in patients with pathologic CRM involvement [22,27]. As such, CRM pathological involvement is one of the key prognostic factors of local tumor recurrence in patients who undergo TME with or without preoperative NAT. MRI shows 66% accuracy in the prediction of CRM involvement during restaging after NAT, with a strong negative predictive value of 98% [92,93].

The interpretation of CRM involvement after NAT is problematic because hypointense fibrotic change frequently remains at the initial tumor area (Fig. 5). To overcome this issue, a few groups have suggested specific morphologic patterns on MRI for determining MRF involvement after ECRT in addition to applying the distance from MRF. Specifically, if MRF infiltration/penetration by thick fibrotic or tumor tissue is present along with fibrotic thickening of MRF itself, a higher risk of pCRM involvement after ECRT is suggested compared to MRF threatening only by spiculated fibrotic change or treated tumor without thickening of MRF itself. Gollub et al. have also reported the potential value of DWI to predict tumor clearance at the MRF after ECRT [33]. In this study, the positive predictive value for MRF involvement was significantly higher with combined T2-W MRI and DWI (82–91%) than with T2W imaging alone (30–45%) ($P \leq 0.025$) [33].

In such setting, the GRERCAR group agrees to consider CRM involvement as (*i*), Residual tumor/EMVI/TD SI on T2W sequence lying ≤ 1 mm to the MRF; (*ii*), Dense and thick fibrotic changes lying ≤ 1 mm to the MRF; (*iii*), Diffusion restriction signal lying ≤ 1 mm to the MRF and no CRM involvement as: (*i*), Residual tumor/EMVI/TD SI on T2W sequence > 1 mm to the MRF; (*ii*), Thin fibrotic changes lying ≤ 1 mm to the MRF; and (*iii*), Diffusion restriction signal lying > 1 mm to the MRF

5. Conclusion

Optimal treatment of rectal cancer involves a multidisciplinary approach with collaboration between radiologists, oncologists, surgeons and pathologists to achieve local control and low recurrence rates. MRI assessment of tumor response in rectal cancer remains challenging. Standardized MRI techniques and structured reporting are recommended to enable consistent accuracy and help select the best therapeutic approach.

Human rights

The authors declare that the work described has been performed in accordance with the Declaration of Helsinki of the World Medical Association revised in 2013 for experiments involving humans.

Informed consent and patient details

The authors declare that this report does not contain any personal information that could lead to the identification.

Disclosure of interest

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