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FULL PAPER

Prospective evaluation of free-breathing diffusion-weighted imaging for the detection of inflammatory bowel disease with MR enterography in childhood population

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Objective: To evaluate prospectively the performance of diffusion-weighted imaging (DWI) for the detection of active lesions on MR enterography (MRE) in children with inflammatory bowel disease (IBD).
Methods: MRE of 48 children (mean age 13 years) with suspected or known IBD were blindly analysed by 2 independent readers for the presence of active lesions. Two sets of imaging including DWI and gadolinium-enhanced imaging (GEI) were reviewed. A reader consensus was obtained. The gold standard was histopathological findings. In patient-level analysis and segment-level analysis, sensitivity and specificity were calculated for DWI and GEI and compared using McNemar's test or logistic random-effects models.
Results: At least 1 active lesion was confirmed in 42 (87.5%) children. Sensitivity and specificity for the detection of at least one lesion were 88.1% (95% CI, 74.3–96.1) and 83.3% (95% CI, 35.9–99.6), respectively, for DWI and 66.7% (95% CI, 50.4–80.4) and 83.3% (95% CI, 35.9–99.6), respectively, for GEI. In segment-level analysis, sensitivity and specificity for the detection of specific segment lesions were 62.5% (95% CI, 48.1–75) and 97.1% (95% CI, 93.5–98.7), respectively, for DWI and 45.7% (95% CI, 30.8–61.3) and 98.2% (95% CI, 95.3–99.4), respectively, for GEI. The sensitivity of DWI was significantly better than that of GEI per patient ($p = 0.004$) and per segment ($p = 0.028$).
Conclusion: DWI demonstrates better performance than GEI for the detection of active lesions in children with IBD.
Advances in knowledge: Examination with no intravenous injection–DWI can replace T_1 weighted images when paediatric patients are screened with MRE for IBD. Examination performed in free breathing is better tolerated by children.

INTRODUCTION

Inflammatory bowel disease (IBD) refers to three specific entities: Crohn's disease (CD), ulcerative colitis (UC) and undetermined colitis (UnC). In Europe, 2.2 million people are affected by IBD.[1] The incidence in the paediatric population has increased in recent decades.[2,3] In northern France, among a population of approximately 6 million people, the incidence of CD has increased by >70% between 1988 and 2007[4,5] in the 10–19-year age group. The diagnosis of IBD is based on clinical examination, imaging, biological, endoscopic and histological results.[6] The gold standard for the diagnosis of IBD remains endoscopy with biopsy and histological confirmation.[7] Diagnosing IBD and defining its precise type is a challenge for both clinicians and radiologists. CD and UC share the same chronic evolution, alternating bouts of recurrences and periods of remission.[8]

The follow-up of affected children and optimization of their treatment require frequent evaluation by imaging techniques. Ultrasound is widely used as the first-line imaging technique in children for screening patients suspected of having IBD.[9] Ultrasound has several limitations such as interobserver variability and poor visualization of some segments of the digestive tract.[10] Therefore, MR enterography (MRE) has gained popularity and is considered as the imaging modality of choice for IBD in children.[11–13] Classical MRE protocol includes T_2 and T_1 weighted pre- and post-contrast sequences[13–16] that are intended to differentiate between active inflammation and fibrosis. Acute bowel inflammation is characterized by an increased bowel wall thickness (>3 mm) and high mural signal intensity relative to the adjacent muscle on T_2 weighted images. Recently, two studies[17,18] have demonstrated that active disease is characterized by mucosal

enhancement.[18] However, it also necessitates the placement of an intravenous catheter, that it could be poorly tolerated by younger children below 10 years.[19]

More recently, Diffusion-weighted imaging (DWI) sequences have been developed for MRE. Diffusion-weighted images are produced on the basis of the random (Brownian) motion of water. DWI MRI reflects the changes in the water mobility caused by interactions with cell membranes, macromolecules and alterations of the tissue. So, in water, molecules are free and the signal intensity on DWI is low and in a tissular environment, the molecular motion is restricted and the signal intensity on DWI is high. Some studies have been shown to characterize inflammatory[20–24] and neoplastic conditions.[25,26] Studies in adults have shown that DWI depicts inflammatory lesions in IBD, thanks to a restriction of diffusion.[20–22] Only two retrospective studies had investigated the contribution of DWI in children.[27,28] DWI appears well adapted for children, thanks to faster image acquisition, the possibility of free-breathing mode, reduced motion artefacts, high tissue contrast and because it obviates the need for contrast enhancement.

The objectives of our study were to evaluate prospectively the performance of DWI for the detection of active lesions of IBD and to compare the performance of diffusion-weighted images with T_1 weighted images after gadolinium injection compared with histopathological findings as the standard reference.

METHODS AND MATERIALS

The protocol of this prospective study was approved by our institutional review board.

Patients

From April 2013 to December 2014, 100 MRE were performed in 100 consecutive children, who were clinically suspected of having an IBD or known to have IBD and needed a mapping of the lesions. Exclusion criteria of the study were MRE without endoscopic or histological confirmation, MRE in the supine position, MRI with a nasogastric tube, general contraindications to MRI and age over 18 years.

MR enterography protocol

All MR examinations were performed using 1.5-T MR units (SIEMENS Magnetom® AERA XQ MRI (Siemens Healthcare, Erlangen, Germany) and General Electric Signa® MRI (GE Healthcare, Milwaukee, WI), with 18-channel phased-array body coils and 8-channel phased-array cardiac coils, respectively. The children fasted for 4 hours before MRI and were asked to drink 500–1000 ml (volume adapted to the age) of a hyperosmotic solution of water mixed with Mannitol 20% (Macopharma, Mouvaux, France) 45 min before the examination. Images were acquired with patients in the prone position.[29] All patients had first T_2 weighted half-Fourier single-shot turbo spin-echo and true free-induction steady-state-free precession MR sequences in the axial and coronal planes of the abdomen.

DWI was performed thereafter with a single-shot spin-echoplanar diffusion-weighted technique in the axial plane with two diffusion factors ($b = 0$ and 1000 s mm^{-2} for GE and $b = 50$ and 800 s mm^{-2} for Siemens). For the examinations performed on the GE magnet, the sequence of DWI covered the entire abdomen in one single acquisition during 166 s. For the Siemens magnet, two acquisitions of DWI were needed to cover the entire abdomen, and each sequence of DWI lasted for 86 s. Fat suppression was obtained with a frequency selective for fat saturation to reduce chemical-shift artefacts for the Siemens magnet. A selective excitation of water was used for the GE equipment.

These sequences were followed by a coronal fat-saturated 3D low-angle volumetric interpolated breath-hold T_1 weighted gradient-echo MR sequence (VIBE for Siemens and LAVA for GE) before and after intravenous administration of 0.2-ml Kg gadoterate meglumine (Dotarem, Guerbet, Aulnay-sous-Bois, France) at the rate of 2 ml s^{-1}. Images were acquired during arterial- and portal-venous phases. They were followed by an axial fat-saturated two-dimensional fast spoiled gradient-echo breath-hold T_1 weighted MR sequence. No spasmolytic was administrated. The MRI characteristics used are further detailed in Table 1.

Image analysis

MRE images were reviewed on a picture archiving and communication system viewing station (iSite 4.1.114 PACS; Philips Healthcare Informatics, Foster City, CA) by two radiologists with 5 (EAB) and 2 (CD) years' experience in abdominal imaging using a standardized evaluation form. Both were blinded to the clinical patient information. The bowel was divided into seven segments: the jejunum, ileum, terminal ileum and ileocaecal junction, ascending colon, transverse colon, descending colon and rectosigmoid colon. We discriminate the jejunum from ileum by the number of folds (jejunum >3 folds per inch and ileum <5 folds per inch). The length of the terminal ileum used for this study was 20 cm.

After a common training session, each reader scored independently the likelihood for the presence of an active lesion using a three-point scale on DWI (1= no increased signal intensity, 2= moderate increased signal intensity and 3= marked increased signal intensity) and on gadolinium imaging (1= no contrast enhancement, 2= moderate contrast enhancement and 3= marked contrast-enhancement). On DWI, an active lesion of IBD was considered if an increased signal intensity was noted on high b-value.[16] Segments graded 2 or 3 for DWI and contrast enhancement images were considered significant for an active lesion. The image quality of diffusion-weighted and gadolinium-enhanced MR images was evaluated semi-quantitatively using a three-point scale as follows: 1= poor quality (with numerous artefacts), 2= moderate quality (with a few artefacts) and 3= optimal quality (without artefact).

The readers first evaluated diffusion-weighted images as a single set. During the second reading, the readers reviewed gadolinium-enhanced MR images as a single set. In the third reading session, all MR sequences (T_2+DWI and T_1+gadolinium enhanced) were reviewed together, and discrepancies were resolved by consensus. To minimize recall bias, the three reading sessions were performed 4 weeks apart from each other.

Table 1. Imaging parameters used for MR enterography

MRI	MR sequence	Acquisition time (s)	Flip angle (degrees)	Repetition time (ms)	Echo time (ms)	Section thickness/ gap (mm)	Acceleration factor	Receiver bandwidth (KHz/pixel)	Fat suppression
SIEMENS	T_2 HASTE axial	48	170	1000	96	4.0/0.0	2	401	No
	T_2 HASTE coronal	44	180	1000	96	4.0/0.0	2	399	No
	T_2 Truefisp axial	16	58	4.09	2.05	4.0/0.0	2	488	No
	T_2 Truefisp coronal	14	59	3.95	1.98	4.0/0.0	3	488	No
	DWI	86		4800	54	5.0/0.2	2	1468	Yes
	Coronal Gd-enhanced 3D T_1 weighted VIBE	18	10	3.19	1.24	1.6/0.2	2	450	Yes
	Axial Gd-enhanced 2D T_1 weighted VIBE	22	10	3.19	1.24	1.4/0.2	2	450	Yes
GE	T_2 SSFSE axial	279	90	4000	120	4.0/0.6	1	83.33	No
	T_2 SSFSE coronal	150	90	4000	120	4.0/0.0	1	83.33	No
	T_2 Fiesta axial	151	85	4.80	2.17	4.0/0.5	1	62.50	Yes
	T_2 Fiesta coronal	99	85	5	2.25	4.0/0.0	1	62.50	Yes
	DWI	166	-	6400	73	4.0/1.5	1	250	No
	Coronal Gd-enhanced 3D T_1 weighted LAVA	166	15	2.92	1.4	3.6/1.8	1	125	Yes
	Axial Gd-enhanced 2D T_1 weighted LAVA	21	12	3.78	1.77	3.6/1.8	1	62.50	Yes

2D, two-dimensional; 3D, three-dimensional; DWI, diffusion-weighted imaging; SSFSE, single shot fast spin echo.

Standard of reference

The standard of reference for the presence of active lesion of IBD was histopathological findings (obtained by biopsy during endoscopic examination in 44 cases and following surgery in 4 cases: 1 lesion of the jejunum and 3 lesions of the ileum). Endoscopic examination was performed within 8 weeks after MRE.

Transmucosal infiltration, focal or diffuse basal plasmacytosis, the presence of neutrophils, cryptitis, cryptitis abscesses and the absence of granuloma were histopathological findings suggesting ulcerative colitis. Epithelioid granuloma is surely a key feature of CD on histological examination but is not specific and not always present (between 15% and 85%). Other histological features suggesting CD were apthoid ulcers, fissure ulcers, transmural inflammation, fistulas and lymphangiectasia. The diagnosis of CD is ascertained when an epithelioid granuloma is present along with any other criteria. The presence of three histological features without granuloma is diagnostic as well.[30]

Statistical analysis

Results were expressed as the median, interquartile range and range for continuous variables and as frequencies and percentages for qualitative variables. Image quality was compared between the diffusion-weighted and gadolinium-enhanced images by using the Bhapkar's test, which generalizes the McNemar's test when more than two categories are involved.[31] The level of agreement between the senior and junior radiologists in the visual assessment of segments with active lesions was evaluated using the weighted kappa (κ) coefficient for three-point scale (1= no lesion, 2= probably lesion, 3= active lesion) and simple κ coefficient for a significant active lesion (defined as Grades 2 or 3); κ values <0 indicated no agreement, 0–0.20 indicated slight agreement, 0.21–0.40 indicated fair agreement, 0.41–0.60 indicated moderate agreement, 0.61–0.80 indicated substantial agreement and 0.81–1.00 indicated almost perfect agreement.[32] Using the consensus between the two radiologists for the detection of a significant active lesion, we assessed the diagnostic performance of diffusion-weighted and T_1 weighted images after gadolinium injection using histopathological findings as the gold standard. We firstly performed a patient-level analysis to evaluate the diagnostic performance for the detection of IBD disease (*i.e.* at least one lesion at any segment) and secondly a segment-level analysis, taking into account multiple observations per patient to evaluate the diagnostic performance for the detection of specific-segment lesion.[33] For patient- and segment-level analyses, we have calculated the sensitivity, specificity, positive-predictive value (PPV), negative-predictive value (NPV) and accuracy of each MRE imaging for the detection of active disease. In patient-level analysis, exactly 95% confidence intervals (CIs) for the diagnostic criteria were calculated, and sensitivity was compared between the two MRE imaging using the exact McNemar's test. In segment-level analysis, we used a logistic random-effects model to estimate the diagnostic criteria and their 95% CIs and to compare the sensitivity and specificity values between the two MRE imagings;[33] this model takes into account the correlation between segment measures within patients. For segment-level analysis, we assessed the sensitivity and specificity of each MRE imaging according to the type of MRI scanner (Siemens *vs* GE). Statistical testing was performed at the two-tailed level of 0.05. Data were analysed using the SAS® software package, release 9.3 (SAS Institute, Cary, NC).

RESULTS

During the period of the study, 100 MRE were performed in our hospital. We excluded 52 patients: 42 patients without endoscopic results or with incomplete endoscopic results, 9 patients with MRE with complete endoscopic and histopathological results but performed in supine position and 1 patient with MRE under general anaesthesia (supine position and MRI with nasogatric tube).

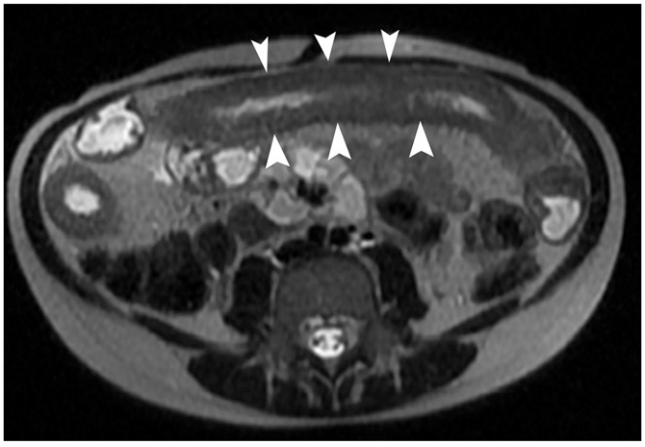
48 children (25 females and 23 males) could finally be included, with a median age of 13 years (range, 5–18 years). 25 (52.1%) children had a clinical suspicion of IBD and 23 (47.9%) children had follow-up examinations for known IBD, including 15 children with CD, 5 children with UC and 3 children with UnC. Two patients had had previous bowel surgery (colectomy for

Table 2. Patient characteristics

Characteristics	Values
Number of patients	48
Age, median (IQR), years	13 (12–15)
Males, *n* (%)	23 (47.9)
Disease duration, median (IQR), months	23 (12–38)
Prior surgery, *n* (%)	7 (14.6)
Crohn's disease[a], *n* (%)	33 (68.8)
Age at diagnosis: A1	*23 (47.9)*
A2	*10 (20.8)*
A3	*0 (0.0)*
Location: L1	*8 (16.7)*
L2	*8 (16.7)*
L3	*12 (25.0)*
L1L4	*1 (2.1)*
L2L4	*3 (6.3)*
L3L4	*1 (2.1)*
Behaviour: B1[b]	*19 (39.6)*
B2	*4 (8.3)*
B3	*10 (20.8)*
Ulcerative colitis[a], *n* (%)	8 (16.7)
E1	*1 (2.1)*
E2	*2 (4.2)*
E3	*5 (10.4)*
Underterminate colitis, *n* (%)	3 (6.3)

IQR, interquartile range.
[a]Montreal classification for Crohn's disease or extent for ulcerative colitis.
[b]10 patients had concomitant perianal disease (6 patients with B1, 1 patient with B2 and 3 patients with B3).

Figure 1. MR enterography in 7-year-old female with Crohn's disease. (a) Axial T_2 single shot fast spin echo shows a long wall thickening (arrowheads) of the small bowel. (b) Axial diffusion-weighted imaging ($b = 1000\,s\,mm^{-2}$) shows a hyperintense signal of the small bowel with no artefact. (c) Axial T_1 LAVA fat saturation after gadolinium enhancement shows a sequence with multiple artefacts. The enhancement is less well visualized as compared with DWI (b).



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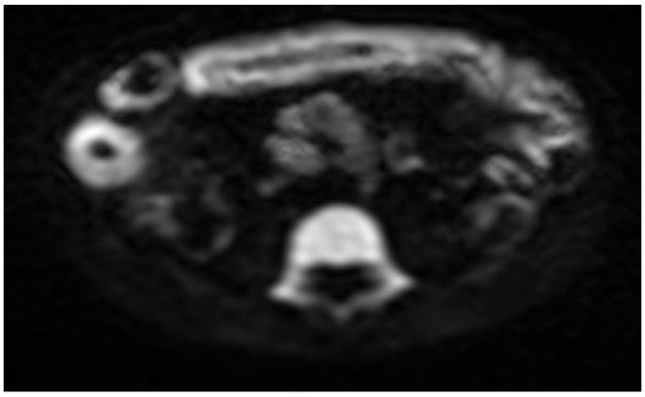

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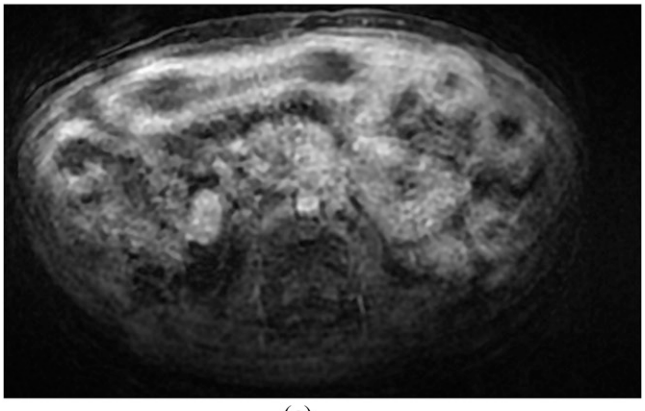


(c)

Hirschsprung disease and colectomy for indeterminate colitis) and five patients had had previous perineal surgery. Patient characteristics are summarized in Table 2.

MRE was performed successfully without side effects in all children. The quality of diffusion-weighted images was significantly better than that of T_1 weighted images after gadolinium injection (Bhapkar's test: $p < 0.0001$). No artefact was found in 37 MRE (77.1%) with diffusion-weighted images in comparison with 21 MRE (43.8%) with T_1 weighted images after gadolinium injection (Figure 1). The overall interreader agreement for graded active lesions was excellent with diffusion-weighted images [accuracy = 94.5%; k (95% CI) = 0.83 (0.77–0.89)] as well as with T_1 weighted images after gadolinium injection [accuracy = 95.7%; k (95% CI) = 0.82 (0.75–0.89)] (Table 3). When considered Grades 2 and 3 as significant for active lesion, the proportion of concordance was 98.5% [k (95% CI) = 0.95 (0.91–0.99)] in diffusion-weighted images and 97.0% [k (95% CI) = 0.89 (0.82–0.96)] in T_1 weighted images when considering Grades 2 or 3 as significant lesions. Among the five discordances in diffusion-weighted images, the senior radiologist did not confirm the junior radiologist's diagnosis of active lesion in one case. For T_1 weighted images, the senior radiologist did not confirm the junior radiologist's diagnosis of active lesion in four cases.

At least one active lesion of IBD was demonstrated in 42 (87.5%) cases using histopathological findings. Active lesion was most frequently diagnosed in the rectosigmoid colon (56.3%, $n = 27$), followed by in the descending colon (45.8%, $n = 22$), ascending colon (39.6%, $n = 19$), terminal ileum and ileocaecal junction (39.6%, $n = 19$), transverse colon (35.4%, $n = 17$), ileum (6.2%, $n = 3$) and jejunum (2.1%, $n = 1$) (Table 4).

Diagnostic performances of diffusion-weighted images and T_1 weighted images after gadolinium injection

Diagnostic performances of diffusion-weighted and gadolinium-enhanced images for the detection of active IBD lesion using histopathological findings as the gold standard are shown in Table 4 for all segments and according to each single bowel segment.

Patient-level analysis

When considering all bowel segments (*i.e.* a diagnosis of ≥1 IBD lesion whatever the segment), 37 true-positive and 5 true-negative results were found on DWI. One false-positive case corresponded to a normal terminal ileum at the endoscopic examination in a 17-year-old female. Five false-negative cases were found including four children with colonic lesion (one UC, one CD and two UnC) and one child with terminal ileum and colonic lesions (CD). The corresponding sensitivity, specificity, PPV, NPV and accuracy were 88.1% (95% CI, 74.3–96.1), 83.3% (95% CI, 35.9–99.6), 97.4% (95% CI, 86.2–99.9), 50.0% (95% CI, 18.7–81.3) and 87.5% (95% CI, 74.7–95.3), respectively.

Analysing the gadolinium-enhanced set, 28 true-positive and 5 true-negative results were found. One false-positive case was found and it was the same as with DWI. Nine supplementary false-negative cases were found compared with DWI including seven children with colonic lesion and two children with terminal ileum lesion. The corresponding sensitivity, specificity, PPV, NPV and accuracy were 66.7% (95% CI, 50.4–80.4), 83.3% (95% CI, 35.9–99.6), 96.6% (95% CI, 82.2–99.9),

Table 3. Observed proportion of interreader agreement for graded active lesions, overall and according to bowel segments

Bowel segments	Diffusion-weighted images		T_1 weighted images	
	3-point scale	Active disease[a]	Three-point scale	Active disease[a]
Jejunum	97.9 (47/48)	97.9 (47/48)	97.9 (47/48)	97.9 (47/48)
Ileum	93.8 (45/48)	97.9 (47/48)	95.8 (46/38)	97.9 (47/48)
Terminal ileum and ileocaecal junction	89.6 (43/48)	100.0 (48/48)	89.6 (43/48)	100.0 (48/48)
Ascending colon	89.6 (43/48)	100.0 (48/48)	91.7 (44/48)	100.0 (48/48)
Transverse colon	89.6 (43/48)	97.9 (47/48)	93.8 (45/48)	97.9 (47/48)
Descending colon	93.8 (45/48)	100.0 (48/48)	89.6 (43/48)	93.8 (45/62)
Rectosigmoid colon	87.5 (42/48)	95.9 (46/48)	91.7 (44/48)	93.8 (45/48)
All segments	*94.5 (308/336)*	*98.5 (331/336)*	*95.7 (312/336)*	*97.0 (326/336)*

Values are percentage (numbers).
[a]Segments graded as 2 or 3 were considered to have active disease, and segments graded as 1 were considered inactive.

26.3% (95% CI, 9.1–51.2) and 68.8% (95% CI, 53.7–81.3), respectively.

Sensitivity for the detection of ≥1 active IBD lesion was significantly better with DWI than with T_1 weighted imaging after gadolinium injection (McNemar's test: $p = 0.004$), whereas the specificity was similar. Regarding sensitivity, when analysis was stratified by bowel segments, a similar difference between diffusion-weighted and T_1 weighted images after gadolinium injection was observed in the most frequent sites of the IBD lesion (Table 4) (Figure 2).

Segment-level analysis

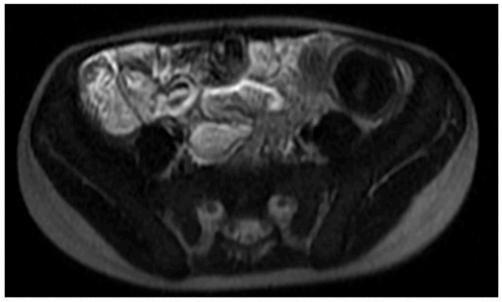
In segment-level analysis (Table 5), we also found that the sensitivity of DWI to detect a specific-segment lesion (62.5%) was better than that of T_1 weighted images after gadolinium

Table 4. Diagnostic performance for active IBD lesion on DWI and gadolinium using endoscopic or surgery findings as gold standard in patient-level analysis, overall and by bowel segments

DWI and gadolinium results	Sensitivity	Specificity	PPV	NPV	Accuracy
DWI results					
All segments	88.1 (37/42)[a]	83.3 (5/6)	97.4 (37/38)	50.0 (5/10)	87.5 (42/48)
Jejunum	0.0 (0/1)	100.0 (47/47)	–	97.9 (47/48)	97.9 (47/48)
Ileum	66.7 (2/3)	93.3 (42/45)	40.0 (2/5)	97.7 (42/43)	91.7 (44/58)
Terminal ileum and ileo-caecal junction	79.0 (15/19)	93.1 (27/29)	88.2 (15/17)	87.1 (27/31)	87.5 (42/48)
Ascending colon	47.4 (9/19)	96.6 (28/29)	90.0 (9/10)	73.7 (28/38)	77.1 (37/48)
Transverse colon	41.2 (7/17)	96.8 (30/31)	87.5 (7/8)	75.0 (30/40)	77.1 (37/48)
Descending colon	59.1 (13/22)	100.0 (26/26)	100.0 (13/13)	74.3 (26/35)	81.2 (39/48)
Rectosigmoid colon	63.0 (17/27)	100.0 (21/21)	100.0 (17/17)	67.7 (21/31)	79.2 (38/48)
Gadolinium results					
All segments	66.7 (28/42)	83.3 (5/6)	96.6 (28/29)	26.3 (5/19)	68.7 (33/48)
Jejunum	0.0 (0/1)	100.0 (47/47)	–	97.9 (47/48)	97.9 (47/48)
Ileum	66.7 (2/3)	93.3 (42/45)	40.0 (2/5)	97.7 (42/43)	91.7 (44/48)
Terminal ileum and ileocaecal junction	63.2 (12/19)	96.6 (28/29)	92.3 (12/13)	80.0 (28/35)	83.3 (40/48)
Ascending colon	42.1 (8/19)	100.0 (29/29)	100.0 (8/8)	72.5 (29/40)	77.1 (37/48)
Transverse colon	35.3 (6/17)	100.0 (31/31)	100.0 (6/6)	73.8 (31/42)	77.1 (37/48)
Descending colon	40.9 (9/22)	100.0 (26/26)	100.0 (9/9)	66.7 (26/39)	72.9 (35/48)
Rectosigmoid colon	44.4 (12/27)	100.0 (21/21)	100.0 (12/12)	58.3 (21/36)	68.7 (33/48)

DWI, diffusion weighted imaging; IBD, inflammatory bowel disease; NPV, negative-predictive value; PPV, positive-predictive value.
Values are percentage (numbers).
[a]$p < 0.05$ for comparison with sensitivity of gadolinium by exact McNemar's test.

Figure 2. MR enterography in 6-year-old female with ulcerative colitis. (a) Axial T_2 single shot fast spin echo shows no colonic distension and no wall thickening. (b) Axial diffusion-weighted imaging ($b = 1000\,s\,mm^{-2}$) shows a hyperintense signal of the descendant colonic. (c) Axial T_1 LAVA fat saturation after gadolinium enhancement shows mild enhancement. (d) Macroscopic photography of the endoscopy shows ulcerative lesions of the left colonic: diffuse erythema with mucosal granularity (arrowheads).



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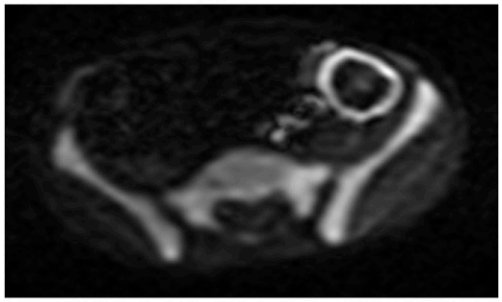

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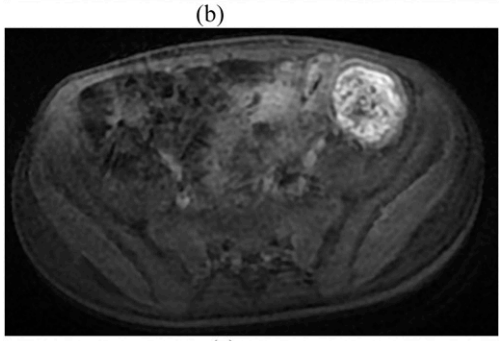
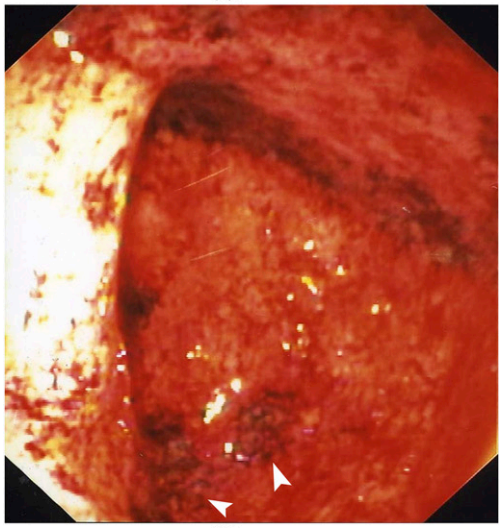


(c)



(d)

injection (45.7%, logistic random-effect model: $p = 0.028$) (Figure 2). No significant difference was noted for the specificity of diffusion-weighted images and T_1 weighted images after gadolinium injection (97.1% *vs* 98.2%, $p = 0.36$). When segment-level analysis was stratified accordingly between the two manufacturers, the sensitivity of diffusion-weighted images remained higher than the sensitivity of T_1 weighted images after gadolinium injection, although no significant difference was noted ($p = 0.19$ for Siemens, and $p = 0.07$ for GE). The sensitivity of diffusion-weighted images was 65.9% (95% CI, 46.0–81.4) for Siemens and 54.4% (95% CI, 31.7–75.4) for T_1 weighted images after gadolinium injection. The corresponding values obtained with GE were 59.4% (95% CI, 36.8–78.6) and 36.9% (95% CI, 18.6–59.9). Specificities of diffusion-weighted images and T_1 weighted images after gadolinium injection were equally high in both manufacturers (>96%).

DISCUSSION

MRE combining T_2 and T_1 weighted images after gadolinium injection sequences is considered as an optimal imaging technique for the detection of active IBD in the adult and paediatric population. In a retrospective study, using histology as a gold standard, Dillman et al[34] have shown that classical sequences (T_2 weighted imaging and T_1 weighted imaging after gadolinium injection) have a sensitivity of 94% for the detection of small-bowel and colonic lesions in case of CD. Gee et al[35] reported similar results in a prospective study including 21 patients. They achieved a sensitivity of 90% and a specificity of 82.6% for MRE with histopathological findings as gold standard. Recently, Seo et al[36] have shown in 44 adults that DWI MRE is not inferior to contrast material-enhanced MRE for the evaluation of inflammation in Crohn's disease, except for the diagnosis of penetration. However, the "classical" technique using T_2 and contrast-enhanced T_1 sequences has disadvantages in children: the length of the examination, the need for contrast enhancement and catheter placement. Therefore, it would be interesting if the examination could be simplified and shortened. Our study shows that the use of DWI could achieve this.

A retrospective study by Oto et al in 2009[20] has shown in 11 adult patients that the inflammation of the bowel wall induces a restriction of diffusion with SE = 84% and Sp=91% for the detection of active lesions of CD with a apparent diffusion coefficient (ADC) threshold of 2. A second study[22] including 18 patients and using histology and endoscopy as the gold standard showed a better sensitivity of ADC values for the detection of inflammatory lesions as compared with patterns of enhancement on T_1 weighted images. In another study, Kyriu et al[21] has shown that DWI had SE = 86% and an accuracy of 82.4% in the detection of active disease compared with conventional barium study or surgery (17 patients). These studies were interesting but included only small samples of adults or did not use a well-defined gold standard. Buisson et al,[37] in a prospective study including 31 adult patients, showed excellent sensitivity (SE = 100%) of DWI as compared with conventional MRE. The NPV was 100%. In the paediatric population, only retrospective studies investigating the role of DWI in IBD are available. In 2012, Neubauer et al[27] performed a retrospective study in a paediatric population of 33 children. They reported

Table 5. Summary estimates of the diagnostic criteria and their 95% confidence intervals (CIs) for active IBD lesion on DWI and gadolinium using endoscopic or surgery findings as the gold standard in segment-level analysis

	DWI	Gadolinium	*p*-value[a]
Sensitivity, %	62.5 (48.1–75.0)	45.7 (30.8–61.3)	0.028
Specificity, %	97.1 (93.5–98.7)	98.2 (95.3–99.4)	0.36
PPV, %	90.3 (79.4–95.7)	92.3 (79.3–97.4)	
NPV, %	86.2 (78.9–91.3)	81.4 (74.0–87.0)	
Accuracy, %	86.9 (80.6–91.3)	83.1 (76.5–88.1)	

DWI, diffusion-weighted imaging; IBD, inflammatory bowel disease; NPV, negative-predictive value; PPV, positive-predictive value.
[a]Sensitivity and specificity were compared between DWI and gadolinium using a using a logistic random-effects model.

that the diffusion-weighted sequence combined with T_2 sequences had diagnostic performances equal or superior to T_1 weighted contrast-enhanced sequences for the detection of active inflammatory lesions and extraluminal complications of CD. In another retrospective study, Ream et al[28] have shown that restriction of diffusion can be found in patients when active small-bowel inflammation lesions are present. Sohn et al[38] showed in a retrospective study of 15 children that all MRE sequences (T_2, motility imaging, DWI and dynamic enhancement imaging) have a high lesion detectability with SE = 90.2% on DWI compared with SE = 92.7–95.1% using contrast-enhanced MR. Recently, Shenoy-Bhangle et al[39] have shown that the combination of DWI and MRE increased the imaging accuracy for the detection of disease activity compared with either technique alone.

To our knowledge, our study is the first that has evaluated prospectively the performance of DWI with gadolinium-enhanced sequences in the detection of active lesions of IBD in children and used anatomopathological findings as the reference standard. Our excellent results (SE = 88.1%, Sp = 83.3%, PPV = 97.4%, NPV = 50.0% and accuracy = 87.5%) are similar to those from retrospective studies.[20,21] Our study demonstrates that MR images obtained with DWI could replace gadolinium chelate-enhanced MRI to detect active lesions of IBD in the protocol of MRE in a paediatric population.

Recently, Kim et al[40] evaluated the performance of DWI per segment, in an adult population, and showed that DWI had a sensitivity of 83% in the terminal ileum and 60% in the colon rectum.

To our knowledge, our study was the first in children to evaluate per segment the performance of DWI compared with histopathological results. However, by comparison with patient-level analysis, the sensitivity decreased at the segment level, since every IBD lesions need to be identified separately in order to count as true positive, and thus the opportunity to miss a lesion in an individual segment increases.[33] However, our results per segment (SE = 79% for the terminal ileum, SE comprised between 41.2% and 63% for the colon) are similar to those from a previous study.[40] From these data, it can be concluded that DWI is an excellent screening tool, but probably lacks precision for the exact topographic diagnosis of the lesions. Furthermore, diagnostic performances are better for the evaluation of the small bowel than for the colon. Still, DWI had better diagnostic performances than gadolinium injection sequences. DWI could be less dependent on a good distension of the digestive tract.

There are other advantages in using DWI instead of T_1 weighted imaging after gadolinium injection: a shorter duration of examination (if gadolinium MR imaging is not performed) and no need for catheter placement. In our study, images obtained by DWI displayed better image quality ($p < 0.0001$). This difference of quality may be due to a longer time of examination with T_1 weighted imaging and artefacts of movements, especially at the end of MRE. Furthermore, gadolinium MR imaging is performed in apnoea, while DWI MR imaging can be performed in free breathing, which is better tolerated by paediatric patients. There are other technical explanations to the overall good performance of MRE in our study. Indeed, unlike other studies,[27,28] we did not use spasmolytic medications in order to simplify the examinations in children. Also, we placed the patients in a prone position and obtained a good distension of the bowel without many artefacts from the small bowel.[29] Still, there are some disadvantages of using DWI. DWI has a poorer spatial resolution that requires a joint analysis with T_2 sequences; for this reason, the MR protocol requires the performance of T_2 weighted imaging together with DWI. This lower spatial resolution also probably explains the lower topographic diagnostic value of DWI.

Our study has several limitations; first, the relatively small size of included patients. However, our number is larger than that in previous studies.[20,21] We excluded 42 patients for whom we had no endoscopic or surgical diagnosis and 9 patients because MRE was performed in the supine position and 1 patient with MRE performed under general anaesthesia. Therefore, we could not exclude a selection bias. Another limitation of our study was the small number of true-negative patients. For ethical reasons, it was difficult to justify performing invasive examinations such as endoscopy in children with no abnormalities on MRE and moderate or low suspicion of IBD. However, in segment analysis, true-negative bowel segments were important, which allows us to accurately estimate the specificity. Another limitation of the study was that DWI evaluation was based on qualitative visual inspection rather than quantitative DWI analysis. Future studies with quantitative evaluation could be valuable.

CONCLUSION

Our study shows that DWI had better diagnostic accuracy than gadolinium MR images and might replace gadolinium MR images for screening IBD.

This would avoid the injection of contrast, reduce the examination time and is better tolerated by young paediatric patients. However, gadolinium is still necessary to detect abscess or fistulae. The respective role of T_2 weighted images, DWI and T_1 weighted images after gadolinium injection for the diagnosis between fibrosis and active lesions in children should be evaluated in future studies.

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