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REPEATABILITY OF MAGNETIC RESONANCE MEASUREMENTS USED FOR ESTIMATING CROHN'S DISEASE ACTIVITY

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The MR activity indices used for quantification and follow-up of Crohn's disease are composed of a number of subjectively determinable components with equivocal repeatability. The purpose of this article was to assess the repeatability of measurements used for quantitative estimation of Crohn's disease activity in the terminal ileum. In five adults (23–57 y.o.) and 12 children (10–17 y.o.) with active terminal ileitis, the inflamed bowel was divided into 3 cm segments (n = 32 in adults, n = 46 in children), and measurements for the calculation of MaRIA and Clermont scores were performed. Parameters included apparent diffusion coefficients (ADC) for diffusion-weighted imaging (DWI) sequences with selective and non-selective fat suppression, wall signal enhancement before (WSI-preGd) and after (WSI-preGd) gadolinium enhancement, bowel thickness, and presence of ulcers. The measurements were standardised (accurate site-to-site comparison, exact ROI size, where applicable) and repeated by the same researcher after two months. Intra-observer agreement for ADC, WSI-preGd and WSI-postGd, bowel thickness was assessed with a paired t-test, and the significant difference in presence/absence of ulcers was assessed by the Pearson ^{2} test. Absolute difference was not found between the 1st and 2nd measurements of ADC, WSI-preGd, WSI-postGd and wall thickness. There was systematic difference in the presence of bowel ulcers. In standardised conditions the repeatability of ADC, WSI-preGd and WSI-postGd is high. Efforts must be made to precisely define the size and appearance of ulcers that may be included in the index calculation.

Key words: *Terminal ileitis, magnetic resonance enterography, Clermont score, MaRIA, activity indices, intra-observer agreement.*

INTRODUCTION

Crohn's disease (CD) is a chronic relapsing inflammatory bowel disease affecting any part of the gastrointestinal tract, but most commonly, the terminal ileum (Horsthuis *et al*., 2008). The overall goal of CD treatment is to achieve and maintain remission. Therefore, monitoring disease activity is crucial during the course of the disease. Ileocolonoscopy with histopathological sampling is the method of choice in assessment of IBD. However, apart from causing general patient discomfort (Buisson *et al*., 2017), visualisation rendered by endoscopy is limited to the terminal ileum and colon, and only superficial tissues from the luminal side can be viewed and sampled (Van Rheenen *et al*., 2010). Wireless capsule endoscopy allows an advance beyond the reach of a conventional endoscope by visualising intestinal mucosa throughout its entire length in case of a non-stricturing disease (Triester *et al*., 2006). Nevertheless, this modality, like conventional endoscopy, does not allow assessment of bowel wall tissue beyond mucosa. Therefore, cross-sectional imaging is the only solution to assess the bowel wall throughout its entire thickness.

When considering the superior soft-tissue resolution, non-invasiveness and ability to obtain findings within entire bowel wall thickness and around the bowel, and lack of ion-

ising radiation, magnetic resonance enterography (MRE) has been shown to be an informative imaging modality, capable of evaluating disease activity in IBD (Foti *et al*., 2015). Numerous attempts have been made to develop scoring systems for less invasive but informative quantification of disease activity in the intestines. Examples of these scoring systems include: Magnetic Resonance Index of Activity (MaRIA), Clermont score, Crohn's disease MRI index (CDMI), Magnetic Resonance Enterography Global Score (MEGS), Lemann index (Rozendorn *et al*., 2018), as well as London index (Steward *et al.,* 2012). Presently, the MaRIA score is the only validated radiological CD activity index tested in large patient populations (Dohan *et al.,* 2016), which has high and significant correlation with the Chron's Disease Endoscopic Activity Index. The MaRIA score is composed of values of intestinal wall thickness and relative contrast enhancement (RCE), as well as rating of presence of oedema and ulcers in the bowel wall. RCE is calculated from wall signal intensity (WSI) series before (WSI-preGd) and after (WSI-postGd) administration of gadolinium contrast agent (Rimola *et al*., 2009). However, gadolinium administration is related to potentially severe adverse reactions like systemic nephrogenic fibrosis (Broome *et al.,* 2008) and accumulation of gadolinium deposits in the brain (Gulani *et al*., 2017) and other body tissues (Quattrocchi *et al.,* 2017). The Clermont score, an alternative MRI index of activity, has been developed on the basis of diffusion weighted imaging (DWI) by replacing RCE with the apparent diffusion coefficient (ADC), which is a numerical measurement of diffusion restriction and is calculated from DWI images (Hordonneau *et al*., 2014). The Clermont score is, therefore, also called DWI-MaRIA. It is reported to have an excellent correlation with the MaRIA score (Rimola *et al*., 2009) and a moderate correlation with CDEIS (Buisson *et al.,* 2017), but further confirmatory studies are needed to validate the Clermont score.

There is equivocal data available on the repeatability of measurements used for calculation of MaRIA and Clermont scores. No standardised technique of performing measurements and assessment of ulcers is described in most of the available publications, possibly influencing repeatability. The goal of our study was therefore to assess intra-observer agreement on measurements performed for calculation of MaRIA and Clermont scores. Measurements such as ADC-DWI, wall signal intensity (WSI) before (WSI-preGd) and after (WSI-postGd) administration of gadolinium contrast medium contributing in relative contrast enhancement (RCE), were performed to define the proper size of region of interest (ROI) and to provide accurate site-to-site comparison. Intra-observer variability of the wall thickness and detection of presence of ulcers was also analysed.

MATERIALS AND METHODS

This prospective observational cross-sectional study was conducted in accordance with the Declaration of Helsinki. Before inclusion in the study, written informed consent was received from all patients or their legal representatives. Approval (permission number 6/10.09.2015) was obtained from the Ethics Committee of Rīga Stradiņš University.

Table 1. Demographic data of patients included in the study

Data	Adult group	Paediatric group
Gender	Males, n = 4; females, n = 1	Males; n = 9, females; n = 3
Age	23 y.o.; n = 1, 25 y.o.; n = 1, 36 y.o.; n = 1, 40 y.o.; n = 1, 57 y.o.; n = 1	11 y.o.; n = 2, 12 y.o.; n = 3, 13 y.o.; n = 1, 14 y.o.; n= 4, 17 y.o.; n = 2

Patients. The study involved 17 patients (five adults, 23–57 y.o., and 12 children, 10–17 y.o.; see Table 1 for details) with faecal calprotectin levels over 1000 μg/mg and histologically proven active Crohn's non-stricturising and non-penetrating disease in the terminal ileum, and signs of active Crohn's disease in MRE examination. These signs included: 1) small bowel wall thickness > 3 mm, 2) presence of mural oedema — hyperintensity of the bowel wall in T2-weighted images compared to that in the psoas muscle (Rimola *et al.,* 2009), 3) signs of active inflammation in conventional DWI sequence — high SI in DWI tracking images of b = 800 s/mm^2, 4) low signal intensity (SI) in the ADC map, and 5) early mucosal hyperenhancement in the series following administration of gadolinium contrast agent (post-Gd) (Moy *et al.,* 2016). CD located outside the terminal ileum, areas of bowel thickness less than 3 mm, lack of signs of active bowel wall inflammation in DWI, DWIBS and post-Gd T1 series within one and the same segments, and dynamic blurring in either of the DWI or T1 post-Gd images were not accepted for performing measurements.

According to the Montreal and Paris classification of CD (Moon, 2019), the phenotype of 10 patients was A1 L1 B1; the phenotype of the remaining seven patients was A2 L1 B1.

MRI technique. All patients were examined without prior bowel cleansing. Fasting was required six hours prior to MRE procedures. Patients were asked to slowly intake 1.000–1.500 ml of 2.5% peroral mannitol solution 45 minutes prior to the MRI procedure, and then to lie in the right decubitus position, drinking extra 250 ml of 2.5% mannitol solution for another 20 minutes. The MRE examinations were performed with a 1.5T MRI scanner (Ingenia, Philips Medical Systems, Best, the Netherlands) covering the region from the diaphragm to the pelvis with a 16-channel body coil. All patients were scanned in the prone position.

The MRE protocol included:

1) coronal breath-hold balanced turbo field echo (bTFE) cine sequence for real-time assessment of the bowel peristalsis,

2) axial and coronal breath-hold Turbo Spin Echo, T2-weighted sequences without fat suppression (T2 TSE),

3) axial and coronal breath-hold Spectral Attenuated Inversion Recovery T2-weighted sequences with fat suppression (T2 SPAIR),

4) axial respiratory triggered Spectral Presaturation Inversion Recovery (SPIR) based DWI sequence using diffusion factors b fixed at 0, 600 and 800 s/mm^2 with the corresponding ADC map,

5) axial free-breathing Short Tau Inversion Recovery (STIR)-based DWI sequence using diffusion factors b fixed at 0, 600 and 800 s/mm^2 with the corresponding ADC map,

6) coronal respiratory triggered T2 fat suppression magnetic resonance cholangiopancreatography (MRCP) sequence with radial 3D reconstructions,

7) coronal breath-hold dynamic T1-weighted High-Resolution Isotropic Volume (THRIVE), where scanning was started simultaneously with intravenous administration of gadolinium contrast media. Gadodiamide (Omniscan) 0.05 mmol/ml, GE Healthcare, dosage 0.2 ml/kg, or 0.1 mmol/kg was used in patients before October 2018, except in two children examined after October 2018, who received gadobutrol (Gadovist) 1 mmol/ml, Bayer, dosage 0.1 ml/kg, or 0.1 mmol/kg.

To stop intestinal peristalsis, hyoscine butylbromide (Buscopan, Sanofi) was administered in slow intravenous injection prior to SPIR-DWI and STIR-based DWI sequences as well as the dynamic contrast sequences. A dosage of 10 mg was used in patients under 50 kg, increased to 20 mg in patients of 50 kg or above, and the dose was diluted in 20 ml of saline solution.

MRI image analysis. The measurements were performed by one radiologist with 19 years of experience in gastrointestinal MRI imaging, and repeated by the same radiologist after two months.

The measurement approach was standardised. Prior to measurements, the whole parts of the inflamed terminal ileum were divided into approximately 3 cm long segments (n = 32 in adult patients, n = 46 in children), and the below process was performed when taking measurements in each of the segments: 1) one measurement of bowel wall thickness was performed in the location of the largest thickness; 2) presence/absence of ulcers was defined (1 – yes, 0 – no); 3) three measurements of ADC of the SPIR-based DWI (Fig. 1a), and ADC of the STIR-based DWI (Fig. 2a) were performed at the site of the maximum signal intensity (SI) within the inflamed bowel wall. The ADC value along with the chosen region of interest (ROI) was automatically propagated on the corresponding ADC map (Figure 1b for STIR- based DWI and 2.b for STIR-based DWI); 4) three measurements of wall signal intensity (WSI) were taken before (WSI-preGD) and after (WSI-postGd) administration of gadolinium contrast medium in exactly the same locations of the highest SI in the bowel wall in both DWI sequences, 5) three measurements of the image noise — standard deviation (SD) were performed outside the patient's body before (SD-preGd) and after (SD-postGd) administration of the contrast medium (Rimola *et al.*, 2009). The ADC, WSI and SD measurements were performed using the

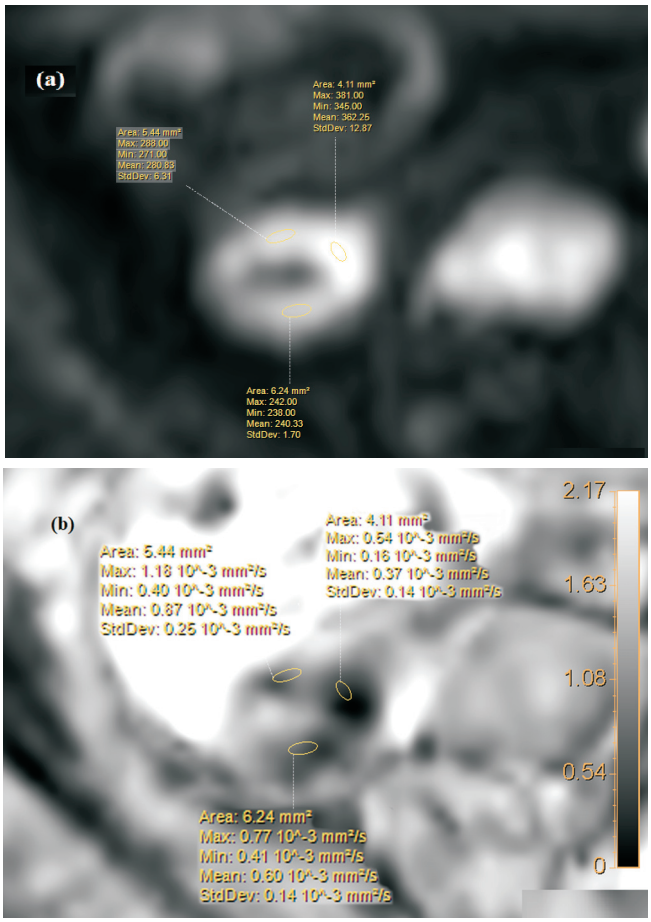

Fig. 1. Selecting the ROI in SPIR-based DWI images (b = 800 s/mm2) of 56 y.o. female (a). On the corresponding ADC map (b), the chosen ROI appears automatically.

4–9 mm^2 oval region of interest (ROI). The average values of the three measurements of ADC, WSI and SD were used for further calculations.

In each inflamed segment, the segmental MaRIA score was calculated per equation:

1.5 × bowel thickness(mm) + 0.02 × RCE + 5 × oedema + 10 × ulceration.

The presence of ulcers was rated as 1 and absence of ulcers – as 0. RCE was calculated as: RCE = (WSI-postGd – WSI-preGd)/(WSI-preGd)) × 100 × (SD-preGd/SD-postGd), where the SD-preGd and SD-postGd corresponded to the mean of the three SD values of the SI. This was measured outside of the body before and after administration of gadolinium contrast medium, accordingly (Rimola *et al.*, 2009). Since oedema was a criterion of inclusion in the study, it was present in all patients and was always equal to 1.

The Clermont score, or DWI-MaRIA, for both SPIR- and STIR-based DWI sequences, was calculated as:

DWI-MaRIA = 1.646 × bowel thickness - 1.321 × ADC + 5.613 × oedema + 8.306 × ulceration + 5.039 (Hordonneau *et al.*, 2014).

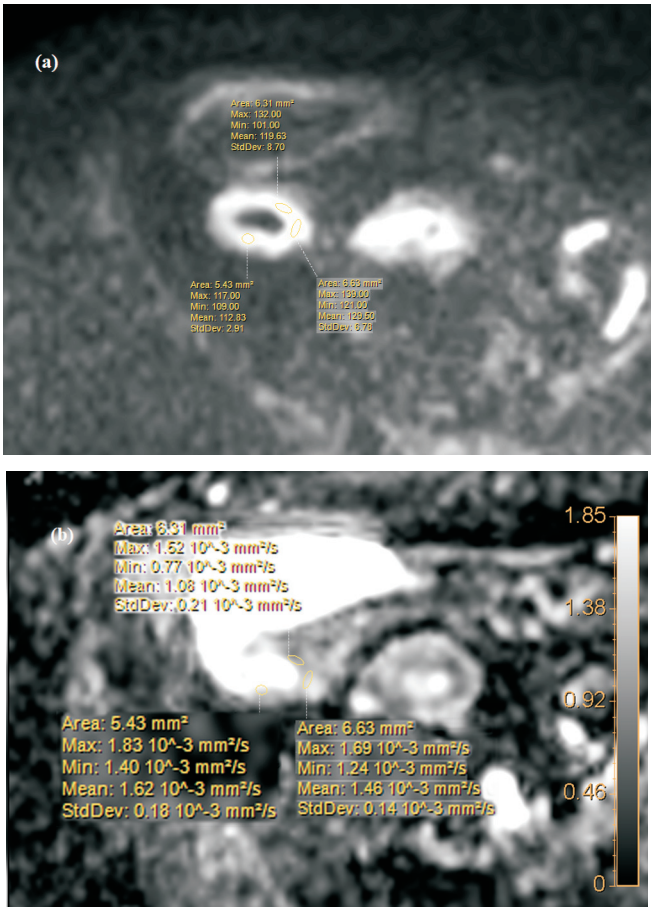

Fig. 2. Selecting the ROI in STIR-based DWI images of 56 y.o. female (b = 800 s/mm2) (a). On the corresponding ADC map (b), the chosen ROI appears automatically.

Similar to the calculation of the MaRIA score, presence of ulcers was rated as 1, absence of ulcers as 0, and presence of oedema was rated as 1.

The assessment of images and measurements of ADC values was performed using a dedicated post-processing server Philips Intellispace Portal 5.0 (Philips Medical Systems, Best, The Netherlands). WSI and image noise measurements were performed using a Clear Canvas DICOM Viewer, v. 13.2 (Synaptive Medical, Toronto, Canada, 2019).

Statistical analysis. Statistical analysis was performed using software Stata/IC (StataCorp LLC, Texas, USA). The mean values and standard deviations were calculated for SPIR- and STIR-based ADC, as well as RCE, MaRIA and Clermont scores. The mean values of the first and second measurement were compared, and statistical significance of the differences was tested using a paired t-test; 95% confidence intervals (CI) were calculated for differences. The statistical significance of differences was determined using one-way ANOVA with Bonferroni correction. A p value of < 0.05 was considered as statistically significant. Differences in the presence/absence of ulcers was evaluated with the Pearson's χ^2 test.

RESULTS

No statistically significant difference was observed between the two measurements performed by a single observer neither in the measurement of the bowel wall thickness (p = 0.42), nor in the assessment of ADC values of SPIR-based DWI (p = 0.65) and ADC values of STIR-based DWI (p = 0.23). There was also no statistically significant difference between the two measurements performed by a single observer in assessment of WSI-preGd (p = 0.06) or WSI post-Gd (p = 0.57). The highest absolute difference between two measurements was observed for WSI-preGd measurements (8%), and the lowest absolute difference for SPIR-based ADC measurements (1%). The results of measurements, along with absolute differences between the two measurements, are presented in the Table 2.

For the assessment of presence of bowel ulcers between the 1st and the 2nd assessment, the Pearson χ^2 was 13.70 ($p <$ 0.0005), indicating a systemic difference between the two assessments for presence of ulcers. The results of the assessment of presence/absence of ulcers are presented in Table 3.

DISCUSSION

The therapeutic endpoint of CD treatment is to achieve and maintain remission. Therefore, assessment of disease activity is crucial for guiding therapeutic decisions in treatment of patients with CD. Apart from the resolution of symptoms as the primary target (Shi *et al.*, 2018), different grades of activity such as clinical, biochemical and histopathological activity, are considered. The concept of mucosal healing has been under discussion for decades (Rogler *et al.*, 2013) being associated with lower demand for steroids, reduced admissions to hospital, and reduced need for surgical treatment in case of complicated CD (D'Haens *et al.*, 2008).

Table 2. Numerical values of the 1st and 2nd measurements of the bowel wall thickness SPIR- and STIR-based ADC, WSI-preGd, and WSI-postGd

Measurement	First assessment (mean)	Second assessment (mean)	Difference	
			Difference (%)	p
Wall thickness (mm)	6.4	6.6	0.2 (5%)	0.42
ADC of SPIR-based DWI (mm^2/s)	1.219 (SD 0.320)	1.227 (SD 0.321)	0.008 (1%)	0.65
ADC of STIR-based (mm^2/s)	1.180 (SD 0.505)	1.132 (SD 0.478)	0.048 (4%)	0.23
WSI-preGd	162.925 (SD 127.57)	150.305 (SD 99.68)	12.61 (8%)	0.06
WSI-post Gd	336.39 (SD 235.35)	316.11 (SD 212.90)	20.33 (6%)	0.57

ADC, apparent diffusion coefficients; WSI, wall signal intensity

Table 3. Evaluation of 1st and 2nd measurements of the presence/absence of ulcers

Evaluation	Ulceration	No. of segments	%	Pearson χ^2	*p*-value
First	Absence	43	55.13	13.70	< 0.0005
	Presence	35	44.87		
Second	Absence	26	33.33		
	Presence	52	66.67		

Mucosal healing has been accepted as an optimal therapeutic target in clinical practice for many years; however, in patients with sustained mucosal healing, transmural inflammation may persist (Nardone *et al*., 2019). Transmural healing is associated with better long-term outcomes than mucosal healing, therefore transmural healing has recently been proposed as a new target for CD treatment (Castiglione *et al*., 2019). Since endoscopy does not provide transmural evaluation even in the accessible regions of the gastrointestinal tract, cross-sectional imaging studies (MR) have become the mainstay of intestinal wall evaluation (Buisson *et al*., 2019). Both mucosal and transmural healing can be assessed with MRI (Panes *et al*., 2013; Maaser *et al*., 2019), and according to the newest joint guidelines by European Crohn's and Colitis Organisation (ECCO) and the European Society of Gastrointestinal and Abdominal Radiologists (ESGAR), MRI can be used as alternative for assessment of disease activity (Maaser *et al*., 2019).

Calculations of MaRIA and Clermont indices include several variables that are common to both indices, such as the presence of ulcers and bowel wall oedema, and the thickness of the gut wall. In the Clermont index, also called as DWI-MaRIA, gadolinium contrast medium administration is replaced by DWI (Rimola *et al*., 2009; Hordonneau *et al*., 2014). Since 2009, this has been proven to be effective for assessment of bowel inflammation. It has potential benefits in the assessment of disease activity (Dohan *et al*., 2016) and is used to replace contrast medium (Neubauer *et al.,* 2013). DWI reflects both anatomical and functional information, providing data on diffusion restriction in the intestinal wall that characterises an active inflammation (Dohan *et al*., 2016), and is proven to be capable of detecting lesions before their appearance in conventional images (Baliyan *et al*., 2016). The DWI technique is however very sophisticated, since it requires ideal magnetic field homogeneity, very strong gradients and infinitively fast acquisition that is not achievable with existing MRI machines. The quality of DWI images is therefore lesser than that of conventional MR images, due to low resolution, noise, distortions, and limited morphological interpretability (Chilla *et al*., 2015); therefore, DWI provides functional rather than anatomical information. Opinions on reproducibility of ADC-DWI measurements used in the Clermont score varies among authors, and despite good to excellent repeatability reported from certain authors (Yu *et al*., 2019), contrary concerns on low reproducibility based on research data also exist (Watson *et al*., 2018). Due to equivocal data on repeatability of measurements the form the MaRIA and Clermont score, our interest was to assess the repeatability of measurements contributing to both of these indices — WSI-preGd and WSI-postGD forming RCE in MaRIA, ADC-DWI used in the Clermont score, as well as bowel thickness and estimation of presence of bowel ulcers, which are common to both MaRIA and Clermont scores.

There are numerous DWI techniques, all of which are based on fat suppression, which is necessary for artefact reduction (Takahara *et al*., 2004). These techniques can be classified into fat, or spectral, selective and non-selective ones, based on different behaviour among lipid protons and hydrogen protons from water during MR imaging. In selective fat suppression, protons of proper resonance frequency of fat are suppressed, whereas in non-selective fat suppression the difference in T1 between protons in water and fat tissue is used to suppress the fat signal with inversion-recovery technique (Delfaut *et al*., 1999). In our institution, apart from selective SPIR-based DWI, a non-selective STIR-based fat suppression technique was evaluated in the study due to better image quality (Ouyang *et al*., 2014), i.e. visually sharper images and more clearly differentiated contours of structures (Fig. 3), and superiority of ADC measurements over DWI with selective fat suppression in assessment of other tissues, such as breast lesions (Stadlbauer *et al*., 2009). This technique could theoretically improve the accuracy of the assessment of disease activity in the intestinal wall. In our study, intra-observer reproducibility of both SPIR- and

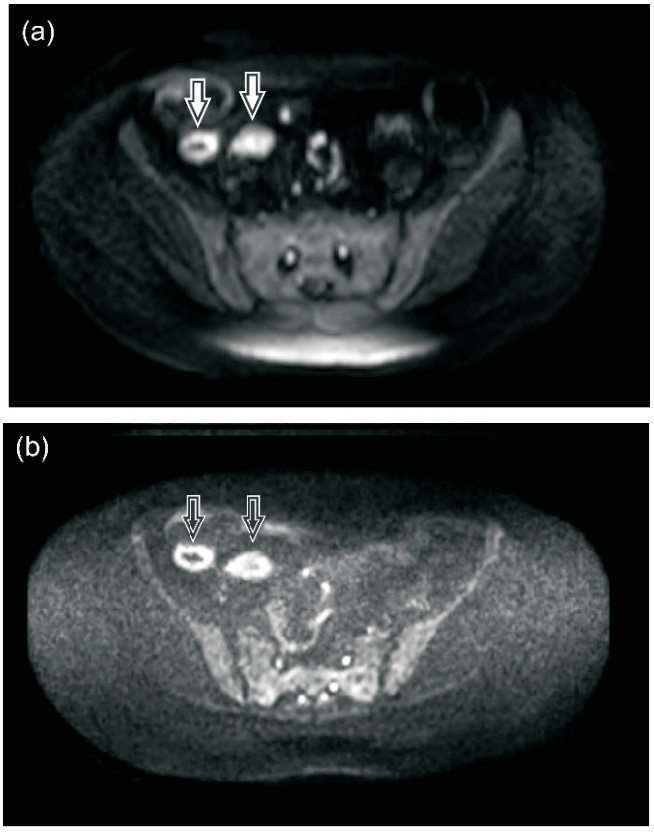

Fig. 3. DWI (a) and DWIBS (b) images of high diffusion gradient b value = 800 mm^2/s in a 56-year-old female patient with active Crohn's disease. Inflamed bowel walls present high signal intensity. The resolution of inflamed bowel and delineation of contours is better in the STIR-based DWI image (black arrows) than in the DWI image (white arrows).

STIR-based DWI techniques was good, since no statistically significant difference was found between mean values in both ADC of SPIR-based DWI (p = 0.65), as well as ADC of STIR-based DWI (p = 0.23), and difference between mean values of ADC was only 1% in SPIR-based DWI and 4% in STIR-based DWI (Table 1). However, unlike breast tissue, ADC measurements of STIR-based DWI quantitative may not be of practical importance in assessment of bowel walls, due to non-selectivity of fat suppression; not only signals from fat, but other media of short T1 time, such as proteinaceous, viscous and mucous substances, methaemoglobin products (Grande *et al*., 2014), as well as chime and faeces (Kwee *et al*., 2008) are suppressed. Since DWI has a strong partial volume effect (Scherrer *et al*., 2011), the measured ADC values in STIR-based images could be artificially lower in the presence of these substances (Apine *et al.*, 2019).

Several authors found poor repeatability of RCE measurements (Sharman *et al*., 2009; Tielbeek *et al*., 2013). We found no statistically significant difference in WSI-preGd (p = 0.06), or in WSI post-Gd (p = 0.57) values used in calculating of RCE. We believe that a strict definition of ROI size and accurate site-by-site WSI-preGd and post-Gd measurement in one and the same bowel segment, would result in good inter-observer agreement. It has however to be noted that our results show high standard deviations in both WSI-preGD (SD 127.57 for the 1st assessment and SD 99.68 for the 2nd assessment) and WSI-post-Gd measurements (SD 235.35 for the 1st assessment and SD 212.9 for the 2nd assessment) covering 66–78% of the WSI values. Our observations suggest that, if WSI-preGd values were in the tens, the WSI-post Gd values would also be in the tens; if WSI-preGd values were in the hundreds, this would also be replicated in the WSI-post Gd values. We explain this observation through individual tissue characteristics of patients, magnetic field inhomogeneity and linearity of gradients yielding wide distribution of WSI values. Detailed analysis of this finding, however, is beyond the scope of our current research.

Tielbeek *et al.* (2013) reported moderate repeatability of bowel thickness measurements and excellent repeatability when the thickness measurements were performed by an experienced radiologist. In our study, no statistically significant difference was found between the 1st and the 2nd measurements. It should, however, be noted that wall thickness differed within one and the same bowel segment, and the maximum thickness was always chosen for the calculations. However, identifying the same exact location of the maximum thickness often was not possible in DWI images due to their low spatial resolution. Similarly, in the pre- and post-contrast series, bowel thickness was always measured in the axial images but pre- and post-T1 images were acquired in the coronal plane.

In our study, there was a systematic difference in the assessment of ulcers. The inconsistency of ulcer detection in our study could be associated with lack of strict consensus regarding standardised MR definition of an ulcer. Developers of the MaRIA index defined ulcers as deep depressions in the mucosal surface (Rimola *et al*., 2009). However, MRI reveals a wide range of ulcers. Even small aphthous ulcers can be seen in MRI images (Ram *et al*., 2016), and there is no clear definition of the size and appearance of ulcers that should be included in calculation of disease activity indices or excluded from it. Intra-observer agreement of the ulcer rating could be improved with a 3T MR scanner, as this provides better spatial and temporal resolution, and literature data indicates that the resolution of 3T MR in ulcer diagnosis is superior compared to that of the 1.5T device (Fiorino *et al*., 2013).

Due to lack of data, histopathological findings were not used as the reference standard in our study. The patients were enrolled in the study only by visual MRE signs of Crohn's disease, i.e. thickened, oedematous bowel wall and significantly increased SI in the DWI images with diffusion gradient value of b = 800 s/mm^2, and low SI on the ADC map. However, the aim of our study was not to investigate the relationship of visual findings with histological findings, but rather whether repeated measurements, based on certain defined MRE criteria for the evaluation of Crohn's disease activity, produced comparable results. Literature provides a broad picture of the correlation not only between MRE and endoscopic findings, but also between MRE and surgical specimens of resected intestinal segments, with certain defined criteria, along with conclusion that MRI is an informative and sufficiently accurate method to assess altered bowel wall. Based on these observations, for several years now when referring patients for MRE examinations, clinicians do not duplicate its results with invasive endoscopy, which is cumbersome for patients. Consequently, in 2019, for the first time, the ECCO-ESGAR guidelines (Maaser *et al*., 2019) came up with a revolutionary statement that radiological cross-sectional imaging methods, including MR, can be used as an alternative to endoscopy to assess Crohn's disease activity. Therefore, although all patients in our study had endoscopically confirmed Crohn's disease, the results of the MRE examination were not duplicated by the endoscopic findings in any cases. Consequently, the correlation of the MR activity indices with the histopathological and endoscopic activity indices was not possible. It should also be noted that the correlation of the MR findings with the endoscopic image is still relative. The endoscopical and histopathological findings, including endoscopically obtained tissue specimens, reflect changes in the intestinal mucosa, whereas the MR activity indices include not only mucosal but also transmural components. Both literature data and the experience from our hospital indicate situations when intact intestinal mucosa is observed endoscopically in active Crohn's disease. The correlation of histopathological-radiological findings could be most accurately reflected in the resection specimen after bowel surgery. Resection of the altered intestinal segment was performed only in one of the patients enrolled in our study.

There may be a methodological error in using correlation between MaRIA and Clermont score, since these indices

mostly contain the same components, except that RCE is used in MaRIA and ADC value in Clermont score, leading to overestimation of actual correlation. However, the goal of this study was to assess the repeatability of all necessary measurements without analysing the shortcomings of methodology of assessment of their correlation. A wider discussion on the application of the correlation coefficient, with references to literature sources, will be discussed in another publication currently awaiting approval.

In our opinion, the strengths of our study were: 1) the prospective study design, 2) exact site-by-site comparison in the same bowel segment, and 3) exact ROI size that was not defined in studies on MaRIA and Clermont scores. The limitations of our research were as follows: 1) the relatively low number of participants in the study groups, 2) the study group included both adults and paediatric patients causing lack of homogeneity regarding the length of the disease or treatment status. However, a mixed data poll of adult and paediatric patients was chosen because the methodology of all measurements (bowel wall thickness, WSI-preGd, WSI-postGd, ADC of SPIR-based DWI, ADC of STIR-based DWI and estimation of ulcers) was identical for both adults and children. Therefore, the estimations of intra- observer agreement were not influenced by the age of patients. Unlike adults, estimation of disease activity in children does not rely on endoscopy findings due to its invasiveness, but rather on the Paediatric Crohn's Disease Activity Index (PCDAI) (Rozendorn *et al*., 2018). In children, the utility of MaRIA and Clermont score is still unclear, and accordingly, the relationship of RCE and DWI-based ADC with actual Crohn's disease activity is unclear.

CONCLUSIONS

The reproducibility of ADC-DWI, WSI-preGd and WSI-post Gd measurements used in calculation of MRE-based indices for quantification of Crohn's disease inflammation is high when standardised conditions, such as proper ROI size and exact site-to site comparison are clearly defined and observed. Effort still needs to be made in defining the size and appearance of ulcers that should either be included in the calculation of Crohn's disease activity indexes, or excluded from it.

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KRONA SLIMĪBAS AKTIVITĀTES IZVĒRTĒŠANĀ IZMANTOTO MAGNĒTISKĀS REZONANSES MĒRĪJUMU ATKĀRTOJAMĪBA

Pētījuma mērķis bija izvērtēt ileum distālajā cilpā lokalizētas Kroina slimības aktivitātes noteikšanas parametru atkārtojamību. Pētījumā tika iekļauti 5 pieaugušie (23-57 g.v.) un 12 bērni (11-17 g.v.) ar aktīvu terminālo ileītu. Iekaisuma skartā zarnas siena tika sadalīta 3 cm garos segmentos (n = 32 pieaugušiem, n=46 bērniem), un veikti MaRIA indeksa un Klērmontas indeksa aprēķināšanai nepieciešamie mērījumi: acīmredzamās difūzijas koeficienti (ADC) difūzijas uzsvērto attēlu (DWI) sekvencēs ar selektīvu un neselektīvu tauku nospiešanu, zarnas sieniņu signāla intensitāte (WSI - *Wall Signal intensity*) pirms (WSI-preGd) un pēc (WSI-post-Gd) i/v gadolīnijas kontrastvielas ievades, zarnu sieniņas biezums, kā arī noteikta čūlu klātbūtne. Mērījumus, veicot precīzu segmentu salīdzināšanu noteiktās lokalizācijās un definējot noteiktu izpētes apgabala (ROI - *Region of Interest*) lielumu, standartizēja un pēc 2 mēnešiem atkārtoja viens un tas pats radiologs. ADC, WSI-preGd un WSI-postGd, zarnu sieniņu biezuma, mērījumu atkārtojamība viena novērotāja robežās tika izvērtēta ar pāru t-testu. Čūlu klātbūtnes vērtējuma atkārtojamība tika izvērtēta ar Pearson χ^2 testu. Starp 1. un 2. mērījumu netika konstatēta statistiski ticama ADC, WSI-preGd, WSI-postGd un sienas biezuma mērījumu atšķirība. Konstatēta statistiski nozīmīga atšķirība čūlu klātbūtnes izvērtēšanā. Standartizētos apstākļos ADC, WSI-preGd un WSI-postGd atkārtojamība ir augsta. Nepieciešami tālāki pētījumi, lai noteiktu kritērijus čūlu lieluma un izskata definējumam.