Diagn Interv Radiol 2012; 18:374–386


ABDOMINAL IMAGING

REVIEW

# Magnetic resonance enterography in Crohn's disease: techniques, interpretation, and utilization for clinical management

Diego R. Martin, Bobby Kalb, Cary G. Sauer, Adina Alazraki, Steve Goldschmid

ABSTRACT

Crohn's disease treatment has improved significantly with the development of immunosuppressive and immunomodulatory agents, while surgery remains an important option in selected patients. However, a relative lag in diagnostics has become apparent with a growing need for the capacity to non-invasively and safely evaluate the tissue changes of Crohn's disease within the bowel wall and deeper tissues. We have noted marked technical improvements in magnetic resonance enterography (MRE) and in our understanding of the different facets of Crohn's disease that can be elucidated by optimized MRE, in contrast to other diagnostics. This review will provide an integrated understanding of MRE related to other available tests and recommendations for the optimal use of MRE for the clinical management of Crohn's disease. We will review the relative strengths and limitations of MRE as applied to clinical evaluation and therapeutic decisions, including the use of the unique capacity to delineate active inflammation and fibrosis in the submucosal and deeper enteric tissues, which is beyond the diagnostic reach of endoscopy and biopsy.

*Key words:* • *Crohn's disease* • *magnetic resonance imaging* • *inflammatory bowel disease*

From the Departments of Radiology (D.R.M. ✉ *dmartin@radiology.arizona.edu*, B.K.) and Internal Medicine (S.G.), University of Arizona School of Medicine, Tucson, Arizona, USA; the Departments of Pediatric Gastroenterology, Hepatology, and Nutrition (C.G.S.), and Radiology (A.A.), Emory University School of Medicine, Atlanta, Georgia, USA.

Received 13 October 2011; revision requested 19 October 2011; revision received 3 November 2011; accepted 3 November 2011.

Published online 19 April 2012
DOI 10.4261/1305-3825.DIR.4893-11.2

In the evaluation of Crohn's disease, multiple diagnostic imaging methods have been developed, yet there remains a need for education on and further validation of the optimal utilization of the available imaging techniques in conjunction with endoscopy and biopsy. The use of computed tomography (CT) has exponentially increased over the past ten years (1), yet the optimal use of CT imaging in Crohn's disease should be assessed in the context of balancing its potential benefits against the risks of CT radiation-induced cancer. Ionizing radiation increases the risk of cancer, a phenomenon directly related to radiation dose (2–9). Younger individuals are more vulnerable to increased cancer risk from radiation exposure, and Crohn's disease in particular has been associated with high radiation exposure in both adults and children, predominantly due to repeat CT scans (10–12). This should be balanced against more recently developed diagnostic capabilities using non-X-ray-based magnetic resonance enterography (MRE).

Small bowel involvement in Crohn's disease can be difficult to diagnose and monitor. Endoscopy with biopsy is still generally viewed as a reference standard. However, little of the small bowel is visualized, and these tests only evaluate the mucosa. Video capsule endoscopy (VCE) can visualize mucosal disease but is unable to provide tissue samples. Small bowel follow-through (SBFT) is relatively insensitive to mucosal disease, provides limited delineation of submucosal or deeper disease, and requires the use of ionizing radiation. Enteroclysis, wherein contrast is administered into the duodenum with the use of a nasogastric tube, is cumbersome, and although it provides improved bowel distention and bowel wall morphologic imaging compared to SBFT, it has similar limitations overall.

It must be emphasized that endoscopic tests and biopsies will evaluate the mucosa but do not evaluate inflammation or fibrosis within the submucosa or deeper tissues. Endoscopic techniques alone may under-represent the full extent of disease, particularly when considering that the mucosa has a high capacity for repair. Crohn's disease is a transmural disease in which submucosal inflammation is responsible for tissue-destructive and penetrating disease, fibrotic disease, strictures, and fistulae, which are the processes responsible for the most serious morbidities. In contrast, disease restricted only to the mucosa likely does not cause such serious comorbidities. Currently, CT enterography and MRE are the only two imaging modalities that enable the visualization of submucosal tissues throughout the entire small bowel; however, MRE does not expose patients to ionizing radiation (Table 1), and it provides additional technical and diagnostic advantages.

## MRE technique: historical perspective and current status

MRE is a generic term used to describe bowel imaging that utilizes magnetic resonance imaging (MRI). Early reports frequently described

MRE exams performed in combination with small bowel enteroclysis (MR-enteroclysis) (13–15). This technique involves administering a large volume of fluid by an enteric tube and acquiring thick-section (5–8 cm) single-shot echo train spin-echo images with strong T2-weighting (T2W) to obtain images that resemble fluoroscopic small bowel images. Although both bright and dark lumen contrast agents have been proposed, water-based methods are relatively easy to implement and provide excellent signal characteristics, resulting in a bright lumen on T2W and a dark lumen on T1W techniques. To slow the absorption of the water that normally would occur rapidly in the jejunum, osmotic and viscosity agents are added. Some researchers, in the early development of MRE, have proposed the routine use of enteroclysis via a naso-jejunal tube for the administration of intra-luminal contrast to provide superior small bowel distension (14).

Currently, techniques for MRE emphasize sequences that are optimized to obtain findings that most significantly affect patient management decisions (16, 17). These findings can include acute inflammation (18) and chronic disease without inflammation, which, if associated with proximal bowel distension, defines a fibrotic stricture (19, 20). Furthermore, other MRE findings may include intra-abdominal complications such as fistulae, tethering (which may be the start of a fistula) and abscesses. There are a variety of T1W and T2W sequences to choose from, but the most useful for bowel imaging include the three-dimensional-gradient echo (3D GRE) T1W and the single-shot T2W techniques, as reviewed in detail previously (17). T1W images are acquired after the administration of gadolinium-based contrast to selectively enhance the diseased bowel wall. Fat surrounds the bowel and can interfere with the visualization of the disease; inflamed bowel and fat both produce high signals on T2W and gadolinium-enhanced T1W images. Fat-suppression techniques are critical to improve disease conspicuity. The diseased bowel generates a high signal, which becomes highly conspicuous only if the adjacent fat is completely darkened by fat suppression (21). T1W gadolinium-enhanced fat-suppressed and T2W single-shot images with and without fat suppression are the foundation for diagnosing and characterizing Crohn's disease. Regular T2W single-shot images depict bowel wall morphology. Fat-suppressed single-shot T2W images are critical to assess edema and inflammation related to active Crohn's disease, optimized with a spectral adiabatic inversion recovery (SPAIR) fat-suppression technique (22).

Patient preparation before performing MRE can improve the results (16, 17, 23). Oral, water-based contrast agents containing 2.5% mannitol, a non-digested carbohydrate, provide an osmotic load that slows water absorption (24). The further addition of a viscous agent further improves small bowel distension. Between 1000 mL and 1200 mL of the water-based contrast can be given to the patient for oral ingestion 20 to 30 min prior to the examination, and 20 mg of metoclopramide or 100 mg of erythromycin can be given intravenously to

**Table 1.** Diagnostic characteristics of MRE, CT, and endoscopy in Crohn's disease

| Structures and disease processes | MRE | CT | Endoscopy with/without mucosal biopsy |
|---|---|---|---|
| Mucosa | • Insensitive | • Insensitive | • Highly sensitive<br>• Moderately specific |
| Submucosa and deeper tissues | • Sensitive even with poor bowel preparation<br>• High specificity between inflammation and chronic without inflammation | • Sensitive with excellent bowel preparation (distension)<br>• Insensitive if bowel not well prepared<br>• Poor specificity between inflammation and chronic without inflammation | • Insensitive |
| Fistula | • Sensitive<br>• Sensitive and specific regarding extra-enteric soft tissues, including genito-urinary structures | • Sensitive<br>• Moderate to poor sensitivity and specificity for extra-enteric soft tissues | • Insensitive |
| Perianal fistula | • Sensitive | • Insensitive | • Insensitive |
| Abscess | • Sensitive and specific regarding inflammation | • Sensitive but non-specific regarding inflammation or soft tissues involved | • Insensitive |
| Obstruction | • Moderate to high sensitivity, dependent upon degree of distension<br>• High specificity, often showing tethering fibrotic bands or foci of adhesion | • Moderate to high sensitivity, dependent upon degree of distension<br>• High specificity dependent upon morphology of bowel showing stricture or tenting related to tethering | • Moderate to poor sensitivity<br>• Poor specificity |

MRE, magnetic resonance enterography; CT, computed tomography.

promote gastric emptying. The addition of a rectal water enema provides improved visualization of the terminal ileum and may be considered an adjunct to facilitate the evaluation of the large bowel in addition to the small bowel (25, 26). Prior to the motion-sensitive T1W 3D GRE sequences, 1 mg of glucagon may be administered intravenously to reduce artifacts from bowel peristalsis.

A potential disadvantage of not performing MR-enteroclysis during MRE exams is suboptimal bowel distension. However, progressive experience over the past 10 years has led to the following conclusions, which contrast both with the early descriptions of MRE and with CT and fluoroscopy techniques:

1) By achieving significant improvements in the diagnostic quality of MRE sequence techniques, active and chronic disease states may be visualized even with suboptimal bowel lumen distention (27).
2) These sequence techniques rely on T2W single-shot imaging, in combination with SPAIR for optimal fat suppression (22), and T1W contrast-enhanced imaging, using the latest-generation 3D GRE, which achieves improved soft tissue contrast and edge sharpness.
3) An enteroclysis level of distention is often not necessary, and pre-procedure oral contrast is sufficient in most patients (28).
4) Routine water-based contrast agents used for CT are equally useful for MRE (17).
5) Even if the patient is unwell and unable to take oral agents, the examination can proceed, and these studies can be frequently diagnostic in the setting of chronic or active Crohn's disease.
6) In comparison, CT and fluoroscopic techniques are usually non-diagnostic without an enteroclysis level of bowel distention (29).
7) MR remains diagnostically sensitive even in lean patients, as it generates ample bowel wall contrast, while CT benefits progressively from increased levels of intra-abdominal fat to separate bowel loops.
8) While prior MRE studies have shown the benefits of rectal water enemas for diagnosing the terminal ileum Crohn's disease, further improvements in the MRI techniques have reduced the need for colon water distension.
9) The differentiation between pathological and non-pathological bowel wall thickening and the differentiation between fibrosis and inflammation are key diagnostic strengths of MRE over CT.

The benefits of a simplified MRE technique include a faster exam, optimal patient comfort, improved compliance with the study and improved diagnostic yield. Employing oral contrast agents prior to imaging allows for improved bowel distention and bowel wall visualization; a simplification of oral contrast administration is achieved with readily available and inexpensive CT oral contrast. By reducing the required degree of bowel lumen contrast distension (as compared to MR-enteroclysis), MRE without enteroclysis becomes markedly more convenient for technologists and comfortable for patients. These are important developments and advantages, particularly when compared to other diagnostic techniques and when considering the young age of many Crohn's disease patients.

**Summary of MRE findings in Crohn's disease** (Table 2)

1) Possible findings on T1W images:
   - Bowel wall thickening with increased enhancement in the delayed images
   - Stranding extending into the mesenteric border fat and increased size and number of vessels
   - Accordion-like compression and thickening of folds asymmetrically, involving the mesenteric side of the small bowel having a tethered appearance
   - Reactively enlarged adjacent mesenteric nodes
2) Possible findings on T2W images:
   - Bowel wall thickening with increased signal in and adjacent to the abnormal bowel (on fat-suppressed [FS] images) showing active inflammation
   - Fluid accumulation in adjacent intraperitoneal and mesenteric spaces
3) General interpretive approach to a thickened bowel wall segment:
   - *Active inflammation;* bowel wall thickening and enhancement on post-gadolinium T1W images plus high signal intensity on T2W-SPAIR FS images (Fig. 1)
   - *Chronic disease without active inflammation;* bowel wall thickening and enhancement on post-gadolinium T1W images plus low signal intensity on T2W-SPAIR FS images with possible stenosis and obstruction (Figs. 2 and 3)
   - *Chronic disease with active inflammation;* these features can overlap with active inflammation, requiring longitudinal repeated scanning (discussed below) (Fig. 1)

**Table 2.** MRE findings of normal bowel, active inflammation, and chronic disease

| | BWT | BWE | T2W signal |
|---|---|---|---|
| Normal bowel | - | - | - |
| Active inflammation | + | + | + |
| Chronic disease | + | + | - |
| Active inflammation with chronic disease[a] | + | + | + |

[a]Active inflammation may mask chronic disease and fibrosis. Best possible measure of underlying fibrosis is achieved on follow-up MRE after treatment and resolution of acute disease.
MRE, magnetic resonance enterography; BWT, bowel wall thickening on post-gadolinium T1W images; BWE, bowel wall enhancement on T1W images; T2W signal, increased signal on T2W SPAIR fat-suppressed images.

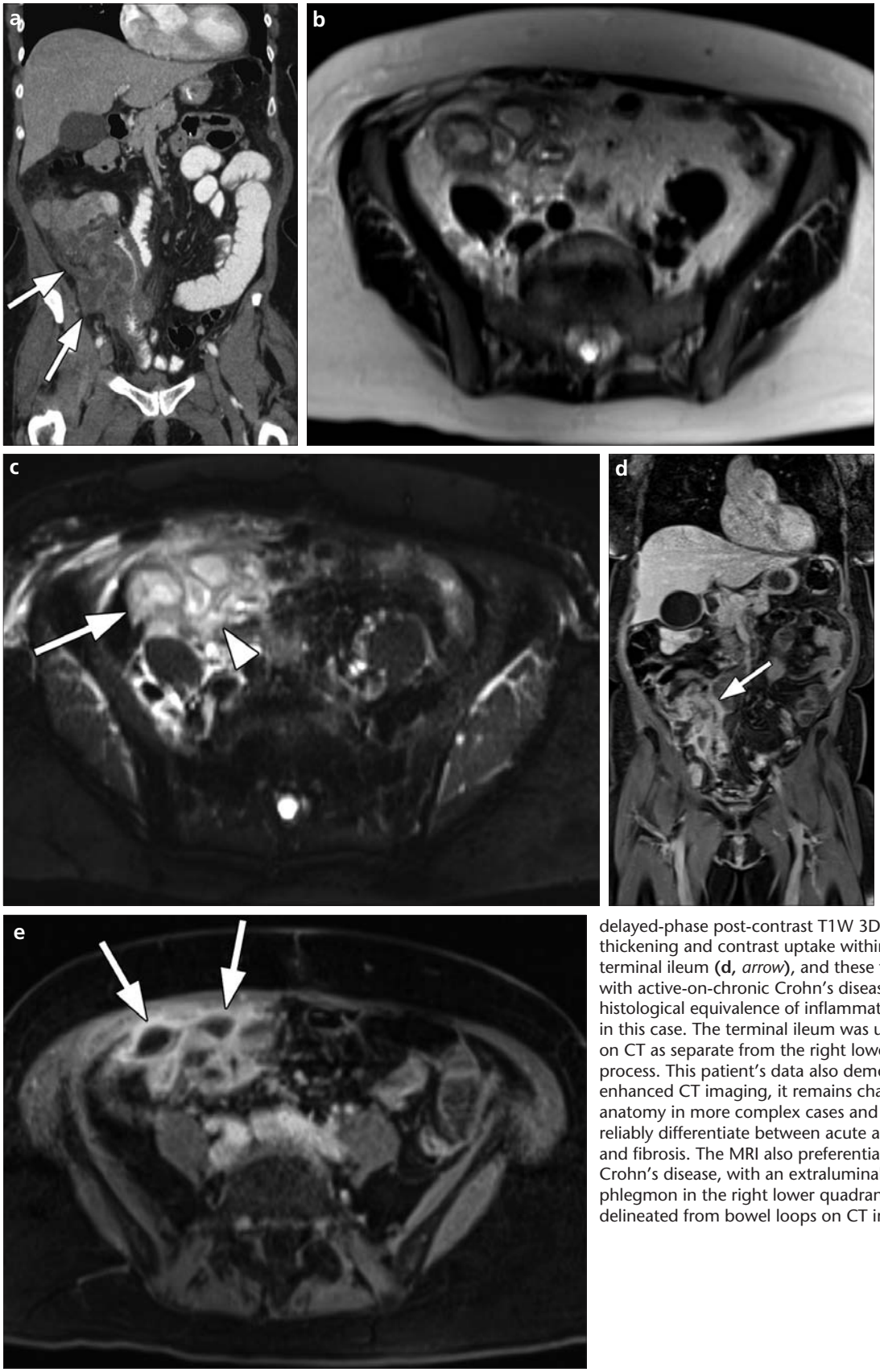


**Figure 1. a–f.** A 68-year-old female with acute abdominal pain. Abdominal and pelvic coronal CT **(a)** demonstrates an extensive soft tissue mass in the right lower quadrant *(arrows)*. We were unable to differentiate among thickened bowel loops from inflammation, fibrosis, and other soft tissue processes. The differential diagnosis was made in light of the patient history and favored either inflammatory bowel disease or appendicitis. An MRI, performed for differentiation, including axial single-shot T2W images without **(b)** and with **(c)** SPAIR fat suppression, demonstrates extensive, abnormally high signal involving distal ileal loops **(c**, *arrow***)** and extending into the adjacent mesentery **(c**, *arrowhead***)**. The high T2 signal identified in the thickened bowel walls and surrounding mesentery is the foundation for characterizing this patient's disease as active; the elevated abnormal signal is directly related to the severity of edema and inflammation but is inconspicuous without fat suppression **(b**, **c)**. Coronal **(d)** and axial **(e)** delayed-phase post-contrast T1W 3D GRE images show abnormal thickening and contrast uptake within the thickened wall of the terminal ileum **(d**, *arrow***)**, and these findings are compatible with active-on-chronic Crohn's disease and correspond to the histological equivalence of inflammation and submucosal fibrosis in this case. The terminal ileum was unable to be clearly identified on CT as separate from the right lower quadrant inflammatory process. This patient's data also demonstrate that on contrast-enhanced CT imaging, it remains challenging to distinguish the anatomy in more complex cases and that it is not possible to reliably differentiate between acute and chronic inflammation and fibrosis. The MRI also preferentially shows other sequelae of Crohn's disease, with an extraluminal abscess **(e**, *arrows***)** and phlegmon in the right lower quadrant, features that are not delineated from bowel loops on CT imaging.

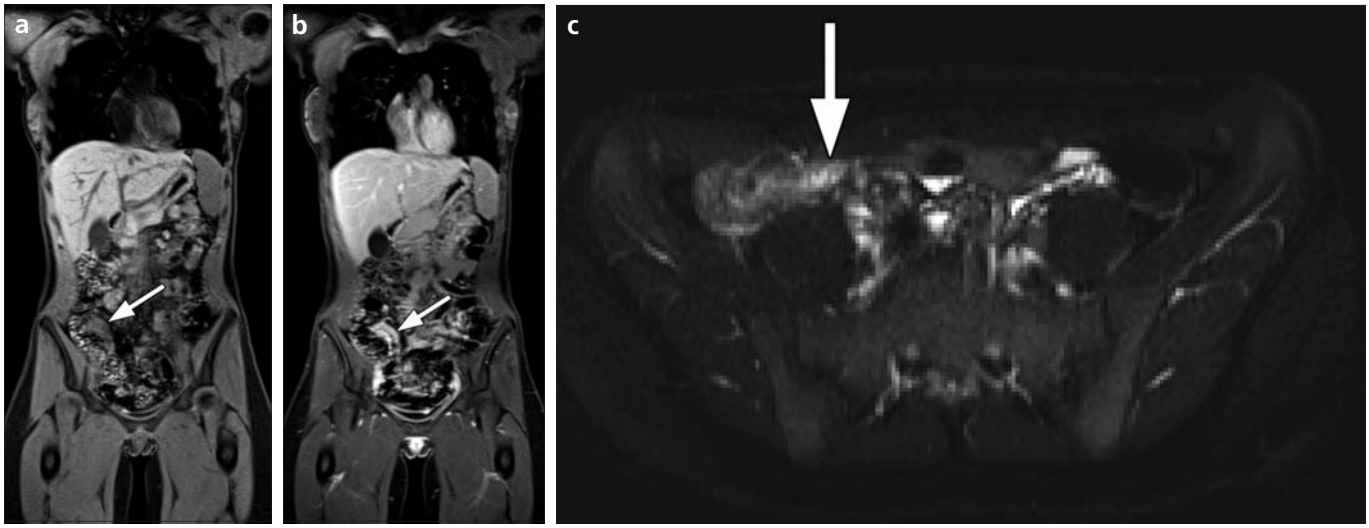


**Figure 2. a–c.** A 20-year-old female with recurrent abdominal pain. An extensive diagnostic evaluation with ultrasound, CT, colonoscopy with the terminal ileum biopsy and capsule endoscopy showed no abnormalities. The patient was diagnosed with irritable bowel syndrome based upon symptoms combined with exclusion of other considerations by objective studies. On further referral for continued symptoms, MRE was performed. Coronal precontrast **(a)** and delayed postcontrast **(b)** T1W 3D GRE images demonstrate a thickened, abnormally enhancing terminal ileum *(arrows)*. Axial, fat-suppressed single-shot T2W image **(c)** demonstrating a minimally elevated T2 signal within the thickened wall of the terminal ileum *(arrow)* and no abnormal signal within the adjacent mesentery. Taken together, these findings concur with the predominance of fibrosis of the terminal ileum with minimal inflammatory changes, a pattern of chronic Crohn's disease. The clinical exam is characteristically nonspecific, and criteria for distinction between irritable bowel syndrome and irritable bowel disease, for example, rely on objective measures of disease. Optical endoscopy and endoscopic biopsy may be insensitive to disease restricted to the submucosa and deeper tissues. In this patient, the mucosa had presumably healed over the submucosal disease, a pattern that has been previously reported (28).

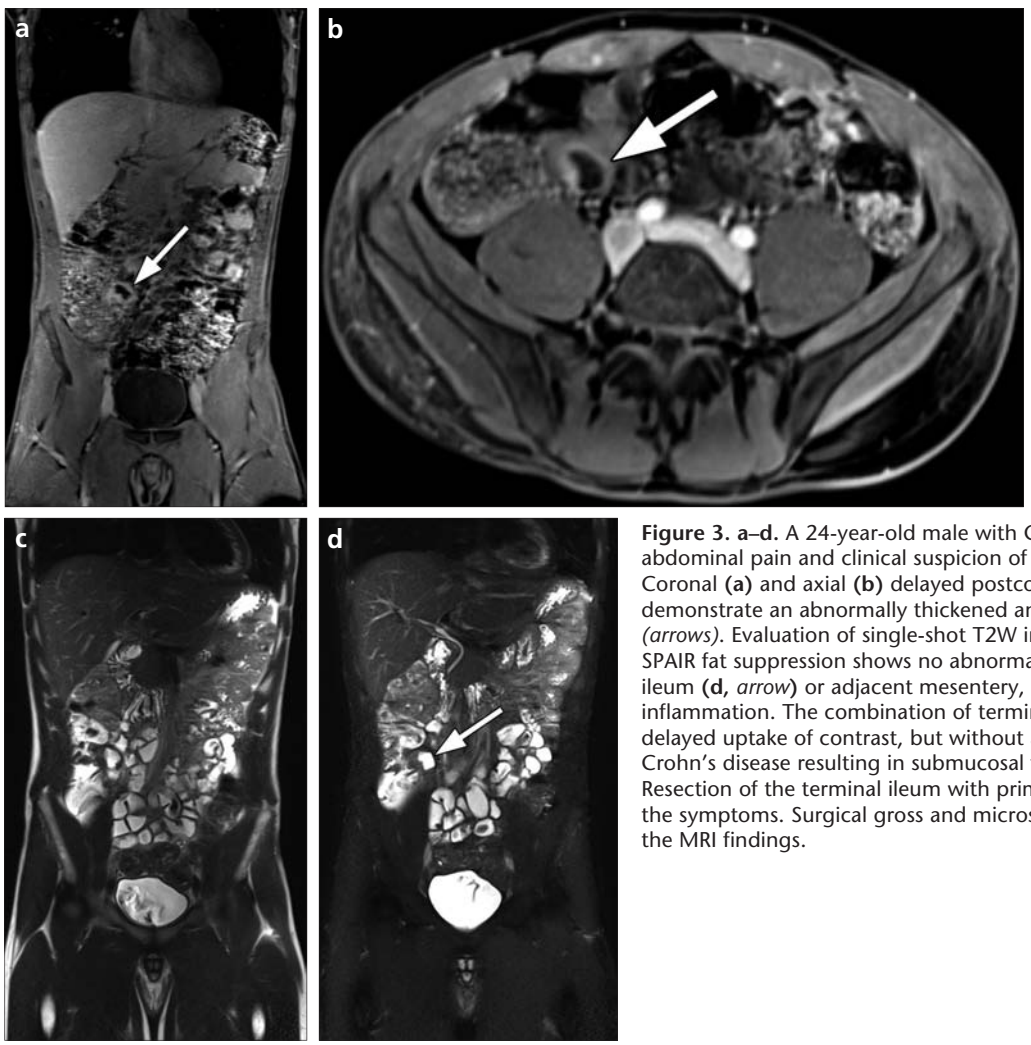


**Figure 3. a–d.** A 24-year-old male with Crohn's disease, recurrent abdominal pain and clinical suspicion of repeated acute disease flaring. Coronal **(a)** and axial **(b)** delayed postcontrast T1W 3D GRE images demonstrate an abnormally thickened and enhancing terminal ileum *(arrows)*. Evaluation of single-shot T2W images without **(c)** and with **(d)** SPAIR fat suppression shows no abnormally elevated signal in the terminal ileum **(d**, *arrow***)** or adjacent mesentery, indicating an absence of active inflammation. The combination of terminal ileum wall thickening with delayed uptake of contrast, but without any edema, indicates chronic Crohn's disease resulting in submucosal fibrosis of the terminal ileum. Resection of the terminal ileum with primary ileocolic anastomosis resolved the symptoms. Surgical gross and microscopic pathology corresponded to the MRI findings.

4) Crohn's disease complications:
   - Fistulae, tethering, and strictures (Fig. 4)
   - Bowel obstruction (Fig. 5)
   - Extra-enteric collections and abscesses (Figs. 1 and 6)
   - Peri-anal disease optimally visualized on pelvic MRE (Fig. 7)
   - Extra-enteric complications of Crohn's disease or other causes of abdominal pain visualized on MRE, including liver or gallbladder disease (sclerosing cholangitis), mesenteric vascular thrombi, abdominal masses, tumors, and pancreatic abnormalities (Fig. 8)

Identifying active inflammation is rarely an interpretive problem in MRE. One important aspect of MRE interpretation is that active inflammation can mask underlying fibrosis related to chronic disease of the bowel wall (Table 2). The presence or absence of underlying fibrosis in this setting is of lesser immediate consequence as active inflammation that requires treatment. In the setting of active inflammation, longitudinal MRE evaluation is implemented to confirm improvements of active inflammation and to then evaluate the presence of unmasked chronic fibrotic disease. After therapy for active inflammation, the fibrotic burden can be assessed, and this information can be used for management decisions, including the need for surgery, as discussed later in this review (Figs. 1 and 2).

### Clinical use of small bowel MRE

Techniques used to assess disease activity include endoscopy, capsule endoscopy, and/or surgical techniques in conjunction with tissue biopsy (29–32). However, these techniques are invasive (endoscopy) or may have contraindications (capsule endoscopy) in the setting of suspected bowel stenosis and obstruction. An underappreciated concern is that endoscopy and capsule endoscopy, and even endoscopy with biopsy, will evaluate only the extent of mucosal disease; as a result, submucosal and serosal-mesenteric disease will not be fully appreciated (17).

MRE can be used for transmural small bowel evaluation. Prior studies have focused on the perfusion characteristics of the bowel wall after intravenous gadolinium administration to assess disease activity (33). The combination of T2W and T1W gadolinium-enhanced sequences can provide a high diagnostic accuracy in these patients (34). Other authors have proposed an MRE-based scoring system for the assessment of inflammatory activity that includes features such as bowel wall thickening, lumen narrowing and the number of peri-intestinal lymph nodes (35). Although feasible, these evaluation algorithms are relatively demanding, which may ultimately limit clinical utilization. In particular, acquiring a series of carefully timed arterial-, venous-, and delayed-phase gadolinium-enhanced T1W images of the entire abdomen and pelvis will often require compromising the field of view at the top of the abdomen and result in sub-optimal assessment of the solid organs, including the liver. In addition, T1W images are more prone to technical complications from respiratory or bowel motion or from magnetic field distortions, as may result from surgical clips or bowel gas. Our experience has led us to propose a relatively simple approach for the evaluation of Crohn's disease activity using FS T2W single-shot fast spin-echo MRI (16, 17). FS T2W imaging is sensitive to edema in or adjacent to the bowel wall (22). Combining late vascular- or interstitial-phase gadolinium-enhanced T1W images with the FS T2W images allows for comprehensive evaluation and discrimination between quiescent disease and active inflammation (Figs. 1–3) and for the evaluation of complications, including abscesses, obstruction, and fistulae (Figs. 1, 4–8).

The presence and magnitude of bowel wall edema correlates with active inflammation (36–38). We have evaluated the accuracy of detecting abnormally high signals on FS T2W images in conjunction with contrast-enhanced T1W MRE to differentiate between active inflammatory and chronic fibrotic bowel disease. In our study of 81 patients with Crohn's disease, we showed that the use of gadolinium-enhanced interstitial-phase T1W images plus FS T2W for assessing edema, as a measure of inflammation and disease activity, provided a high degree of accuracy compared to other measures of disease activity based on the combination of available endoscopy, biopsy, or surgical pathology (39). Although other studies have examined the correlation between the disease activity and MRE findings (36, 38, 40), the significance of the recently improved, high-quality FS single-shot T2W imaging is only now becoming fully appreciated. Technically, the single-shot T2W images are easy to acquire and are extremely robust, providing a consistent image quality that is resistant to motion deterioration and artifacts from gas or surgical clips (21). Interestingly, the discordance reported between MRE and endoscopy or biopsy has helped to further demonstrate what has been shown previously on pathological specimens: that the mucosal evaluation by endoscopy, capsule endoscopy, and biopsy may significantly under-represent submucosal disease compared to surgical specimens (37). Conversely, small bowel MRE is insensitive to early changes of Crohn's disease restricted to only the mucosa (28). The combination of optical methods with MRE provides a comprehensive evaluation of early disease affecting the mucosa (endoscopy, capsule endoscopy, and biopsy) and more extensive disease affecting the submucosa and mesentery.

The drawback of MRE is that the expertise and availability of examinations are still somewhat limited. These may constitute the main limitation of MRE at this time. Further, an MRE study requires approximately 30 min. While this compares favorably to fluoroscopic studies (SBFT or enteroclysis), it is approximately twice as long as the room time for a CT scan. However, when considering the entire length of the examination, starting with any prior bowel preparation and consumption of pre-scanning oral contrast, the differences in room time between MRE and CT become less important. For very young children and for patients with claustrophobia, sedation may be required prior to performing an MRE study. Absolute contraindications to MRE include metallic fragments in the orbits. MRE can provide a measurement of disease activity that impacts the therapeutic decision pathway, including medical and surgical management (Table 3). MRE may also be used prior to capsule endoscopy to provide information on the transmural disease location and extent and to detect bowel stenoses or obstructions that may contraindicate capsule endoscopy.

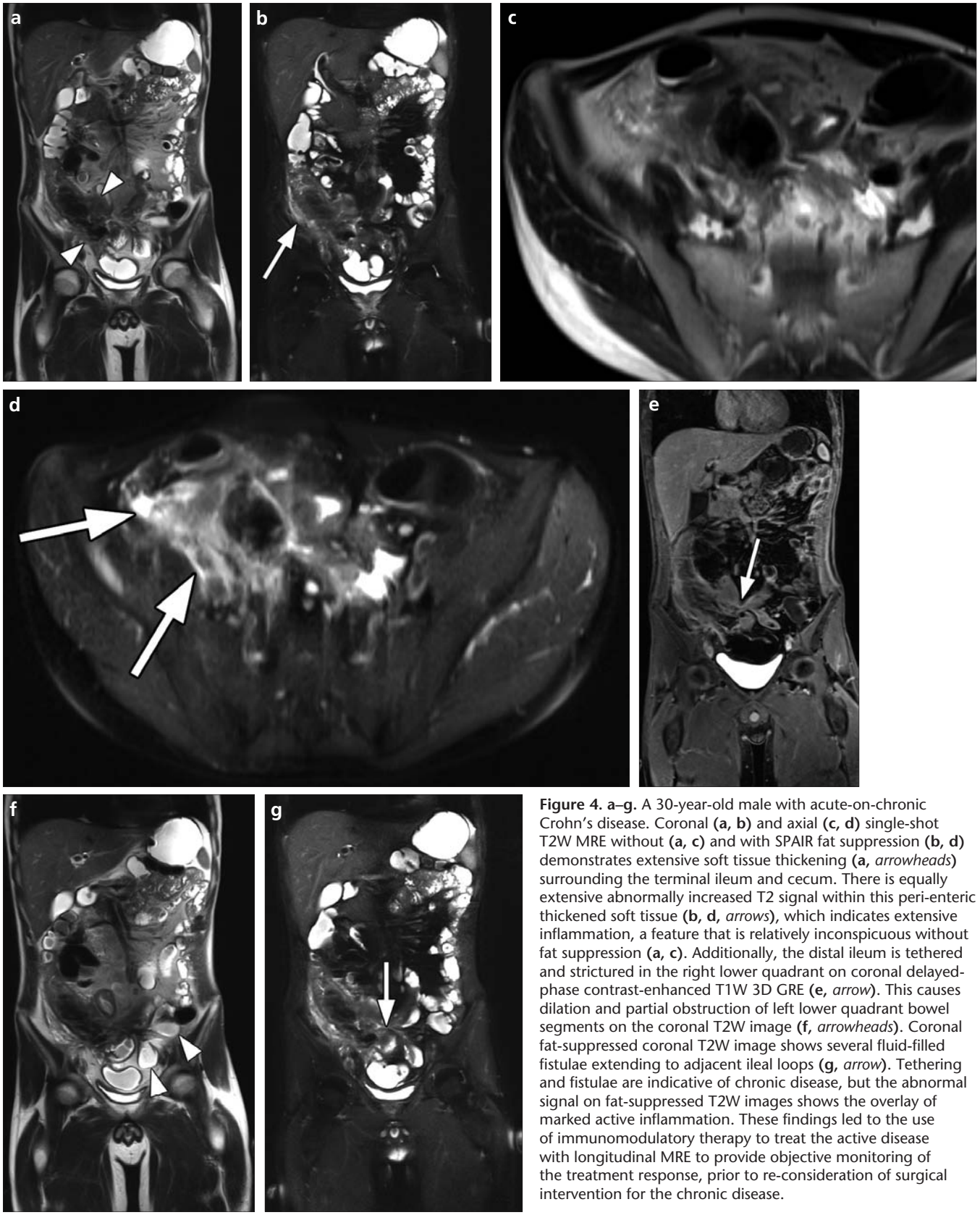


**Figure 4. a–g.** A 30-year-old male with acute-on-chronic Crohn's disease. Coronal **(a, b)** and axial **(c, d)** single-shot T2W MRE without **(a, c)** and with SPAIR fat suppression **(b, d)** demonstrates extensive soft tissue thickening **(a,** *arrowheads***)** surrounding the terminal ileum and cecum. There is equally extensive abnormally increased T2 signal within this peri-enteric thickened soft tissue **(b, d,** *arrows***)**, which indicates extensive inflammation, a feature that is relatively inconspicuous without fat suppression **(a, c)**. Additionally, the distal ileum is tethered and strictured in the right lower quadrant on coronal delayed-phase contrast-enhanced T1W 3D GRE **(e,** *arrow***)**. This causes dilation and partial obstruction of left lower quadrant bowel segments on the coronal T2W image **(f,** *arrowheads***)**. Coronal fat-suppressed coronal T2W image shows several fluid-filled fistulae extending to adjacent ileal loops **(g,** *arrow***)**. Tethering and fistulae are indicative of chronic disease, but the abnormal signal on fat-suppressed T2W images shows the overlay of marked active inflammation. These findings led to the use of immunomodulatory therapy to treat the active disease with longitudinal MRE to provide objective monitoring of the treatment response, prior to re-consideration of surgical intervention for the chronic disease.

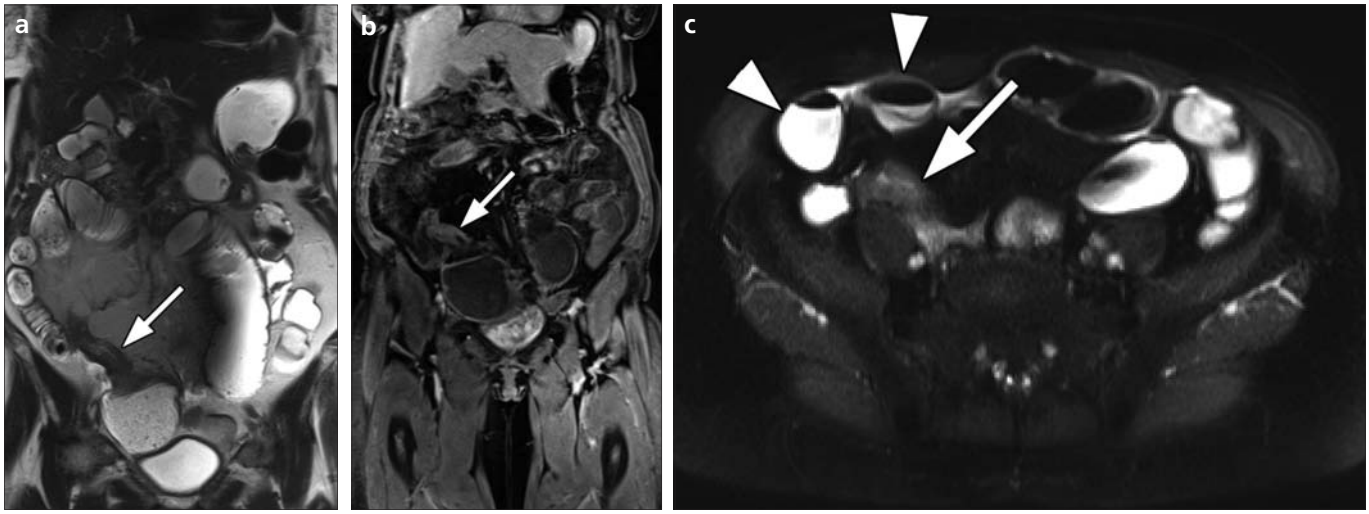


**Figure 5. a–c.** A 73-year-old female with long-standing Crohn's disease. Coronal single-shot T2W **(a)** and coronal contrast-enhanced delayed-phase T1W 3D GRE **(b)** images demonstrate a thickened terminal ileum **(a,** *arrow***)** with abnormally increased contrast uptake **(b,** *arrow***)**. Axial SPAIR fat-suppressed T2W image **(c)** shows no abnormally increased signal, indicating no active inflammatory component to this segment of diseased bowel **(c,** *arrow***)**, implying a chronic, fibrotic stricture. The terminal ileum stricture causes proximal small bowel dilatation and air fluid levels **(a,** *mid-abdominal small bowel loops*; **c,** *arrowheads***)**, suggesting mechanical obstruction. The lack of active inflammation and the associated bowel obstruction triaged this patient directly to surgical management.

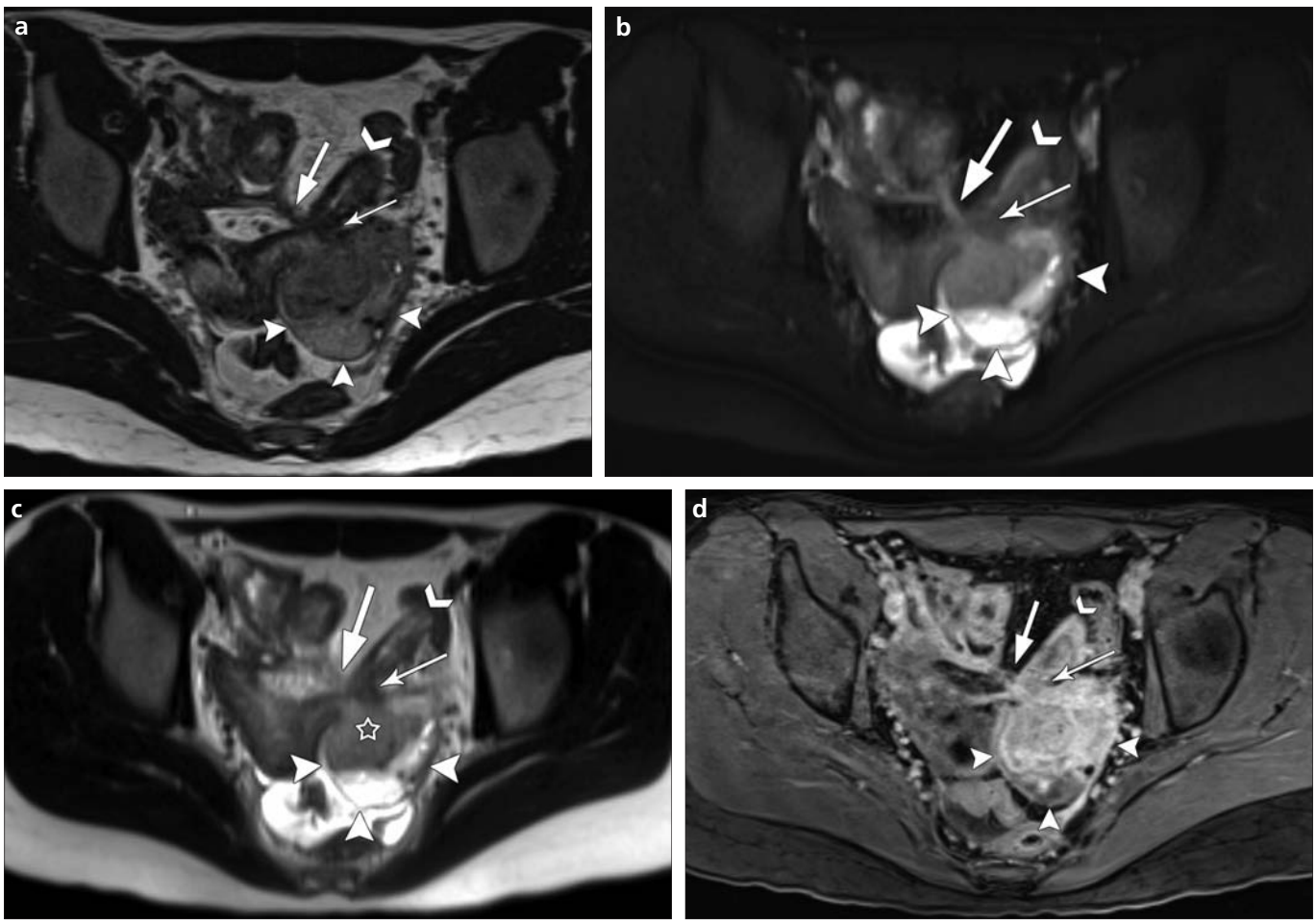


**Figure 6. a–d.** A 22-year-old female with Crohn's disease and persistent pelvic pain. An abnormally thickened loop of distal ileum is present in the pelvis **(a–d,** *chevron***)**. Note the wide-mouthed fistulous connection **(a–d,** *small arrows***)** with the left ovary **(a–d,** *arrowheads***)**, which has become enlarged with an intra-ovarian phlegmon **(c,** *asterisk***)** as a sequela of long-standing Crohn's disease. There is also tethering of this diseased bowel to adjacent small bowel loops in the pelvis **(a–d,** *large arrows***)**, but no severe, active inflammation is identified on fat-saturated T2W images **(a–d)**.


**Figure 7. a–c.** A 36-year-old female with Crohn's disease and perianal fistula. A fluid-filled fistula is identified on the axial 3D T2W 1 mm isotropic resolution image **(a,** *arrow***)** and extends from the anorectal junction on the right, tracking posteriorly through the perineal soft tissues and draining through the medial gluteal skin surface on the right. Axial SPAIR fat-suppressed single-shot T2W image showing abnormally increased signal **(b,** *arrowheads***)** indicates mildly active inflammation within the perineum. The combined observation of mild T2 signal abnormality (**b,** *arrowheads*) and a markedly thickened and enhancing fistula track wall on axial contrast-enhanced delayed-phase T1W 3D GRE **(c,** *arrow***)** indicates a chronic fistula with fibrosis.

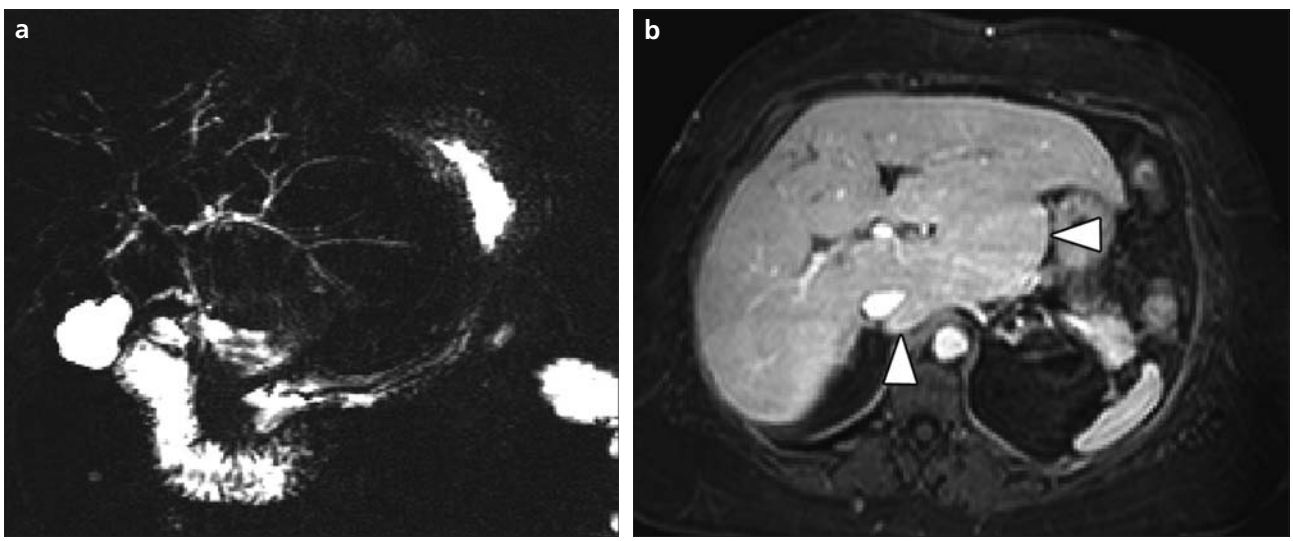


**Figure 8. a, b.** A 56-year-old female with inflammatory bowel disease. Coronal thick-section single-breath-hold T2W MR cholangiopancreatography **(a)** demonstrates marked, irregular dilatation and beading of the intrahepatic biliary system. Axial postcontrast delayed-phase T1W 3D GRE image **(b)** demonstrates irregular beading of regional foci of peripheral intrahepatic bile ducts and also shows the coexistent changes of chronic liver disease. The features of chronic liver disease are, in this case, characteristic of primary sclerosing cholangitis that includes caudate hypertrophy **(b,** *arrowheads***)** and early hepatic fibrosis along the periphery of the right hepatic lobe. This case illustrates the ability to use MRI for comprehensive digestive system evaluation in the setting of inflammatory bowel disease to provide concurrent diagnostic evaluation of the liver, in addition to evaluation of the bowel and adjacent soft tissues.

### Comparison of MRE to disease activity index

Crohn's disease activity measurements are predominantly subjective measurements. They include physician global assessment, Harvey-Bradshaw Index, Crohn's Disease Activity Index (CDAI) and Pediatric Crohn's Disease Activity Index (PCDAI) (41–43). As expected, comparing objective measures of disease inflammation with MRE to subjective measures of clinical activity has resulted in conflicting data.

Multiple studies have demonstrated no correlation between MRE findings and CDAI (24, 32, 44, 45). Meanwhile, other studies have demonstrated a correlation between MRE and CDAI (33, 46, 47) and a correlation between MRE and laboratory markers of inflammation (erythrocyte sedimentation rate/C-reactive protein) (41–43). Only two pediatric studies compared MRE to PCDAI, one demonstrating a statistically significant correlation between disease on MRE and PCDAI (48) and the other demonstrating no correlation between MRE and PCDAI (49).

Subjective clinical activity measurements do not necessarily reflect mucosal findings, and studies that have used them show discordance between inflammation on endoscopy and subjective activity index measurements.

### Comparison of MRE to VCE

VCE visualizes the mucosa throughout the entire small intestine with the use of a wireless video capsule. Three studies, each with approximately 20 patients, compared MRE to VCE for the detection of intestinal lesions (36, 50, 51). All three studies concluded that both MRE and VCE identified diseased small bowel; however, VCE was better at identifying small aphthous lesions and often identified more lesions (36), which agrees with our contention that MRE is insensitive to early mild disease restricted to the mucosa.

### Comparison of MRE to SBFT/ conventional enteroclysis

Historically, SBFT has been recommended for the evaluation of the small bowel to detect both ulceration and strictures in Crohn's disease. Gourtsoyiannis et al. (52) published the largest study comparing MRE (utilizing MR-enteroclysis) to SBFT in 52 Crohn's disease patients. MRE (with MR-enteroclysis) and SBFT were in full agreement in revealing, localizing, and estimating the length of bowel involved. MRE (with MR-enteroclysis) was poor at detecting superficial ulcers but performed well in identifying deep ulcers and stenosis.

These earlier studies were likely limited by the use of older sequences because they did not yet have access to the most optimized T1W and T2W techniques (16, 17, 39). Current MRE imaging (without MR-enteroclysis) yields significant improvements over fluoroscopic techniques (53).

### Comparison of MRE to CT

Concerns over radiation risks may lead to the under-utilization of CT for the longitudinal management of Crohn's disease. There is a clinical need to optimize the use of cross-sectional imaging that is at the same time safer than and at least as diagnostic as CT. MRE meets that need by providing a safe, non-ionizing technology that can be obtained when required and without additive or long-term harm. In addition, evolving experience is showing that MRE may more accurately describe the submucosal pathology of transmural Crohn's disease, including detecting and quantifying inflammation, fibrotic disease, and other intra-abdominal complications, compared to other diagnostics, including CT (Table 1). A particular diagnostic strength of MRE over CT is the ability to differentiate inflammation from fibrosis within the submucosa of the bowel wall and in the peri-enteric tissues (Tables 1 and 2). MRE can show extra-intestinal disease, including bowel obstruction, abscesses, webs, tethering, and fistulae. These disease processes may be visualized on MRE with less dependence on enteroclysis-level bowel distension as is necessary for optimal CT, representing an additional important technical advantage of MRE.

The advantages of CT include its availability and a slight cost differential, although the overall cost-benefit balance is a key measure that remains incompletely evaluated. Studies comparing MRE to CT for the evaluation of small bowel pathology have indicated similar sensitivities in some studies (53, 54), better sensitivity for CT in one study (55), and better sensitivity for MRE in a fourth study (56). As we discussed for SBFT, this variety of results can be attributed to the fact that these studies were performed without the advantages of current, optimized MRE techniques.

### Comparison of MRE to surgical resection specimens

The gold standard of evaluating MRE findings remains comparison to surgical specimens. Punwani et al. (18) evaluated MRE prior to surgical resection in Crohn's disease (7 fibrostenotic disease and 11 ileal disease unresponsive to treatment). Their results suggest that increased mural thickness and high mural signal intensity reflect the histological features of small bowel inflammation in Crohn's disease. The enhancement pattern differed in fibrostenotic compared to inflammatory tissue, with homogenous enhancement more often observed in inflammation and layered/non-homogenous enhancement visualized in fibrostenotic disease. They concluded that MRE images correlated with the histological examination of surgical specimens and validated the MRE findings against matched histology specimens.

### Summary of MRE findings in Crohn's disease

The MRE technique has evolved to produce reproducible, high-quality examinations of the small and large bowel to a degree that significantly advances its sensitivity and specificity in detecting Crohn's disease changes. Much of the comparative literature on MRE was published before the development of optimized techniques, and this accounts for the wide range of results in these studies. In our recent experience, CT does not match MRE for producing the soft tissue contrast necessary to reliably delineate between inflammation and chronic changes related to fibrosis; both processes may look identical on CT. On MRE, the T2 signal increases with inflammation and edema, a marker of active Crohn's disease (22, 39). The use of single-shot T2 combined with fat suppression employing the SPAIR technique is critical to optimize the sensitivity and specificity of MRE for diagnosing active Crohn's disease (21, 22); the majority of earlier publications either did not use FS T2 or did not use the SPAIR technique. Other forms of fat suppression, using simple inversion recovery or chemical shift spoiling,

**Table 3.** Relationship between MRE findings and therapy optimization in symptomatic patients

| | MRE findings[a] | |
|---|---|---|
| Obstruction/fistula | E+T2hi | E+T2lo |
| Obstruction[b] | • Treat active disease (e.g., steroids) | • Surgical resection |
| No obstruction or fistula | • Treat active disease (e.g., steroids) and consider maintenance regimen (immunomodulators)<br>• Use MRE for longitudinal evaluation to show resolution of inflammation (T2hi) and to document baseline underlying fibrosis (E), i.e., conversion of the patient to the next column | • Continue or initiate maintenance regimens (immunomodulators)<br>• Consider fibrotic peritoneal tethering causing mechanical pain treatable by surgery<br>• Consider longitudinal follow-up MRE to evaluate fibrotic bowel wall thickening for possible fibrotic remodeling and improvement while on maintenance therapy |
| Fistula | • Treat active disease (e.g., steroids), consider immunomodulators, and monitor fistula for healing using follow-up MRE<br>• Treat abscess by percutaneous drainage and antibiotics | • Treat persistent fistula by surgical resection |

[a]It is critical that both enhanced T1W and T2 imaging be performed with fat suppression.
[b]Obstruction is defined as marked dilation of bowel above the diseased segment.
MRE, magnetic resonance enterography;
E, bowel wall thickening and enhancement on post-gadolinium T1W images;
T2hi, high signal intensity in or around the thickened bowel wall, indicative of edema and active inflammatory disease;
T2lo, low, normal range, signal intensity in or around the thickened bowel wall, showing no edema and associated with quiescent disease.

will be affected by higher noise, less uniform fat suppression, or increased through-plane motion sensitivity to bowel peristalsis.

MRE does not detect mild, early disease limited to the mucosa. This accounts for the different results when comparing endoscopic, biopsy and capsule techniques, which only see mucosal disease. However, submucosal and deeper disease is often under-represented on endoscopic examinations but detected by MRE.

## Recommendations for clinical applications of MRE in Crohn's disease

MRE can aid in the clinical management of Crohn's disease and provide a more complete picture of the disease burden. The complementary use of MRE with mucosal visualization and biopsy can lead to better management decisions and therapeutic options. MRE can provide a non-invasive longitudinal measure of disease activity and a measure of submucosal fibrosis. It is expected that MRE will improve the utilization of medical and surgical treatments and improve outcomes while decreasing radiation risks from repeated CT scans. Specifically, MRE may be used in clinical applications in Crohn's disease for the following:

1) Evaluation of the extent of small bowel disease at diagnosis
2) Evaluation of disease burden in symptomatic patients to direct therapeutic management
3) Evaluation of fibrostenotic disease, which may respond better to surgery than to escalation of medical therapy
4) Confirmation of clinical remission and consideration for escalation of medical therapy if there is persistent submucosal disease despite clinical remission
5) Evaluation of intra-abdominal complications, including fistulae, tethering, stenosis, and abscesses
6) Evaluation of perianal disease

## Research applications of MRE in Crohn's disease

MRE presents numerous translational research opportunities, including the study of the pathogenesis of penetrating/stricturing disease and investigating the mechanisms related to the clinical symptoms of diarrhea and pain. Longitudinal documentation of patients using MRE will yield insights into the nature of submucosal inflammation and its relationships to mucosal disease, fibrostenotic disease, fat wrapping, and changes that occur with medical treatment, including the potential role of medical management in altering the natural course of Crohn's disease. MRE may also be used to monitor fibrosis, which will allow the evaluation of potential therapeutic remodeling of the fibrotic bowel wall, a phenomenon that remains not fully explored.


### Acknowledgments

In loving memory of Shanthi Sitaraman, MD, PhD, a former classmate, colleague and mentor, known to all as a major contributor to our understanding of inflammatory bowel disease.


### Conflict of interest disclosure

The authors declared no conflicts of interest.

### References


1. Brenner DJ, Hall EJ. Computed tomography--an increasing source of radiation exposure. N Engl J Med 2007; 357:2277–2284.
2. Cardis E, Vrijheid M, Blettner M, et al. The 15-Country Collaborative Study of Cancer Risk among Radiation Workers in the Nuclear Industry: estimates of radiation-related cancer risks. Radiat Res 2007; 167:396–416.
3. Fazel R, Krumholz HM, Wang Y, et al. Exposure to low-dose ionizing radiation from medical imaging procedures. N Engl J Med 2009; 361:849–857.
4. Fucic A, Brunborg G, Lasan R, Jezek D, Knudsen LE, Merlo DF. Genomic damage in children accidentally exposed to ionizing radiation: a review of the literature. Mutat Res 2008; 658:111–123.
5. Martin DR, Semelka RC. Health effects of ionising radiation from diagnostic CT. Lancet 2006; 367:1712–1714.

6. Preston DL, Pierce DA, Shimizu Y, et al. Effect of recent changes in atomic bomb survivor dosimetry on cancer mortality risk estimates. Radiat Res 2004; 162:377–389.
7. Preston DL, Ron E, Tokuoka S, et al. Solid cancer incidence in atomic bomb survivors: 1958-1998. Radiat Res 2007; 168:1–64.
8. Preston DL, Shimizu Y, Pierce DA, Suyama A, Mabuchi K. Studies of mortality of atomic bomb survivors. Report 13: Solid cancer and noncancer disease mortality: 1950-1997. Radiat Res 2003; 160:381–407.
9. Sodickson A, Baeyens PF, Andriole KP, et al. Recurrent CT, cumulative radiation exposure, and associated radiation-induced cancer risks from CT of adults. Radiology 2009; 251:175–184.
10. Desmond AN, O'Regan K, Curran C, et al. Crohn's disease: factors associated with exposure to high levels of diagnostic radiation. Gut 2008; 57:1524–1529.
11. Newnham E, Hawkes E, Surender A, James SL, Gearry R, Gibson PR. Quantifying exposure to diagnostic medical radiation in patients with inflammatory bowel disease: are we contributing to malignancy? Aliment Pharmacol Ther 2007; 26:1019–1024.
12. Palmer L, Herfarth H, Porter CQ, Fordham LA, Sandler RS, Kappelman MD. Diagnostic ionizing radiation exposure in a population-based sample of children with inflammatory bowel diseases. Am J Gastroenterol 2009; 104:2816–2823.
13. Maglinte DD, Siegelman ES, Kelvin FM. MR enteroclysis: the future of small-bowel imaging? Radiology 2000; 215:639–641.
14. Gourtsoyiannis N, Papanikolaou N, Grammatikakis J, Prassopoulos P. MR enteroclysis: technical considerations and clinical applications. Eur Radiol 2002; 12:2651–2658.
15. Gourtsoyiannis N, Papanikolaou N, Grammatikakis J, Maris T, Prassopoulos P. MR imaging of the small bowel with a true-FISP sequence after enteroclysis with water solution. Invest Radiol 2000; 35:707–711.
16. Martin DR, Danrad R, Herrmann K, Semelka RC, Hussain SM. Magnetic resonance imaging of the gastrointestinal tract. Top Magn Reson Imaging 2005; 16:77–98.
17. Martin DR, Lauenstein T, Sitaraman SV. Utility of magnetic resonance imaging in small bowel Crohn's disease. Gastroenterology 2007; 133:385–390.
18. Punwani S, Rodriguez-Justo M, Bainbridge A, et al. Mural inflammation in Crohn disease: location-matched histologic validation of MR imaging features. Radiology 2009; 252:712–720.
19. Fornasa F, Benassuti C, Benazzato L. Role of magnetic resonance enterography in differentiating between fibrotic and active inflammatory small bowel stenosis in patients with Crohn's disease. J Clin Imaging Sci 2011; 1:35.
20. Ha CY, Kumar N, Raptis CA, Narra VR, Ciorba MA. Magnetic resonance enterography: safe and effective imaging for stricturing Crohn's disease. Dig Dis Sci 2011; 56:2906–2913.
21. Lauenstein TC, Sharma P, Hughes T, Heberlein K, Tudorascu D, Martin DR. Evaluation of optimized inversion-recovery fat-suppression techniques for T2-weighted abdominal MR imaging. J Magn Reson Imaging 2008; 27:1448–1454.
22. Udayasankar UK, Martin D, Lauenstein T, et al. Role of spectral presaturation attenuated inversion-recovery fat-suppressed T2-weighted MR imaging in active inflammatory bowel disease. J Magn Reson Imaging 2008; 28:1133–1140.
23. Leyendecker JR, Bloomfeld RS, DiSantis DJ, Waters GS, Mott R, Bechtold RE. MR enterography in the management of patients with Crohn disease. Radiographics 2009; 29:1827–1846.
24. Schunk K, Kern A, Oberholzer K, et al. Hydro-MRI in Crohn's disease: appraisal of disease activity. Invest Radiol 2000; 35:431–437.
25. Ajaj W, Lauenstein TC, Langhorst J, et al. Small bowel hydro-MR imaging for optimized ileocecal distension in Crohn's disease: should an additional rectal enema filling be performed? J Magn Reson Imaging 2005; 22:92–100.
26. Narin B, Ajaj W, Gohde S, et al. Combined small and large bowel MR imaging in patients with Crohn's disease: a feasibility study. Eur Radiol 2004; 14:1535–1542.
27. Negaard A, Paulsen V, Sandvik L, et al. A prospective randomized comparison between two MRI studies of the small bowel in Crohn's disease, the oral contrast method and MR enteroclysis. Eur Radiol 2007; 17:2294–2301.
28. Lawrance IC, Welman CJ, Shipman P, Murray K. Small bowel MRI enteroclysis or follow through: which is optimal? World J Gastroenterol 2009; 15:5300–5306.
29. Mako EK, Mester AR, Tarjan Z, Karlinger K, Toth G. Enteroclysis and spiral CT examination in diagnosis and evaluation of small bowel Crohn's disease. Eur J Radiol 2000; 35:168–175.
30. Erber WF, Erber JA. Meta-analysis of the yield of capsule endoscopy in patients with Crohn's disease. Am J Gastroenterol 2006; 101:2669.
31. Mary JY, Modigliani R. Development and validation of an endoscopic index of the severity for Crohn's disease: a prospective multicentre study. Groupe d'Etudes Therapeutiques des Affections Inflammatoires du Tube Digestif (GETAID). Gut 1989; 30:983–989.
32. Miao YM, Koh DM, Amin Z, et al. Ultrasound and magnetic resonance imaging assessmentof active bowel segments in Crohn's disease. Clin Radiol 2002; 57:913–918.
33. Florie J, Wasser MN, Arts-Cieslik K, Akkerman EM, Siersema PD, Stoker J. Dynamic contrast-enhanced MRI of the bowel wall for assessment of disease activity in Crohn's disease. AJR Am J Roentgenol 2006; 186:1384–1392.
34. Maccioni F, Bruni A, Viscido A, et al. MR imaging in patients with Crohn disease: value of T2- versus T1-weighted gadolinium-enhanced MR sequences with use of an oral superparamagnetic contrast agent. Radiology 2006; 238:517–530.
35. Ajaj WM, Lauenstein TC, Pelster G, et al. Magnetic resonance colonography for the detection of inflammatory diseases of the large bowel: quantifying the inflammatory activity. Gut 2005; 54:257–263.
36. Albert JG, Martiny F, Krummenerl A, et al. 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.
37. Ochsenkuhn T, Herrmann K, Schoenberg SO, Reiser MF, Goke B, Sackmann M. Crohn disease of the small bowel proximal to the terminal ileum: detection by MR-enteroclysis. Scand J Gastroenterol 2004; 39:953–960.
38. Shoenut JP, Semelka RC, Magro CM, Silverman R, Yaffe CS, Micflikier AB. Comparison of magnetic resonance imaging and endoscopy in distinguishing the type and severity of inflammatory bowel disease. J Clin Gastroenterol 1994; 19:31–35.
39. Udayasankar UK, Burrow B, Sitaraman SV, Rutherford R, Martin DR. Evaluation of Crohn disease activity using MRI: correlation with T2 signal intensity on fat-suppressed single shot imaging. Presented at 2007 International Society of Magentic Resonance in Medicine; May 24, 2007; Berlin, Germany.
40. Sempere GA, Martinez Sanjuan V, Medina Chulia E, et al. MRI evaluation of inflammatory activity in Crohn's disease. AJR Am J Roentgenol 2005; 184:1829–1835.
41. Best WR, Becktel JM, Singleton JW, Kern F Jr. Development of a Crohn's disease activity index. National Cooperative Crohn's Disease Study. Gastroenterology 1976; 70:439–444.
42. Harvey RF, Bradshaw JM. A simple index of Crohn's-disease activity. Lancet 1980; 1:514.
43. Hyams JS, Ferry GD, Mandel FS, et al. Development and validation of a pediatric Crohn's disease activity index. J Pediatr Gastroenterol Nutr 1991; 12:439–447.
44. Koh DM, Miao Y, Chinn RJ, et al. MR imaging evaluation of the activity of Crohn's disease. AJR Am J Roentgenol 2001; 177:1325–1332.
45. Martinez MJ, Ripolles T, Paredes JM, Blanc E, Marti-Bonmati L. Assessment of the extension and the inflammatory activity in Crohn's disease: comparison of ultrasound and MRI. Abdom Imaging 2009; 34:141–148.
46. Del Vescovo R, Sansoni I, Caviglia R, et al. Dynamic contrast enhanced magnetic resonance imaging of the terminal ileum: differentiation of activity of Crohn's disease. Abdom Imaging 2008; 33:417–424.
47. Madsen SM, Thomsen HS, Munkholm P, et al. Inflammatory bowel disease evaluated by low-field magnetic resonance imaging. Comparison with endoscopy, 99mTc-HMPAO leucocyte scintigraphy, conventional radiography and surgery. Scand J Gastroenterol 2002; 37:307–316.
48. Laghi A, Borrelli O, Paolantonio P, et al. Contrast enhanced magnetic resonance imaging of the terminal ileum in children with Crohn's disease. Gut 2003; 52:393–397.

49. Alexopoulou E, Roma E, Loggitsi D, et al. Magnetic resonance imaging of the small bowel in children with idiopathic inflammatory bowel disease: evaluation of disease activity. Pediatr Radiol 2009; 39:791–797.
50. Golder SK, Schreyer AG, Endlicher E, et al. Comparison of capsule endoscopy and magnetic resonance (MR) enteroclysis in suspected small bowel disease. Int J Colorectal Dis 2006; 21:97–104.
51. Tillack C, Seiderer J, Brand S, et al. Correlation of magnetic resonance enteroclysis (MRE) and wireless capsule endoscopy (CE) in the diagnosis of small bowel lesions in Crohn's disease. Inflamm Bowel Dis 2008; 14:1219–1228.
52. Gourtsoyiannis NC, Grammatikakis J, Papamastorakis G, et al. Imaging of small intestinal Crohn's disease: comparison between MR enteroclysis and conventional enteroclysis. Eur Radiol 2006; 16:1915–1925.
53. Lee SS, Kim AY, Yang SK, et al. Crohn disease of the small bowel: comparison of CT enterography, MR enterography, and small-bowel follow-through as diagnostic techniques. Radiology 2009; 251:751–761.
54. Siddiki HA, Fidler JL, Fletcher JG, et al. Prospective comparison of state-of-the-art MR enterography and CT enterography in small-bowel Crohn's disease. AJR Am J Roentgenol 2009; 193:113–121.
55. Schmidt S, Lepori D, Meuwly JY, et al. Prospective comparison of MR enteroclysis with multidetector spiral-CT enteroclysis: interobserver agreement and sensitivity by means of "sign-by-sign" correlation. Eur Radiol 2003; 13:1303–1311.
56. Low RN, Francis IR, Politoske D, Bennett M. Crohn's disease evaluation: comparison of contrast-enhanced MR imaging and single-phase helical CT scanning. J Magn Reson Imaging 2000; 11:127–135.