



## Diffusion weighted imaging improves diagnostic ability of MRI for determining complete response to neoadjuvant therapy in locally advanced rectal cancer

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### ABSTRACT

**Purpose:** To assess the diagnostic performance, interobserver agreement and confidence level for determining response to neoadjuvant chemoradiotherapy (NACRT) using morphology based MR-tumour regression grade (MR TRG), diffusion weighted imaging (DWI) patterns and their combination in patients with locally advanced rectal cancer.

**Methods:** This was a retrospective study including patients with locally advanced rectal cancer treated with NACRT and subsequent surgery. Two independent radiologists blinded to the histopathology reviewed staging and restaging MRI. Diagnostic performance of morphology based MR-TRG, DWI patterns and their combination for determining complete (CR) and incomplete (IR) response was assessed with pathological response as the reference. Likert's scale was used to assess the radiologist's level of confidence. Interobserver agreement was determined using Kappa statistics.

**Results:** The study included 251 patients (mean age of 47.9 +/-14 (range 19–86) years, M:F = 164:87). Rate of pathological CR was 14.7 % (n = 37). Pattern based interpretation of DWI and combined approach (DWI + T2-HR) had superior diagnostic performance than morphology based assessment alone with area under curve (AUC) for T2HR, DWI and their combination being 0.531, 0.887, 0.874 respectively for observer 1 and 0.558, 0.653, 0.678 respectively for observer 2, p < 0.001. Interobserver agreement was substantial (k = 0.688) for combined approach, moderate (k = 0.402) for DWI patterns and fair (k = 0.265) for T2 HR MRI with both observers exhibiting highest level of confidence for determining response with the combined approach.

**Conclusion:** Complete response to neoadjuvant chemoradiotherapy can be determined with excellent accuracy, substantial interobserver agreement and high level of confidence by combined interpretation of DWI and T2 high resolution MRI.

### 1. Introduction

In patients with rectal cancer, excellent long-term outcomes have been demonstrated for the 'watch and wait' strategy, after a complete

clinical response (cCR) to neoadjuvant chemoradiotherapy (NACRT). This has led to the concept of organ preservation in rectal cancer [1–3]. Patients with rectal cancer receiving NACRT have a pathological complete response (pCR) rate varying from 10 to 20% [2,4]. MRI is being

**Abbreviations:** NACRT, neoadjuvant chemoradiotherapy; LCCRT, neoadjuvant long course chemoradiotherapy; MR, TRG MR-tumour regression grade; p-TRG, pathological tumour regression grade; DWI, diffusion weighted imaging; T2-HR MRI, T2 high resolution MRI; cCR, clinical complete response; pCR, pathological complete response; IR, incomplete response; AUC, area under the curve; AJCC, American Joint Committee on Cancer; MERCURY, Magnetic Resonance Imaging and Rectal Cancer European Equivalence Study

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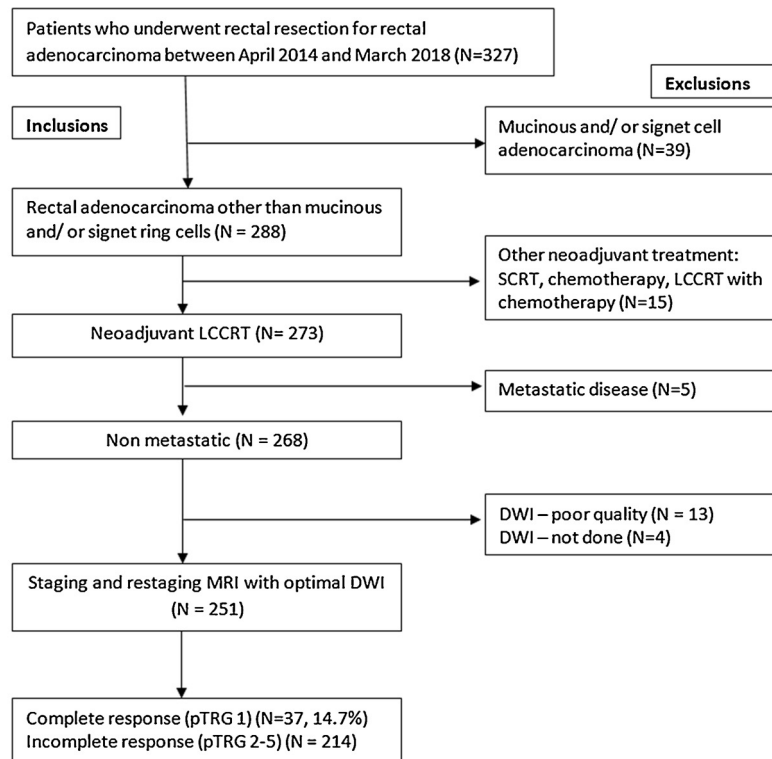


Fig. 1. Consort flow chart showing patients included in the study.

Table 1

MRI imaging protocol used in 3T and 1.5T scanners for both T2 high resolution (T2-HR) MRI and diffusion weighted imaging (DWI).

Scan parameters	Intera 22 Achieva 3.0 T		Magnetom Avanto fit, 1.5T	
	T2-HR	DWI	T2-HR	DWI
Repetition Time	3500	3750	4000	3000
Echo time	90	75	105	61
Slice thickness (mm)	3	5	3	5
FOV (cm)	20	25	18 - 20	22
Matrix	368 × 290	128 × 116	325 × 250	128 × 116
Sensitivity encoding factor	2-2.5	1.7	2	1.9
Echo train length	25	1	12	1
No. of signal averages	2-6	4-6	2-6	4-6
No. of slices	20-40	20-30	20-40	20-30
Acquisition time (minutes)	3-4	3-4	4-6	5
B-values	-	0, 400, 800	-	0, 400, 800
Echo planar imaging factor	-	77	-	108
Fat suppression technique	-	SPAIR	-	SPAIR

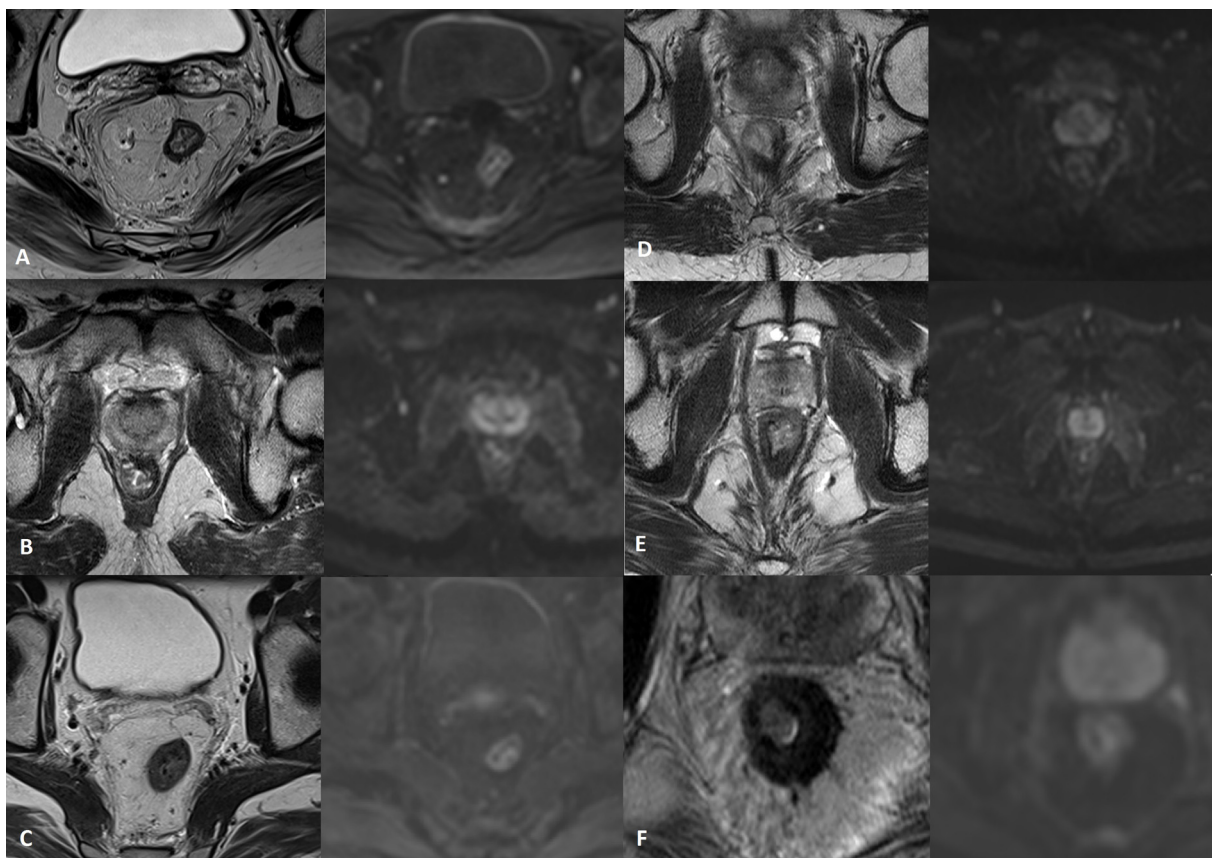
increasingly performed following NACRT in order to assess the response and to identify the local stage since these have important bearing on subsequent treatment plan and the outcome [5]. The five-point MR-tumour regression grade by the Magnetic Resonance Imaging and Rectal Cancer European Equivalence Study (MERCURY) study group, adapted from pathological tumour regression grade, and similar three-point scoring system by ESGAR consensus meeting, both of which are based on assessment of T2 high resolution MR images, are being used to assess response to NACRT [6–9]. However, the currently available methods of determining complete response to NACRT are suboptimal in predicting pCR, with a diagnostic accuracy between 50.2 % to 88 %; correlate poorly with pCR and only have fair interobserver agreement [8,10]. Post treatment related edema, fibrosis, necrosis and poor interface between tissues often lead to over staging and over estimation of tumour extent. Diffusion weighted imaging (DWI) has shown promising results in this area [10–14]. Through this large retrospective study, we aimed to assess the diagnostic performance, interobserver agreement and the level of radiologist’s confidence for determining complete response using T2 high resolution (T2-HR) MRI morphology based MR-tumour regression grade (MR-TRG), DWI patterns matching MR-TRG and a combination of both.

Table 2

Criteria for response assessment on post neoadjuvant chemoradiotherapy (NACRT) MRI using T2-high resolution (T2-HR) MRI based MR-TRG by MERCURY study group [7], diffusion weighted imaging (DWI) patterns and their combination.

MR-TRG	T2-HR MRI <sup>a</sup> MERCURY (2012)	DWI	Combination of T2 HR and DWI
1	Normal rectal wall or thin band of fibrosis	No foci of restricted diffusion	T2 HR 1/2/3 + DWI 1
2	Thick band of fibrosis with doubtful residual tumor	Few scattered foci of restricted diffusion	T2 HR 2/3 + DWI 2
3	Fibrosis/ mucin > 50 % with tumor	C-shaped band or nodular focus of restricted diffusion	T2 HR 2/3 + DWI 3
4	Little fibrosis, mostly tumour	Smaller than pre-Rx MR	T2 HR 4 + DWI 4
5	No response or progression	No change since previous	T2 HR 5 + DWI 5

<sup>a</sup> MERCURY - Magnetic Resonance Imaging and Rectal Cancer European Equivalence Study (7).



**Fig. 2.** Restaging MRI of six different patients with pathological complete response show the spectrum of appearances of complete response on T2 HR images and DWI. (A–C) In three different patients who had features of complete response on both T2 HR images and DWI, there was with thin hypointense band of fibrosis in patient 1(A) and patient 2(B) and there was normalisation of rectal wall in patient 3(C). All three patients had no restricted diffusion on DWI. (D–F) MRI of three different patients who had features of complete response on DWI (dwi-TRG-1), but were either called as mrTRG-2 (D,E) due to thick band of fibrosis or mrTRG-3 (F) due to thick band of predominant fibrosis interspersed by intermediate signal areas on T2 HR images.

## 2. Materials and methods

### 2.1. Setting

This was an institutional review board approved IRB min no: 12011 retrospective review conducted on patients who underwent surgery for rectal cancer between April 2014 – March 2018 in a dedicated Colorectal Surgery unit of a 3000 bedded tertiary care teaching hospital.

#### 2.1.1. Patients

Patients with locally advanced rectal adenocarcinoma who underwent neoadjuvant long course chemoradiotherapy (LCCRT) followed by surgery, and had a staging MRI and post LCCRT restaging MRI, were included in the study. Patients who underwent upfront surgery, or received other forms of neoadjuvant therapy apart from LCCRT, as well as those not having appropriate or optimal imaging were excluded. Patients with mucinous and signet ring cell tumours were also excluded. Standard LCCRT protocol included 45–50 Gy radiation in 25–28 fractions with a 5.4 Gy boost with intravenous 5-fluorouracil infusion or oral capecitabine in standard radio sensitising doses during NACRT. Fig. 1 shows the consort flow chart of patients included and excluded from the study.

**2.1.1.1. Sample size.** For a 10 % precision, 80 % power, 5% error and assumption that there might be 40 % discordance between morphology based assessment on T2 HR MRI and DWI patterns, a sample size of 40 pathological complete responders and 145 pathological incomplete responders was calculated. The number of patients included in the

study matched the sample size calculation.

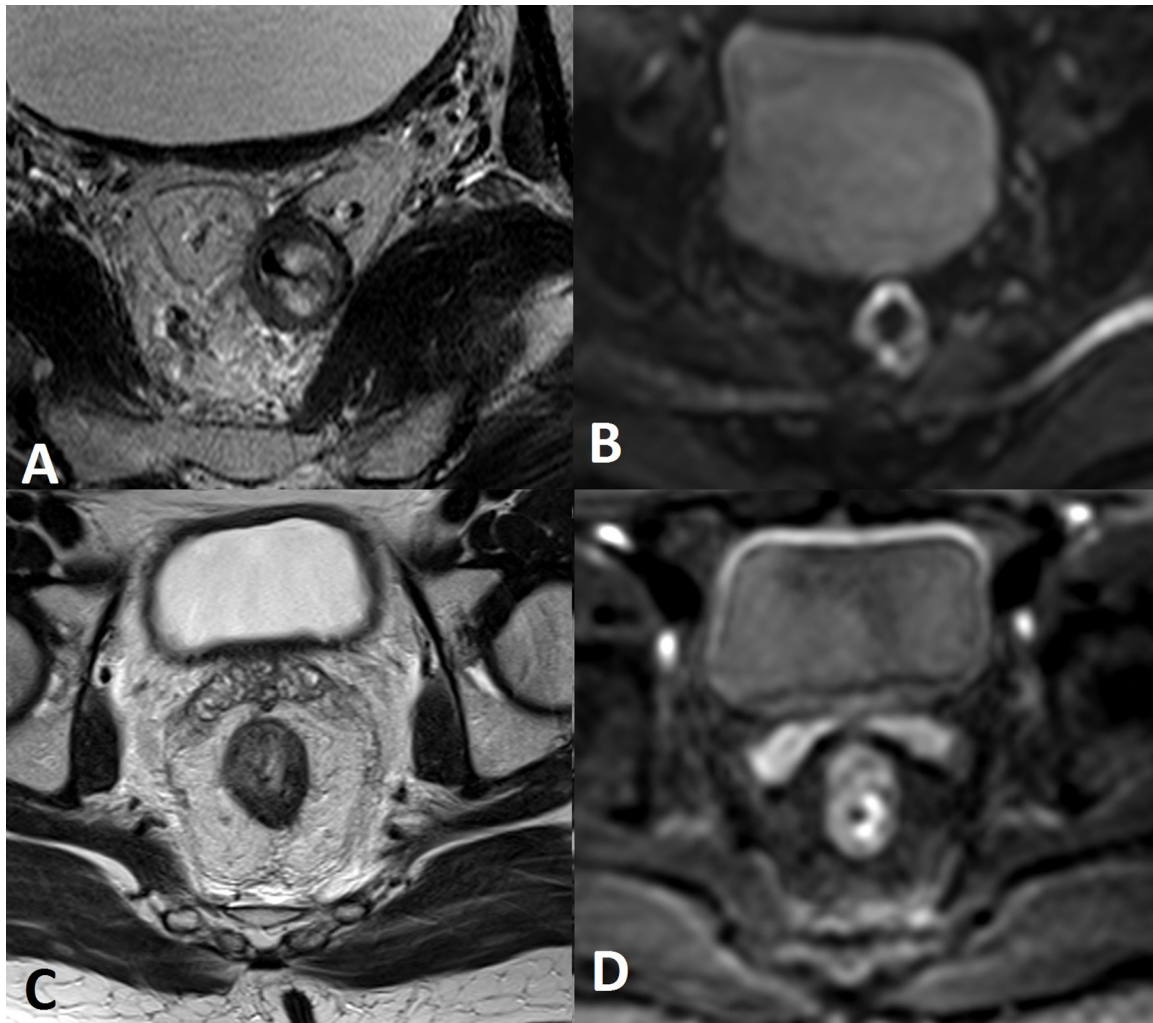
#### 2.1.2. MRI protocol

All the patients underwent MRI scans in one of the following two MRI scanners: Intera 22 Achieva 3.0 T<sup>TM</sup> (Philips Healthcare, Best, Netherlands) with a 16 channel phased-array body coil and Magnetom Avanto fit, 1.5 T (Siemens Healthcare, Erlangen, Germany) with an 18 channel body coil using Tim 4G coil technology. Table 1 shows the imaging protocol used in these scanners. No bowel preparation or spasmolytics were used in our patients. Standard T2 HR MRI of the pelvis was performed in sagittal, oblique axial (perpendicular to the rectum) and oblique coronal (parallel to the rectum) planes. Axial DWI was obtained using respiratory-triggered, single-shot echoplanar imaging with  $b$ -values of 0, 400 and 800  $s\ mm^{-2}$ . Depending on the respiratory efficiency of each patient, the acquisition time for this sequence ranged from 3 to 5 min. ADC maps were automatically generated in the system.

#### 2.1.3. Image interpretation and response evaluation

Images were reviewed on picture archiving and communication system (GE Health system, Barrington, IL) by two independent radiologists with 8 years and 2 experience in interpreting rectal cancer MRI. Radiologists were blinded to the surgical findings and histopathology reports.

The readers assessed response on post NACRT restaging MRI by using T2 high resolution MRI, diffusion weighted imaging and their combination in a pre-decided order. Staging MRI was available for comparison while assessing response on post NACRT restaging MRI. T2 HR sagittal images of staging and post NACRT restaging MRI were



**Fig. 3.** Restaging MRI of two different patients with pathological incomplete response (pTRG-2). (A,B) Patient 1 was called as complete response based on T2 HR image (mr-TRG1), but DWI showed few scattered foci of restricted diffusion suggestive of incomplete response (dwi-TRG-2). (C,D) Patient 2 had thick band of fibrosis on T2 HR images (mr-TRG-2) and the DWI showed few scattered foci of restricted diffusion suggestive of dwi-TRG 2.

compared in order to accurately locate the site of the rectal growth. This was followed by review of T2 HR images, DWI and subsequently both together, with documentation of response assessment and the level of confidence for each. Response on T2 HR images were assessed according to 5-point MR-TRG scores of the MERCURY study group [7,15].

We used the patterns of response described on high *b*-value DWI by previous workers [9,13] and compared these patterns to Mandard's pathological TRG (p-TRG) in a cohort of 64 patients of our previous study [16] who were outside of the current study population. We did this exercise in order to correctly identify the DWI patterns that best identifies with p-TRG. Following this, two observers independently read the DWI images to determine response based on DWI patterns. ADC maps were used to facilitate pattern based response assessment on DWI. Table 2 summarises the description of MR-TRG and DWI patterns. Figs. 2–4 show examples comparing the responses on T2HR images and DWI on restaging MRI.

A five point Likert's scale was used to document the level of confidence in assessing response using MRI criteria in Table 2, with 5 being very confident and 1 not confident at all.

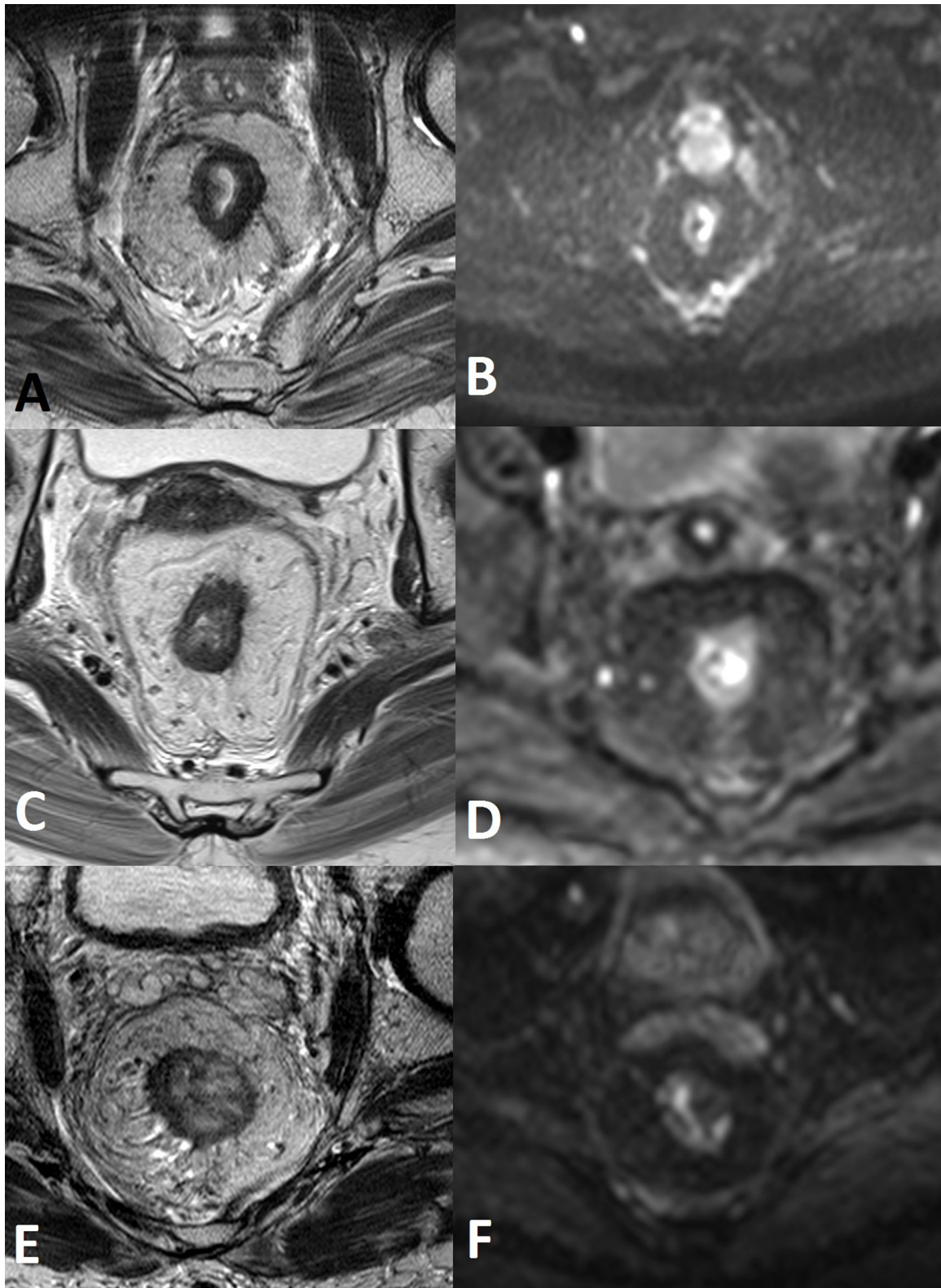
#### 2.1.4. Reference standard

Surgical histopathology including pathological tumor regression grade (pTRG) by Mandard et al. [17] was the reference standard. The pathology specimens were reviewed by a single pathologist with 10

years of experience in pathology of colorectal cancer. Staging was performed in accordance with the 7th edition of American Joint Committee on Cancer (AJCC) guidelines. Patients with no viable tumour at the primary location or in the lymph nodes (ypT0N0) were considered to have pathological complete response (ypCR). All other patients including those with positive nodes (ypN+) and positive extramural vascular invasion (ypEMVI+) on histopathology were considered as incomplete response (ypIR).

#### 2.2. Statistical analysis

Statistical analysis was performed using IBM SPSS Analytics 22.0 software. Descriptive statistics were reported as mean  $\pm$  2SD and range for continuous variables and number with percentage for categorical variables. The rate of complete response was determined and given as a percentage. Diagnostic performance of determining response using T2-HR MRI morphology, DWI patterns and their combination was determined using two by two contingency tables with pathology as the reference standard. Interobserver agreement between the two radiologists was determined by Kappa statistics and was interpreted as follows:  $k < 0$ , poor agreement;  $k 0-0.2$ , slight agreement;  $k 0.21-0.40$ , fair agreement;  $k 0.41-0.60$ , moderate agreement;  $k 0.61-0.80$ , substantial agreement; and  $k 0.81-1.00$ , almost perfect agreement. Mode of Likert's scale was determined to assess the most common level of



**Fig. 4.** Restaging MRI of three different patients with incomplete response (pTRG-3). (A) Patient 1 showed thick band of fibrosis (mr-TRG-2) on T2 HR images and DWI showed a C-shaped restricted diffusion along the left wall of the rectum suggestive of dwi-TRG-3. (B) Patient 2 had greater than 50 % fibrosis with intermediate signal intensity areas along the left wall of rectum (mrTRG-3). DWI showed a nodular focus of restricted diffusion suggestive of dwi-TRG-3. (C) Patient 3 had less than 50 % tumor signal areas than fibrosis on T2 HR images and was called mr-TRG-4. DWI showed curvilinear C shaped focus of restricted diffusion from 4-10 O'clock suggestive of dwi-TRG3.

**Table 3**  
Comparison of patient and tumor characteristics between pathological complete (pCR) and incomplete responders (pIR).

Characteristics	Total N = 251	Pathological complete response (pCR) N = 37	Pathological incomplete response (pIR) N = 214	p-value
Age	47.7 +/-12.1 years (22–70 years)	48.3 +/-14.3 years (19–86 years)		0.301
Male: Female	26:11	138:76		0.495
Pre-treatment biopsy: Well to moderately differentiated	8 (21.6 %)	48 (22.4 %)		0.584
Moderately differentiated	24 (64.8 %)	147 (68.6 %)		
Poorly differentiated	5 (13.5 %)	19 (8.7 %)		
Length of tumor	4.6 +/- 1.8 cm (1.8–10.6 cm)	5.3 +/-1.9 cm (2–14 cm)		0.066
Location				< 0.001
Low/ low mid	26 (70.2 %)	92 (42.9 %)		
Mid/ mid high	9 (24.4 %)	59 (27.5 %)		
High	2 (5.4 %)	42 (19.6 %)		
Long segment	–	21 (9.8 %)		
Annular	17 (45.9 %)	124 (57.9 %)		0.174
Semi-annular	20 (54.1 %)	90 (42.1 %)		
Intermediate signal intensity	32 (86.5 %)	181 (84.6 %)		0.949
Hyperintense	2 (5.4 %)	14 (6.5 %)		
Mixed signal intensity	3 (8.1 %)	19 (8.9 %)		
DWI appearance on pretreatment MRI:				0.237
Entire tumor showed diffusion restriction	22 (59.5 %)	130 (60.7 %)		
Few scattered foci of diffusion restricted	11 (29.6 %)	49 (22.9 %)		
Facilitated diffusion with no foci of diffusion restricted	4 (10.8 %)	8 (3.7 %)		
No restricted diffusion or facilitated diffusion	0	27 (12.6 %)		
T-stage on pretreatment staging MRI:				0.211
mrT2	5 (13.5 %)	17 (8 %)		
mrT3	26 (70.3 %)	147 (68.7 %)		
mrT4	6 (16.2 %)	50 (23.4 %)		
mrN0	24 (64.9 %)	72 (33.6 %)		0.001
mrN1	6 (16.2 %)	97 (45.3 %)		
mrN2	7 (18.9 %)	45 (21.0 %)		
CRM = 0 mm	24 (64.9 %)	135 (63.1 %)		0.467
EMVI positive	7 (18.9 %)	81 (37.9 %)		0.003
Pelvic sidewall disease	3 (8.1 %)	18 (8.4 %)		0.951
y-mrT-stage:				
ymrT0 = 30 (30/251 = 11.9 %)				
ymrT1/2 = 101/251 (40.2 %)				
ymrT3 = 86/251 (34.2 %)				
ymrT4 = 34/251 (13.5 %)				
y-mrN -stage				
y-mr- N0 = 167 (66.5 %)				
y-mr- N1 = 71 (28.3 %)				
y-mr- N2 = 13 (5.2 %)				
y-pT-stage				
ypT0 = 37(14.7 %)				
ypTis = 5 (2%)				
ypT1/T2 = 84 (33.5 %)				
ypT3 = 113 (45 %)				
ypT4 = 12 (4.8 %)				
y-pN-stage				
pN0 = 175 (69.7 %)				
pN1 = 57 (22.7 %)				
pN2 = 19 (7.6 %)				

confidence entered for each category of response assessment using T2 HR MRI based MR-TRG, pattern based interpretation of DWI and their combination.

### 3. Results

#### 3.1. Patients and tumour characteristics

A total of 251 patients (164 males, 87 females) with a mean age of

47.9 +/- 14 years (range 19–86 years) were included in the study. Restaging MRI following NACRT was performed after a mean duration of 8 weeks (range of 6–14 weeks) following NACRT and within a mean of 7 days (range of 1–44 days) prior to the surgery. Table 3 compares the patient and tumour characteristics between pathological complete response (pCR) and incomplete response (pIR). Of the 251 patients, 14.7 % (N = 37) had pCR and the rest had pIR (N = 214). Experienced radiologist gave an assessment of y-mrT0 in 30 (11.9 %) patients. There was significant association between y-mrT and y-mrN stage with the y-pT and y-pN stage (p < 0.001).

#### 3.2. Comparison of response assessment using MRI with reference standard

Table 4 shows the comparison of the response assessment using T2 HR MRI based MR-TRG, patterns of DWI and their combination with the pathological response. Though there was significant association between the response assessed using T2-HR MRI morphology and pathological response (chi square = 63.8, p < 0.001), there was no agreement between the two (k = 0.008, p = 0.033). There was significant association (chi square = 148.8, p < 0.001) and substantial agreement (kappa = 0.765, p < 0.001) between response assessed using DWI patterns and the pathological response. Similarly, there was a significant association (chi square = 170.02, p < 0.001) and excellent agreement (kappa = 0.811, p < 0.001) between the response assessed using a combination of T2HR MRI based MR-TRG plus patterns on DWI and the pathological response.

#### 3.3. Diagnostic performance and interobserver agreement

Table 5 compares the diagnostic performance of both the observers using the three MRI strategies. Both the observers were able to call complete response in significantly more number of patients on DWI and the combination of T2 HR + DWI when compared to only T2 HR MRI. A similar trend was also observed in the sensitivity and the positive predictive value (PPV). Sensitivity and PPV for determining complete response using MR-TRG on T2 HR MRI alone was very low (8% and 42.8 % respectively for observer 1 and 13.5 %, 55.5 % respectively for observer 2). On the other hand, the sensitivity and PPV for DWI patterns was 81 % and 79 % respectively for observer 1; 75 % and 73.5 % respectively for observer 2. The specificity for determining complete response on MRI was very high (~ 98 %) for all three methods. However, the NPV was higher for DWI patterns and combined T2HR + DWI when compared to T2 HR MRI alone. The area under the curve (AUC) for T2 HR MRI, DWI and their combination was 0.531, 0.887, 0.874 respectively for observer 1 and 0.558, 0.653, 0.678 respectively for observer 2 with p < 0.001.

The interobserver agreement was only fair (0.231, p < 0.001) for determining response using T2 HR MRI based MR-TRG; moderate (0.402, p < 0.001) for DWI patterns and substantial (0.688, p < 0.001) for the combination of both.

#### 3.4. Level of confidence

The level of confidence for each assessment category for both observers combined is shown in Table 6. In all the three methods, the radiologists called MR-complete response (MR-CR) only when confident. However, there was significant difference in the total number of MR-CR for both readers combined using the three methods with 16, 54 and 49 MR-CR using T2 HR MRI morphology, DWI patterns and their combination respectively. Similarly, higher percentage of responses matched the most common level of confidence with DWI (77 %) and combined approach (79.6 %) when compared to T2 HR images (62.5 %). From being not at all confident and less confident with MR-TRG 2 and 3 responses, the confidence level rose to 'confident' and 'very confident' with a combined approach in over 60 %. Addition of DWI and the combined approach did not add value in MR-TRG 4 and 5

**Table 4**

Comparison between the reference standard and the response assessment using T2 high resolution MRI, diffusion weighted imaging and their combination.

MR-TRG	T2-HR MRI				DWI				Combination of T2 HR and DWI			
	Observer 1		Observer 2		Observer 1		Observer 2		Observer 1		Observer 2	
	pCR N =	pIR N =	pCR N =	pIR N =	pCR N =	pIR N =	pCR N =	pIR N =	pCR N =	pIR N =	pCR N =	pIR N =
	37	214	37	214	37	214	37	214	37	214	37	214
1	3	4	5	4	30	8	12	4	28	2	14	5
2	24	26	13	12	6	72	10	38	6	52	6	19
3	8	94	10	93	0	61	7	90	1	78	6	75
4	2	77	9	101	1	61	8	77	2	70	11	109
5	0	13	0	4	0	12	0	4	0	12	0	4

**Table 5**

Diagnostic performance of response assessment using T2 high resolution MRI, diffusion weighted imaging and their combination.

	Observer 1			Observer 2		
	T2HR	DWI	T2 + DWI	T2HR	DWI	T2 + DWI
CR	7	38	30	9	16	19
IR	244	213	221	242	235	232
Sensitivity	8.1	81.1	75.6	13.5	32.4	37.8
Specificity	98.1	96.2	99	98.1	98.1	97.6
PPV	42.8	78.9	93.3	55.5	75	73.6
NPV	86	96.7	95.9	86.7	89.3	90
Accuracy	84.8	94	95.6	85.6	88.4	88.8
AUC	0.531	0.887	0.874	0.558	0.653	0.678

responses since there was a high level of confidence with all three approaches.

**4. Discussion**

The growing interest in organ preserving treatment strategy as an alternative to surgery in patients with locally advanced rectal cancer and complete clinical and radiological response to neoadjuvant chemoradiotherapy (NACRT) has created the need for accurate response assessment on post NACRT restaging MRI. While response assessment on T2 high resolution MRI using MR-TRG has suboptimal accuracy and interobserver agreement, DWI has shown promising results [10,11,13,16]. We assessed the diagnostic performance; inter reader agreement and level of confidence of determining response to NACRT on restaging MRI using MR-TRG of MERCURY study group, DWI patterns and their combination.

We found substantial agreement (k = 0.765) between DWI patterns and pTRG and excellent agreement (k = 0.811) between the combined approach (T2 HR MRI + DWI) and pTRG. This finding is supported by previous work by Iennicelli E et al. which showed good correlation (p = 0.700) between DWI incorporated MR-TRG and pTRG [9]. We have shown that the response assessment using DWI patterns and the

combination of T2 HR MRI + DWI patterns outperformed T2 HR MRI based MR-TRG. There were large improvements in sensitivity and PPV for DWI patterns and the combined approach when compared to T2 HR MRI based assessment alone. These differences were more marked with higher experience of the radiologist. Specificity was very high (> 95 %) for all the three approaches. Our results are supported by the results of several previous studies, which showed similar improvements in the diagnostic accuracy for determining treatment response following NACRT using DWI [16,18–23]. A recent work on pattern based approach of assessing response to NACRT using a combination of T2 HR MRI and DWI patterns was shown to have a sensitivity, specificity, PPV, NNV and accuracy of 94 %, 77 %, 88 %, 87 % and 88 % respectively, which is similar to our results [13]. A simplified 3-point DWI incorporated mrTRG by Lee MA et al. showed accuracy of 70 % [9]. We found moderate (0.402) and substantial agreement (k = 0.688) between the two observers for pattern based assessment using DWI and the combined approach similar to the other study which had substantial agreement (k = 0.77) using DWI patterns [9].

It was observed that both readers called complete response (MR-TRG 1) and no response (MR-TRG 5) with high levels of confidence using T2 HR MRI morphology. But the confidence level for MR-TRG 2 or 3 assessments were low. This explains the low sensitivity and the tendency for over staging using T2 HR MRI morphology alone. Radiologists had better levels of confidence for determining the response with a combined approach, especially in MR TRG1 to 3 scenarios. This could be due to the complementary nature of T2 HR and DWI. While it is easier to locate the site of treated rectal tumour on T2 HR MRI, DWI is capable of identifying tumour positive fibrosis from tumour negative fibrosis. Moreover, interpreting these together would help with better assessment of tumor when there is fluid in the lumen, mucin reaction and bowel wall oedema, which are the most common causes of incorrect assessments and lack of radiologist’s confidence while interpreting restaging MRI.

We did not use bowel preparation or spasmolytics. However, considering the total number of patients studied, only 13/268 patients (4.8 %) who had poor quality DWI had to be excluded. We used both 1.5 T and 3.0 T magnets from different vendors and used B-800 for high B-

**Table 6**

Mode of the level of confidence for each assessment category for both the observers combined. Likert’s scale used for the level of confidence is as follows: 5 - very confident, 4 - confident, 3 - not sure, 2 - less confident and 1 - not at all confident.

MR-TRG	T2 HR MRI		DWI		T2 HR + DWI	
	Mode of the level of confidence	(N/TR) and %	Mode of the level of confidence	(N/TR) and %	Mode of the level of confidence	(N/TR) and %
1	4	(10/16) 62.5	4	(42/54) 77	5	(39/49) 79.6
2	1	(52/75) 69.3	2	(52/126) 41.2	4	(51/83) 61.4
3	2	(63/205) 30.7	4	(113/158) 71.5	5	(106/160) 66.2
4	5	(153/189) 80.9	5	(128/147) 87	5	(143/192) 74.4
5	5	(15/17) 88.2	5	(12/16) 75	5	(15/16) 93.7

\* (N/TR) and % = number of responses for the mode of level of confidence divided by the total number of responses in that category for both observers combined and their percentage.

value DWI. Though we did not separately study the effect of different equipments and magnetic strengths on our results, in real practice these factors had no effect on the image interpretation. Our results emphasise the usefulness of incorporating DWI as a part of the standard imaging protocol as also recommended by recent expert consensus guidelines of European society of gastrointestinal and abdominal radiology (ESGAR) [8].

This study has a few limitations related to its retrospective nature. Post NACRT T2 HR images, DWI and their combination was reviewed at the same sitting and this may have introduced bias and may have positively contributed to the interpretation using the combined approach. The experience of the two observers was unequal. The value of experience and training in the interpretation of post NACRT MRI was clearly seen in the results of our study. While a large multi-center study is justified to prove the usefulness of the approach described by us, our results reflect the real life situation where radiologists of varying experience are likely to be interpreting MRI studies following NACRT.

## 5. Conclusion

There is significant association and excellent agreement between pathological and MRI response assessment using DWI patterns and its combination with T2HR MRI based MR-TRG. Combination of DWI patterns and T2 HR MRI based MR-TRG improves diagnostic performance of MRI for predicting complete pathological response. It also improves interobserver agreement and the level of confidence of the interpreting radiologists.

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## CRedit authorship contribution statement

**Anuradha Chandramohan:** Conceptualization, Methodology, Validation, Investigation, Resources, Data curation, Writing - original draft, Writing - review & editing, Visualization, Supervision, Project administration. **Umar M. Siddiqi:** Methodology, Investigation, Resources, Data curation, Writing - original draft, Writing - review & editing, Visualization, Supervision, Project administration. **Rohin Mittal:** Conceptualization, Methodology, Validation, Investigation, Resources, Data curation, Writing - original draft, Writing - review & editing, Visualization, Supervision, Project administration. **Anu Eapen:** Methodology, Validation, Investigation, Resources, Data curation, Writing - review & editing, Project administration. **Mark R. Jesudason:** Methodology, Validation, Investigation, Resources, Writing - review & editing, Project administration. **Thomas S. Ram:** Methodology, Validation, Investigation, Resources, Writing - review & editing, Project administration. **Ashish Singh:** Methodology, Investigation, Resources, Writing - review & editing, Project administration. **Dipti Masih:** Methodology, Validation, Investigation, Resources, Writing - review & editing, Project administration.

## Declaration of Competing Interest

None of the authors have any conflict of interests.

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