RESEARCH ARTICLE



Application value of simultaneous multislice readout-segmented echo-planar imaging for diffusion-weighted MRI in differentiation of rectal cancer grade

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Abstract

Objective To analyze the association of apparent diffusion coefficient (ADC) values measured by readout-segmented echoplanar imaging (rs-EPI) using different simultaneous multislice (SMS) acceleration factors and the differentiation of rectal cancer grade.

Materials and methods Patients with non-mucinous rectal adenocarcinoma diagnosed by biopsy (endoscope-guided biopsy or surgical resection) were retrospectively collected, and each patient underwent an MRI examination. ADC values of rs-EPI, $2 \times SMS$ rs-EPI, and $3 \times SMS$ rs-EPI were recorded as ADC₁, ADC₂, and ADC₃, respectively.

Results The scanning time of $2 \times SMS$ rs-EPI was 60 s, 56.2% shorter than 137 s of rs-EPI sequence, while that of $3 \times SMS$ rs-EPI was 51 s, 72.8% less than that of rs-EPI time. The ADC value of the three groups dropped with the decrease in cancer grade (p < 0.05). The AUC values of ADC₁, ADC₂, and ADC₃ in predicting highly differentiated rectal cancer were 0.74, 0.729, and 0.687, respectively. The difference in AUC values between ADC₁ and ADC₂ was not statistically significant (p = 0.889).

Discussion SMS technology with an acceleration factor of 2 could be applied clinically to evaluate the pathological differentiation of rectal cancer grade.

Keywords Rectum \cdot Readout-segmented echo-planar imaging \cdot Simultaneous multislice \cdot Apparent diffusion coefficient \cdot Differentiation grade

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Introduction

Colorectal cancer is among the most common malignant neoplasms and the tenth most deadly cancer worldwide. Among all colorectal cancer, 30–35% arise in the rectum [1]. The tumor-node-metastasis (TNM) staging system is the most common method to predict clinical outcomes and guide therapeutic management in rectal cancer. Moreover, mesenteric fascia, histopathological grade, and vascular invasion are adjunctive prognosticators for further stratification of colorectal cancer patients [2]. However, it remains debatable whether conventional histologic differentiation grading is less suited for resected rectal cancer following neoadjuvant chemoradiation [2]. Therefore, a non-invasive and accurate assessment of rectal cancer grading is of great clinical significance for guiding subsequent clinical treatment.

Diffusion-weighted imaging (DWI) is a non-invasive MR imaging tool based on signal contrast generation and differences in Brownian motion that can reflect biological activity [3] and can be used to evaluate the molecular function and micro-architecture of the human body [4]. The apparent diffusion coefficient (ADC) from DWI provides biological implications for cell density and can identify tumor progression [5]. However, the application of traditional DWI sequences based on single-shot echoplanar imaging (ss-EPI) is limited by factors including low resolution, geometric distortion, and sensitivity to artifacts [6]. Compared with ss-EPI, the K-space acquisition of readout-segmented Echo-planar imaging (rs-EPI) can improve the imaging quality of DWI in various organs by reducing geometric distortion, providing shorter echo intervals, and improving spatial resolution [7]. Yet, its application is limited by the long scanning time.

Multi-layer data can be obtained by simultaneous multislice (SIMULTANEOUS multislice/SMS) and can significantly shorten the image acquisition time [8]. Furthermore, several recent studies have shown that ADC values based on ss-EPI and rs-EPI can be used to evaluate preoperative and prognostic factors of different cancers, including rectal cancer [9–11]. Moreover, rs-EPI technology combined with SMS has been successfully applied to evaluate the image quality of nasopharyngeal carcinoma, breast and parotid gland, and pancreas [12–15]. However, no studies have explored the relationships between ADC values measured on rs-EPI combined with SMS and rectal cancer grade differentiation. Also, the impact of rs-EPI combined with different SMS acceleration factors on the ADC values of rectal cancer is still unclear.

In this study, we analyzed the association of ADC values measured by rs-EPI using different SMS acceleration factors with the pathological differentiation of rectal cancer grade.

Materials and methods

Ethics statement

This retrospective study was approved by the Institutional Review Board. The need for written informed consent was waived by the institutional review board due to the retrospective design of the study.

Study population

Patients with non-mucinous rectum adenocarcinoma diagnosed by biopsy between December 2021 and July 2022 were included in the study. The inclusion criteria were: (1) patients with biopsy-proven rectal cancer either after endoscopic-guided biopsy or surgical resection; (2) patients with complete MRI images; (3) those who did not receive neoadjuvant radiotherapy at the time of the MRI scan. The exclusion criteria were: patients who had rectal surgery or radiochemotherapy before the examination; with poor image quality; the tumor not visible on the MRI image; unresectable or metastatic diseases; the existence of mucinous cystadenoma.

Imaging protocol

A 3 T scanner (MAGNETOM Vida, Siemens Healthiness) and 18 channel body array coils were used for MRI. Creatine-50 min was used to clean the intestinal tracts before the examination. In addition, patients were given 20 mg of scopolamine butyl bromide (Bus Copan, Boehringer Ingelheim) intramuscularly 30 min before MRI to reduce bowel motion. No rectal dilation was seen prior to the MRI examination. Conventional MRI plain scan (including sagittal, axial, and coronal T2-weighted imaging) and three rs-EPI sequences, including rs-EPI and SMS rs-EPI sequence with an acceleration factor of 2 (2×SMS rs-EPI), and SMS rs-EPI sequence with an acceleration factor of 3 ($3 \times SMS$ rs-EPI) were all in free respiration scanning mode, and the scanning direction was perpendicular to the diseased bowel. The parameters are shown in Table 1. The conventional MR techniques for rectal cancer included routine standardized sagittal T2 and axial T1 fast spin echo (FSE) sequences together with high-resolution axial and coronal T2 FSE sequences: an axial T1 FSE sequence [repetition time/ echo time (TR/TE), 500/11 ms; section thickness, 5 mm; gap, 1 mm; matrix, 320×224; FOV, 380×380 mm²]; an axial T2 FSE sequence (TR/TE, 4050/85 ms; section thickness, 5 mm; gap, 1 mm; matrix, 320×324; FOV, 380×380 mm²); a sagittal T2 sequence (TR/TE, 5310/113 ms; section thickness, 3 mm; gap, 0 mm; matrix, 320×320; FOV, 250×250 mm²); oblique high-resolution axial and coronal

Parameters	rs-EPI	2×SMS rs-EPI	3×SMS rs-EPI
<i>b</i> value (s/mm ²)	0.1000	0.1000	0.1000
Fat suppression	SPAIR	SPAIR	SPAIR
TR (ms)	5000	2270	1800
TE (ms)	51	52	54
Inversion time	210	210	210
FOV (mm)	216×216	216×216	216×216
Matrix	128×128	128×128	128×128
Voxel (mm ³)	$1.7 \times 1.7 \times 4.5$	$1.7 \times 1.7 \times 4.5$	$1.7 \times 1.7 \times 4.5$
Slice thickness (mm)	4.5	4.5	4.5
Interlayer spacing (mm)	0.45	0.45	0.45
Number of slices	24	24	24
Slice acceleration factor		2	3
Bandwidth (Hz/Px)	998	998	998
Acquisition time (s)	137	60	51

T2 sequences (TR/TE, 5629/85 ms; section thickness, 2 mm; gap, 0 mm; matrix, 448×314 ; FOV, 200×200 mm²). The axial imaging was perpendicular to the long axis of the rectal tumor, as identified by sagittal T2 imaging.

All the *b* values of the DWI sequence were 0 and 1000 s/ mm^2 . The device automatically created ADC figures.

Image analysis

The MRI images were independently reviewed by two radiologists (Y. T. Wang and G. H. Yan, with 10 and 15 years of experience in reading Rectal MRI, respectively) who were blind to clinicopathological results but were aware that patients were diagnosed with rectal cancer. For intratumoral ADC measurements, regions of interest (ROI_s) included the largest tumor area, avoiding cystic, necrotic, and visible vascular structures on T2-weighted images. Two radiologists manually drew ROI using b = 0 s/mm² of rs-EPI or SMS rs-EPI independently and then copied the ROI to the ADC map (Fig. 1) for recording the ADC values. ADC values of RS-EPI, $2 \times$ SMS RS-EPI, and $3 \times$ SMS RS-EPI were recorded and specified as ADC₁, ADC₂, and ADC₃, respectively.

Statistical analysis

SPSS version 22 (IBM Corporation) and MedCalc (Version 16.8) were used for statistical analyses. A two-way mixed model was used to calculate the intraclass correlation coefficients (ICCs) with an absolute agreement for evaluating the agreement between the ADC values from the two radiologists. Eighty-three patients were randomly selected for ICC, which was classified as poor (ICC < 0.5), moderate $(0.5 \le ICC < 0.75)$, good $(0.75 \le ICC < 0.9)$, and excellent (ICC ≥ 0.9) [16]. The mean value of the ADC values measured by two radiologists was adopted for further study. Freidman test was conducted to compare the ADC values between various differentiation grades and between ADC groups with different differentiation grades in each group. Pairwise comparison was further performed using paired Wilcoxon signed rank-sum test for statistically significant difference (p < 0.05). Nonparametric Spearman rank correlation was conducted for evaluating the correlation between ADC₁, ADC₂, ADC₃, and differentiation grade of rectal cancer pathological tissues; r value from 0 to 0.25 was taken to represent little or no correlation: 0.25–0.5 indicated moderate correlation, 0.5–0.75 indicated a good correlation, and from 0.75 to 1.0 represented very good or excellent correlation [17].

The receiver-operating characteristic (ROC) curve was adopted to determine the predictive value of ADC values of different groups to differentiated rectal cancer, indicated by the area under the curve (AUC). The DeLong test was used to compare the AUC of ADC₁ and ADC₂. Optimal cutoffs for each ADC parameter were determined at points that maximized Youden's J index based on receiver-operating characteristic (ROC) curves. Youden's index was calculated by specificity + sensitivity-1 [18]. A two-sided *p* value < 0.05 represented statistical significance.

Results

Patients

Based on the clinical history and physical examination results, 203 patients with clinically suspected rectal cancer were enrolled. One hundred and twenty patients were excluded based on the exclusion criteria: (1) insufficient image quality due to gas-induced susceptibility artifacts or movement artifacts which prevented accurate measurement of the region of interest (ROI) (n = 54); (2) tumor not visible on the MRI image (n = 15); (3) unresectable or metastatic diseases (n = 21); (4) the existence of mucinous cystadenoma, whose cell density was low (high ADC values) (n = 30).

Finally, 83 patients (55 males and 28 females, 22–76 years old, with a mean age of 54.6 ± 11.9 years) who underwent MRI were included in this study. The clinicopathological features of the patients are shown in Table 2. According to the glandular and ductal morphological features, rectal cancer was classified as a moderately and or poorly differentiated tumor [3].

Fig. 1 Male, 53 years old, with moderately differentiated rectal cancer. a, b Conventional rs-EPI sequence with b value of 1000 s/mm² and ADC map, respectively. The ADC value was 1.16×10^{-3} mm²/s, and the SNR was 45.36. c, d 2×SMS rs-EPI sequence with b value of 1000 s/mm² and ADC map, respectively. The ADC value was 1.04×10^{-3} mm²/s, and the SNR was 42.36. e, f 3×SMS rs-EPI sequence with b value of 1000 s/mm² and ADC map, respectively. The ADC value was 1.18×10^{-3} mm²/s, and the SNR was 40.21. **g–i** Highly (g), moderately (h), and poorly (i) differentiated rectal cancer, respectively. The red line points to a tumor. \mathbf{j} The axial T2WI image



Table 2	Clinicopathologica	l characteristics	of the	patients
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Clinicopathological characteristics	n Percentage (%)
Gender	
Male	44 (53.01)
Female	39 (46.99)
Age (years)	58.82 (11.71)
BMI/(kg m ⁻²)	22.82 (1.91)
Location of tumor	
Upper-middle segment	34 (40.96)
Lower segment	49 (59.04)
Differentiation grade	
Well	13 (15.7)
Moderate	64 (77.1)
Poor	6 (7.2)
CEA	
+	55 (66.27)
-	28 (33.73)
CA19-9	
+	40 (48.19)
-	43 (51.81)
Nerve invasion	
+	56 (67.5)
-	27 (32.5)
Vascular cancer embolus	
+	61 (73.5)
-	22 (26.5)
Cancer nodules	
+	68 (81.9)
-	15 (18.1)

1.5

Acquisition time

The scanning time of $2 \times SMS$ rs-EPI was 60 s, 56.2% shorter than 137 s of rs-EPI sequence, while that of $3 \times SMS$ rs-EPI was 51 s, 72.8% less than that of rs-EPI time.

Interobserver agreement of ADC parameters

Interobserver agreement was excellent for ADC_1 [intraclass correlation coefficient (ICC), 0.935; 95% CI 0.467–0.979], ADC_2 (ICC, 0.947; 95% CI 0.167–0.986), and ADC_3 (ICC, 0.946; 95% CI 0.213–0.986).

The relationship between ADC values of the three sequences and the differentiation grade of pathological tissues

The comparison of ADC value and differentiation grade of pathological tissues of rs-EPI sequence in the three groups is shown in Fig. 2 and Table 3. Among 83 patients with rectal cancer, 15.7% (13/83) were with highly differentiated rectal cancer, 77.1% (64/83) with moderately differentiated rectal cancer, and 7.2% (6/83) with poorly differentiated rectal cancer. The ADC value of the three groups dropped with the decrease in the pathological grade. ADC₁ and ADC₂ between the highly differentiated group and a moderately differentiated group showed no significant differences (p > 0.05); there were significant differentiation, moderate differentiation and poor differentiation (p < 0.05), while differences among various differentiated groups in ADC₃ were statistically significant (all p < 0.05).

highly differentiated

moderately differentiated Differentiation grade



poorly differentiated

ADC1

ADC3

ADC2

In the highly differentiated rectal cancer group, differences among ADC₁, ADC₂, and ADC₃ groups were not statistically significant (p = 0.219).

In the moderately differentiated rectal cancer group, the difference between the three groups was significant (p < 0.001). Pairwise comparison showed no significant difference between ADC₁ and ADC₂ (p = 0.109) but significant differences between ADC₁ and ADC₃ (p < 0.001) and between ADC₂ and ADC₃ (p < 0.001).

In the poorly differentiated rectal cancer group, the differences among ADC₁, ADC₂ and ADC₃ groups were statistically significant (p = 0.009). Pairwise comparison showed no statistically significant difference between ADC₁ and ADC₂ (p=0.752) but a significant difference between ADC₁ and ADC_3 (p=0.028) and between ADC_2 and ADC_3 (p=0.028).

According to correlation analysis (Table 4), ADC₁, ADC₂ and ADC₃ were positively correlated with the differentiated histological degree of rectal cancer (p < 0.05), among which ADC_1 had the highest correlation, followed by ADC_2 .

Diagnostic efficiency on ADC value of rs-EPI sequence in highly differentiated rectal cancer in these three groups

Table 5 shows that the AUC values of ADC_1 , ADC_2 and ADC₃ in predicting highly differentiated rectal cancer were 0.74, 0.729, and 0.687, respectively, with respective sensibilities of 84.6%, 92.3%, and 69.2%, respectively; specificities of 55.7%, 51.4%, and 88.6%, respectively; thresholds of 1.185×10^{-3} mm²/s, 1.135×10^{-3} mm²/s, and 1.155×10^{-3} mm²/s, respectively. The ROC curve is shown in Fig. 3. The AUC values of ADC1 and ADC2 were not statistically different (p = 0.889).

Discussion

Our data suggested that compared with rs-EPI, SMS technology with an acceleration factor of 2 significantly reduces the scanning time and maintains stable diagnostic performance to highly differentiated rectal cancer, and could therefore be applied to evaluate the pathological differentiation grade of rectal cancer and be further extended in clinical practice.

ADC value obtained by DWI-MR imaging can reflect the microanatomical structure information of tissues [19]. Some studies have suggested using ADC as a non-invasive marker of tumor aggressiveness. A previous study reported that lower ADC values are associated with a more aggressive tumor profile for rectal cancer, and significant correlations were found between mean ADC values and differentiation grade with peritumoral edema [20]. Yang et al. found that the mean ADC value could predict a pathologic complete response after undergoing preoperative chemoradiotherapy [21]. Therefore, DWI has been increasingly used in detecting

Table 3The comparison ofADC value and differentiationgrade of pathological tissuesof rs-EPI sequence in the threegroups	Differentiation grade	$ADC_1 (\pm SD)$	$ADC_2 (\pm SD)$	$ADC_3 (\pm SD)$
	Highly differentiated $(n=13)$	1.27 (±0.12)	1.25 (±0.10)	1.12 (±0.22)
	Moderately differentiated $(n=64)$	$1.15 (\pm 0.17)$	$1.13 (\pm 0.17)$	$1.04 (\pm 0.12)$
	Poorly differentiated $(n=6)$	$0.82 (\pm 0.09)$	$0.81 (\pm 0.14)$	$0.63 (\pm 0.06)$
	p value	0.011	0.009	0.011
	Highly differentiated versus moderately differentiated tumor	0.906	0.307	0.046
	Highly differentiated versus poorly differentiated tumor	0.027	0.028	0.028
	Moderately differentiated versus poorly differentiated tumor	0.028	0.027	0.028

Table 4	The correlation of ADO	C value and differenti	ation grade of	pathological tissu	ues of rs-EPI sequence in th	e three groups
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Parameters	ADC ₁	ADC ₁		ADC ₂		ADC ₃	
Differentiation grade	r value	p value	<i>r</i> value <i>p</i> value		r value p valu		
	0.455	< 0.001	0.436	< 0.001	0.419	< 0.001	

Table 5 Diagnostic efficiency on ADC value of rs-EPI	Parameters	AUC	Cutoff value	Sensitivity (%)	Specificity (%)	p value
sequence in highly differentiated rectal cancer in these three groups	Well versus moderate-po ADC ₁ (× 10 ⁻³ mm ² /s) ADC ₂ (× 10 ⁻³ mm ² /s) ADC ₃ (× 10 ⁻³ mm ² /s)	or differentiation 0.74 (0.632, 0.830) 0.729 (0.620, 0.820) 0.687 (0.576, 0.784)	1.185 1.135 1.155	0.846 0.923 0.692	0.557 0.514 0.886	0.006 0.009 0.033



Fig. 3 Receiver operating characteristic curves of the performance of ADC₁, ADC₂, and ADC₃. ADC values of rs-EPI, $2 \times SMS$ rs-EPI, and $3 \times SMS$ rs-EPI were recorded as ADC₁, ADC₂, and ADC₃, respectively

and characterizing rectal cancer and monitoring rectal cancer after neoadjuvant chemotherapy [20]. However, it is susceptible to image blur and spatial deformation when standard DWI based on single-shot echo plane imaging is used [6].

Rs-EPI has been suggested as a good variant of EPI for high-resolution imaging, particularly when combined with parallel imaging. This is because it can shorten the echo interval, reduce the geometric distortion, and obtain better image quality and diagnostic efficiency, compared with the traditional EPI sequence. However, its ADC value has no statistical difference compared to traditional DWI [22]. In addition, it has the disadvantage of a long scanning time [7].

SMS technology is a relatively novel MRI technology that uses parallel image reconstruction, which is simultaneously excited by multiple frequency composite of pulses and multiple imaging levels [8]. Compared with conventional ss-EPI sequence, b = 1000 s/mm² images in 2×SMS ss-EPI sequence show no significant difference in overall image quality, lesion significance, and anatomical details. Also, the comparison between rectal and background tissue is sharp, and there are no obvious artifacts [23]. However, to the best of our knowledge, no study explored the relationships between the differentiation grades of rectal cancer by combining SMS technology with rs-EPI. Therefore, the acceleration factor of SMS and rs-EPI in terms of ADC values needs to be studied systematically to determine the balance between scan time minimization and image quality.

Different SMS acceleration factors by referring to the relationships between the different ADC values measured by

rs-EPI and the rectal cancer grade differentiation were evaluated in this study. The differentiation of rectal cancer grade is one of the important factors affecting the prognosis [2]. With the decrease of tumor differentiation, the malignant structure becomes more complex, with more neovascularized and necrotic structures and greater heterogeneity, thus significantly restricting the movement of water molecules [24]. Our results show that the ADC values of the three sequences decreased with the decrease of differentiation, and there was statistical significance for the differences in ADC values at different levels of tissue differentiation (p < 0.05), which was consistent with previous research results [19, 20, 25, 26]. This resulted from the fact that with the increase of the degree of the malignant tumor, the proliferation of tumor cells significantly accelerated, and the ratio of the nucleus and the cell density per unit volume increased, leading to the decrease of the extracellular space distance and that of free diffusion of water molecules, limitation of diffusion, and in turn, lower ADC value [20]. However, there are controversial results of no significant difference between RESOLVE ADC values and different degrees of pathologic differentiation in Cui's study [3], which may be attributed to the different selected b values and a small number of cases with high and poor differentiation. In this study, the ADC images were obtained at 1000 s/mm², and the ADC values were measured, improving the sensitivity of DWI and effectively overcoming the influence of perfusion and the T2 shinethrough effect. In addition, the accuracy of ADC values was improved [27]. There were no statistical differences between high and medium differentiation for the ADC values of the three groups, indicating that the micro-environment of cells is similar in highly and moderately differentiated tissues, and the diffusion degree of water molecules is also similar.

This study showed that when the SMS acceleration factor was 3, the ADC₃ value was significantly lower than that of ADC₁, and the difference was statistically significant (p < 0.05), indicating that SMS with an acceleration factor of 2 could obtain ADC values as stable and accurate as rs-EPI and that the scanning time was significantly shortened. However, when comparing moderately and poorly differentiated tissues, ADC₃ was statistically different from ADC₁ and ADC₂, which was mainly attributed to the fact that high SMS accelerators caused instability in the measurement of ADC values at high levels of cell malignancy. Hence, SMS with an acceleration factor of 3 could significantly reduce the scanning time, but caution should still be exercised in rectal applications.

In the present study, according to ROC curve analysis, ADC₁ obtained by rs-EPI had the highest diagnostic efficacy for highly differentiated rectal cancer (AUC = 0.74), the lowest diagnostic efficacy for $3 \times SMS$ rs-EPI (0.687), and the highest sensitivity for $2 \times SMS$ rs-EPI for highly differentiated rectal cancer (0.923), meanwhile, the diagnostic efficacy

of 2×SMS rs-EPI was not significantly different from rs-EPI (0.729 vs. 0.74). The cutoff of the three sequences was stable, with an average value of 1.158×10^{-3} mm²/s. The correlation between ADC₁ and the differentiation degree of rectal cancer was the highest (r=0.455) and the lowest for ADC₃ (r=0.419), which were moderately correlated due to the heterogeneity of tumor, as different degrees of differentiation may exist within the same tumor [28]. Therefore, combining the diagnostic efficiency of differentiation grade and scanning time, it can be inferred that SMS with an acceleration factor of 2 is provided with a certain potential in studying pathological differentiation of rectal cancer.

This study has a few limitations. First, only one MR 3.0 T scanner was used instead of scanners with different field strengths, making it impossible to evaluate the impact of different field strengths on the application of SMS technology. Second, manual measurement of ROI increased the possibility of sample error, and different degrees of differentiation within the same tumor could be observed due to the heterogeneity of tumor differentiation. To this end, further studies are expected to be carried out on the correlation between different ROI measurement methods and differentiation grades. Third, moderately and poorly differentiated rectal cancer was combined for detailed research, and larger sample sizes were needed to assess histological types of rectal cancer, since there were only six poorly differentiated cases.

In conclusion, compared with rs-EPI, SMS technology with an acceleration factor of 2 significantly reduces the scanning time and can be applied to evaluate the pathological differentiation grade of rectal cancer.

Declarations

Conflict of interest All authors declare that they have no conflict of interest.

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