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MR enterography in pediatric and adult Crohn's disease: analyzing the apparent diffusion coefficient to assess active bowel wall inflammation

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Aims and objectives

Crohn's disease (CD) is a chronic idiopathic inflammatory condition potentially affecting any portion of the gastrointestinal tract, from mouth to anus, and characterized by a relapsing-remitting clinical behavior. In the past, treatment goals focused only on symptomatic control, but the discrepancy between clinical symptoms and active inflammation, and the introduction of more aggressive medical therapies (using biological and immunosuppressant agents) have made it necessary to reconsider our approach, focusing on clinical, laboratory and imaging data. A key issue in the management of patients with CD concerns how best to assess the disease's extent and inflammatory activity, detect potential complications, and measure treatment response.

Magnetic resonance enterography (MRE) has become the first-line imaging technique for assessing patients with CD. Besides the advantages of avoiding any ionizing radiation and obtaining a better soft tissue contrast resolution than with CT, MRE has the ability to investigate both intestinal and extra-intestinal disease activity, and it helps to differentiate between active disease and fibrosis, with important implications for disease management [1-6].

Signs of active bowel disease include [7]:

- Mural thickness: the hallmark of CD on cross-sectional imaging is bowel wall thickening (from 4 to 12 mm), usually in association with luminal stenosis. A normal bowel wall thickness, when adequately distended, should not exceed 3 mm. The most common site of involvement is the terminal ileum (sometimes with contiguous disease in the caecum). Discontinuous skip lesions may be seen more proximally in the small bowel or in the colon;
- Bowel wall signal intensity on T2-weighted images: a higher signal intensity is due to the presence of mucosal or submucosal edema;
- Pre-stenotic dilation: this can occur upstream from either an inflammatory stenosis or a fibrostenotic stricture. It becomes significant when the small bowel diameter is >3 cm;
- Mural enhancement: an increase in bowel wall enhancement compared with adjacent uninvolved bowel. A less avid mural enhancement is seen in fibrostenotic disease [8];
- Stratified mural enhancement: this is due to the presence of submucosal edema, where there is avid enhancement of the mucosa and muscularis propria/serosa, but relatively limited enhancement of the submucosa [9,10];
- The 'comb' sign and mesenteric adenopathy: in active inflammation, the vascular arcades (vasa recta) supplying the bowel segment involved become engorged;
- Fibro-fatty proliferation: sometimes found; and in penetrating disease: mesenteric phlegmon, abscess, fistulae.

In recent years, diffusion-weighted imaging (DWI) has been studied in conjunction with MRE with a view to improving the accuracy of disease activity assessments.

The DWI technique uses the diffusion of water molecules (random Brownian motion) in biological tissue to create images that reflect changes in water motility caused by interactions with cell membranes, macromolecules, and tissue alterations. Using this method helps to quantify the restriction of Brownian motion. DWI is performed using a T2-weighted fat-suppressed MR sequence with the addition of a diffusion gradient, which is quantified with a diffusion coefficient called the "b-value". Increasing the diffusion coefficient makes the signal in areas of free diffusion decrease more rapidly than in regions where diffusion is restricted. A single parametric map called the apparent diffusion coefficient (ADC) provides numerical values to help quantify the restriction of the water molecules' diffusion [11, 12]. DWI can thus provide additional information on a tissue's structural organization.

Numerous published studies have demonstrated the association between active bowel inflammation in CD and restricted mural diffusion on DWI [13-17].

Aims of the study were to compare DWI findings with morphological MRE sequences in cohorts of pediatric and adult patients with different stages of CD, and to quantify the mean ADC for inflamed intestinal segments and areas of inactive disease.

Images for this section:

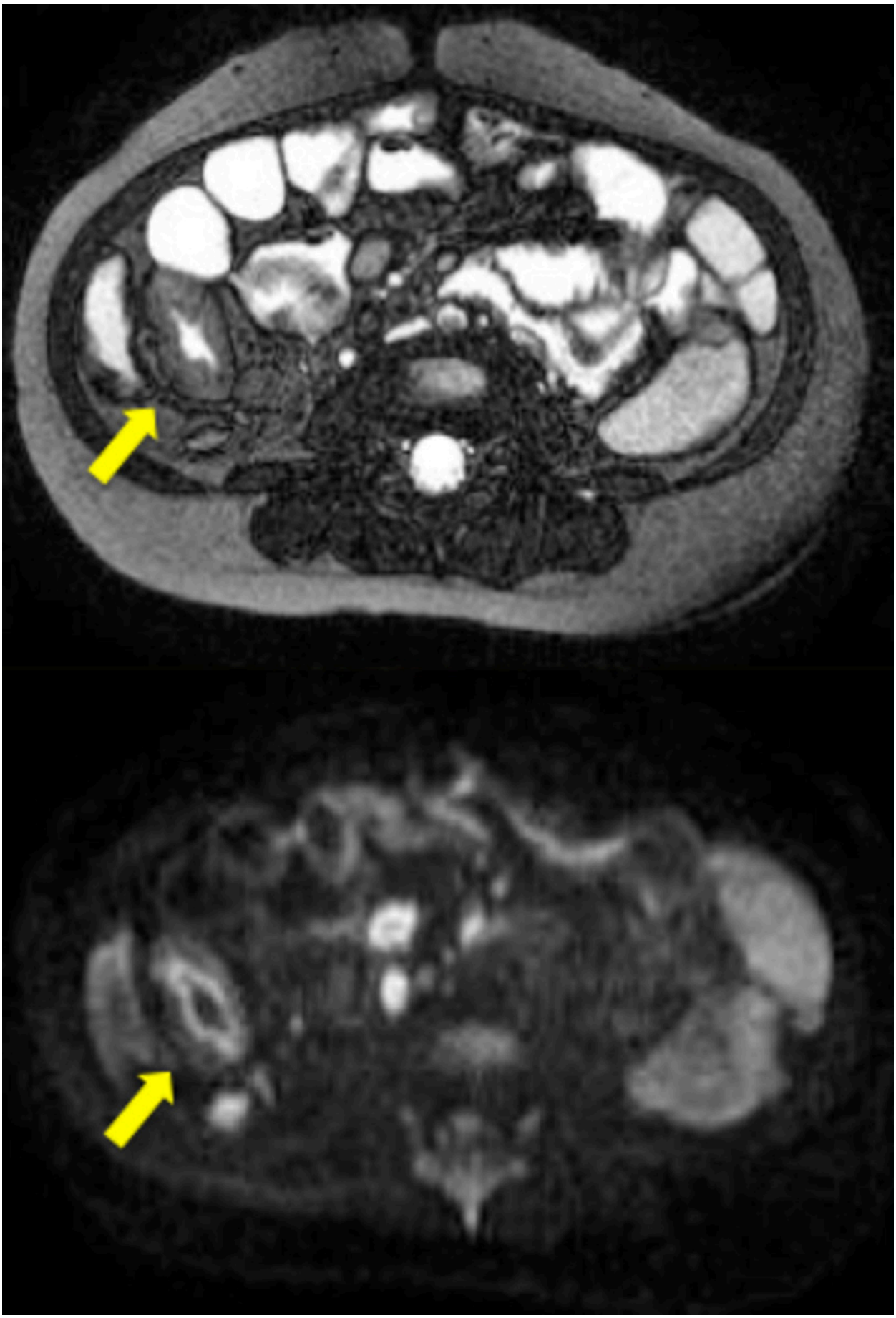

Fig. 1: Caecum: correlation between mural thickening and altered DWI signal.

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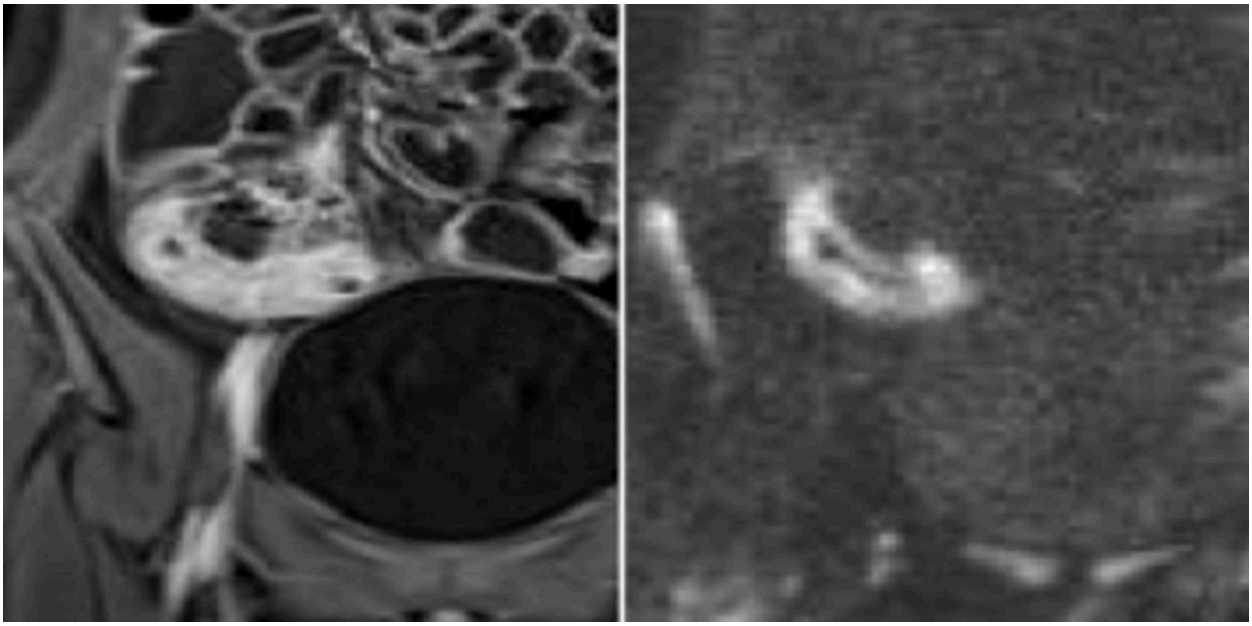

Fig. 2: Terminal ileum: correlation between mural enhancement (T1-weighted sequence) and altered DWI signal.

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Methods and materials

A single-center retrospective study was conducted over the years 2013-2015 at the Radiology Department of the University of Padua. There were 74 patients enrolled in the study (41 M; 33 F), including 45 of pediatric age (0-18 year-olds; mean age: 12,7 years) and 29 adults (mean age: 26,2 years). All patients had histopathologically confirmed CD. All patients, or their parents for the pediatric cases, were informed about the examination and gave their written consent. They underwent MRE (1,5 T) using a standardized protocol.

From four days before the procedure, patients adopted a low-fiber diet. On the day before the examination, they drank 2 liters of a water solution containing 4 sachets (34,8 g each or 17,4 g in pediatric cases) of PEG (polyethylene glycol) 4000. Patients fasted for 6 hours before the procedure, and 40 minutes beforehand they were given oral PEG 4000 (34.8 g in adults, 17.4 g in pediatric cases) dissolved in 20 ml of water per kilogram of body weight. Immediately before the examination, they were administered a bolus of 10 mg of hyoscine butylbromide in 10 ml of physiological solution. A further bolus of the same amount was administered before the contrastographic phases. The use of hyoscine butylbromide has been suggested in the recent literature as an anti-peristaltic agent. Patients were placed in the supine position, head first. After performing localizer sequences, the following were obtained: T2 TRUE-FISP sequences on the coronal and axial planes, with a thickness of 4 mm for adult patients and 3 mm for pediatric patients; T2 HASTE sequences with the same planes and thicknesses; T2 HASTE sequences with fat saturation (FS) on the coronal plane (3 mm thickness); T1 VIBE FS sequences on the coronal plane (3 mm thickness); T1 VIBE FS sequences with contrast medium on the coronal and axial planes 30 seconds (arterial phase), 70 seconds (portal phase), and 150 seconds (late phase) after administering the contrast agent, on the coronal and axial planes (3 mm thickness). The contrast medium was gadodiamide (Omniscan, GE Healthcare) 0.01 mmol/kg in adults and gadolinium chelate (Dotarem, Guerbet) 0.01 mmol/kg in pediatric patients. Then DWI sequences were obtained with b=0, 400, 800 s/mm^2 on the axial plane (6 mm thickness). Subtraction sequences of the various dynamic phases were also recorded.

ADC maps were generated from the DWI sequences. The ADC was measured by placing specific regions of interest (area <10 mm^2) in appropriately selected segments of ileum and colon with active and inactive disease.

A two-tailed statistical t-test was conducted. The statistical software used was IBM SPSS Statistics 24.

Results

Diffusivity was always restricted in inflamed bowel walls, identified on morphological MRE sequences from the typical signs (mural thickening, enhancement, etc.).

At higher b values (b=800 s/mm^2), the difference in mean ADC between inflamed loops and uninflamed loops was found statistically significant: the mean ADC was 1.07±0.33 x10^{-3}mm^2/s for inflamed loops, and 3.11±0.35 x10^{-3}mm^2/s for uninflamed loops (p=0.003). These values were uninfluenced by patients' age (pediatric cases: 1.04±0.29 vs 3.10±0.34 x10^{-3}mm^2/s; adults: 1.11±0.38 vs 3.12±0.37 x10^{-3}mm^2/s) or gender (males: 1.13±0.35 vs 3.13±0.39 x10^{-3}mm^2/s; females: 1.00±0.28 vs 3.07±0.30 x 10^{-3}mm^2/s).

Images for this section:

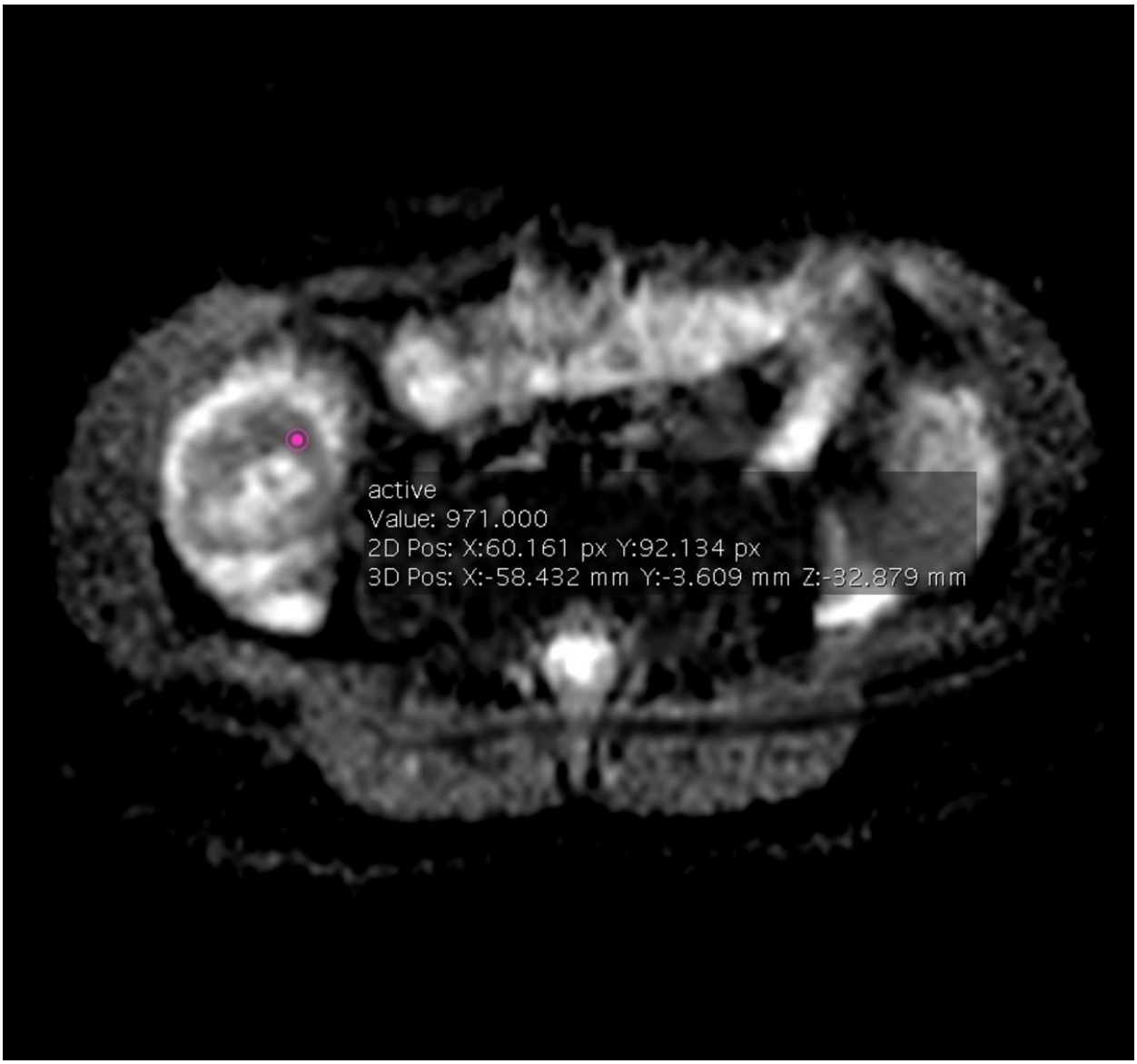

Fig. 3: ROI on a inflamed bowel wall (M; 15 y.). Medium ADC value is 0,97 x 10(-3) mm(2)/s.

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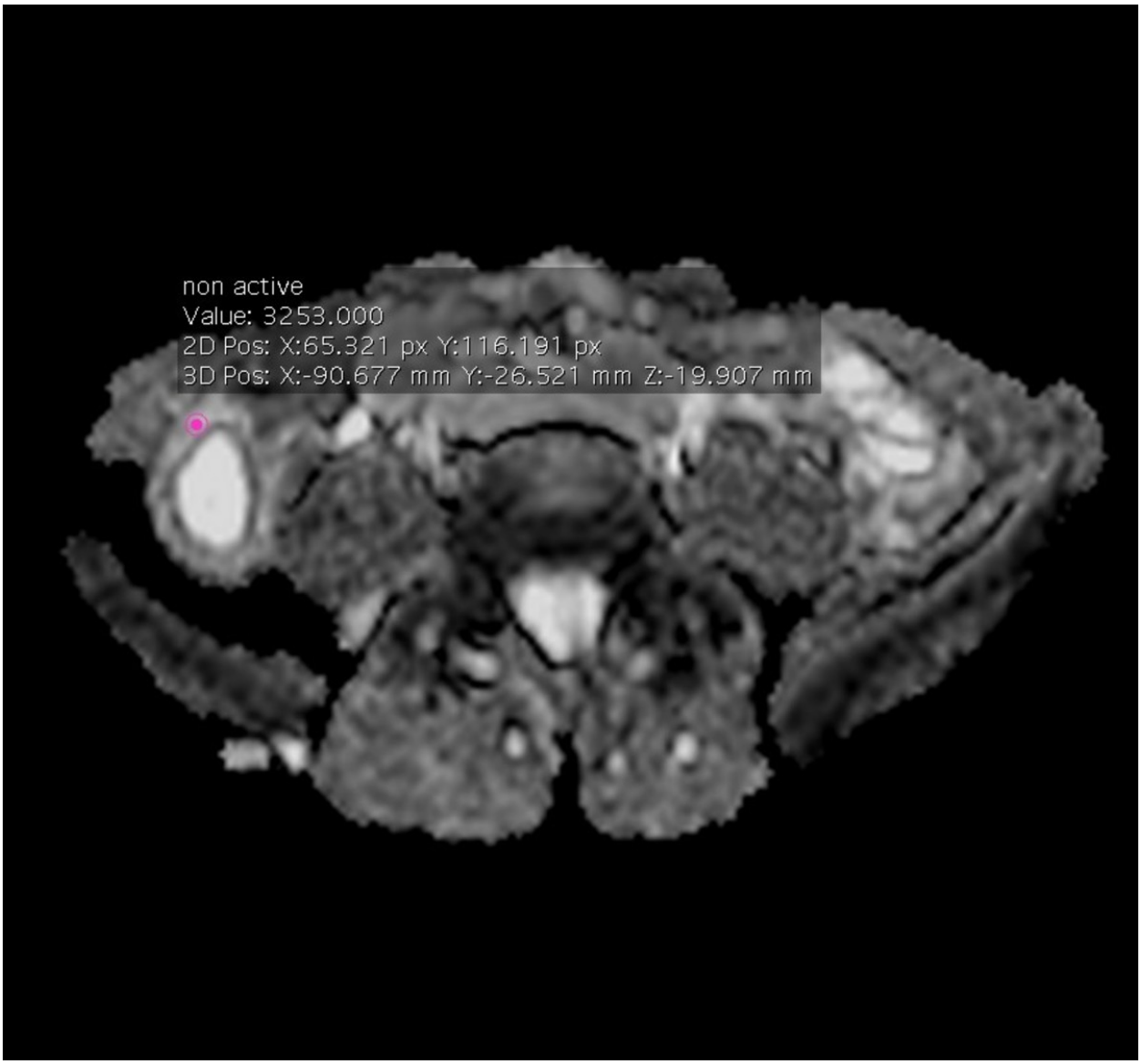

Fig. 4: ROI on a inactive bowel wall (M; 11 y.). Medium ADC value is 3,25 x 10(-3) mm(2)/s

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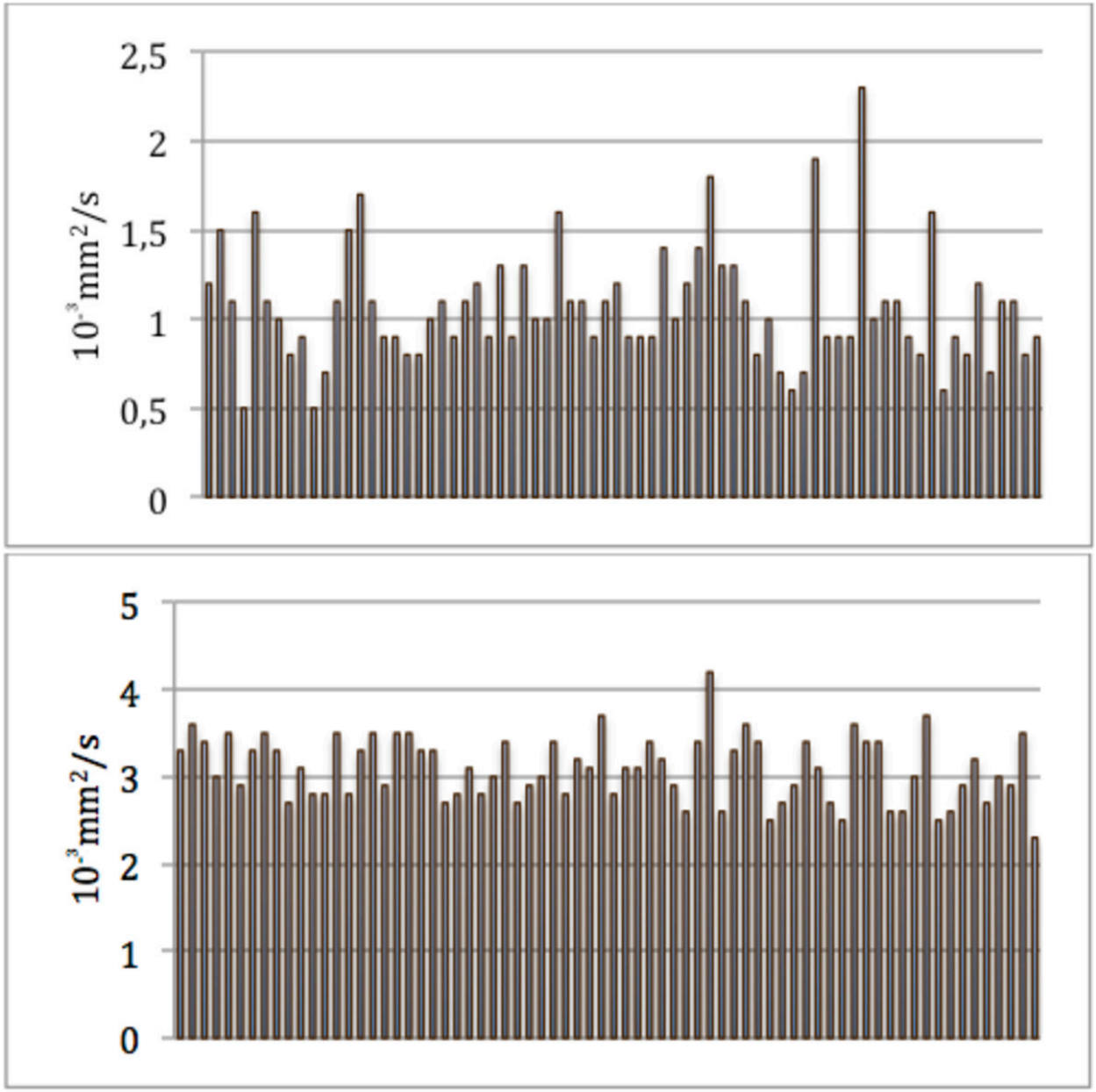

Fig. 5: ADC values in inflamed bowel loops (above) and in inactive bowel loops (below).

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Conclusion

In Crohn's disease, the mean ADC was found significantly higher in bowel segments with active as opposed to inactive Crohn's disease. DWI sequences and ADC maps might be used alongside traditional MRE sequences to facilitate a quantitative analysis of disease activity. Combining DWI with traditional MRE images improves accuracy in determining the extent of disease activity. DWI sequences should always be included in study protocols involving both pediatric and adult patients.

Especially in pediatric cases, or in patients for whom the administration of a contrast medium is contraindicated, the ADC obtained from DWI sequences could serve as an effective alternative to post-contrast study.

DWI can also have a role in the follow-up of patients under pharmacological treatment for the purpose of assessing the activity of the disease at different stages.

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