Prospective Comparison of State-of-the-Art MR Enterography and CT Enterography in Small-Bowel Crohn's Disease

Hassan A. Siddiki[1]
Jeff L. Fidler[1]
Joel G. Fletcher[1]
Sharon S. Burton[1]
James E. Huprich[1]
David M. Hough[1]
C. Daniel Johnson[1]
David H. Bruining[2]
Edward V. Loftus, Jr.[2]
William J. Sandborn[2]
Darrell S. Pardi[2]
Jayawant N. Mandrekar[3]

OBJECTIVE. The objective of our study was to prospectively obtain pilot data on the accuracy of MR enterography for detecting small-bowel Crohn's disease compared with CT enterography and with a clinical reference standard based on imaging, clinical information, and ileocolonoscopy.

SUBJECTS AND METHODS. The study group for this blinded prospective study was composed of 33 patients with suspected active Crohn's ileal inflammation who were scheduled for clinical CT enterography and ileocolonoscopy and had consented to also undergo MR enterography. The MR enterography and CT enterography examinations were each interpreted by two radiologists with disagreements resolved by consensus. The reports from ileocolonoscopy with or without mucosal biopsy were interpreted by a gastroenterologist. The reference standard for the presence of small-bowel Crohn's disease was based on the final clinical diagnosis by the referring gastroenterologist after reviewing all of the available information.

RESULTS. All 33 patients underwent CT enterography and ileocolonoscopy, 30 of whom also underwent MR enterography. The sensitivities of MR enterography and CT enterography for detecting active small-bowel Crohn's disease were similar (90.5% vs 95.2%, respectively; $p = 0.32$). The image quality scores for MR enterography examinations were significantly lower than those for CT enterography ($p = 0.005$). MR enterography and CT enterography identified eight cases (24%) with a final diagnosis of active small-bowel inflammation in which the ileal mucosa appeared normal at ileocolonoscopy. Furthermore, enterography provided the only available imaging in three additional patients who did not have ileal intubation.

CONCLUSION. MR enterography and CT enterography have similar sensitivities for detecting active small-bowel inflammation, but image quality across the study cohort was better with CT. Cross-sectional enterography provides complementary information to ileocolonoscopy.

Keywords: Crohn's disease, CT enterography, inflammatory bowel disease, MR enterography, small bowel

DOI:10.2214/AJR.08.2027

Received October 29, 2008; accepted after revision December 17, 2008.

This study was funded in part by a research grant awarded to J. L. Fidler from Bracco.

C. D. Johnson holds a CT colonography license with GE Healthcare.

[1]Department of Radiology, Mayo Clinic, 200 First St., SW, Rochester, MN 55905. Address correspondence to J. L. Fidler (fidler.jeff@mayo.edu).

[2]Miles and Shirley Fiterman Center for Digestive Diseases, Mayo Clinic, Rochester, MN.

[3]Division of Biostatistics, Department of Health Sciences Research, Mayo Clinic, Rochester, MN.

AJR 2009; 193:113–121

0361–803X/09/1931–113

The prevalence of inflammatory bowel disease (IBD), including Crohn's disease, is increasing in the United States, with an estimated 31% increase in the prevalence of Crohn's disease since 1991 [1]. The risk of morbidity and mortality in inaccurately diagnosed or assessed Crohn's disease patients is increased because of either gastrointestinal complications arising directly from the disease process [2–6] or prolonged immunosuppression from medical treatment [7–9]. This increased risk warrants accurate and reliable methods of correctly quantifying the extent and severity of disease activity.

Cross-sectional imaging techniques are playing an increasing role in the imaging of patients with Crohn's disease. Historically, ileoscopy and biopsy of the terminal ileum have been incorporated into the reference standard for modern studies estimating the performance characteristics of cross-sectional enterography [10–12]. In a recent prospective, blinded, four-way head-to-head trial comparing wireless capsule endoscopy, ileocolonoscopy, CT enterography, and small-bowel follow-through, the sensitivity of CT enterography for the detection of active inflammatory small-bowel Crohn's disease was not significantly different from that of wireless capsule endoscopy ($p = 0.63$) [13]. However, CT enterography had a superior specificity compared with wireless capsule endoscopy (89% vs 53%, respectively; $p = 0.02$). CT enterography has also been shown to have a higher sensitivity than barium small-bowel follow-through [13, 14]. At some institutions, CT enterography combined with ileocolonoscopy has become a first-line test for the diagnosis and staging of Crohn's disease [13].

Radiology imaging alternatives to CT enterography include barium small-bowel follow-through and MR enterography. Given the concerns of the public and medical professionals about radiation-induced cancer arising from medically related CT [15], particularly in the setting of a chronic and remitting disease such as Crohn's, which can lead to multiple CT examinations in young patients, the role of CT enterography in assessing younger patients is being increasingly discussed [16, 17]. There is a need for a small-bowel imaging technique that has the advantages of CT enterography—that is, the ability to show the entire small bowel, detect transmural inflammation, grade the severity of inflammation, and detect extracolonic inflammation—but does not require ionizing radiation. MR enterography does not require ionizing radiation and has been shown in some studies to have excellent sensitivity for detecting active Crohn's disease [18]. Therefore, MR enterography could potentially replace CT enterography for the imaging of Crohn's disease. However, comparing MR enterography with CT enterography studies is difficult because reference and selection bias can significantly skew results. Limited studies comparing MR enterography with CT enterography for detecting active Crohn's disease have been performed in the same patients, and the results of those studies are inconsistent [19, 20]; moreover, only one used state-of-the-art CT enterography techniques [20].

The purpose of our study was to compare state-of-the-art MR enterography and CT enterography in the detection of small-bowel inflammation using a prospective blinded study design and a comprehensive clinical reference standard that included ileocolonoscopy performed as part of routine clinical practice.

Subjects and Methods

This study was approved by the institutional review board at our institution and fulfilled the regulations of the HIPAA.

Patients with suspected active small-bowel Crohn's disease who were scheduled for CT enterography and ileocolonoscopy that had been ordered as part of routine clinical practice by a gastroenterologist and who consented prospectively to undergo an additional MR enterography examination were included in the study. Exclusion criteria were the presence of a contraindication to MRI, the inability to receive gadolinium or iodinated contrast material (allergy, renal insufficiency), and claustrophobia. Patients who had difficulty tolerating the oral contrast agent at CT enterography (e.g., nausea or vomiting) did not undergo subsequent MR enterography. All examinations were required to be performed within 30 days of each other.

CT Enterography Technique

CT enterography was performed in each patient using a helical 16-MDCT system (LightSpeed Pro, GE Healthcare). A neutral enteric contrast agent (barium preparation [VoLumen, Bracco]) was initially administered orally to achieve small-bowel distention. Patients consumed three bottles (total volume = 1,350 mL) of the oral contrast agent one at 60, one at 45, and one at 30 minutes before scanning. Fifteen minutes before scanning, participants were asked to drink an additional 500 mL of water. Immediately before scanning, patients were given 0.5 mg of glucagon IV over 30 seconds.

Contrast-enhanced CT was performed using 310 mA, 120 kVp, a 0.5-second tube rotation time, a detector configuration of 16 × 0.625, and a pitch of 0.9375. IV contrast material (150 mL of iohexol [Omnipaque 300, GE Healthcare]) was injected at a rate of 4 mL/s, and scanning was initiated after a 50-second delay [21]. Images were obtained with a 2.5-mm section thickness and an interval of 1.25 mm. Overlapping 2-mm coronal images were reconstructed from overlapping 1.25-mm slices.

MR Enterography Technique

Twenty-three patients underwent MR enterography immediately after CT enterography, and seven patients underwent repeated administration of oral contrast material for MR enterography on a separate day. Patients taken to MR enterography immediately after CT enterography were given an additional bottle of 500 mL of water and were instructed to continue drinking until they were placed on the scanner. For patients who had a standalone examination, the drinking algorithm was the same as that for CT enterography. MR enterography was performed within 21 days of CT enterography without any intervening treatment in all patients.

MR enterography was performed using a 1.5-T magnet (Signa, GE Healthcare). Patients were scanned in the supine position with a 16-channel torso array coil using the following protocol: coronal single-shot fast spin-echo (SSFSE) (TR/TE, 2,000/90; matrix size, 256 × 256; slice thickness, 5 mm; gap, 0 mm), coronal 2D true fast imaging with steady-state precession (FISP) (matrix, 193 × 340; slice thickness, 5 mm; gap, 0 mm), axial SSFSE (2,000/90; matrix, 256 × 256; slice thickness, 6 mm; gap, 0 mm), axial 2D true FISP (matrix, 192 × 340; slice thickness, 6 mm; gap, 0 mm), and axial 2D true FISP with fat suppression (matrix, 192 × 340; slice thickness, 6 mm; gap, 0 mm). All patients, regardless of whether the MR enterography examination was performed on the same day as CT enterography, were then given 0.5 mg of glucagon IV. After the administration of 0.2 mmol/kg of gadodiamide (Omniscan, GE Healthcare) at 3 mL/s and a 45-second scanning delay, coronal 2D fast spoiled gradient-recalled echo (FSPGR) (TR, 150 milliseconds; matrix, 320 × 160; slice thickness, 6 mm; gap, 0 mm), coronal 3D liver acquisition volume acceleration (LAVA) (matrix, 384 × 224; slice thickness, 4 mm; gap, 0 mm), and axial 3D LAVA (matrix, 320 × 192; slice thickness, 4 mm; gap, 0 mm) sequences were performed. Parallel imaging was used for all contrast-enhanced sequences. All sequences were performed during breath-holding.

Endoscopy

All ileocolonoscopy examinations were performed in a clinical setting by a board-certified gastroenterologist using standard techniques. The gastroenterologist had access to all clinical data except the CT enterography and MR enterography results because those examinations were performed after ileocolonoscopy in all patients. Each ileocolonoscopy procedure was performed by a gastroenterologist from a large group of gastroenterologists as part of routine clinical practice. The endoscopist knew that the indication for the procedure was Crohn's disease but did not necessarily know that the patient was participating in a comparative study of MR enterography and CT enterography, was not given specific instructions to intubate the terminal ileum or to obtain mucosal biopsy samples, was not given any standardized criteria for determining the presence of ileal inflammation or grading its severity, and was not asked to prospectively determine whether ileal inflammation was present or to grade its severity.

After the clinically indicated ileocolonoscopy examinations (with or without mucosal biopsy) were performed, a single gastroenterologist reviewed the ileocolonoscopy and pathology reports. Ileocolonoscopy findings without mucosal biopsy were classified as active small-bowel Crohn's disease when ulcerations, erosions, granularity, friability, or erythema was identified in the ileocolonoscopy report. Ileocolonoscopy with mucosal biopsy was classified as showing active small-bowel Crohn's disease when ulcerations, erosions, granularity, friability, or erythema was identified in the ileocolonoscopy report, when acute or chronic active ileitis was identified in the pathology report, or both.

Study Design and Reference Standard

Cross-sectional enterography examinations were independently reviewed by four radiologists

(two for MR enterography, two for CT enterography) blinded to all clinical information. Reviewers indicated the global disease assessment (1 = definitely active, 2 = suspicious, 3 = inactive, 4 = absent) based on findings indicative of active inflammation including segmental mural hyperenhancement, increased wall thickness (> 3 mm), or the presence of penetrating disease (sinus tract, fistula, abscess). Maximum small-bowel wall thickness was recorded in millimeters, and other imaging features of active small-bowel inflammation were recorded (i.e., mural stratification, high T2 mural MR signal, presence of the comb sign, adenopathy). Findings were recorded for the following bowel segments: duodenum, proximal jejunum, distal jejunum, proximal ileum, distal ileum, and terminal ileum.

For statistical purposes, imaging interpretations classified as definitely active or suspicious were considered to have active disease present, whereas those categorized on imaging as inactive or absent were considered to have active disease absent. For cases in which there were discrepant interpretations between the two reviewers (active vs inactive), a second review with both readers was performed to obtain a consensus interpretation.

The electronic medical record was reviewed to create the comprehensive clinical reference standard. Each patient was seen by a clinical gastroenterologist who is an expert in the diagnosis and management of IBD after the performance of ileocolonoscopy, MR enterography, and CT enterography. The gastroenterologist had an unblinded review of all the clinical data (e.g., MR enterography, CT enterography, ileocolonoscopy, mucosal biopsy, surgical reports, surgical pathology, physical examination, serum laboratory test results) to determine whether active small-bowel inflammation was present. All of this information was incorporated into the gastroenterologist's discharge impression, which was used to categorize cases as active, inactive, or absent with respect to small-bowel Crohn's disease. In equivocal cases, the gastroenterologist was contacted for confirmation of his or her impression. To assess the accuracy of MR enterography and CT enterography to diagnose penetrating disease, all participating radiologists performed a consensus review of all MR enterography and CT enterography examinations in which at least one reader identified a sinus tract, fistula, or abscess.

To evaluate MR enterography and CT enterography image quality for displaying small-bowel anatomy in detail, a subspecialized gastrointestinal radiologist not participating in the prospective reads rated the quality of the MR enterography and CT enterography data sets on a 5-point ordinal scale, where 5 was excellent quality; 4, minimum artifacts, no effect on confidence; 3, moderate artifacts, mild to moderate decrease in reader confidence; 2, moderately severe artifacts, markedly diminished confidence; and 1, uninterpretable. The artifacts that were assessed included patient motion, bowel peristalsis, and artifacts related to pulse sequences. Bowel distention was not incorporated into the classification. This reviewer also determined the probable cause for any false-negative and false-positive MR enterography and CT enterography examinations compared with the comprehensive clinical reference standard. Ileocolonoscopy reports were reviewed separately in a blinded fashion by a gastroenterologist and gastrointestinal radiologist, and the results were grouped in one of five different categories: 1, terminal ileum not intubated; 2, ileoscopy negative and mucosal biopsy negative; 3, ileoscopy negative and mucosal biopsy positive; 4, ileoscopy positive and mucosal biopsy not performed; and 5, ileoscopy positive and mucosal biopsy positive.

Statistical Analysis

The primary outcome variables were the sensitivity and specificity of MR enterography and CT enterography using a comprehensive clinical reference standard for each case. The 95% exact binomial CIs for these estimates were calculated. Sensitivities and specificities were compared using the McNemar test for paired categoric observations of two groups. Interobserver agreement scores were calculated between the two readers for global assessment of disease activity (active vs not active) on MR enterography and CT enterography.

For exploring assessment of imaging signs of Crohn's disease at MR enterography and CT enterography, we calculated interobserver agreement scores (kappa scores or intraclass correlation coefficients) and reported the kappa scores for the two pairs of readers using a commonly used rating system [22]. For the purposes of analysis, segments were classified as distal disease (terminal and distal ileum) or as proximal disease (duodenum, jejunum, and proximal ileum). We compared the image quality scores of MR enterography and CT enterography examinations using a two-tailed Student's *t* test.

Results

Thirty-three consecutive patients were recruited into this prospective study between April 2005 and May 2008. Eighteen (55%) were men (mean age, 40 years; age range, 20–60 years), and 15 (45%) were women (mean age, 39 years; age range, 21–63 years). Twenty-two patients (67%) had active disease, two (6%) had inactive disease, and nine (27%) did not have Crohn's disease by the comprehensive clinical reference standard. The results of imaging, ileocolonoscopy, mucosal biopsy, and the clinical reference standard are listed in Table 1.

All 33 patients underwent CT enterography and ileocolonoscopy, and 30 patients also underwent MR enterography. Three participants could not tolerate ingestion of the entire volume of oral contrast agent during CT enterography and did not undergo MR enterography. Nonetheless, they underwent the CT enterography examination, and the data sets had acceptable diagnostic image quality. On retrospective evaluation, none of these patients had small-bowel obstruction.

The head-to-head comparison of MR enterography and CT enterography for the 30 patients who successfully underwent both studies is given in Table 2. Although MR enterography had a slightly lower sensitivity and specificity, this difference was not statistically significant. For all 33 cases that had ileocolonoscopy, CT enterography had a sensitivity of 91% (20/22) for each reader, a sensitivity of 95% (21/22) for the consensus read, a specificity of 64% (7/11) and 73% (8/11) for both readers, and a specificity of 82% (9/11) for the consensus read.

Interobserver agreement scores of the MR enterography and CT enterography data sets for the global assessment of disease activity between the two readers for each technique are shown in Table 3. For overall disease assessment, agreement for both MR enterography and CT enterography was in the range of substantial agreement (0.6–0.8), with slightly worse agreement for MR enterography. The MR enterography sign of mural stratification of proximal disease and the CT enterography sign of mural hyperenhancement of proximal disease segments scored in the highest tier of agreement range (> 0.8, almost perfect agreement). The comb sign was in the almost-perfect agreement range for both MR enterography and CT enterography.

The quality score for all CT enterography examinations was noted as excellent (i.e., a score of 5 on our quality scale). The mean and median MR enterography quality scores were 4.7 and 5, respectively (range, 3–5). Six MR enterography data sets had minimum artifacts (score = 4) and two, moderate (score = 3), which resulted in significantly lower grading scores than CT enterography ($p = 0.005$). No significant difference in the MR enterography quality score was seen for examinations performed the same day as CT enterography

TABLE 1: Results of MR Enterography, CT Enterography, Ileoscopy, Mucosal Biopsy, and Clinical Reference Standard

Case No.	MR Enterography			CT Enterography			Ileoscopy	Mucosal Biopsy	Clinical Reference Standard
	Reviewer 1	Reviewer 2	Consensus	Reviewer 1	Reviewer 2	Consensus			
1	Active	Active	Active	Active	Active	Active	No intubation	NP	Active
2	Absent	Absent	Absent	Absent	Absent	Absent	Normal	NP	Absent
3	Active	Active	Active	Active	Active	Active	Normal	NP	Active
4	Active	Suspicious	Active	Active	Inactive	Active	Positive	Normal	Active
5	Active	Active	Active	Active	Active	Active	Positive	Positive	Active
6	Absent	Suspicious	Suspicious	Absent	Absent	Absent	Normal	NP	Absent
7	Active	Absent	Suspicious	Suspicious	Absent	Absent	Positive	Normal	Absent
8	Active	Absent	Absent	Absent	Active	Absent	Normal	NP	Absent
9	Absent	Absent	Absent	Active	Absent	Absent	Normal	NP	Absent
10	Absent	Absent	Absent	Suspicious	Suspicious	Suspicious	Normal	Normal	Absent
11	Active	Active	Active	Suspicious	Suspicious	Suspicious	No intubation	NP	Active
12	Active	Suspicious	Active	Active	Suspicious	Active	Positive	Positive	Active
13	Active	Active	Active	Active	Active	Active	No intubation	NP	Active
14	Active	Active	Active	Active	Active	Active	Positive	Positive	Active
15	Absent	Absent	Absent	Absent	Absent	Absent	Positive	Positive	Active
16	Suspicious	Suspicious	Suspicious	Absent	Absent	Absent	Normal	Normal	Absent
17	Active	Active	Active	Active	Active	Active	Normal	NP	Active
18	Active	Active	Active	Active	Active	Active	Negative	Normal	Active
19	Absent	Absent	Absent	Active	Active	Active	Normal	NP	Active
20	Absent	Absent	Absent	Absent	Absent	Absent	Normal	NP	Absent
21	Active	Active	Active	Active	Active	Active	Positive	Positive	Active
22	Active	Active	Active	Active	Active	Active	Normal	Normal	Active
23	Inactive	Active	Active	Suspicious	Absent	Active	Positive	Positive	Active
24	Active	Active	Active	Suspicious	Active	Active	Positive	Positive	Active
25	Active	Active	Active	Active	Active	Active	Normal	Normal	Active
26	Active	Suspicious	Active	Suspicious	Active	Active	Positive	Positive	Active
27	Active	Absent	Active	Active	Suspicious	Active	Negative	Normal	Active
28	Absent	Absent	Absent	Absent	Inactive	Absent	Normal	NP	Absent
29	Active	Active	Active	Active	Active	Active	Normal	Normal	Active
30	Active	Active	Active	Active	Active	Active	Positive	Positive	Active
31	NP	NP	NP	Active	Suspicious	Active	Normal	NP	Inactive
32	NP	NP	NP	Absent	Inactive	Inactive	Normal	Normal	Inactive
33	NP	NP	NP	Absent	Suspicious	Active	Positive	NP	Active

Note—NP = not performed.

in comparison with examinations performed on different days ($p = 0.08$).

In our cohort of 33 patients, seven patients were found to have penetrating complications. The reference standard confirmed six patients as indeed having penetrating complications and indicated that one patient did not and that MR enterography was overcalled in that case. The kappa score for penetrating disease, which was higher for MR enterography, is reported in Table 3.

There were three cases in which CT enterography was discordant with the reference standard. One of these cases was a false-negative; the patient had mild active disease at ileocolonoscopy and mucosal biopsy. The other two cases were false-positives. The false-positive CT enterography results were thought to be secondary to luminal collapse giving the appearance of wall thickening.

The MR enterography findings were discordant with the reference standard in five cases: Two were false-negatives, and three were false-positives. One false-negative case was the same as the false-negative CT enterography (occult disease at imaging), and the other was negative because of perception errors (Fig. 1). The three false-positive cases were thought to be due to bowel wall collapse ($n = 1$), fibrosis ($n = 1$), and a combination of bowel wall collapse and motion artifact ($n = 1$).

Cross-sectional enterography provided new and complementary information to ileo-

TABLE 2: Head-to-Head Analysis Between MR Enterography and CT Enterography

Technique	Sensitivity (%)	95% CI	Specificity (%)	95% CI	Interobserver Agreement	95% CI
MR enterography (n = 30)					0.63	0.31–0.92
Consensus	90.5 (19/21)	70–99	66.7 (6/9)	30–93		
Reader 1	85.7 (18/21)	64–97	66.7 (6/9)	30–93		
Reader 2	85.7 (18/21)	64–97	77.8 (7/9)	40–97		
CT enterography (n = 30)					0.76	0.5–1.0
Consensus	95.2 (20/21)	76–100	88.9 (8/9)	52–100		
Reader 1	95.2 (20/21)	76–100	66.7 (6/9)	30–93		
Reader 2	90.5 (19/21)	70–99	88.9 (8/9)	52–100		

TABLE 3: Interobserver Agreement Scores for MR Enterography and CT Enterography

	Interobserver Agreement Score (95% CI)			
	MR Enterography		CT Enterography	
Imaging Features	Proximal Disease[a]	Distal Disease[b]	Proximal Disease[a]	Distal Disease[b]
Mural hyperenhancement	0.70	0.73	0.86	0.59
Mural stratification	0.83	0.35	0.56	0.49
Mural high T2 signal	0.53	0.49	NA	NA
Comb sign	0.90	1.00	0.93	0.70
Overall assessment of active disease	0.61		0.71	
Penetrating disease[c]	0.62		0.43	
Maximum wall thickness[d]	0.51 (0.12–0.77)		0.73 (0.52–0.87)	

Note—NA = not applicable.
[a]Terminal and distal ileum.
[b]Duodenum, jejunum, and proximal ileum.
[c]Agreement was assessed on a per-patient basis.
[d]Agreement for wall thickness of abnormal segment is reported using interclass correlation coefficients.

colonoscopy in 11 patients. In three patients, the terminal ileum was not intubated, so the ileal mucosa could not be examined optically (Fig. 2). In two of these three patients, stricturing at the ileocolonic anastomosis prevented passage of the colonoscope into the terminal ileum. In the third patient, cecal inflammation prevented visualization of the ileocecal valve. Ileocolonoscopy showed a normal-appearing ileal mucosa in eight additional patients, three without biopsy and five with negative biopsy results (Fig. 3). In the eight cases of endoscopically occult active small-bowel inflammation, the reference standard identified small-bowel inflammation in the proximal small bowel in four patients (i.e., skipping of "terminal" terminal ileum) (Fig. 4), intramural disease in four patients (as manifested by mural hyperenhancement, wall thickening, or mural stratification on MR enterography and CT enterography at the terminal ileum or neoterminal ileum), and penetrating disease in one patient.

Discussion

MR enterography and CT enterography showed excellent and similar sensitivities. Although the specificity of MR enterography tended to be lower than that of CT enterography, this difference was not significant.

Prospective recruitment and state-of-the-art imaging techniques with correlative ileocolonoscopy are strengths of the current study. The inclusion of four readers, inclusion of an additional gastroenterologist and a

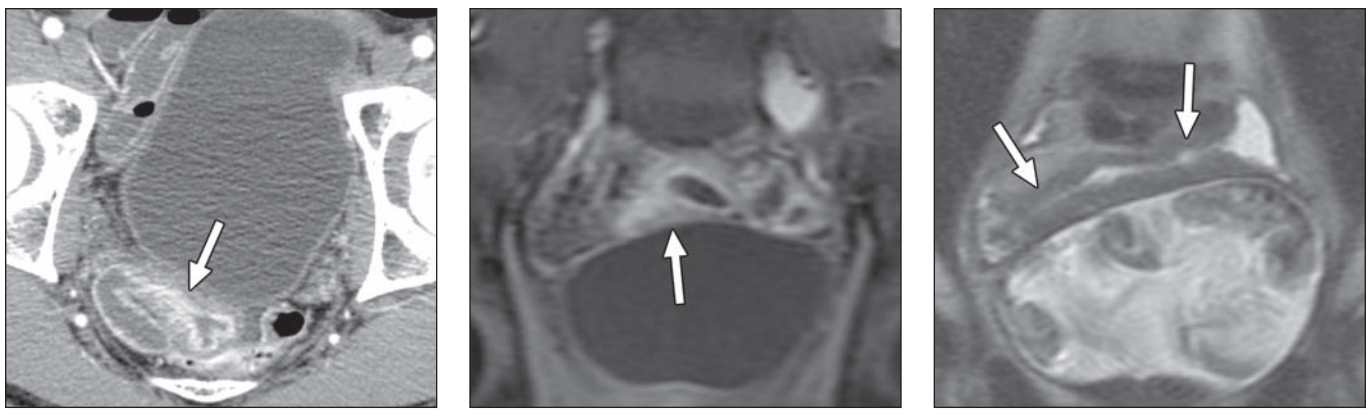

Fig. 1—False-negative MR findings in 29-year-old man who presented with fluctuating abdominal symptoms of 9 years' duration. Ileocolonoscopy was performed for suspicion of Crohn's disease but did not show any abnormalities and biopsies were not performed.
A, Axial CT enterography image was interpreted as positive for 20-cm-long small-bowel segment with active inflammation consisting of mucosal hyperenhancement and mural wall thickening (*arrow*) 10 cm proximal to ileocecal valve.
B, Coronal 2D fast spoiled gradient-recalled echo MR enterography image was interpreted as negative but in retrospect shows wall thickening and hyperenhancement (*arrow*), findings similar to CT enterography. This perceptual error could have been secondary to proximity of pelvic structures without intervening mesenteric fat and decreased bowel distention.
C, Coronal 2D steady-state fast spin-echo MR enterography image was interpreted as negative but in retrospect shows wall thickening (*arrows*), finding similar to CT enterography. This perceptual error could have been secondary to proximity of pelvic structures without intervening mesenteric fat and decreased bowel distention.

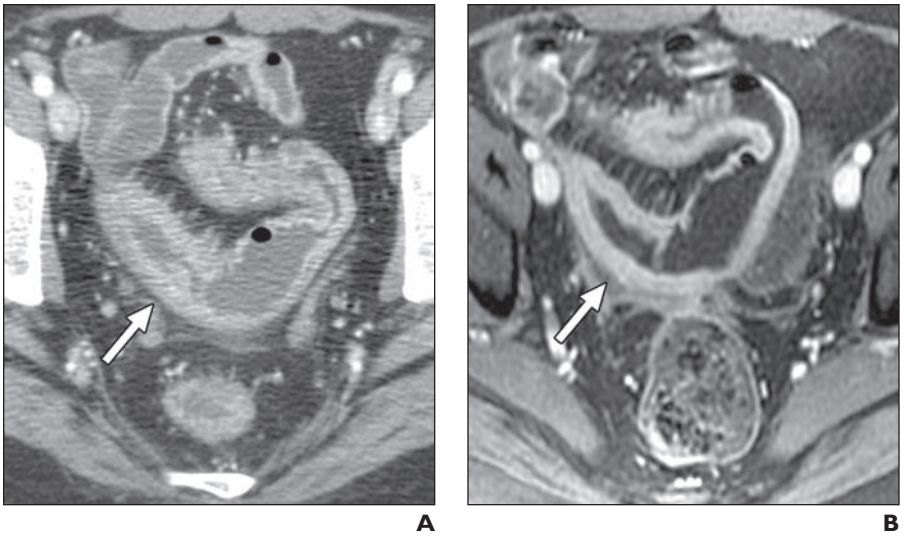

Fig. 2—Positive CT enterography and MR enterography findings with failed intubation in 23-year-old man with prior small-bowel resections.
A, Axial CT enterography image was interpreted as positive with wall thickening and mucosal hyperenhancement (*arrow*). Endoscopist was unable to intubate terminal ileum.
B, Axial 3D liver acquisition volume acceleration (LAVA) MR enterography image was interpreted as positive with wall thickening and mucosal hyperenhancement (*arrow*). Endoscopist was unable to intubate terminal ileum.

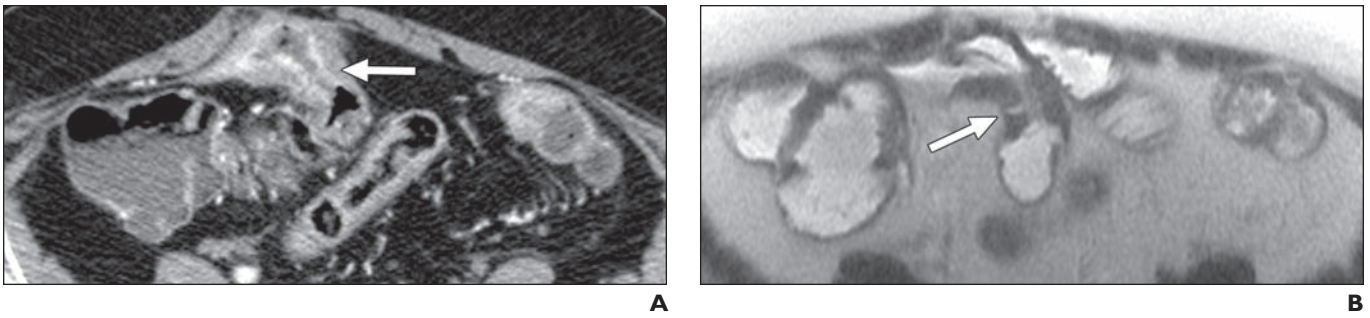

Fig. 3—False-negative ileoscopy in 49-year-old woman with diarrhea and 40-year history of known Crohn's disease and extensive bowel resections who underwent evaluation to rule out short gut syndrome from active disease. Ileocolonoscopy did not show evidence of active Crohn's disease.
A, Axial CT enterography image shows active inflammation with wall thickening and hyperenhancement (*arrow*) just proximal to ileocolonic anastomosis.
B, Axial single-shot fast spin-echo MR enterography image shows active inflammation with wall thickening and deep ulceration (*arrow*) just proximal to ileocolonic anastomosis.

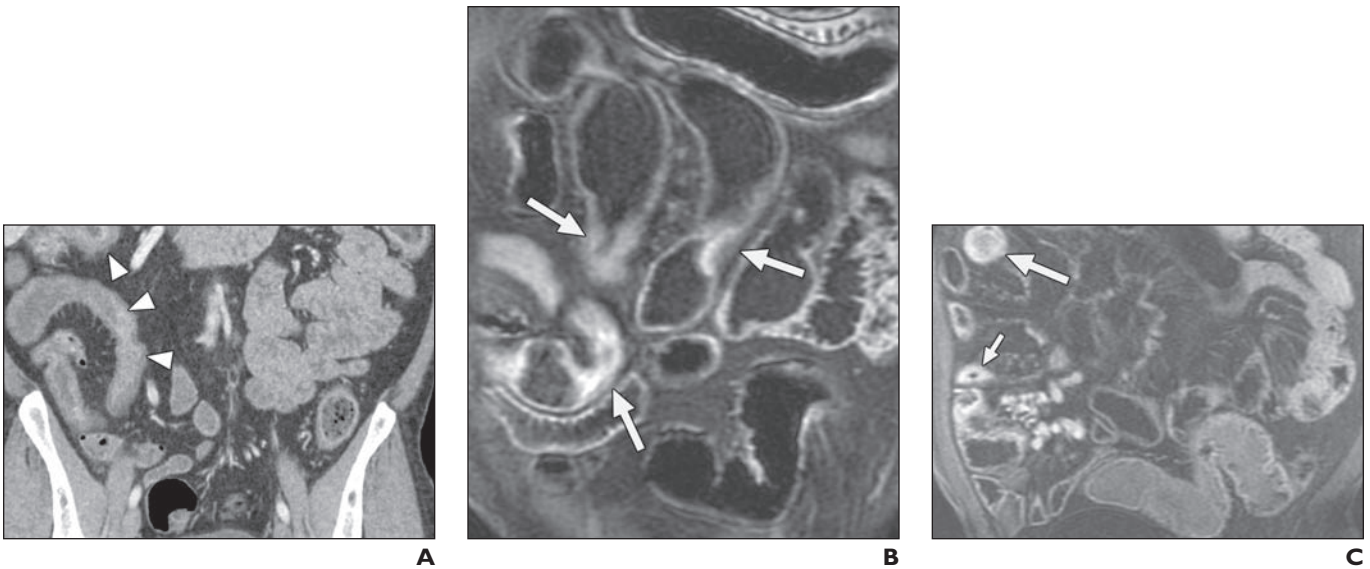

Fig. 4—Proximal small-bowel inflammation in 45-year-old steroid-dependent man with known diagnosis of Crohn's disease who developed obstructive symptoms. Ileocolonoscopy showed patchy involvement from sigmoid to cecum, but ileum was reported to be normal 15 cm beyond ileocecal valve.
A, Coronal CT enterography image shows active disease (*arrowheads*) in proximal small bowel with scattered areas of wall thickening and increased enhancement.
B and **C,** Coronal 3D liver acquisition volume (LAVA) images show active disease (*arrows*) in proximal small bowel with scattered areas of wall thickening and increased enhancement.

gastrointestinal radiologist to analyze false-positive and false-negative examinations, and the use of a comprehensive clinical reference standard are innovative and appropriately increase the external validity of the study results.

Although no study to our knowledge has compared MR enterography and CT enterography in a head-to-head manner using overall disease assessment as well as individual MR and CT signs, there have been studies giving side-by-side comparison of mural signs of inflammation. Low et al. (2000) [19] found that in the depiction of mural thickness and hyperenhancement, MR enterography was superior to CT enterography. In contrast, Schmidt et al. (2003) [20] showed better interobserver agreement and sensitivity for bowel wall thickening and enhancement for CT enterography when compared with MR enterography.

In our study, the interobserver agreement scores for mural hyperenhancement were similar at MR enterography and CT enterography, with MR enterography having slightly worse interclass correlation coefficients for wall thickness measurement. Additionally, we did not find a difference between MR enterography and CT enterography in the detection of complications (fistula, phlegmon, abscess). Although the mean image quality scores for both MR enterography and CT enterography were high, image quality scores were significantly lower for MR enterography. In our experience, MR enterography is occasionally compromised by idiosyncratic factors including motion, artifacts, and signal inhomogeneity. In these instances, correlative ileoscopy, wireless capsule endoscopy, or CT enterography may be helpful.

Early feasibility studies developing and refining CT enterography necessarily used clinically accepted radiologic studies as a reference standard. In 2001, wireless capsule endoscopy was approved for use by the U.S. Food and Drug Administration for mucosal assessment of the small bowel, and its integration into the study of the small intestine quickly led to the realization that radiologic examinations underestimate mucosal disease even when meticulous technique is used [13, 23–27]; consequently, mucosal assessment was integrated into reference standards for CT enterography and MR enterography. Although numerous studies on CT enterography have been published, only a minority used a clinical gold standard that includes the results of ileocolonoscopy (with or without mucosal biopsy) [10, 11, 13, 14, 23, 26–28]. The same holds true for studies estimating the performance of MR enterography in detecting patients with Crohn's disease [12, 29]. Maglinte [30] and Maglinte et al. [31] quickly observed that the incremental benefit of imaging is in the ability of imaging to display the small-bowel wall and perienteric tissues, which are obscure at mucosal assessment. A unique contribution of our study is that it shows the incremental benefit and how mural and perienteric cross-sectional imaging assessment complements optical mucosal assessment by ileocolonoscopy.

Endoscopically occult inflammation can be due to normal mucosa with underlying mural inflammation (as confirmed by mucosal biopsy or imaging), inflammation proximal to the extent of the endoscopy (skipping of the "terminal" terminal ileum), or penetrating disease. When biopsy is performed, sampling error can occur (e.g., biopsying a normal portion of the ileal wall in an ileum with patchy inflammation [skip lesions]) (Fig. 5). Hence, we now understand that studies that have necessarily used ileoscopy with or without mucosal biopsy to assess the performance of cross-sectional enterography may have underestimated sensitivity and specificity. Moreover, the effect of selection bias caused by excluding cases without successful intubation probably exacerbated this underestimation in retrospective studies [10, 11].

The complementary nature of endoscopy and cross-sectional imaging, as reported recently [13], makes the use of a comprehensive clinical gold standard all the more appropriate. Moreover, the converse is also true. We and others have diagnosed small-bowel inflammation that was occult at cross-sectional imaging but was obvious at ileoscopy or wireless capsule endoscopy [13, 23, 26]. It should be emphasized that our study also shows the complementary nature of mucosal inspection by ileocolonoscopy with CT enterography and MR enterography, given that ileocolonoscopy identified patients with inflammation missed at cross-sectional enterography. Moreover, endoscopic examination of the colon is supplemented by random biopsy, and enterography is not optimized to display colonic inflammation.

Although our results show that MR enterography can be used to replace CT enterography in certain scenarios, each technique has unique advantages and limitations in clinical practice. The advantages of MR enterography include the elimination of ionizing radiation and the ability to perform the examination in patients with impaired renal function. If necessary, the examination can be performed without IV contrast material for patients with a low glomerular filtration rate who are at risk for nephrogenic systemic fibrosis or pregnant patients. Limitations of MR enterography include the examination time and interpretation time, which are longer for MR enterography than for CT enterography. In our practice, CT enterography examinations are scheduled every 15 minutes in comparison with every 45 minutes for MR enterography. Some of the sequences may be omitted for MR enterography to reduce the scanning time; however, further studies assessing the accuracy of more abbreviated examinations will be needed. The cost of MR enterography is approximately twice that of CT enterography. Finally, for uncooperative patients or patients who have difficulty with breath-holding, CT enterography may be preferred because of the associated artifacts.

Our study has several limitations. We did not include pediatric patients. We did not perform MR enterography using the enteroclysis technique; however, we think that this should not affect our results because published studies have shown these two techniques for MRI of the abdomen to be similar in diagnostic accuracy [32, 33]. We acknowledge that the current sample size ($n = 33$) had limited power and thus allowed us to detect only large differences in test performance. In addition, the ileocolonoscopies were performed in a clinical fashion by different gastroenterologists who likely were not aware of patient involvement in our study. If the gastroenterologist had known of potential recruitment, the ileocolonoscopy results may have been influenced by a more vigorous attempt at ileal intubation, a closer mucosal inspection, and more random biopsies.

Nevertheless, we believe that these results are a standard representation of our clinical practice. Future prospective studies that incorporate findings of ileocolonoscopy and a consensus gold standard should use a standardized protocol for ileocolonoscopy that includes specific instructions to intubate the terminal ileum, specific instructions to obtain mucosal biopsies from the ileal mucosa even if it appears endoscopically normal, and the use of standardized criteria for determining the presence of ileal inflammation and grading its severity.

In conclusion, we found that the sensitivities of MR enterography and CT enterography to detect active small-bowel Crohn's disease

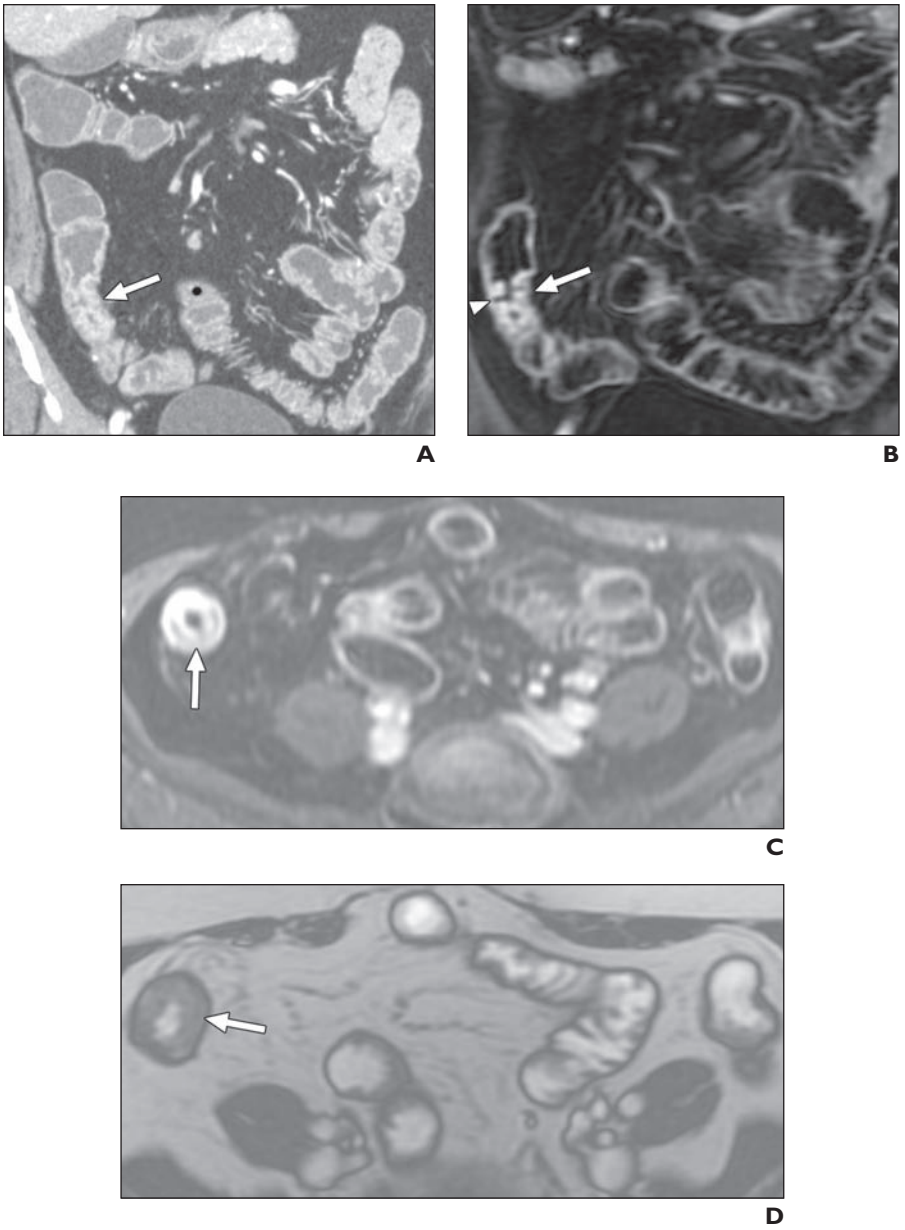

Fig. 5—False-negative ileoscopy with sampling error. 63-year-old symptomatic woman who presented with long history of known Crohn's disease. Ileocolonoscopy and biopsy did not show any evidence of active disease. Negative biopsy and presence of active disease seen on cross-sectional imaging well within reach of endoscope raise possibility of sampling error.
A, Coronal CT enterography image shows wall thickening and mucosal hyperenhancement (*arrow*) just proximal to ileoascending anastomosis.
B, Coronal 2D fast spoiled gradient-recalled echo (FSPGR) MR enterography image shows wall thickening and mucosal hyperenhancement (*arrow*) just proximal to ileoascending anastomosis. Also note deep ulcerations (*arrowhead*).
C, Axial 2D FSPGR MR enterography image shows wall thickening and stratified mucosal hyperenhancement (*arrow*) just proximal to ileoascending anastomosis.
D, Axial 2D true fast imaging with steady-state precession MR enterography image shows wall thickening (*arrow*) just proximal to ileoascending anastomosis.

are similar. Cross-sectional enterography provides new and complementary information compared with mucosal assessment by optical ileoscopy. Enterography can show mural or proximal inflammation or penetrating disease even in the presence of normal overlying ileal mucosa. It also provides an alternative diagnostic pathway when the ileum cannot be intubated. Reliance on mucosal inspection alone as a reference standard for Crohn's disease–related small-bowel inflammation may underestimate the performance of cross-sectional enterography techniques and vice versa. Integration of imaging end points and mucosal inspection and biopsy of the small bowel will yield the most accurate representation of small bowel inflammation. Based on the results of our study, MR enterography appears to be an accurate technique for evaluating the small bowel for Crohn's disease. MR enterography may be the preferred imaging technique for patients with small-bowel Crohn's disease who are undergoing serial radiologic evaluations to reduce the total lifetime radiation exposure.

References

1. Loftus CG, Loftus EV Jr, Harmsen WS, et al. Update on the incidence and prevalence of Crohn's disease and ulcerative colitis in Olmsted County, Minnesota, 1940–2000. *Inflamm Bowel Dis* 2007; 13:254–261
2. Canavan C, Abrams KR, Mayberry JF. Meta-analysis: mortality in Crohn's disease. *Aliment Pharmacol Ther* 2007; 25:861–870
3. Card T, Hubbard R, Logan RF. Mortality in inflammatory bowel disease: a population-based cohort study. *Gastroenterology* 2003; 125:1583–1590
4. Danzi JT. Extraintestinal manifestations of idiopathic inflammatory bowel disease. *Arch Intern Med* 1988; 148:297–302
5. Ekbom A, Helmick CG, Zack M, Holmberg L, Adami HO. Survival and causes of death in patients with inflammatory bowel disease: a population-based study. *Gastroenterology* 1992; 103: 954–960
6. Jess T, Loftus EV Jr, Harmsen WS, et al. Survival and cause specific mortality in patients with inflammatory bowel disease: a long term outcome study in Olmsted County, Minnesota, 1940–2004. *Gut* 2006; 55:1248–1254
7. Colombel JF, Loftus EV Jr, Tremaine WJ, et al. The safety profile of infliximab in patients with Crohn's disease: the Mayo Clinic experience in 500 patients. *Gastroenterology* 2004; 126:19–31
8. Hutfless SM, Weng X, Liu L, Allison J, Herrinton LJ. Mortality by medication use among patients with inflammatory bowel disease, 1996–2003. *Gastroenterology* 2007; 133:1779–1786
9. Siegel CA, Hur C, Korzenik JR, Gazelle GS, Sands BE. Risks and benefits of infliximab for the treatment of Crohn's disease. *Clin Gastroenterol Hepatol* 2006; 4:1017–1024
10. Bodily KD, Fletcher JG, Solem CA, et al. Crohn disease: mural attenuation and thickness at contrast-enhanced CT enterography—correlation

with endoscopic and histologic findings of inflammation. *Radiology* 2006; 238:505–516

11. Booya F, Fletcher JG, Huprich JE, et al. Active Crohn disease: CT findings and interobserver agreement for enteric phase CT enterography. *Radiology* 2006; 241:787–795
12. 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
13. Solem CA, Loftus EV Jr, Fletcher JG, et al. Small-bowel imaging in Crohn's disease: a prospective, blinded, 4-way comparison trial. *Gastrointest Endosc* 2008; 68:255–266
14. Hara AK, Leighton JA, Heigh RI, et al. Crohn disease of the small bowel: preliminary comparison among CT enterography, capsule endoscopy, small-bowel follow-through, and ileoscopy. *Radiology* 2006; 238:128–134
15. Brenner DJ, Hall EJ. Computed tomography: an increasing source of radiation exposure. *N Engl J Med* 2007; 357:2277–2284
16. Jaffe TA, Gaca AM, Delaney S, et al. Radiation doses from small-bowel follow-through and abdominopelvic MDCT in Crohn's disease. *AJR* 2007; 189:1015–1022
17. Peloquin JM, Pardi DS, Sandborn WJ, et al. Diagnostic ionizing radiation exposure in a population-based cohort of patients with inflammatory bowel disease. *Am J Gastroenterol* 2008; 103:2015–2022
18. Prassopoulos P, Papanikolaou N, Grammatikakis J, Rousomoustakaki M, Maris T, Gourtsoyiannis N. MR enteroclysis imaging of Crohn disease. *RadioGraphics* 2001; 21[spec no]:S161–S172
19. 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
20. 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
21. Schindera ST, Nelson RC, DeLong DM, et al. Multi-detector row CT of the small bowel: peak enhancement temporal window—initial experience. *Radiology* 2007; 243:438–444
22. McGinn T, Wyer PC, Newman TB, et al. Tips for learners of evidence-based medicine. 3. Measures of observer variability (kappa statistic). *CMAJ* 2004; 171:1369–1373 [Erratum in *CMAJ* 2005; 173:18]
23. Hara AK, Leighton JA, Sharma VK, Fleischer DE. Small bowel: preliminary comparison of capsule endoscopy with barium study and CT. *Radiology* 2004; 230:260–265
24. Liangpunsakul S, Chadalawada V, Rex DK, Maglinte D, Lappas J. Wireless capsule endoscopy detects small bowel ulcers in patients with normal results from state of the art enteroclysis. *Am J Gastroenterol* 2003; 98:1295–1298
25. Triester SL, Leighton JA, Leontiadis GI, et al. A meta-analysis of the yield of capsule endoscopy compared to other diagnostic modalities in patients with non-stricturing small bowel Crohn's disease. *Am J Gastroenterol* 2006; 101:954–964
26. Voderholzer WA, Beinhoelzl J, Rogalla P, et al. Small bowel involvement in Crohn's disease: a prospective comparison of wireless capsule endoscopy and computed tomography enteroclysis. *Gut* 2005; 54:369–373
27. Wold PB, Fletcher JG, Johnson CD, Sandborn WJ. Assessment of small bowel Crohn disease: noninvasive peroral CT enterography compared with other imaging methods and endoscopy—feasibility study. *Radiology* 2003; 229:275–281
28. Hassan C, Cerro P, Zullo A, Spina C, Morini S. Computed tomography enteroclysis in comparison with ileoscopy in patients with Crohn's disease. *Int J Colorectal Dis* 2003; 18:121–125
29. 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
30. Maglinte DDT. Science to practice: do mural attenuation and thickness at contrast-enhanced CT enterography correlate with endoscopic and histologic findings of inflammation in Crohn disease? *Radiology* 2006; 238:381–382
31. Maglinte DDT, Sandrasegaran K, Chiorean M, Dewitt J, McHenry L, Lappas JC. Radiologic investigations complement and add diagnostic information to capsule endoscopy of small-bowel diseases. *AJR* 2007; 189:306–312
32. 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
33. Schreyer AG, Geissler A, Albrich H, et al. Abdominal MRI after enteroclysis or with oral contrast in patients with suspected or proven Crohn's disease. *Clin Gastroenterol Hepatol* 2004; 2:491–497