

Diagnostic accuracy of three different MRI protocols in patients with inflammatory bowel disease

Kayalvily Jesuratnam-Nielsen^{1,2}, Vibeke Berg Løgager¹, Pia Munkholm^{2,3} and Henrik S Thomsen^{1,2}

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Abstract

Background: Magnetic resonance imaging (MRI) is used for workup and control of inflammatory bowel disease (IBD); however, disagreement remains as to how the MRI should be performed.

Purpose: To compare prospectively the diagnostic accuracy of MRI with neither oral nor intravenous contrast medium (plain MRI), magnetic resonance follow-through (MRFT) and MR enteroclysis (MRE) using MRE as the reference standard in patients with inflammatory bowel disease.

Material and Methods: Plain MRI and MRE were carried out in addition to MRFT. All patients underwent both plain MR and MRFT on the same day and MRE within seven days. For the evaluation, the bowel was divided into nine segments. One radiologist, blinded to clinical findings, evaluated bowel wall thickness, diffusion weighted imaging (DWI), mural hyperenhancement, and other inflammatory changes in each bowel segment.

Results: Twenty patients (6 men, 14 women; median age, 43.5 years; age range, 26–76 years) underwent all three examinations; 10 with Crohn's disease (CD), three with ulcerative colitis (UC), and seven with IBD unclassified (IBD-U). Sensitivity, specificity, and accuracy were in the range of 0–75%, 81–96%, and 75–95% for wall thickening, and 0–37%, 59–89%, and 50–86% for DWI in plain MRI, respectively. Sensitivity, specificity, and accuracy were in the range of 0–50%, 96–100%, and 90–100% for wall thickening, 0–50%, 84–97%, and 82–95% for DWI, and 0–71%, 94–100%, and 85–100% for mural hyperenhancement in MRFT, respectively.

Conclusion: The use of oral and intravenous contrast agent improves detection of bowel lesions resulting in MRFT remaining the superior choice over plain MRI for diagnostic workup in patients with IBD.

Keywords

Crohn's disease, inflammatory bowel disease, magnetic resonance enteroclysis (MRE), magnetic resonance follow-through (MRFT), magnetic resonance imaging (MRI), ulcerative colitis

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Introduction

Endoscopy and small-bowel follow-through examination (SBFT) or barium enteroclysis (BE) have been first choice examinations for many years in patients with inflammatory bowel disease (IBD). Both methods lack the capability of visualizing the transmural or extramural extent of disease. SBFT and enteroclysis have high accuracy for mucosal abnormality and are widely available. However, radiation exposure is a major limitation of nasojejunal tube (NJT) in enteroclysis and it is often regarded as painful by patients (1). Due to these drawbacks, the use of cross-sectional imaging techniques has increased rapidly.

Three cross-sectional imaging modalities are available: ultrasonography (US), computed tomography

¹Department of Diagnostic Radiology, Copenhagen University Hospital Herlev, Herlev, Denmark

²Faculty of Medical and Health Sciences, University of Copenhagen, Copenhagen, Denmark

³DEEP – Danish Centre for eHealth & Epidemiology, North Zealand Hospital, University of Copenhagen, Denmark

Corresponding author:

Kayalvily Jesuratnam-Nielsen, Department of Diagnostic Radiology, Copenhagen University Hospital Herlev, Herlev Ringvej 75, 2730 Herlev, Denmark.

Email: Kayalvily.nielsen@gmail.com



(CT), and magnetic resonance imaging (MRI). The disadvantage of US is that it is highly operator-dependent and sometimes unable to assess certain anatomical regions and for the CT the exposure to radiation (2,3). Since the 1990s, the use of MRI in diagnosis and control of IBD has been recommended (4).

MRI has the major advantage of being able to visualize luminal, mural, and extramural abnormalities. Advantages of MRI include the lack of ionizing radiation, the ability to provide real-time and functional imaging, and the use of small amounts of intravenous contrast media. Limitations of MRI are its high cost, longer examination times, lower spatial resolution, and variable image quality.

The European Crohn's and Colitis Organisation (ECCO) guidelines and International Organization for the Study of Inflammatory Bowel Diseases recommend MR or CT enterography/enteroclysis as the imaging technique to diagnose and to evaluate mucosal healing in Crohn's disease (CD) (5). MRI can be performed in several ways; plain MRI (neither oral nor intravenous contrast), MRI follow-through (MRFT) and MR enteroclysis (MRE). To the best of our knowledge, these three protocols have never been compared. Therefore, we undertook the present prospective study in order to compare the diagnostic accuracy of plain MRI, MRFT, and MRE, using MRE as the reference standard in patients with IBD. This study is an extension of a study published previously by the same group (6).

Material and Methods

The local ethics committee for medical research of the Capital Region (study number H-2-2010-149), the Danish Data Protection Agency (ID-number: 2007-58-0015/HEH.750.8-14) and Clinical Trials (ID: NCT02255019) approved this study. Written informed consent was obtained from all patients.

Study population

The study included all patients diagnosed with CD, ulcerous colitis (UC), and inflammatory bowel disease unclassified (IBD-U) referred to MRI. Patients who did not met all criteria for either CD or UC but still had symptom and required IBD treatment were classified as IBD-U (7). Exclusion criteria were: age younger than 18 years; previous moderate or serious reactions to gadolinium-based contrast medium; pregnancy; ferromagnetic implants; estimated glomerular filtration rate <30 mL/min 1.73 m²; or known cancer.

All patients were scheduled to undergo three MRI examinations: plain MRI, MRFT, and MRE. Plain MRI and MRFT were done on the same day within a 2 h interval. MRE was done within 7 days of the first two examinations. All three examinations were done in a 1.5T scanner (Achieva Philips Healthcare, Best, The Netherlands) equipped with a torso 16-channel phased array coil. The sequences performed in the MRI examinations are listed in Table 1.

Table 1. MRFT parameters.

Parameter	SSH T2	SSH fat.sat.	T2 TSE (BH)	DWI	T1 TSE	GRE 3D	GRE 3D fat. sat.
Imaging plans	Coronal	Coronal	Axial	Axial	Coronal	Coronal	Coronal
TR/TE (ms)	725/100	726/100	399/80	11254/77	539/7	4.4/2.1	4.4/2.1
Flip angle (°)	90	90	90	90	90	10	90
FOV (mm)	450 × 450	450 × 450	375 × 296	300 × 300	400 × 400	400 × 400	450 × 481
Selection thickness (mm)	7	7	5	5	5	2	5
Max. slices per breath-hold	25	25	35	Free-breathing	15	25	10
Bandwidth (Hz)	432.9	432.9	704	11	218.3	378.1	218.3
Weighting	T2	T2	T2	–	T1	T1	T1
Matrix	308 × 185	308 × 185	268 × 182	148 × 117	368 × 291	228 × 243	368 × 291
NSA	1	1	1	2	1	2	1
Sense factor	No	No	1	No	1	1	1
B-value s/mm ²				0, 100, 200, 500, 700, 800, 1000			
Protocol	All three	All three	All three	All three	All three	MRFT and MRE	MRFT and MRE
Intravenous contrast						+	+

BH, breath-hold; DWI, diffusion-weighted imaging; FOV, field of view; GRE, gradient echo sequences; MRFT, magnetic resonance follow-through; NSA, number of signal averages; Sat, saturation; SSH, single-shot spin echo; TE, time to echo; TR, time to repeat; TSE, turbo spin echo.

Plain MRI protocol

Plain MRI was the first examination performed. Patients were instructed to fast for 4 h prior to the MRI. No bowel cleansing was done. The imaging was done with the patient in the prone position and only in supine position if the prone position was impossible for any reason. All patients were scanned from diaphragm to perineum. Scopolaminbutylbromide 20 mg (Buscopan®, Boehringer Ingelheim, Ingelheim am Rhein, Germany) was administered intravenously to reduce motion artifacts from peristalsis during the procedure.

MRFT and MRE protocols

MRFT and MRE were performed using the same protocol, except for the administration of the contrast agent. In MRFT, the contrast agent was ingested orally and in MRE, injected through a NJT. The NJT was placed under fluoroscopic guidance. MRE was used as the reference standard for evaluation of IBD extension and severity. The patients were instructed to drink 1.350 mL of a barium sulphate suspension (VoLumen®; Bracco Diagnostics, Milan, Italy) within 45–60 min in MRFT and the same amount was given through NJT in MRE.

Scopolaminbutylbromide 20 mg was used twice in both protocols and was administered right before the imaging procedure started and again when 0.1 mmol/kg of gadoterate (gadoterate meglumine; Dotarem®, Guerbet, Roissy, France) was given; maximum was 20 mL. The average duration of the MRI exam was approximately 30 min. All images were transferred to our Picture Archiving and Communication System (iSite, Philips Healthcare).

Image analysis

An experienced radiologist with 16 years of MR experience evaluated the bowel from jejunum to rectum. The examinations were randomized and the radiologist was blinded to all clinical information. The small bowel was divided into jejunum and ileum, while the terminal ileum was considered alone. The colon was divided into six segments; cecum, ascending colon, transverse colon, descending colon, sigmoid colon, and rectum. The terminal ileum was defined as 20 cm of the distal end of the ileum nearest to the ileo-cecal valve. For all evaluations, a standardized data sheet was used to record inflammatory changes in each bowel segment. The statistical calculations were performed for the parameters considered the most important for active inflammation (bowel wall thickening, DWI, and hyperenhancement).

Three and 6 mm wall thicknesses were considered to be normal in the small bowel and colon, respectively.

Restricted diffusion was defined as a high signal intensity in DWI in 1000 b-value images combined with low signal intensity in apparent diffusion coefficient (ADC) images. Mural hyperenhancement is a segmental hyperattenuation of a distended bowel loop when compared to adjacent normal loops.

Statistical analysis

The sensitivity, specificity, accuracy, positive predictive values (PPV), and negative predictive values (NPV) for plain MRI and MRFT were calculated compared to the reference standard, MRE. Descriptive statistics were applied. The statistical analyses were performed using the software package “R” (8).

Results

Patients

A total of 115 patients were enrolled from June 2011 to October 2012. Prior to the first examination, seven patients withdrew for various reasons. Another 88 patients did not undergo all three MRI examinations. Of these, 74 refused to undergo MRE due to the discomfort of the NJT, while 14 had other reasons not to participate in MRE. Thus, only 20 patients completed all three MRI examinations. The study included six men and 14 women with a median age of 43.5 years (age range, 26–76 years). Eleven had CD, four had UC, and five had IBD-U. Sixty MRI examinations were performed; 57 in prone position and three in supine position, the latter consisting of a complete set of MRI exams for a single patient with stoma. Two of the patients had hemi-colectomy and one had an ileostomy. In total, 170 segments were evaluated in each MRI protocol.

Wall thickening in MRI

Eight of 170 (5%) segments had bowel wall thickening in the reference standard, MRE. Plain MRI identified five (63%) of the eight segments and MRFT identified three (38%). However, plain MRI had 13 false positive findings, while MRFT only had four. On average, the patients ingested 1115 mL of contrast in MRFT and 1148 mL was administered in MRE.

DWI in MRI

Overall, 12 of 170 (7%), segments in MRE had restricted diffusion. Plain MRI found three (25%) of the 12 lesions whereas MRFT found five (42%). Plain MRI failed to find nine of the lesions and MRFT seven.

Hyperenhancement in MRI

Mural hyperenhancement was seen in 10 segments in the reference standard and MRFT identified six of them. Hyperenhancement in the colon had high sensitivity, specificity, and accuracy compared to the terminal ileum. The low sensitivity in terminal ileum also reflects the low number of segments ($n=20$) compared (Fig. 1). For the small bowel, no true positive findings were recorded, resulting in 0% sensitivity, 100% specificity, and 100% accuracy.

Hyperenhancement was not scored in plain MRI, as the protocol did not include contrast medium administration.

Discussion

The aim of this study was to compare prospectively the diagnostic accuracy of plain MRI and MRFT with MRE in patients with inflammatory bowel disease. However, it was a challenge to recruit patients to this study as 74 patients refused to undergo MRE due to the discomfort of the NJT. Our study finds that the use of both oral and intravenous contrast significantly improves the detection of bowel lesions.

Our department routinely performs MRFT. The MRE was incorporated in this study to function as an MRI reference standard. When patients were offered MRE to obtain more precise results, they declined. It is known from other studies that patients' participation in a clinical trial can be low for a variety of reasons (9,10). Research and their own health issues may overwhelm patients. Women, older patients, and low income patients often decline participation in research trials (9,11). In the current study four patients were aged older than 60 years and six of the 20 patients were men.

Wanger et al. report that pain is not one of the major reasons for declining to participate in a study (9). However, this was not the case in our study. Patients

were afraid of the unpleasantness and the possible pain due to NJT. A declining rate of participating in a study could be due to the patients' views on health service.

When we asked the current patients about their preferences regarding MRE and MRFT (unpublished data), 12 (60%) preferred MRFT, six (30%) MRE and two (10%) had no preference. This is in accordance with other studies (12,13). IBD patients generally find it hard to ingest contrast, orally or by tube, as they already suffer from severe abdominal pain. However, it is important that the amount of contrast be the same in MRE and MRFT to be able to compare these methods. This was the case in the current study, with the patients ingesting on average 1115 mL contrast in MRFT and 1148 mL in MRE.

We chose VoLumen as the oral contrast as it is the contrast we routinely use in our department. VoLumen is a biphasic contrast agent as water, mannitol, sorbitol, and polyethylene glycol. These agents demonstrate low signal intensity on T1-weighted images and high signal intensity on T2-weighted (T2W) images (14). The choice of oral contrast medium varies from department to department.

Several studies point out that a collapsed and insufficiently dilated bowel can mimic or mask lesions (15,16). This was also the case in our study; in plain MRI, 13 false positive bowel thickening findings were present. In comparison, only four were present in MRFT. In several segments, particularly in the colon, there was a high rate of false positive findings. This is a problem for patients who are healthy, but misdiagnosed as being sick. The consequences for these patients may be that they have to undergo further examinations and possibly take medication. Plain MRI remains viable in the detection of severe wall thickening (Fig. 2).

The low number of subjects in our study may have influenced the outcome. However, this current study is an extension of a study published previously by the same group where plain MRI was compared with

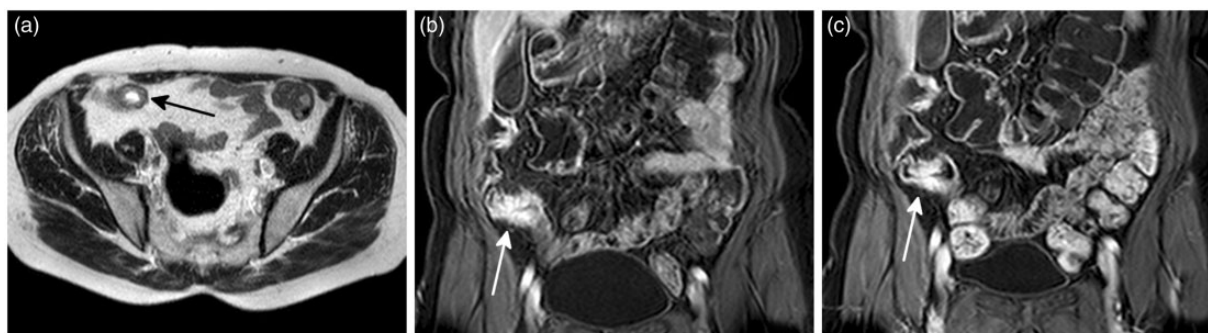


Fig. 1. A 57-year-old woman known with CD for over 30 years. The axial T2W image in plain MRI (a) shows a wall thickening of the terminal ileum (arrow). The corresponding coronal image after intravenous contrast administration in MRFT (b) and MRE (c) show segmental mural hyperenhancement and wall thickening at the same location (arrow), indication terminal ileum inflammation.

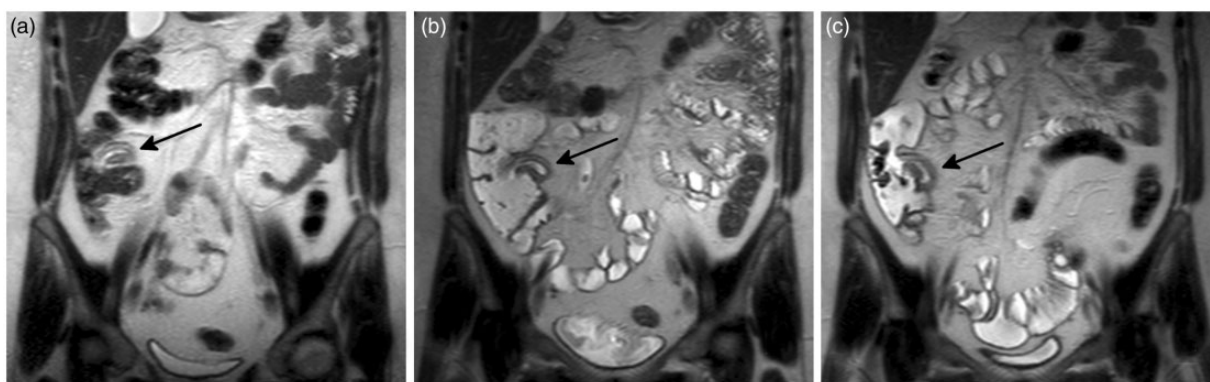


Fig. 2. Active terminal inflammation in a 41-year-old woman with CD. Coronal T2W image shows identical wall thickening and increase mural T2-signal intensity in the terminal ileum wall (arrows) in all three protocols; plain MRI (a), MRFT (b), and MRE (c). MRFT and MRE shows identical distension of the bowel whereas the bowel in plain MRI have no oral contrast.

Table 2. Sensitivity, specificity, PPV, NPV, and accuracy in plain MRI. The findings of bowel wall thickening and DWI in plain MRI using the MRE as the standard of reference in IBD patients.

	Sensitivity (%) [95 % CI]	Specificity (%) [95 % CI]	PPV (%) [95 % CI]	NPV (%) [95 % CI]	Accuracy (%) [95 % CI]	P value
<i>Wall thickening</i>						
Small bowel	0 [0]	96 [95–95]	0 [0]	100 [100]	95 [95–95]	1.00
Terminal ileum	50 [10–89]	81 [71–91]	4 [8–71]	87 [76–97]	75 [59–91]	0.25
Colon	75 [23–99]	93 [91–93]	27 [8–36]	99 [97–100]	92 [88–94]	0.003
<i>DWI</i>						
Small bowel	0 [0–95]	80 [80–82]	0 [0–11]	97 [97–100]	78 [78–82]	1.00
Terminal ileum	0 [0–66]	59 [59–70]	0 [0–28]	77 [77–92]	50 [50–70]	0.52
Colon	37 [11–72]	89 [87–91]	21 [6–41]	95 [93–98]	86 [81–92]	0.063

DWI, diffusion-weighted imaging; MRE, magnetic resonance enteroclysis; NPV, negative predictive value; PPV, positive predictive value.

MRFT (6). The MRFT was used as the reference standard in 100 IBD patients and the same pattern was found. The plain MRI had too many false positive findings.

Four other studies have compared MRFT and MRE (1,17–19). Negaard et al., Masselli et al., and Lawrance et al. compared the distension of bowel and found that the dilation was greater in MRE (17–19). Three of the studies found the accuracy of lesion detection were very similar. However, Masselli et al. showed a higher detection rate of superficial abnormalities with MRE (17).

DWI in plain MRI detected no true positive lesions in the small bowel and the terminal ileum. The same applied to MRFT in the small bowel. This reflects the low sensitivity for DWI in both protocols (Tables 2 and 3). As with bowl wall thickening, the false positive rate for DWI was high particularly in the colon, in both plain MRI and MRFT. The same pattern was observed by Kiryu et al. who found high DWI signal in inactive segments which occurred more frequently in the colon

(20). Two other studies found DWI to be a reliable tool to identify inflammation in the colon and rectum in UC (21,22).

Apparent diffusion coefficient (ADC) is a tool to avoid most of the false interpretation of DWI (23). ADC is a quantifiable method to identify lesion with restricted diffusion (24). In theory increased DWI signal intensity with a high b-value and a low ADC value are seen in active disease (24). In the current study, a lesion in DWI with high signal intensity was only regarded as restricted DWI when ADC showed low signal intensity at the same time. However, we did not measure the ADC value.

DWI and ADC are relative new sequences when it comes to the bowel lesions. No definitive agreement has been reached regarding bowel lesions. There are still too many contradicting results.

Some studies have suggested that degree and layered pattern of the enhancement could be used to distinguish between, active inflammation and fibrosis (25–29).

Table 3. Sensitivity, specificity, PPV, NPV and accuracy in MRFT. The findings of bowel wall thickening, DWI, and hyperenhancement in MRFT using the MRE as the standard of reference in IBD patients.

	Sensitivity (%) [95 % CI]	Specificity (%) [95 % CI]	PPV (%) [95 % CI]	NPV (%) [95 % CI]	Accuracy (%) [95 % CI]	P value
<i>Wall thickening</i>						
Small bowel	0 [0]	100 [100]	0 [0]	100 [100]	100 [100]	1.00
Terminal ileum	50 [11–50]	100 [90–100]	100 [21–100]	89 [80–89]	90 [74–90]	0.03
Colon	25 [1–74]	96 [95–98]	20 [1–59]	97 [96–99]	94 [92–97]	0.172
<i>DWI</i>						
Small bowel	0 [0–91]	97 [97–100]	0 [0–91]	97 [97–100]	95 [95–100]	1.00
Terminal ileum	33 [2–65]	94 [89–100]	50 [3–97]	89 [84–94]	85 [76–94]	0.28
Colon	50 [18–82]	84 [82–87]	20 [7–33]	96 [93–98]	82 [77–86]	0.035
<i>Hyperenhancement</i>						
Small bowel	0 [0]	100 [100]	0 [0]	100 [100]	100 [100]	1
Terminal ileum	33 [2–65]	94 [89–100]	50 [3–97]	89 [84–94]	85 [76–94]	0.28
Colon	71 [33–95]	95 [93–97]	50 [23–66]	98 [95–100]	94 [89–97]	0.000

DWI, diffusion-weighted imaging; MRE, magnetic resonance enteroclysis; MRFT, magnetic resonance follow-through; NPV, negative predictive value; PPV, positive predictive value.

In the current study the layered pattern of bowel enhancement was interpreted as acute inflammation and low inhomogeneous enhancement as fibrosis. Fibrosis was found in only one case in the terminal ileum. This was detected in MRE whereas plain MRI and MRFT showed no abnormalities.

The differences in true positives, true negatives, false positives, and false negatives for wall thickening, DWI and hyperenhancement are small in almost all segments in MRFT compared to plain MRI. The contingency table indicates that wall thickening and DWI are not as trustworthy in plain MRI as in MRFT.

Plain MRI is very appealing to patients for various reasons. Patients do not have to be at the hospital 1 h before the examination to drink the contrast. Another advantage is that the patients avoid the all discomforts due to the oral contrast media. However, plain MRI currently does not perform as well as MRFT and MRE in identifying lesions. A suggestion to improve the plain MRI would be the administration of an intravenous contrast. This might reduce the probability of poorly distended bowel loops being mistakenly diagnosed as disease. A pilot study with this modification of the protocol is being performed by the authors.

The main limitation in our current study is the small number of the patients completing all three procedures. Another limitation is that we did not perform any endoscopy to confirm our MRI findings. We also deliberately chose to make an overall statistic for all three patients groups due to the limited number of patients. Lastly, the lack of inter-observer agreement is also a limitation to this study. The strength of the current

study is that plain MRI and MRFT were performed on the same day. If the patients were taking medicine, the effects would have the same influence on plain MRI and MRFT. Another advantage of plain MRI is that the patients avoid the oral contrast media and thereby all the related discomforts.

In conclusion, patients with IBD overwhelmingly decline MRE due to the discomfort of the NJT. The use of oral and intravenous contrast agent improves detection of bowel lesions resulting in MRFT remaining the superior choice over plain MRI for diagnostic workup in patients with IBD.

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Conflict of interest

None declared.

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