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ABDOMINAL IMAGING
ORIGINAL ARTICLE

Can diffusion-weighted MRI determine complete responders after neoadjuvant chemoradiation for locally advanced rectal cancer?

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PURPOSE
We aimed to prospectively determine if analyzing pre- and post-chemoradiotheraphy (CRT) changes in the signal intensity (SI) and apperent diffusion coefficient (ADC) values from diffusion-weighted magnetic resonance imaging (DW-MRI) can accurately predict complete responders for locally advanced rectal cancer.

MATERIALS AND METHODS
Thirty patients (mean age, 54.3 years) with locally advanced rectal cancer who underwent neoadjuvant CRT and subsequent surgery were included in this study. All patients were evaluated pre- and post-CRT by standardized turbo spin echo and DW-MRI. Pre- and post-CRT tumor and normal rectal wall SI (which were gradually scored as very high, high, intermediate, low, and no signal) and ADC values were recorded.

RESULTS
Tumor SIs were decreased in all of the patients that had a therapy response. However, complete tumor SI loss was only seen in two (22.2%) of nine patients with a pathological complete response, while it regressed to low and/or intermediate SI levels in the remaining seven patients (77.8%). Post-CRT ADC values of rectal tumors were significantly higher from the pre-CRT ADC values ($P < 0.0001$; Z=-9.39). However, post-CRT ADC values from the complete and partial/no response patient groups were not significantly different ($P = 0.071$; Z=-1.99).

CONCLUSION
In re-staging of rectal tumors by DW-MRI, an increase in ADC values and decrease in SIs can predict therapy response but cannot unequivocally determine a complete response.

Key words: • *colorectal carcinoma* • *neoadjuvant therapy* • *treatment outcome* • *diffusion magnetic resonance imaging* • *diagnostic imaging*

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Neoadjuvant chemoradiotheraphy (CRT) improves tumor downstaging, pathological complete response (pCR), and local control (1, 2). pCR rates of 13%–30% have been reported in phase II and phase III trials following 5-fluorouracil-based preoperative CRT (3, 4). Currently, management of patients with clinical complete response (cCR) remains controversial (5–8).

A recent meta-analysis including 218 phase I/II or retrospective studies and 28 phase III trials of adjuvant CRT reported that T3 rectal cancer is associated with high local recurrence rates after nonsurgical treatment (9). In addition, similiar results were recently shown from a study using a "wait-and-see" policy after CRT (10).

Accurate imaging methods are needed to evaluate CRT responses, and post-CRT magnetic resonance imaging (MRI) is frequently used for this purpose. However, the method has low accuracy in predicting the pathological stage of the tumor and can often overstage T1 and T2 tumors due to the limited capability of MRI to differentiate viable tumor, residual fibrotic nontumoral tissue, and a desmoplastic reaction. Understaging of irradiated rectal cancer can affect treatment planning, including the surgical strategy, and thus affects the tumor recurrence rate and prognosis (11).

Diffusion-weighted (DW)-MRI is a functional imaging technique that yields qualitative and quantitative information and provides unique insights regarding tumor cellularity, integrity of cell membranes, and microcirculation. The motion of water molecules is more restricted in tissues with a high cellular density that are associated with numerous intact cell membranes (e.g., tumor tissue). Apparent diffusion coefficients (ADCs), which are quantitative expressions of diffusion characteristics of tissues, tend to decrease in diffusion restricted areas, whereas diffusion signal intensity (SI), which is the qualitative parameter of diffusion, increases in those areas (12).

DW-MRI has been used in the diagnosis of rectal tumors since the 1990s. In recent years, researchers have used this technique to determine the therapeutic efficacy of CRT in locally advanced rectal tumors (12, 13). However, a limited number of retrospective studies exists in the literature that have assessed DW-MRI for the determination of CR to neoadjuvant CRT (14–16).

In this study, we prospectively examined whether DW-MRI can accurately predict CRs in patients with locally advanced rectal cancer by analyzing pre- and post-CRT changes in qualitative (SI) and quantitative (ADC) parameters.

Materials and methods

Patients

Between May 2007 and April 2010, 30 patients (mean age, 54.3 years; range, 37–74 years; 8 females and 22 males) who had locally advanced

(≥T3 and/or lymph node positive) rectal cancer based on pre-CRT MRI and/or endorectal ultrasonography were prospectively included in this study. The patients were confirmed to have rectal cancers without metastatic disease based on an endoscopic colonoscopy. This study was approved by the local research and ethics committee, and informed consent was obtained from each patient before participation.

MRI technique

All patients underwent a pre-CRT MRI for primary tumor staging and a second, restaging MRI for response evaluation six weeks after completion of CRT. Distant metastasis analysis was conducted with thoracal computed tomography (CT) and abdominal CT or MRI. The median time between the second MRI and surgery was 15 days (range, 14–17 days).

MRI studies were performed using a 1.5 Tesla MRI (Symhony, Siemens Medical Solutions, Erlangen, Germany) system and a four-element body phased-array coil, before and after neoadjuvant CRT. Standart pelvic turbo spin echo (TSE) and DW-MRI techniques were used.

Standard TSE pelvic MRI protocol

The T1-weighted MR sequence was performed in the transverse plane, and the first T2-weighted MR sequence was performed in the sagittal plane. The sagittal images were then used to help plan the thin-slice transverse and coronal T2-weighted images (Table 1). The tranverse and coronal oblique images were obtained orthogonal and parallel to the long axis of the rectum. All sequences were obtained with no fat saturation. The patients did not receive intravenous (IV) gadolinium or antiperistaltic agents.

The patients were asked to perform rectal cleaning 2–3 hours prior to the MRI using a fleet enema (133 mL; 19 g sodium phosphate monobasic and 7 g sodium phosphate dibasic; CB Fleet Co. Inc., Lynchburg, Virginia, USA). Warm water was administered with a balloon-tipped rectal tube while the patient was in the MRI suite, and the rectum was filled until the patient felt full. The volume of water ranged from 150 to 400 mL. The rectal tube was removed after instillation.

TSE-MRI interpretation

Pre-CRT diagnostic criteria for the T3 stage included extention of the tumor through the muscle layer into perirectal fat with obliteration of the interface between muscle and perirectal fat (17). Morphologic criteria for positive lymph nodes were greater than 3 mm in size, mixed signal intensity, irregular margins, and a shape that was spherical rather than ovoid or flat (18).

DW-MRI protocol

DW images were obtained in the axial plane using a multisection single-shot inversion recovery echo planary sequence (IR-EPI) and b-values of 50, 400, and 800 s/mm² without breath-holding (Table 1). Images with a b-value of 800 s/mm² were used for the evaluation.

DW-MRI interpretation

All images were reviewed on a picture archiving and communication system workstation monitor by two gastrointestinal system radiologists (G.E., R.S.), each with at least three years of clinical experience interpreting rectal MRI. The images were analyzed by consensus between the two reviewers. Both radiologists were blinded to information obtained either at the time of surgery or the pathological analysis reviewed from pre- and post-CRT DW-MRI. For qualitative information, tumor SI was scored as very high, high, intermediate, low, or no signal, according to the normal rectal wall on the b-800 value images. The light bulb appearance was considered to be a very high signal. For quantitative analysis, rectal wall with a normal apprearance and rectal tumor ADC values were recorded from three regions of interest on the ADC mapping images by using dedicated software at the workstation. The measurements from the three regions of interest were averaged. A circular region of interest of at least 4 mm² (larger than 2 mm in minimum diameter) was placed within three sections of the tumor to obtain average ADC values of the heterogeneous tumor.

After CRT, a decrease or absence of SI and increase of ADC values in the tumor were considered to represent a good therapeutic response. CR was predefined as an unidentified mass or wall thickening without any identifiable residual tumor SI. These findings were correlated with pathological results after surgery.

Table 1. Technical parameters for TSE and DW-MRI

	Pelvic area		Tumor area		
Parameters	T1W axial	T2W axial/sagittal	T2W axial/coronal	STIR coronal	DW axial
FOV (mm)	350	350	350	236	400
Matrix	512×512	512×512	512×512	512×512	192×192
TR (ms)	675	7000	7000	9530	4400
TE (ms)	14	134	134	101	85
Section thickness (mm)	5	5	3	3	4
Intersection gap (mm)	1	1	0	0	0
Fat suppression	-	-	-	STIR	STIR
EPI factor	-	-	-	-	192
Parallel imaging factor	-	-	-	-	2
NSA	-	-	-	-	5
Partial fourier factor	-	-	-	-	6/8
Band length (Hz per pixel)	-	-	-	-	1370
Voxel (mm)	-	-	-	-	2.1×2.1×5.0

TSE, turbo spin echo; T1W, T1-weighted; T2W, T2-weighted; STIR, short time inversion recovery; DW, diffusion-weighted; FOV, field of view; TR, repetition time; TE, echo time; EPI, echo planar imaging; NSA, number of signal averages.

Neoadjuvant CRT protocol

Preoperative radiation therapy (RT) was applied using the three planes technique (postero-anterior and two lateral regions) with 45 Gy per 25 fractions administered to the reference points over the course of 5–6 weeks. The rectal tumor, total mesorectum, common and internal iliac, and pelvic lymph nodes were included in the clinical target volume. The small bowels and bone marrow were sheltered with the collimator. A three-dimensional (3D) therapeutic planning system was used with the CT.

The patients received continuous IV injection of 5-fluorouracil (225 mg/m^2) concurrent with RT. All patients waited eight weeks between the completion of neoadjuvant CRT and surgery.

Reference standard

Pathological staging served as the reference standard and was based on the TNM staging system and the Dworak tumor response grading system (19, 20) (Table 2).

Table 2. The Dworak tumor response grading system (19, 20)

Grade	Definition
Grade 0	No response
Grade 1	Minimal response (dominant tumor mass with obvious fibrosis, vasculopathy)
Grade 2	Moderate response (dominant fibrotic changes with a few easy-to-find tumor cells or groups)
Grade 3	Near complete response (few microscopically difficult-to-find tumor cells in fibrotic tissue with or without mucous substance)
Grade 4	Complete response (no tumor cells, only fibrotic mass or acellular mucin pools)

Table 3. Pre- and post-CRT qualitative assessment findings with DW-MRI

Tumor SI	Pre-CRT, n (%)	Post-CRT, n	*P*
Very high	14 (46.7)	-	
High	13 (43.3)	2	
Intermediate	3 (10)	11	< 0.0001 (Z=4.8)
Low	-	15	
No signal	-	2	
Total	30	30	

SI, signal intensity; CRT, chemoradiotherapy.

Table 4. Correlation of post-CRT diffusion SI score and pathologic grade of rectal tumors

	DW-SI scores					
Pathologic grade	0	1	2	3	4	Total
4	2	5	2	-	-	9
3	-	2	1	-	-	3
2	-	4	4	-	-	8
1	-	4	3	2	-	9
0	-	-	1	-	-	1
Total	2	15	11	2	-	30

SI, signal intensity; CRT, chemoradiotherapy.
DW-SI scores: 0, no signal; 1, low signal; 2, intermediate signal; 3, high signal; 4, very high signal.
Data represent number of patients.

Statistical analysis

Statistical analysis was performed using a computer software (Statistical Package for Social Sciences version 10.0, SPSS Inc., Chicago, Illinois, USA). Pairwise comparison and agreement evaluation were calculated by nonparametric Wilcoxon test and Spearman's rho correlation coefficient with a 95% confidence level, respectively. R values of ≥0.75, 0.74–0.50, and <0.50 represent very good, good, and poor agreement, respectively. The Wilcoxon signed rank test was used to test the significance of the difference in tumor SI before and after CRT. The differences in pre- and post-CRT ADC values of normal rectal wall and rectal tumor were tested by Spearman's rho correlation coefficient and Wilcoxon signed rank test. Differences in tumor ADC values with CRT between pathological regression score (pRS) 4 and pRS 0–3 tumors were assessed by using the Wilcoxon signed rank test. The exact 95% confidence intervals (CIs) for these values were calculated with the assumption of a binomial distribution.

Results

Before adjuvant CRT, all rectal tumors were staged as T3 based on the TNM staging system. Three tumors were localized in the upper rectum, 18 tumors were in the middle rectum, and nine tumors were in the lower rectum. None of the patients had distant metastases.

Qualitative analysis

Before CRT, all rectal tumors, including two mucinous subtypes, showed SI between intermediate and very high levels on the b-800 value DW-MR images. In 27 (90%) of 30 rectal tumors, very high and high SIs were seen (Table 3). The tumor diffusion SI was significantly decreased in all of the patients that demonstrated a response to therapy (P < 0.001; Z=4.8) (Table 4 and Fig. 1). In two patients with a mucinous subtype, the tumor diffusion SIs decreased from high to low or intermediate levels. However, complete loss of tumor diffusion SI was only seen in two (22.2%) of nine patients with a pCR, while it regressed to low (n=5) and/or intermediate (n=2) SI levels in the remaining seven patients (77.8%) (Table 4 and Fig. 2). In one patient with no CRT response, the SI regressed from intermediate to low.

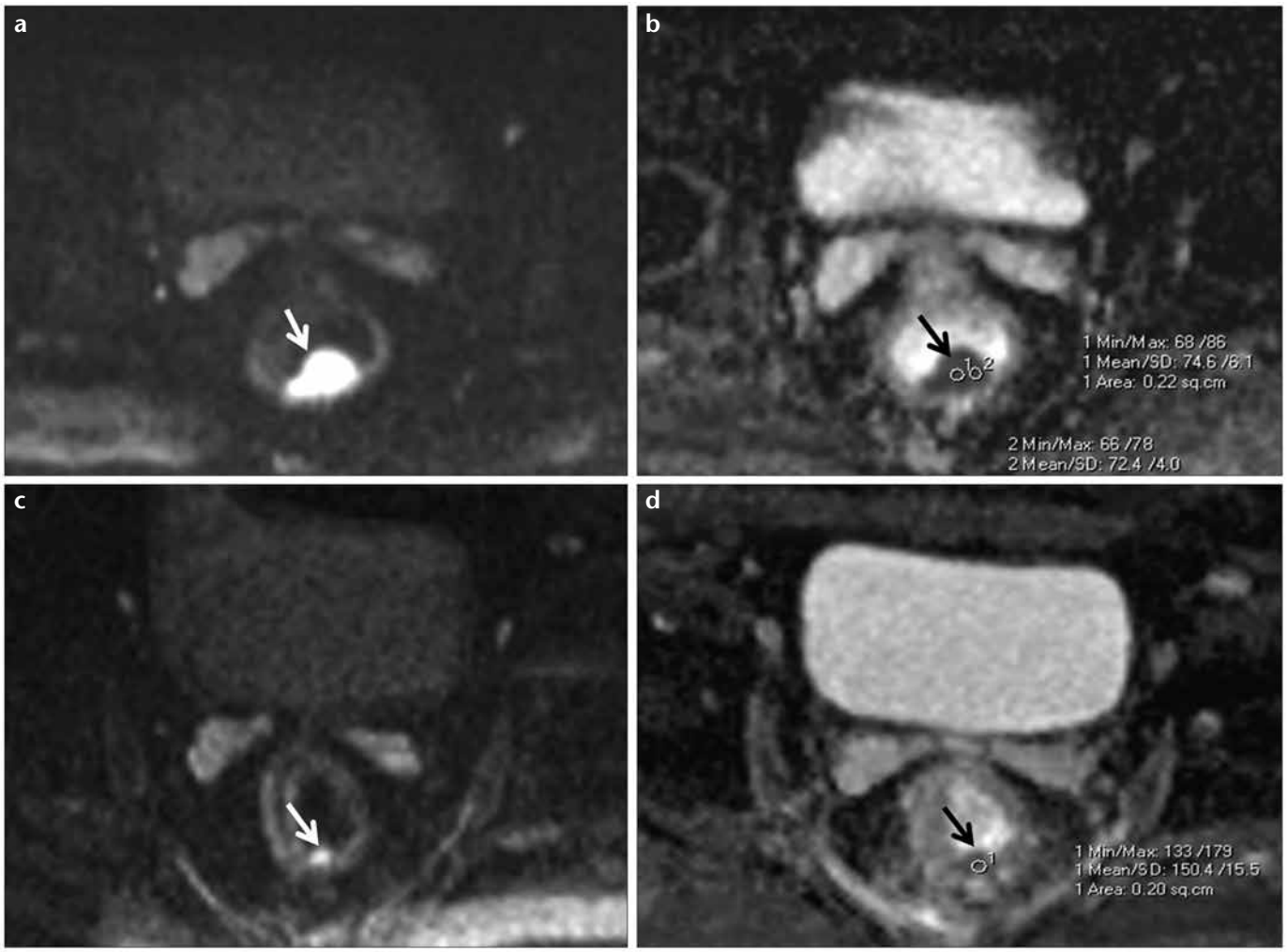

Figure 1. a–d. A rectal adenocarcinoma of a 47-year-old male patient (PT2N0, pRS: 1, 0.28 cc). Pre-chemoradiation therapy (CRT) DW-MR image (b=800 s/mm²) **(a)** shows a 4.8 cc, polipoid rectal tumor with very high signal intensity (*arrow*). The ADC mapping image **(b)** shows that the ADC values from the area of interest were 0.72–0.75×10^{-3} mm²/s (*arrow*). Post-CRT DW-MR image (b=800 s/mm²) **(c)** shows a significant decrease in tumor volume (1 cc). Residual tumor with intermediate signal intensity limited to the mucosa and submucosa can be seen (*arrow*). After CRT **(d)**, significant increases in ADC values in the ADC mapping images were observed (1.50×10^{-3} mm²/s) (*arrow*).

Quantitative analysis

Pre-CRT mean ADC values of the normal rectal wall and rectal tumors were 1.70×10^{-3}±0.13 mm^2/s (95% CI, 1.49–1.97 mm^2/s) and 0.84×10^{-3}±0.14 mm^2/s (0.61–1.25 mm^2/s), respectively (Table 5). These values were statistically different and did not overlap (P < 0.001; Z=4.62). In two patients with a mucinous subtype of tumor, the mean pre-CRT rectal tumor ADC values were 0.72×10^{-3}±0.28 mm^2/s (0.70–0.74 mm^2/s). Post-CRT mean ADC values of the normal rectal wall and rectal tumors were 1.78×10^{-3}±0.23 mm^2/s (1.49–2.20 mm^2/s) and 1.17×10^{-3}±0.19 mm^2/s (0.61–1.90 mm^2/s), respectively. Both mucinous rectal tumors had a mean post-CRT ADC value of 1.01×10^{-3} mm^2/s. Pre- and post-CRT mean ADC values of normal rectal wall were not statistically different (P = 0.09; Z=1.8) (Table 5). However, the post-CRT mean ADC values of rectal tumors were significantly higher than that of the pre-treatment rectal tumor ADC values (P = 0.002; Z=-9.39) (Table 5, Figs. 1 and 2). However, the mean ADC values of pRS 4 (n=9) and pRS 0–3 (n=21) were not statistically diffferent (P = 0.071; Z=-1.99; 95% CI, -34.09–0.49) (Table 6).

Surgical therapy

All patients recevied a total mesorectal excision eight weeks after neoadjuvant CRT. Based on the MRI findings, low anterior resection (n=19), abdominoperineal resection (n=8), proctectomy (n=2), or resectional biopy (n=1) was administered.

Pathological findings after surgery

Upon pathological evaluation after surgery, 21 patients with residual rectal tumors were staged as T2 (n=7) or T3 (n=14). Two patients had a mucinous histopathologic subtype of tumor. The N staging results of all patients showed tumor staging of N0 (n=26), N1 (n=2), or N2 (n=2). The mean residual tumor volume was 4.5±7.0 cm^3 (range, 0.0–28.1 cm^3). Based on the Dworak tumor response grading system, the patient evaluation showed RS 0 in one patient, RS 1 in nine patients, RS 2 in eight patients, RS 3 in three patients, and RS 4 in nine patients.

Discussion

In this study, we prospectively investigated the efficiency of DW-MRI

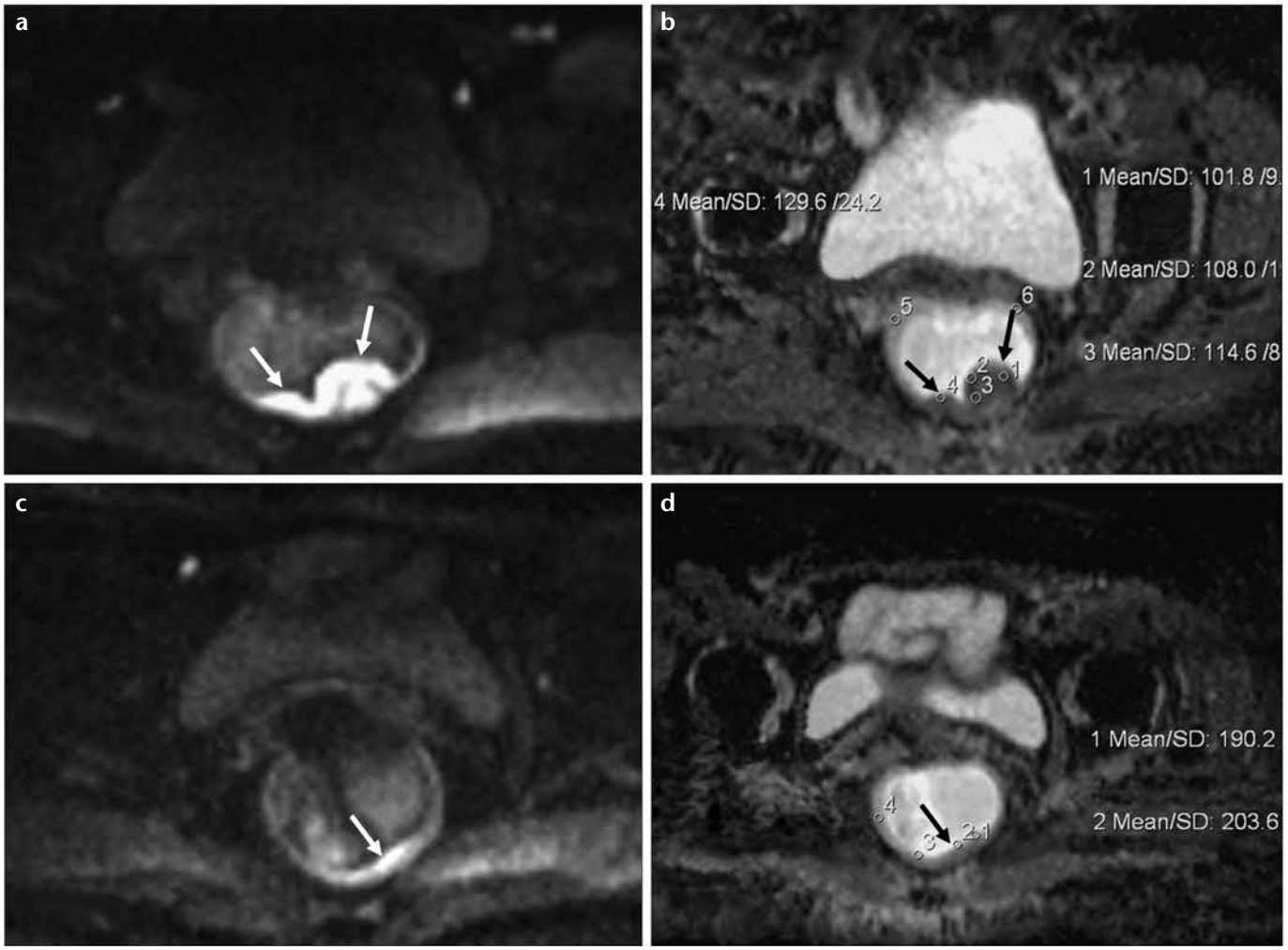

Figure 2. a–d. A rectal adenocarcinoma from a 71-year-old female patient (PT0N0, pRS: 4). Pre-chemoradiation therapy (CRT) DW-MR image (b=800 s/mm²) **(a)** shows a 9.5 cc, polipoid rectal tumor with very high signal intensity (*arrows*). The ADC mapping image **(b)** shows that the ADC values from the area of interest were 1.10–1.14×10^{-3} mm²/s (*arrows*). Post-CRT DW-MR image (b=800 s/mm²) **(c)** shows a significant decrease in tumor volume (1.4 cc). Residual tumor with low signal intensity limited to the mucosa and submucosa can be seen (*arrow*). After CRT **(d)**, significant increases in ADC values in the ADC mapping images were observed (1.90–2.03×10^{-3} mm²/s) (*arrow*).

for the prediction of neoadjuvant therapy response in locally advanced rectal cancer. Although there is controversy regarding the necessity of aggressive surgery in patients with pCR after CRT (5–8), informing colorectal surgeons of an accurate tumor response to neoadjuvant CRT before surgery by using DW-MRI is beneficial for complete responders because they would benefit from less extensive resection, such as sphincter-preserving surgery. Our study focused on determining if complete responders can be accurately predicted by measuring pre- and post-CRT changes in the ADC values and SI. In previous studies of therapy response using DW-MRI as a method for evaluation, changes in ADC values were described; however, in this study, we also analyzed SI changes.

A number of previous studies have shown that bright SI or lower ADC values based on DW-MRI are associated with more viable tumor tissue, in which diffusion is more restricted because of intact cellular membranes (21–23). Ichikawa et al. (24) evaluated the usefulness of high-b-value DW-MRI with qualitative (SI) analyses for the detection of colorectal adenocarcinoma in 33 patients. According to their preliminary results, the mean sensitivity and specificity of high-b-value DW-MRI for the detection of colorectal adenocarcinoma were 90.9% (30/33; 95% CI, 74.5%–97.6%) and 100% (15/15; 95% CI, 74.6%–100%), respectively. Similiarly, Rao et al. (25) proved the added value of DW-MRI imaging to conventional T2-weighted imaging in the detection of rectal cancer. In this study, all rectal tumors were visible before treatment and had higher SIs relative to the normal rectal wall on DW-MR images with b-800 values. Moreover, the SIs were very high or high in 27/30 (90%) of the rectal tumors.

Preliminary studies related to quantitative DW-MRI showed that ADC measurements may be able to differentiate the normal rectum from neoplastic involvement in addition to distinguishing inflammatory and neoplastic involvements. In a small retrospective series, ADC values of the normal rectum and rectosigmoid malignancy groups and rectosigmoid carcinoma

Table 5. The findings of quantitative assessment with DW-MRI

	ADC (mm^2/s)		Sperman test		Wilcoxon test	
	Pre-CRT	Post-CRT	R^a	P	Z	P
Normal rectal wall	1.70×10^{-3} (1.49–1.97)	1.78×10^{-3} (1.49–2.20)	-0.86	< 0.01	1.8	0.09
Rectal tumor						
Total (n=30)	0.84×10^{-3} (0.61–1.25)	1.17×10^{-3} (0.61–1.90)	0.5	0.002	-9.39	< 0.001
CR (n=9)	0.88×10^{-3} (0.61–1.25)	1.29×10^{-3} (0.92–1.90)				
pRS 0–3	0.83×10^{-3} (0.61–1.25)	1.11×10^{-3} (0.64–1.10)				
pRS 3 (n=3)	0.95×10^{-3} (0.84–1.05)	1.22×10^{-3} (1.07–1.46)				
pRS 2 (n=8)	0.82×10^{-3} (0.70–0.91)	1.06×10^{-3} (0.95–1.32)				
pRS 1 (n=9)	0.80×10^{-3} (0.65–1.10)	1.14×10^{-3} (0.94–1.48)				
No response (n=1)	0.83×10^{-3}	1.07×10^{-3}				

DW, diffusion-weighted; CRT, chemoradiotherapy; ADC, apparent diffusion coefficent; CR, complete response, pRS; pathological regression score.
[a] *R* values of ≥0.75, 0.74–0.50, and <0.50 correspond very good, good, and bad agreement, respectively.
Data represent mean (95% confidence interval).

Table 6. ADC differences of the patients with pRS 4 and pRS 0–3

	Z	P^a	95% confidence interval
Pre-CRT tumor ADC			
pRS 4	-0.84	0.066	-16.17–6.7
pRS 0–3			
Post-CRT tumor ADC			
pRS 4	-1.99	0.071	-34.09–0.49
pRS 0–3			

ADC, apparent diffusion coefficent; CRT, chemoradiotherapy; pRS, pathological regression score.
[a] Wilcoxon test.

and inflammatory bowel disease groups were significantly different (P < 0.01). A cut-off value for carcinomas of 1.14×10^{-3} mm^2/s yielded a sensitivity and specificity of 93.3% and 93.3%, respectively (26). In a recent study, Song et al. (23) reported that the mean ADC of the viable tumor group was significantly lower than that of the non-viable tumor group. They concluded that adding DWI to T2-weighted imaging is helpful for detecting viable tumour after neoadjuvant CRT compared to T2-weighted imaging alone or to positron emission tomography (PET)/CT in patients with locally advanced rectal cancer. In our current study, the pre-treatment mean ADC values of the normal rectal wall and rectal tumors were 1.70×10^{-3} mm^2/s (1.49–1.97 mm^2/s) and 0.84×10^{-3} mm^2/s (0.61–1.25 mm^2/s), respectively, which were statistically different (P < 0.001; Z=4.62).

In recent years, there have only been a few, small, preliminary studies of the use of DW-MRI for evaluating pCR to neoadjuvant CRT (27–29). In a recent, retrospective, multicenter trial, the added value of DW-MRI in the evaluation of pCR to neoadjuvant CRT was investigated in patients with 120 locally advanced rectal cancer. The sensitivity for the selection of complete responders ranged from 0% to 40% by standard MRI compared to 52%–64% with DW-MRI, and resulted in less overestimation of tumors in patients with a pCR after the addition of DW-MRI (14). In the current study, tumor diffusion SIs were significantly decreased in all patients who had a response after CRT (P < 0.001; Z=4.8). However, the quantitative analysis on DW-MRI was not considered to be a reliable method for the differentiation of complete and partial responders, because scores of 1–2 level tumor SIs were still present in 77.8% of the patients with pCR.

Kim et al. (15) showed that adding DW-MRI to conventional MRI yields better diagnostic accuracy than the use of conventional MRI alone in the evaluation of CR to neoadjuvant CRT in patients with locally advanced rectal cancer. They stated that the mean ADC of the pCR group was significantly higher than that of the non-pCR group (1.62×10^{-3} vs. 1.04×10^{-3} mm^2/s, respectively; P < 0.0001); however, an overlap of ADC values was observed in the two groups (15). In the current study, ADC measurements were taken from the normal rectal wall and rectal tumors. While the ADC values of the normal rectal wall did not change (P = 0.09; Z=1.8) after CRT, the ADC values of the rectal tumors increased significantly (P < 0.0001; Z=-9.39). Unfortunately, there was no significant difference between ADC values of patients with pCR and partial response after neoadjuvant CRT (P = 0.071; Z=-1.99). This finding suggests that ADC values can not be used to accurately differentiate complete responders from partial responders.

Recently, Curvo-Semedo et al. (16) stated similar results in assessing pCR in patients with locally advanced rectal cancer after CRT and found that ADC measurements were not reliable for this purpose. It is believed that

the presence of microscopic residual tumor cell nests in fibrotic areas or in the mucinous subset is the main reason for indiscrimination of CR from near CR by DW-MRI (15). In our study, this hypothesis was supported by the determination that there was no relationship between post-CRT ADC values and SI changes with pRS in rectal tumors. Even with the recent technical advances in DW-MRI, the cellular heterogeneity of the tumor in response to neoadjuvant CRT cannot be overcome, because even high-spatial-resolution reconstructed ADC mapping based on minute voxels cannot be used to determine the tumor response at each individual cellular level (30). Therefore, further studies of novel functional imaging modalities are needed to detect microscopic residual tumor cell nests. PET-CT has similiar limitations for identifying microscopic residual tumor cell nests besides the low spatial resolution and high cost. Currently, perfusion imaging represents one of the most interesting fields of CT development. This technique has shown promise in predicting the response to neoadjuvant treatment (31, 32).

Our study had several limitations. First, the size of the pCR patient group in this study was relatively small. Second, the images were analyzed by consensus between two reviewers, and therefore the interobserver variability of ADC measurements was not tested. Third, the limited spatial resolution and the relatively poor signal-to-noise ratio of high b-value DW-MRI should be considered as a limitation. Therefore, it was impossible to identify detailed rectal wall layers on high-b-value DW-MR images alone, as the background signal intensity was suppressed, especially in the normal rectal wall. Moreover, we used a high b-value of 800 s/mm^2 compared to 1000 s/mm^2, and therefore it is possible that the sensitivity of this technique was decreased by the presence of patients with false-positive results (33, 34).

In conclusion, for the re-staging of rectal tumors by DW-MRI, an increase in ADC values and decrease in SIs can predict therapy response but cannot unequivocally determine a complete response. Therefore, further studies of novel functional imaging modalities are needed to identify microscopic residual tumor cell nests.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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