

Diffusion MRI in rectal cancer: ADC measurements before and after gel lumen distension

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Aims and objectives

Rectal carcinoma represents one of the most frequent malignancies of the gastrointestinal tract [1] and the third most common cancer worldwide [2].

The five-year survival rate after radical surgery is about 60%, but it amounts to 80-90% in case of early diagnosis [1].

Therefore, the role of early diagnosis, accurate staging and early treatment is essential to improve survival rate.

According to the National Comprehensive Cancer Network (NCCN), the prognosis of rectal cancer is influenced by several factors.

These factors are represented by degree of tumor invasion into and beyond the bowel wall, number of lymph nodes involved, involvement of the mesorectal fascia (MRF), plasmatic level of carcinoembryonic antigen (CEA) and presence of lymphovascular invasion (LIV) like the tumor differentiation grade [3,4].

Some of these prognostic factors are assessed by histopathological examination of tumor specimens, obtained during surgical intervention [3,5].

Management of rectal cancer has undergone important changes in the last decades with an increasing interest in organ-sparing treatment [6].

This improved the research of pre-operative non-invasive methods which could stratify good-responders after neo-adjuvant therapies and select high-risk patients who benefit from the more aggressive multimodality treatments [3,5,6].

Diffusion-weighted imaging (DWI) has recently been introduced into MR protocol for disease evaluation in oncology, namely in rectal cancer. This sequence provides information on the microanatomy of a tissue by measuring water diffusion influenced by cell density, vascularity, viscosity of extracellular fluid and membrane integrity [3,7].

The proprieties of water diffusion are successively quantified from DWI images and expressed as apparent diffusion coefficient (ADC), which has recently been considered a potential non-invasive imaging biomarker of tumor aggressiveness in rectal cancer [3,5].

Considering the rising importance of ADC in pre-treatment rectal cancer, several studies have shown that the repeatability of ADC values is conditioned by various factors [6].

One of these factors is due to rectal filling during MRI examination with endorectal contrast agent. This way the distention of rectal lumen improves rectal wall depiction and tumor extension estimation [8,9].

Currently there is no scientific data about the possible variations of ADC values due to endorectal contrast agent.

The aim of our prospective study is to compare ADC measurements obtained before and after rectal distension using sonography transmission gel as endoluminal contrast agent.

Methods and materials

Patients

Between January and September 2014, 21 consecutive patients (13 men and 8 women) with a mean age of 60 years (age range 54-73 years) were studied for pre-treatment rectal cancer staging using a 1.5 Tesla MRI.

Selection criteria included the following:

1. histological biopsy of proven rectal carcinoma;
2. primary staging MRI including DWI;
3. no contraindications for 1.5 Tesla (T) MRI examination;
4. DWI obtained before and after rectal distention with ultrasonographic gel.

Exclusion criteria are represented by:

1. no identified tumor signal on a DWI and ADC map both before and after endoluminal distention;
2. insufficient MRI quality images (artifacts owing to severe motion or to metal implants).

The protocol was reviewed and approved by our internal institutional committee and all patients signed a written informed consent.

Study protocol

MRI was performed using a 1.5-T system (Signa HDxt , GE Healthcare, Milwaukee) and an eight channel dedicated phased-array body coil in all patients. The patients did not receive any bowel preparation or antispasmodic medication before the examination.

The exam protocol consisted of two steps: first, sequences were acquired without gel rectal distension, then DW images were repeated after endorectal introduction of ultrasonographic transmission gel ([Fig. 1](#) on page 4).

The rectal filling was obtained placing patient on MR table in left lateral decubitus position with the knees on the chest. Then approximately 60-80 ml of tepid sonography

transmission gel was administrated using an enema syringe. Rectal distension was stopped when the patient indicated a sensation of fullness in the rectum. In the end, patient returned to a supine position on the MR table with feet entering first MR gantry.

The standard imaging protocol ([Fig. 2](#) on page 5) consisted of the following sequences:

- Sagittal T2-weighted Fast Recovery Fast Spin-Echo (FRFSE) images, acquired with repetition time (TR)=4000 ms, Echo Time (TE)=106 ms, Echo Train Length (ETL) 16, Thickness 3 mm, Gap 0-1 mm, Matrix 320x256, Number of Signal Average (NSA)=4.
- Coronal T2-weighted FRFSE images, acquired with TR=4500, TE=101.3 ms, ETL 16, Thickness 3 mm, Gap 0-1 mm, Matrix 320x256, NSA=4; coronal sequences have been placed parallel to the longitudinal rectal axis.
- Axial T2-weighted FRFSE images, acquired with TR=4500, TE=108 ms, ETL 16, Thickness 3 mm, Gap 0-1 mm, Matrix 320x256, NSA=4; axial images were placed perpendicular to the longitudinal rectal axis.
- Axial T1-weighted FSE images, acquired with a TR=400-500 ms, TE=14 ms, ETL=1-3, Thickness 3 mm, Gap 0-1 mm, Matrix 3230x224, NSA=2-3.
- Axial diffusion-weighted images (DWI) obtained with b-value of 0-800, with a TR=5000, TE=85.7ms, Thickness 5 mm, Gap 1 mm, Matrix 160x160, NSA=4. This sequence is acquired twice, before and after rectal distension ([Fig. 3](#) on page 6).

Imaging analysis and statistical technique

DWI Functool software was used to obtain quantitative ADC maps using Advantage workstation VolumeShare 5 GE Healthcare. ADC measurement was calculated on the DWI slice with the largest tumor area, manually tracing a round/oval shaped region of interest (ROI) before and after rectal lumen distension with sonographic transmission gel ([Fig. 4](#) on page 6).

ADC values, obtained in both diffusion sequences, were compared using Wilcoxon matched pairs signed rank test. Correlation was assessed using Pearson analysis.

Images for this section:

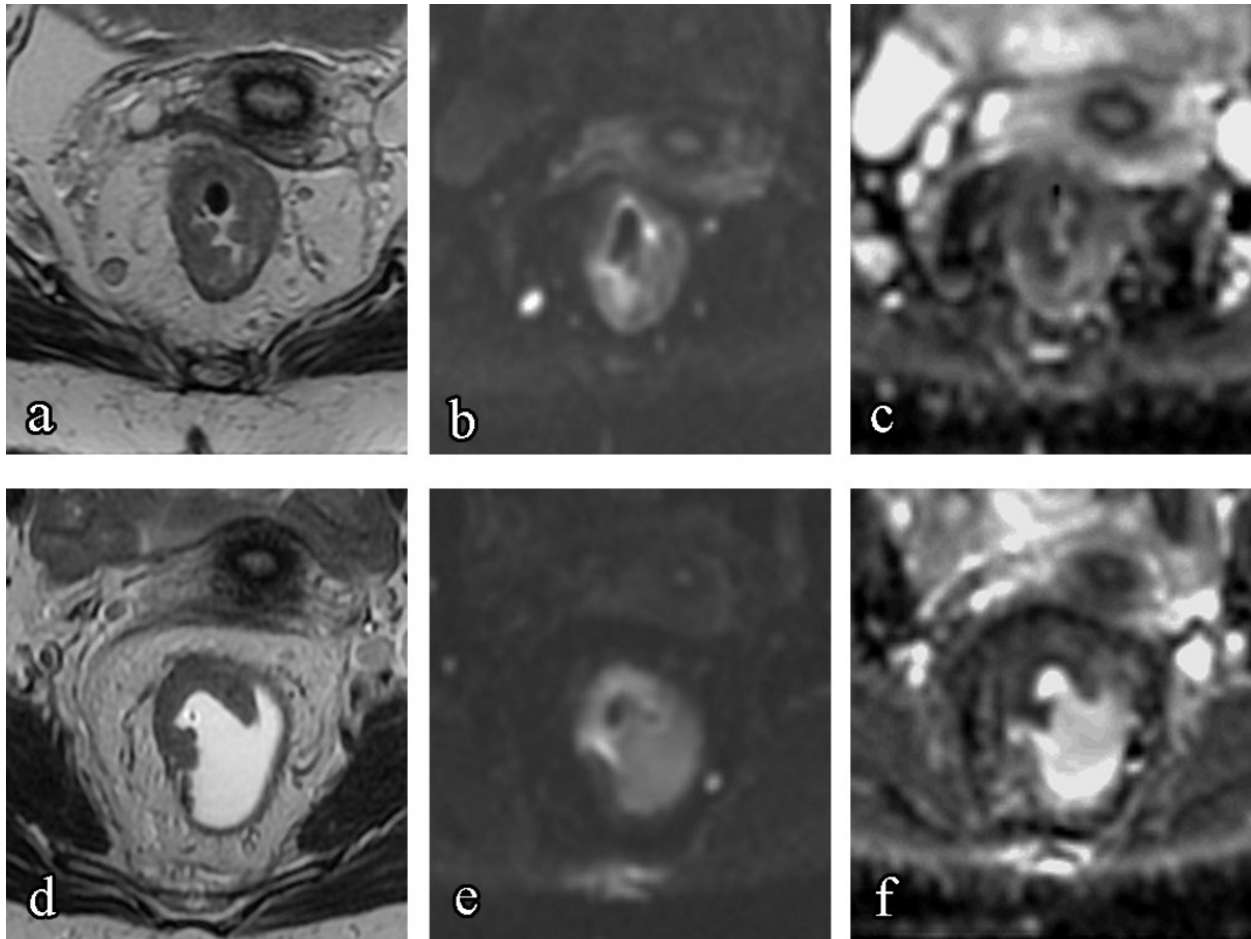


Fig. 1: Example of sequences used in rectal cancer evaluation, before (a-c) and after (d-f) gel lumen distension. Figure a and d exhibit axial T2-weighted images. DW images are shown in figure b and e; respective ADC maps are illustrated in figure c and f.

	FSE T2w	FSE T1w	DWI
TR	4500	400-500	5000
TE	106	14	85.7
ETL	16	1-3	-
Thickness	3 mm	3 mm	5 mm
Gap	0-1 mm	0-1 mm	1 mm
Matrice	320x256	320x224	160x160
Nex	4	2-3	4

Fig. 2: The table represents MRI parameters in T2W, T1W and DW images.

PARAMETERS	FREE BREATHING b800
TR	5425ms
TE	76-85.7
EPI factor	80
Slice thickness	5
Gap	1
Flip angle	90
Acceleration factor	2
FOV	40 cm
NSA	4
Half scan factor	2
Bandwidth	250KHz
Scan percentage	100%
Acquisition voxel	N/A
Reconstruction voxel	N/A
Acquisition matrix	160x160
Reconstruction matrix	256x256
Spatial fat saturation	Yes - Water Excitation
Diffusion directions	All

Fig. 3: The Table illustrates parameters used in b800 diffusion-weighted single-shot echo-planar sequences acquired before and after luminal distension with sonographic transmission gel.

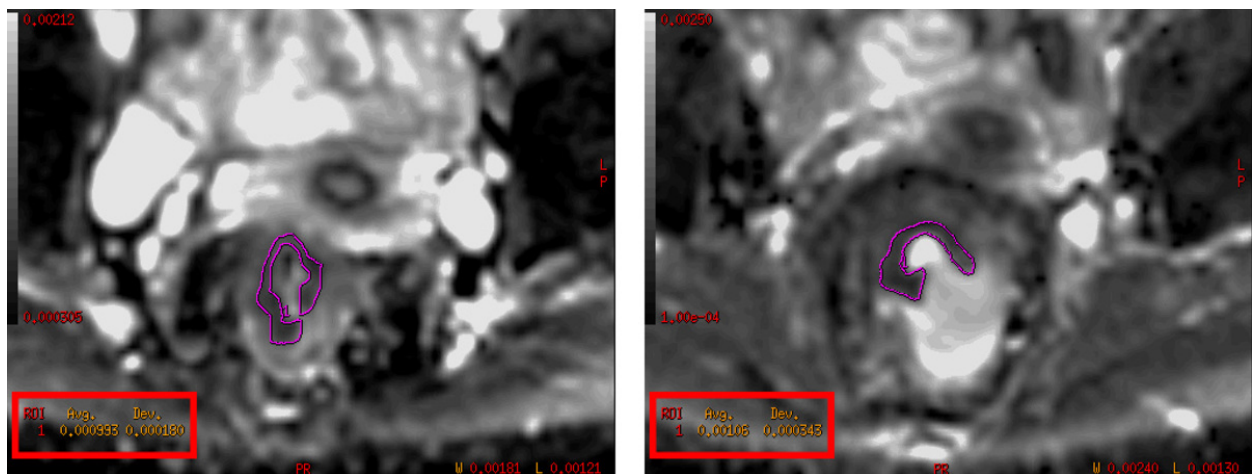


Fig. 4: ADC maps obtained from diffusion weighted single-shot echo-planar images illustrating examples of ROI (Region of Interest), placed in rectal tumor before and after rectal gel distension.

Results

Mean ADC value assessed from diffusion MR sequences acquired with $b=0-800$ without endorectal contrast was 1.24 (95% Confidence Interval=0.91-1.91) while after gel lumen distension, higher mean ADC value of 1.49 was obtained (95% Confidence Interval=1.09-1.95).

Wilcoxon matched pairs signed rank test revealed no statistically significant difference ($p>0.05$) between ADC values obtained before and after rectal lumen distension with sonographic transmission gel (Fig. 5 on page 8).

A very strong Pearson correlation was reported between sequences in both modalities with r value of 0.92.

Images for this section:

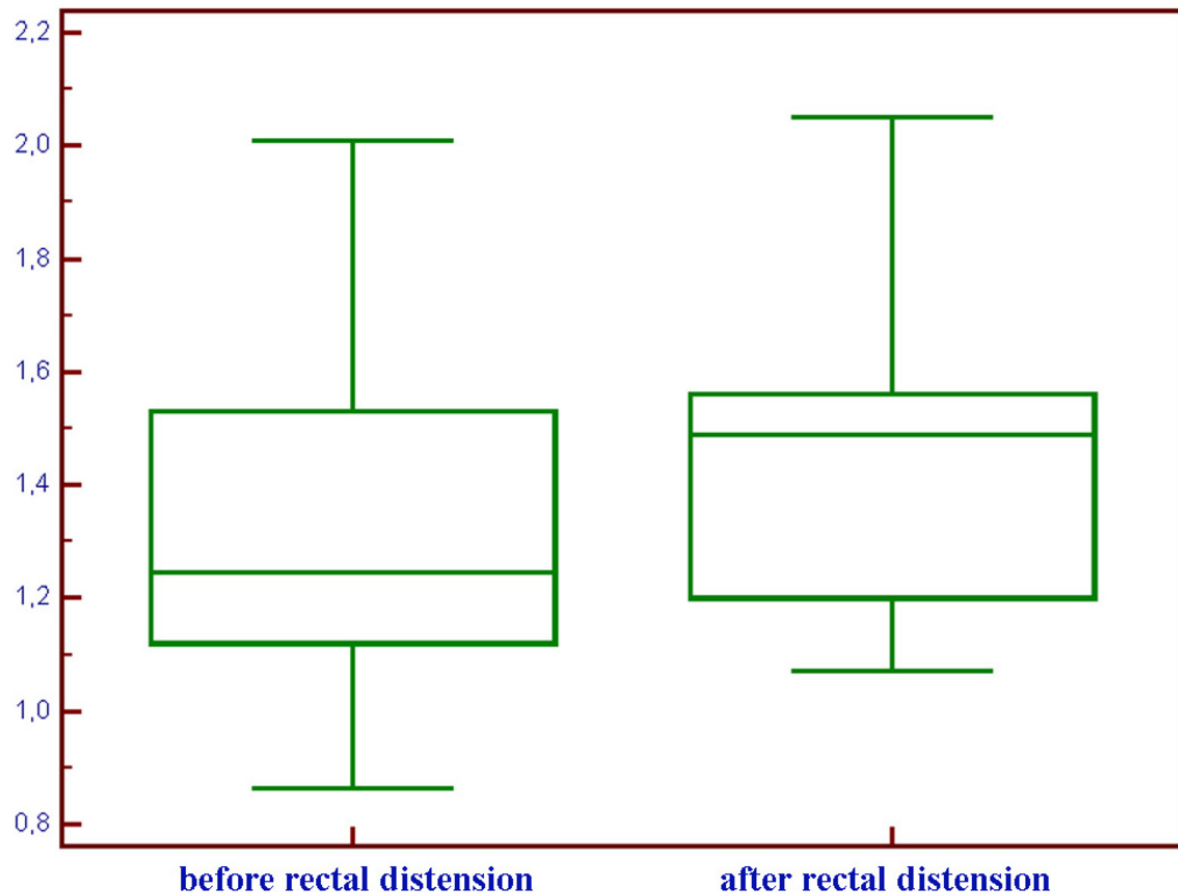


Fig. 5: Box-and-whisker plot for ADC measurements obtained before and after gel endorectal distension: no statistically significant difference was observed.

Conclusion

Analysis of ADC values did not show any statistically significant difference between acquisition before and after rectal distension, although ADC values were slightly higher after introduction of ultrasonographic transmission gel within the rectum.

The ultrasonographic transmission gel used in this study, was considered by some studies the most appropriate endorectal contrast agent.

In fact it shows inert characteristic in the magnetic field, high contrast on T2-weighted fast spin-echo imaging, semisolid consistence and inexpensive, too [10].

Several authors assess that this technique of rectal distension helps to determine a clear distinction between the lumen and the inner rectum wall - distinguishing the lesion from the fecal material - and to better evaluate its extension in the perirectal fat [11, 9, 8].

Some authors prefer not to distend rectal lumen because it may cause alteration of the distance between the tumor and the mesorectal fascia and of the resulting circumferential resection margin (CRM) [12,9].

In addition, if the procedure of rectal filling is not adequately performed, the presence of intrarectal air causes magnetic susceptibility artifacts in DW images ([Fig. 6](#) on page 9).

Furthermore there is no difference in ADC values before and after introduction of gel within the rectum, indicating this potential non-invasive bio-marker could be influenced by other different factors [6].

Further studies are necessary to create a standardized method for quantitative analysis of DWI in rectal cancer.

Images for this section:

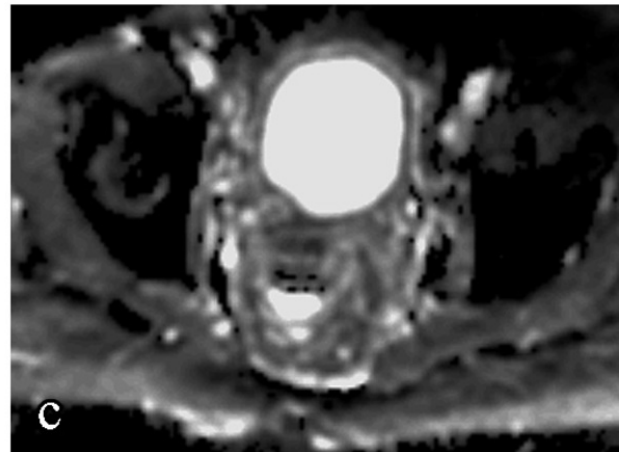
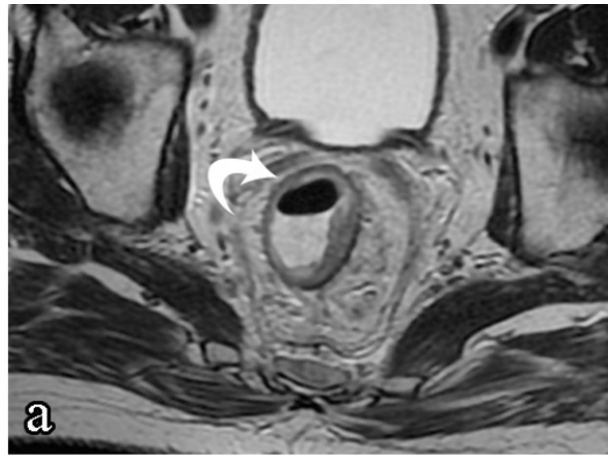


Fig. 6: Magnetic susceptibility artifacts caused by intraluminal air. In a, T2-weighted image shows endorectal air (curved white arrow), causing susceptibility artifacts in DW images (b) and ADC map (c).

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