MR enterography in children: Principles, technique, and clinical applications

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Abstract
MR enterography is a constantly advancing technique for assessment of bowel with newer technology and sequences. It is being increasingly used for the assessment of inflammatory bowel disease and has almost replaced barium follow through examinations in many institutions. Its lack of radiation makes it an attractive alternative for bowel evaluation in children. It has been proved to be highly sensitive in the detection of Crohn disease in adults and children. It is also superior to barium studies in showing extra-enteric findings and detecting complications such as fistulas and abscesses. Even though at present it is almost exclusively used for the evaluation of inflammatory bowel disease, it has the potential to be used in other conditions affecting the bowel. The principles, MR enterography technique pertinent to children, and its utility in the assessment of Crohn disease in children are discussed in this review.

Key words: Children; crohn disease; MR enterography; tuberculosis

Introduction
MR enterography (MRE) is a new technique that has become widespread during the last few years. In children, it is replacing fluoroscopic barium studies as against the transition from CT enterography to MRE in adults. Apart from having distinct advantage of showing extraluminal and mural abnormalities with superior soft-tissue contrast, MRE is well suited for children because of its lack of radiation. The most common indication for MRE is inflammatory bowel disease with Crohn disease much more common than ulcerative colitis. About 25-30% of patients affected with Crohn disease are children.[1]

In this article, we discuss the principles, technique, normal appearances, and range of abnormal findings in inflammatory bowel disease in children. This technique will also be useful for the evaluation of abdominal tuberculosis.

Principles
Normal bowel wall is difficult to image by MR imaging because it is a thin structure, a moving target, and has mixed intraluminal content, especially the gas in it causes obscuration of the wall by artifacts. Moreover, assessment of the bowel wall thickness is correct only when the bowel is optimally distended. Once these challenges are overcome, imaging of the bowel wall becomes possible. Faster sequences and anti-peristaltic agents help to counteract the motion. Luminal contrast agents distend the bowel loops and remove the intraluminal air. So, MRE comprises distension of bowel with intraluminal contrast, reducing the peristalsis by anti-peristaltic agents, and imaging with faster sequences. With the advancement of the technique, real-time assessment of peristalsis by cine sequences and another indicator of inflammation in the form of diffusion-weighted imaging (DWI) have also become an integral part of MRE.

Technique
Preparation
MRE is still limited to older children, usually above 6-7 years of age, who can be scanned awake because the intraluminal contrast cannot be given in those who will need sedation.
or anesthesia for scanning. Children are kept fasting for 4-6 h before the scan.[3]

Intraluminal contrast

Intraluminal contrast can be administered orally as in MRE or by a nasojejunal (NJ) tube. When the contrast is administered by the NJ tube, the technique is called “MR enteroclysis.” It has the advantages of better bowel distension, especially jejunal loops, and better delineation of mucosal ulceration.[4,5] However, placement of the NJ tube under fluoroscopy involves radiation and makes the procedure more invasive. Children may not be compliant for MR enteroclysis. All these factors make MRE a better choice in children. Common choices of biphasic intraluminal contrast (hypointense on T1W and hyperintense on T2W images) include VoLumen (EZ-E-M, Westbury, NY, USA), polyethylene glycol, and 3% sorbitol. We use 3% sorbitol solution prepared by our pharmacy and add some flavoring powder (e.g., Rasna) to it. This is much cheaper than the other agents and well tolerated by most children. There is variability in the amount of oral contrast administered in the literature, with typical amount ranging between 500 and 1500 ml.[2,4,5] The overall amount of intraluminal contrast used is 20 ml/kg of body weight up to a maximum of 1200 ml. Outpatient arrives in the MRI department 1 h prior to start of the scan and starts drinking the contrast at least 45 min prior to start of the scan. Half the total amount (10 ml/kg) is given at the beginning about 45 min before the scan, one-fourth (5 ml/kg) is given half an hour before, and the remaining (5 ml/kg) is given 15 min before the scan. Drinking the oral contrast in 45 min time maintains tight bolus and optimally distends the bowel loops.

Anti-peristaltic and intravenous contrast agents

Anti-peristaltic agents include hyoscine butylbromide (Buscopan; Boehringer Ingelheim, Ingelheim, Germany) and glucagon (Glucagen; Novo Nordisk, Bagsvaerd, Denmark). Buscopan is administered intravenously slowly over 2 min at a dose of 0.3 mg/kg, with a maximum dose of 20 mg. Glucagon is administered intravenously slowly at a dose of 0.25 mg for children with body weight less than 20 kg and at a dose of 0.5 mg for children with body weight over 20 kg. Buscopan is much cheaper than glucagon. The first dose of anti-peristaltic agent is administered after the initial evaluation sequence done for distension of loops and the cine sequence, while the second dose is given at the time of intravenous contrast agent administration. Standard dose (0.1 mmol/kg) of gadolinium-based contrast media is administered intravenously.

Patient positioning

Children are asked to empty their bladder immediately before taking on the table. Prone position has potential advantages of less breathing-related motion, compression of abdomen with less number of slices, and better distension of loops. However, it may not be tolerated by children with distended bowel loops. In supine position, residual intraluminal air goes anteriorly and does not interfere with most of the loops. Residual intraluminal air in the prone position may go posteriorly and cause susceptibility artifacts in the middle of the abdomen.

Sequences

The sequences used for MRE include single-shot T2 fast spin-echo (HASTE/SSFSE), balanced SSFP (TrueFISP/FIESTA/bTFE) and T1 3D gradient-echo (VIBE/LAVA/THRIVE) sequences in axial and coronal planes [Figure 1A-F]. Combination of sequences is listed in Table 1.

Balanced SSFP sequence can also be acquired with respiratory triggering or with breath hold. It is useful to show gross anatomy, bowel wall edema, mesenteric edema, lymph nodes, and collections. It is less susceptible to artifacts including motion and susceptibility. Initial evaluation SSFSE sequence in coronal plane can be acquired without fat saturation for gross anatomy, while the coronal SSFSE after anti-peristaltic agent can be fat saturated to show the bowel wall and mesenteric edema better.

T1-weighted 3D gradient-echo (T1 3D GRE) sequence is typically acquired with breath hold before and after gadolinium-based contrast injection. It is useful to show thickening and enhancement of bowel wall, engorgement of vessels, lymph nodes, fistulous tracts, and abscesses. In

Table 1: Sequences used in MRE

<table>
<thead>
<tr>
<th>Sequence</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>Cor single-shot T2 BH</td>
<td>Cor B-TFE/TruFISP/FIESTA CINE</td>
</tr>
<tr>
<td>A single-shot T2 BH</td>
<td>Inject buscopan or glucagon IV slowly</td>
</tr>
<tr>
<td>Ax B-TFE/TruFISP/FIESTA fatsat RT</td>
<td>Cor B-TFE/TruFISP/FIESTA fatsat BH</td>
</tr>
<tr>
<td>Ax diffusion RT (b-values 0, 100, and 600-800)</td>
<td>PreGd Cor VIBE/THRIVE/LAVA BH</td>
</tr>
<tr>
<td>Gad + IV 2nd dose of buscopan/glucagon</td>
<td>Gd Cor VIBE/THRIVE/LAVA BH</td>
</tr>
</tbody>
</table>
our experience, it is the best sequence that shows location of terminal ileum and bowel wall thickening.

In addition, some authors\textsuperscript{[5]} use fat-saturated axial T2 fast spin-echo images for better assessment of bowel wall signal to differentiate active inflammation (hyperintense wall) from fibrosis (hypointense bowel wall). However, this sequence takes a long time, and peristaltic and breathing artifacts may not be completely eliminated.

**Cine imaging for bowel peristalsis**

Balanced SSFP sequence can be acquired as cine sequence for real-time assessment of the bowel movement. This is typically acquired in coronal plane as a 7-mm slab. Seven to eight such slabs are acquired to cover the bowel loops. Each slab is acquired with breath hold of about 12 seconds. In these 12 seconds, the slab is imaged about 40 times, so that it can be viewed as real-time cine loop.

Motility assessed by cine sequences has been shown to correlate significantly with the levels of inflammatory markers like C-reactive protein.\textsuperscript{[7]} Cine images have also been shown to improve lesion detection in Crohn disease.\textsuperscript{[8]} Cine images can be used in three ways. First, they can help to better assess any undistended loop. If the undistended loop shows normal peristalsis, it may not be inflamed. Second, inflamed bowel loops usually do not move or move less, thus cine images can be one of the ways to detect inflamed bowel loops. And lastly, cine images also help to see strictures. The strictured segment will not distend fully and will be fixed. If narrowing is obstructive, then the proximal bowel will show dilatation. A tight stricture may show a dark jet through it on cine images.

**Diffusion-weighted imaging**

Inflamed bowel wall shows diffusion restriction [Figure 2A-D].\textsuperscript{[9-11]} Its exact mechanism is not clear. However, presumably it is a result of infiltration of inflammatory cells, especially lymphoid aggregates, dilated lymphatic channels, and development of granulomas resulting in narrowed extracellular space and restricted mobility of water molecules.\textsuperscript{[10]} DWI for bowel can be acquired with breath hold, free breathing, or with respiratory triggering. The typical $b$-values used are 50, 400, 800 seconds/mm$^2$.

DWI can be utilized in three ways in the assessment of inflammatory bowel disease: Detection of inflamed bowel segment, assessment of complications like fistula and abscess, and detection of lymph nodes. If, in the future, it is established that restriction always represents inflammation, DWI might replace post-gadolinium imaging.

**Figure 1 (A-F):** Crohn disease in a 14-year-old girl with barium follow through and MR enterography done 6 months apart. (A) Barium follow through spot view of ileocecal junction shows irregular ulcerated terminal ileum (long arrows) and contracted cecum (small arrow). Axial single-shot T2-w (B), axial balanced TFE (C), axial post-gadolinium THRIVE (D), coronal single-shot T2-w (E), and coronal post-gadolinium THRIVE (F) images from MR enterography show marked thickening and enhancement of the terminal ileum (arrows). Also note fibrofatty proliferation and prominent mesenteric vessels giving “comb sign” in the pelvis (arrowheads)
for the detection of inflammation.[11] It is not clear at this stage whether diffusion can differentiate between active inflammation and chronic fibrosis. Abscess and fistulas can be detected by DWI. Lymph nodes, normal or abnormal, stand out on diffusion images and are much easier to detect than any other sequences. Typically multiple tiny lymph nodes are seen around the inflamed bowel segment.

What is normal?

MRE, being a relatively new technique, we are at a learning curve as far as normal appearance of bowel loops, thickening, and other features in children are concerned. This is complicated by inability to distend bowel loops optimally all the time and to distend all the bowel loops uniformly. In optimally distended bowel loops, normal jejumun is slightly thicker than ileum wall. A normal terminal ileal wall is also slightly thicker than the other ileal loops. In all these segments, wall thickness up to 3 mm is considered as normal.[4] A normal bowel enhances slightly. Abnormal thickened and inflamed bowel wall enhances much more than the adjacent normal wall.[4]

Crohn disease

Findings of Crohn disease on MRE include bowel wall thickening, hyper-enhancement, narrowing of the lumen, mesenteric hypervascularity, and inflammatory changes, fibrofatty proliferation, enlarged and/or increased number of lymph nodes, and fistula.[4,12] There are two recent studies assessing the accuracy of MRE in detecting Crohn disease in children. In one study on 32 children with Crohn disease, MRE showed an overall sensitivity of 94% in the detection of Crohn disease.[13] In another study on 21 children with Crohn disease,[10] MRE showed an accuracy of 87% for the detection of active inflammation and 65% for mural fibrosis.

Active inflammation versus fibrostenotic disease

Crohn disease has been divided into three types by some authors: Active inflammatory (without fistulas and stenosis) [Figure 3A-C], penetrating disease (deep ulcers, fistula, and abscess) [Figure 4A and B], and fibrostenotic disease (fibrosis and stricture).[12] By others, it is simply divided into active inflammation and chronic fibrosis or damage.[4,5] Histologically, active inflammation is characterized by neutrophilic infiltration of mucosal crypts, submucosal edema, and superficial and deep ulcerations. Mural fibrosis involves collagen fiber deposition in the bowel wall involving at least submucosal and mucosal layers.[5] Differentiation of active inflammation from chronic damage or fibrostenotic disease is important to decide the different forms of treatment in these cases. However, all the forms of Crohn including active inflammation, penetrating disease, and chronic fibrosis can be seen at the same time in same bowel segment.[12]

Signs of active inflammation on MRE include submucosal edema (indicated by hyperintensity of bowel wall on T2-w images and stratified enhancement), prominent mucosal enhancement followed by progressive mural enhancement, prominent mesenteric vessels, and enhancing lymph nodes.[5,12] Hypointensity of bowel wall on T2-w images, absence of prominent mucosal enhancement, and absence of or minimal transmural enhancement suggest chronic fibrosis in the thickened bowel segment.[5,12] In a recent study on 21 children with Crohn disease, MRE was 87% accurate in detecting active inflammation and 65% accurate in detecting mural fibrosis with histopathology as the reference standard.[5] On further analysis, the authors found that low accuracy of MRE for the detection of mural fibrosis was related to superimposition of active inflammation over mural fibrosis. When these cases of mural fibrosis with superimposed active
inflammation were removed from the analysis, the accuracy of MRE for the detection of mural fibrosis increased to 83%.[5]

In cases with superimposed active inflammation and fibrosis, chronic damage or stricture can be detected by features like proximal dilatation and non-distension of the segment on cine images. Ulcerations, which are an indicator of active inflammation, are difficult to detect by MRE. MRE at present does not have the resolution to detect superficial ulceration. Deep ulcers can be occasionally detected by MRE, but optimal distension of the bowel loop is essential.

**Pitfalls and solutions**

Optimal distension of bowel loops is the most important aspect of MRE technique and its interpretation. Suboptimal or non-distended loops can falsely show wall thickening, enhancement, as well as can obscure true bowel wall inflammation. Inadequate distension can cause artifacts like susceptibility from intraluminal content and obscure bowel wall visualization. Jejunal loops are most commonly affected by suboptimal distension. Features that help to differentiate true inflammation from collapse bowel include associated prominent mesenteric vessels, fibrofatty proliferation, lymphadenopathy, and less or absence of peristalsis on cine images. A collapsed loop on other sequences can distend on cine images and indicate its normalcy. The best way to distend jejunal loops is MR enteroclysis, but it may not be feasible in children. DWI may help in detecting inflamed bowel segment. But we have observed that normal, but collapsed bowel loops, apart from showing false wall thickening and enhancement also show restricted diffusion.

Presence of active inflammatory and chronic fibrotic changes in a loop at the same time poses problems in detecting mural fibrosis and stricture. Cine images may help in these cases by showing fixed non-distending segment with proximal dilatation [Figure 5A and B].

Submucosal edema is considered a sign of active inflammation, but it may also be seen in obstructed but not actively inflamed bowel.[16] It may also be seen in mural fibrosis with superimposed active inflammation.

**Other applications of MR enterography**

MR enterography has been reported to be useful in other small bowel conditions including celiac disease,[14] polyposis syndromes like Peutz-Jeghers disease,[15] and small bowel lymphoma.[16] Considering the similarities in the findings of Crohn disease and tuberculosis, MR enterography has the potential to be a useful test in the evaluation of abdominal tuberculosis.

**Conclusion**

Promising results from initial studies and experiences from large institutions indicate that MRE can be a primary imaging modality in children with Crohn disease. Inability to be performed in children who cannot be scanned awake still remains a major limitation of MRE. There are also a few
pitfalls in the technique and its interpretation, especially with inadequate distension of loops. As the technique advances and all pediatric radiologists as a community pass the initial learning curve, these pitfalls will be resolved. DWI and cine sequences will play an important role in these situations.

References


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