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Diffusion MRI for rectal cancer staging: ADC measurements before and after ultrasonographic gel lumen distension

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ABSTRACT

Objectives: To compare Apparent Diffusion Coefficient (ADC) measurements in rectal neoplastic lesions before and after lumen distension obtained with sonography transmission gel.
Methods: From January 2014 to July 2016, 25 patients (average age 63.7, range 41–85, 18 males) were studied for pre-treatment rectal cancer staging using a 1.5 T MRI. Diffusion MRI was obtained using echo-planar imaging with b = 800 value; all patients were studied acquiring diffusion sequences with and without rectal lumen distension obtained using sonography transmission gel. In both diffusion sequences, two blinded readers calculated border ADC values and small ADC values, drawing regions of interest respectively along tumour borders and far from tumour borders. Mean ADC values among readers – for each type of ADC measurement – were compared using Wilcoxon matched pairs signed rank test. Correlation was assessed using Pearson analysis.
Results: Border ADC mean value for diffusion MR sequences without endorectal contrast was 1.122 mm^2/sec, with 95% Confidence Interval (CI) = 1.02–1.22; using gel lumen distension, higher border ADC mean value of 1.269 mm^2/s (95% CI = 1.16–1.38) was obtained. Wilcoxon matched pairs signed rank test revealed statistical difference ($p < 0.01$); a strong Pearson correlation was reported, with *r* value of 0.69. Small-ADC mean value was 1.038 mm^2/s (95% CI = 0.91–1.16) for diffusion sequences acquired without endorectal distension and 1.127 mm^2/s (95% CI = 0.98–1.27) for diffusion sequences obtained after endorectal gel lumen distension. Wilcoxon analysis did not show statistical difference ($p = 0.13$). A very strong positive correlation was observed, with *r* value of 0.81.
Conclusions: ADC measurements are slightly higher using endorectal sonographic transmission gel; ROI should be traced far from tumour borders, to minimize gel filled-pixel along the interface between lumen and lesion. Further studies are needed to investigate better reliability of ADC in rectal cancer MRI using sonographic gel intraluminal distension.

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1. Introduction

Rectal carcinoma represents one of the most frequent malignancies of the gastrointestinal tract [1] and is the third most common cancer worldwide [2]. Its prevalence increases after the age of 50 years with a male predilection [3]. Rectal cancer shows a worse prognosis for its high risk of metastasis and local recurrence [4]. The five-year survival rate after radical surgery is about 60%, but this rate amounts to 80–90% when diagnosis is made at an early stage [1].

Therefore, the role of tumour staging is essential for treatment planning and prognosis of the patient. According to TNM classification and International Union Against Cancer (UICC) the criteria for rectal cancer staging are based on histologic criteria indicating local status of the tumour (T stage) and the presence or absence of metastatic nodes (N stage) [5].

Even though diagnosis of rectal cancer needs bioptic samples obtained from endoscopic examination, this procedure does not show the depth of the lesion (degree of tumour invasion into and beyond the bowel wall), the number of lymph nodes involved and the involvement of mesorectal fascia [3].

For this reason, MRI is considered the most suitable imaging modality for the preoperative management of rectal carcinoma.

Abbreviations: ADC, apparent diffusion coefficient; FRFSE, fast recovery fast spin echo; TR, repetition time; TE, echo time; ETL, echo train length; NSA, number of signals average; ROI, region of interest; CI, confidence interval; CEA, carcinoembryonic antigen.

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The interpretation of preoperative MR images permits selection of patients with extra-rectal spread who mostly benefit from neo-adjuvant therapies (chemio- and/or radiotherapy) and patients with minimal or absent sphincteral involvement for which sphincter-sparing surgery is recommended [3].

In recent years, MRI has become increasingly interesting in management of rectal cancer, thanks to the possibility of predicting those patients who are "good responders" after neo-adjuvant therapies – adding diffusion weighted imaging (DWI) to the conventional protocol.

DWI is a technique widely used within the MR protocol for disease evaluation in oncology. 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 [6,7]. The application in rectal cancer allows us to localize, to predict treatment responders and to distinguish tumour tissue from non-tumour tissue [8]. The properties of water diffusion of the neoplasm are successively quantified from DWI images and expressed as an apparent diffusion coefficient (ADC) map, which has recently been considered a potential non-invasive imaging biomarker of tumour aggressiveness in rectal cancer [6,9].

Distension of rectal lumen has been considered an important diagnostic tool [10,11], even if its realistic use has been considered controversial for rectal MRI in rectal cancer staging. In this regard, some Authors found that rectal lumen distension improves tumour depiction within the wall and its extension estimation [10,11]. However, the ESGAR consensus paper on MRI of rectal cancer does not recommend the routine use of endorectal filling: the lumen distension could influence distance between rectal tumour and mesorectal fascia, and it does not improve depiction of mesorectal invasion from cancer [12].

Because of the increasing importance of ADC values for the prognosis of patients affected by rectal carcinoma, a standardized MRI protocol is necessary. Several studies have shown that repeatability of ADC values is conditioned by various factors [13]; currently there is no scientific data about the possible variations of ADC values due to endorectal contrast agent. Therefore, 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.

2. Materials and methods

2.1. Study population

Between January 2014 and July 2016, 25 consecutive patients (18 males, 7 females) with a mean age of 63 years (age range 41–85 years) were studied for pre-treatment rectal cancer staging using a 1.5 T MRI.

Selection criteria included the following: 1) histologically proven rectal carcinoma; 2) primary staging MRI including DWI; 3) no contraindications for 1.5 T MRI examination; 4) DWI sequences obtained before and after rectal distension with ultrasonographic gel.

Exclusion criteria are represented by: 1) no identified tumour signal on a DWI and ADC map both before and after endoluminal distension; 2) insufficient MRI quality images (artefacts 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.

2.2. Study protocol

MRI is performed using a 1.5-T system (SignaHDxt, GE Healthcare, Milwaukee) and an eight channel dedicated phased-array body coil in all patients. About three hours before the MR study, all patients performed a rectal cleansing with a water enema; no antispasmodic medication was used before imaging.

The patient is first placed on the MR table in the left lateral decubitus position with knees on the chest; successively a rectal tube, connected to a plastic enema syringe, is introduced into the rectum without gel instillation. Then the patient returns to a supine position locating the centre of magnetic field on the iliac crest. Rectal tube positioning was performed before the beginning of MRI exam in order to avoid changes of patient position on the MR table, namely during the successive procedure of sonographic gel infusion.

The standard imaging protocol consists of the following sequences:

- Sagittal T2-weighted Fast Recovery Fast Spin-Echo (FRFSE) images, acquired with repetition time (TR) = 4000 msec, Echo Time (TE) = 106 msec, Echo Train Lenght (ETL) = 16, thickness = 3 mm, gap interval = 0–1 mm, matrix = 320 × 256, number of signal average (NSA) = 4, field of view = 36 cm;
- Oblique coronal T2-weighted FRFSE images, with TR = 4500 msec, TE = 101.3 msec, ETL = 16, thickness = 3 mm, gap = 0–1 mm, matrix = 320 × 256, NSA = 4; coronal sequences have been placed parallel to the longitudinal rectal axis;
- Oblique axial T2-weighted FRFSE images, perpendicular to the longitudinal axis of the rectum, with TR = 4500 msec, TE = 108 msec, ETL = 16, thickness = 3 mm, gap = 0–1 mm, matrix = 320 × 256, NSA = 4;
- Axial T1-weighted FSE images, acquired with a TR = 400-500 msec, TE = 14 msec, ETL = 1-3, thickness = 3 mm, gap = 0–1 mm, matrix = 320 × 224, NSA = 2-3.

Diffusion-weighted sequences were obtained by Single Shot Echo Planar Imaging technique, with *b* values of 0–800. Diffusion sequences were acquired in axial plane (not angulated perpendicularly to the longitudinal rectal axis). Namely, acquisition parameters were the following: TR = 5000 msec; TE = 85.7 msec; number of excitation = 4; acceleration factor = 2; EPI factor = 80; spacing = 1 mm; field of view = 34–42 cm; thickness = 5 mm; acquisition time = 1 min and 42 s; half scan-factor = 2; band-width = 250 KHz; scan percentage 100%; acquisition voxel = not applicable; reconstruction voxel = not applicable; acquisition matrix = 192 × 160; reconstruction matrix = $256\hat{2}$; spatial fat saturation = yes; water excitation and isotropic motion gradient SI, RL, and AP with Stejskal-Tanner diffusion scheme.

After acquisition of these unenhanced sequences, approximately 60–80 ml of tepid sonography transmission gel are administrated using the enema syringe. Rectal distension was stopped if the patient indicates an unpleasant painful sensation. The enema tube is left in place to mark the rectal lumen. Then, the patient is again positioned into the MR gantry; axial T2-weighed sequences and Diffusion Imaging are repeated with rectal lumen distension (Fig. 1).

Approximately, a total study time of 20 min was needed for completing the MRI protocol.

2.3. Imaging analysis and statistical technique

MR examinations were independently reviewed by two radiologists (reader 1–a senior radiologist with 10 years of experience in body MRI and reader 2–a junior radiologist with 4 years of practice experience). Readers were blinded for their respective reports.

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