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TOPIC HIGHLIGHT

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Magnetic resonance imaging in children and adolescents with chronic inflammatory bowel disease

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Abstract

Inflammatory bowel diseases (IBD) represent challenges, both from a diagnostic, and therapeutic point of view. Deep-seated anatomic structures are difficult to assess by ultrasound technique alone. As radiation-free alternative cross-sectional imaging method, magnetic resonance imaging of the intestinal structures is costly and time-consuming. Examination of pediatric patients imply additional considerations: reduction of body motions in younger children and consideration of the most appropriate preparation, and examination technique. The demanding Sellink technique is the only means for appropriately distending the lesser intestine in order to detect small bowel strictures. Oral intake of contrast medium (CM) alone shows its limitations regarding distensibility. The need for intravenous contrast media application needs to be considered, too. Active inflammation of both intestinal wall, and mesentery can be demonstrated accurately. Nevertheless, viable alternatives to CM application is desirable, considering non-negligible adverse reactions. Recent data suggest diffusion weighted imaging might fill this diagnostic gap. Irrespective of sequence technique chosen, bowel movement remains a major obstacle. Antispasmolytics in their function as smooth muscle relaxants help in improving image quality, however, their use in children might be off-label. Optimal preparation for the examination and appropriate imaging technique allow for diagnosing typical patterns of changes in IBD, such as bowel wall thickening, ulcers, mural stratification, strictures, creeping fat, and comb sign, and lymphadenopathy. The article gives a detailed overview of current significance of magnetic resonance imaging pediatric patients suffering from IBD, considering indications, limitations, and safety aspects.

Key words: Children; Adolescents; Inflammatory bowel disease; Crohn's disease; Ulcerative colitis; Magnetic resonance imaging; Enterography

Core tip: Diagnosis of chronic inflammatory bowel disease (IBD) is partially based on subsequent imaging. Magnetic resonance imaging (MRI) of the gastrointestinal tract (GIT) is established in adults for diagnosing IBD. In children and adolescents MRI is not routinely used up to now. This manuscript presents the commonly used magnetic resonance sequences for the evaluation of the GIT in children and adolescents. Techniques to obtain optimal bowel distension by oral intake or by using a nasally placed tube are described. Typical findings of intestinal and mesentery pathology in children suffering from IBD are shown.

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INTRODUCTION

Population-based studies suggest that inflammatory bowel disease (IBD) is unevenly distributed throughout the world with the highest incidence rate occurring in the Western world. However, emerging data have demonstrated a rising trend of IBD in Eastern countries[1]. In approximately 20%-30% of all affected patients with IBD the disease manifests in childhood[2]. Studies have shown a prevalence of as high as 16.6 per 100000 in the pediatric population[3]. Chronic IBD, namely Crohn's disease (CD) and ulcerative colitis (UC) seem to develop as a result of dysregulation of the immune response to normal gut flora in a genetically susceptible host[4] (Table 1). There are further reasons, like microvascular, infectious, and environmental co-factors to consider[5,6]. Moreover changes in lifestyle and diet, migration-related changes in genetic susceptibility, urbanization, and environmental changes may be relevant cofactors. Epidemiologic data indicate an increase in IBD in children. While CD and UC occur with equal distribution in adults, there are three new CD cases for each new UC case in pediatric age groups[7]. There are patients who, however, can't be classified as CD or UC. They are termed inflammatory bowel disease-undeterminate (IBD-U). In the pediatric population a greater number of IBD are labeled as IBD-U compared to adults. In adult IBD there is an equal ratio of male to female patients, or perhaps more women affected by the disease. In contrast, prepubertal males seem to be more affected than females, with a male predominance of 1.5:1[8]. Rarely, UC can even be found in young children and infants. In children an overlap of clinical findings can be observed, making differentiation of both entities in the pediatric patient difficult. IBD in children often relapses, making repeated imaging necessary.

CD can affect any part of the gastrointestinal (GI) tract, however, in children the distribution tends to be more proximal. The terminal ileum is the most common site of CD; however about 60% of pediatric patients show ileocolonic involvement, whereas 20%-30% have isolated colonic disease[1]. Transmural spread is a distinguishing feature of CD. Up to one third of patients will develop a perianal fistula or abscess at some point in their disease course. Skip lesions, fibrofatty proliferations, and mesenteric lymphadenopathy are common. In the case of chronification, fibrosis of the bowel wall may occur, resulting in stenotic bowel loops.

UC is mostly localized to the colon with the rectum affected primarily. Even if pancolitis is the most common presentation in childhood other features exist[9]. UC is a chronic inflammation involving exclusively the mucosa of the colon. Diarrhea and rectal bleeding is seen commonly in UC (50%-90% of cases)[10]. Contrary, perianal or perirectal disease is not a feature of UC.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Diagnosis of IBD is based on clinical presentation, laboratory and endoscopic assessments, histology and subsequent imaging[11,12]. Proper classification is necessary in order to determine the ideal treatment in children with chronic disease. The Montreal classification was adapted to the pediatric population[13]. In a child with bloody diarrhea a bacterial infection needs to be excluded first. Further differential diagnosis includes vasculitis, ischemic colitis, and hemolytic uremic syndrome. Bleeding without diarrhea is possible in children with fissure, vascular malformations, coagulation disorders, polyps, or Meckel diverticulum. Etiologies that can mimic IBD include appendicitis. Moreover, food allergies like cow's milk protein allergy can result in GI bleeding as early as in infancy. Laboratory studies can help to identify a child suspected to suffer from IBD and to monitor the course of the disease. Diagnostic imaging is necessary to describe the extension and grading of the inflammation. In children, ultrasound can be used with high success. The use of high frequency transducers (7-14 MHz) allows a detailed assessment of the whole bowel. Graded compression allows for displacement of adjacent bowel loops and interfering intraluminal gas. Color Doppler can be used to assess inflammation by demonstrating increased perfusion and vascularization. Significant correlations could be shown by considering bowel wall thickness, vascular pattern, and disease activity. Ultrasound can be used to appreciate extraintestinal findings (lymph node enlargement, abscesses), and to describe the surrounding mesenteric tissue. On the other side, ultrasound can fail to detect IBD in cases of superficial disease or if there are artifacts (*e.g.*, bowel gas). Also, ultrasound is an operator dependent modality; experience is necessary in order to make the correct diagnosis. Plain radiography is reserved for acute diseases. Findings are nonspecific and can include large bowel dilation, and small bowel distension. In the acute abdomen, the toxic megacolon or obstruction can be suspected. These cases have to be followed in order to detect possible bowel perforation. Contrast enema can be helpful for the evaluation of the extension of the disease, moreover, it is helpful to rule out or prove stenosis. Upper gastrointestinal series with small bowel barium follow through (SBFT) has been the cornerstone of small bowel imaging in the past[14]. The more sensitive enteroclysma was considered the gold standard (so-called Sellink technique), but it is not easy to perform, especially in younger children and infants. It requires the insertion of a naso-jejunal tube, for that it is poorly tolerated by children. It comes with a considerable higher radiation dose compared to SBFT[15]. Both methods suffer from one further major disadvantage: its

Table 1 Inflammatory bowel disease in children

	Crohn's disease	Ulcerative colitis
Etiology	Unknown (hereditary, immune response to gut flora)	
Incidence		
Site	Terminal ileum/SB/entire GIT	Colon/backwash ileitis
Pattern	Skip lesions, transmural, deep ulcerations	Diffuse mucosal
Acute complication	Obstruction, toxicity, hemorrhage, perforation	
Chronic complication	Stenosis, fistula, fissures, abscess, GIT cancer, extraintestinal manifestation	Extraintestinal manifestation, colorectal cancer

SB: Small bowel; GIT: Gastrointestinal tract; PSC: Primary sclerosing cholangitis.

very limited information regarding the extraluminal mesenteric extension of the disease. Computed tomography (CT) as a cross-sectional imaging method overcomes this and may be helpful in the acute situation, for planning surgery, especially in the evaluation of stricture or obstruction. Again, CT enteroclysma is poorly tolerated in children[16]. The major disadvantage of CT is the large amount of radiation exposure[17]. So, especially in children, techniques using ionizing radiation should be avoided if possible[18]. Leucocyte scintigraphy using white blood cells labeled with technetium 99m, and also positron emission tomography may be indicative in IBD, however, these techniques are not usually used. Because IBD is a diagnosis which should be proven by endoscopy with biopsy and histologic assessment, they are part of the diagnostic workflow. Endoscopy is the mainstay for evaluation, but provides limited access to the small bowel (terminal ileum and duodenum) and can be more limited in the presence of severe disease or strictures. Capsule endoscopy can overcome parts of these limitations, but has limitations as well especially in stricturing disease. Recent advances in magnetic resonance imaging (MRI) have the potential to emerge as useful imaging technique providing assessment of the whole gastrointestinal tract and to assess extra-intestinal involvement without ionizing radiation.

In adults MRI of the GI tract is now an established method when diagnosing chronic inflammatory bowel disease. In children and adolescents MRI is not routinely used, but some guidelines define MR as first line imaging modality in the investigation of the GI tract in suspected chronic inflammatory bowel disease. Especially the lack of radiation burden would favor the use of MRI. Further advantages include the superior soft tissue contrast and multiplanar imaging. Improvements in MR hardware include the availability of fast breath-hold sequences, decreased scan time and increased spatial resolution.

But, there are some difficulties of the technique in infants that limit the use of MRI. Children at school age have no problems with undergoing MR study, but the younger ones need to be handled gently because of reduced compliance. Numerous articles have been published on this topic discussing the complexity and also the financial impact on management. In the literature only few scientific reports and reviews on MRI of the GI tract in children can be found[19]. The purpose of this article is to present the commonly used MR sequences in children for the evaluation of the GI tract in the diagnosis and follow-up of IBD.

MR IMAGING OF THE BOWEL

Currently, there is no approved standard protocol for the evaluation of IBD using MRI. Applying a standard protocol without bowel distension is not helpful and results in false negative findings. The use of spasmolytics such as n-butylscopolamine (hyoscine) (0.5 mg/kg, up to 20 mg)[20] or glucagon[21] might meet the criteria of off-label use in some countries. Intravenous application of spasmolytics is given immediately before the start of the MR scans. A further bolus can be administered immediately before contrast media application. Metoclopramid (off-label in some countries) (0.15 mg/kg) can be given in the case of nausea. The cleansing preparation of the small bowel consists of a low-residue diet starting 3 d prior to the examination (no milk products, ample fluids, non-carbohydrate in order to avoid the generation of gas).

The cardinal principle to obtain diagnostic images is an optimal bowel distension of the bowel lumen. The loops need to be distended in order to detect changes in luminal diameter, which can be observed in cases with relative bowel stenosis. However, there is no consensus about the technique for optimal small-bowel distension[22]. Commonly used agents include methylcellulose, locust-bean gum, psyllium, and mannitol. There are very different protocols in the literature, ranging from oral application before entering the MR cabin (hydro MRI) to the MR enteroclysma procedure (MR Sellink) using application of methylcellulose while in the MR scanner *via* a nasojejunal tube.

Oral intake of endoluminal agents is mandatory. Some studies have shown, that oral intake is sufficient and increases the patient's compliance (which is necessary especially in follow-up studies)[23]. Unfortunately, sometimes the filling is inadequate and the distal/terminal ileum is not sufficiently distended (Figure 1). The most accurate results can be achieved with the MR enteroclysma technique[24]. Reports in the literature describe numerous different oral contrast media suitable for use, including plain water, mannitol, sorbitol, iron oxide, and barium sulfate, ispaghula husk, locust bean gum, planta ovate, and pineapple juice[25]. Based on their signal intensity in T1 weighted (T1w) and in T2 weighted (T2w) imaging, these contrast substances are divided

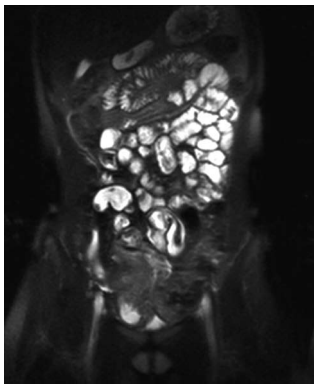

Figure 1 Hydro-magnetic resonance imaging using mannitol orally. Sometimes the filling result is inadequate and the distension of the bowel is insufficient.

into so-called positive (hyperintense in T1w and in T2w sequences) and negative (hypointense in T1w and in T2w sequences) contrast media. Some authors use a combination of barium sulfate and sorbitol as described by Sauer *et al*[26] who administered 450 cm^3 of 0.1% barium sulfate with sorbitol 90 min before imaging and a second amount of 450 cm^3 30 min before imaging[1]. Dagia *et al*[27] administered sorbitol orally (1000-1500 mL) as enteral contrast agent by adding 15 mL of sorbitol to 500 mL of water. Application started 60 min before the scan at a rate of 250-300 mL/15 min. If distension of the proximal small bowel was inadequate on initial MR acquisition (luminal diameter < 3 cm), another 250-300 mL of sorbitol was given[27]. Others use a suspension of polyethylene glycol (PEG; Klean-Prep®, Helsinn Birex Pharmaceuticals Ltd.) one hour before the investigation (1500 mL) after an overnight fasting state[20]. To render these mixtures more palatable, small amounts of orange flavoring may be added[3]. Mannitol and other hypertonic contrast agents may have side-effects, such as excessive diarrhea, which is an important issue, especially in children. The influence of the osmolarity for small bowel distension could be shown in a study by Ajaj *et al*[25] who compared a water solution combined with 2.0% sorbitol and 0.2% locust bean gum (quantity 1500 mL, osmolarity 1148 mOsmol/L) with a solution combined with 2.0% sorbitol and 2.0% barium sulfate (quantity 1000 mL; osmolarity 194 mOsmol/L). The mean loop diameter after solution administration with higher osmolarity increased over time (up to 30 min). The side effect rate of both solutions was low, but the smaller amount was more acceptable for patients[28]. Alexopoulou *et al*[29] used a total amount of 2.5 L of water solution containing 0.1 g/kg body weight of herbal fibres (psyllium) which was administered orally over a period of 4 h before MRI. This mixture has the property of retaining large amounts of water, up to 20 to 30 times its own volume, thus providing adequate distension. This agent also has biphasic properties, demonstrating low signal intensity in T1w images and high signal intensity in T2w images. MR enteroclysma-which the authors prefer-allows for dynamic filling of the small bowel. Thereby, relevant stenosis can be detected dynamically. In this procedure, the patients will be provided with a tube inserted nasally, which will then be proceeded past the ligament of Treitz under fluoroscopic guidance, using a reduced pulse rate (rate 3 pulses/s; fluoroscopy time 1-3 min[27]; authors' own experience: 4 s-1 min; Figure 2). The procedure of inserting and positioning of the catheter is the most challenging part of the entire procedure and can become a very unpleasant or almost intolerable maneuver for both the patient and the radiologist[30]. Approximately 1000-1500 mL prewarmed methylcellulose will be administered manually during the MR scanning process over a time period of up to 15 min using 50 mL syringes. The filling can be automated by a pump which usually needs to be placed outside of the scanner room. The filling process will be followed by using a single-shot heavily T2w sequence with thick slabs (7-10 cm) in coronal orientation which are sequentially acquired during continuous filling of the bowel (Figure 3). This dynamic acquisition results in a film sequence of the filling process which can be helpful in the detection of atonic bowel segments, and hyperperistalsis, or in the delineation of stenosis and luminal diameter changes. If the patient suffers from nausea, the filling process needs to be stopped and may be continued after recovery. The total amount of methylcellulose tolerated is limited by patient compliance and by the amount of backflow of cellulose into the duodenum and the stomach. Filling is finished if the terminal ileum is widened and the coecum/ascending colon start to become distended. Necessity of additional placement of a transrectal catheter and filling of the colon depends on the region of suspected pathology[31].

During the MR procedure the patients may be placed in the prone position, for a mild pressure to the anterior abdominal wall may result in better separation of the small-bowel loops. In case of MR enteroclysma this position will not be tolerated well. So, the authors suggest that the patient is placed in the standard supine position. In case of an unsuccessful separation of the loops the patient can be placed in the prone position at the end of the MR examination.

For MRI a dedicated multi-channel body array coil is used. The main technique involves MRI with ultrafast T2w sequences supplemented by dynamic contrast enhanced T1w scans in combination with fat saturation covering abdomen and pelvis, from the lung bases to the perineum. True steady-state free precession images (TRUFI) are obtained in the coronal plane for overview. T2w half-fourier acquisition single-shot turbo-spin-echo (HASTE) imaging is performed with long time of echo in axial and coronal orientation. T2w sequences are obtained with and without fat saturation. Fast low-angle shot T1w sequences (FLASH) are acquired in axial orientation. For dynamic multiphase contrast studies the authors use 3D sequences (T1-volume interpolated gradient-echo = VIBE) (Figure 4). Gadolinium-based agent at a dose of 0.1 mmol/kg will be administered intravenously. T1w VIBE sequences are acquired imme-

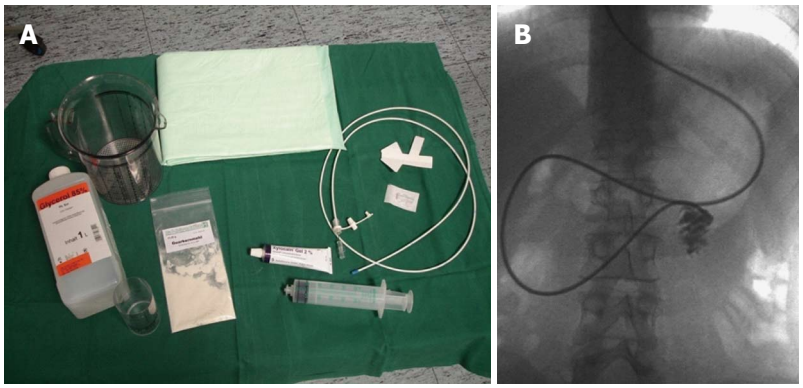

Figure 2 Magnetic resonance enteroclysma requires application of a nasojejunal tube (A) and placement will be guided by pulsed fluoroscopy (B).

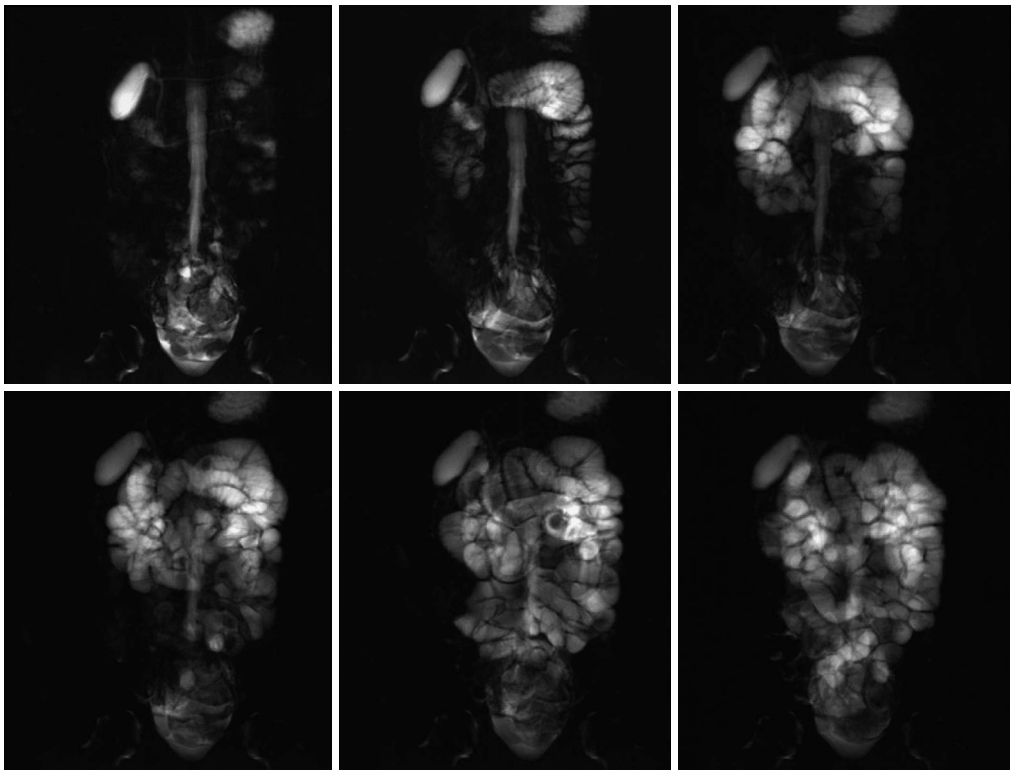

Figure 3 Enteral filling can be followed by using thick slab T2 weighted sequence (7-10 cm thickness).

diately after contrast application and repeated 30, 60, 90, and 180 s post injectionem (*p.i.*). Afterwards an axially oriented T1w FLASH sequence will be sampled in two stacks placed over epi- and mid-gastrium and over the pelvis. In case of suspected perineal/perirectal involvement further high-resolution sequences will be acquired in additional sagittal orientation, optionally with fat suppression (Table 2).

DISEASE EVALUATION USING MRI

MR imaging can detect a number of intestinal and extraintestinal findings which should be included in the report (Table 3). First of all the intestinal distension and caliber changes have to be described. Afterwards intestinal and mesentery pathologies have to be mentioned.

Transmural abnormalities, wall thickening, loss of layering, cobblestoning, ulceration, pseudo polyps, mural abscess, pseudo sacculation appearance, stenosis, strictures, prestenotic dilation can be described without contrast application by assessing high resolution T2w sequences.

Thickening and pronounced enhancement of the intestinal wall

Bowel wall thickness of more than 3 mm is considered pathologic[3]. Swelling of the wall is a result of interstitial edema. Increased signal in the bowel wall in edema sensitive T2w images (*e.g.*, sequence-short tau inversion recovery, STIR) may be suggestive for active disease (Figure 5). Hyperemia results in more or less increased signal intensity on T1w sequences after Gadolinium application, depending on disease activity (Figure 6). The degree of

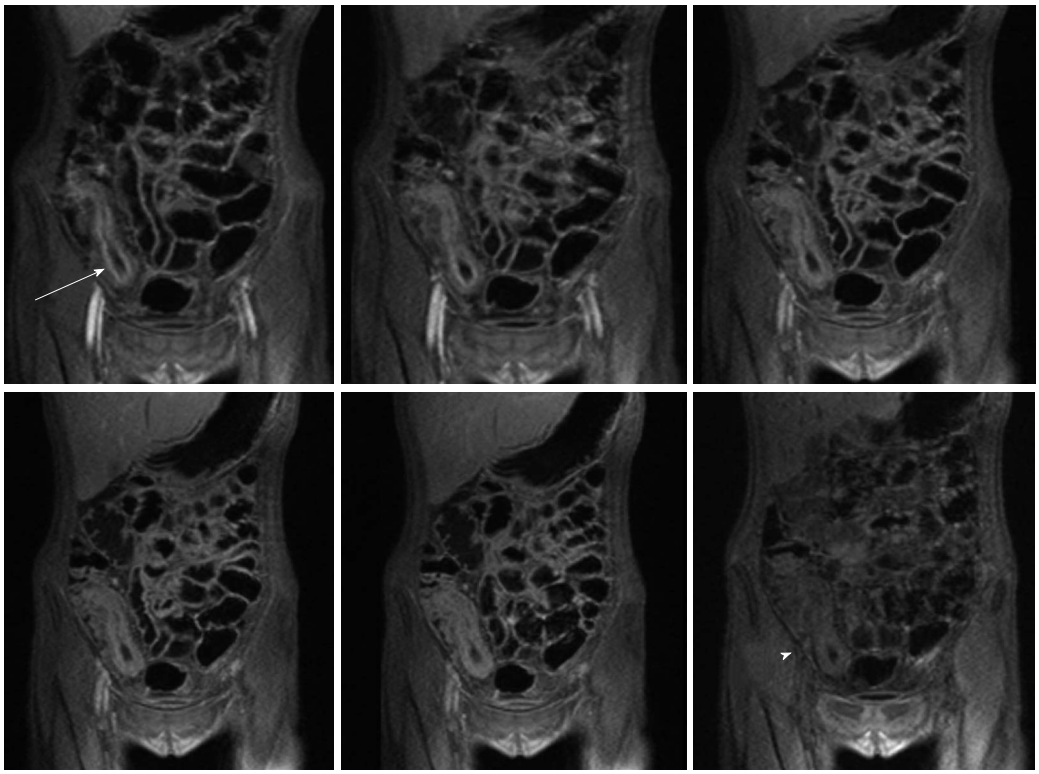

Figure 4 Dynamic contrast enhanced T1-volume interpolated gradient-echo sequence demonstrating different phases of signal increase in the various layers of the bowel wall [at first mucosa (arrow), followed by the serosa, the muscularis, and finally the submucosa (arrowhead)].

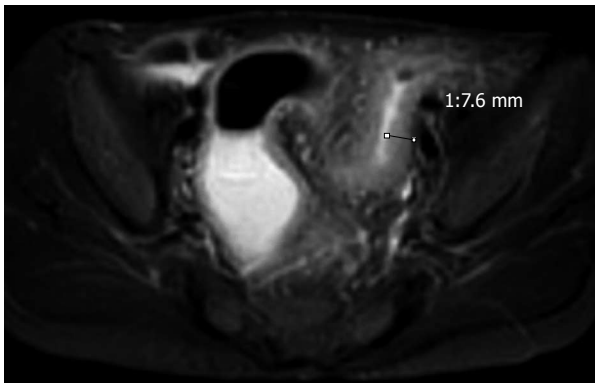

Figure 5 Eleven year old boy with Crohn's disease. T2 weighted sequence with fat saturation (Tirm/Stir) demonstrates thickening of the bowel wall and hyperintense signal corresponding to edema in acute inflammation. Narrowing of the lumen.

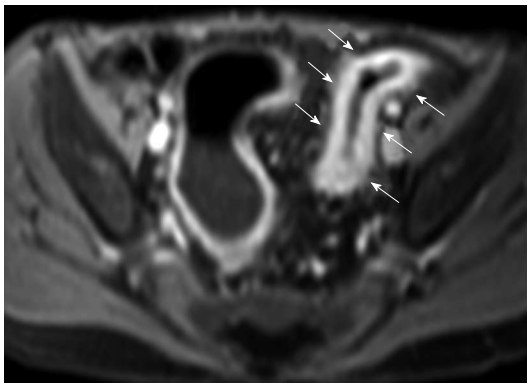

Figure 6 Eleven year old boy with Crohn's disease. T1 weighted contrast enhanced sequence shows strong transmural enhancement (arrows).

bowel enhancement following contrast application (0.1 mmol/kg body weight Gd DTPA *iv*) by evaluation the increase in signal intensity (SI) can help to differentiate active from chronic disease[29]. For quantification, Alexopoulou defined the percentage contrast enhancement as %CE = [(SI bowel postcontrast - SI bowel precontrast)/SI bowel precontrast] × 100. A layered enhancement pattern on T1w scans can be highly specific[29]. The use of contrast-enhanced MRI (CE-MRI) may be useful in diagnosing IBD, as well as in the differentiation between CD and UC[32]. A study in children by Laghi *et al*[33] correlated the semiquantitative score findings of MRI with endoscopic, histological, and CD activity index findings. MR showed a sensitivity of 84% and a specificity of 100%. Other studies showed no correlation between percental contrast enhancement of the bowel wall and the CD activity index in children[29]. New techniques like diffusion weighted imaging (DWI) are helpful adjuncts. DWI can be performed as transverse free-breathing echo planar imaging (EPI) sequence with diffusion-sensitizing gradients applied sequentially along the three orthogonal directions[34,35]. Using a diffusion gradient of three different b values (0, 50, 800 s/mm^2) the sensitivity and specificity compared to surgery and/or conventional enteroclysma was 86% and 97% in adults suffering from CD[34]. Neubauer *et al*[36] could prove DWI in combination with high-resolution T2w-HASTE is equal (if not superior) to CE-

Table 2 Sequence parameters used for magnetic resonance enterography (magnetic resonance avanto, magnetic resonance symphony)

Sequence	Orientation	Slice thickness (mm)	Time of repetition (ms)	Time of echo (ms)	Time of inversion (ms)	Flip angle (°)
TRUFI	Coronal	6	3.8	1.9		80
T2	Coronal	70-100	3000	985		180
TRUFI	Transverse	4	4.3	2.15		80
HASTE	Transverse	4-7	1000	87		150
VIBE	Coronal	2	3.18	1.1		9
FLASH	Transverse	4-5.5	233	1.91		70
TIRM	Transverse	8	5050	91	140	180
DWI	Transverse	5	5500	139		0

TRUE: True steady-state free precession images; HASTE: Half-fourier acquisition single-shot turbo-spin-echo; FLASH: Fast low-angle shot T1w sequences; VIBE: Volume interpolated gradient-echo; DWI: Diffusion weighted imaging.

Table 3 Magnetic resonance imaging features in inflammatory bowel disease in children differentiation active and fibrostenotic phase

Imaging features	Active inflammation	Fibrostenotic disease
Mural thickening	Moderate	Mild
Mural enhancement	Avid	Mild
Stratified enhancement	Yes	Variable
Mural edema	Yes	Mild/absent
Mesenteric adenopathy	Yes	No
Fibrofatty proliferation	Variable	Yes
Abscess, empyema, fistula	Complicated disease	Variable

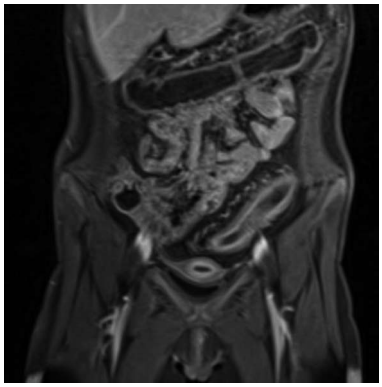

Figure 7 Stratified enhancement in the sigmoid in a female suffering from ulcerative colitis.

MRI for detecting inflammatory lesions in children with CD. Based on these two sequences imaging without the need of contrast media seems to be sufficient for diagnosis, reducing scanning time to less than 10 min. Using a high *b* value of 800 s/mm^2 for DWI the background signal arising from non-inflamed tissue and from body fluids can be largely suppressed, so that inflamed bowel segments are more easily detected. The same authors observed a reduction of the apparent diffusion coefficient (ADC) in the inflamed bowel segments based by an altered diffusivity of extracellular water in inflamed bowel wall tissue. This could also be shown by another study in children with terminal ileitis using a *b* value of 500 s/mm^2[37]. In this study there was a significant correlation between the bowel wall minimum ADC and established MRI markers of disease activity (bowel wall thickening, striated pattern of arterial enhancement, degree of arterial enhancement, degree of delayed enhancement, amount of mesenteric inflammatory changes, and presence of a stricture).

Mural stratification

The inflammatory process in CD results in a complete loss of the intestinal layering which can be detected by high-resolution MRI. The transmural aspect of CD results in homogeneous high signal intensity of the entire bowel wall without normal stratification after administration of Gd. Exclusive involvement of the mucosa is a typical sign of UC. The result is a stratified enhancement the so-called target or double halo appearance (Figure 7). So, in the examination report the two patterns of enhancement can be described as "homogeneous" or "stratified"[22]. The stratified enhancement pattern is typical for long-standing CD with fibrosis or in patients following intensive treatment.

Cobblestones and ulcers

Cobblestone formation is typically found in UC patients and less often in CD. The development of aphthous lesions along the mucosa result in deep linear or stellate lesions. Deep ulcers can be found in CD patients.

Strictures and stenosis

Whenever there is a procedural adequate distension of the bowel a reduction of the diameter (normally around 2.5 cm) is suspected a stricture. Chronic IBD-affected bowel segments may result in strictures. The presence of a pre-stenotic dilation may help in the diagnosis. Long-standing fibrotic strictures with a thick hypointense wall can be diagnosed on heavily T2w sequences. Notice that there is no significant contrast enhancement. Inflamed bowel segments tend to show a reduction of the size of the intraluminal diameter. The strictures can be demonstrated more sensitively using dynamic filling of the bowel with MR enteroclysma technique compared to hydro-MRI technique (Figure 8). In the case of lymph node bulking the bowel diameter can also be reduced. Description of localization and length of the involved bowel segment is necessary for planning surgery.

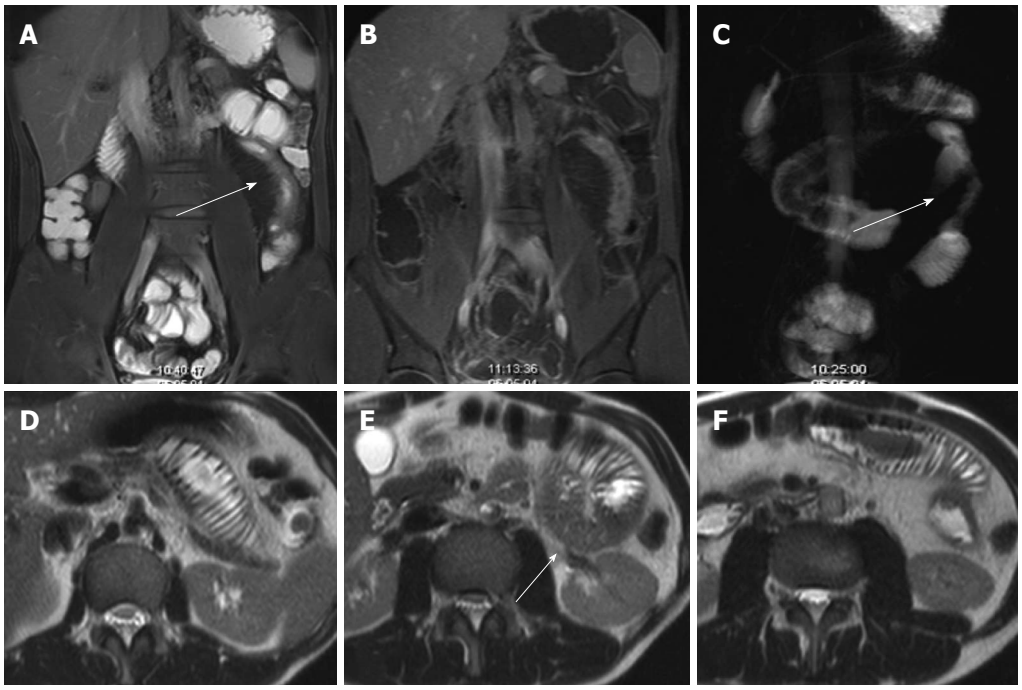

Figure 8 Stricture in inflammatory bowel diseases-chronic phase, no activity of inflammation. There is no edema with reduced signal intensity in T2 weighted sequences (A, D, arrow). The MR enteroclysma does not show any widening of the involved jejuna bowel loop (C, arrow), also seen in axial T2w sequence (D-F). There is moderate enhancement (B).

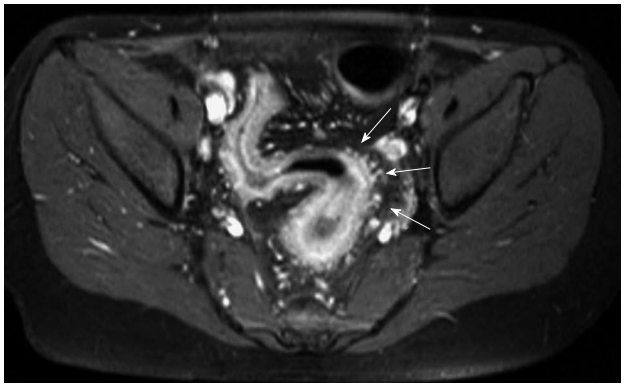

Figure 9 Twelve year old female with Crohn's disease. Comb sign. CE-T1 weighted sequence with fat saturation. Blood vessels within the mesentery (arrows).

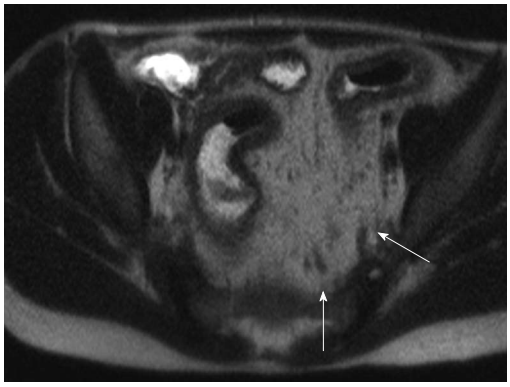

Figure 10 Eleven year old male with Crohn's disease. Creeping fat sign (arrows).

Extramural findings

The extramural signs of IBD such as free fluid, peritoneal fat stranding and enhancement, mesenteric edema, fibrofatty proliferation, the comb sign, mesenteric lymph nodes, abscesses, fistulas can be easily detected by MRI. Especially for the evaluation of perineal complications MRI is the gold standard nowadays. In a meta-analysis including 33 articles. Horsthuis *et al*[38] showed the highest sensitivity in MR enteroclysma compared to hydro MRI, however, in children sensitivity was lower than in adults. One reason may be the lower amount of mesenteric fat which helps in separating the bowel loop segments for image interpretation. Motion artifacts, reduced complicance might be further possible reasons.

Comb sign

This is a sign of active inflammation (typical of CD) describing the vascular engorgement of the vasa recta on the mesenteric side of the bowel wall. The comb sign may be appreciated well on fat-saturated sequences as multiple tubular, sometimes tortuous vessels, aligned like the teeth of a comb (Figure 9).

Creeping fat sign

The chronic inflammation of the mesenteric fatty tissue induces a proliferation of the fat tissue itself together with a fibrotic component along the mesenteric border of inflamed bowel segments. This is the so called fibro-fatty proliferation which is also a typical CD sign. MR imaging can show a pseudo-mass which is surrounding the bowel

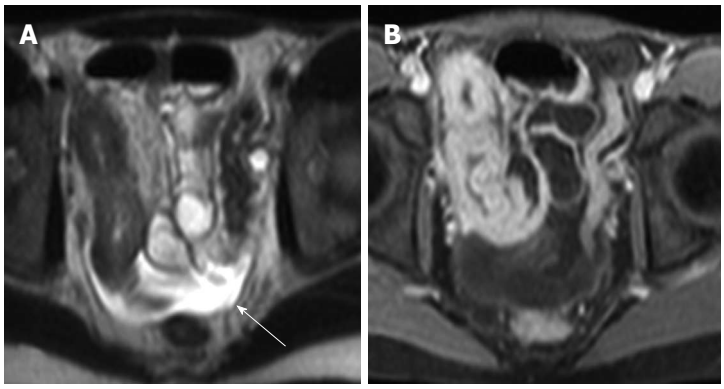

Figure 11 Thirteen years old girl with Crohn's disease. A: T2w image demonstrating strong hyperintense ascites. Arrow marks the free ascites; B: T1w sequence after contrast application. Fluid is not as easily detected as in T2w images. T1w: T1 weighted; T2w: T2 weighted.

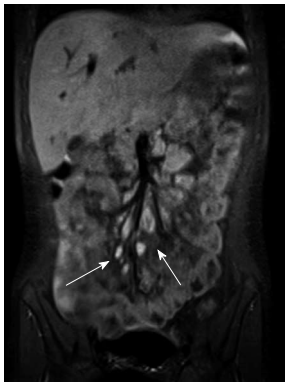

Figure 12 Coronally oriented true steady-state free precession images shows enlarged mesenteric lymph nodes (arrows).

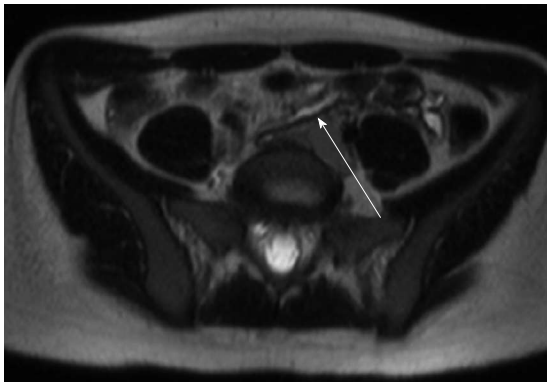

Figure 13 Seventeen years female with Crohn's disease. T2 weighted sequence showing enterocolic fistula (arrow).

loop with intermediate T2w signal intensity corresponding to fibrous or/and fatty components (Figure 10).

Free fluid

The distribution and amount should be described. Using the signal intensity on T1w and T2w sequences different entities (blood, pus, ascites) can be suspected (Figure 11). Diffusion weighted imaging is helpful in distinguishing serous fluid and empyema/pus.

Mesenteric lymph nodes

Mesenteric lymphadenopathy is well-depicted using TRUFI or T2w TSE sequences (Figure 12). In case there are multiple and round lymph nodes larger than 10 mm in diameter lymphoma needs to be excluded. As first choice follow-up imaging using ultrasound is recommended in these patients.

Fistula, abscess, phlegmon

Fistulas can be categorized as enteroenteric, enterocolic, enterovesical, enterocutaneous, or complex perianal (Figure 13). Fistulas are typically found in sites where two inflamed bowel segments are in close proximity to each other or in regions with high-grade bowel stenosis[39]. Typically, the fistulous tract shows strong enhancement which can be differentiated using fat-suppressed T1w high-resolution sequences. The direct visualization of the fistulous tract is not always possible, but indirect signs can be recognized. So, around the sinus tract inhomogeneity and enhancement of the mesenteric fat can be demonstrated. Other extraintestinal findings may be a psoas muscle abscess, and sacroiliitis (Figure 14). In these cases MRI of the pelvis will be recommended.

LIMITATIONS AND DEVELOPMENTS

The greatest limitation of MR enterography especially in children is the dependence on a compliant patient. It should be considered, that the patient is strained by fluid placement, application of contrast agents and motility influencing agents, and breath-holding maneuvers. Artifacts may be the result of bowel, breathing, and patient moving. In order to reduce these motion artifacts, two techniques can be applied: parallel imaging, navigator techniques, and motion correction[40]. The use of higher field strength results in a greater signal-to-noise-ratio and has the potential of reducing scan time and increasing the spatial resolution[5,28]. However, there is a concurrent increase in artifacts, especially chemical shift artifacts and susceptibility artifacts in abdominal imaging using gradient-echo imaging like TRUFI, CE-T1 VIBE, and FLASH. The T2w HASTE is more robust[41]. Con-

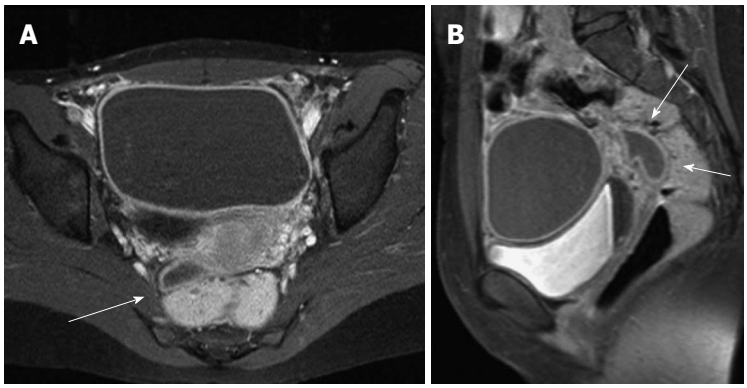

Figure 14 Female with Crohn's disease. Sagittal T1 weighted sequence allows to describe presacral abscess (arrow). Fat saturation was applied. A: Axial image; B: Sagittal image (arrows marking abscess; late contrast phase. Notice sedimentation of different components in the bladder).

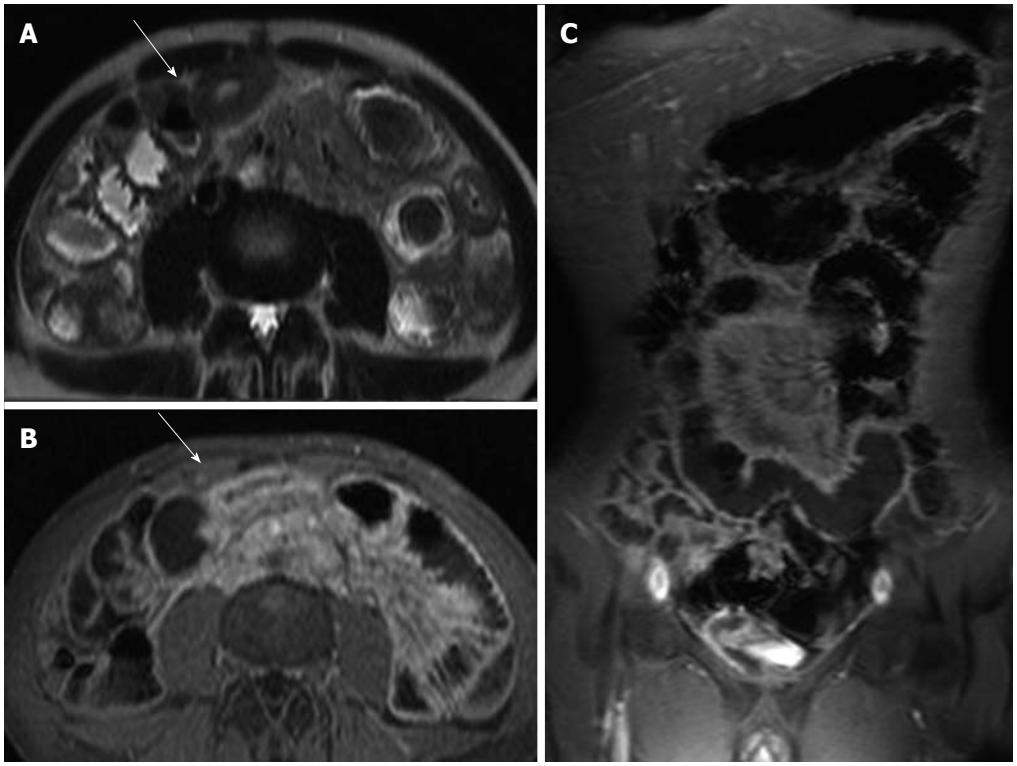

Figure 15 Magnetic resonance enterography allows an overview about involved bowel segments. In this case there was an isolated involvement of the jejunum. A: Axial T2w sequence showing thickened bowel wall without edema; B, C: Axial and coronal fat saturated contrast-enhanced T1w sequence demonstrating transmural enhancement in Crohn's disease. T1w: T1 weighted; T2w: T2 weighted.

sequently, the feasibility of high-field MRI in children suffering from IBD should be studied in the future. The MR study is time consuming and staff-intensive. So, the use of a modified examination consisting of Diffusion weighted imaging with high *b* values from 600 to 1300 s/mm^2[5] and high resolution T2w sequences (isovoxel 3D with multiplanar reformation in three orthogonal directions) has to be evaluated in the future as a standard examination protocol resulting in a scanning time of not more than 10 min. This protocol can be used for routine controls. But, in the case of newly diagnosed IBD and in cases of relapse the examination has to be more extensive.

CONCLUSION

There are still sites that prefer fluoroscopic contrast studies and multislice CT in the diagnosis of IBD, also in children. But, the development of the last decade promises the increasing value of MR imaging in the evaluation of the intestine. MR enterography has definitely advantages including the detection and assessment of disease activity of the entire gut and the ability to evaluate extraluminal disease (Figure 15) and is therefore becoming the standard assessment of the small bowel in many centers. The radiation free ultrasound performed with adequate technique and experience by the sonographer should

be used as initial imaging method. MR imaging should be performed at the initial diagnosis of CD and should considered in any case of treatment changes, especially if surgery is planned.

REFERENCES

1 **Shikhare G**, Kugathasan S. Inflammatory bowel disease in children: current trends. *J Gastroenterol* 2010; **45**: 673-682 [PMID: 20414789 DOI: 10.1007/s00535-010-0241-5]
2 **Mann EH**. Inflammatory bowel disease: imaging of the pediatric patient. *Semin Roentgenol* 2008; **43**: 29-38 [PMID: 18053826 DOI: 10.1053/j.ro.2007.08.005]
3 **Cosgrove M**, Al-Atia RF, Jenkins HR. The epidemiology of paediatric inflammatory bowel disease. *Arch Dis Child* 1996; **74**: 460-461 [PMID: 8669968 DOI: 10.1136/adc.74.5.460]
4 **Scherr R**, Essers J, Hakonarson H, Kugathasan S. Genetic determinants of pediatric inflammatory bowel disease: is age of onset genetically determined? *Dig Dis* 2009; **27**: 236-239 [PMID: 19786746 DOI: 10.1159/000228555]
5 **Gorincour G**, Aschero A, Desvignes C, Portier F, Bourlière-Najean B, Ruocco-Angari A, Devred P, Colavolpe N, Roquelaure B, Delarue A, Petit P. Chronic inflammatory diseases of the bowel: diagnosis and follow-up. *Pediatr Radiol* 2010; **40**: 920-926 [PMID: 20432009 DOI: 10.1007/s00247-010-1627-5]
6 **Schirbel A**, Fiocchi C. Inflammatory bowel disease: Established and evolving considerations on its etiopathogenesis and therapy. *J Dig Dis* 2010; **11**: 266-276 [PMID: 20883422 DOI: 10.111/j.1751-2980.2010.0049.x]
7 **Kugathasan S**, Judd RH, Hoffmann RG, Heikenen J, Telega G, Khan F, Weisdorf-Schindele S, San Pablo W, Perrault J, Park R, Yaffe M, Brown C, Rivera-Bennett MT, Halabi I, Martinez A, Blank E, Werlin SL, Rudolph CD, Binion DG. Epidemiologic and clinical characteristics of children with newly diagnosed inflammatory bowel disease in Wisconsin: a statewide population-based study. *J Pediatr* 2003; **143**: 525-531 [PMID: 14571234 DOI: 10.1067/S0022-3476(03)00444-X]
8 **Van Limbergen J**, Russell RK, Drummond HE, Aldhous MC, Round NK, Nimmo ER, Smith L, Gillett PM, McGrogan P, Weaver LT, Bisset WM, Mahdi G, Arnott ID, Satsangi J, Wilson DC. Definition of phenotypic characteristics of childhood-onset inflammatory bowel disease. *Gastroenterology* 2008; **135**: 1114-1122 [PMID: 18725221 DOI: 10.1053/j.gastro.2008.06.081]
9 **Aloi M**, D'Arcangelo G, Pofi F, Vassallo F, Rizzo V, Nuti F, Di Nardo G, Pierdomenico M, Viola F, Cucchiara S. Presenting features and disease course of pediatric ulcerative colitis. *J Crohns Colitis* 2013; **7**: e509-e515 [PMID: 23583691 DOI: 10.1016/j.crohns.2013.03.007]
10 **Fish D**, Kugathasan S. Inflammatory bowel disease. *Adolesc Med Clin* 2004; **15**: 67-90, ix [PMID: 15272257 DOI: 10.1016/j.admecli.2003.11.012]
11 **de Bie CI**, Buderus S, Sandhu BK, de Ridder L, Paerregaard A, Veres G, Dias JA, Escher JC. Diagnostic workup of paediatric patients with inflammatory bowel disease in Europe: results of a 5-year audit of the EUROKIDS registry. *J Pediatr Gastroenterol Nutr* 2012; **54**: 374-380 [PMID: 21857248 DOI: 10.1097/MPG.0b013e318231d984]
12 **Turner D**, Levine A, Escher JC, Griffiths AM, Russell RK, Dignass A, Dias JA, Bronsky J, Braegger CP, Cucchiara S, de Ridder L, Fagerberg UL, Hussey S, Hugot JP, Kolacek S, Kolho KL, Lionetti P, Paerregaard A, Potapov A, Rintala R, Serban DE, Staiano A, Sweeny B, Veerman G, Veres G, Wilson DC, Ruemmele FM. Management of pediatric ulcerative colitis: joint ECCO and ESPGHAN evidence-based consensus guidelines. *J Pediatr Gastroenterol Nutr* 2012; **55**: 340-361 [PMID: 22773060 DOI: 10.1097/MPG.0b013e3182662233]
13 **Levine A**, Griffiths A, Markowitz J, Wilson DC, Turner D, Russell RK, Fell J, Ruemmele FM, Walters T, Sherlock M, Dubinsky M, Hyams JS. Pediatric modification of the Montreal classification for inflammatory bowel disease: the Paris classification. *Inflamm Bowel Dis* 2011; **17**: 1314-1321 [PMID: 21560194 DOI: 10.1002/ibd.21493]
14 **Stenerson M**, Vittinghoff E, Heyman MB, Kim GE, Gupta N. Role of small bowel follow-through in diagnosing inflammation of the terminal ileum in pediatric patients. *J Pediatr Gastroenterol Nutr* 2010; **51**: 433-436 [PMID: 20562720 DOI: 10.1097/MPG.0b013e318d67ea7]
15 **Stuart S**, Conner T, Ahmed A, Steward M, Maclachlan J, Wylie P, Beal I. The smaller bowel: imaging the small bowel in paediatric Crohn's disease. *Postgrad Med J* 2011; **87**: 288-297 [PMID: 21242573 DOI: 10.1136/pgmj.2010.106641]
16 **Bender GN**, Timmons JH, Williard WC, Carter J. Computed tomographic enteroclysis: one methodology. *Invest Radiol* 1996; **31**: 43-49 [PMID: 8850364 DOI: 10.1097/00004424-199601000-00007]
17 **Gaca AM**, Jaffe TA, Delaney S, Yoshizumi T, Toncheva G, Nguyen G, Frush DP. Radiation doses from small-bowel follow-through and abdomen/pelvis MDCT in pediatric Crohn disease. *Pediatr Radiol* 2008; **38**: 285-291 [PMID: 18183380 DOI: 10.1007/s00247-007-0702-z]
18 **Brenner DJ**. Should computed tomography be the modality of choice for imaging Crohn's disease in children? The radiation risk perspective. *Gut* 2008; **57**: 1489-1490 [PMID: 18941001 DOI: 10.1136/gut.2008.156265]
19 **Hörmann M**. MR imaging of the gastro-intestinal tract in children. *Eur J Radiol* 2008; **68**: 271-277 [PMID: 18762396 DOI: 10.1016/j.ejrad.2008.07.019]
20 **Albert JG**, Martiny F, Krummenerl A, Stock K, Lesske J, Göbel CM, Lotterer E, Nietsch HH, Behrmann C, Fleig WE. Diagnosis of small bowel Crohn's disease: a prospective comparison of capsule endoscopy with magnetic resonance imaging and fluoroscopic enteroclysis. *Gut* 2005; **54**: 1721-1727 [PMID: 16020490 DOI: 10.1136/gut.2005.069427]
21 **Froehlich JM**, Daenzer M, von Weymarn C, Erturk SM, Zollikofer CL, Patak MA. Aperistaltic effect of hyoscine N-butylbromide versus glucagon on the small bowel assessed by magnetic resonance imaging. *Eur Radiol* 2009; **19**: 1387-1393 [PMID: 19190916 DOI: 10.1007/s00330-008-1293-2]
22 **Paolantonio P**, Ferrari R, Vecchietti F, Cucchiara S, Laghi A. Current status of MR imaging in the evaluation of IBD in a pediatric population of patients. *Eur J Radiol* 2009; **69**: 418-424 [PMID: 19144484 DOI: 10.1016/j.ejrad.2008.11.023]
23 **Negaard A**, Sandvik L, Berstad AE, Paulsen V, Lygren I, Borthne A, Klow NE. MRI of the small bowel with oral contrast or nasojejunal intubation in Crohn's disease: randomized comparison of patient acceptance. *Scand J Gastroenterol* 2008; **43**: 44-51 [PMID: 18158695 DOI: 10.1080/00365520701494813]
24 **Sanka S**, Gomez A, Set P, Rimareva N, Davies RJ, Rolfe P, Noble-Jamieson G, Torrente F, Heuschkel R, Zilbauer M. Use of small bowel MRI enteroclysis in the management of paediatric IBD. *J Crohns Colitis* 2012; **6**: 550-556 [PMID: 22398053 DOI: 10.1016/j.crohns.2011.10.014]
25 **Ajaj W**, Goyen M, Schneemann H, Kuehle C, Nuefer M, Ruehm SG, Goehde SC, Lauenstein TC. Oral contrast agents for small bowel distension in MRI: influence of the osmolarity for small bowel distention. *Eur Radiol* 2005; **15**: 1400-1406 [PMID: 15754160 DOI: 10.1007/s00330-005-2711-3]
26 **Sauer CG**, Middleton JP, Alazraki A, Udayasankar UK, Kalb B, Applegate KE, Martin DR, Kugathasan S. Comparison of magnetic resonance enterography with endoscopy, histopathology, and laboratory evaluation in pediatric Crohn disease. *J Pediatr Gastroenterol Nutr* 2012; **55**: 178-184 [PMID: 22513710 DOI: 10.1097/MPG.0b013e3182598465]
27 **Dagia C**, Ditchfield M, Kean M, Catto-Smith T. Imaging for Crohn disease: use of 3-T MRI in a paediatric setting. *J Med Imaging Radiat Oncol* 2008; **52**: 480-488 [PMID: 19032394 DOI:

10.1111/j.1440-1673.2008.01993x]
28 **Rimola J**, Rodríguez S, García-Bosch O, Ricart E, Pagès M, Pellisé M, Ayuso C, Panés J. Role of 3.0-T MR colonography in the evaluation of inflammatory bowel disease. *Radiographics* 2009; **29**: 701-719 [PMID: 19448111 DOI: 10.1148/rg.293085115]
29 **Alexopoulou E**, Roma E, Loggitsi D, Economopoulos N, Papakonstantinou O, Panagiotou I, Pahoula I, Kelekis NL. Magnetic resonance imaging of the small bowel in children with idiopathic inflammatory bowel disease: evaluation of disease activity. *Pediatr Radiol* 2009; **39**: 791-797 [PMID: 19452148 DOI: 10.1007/s00247-009-1272]
30 **Schreyer AG**, Seitz J, Feuerbach S, Rogler G, Herfarth H. Modern imaging using computer tomography and magnetic resonance imaging for inflammatory bowel disease (IBD) AU1. *Inflamm Bowel Dis* 2004; **10**: 45-54 [PMID: 15058527]
31 **Narin B**, Ajaj W, Göhde S, Langhorst J, Akgöz H, Gerken G, Rühm SG, Lauenstein TC. Combined small and large bowel MR imaging in patients with Crohn's disease: a feasibility study. *Eur Radiol* 2004; **14**: 1535-1542 [PMID: 15221267 DOI: 10.1007/s00330-004-2364-7]
32 **Darbari A**, Sena L, Argani P, Oliva-Hemker JM, Thompson R, Cuffari C. Gadolinium-enhanced magnetic resonance imaging: a useful radiological tool in diagnosing pediatric IBD. *Inflamm Bowel Dis* 2004; **10**: 67-72 [PMID: 15168803 DOI: 10.1097/00054725-200403000-00001]
33 **Laghi A**, Borrelli O, Paolantonio P, Dito L, Buena de Mesquita M, Falconieri P, Passariello R, Cucchiara S. Contrast enhanced magnetic resonance imaging of the terminal ileum in children with Crohn's disease. *Gut* 2003; **52**: 393-397 [PMID: 12584222 DOI: 10.1136/gut.52.3.393]
34 **Kiryu S**, Dodanuki K, Takao H, Watanabe M, Inoue Y, Takazoe M, Sahara R, Unuma K, Ohtomo K. Free-breathing diffusion-weighted imaging for the assessment of inflammatory activity in Crohn's disease. *J Magn Reson Imaging* 2009; **29**: 880-886 [PMID: 19306416 DOI: 10.1002/jmri.21725]
35 **Oto A**, Kayhan A, Williams JT, Fan X, Yun L, Arkani S, Rubin DT. Active Crohn's disease in the small bowel: evaluation by diffusion weighted imaging and quantitative dynamic contrast enhanced MR imaging. *J Magn Reson Imaging* 2011; **33**: 615-624 [PMID: 21563245 DOI: 10.1002/jmri.22435]
36 **Neubauer H**, Pabst T, Dick A, Machann W, Evangelista L, Wirth C, Köstler H, Hahn D, Beer M. Small-bowel MRI in children and young adults with Crohn disease: retrospective head-to-head comparison of contrast-enhanced and diffusion-weighted MRI. *Pediatr Radiol* 2013; **43**: 103-114 [PMID: 23212595 DOI: 10.1007/s00247-012-2492-1]
37 **Ream JM**, Dillman JR, Adler J, Khalatbari S, McHugh JB, Strouse PJ, Dhanani M, Shpeen B, Al-Hawary MM. MRI diffusion-weighted imaging (DWI) in pediatric small bowel Crohn disease: correlation with MRI findings of active bowel wall inflammation. *Pediatr Radiol* 2013; **43**: 1077-1085 [PMID: 23949929 DOI: 10.1007/s00247-013-2712-3]
38 **Horsthuis K**, Bipat S, Bennink RJ, Stoker J. Inflammatory bowel disease diagnosed with US, MR, scintigraphy, and CT: meta-analysis of prospective studies. *Radiology* 2008; **247**: 64-79 [PMID: 18372465 DOI: 10.1148/radiol.2471070611]
39 **Chalian M**, Ozturk A, Oliva-Hemker M, Pryde S, Huisman TA. MR enterography findings of inflammatory bowel disease in pediatric patients. *AJR Am J Roentgenol* 2011; **196**: W810-W816 [PMID: 21606274 DOI: 10.2214/AJR.10.5474]
40 **Yang RK**, Roth CG, Ward RJ, deJesus JO, Mitchell DG. Optimizing abdominal MR imaging: approaches to common problems. *Radiographics* 2010; **30**: 185-199 [PMID: 20083593 DOI: 10.1148/rg.301095076]
41 **Dagia C**, Ditchfield M, Kean M, Catto-Smith A. Feasibility of 3-T MRI for the evaluation of Crohn disease in children. *Pediatr Radiol* 2010; **40**: 1615-1624 [PMID: 20689946 DOI: 10.1007/s00247-010-1781-9]

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