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Chapter 2

Small-bowel radiology – an introduction for gastroenterologists

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Summary

The field of radiological small-bowel imaging is changing rapidly, as is small-bowel enteroscopy. New techniques allow the depiction of intraluminal, mural, and extraintestinal features of various small-bowel disorders, such as Crohn's disease, small-bowel polyposis syndromes, small-intestinal malignancies, and coeliac disease. For patients in need of repeated small-bowel imaging, modalities that do not use ionizing radiation, such as ultrasound or magnetic resonance imaging, should be considered.

Introduction

For several decades small-bowel radiology was the only nonoperative modality to investigate the total small bowel. The introduction of video capsule endoscopy (VCE) and balloon-assisted enteroscopy, like double-balloon endoscopy (DBE) and single-balloon endoscopy (SBE), have allowed endoscopic evaluation of the small intestine. Despite these recent major advances in small-bowel endoscopy, radiological imaging remains important for patients with suspected or established small-bowel disease. The advantages of radiological imaging include its low invasiveness and the possibility of investigating extraluminal abnormalities as well as intraluminal changes. However, in most conditions, obtaining biopsy specimens for histological analysis by enteroscopy remains mandatory and small-bowel radiology is often used to select patients who require enteroscopy. Important factors when considering radiological imaging of the small bowel include patient exposure to potentially carcinogenic radiation and the diagnostic accuracy of tests. A problem with the interpretation of studies on radiological small-bowel imaging is that many compare the results of a new modality with a suboptimal reference test, like conventional enteroclysis. Complete balloon-assisted enteroscopy and operative findings are in our view the standard of reference in small-bowel investigation. However, there is only a limited amount of literature using enteroscopy as the reference test. In addition, excellent diagnostic accuracies of many new imaging modalities are only achieved when these tests are performed and interpreted by experts in the field, usually in highly selected patient populations. Therefore, it is unlikely that in daily practice, the same sensitivity and specificity can be achieved.

In this chapter the current techniques of radiological small-bowel imaging and findings in the most prevalent small-bowel disorders are reviewed, with special emphasis on the relationship between endoscopic and radiological methods, in order to demonstrate for gastroenterologists the progress that has been achieved in small-bowel radiology.

Part I: Methods of radiological small-bowel imaging

General issues

The ideal small-bowel imaging method should be non-invasive, not require potentially toxic (intravenous) contrast agents, not use ionizing radiation, and be able to depict the total small-intestinal lumen, bowel wall, and surrounding structures. In addition, the ideal modality should be widely available, result in images that are easy to interpret, and be cost-effective. Although many of these aspects are true for many radiological modalities, there is no modality that fulfils all the criteria of the ideal examination (*table 2.1*). Most patients undergo VCE or enteroscopy because of midgastrointestinal blood loss. In most of these patients, especially those in Western countries, the cause will be angioectasia. These lesions are usually small and flat. Therefore, no radiological modality will be able to detect such lesions with 100% sensitivity. VCE and DBE are clearly superior for detecting intramucosal flat lesions, and should therefore be considered first for patients with midgastrointestinal bleeding (MGIB).

Table 2.1: Comparison between radiological and endoscopic small-bowel imaging methods.

Modality	Invasiveness	Enteral contrast	IV contrast	Radiation exposure	Total SB	Luminal detail	Wall detail	Surrounding structures	Availability	Ease of interpretation	Costs
Plain abdominal X-ray	-	-	-	+	+	-	-	-	+++	+++	+
SBFT	+	+	-	+++	+++	+	++	-	+++	++	++
SB enteroclysis	++	+	-	+++	+++	++	+++	-	++	++	++
Ultrasound	-	-	-	-	-	+	++	++	+++	+	+
CT enterography	+	+	+	+++	+++	++	++	+++	++	++	++
CT enteroclysis	++	+	+	+++	+++	++	+++	+++	++	++	++
MR enterography	+	+	+	-	+++	++	++	+++	+	++	++
MR enteroclysis	++	+	+	+	+++	++	+++	+++	+	++	++
VCE	+	-	-	-	++	+++	-	-	+	++	++
Push enteroscopy	+++	-	-	- (if no fluoroscopy)	-	+++	-	-	+	++	+
Balloon-assisted enteroscopy	+++	-	-	- (if no fluoroscopy)	+	+++	-	-	+	++	+++

Note: CT = computed tomography; IV = intravenous; SB = small bowel; SBFT = small bowel follow through; MR = magnetic resonance; VCE = video capsule endoscopy.

Conventional Radiology and Contrast Studies

Small-bowel follow through and conventional enteroclysis

Small-bowel follow through (SBFT) requires the ingestion of at least 0.5 L of 40–50% barium suspension by mouth. As the barium progresses through the small bowel, fluoroscopy is performed and serial images are obtained. Often manual palpation is necessary to separate individual small-bowel loops to help identify abnormalities.¹ The main advantage of SBFT is the ease of performance. The disadvantages include poor definition of small-bowel fold pattern, poor distension and separation of individual segments, and the use of ionizing radiation.

In general, SBFT has been replaced by enteroclysis, which is considered to be more accurate.² Enteroclysis is performed by administering a low-density barium suspension through a fluoroscopically placed nasojejunal catheter (*figure 2.1*). The administration of the contrast medium directly into the small bowel is usually followed by administration of methylcellulose suspension or air to enable optimal distension of individual small-bowel loops.^{1,2} As with SBFT, fluoroscopy is performed and serial images are obtained. In general, small-bowel enteroclysis, especially if performed using double contrast, enables a more detailed examination of the small-bowel lumen and wall. Compared with cross-sectional imaging, the information about trans- and extraluminal abnormalities is limited. The need for nasojejunal intubation makes small-bowel enteroclysis more invasive than SBFT, CT enterography, and MR enterography.

Ultrasound

Although ultrasound investigation of the abdomen is often hampered by the presence of intestinal gas and by collapse of the small-intestinal lumen, this can be overcome by filling the small bowel with anechoic fluid. The main advantages of ultrasound include its wide availability, low cost and lack of ionising radiation. In addition, ultrasound enables better functional evaluation than many other small-bowel imaging modalities. For instance, the presence of intussusception can be reliably depicted with ultrasound (*figure 2.2*).³ The diagnostic accuracy of sono-enteroclysis has been reported to be comparable to that of barium enteroclysis.³ However, in general, ultrasound is most often only used in patients with (suspected) Crohn's disease and to demonstrate the presence of small-bowel obstruction or paralytic ileus.⁴

Cross-sectional imaging

Computed Tomography

In routine settings, opacification of the small bowel during CT is achieved by administering oral contrast agent by mouth. A possible drawback of this method is that the small-intestinal lumen might remain collapsed and the bowel wall is not visualized in detail. This situation can be overcome by increasing the dose of orally ingested contrast medium (CT enterography) or by administering methylcellulose (neutral enteral contrast) or barium (positive enteral contrast) directly into the small bowel using an enteroclysis catheter (CT enteroclysis).⁵

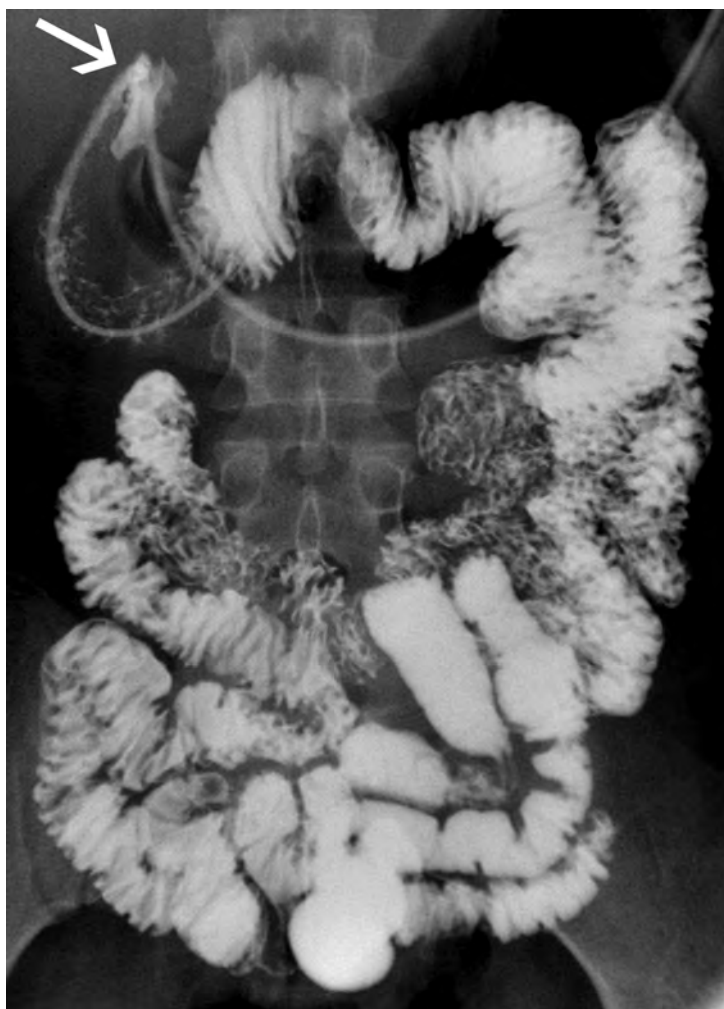


Figure 2.1: Normal conventional enteroclysis shows the nasoduodenal tube following the greater curvature of the stomach, through the pylorus (arrow) and with an acute angle entering the descending part of the duodenum.

MR imaging

The development of fast imaging sequences has enabled small-bowel imaging by MR (**figure 2.3**). As in CT imaging of the small bowel, luminal distension is a prerequisite for adequate depiction of luminal abnormalities. Several luminal contrast agents can be used: Positive contrast agents (such as gadolinium chelate) produce high signal intensities on T1-weighted and T2-weighted sequences, whereas negative contrast agents (such as perfluoro-octyl bromide) produce low signal intensity on T1-weighted and T2-weighted sequences. Biphasic contrast agents (like polyethylene glycol and methylcellulose) produce

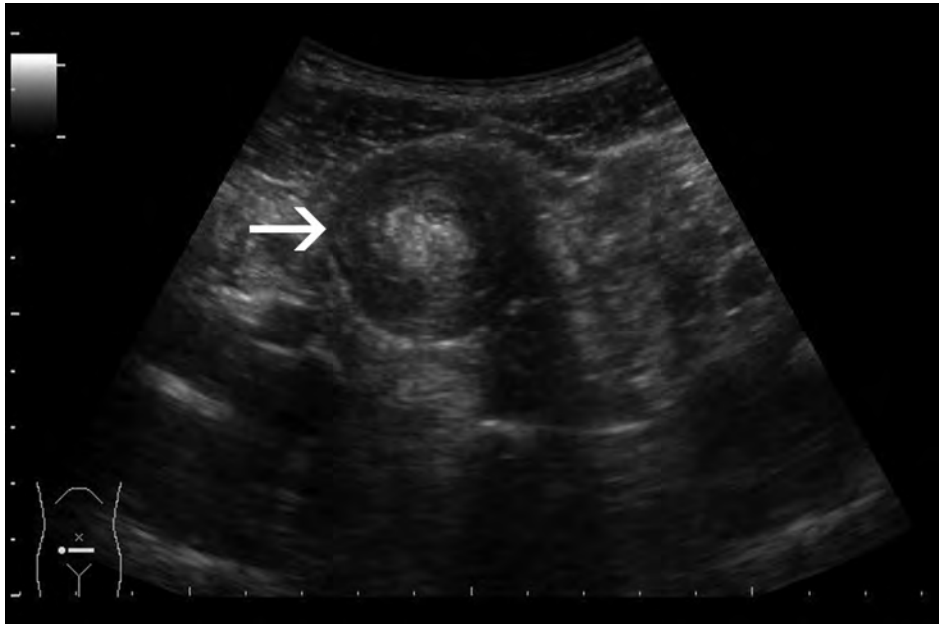


Figure 2.2: Transabdominal ultrasound image, obtained in a patient with Peutz-Jeghers disease and recurrent small-bowel obstruction, shows a bowel-in-bowel sign (arrow), consistent with a diagnosis of intussusception.

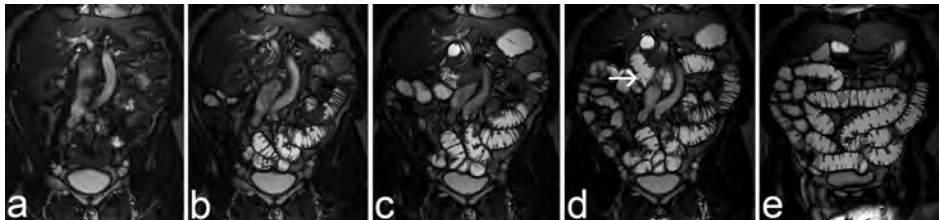


Figure 2.3: Consecutive sequences of a normal MR enteroclysis demonstrate the gradual filling of the small intestine during the study. (a) The small-bowel lumen is collapsed. (b) The first contrast enters the proximal jejunum through a nasojejunal catheter. (c) The filling of the jejunum continues. (d) Further filling of the jejunum. Retrograde duodenal distension and the enteroclysis catheter can be observed (arrow). (e) The ileum is filled as well, while the jejunum remains distended as well, which is a hallmark of an enteroclysis study.

different patterns of contrast depending on the sequence used.⁶ The luminal contrast agent can be delivered by mouth (MR enterography) or by means of a nasojejunal catheter, positioned using fluoroscopic guidance (MR enteroclysis). Enteroclysis in general gives superior luminal distension, especially of the jejunum.⁷ The main advantages of MR imaging are the lack of exposure to ionizing radiation and excellent soft-tissue contrast.⁸

In expert hands, MR enteroclysis is probably the best radiological modality for examination of the small bowel, especially if repeated examinations are expected. Drawbacks include limited availability, high cost, and the need for jejunal intubation.

Part II: Radiological findings in selected small-bowel diseases

Midgastrointestinal bleeding (MGIB)

If we define MGIB as bleeding from a small-intestinal site beyond the reach of conventional oesophagogastroduodenoscopy or ileocolonoscopy, it accounts for approximately 5% of all gastrointestinal bleedings.⁹ Suspected MGIB is the most common indication for VCE, accounting for almost 70% of all VCE-examinations being performed.¹⁰ The diagnostic yield for VCE for this indication has been reported to be around 60%.¹⁰ However, the definitions of positive findings vary in studies on the subjects, and many studies lack a reference test. The causes of MGIB are diverse, but in Western populations flat angioectasia, usually between 2–10 mm in diameter, are the most common cause.^{9, 11} These lesions can usually not be identified with any radiological modality, so in patients with suspected MGIB without other abdominal symptoms, VCE should be the first investigation performed, and the role for radiology is in most cases limited.¹² If lesions are identified, the optimal endoscopic approach can be determined and enteroscopy can be performed to treat these lesions. The optimal strategy after negative VCE is not clear. Both a repeat VCE as DBE have been shown to be useful investigations in patients with continuing MGIB and a negative initial VCE.¹³⁻¹⁵

In approximately 10–20% of the patients with MGIB, this is caused by small intestinal neoplasms.⁹ A neoplastic cause should especially be suspected in case of additional symptoms, such as abdominal pain, vomiting or weight loss. In these circumstances, a stenosis should be suspected, and VCE should not be performed before more information on the patency of the intestinal tract has been acquired. There are two ways to do this: using a patency capsule, or by radiological depiction of the small bowel. The diagnostic accuracy of CT and MR enteroclysis in the detection of small intestinal neoplasms is very high^{16, 17} Therefore, one could argue that in patients with MGIB and other symptoms like weight loss or abdominal pain, cross-sectional enteroclysis should be preferred. VCE can then be performed when cross-sectional enteroclysis studies are normal and the presence of a tumour is thus low.

In acute and life-threatening MGIB, a different approach to small bowel imaging is needed. Often, there is no time to perform VCE, and immediate enteroscopy is performed, which allows therapeutic interventions.

Crohn's disease

General considerations

It is estimated that 0.6–3% of the cumulative risk of cancer in the general population can be attributed to the medical use of radiography.¹⁸ The increased risk of radiation-induced

cancer may be of particular concern in patients with Crohn's disease, who are often exposed to radiological imaging starting in childhood. In 15.5% of patients with Crohn's disease, the cumulative effective dose exceeded 75 mSv, which can be translated to an excess risk of cancer mortality of 7.3%.¹⁹ Factors associated with high cumulative exposure in patients with Crohn's disease are age <17 years at diagnosis, small-bowel involvement, penetrating disease, and requirement for intravenous steroids, infliximab, or multiple surgeries.¹⁹

As in all patients in whom radiological imaging with ionizing radiation is considered, the potential benefits should be weighed against the potential long-term risks, and imaging modalities that do not expose the patient to ionizing radiation (such as ultrasound or MR imaging) should be considered (*table 2.2*).²⁰⁻²² The main problems when interpreting research results of radiological imaging in Crohn's disease are the often heterogeneous study populations (especially when patients with suspected Crohn's disease are studied) and the lack of a solid reference test. These problems often apply to studies comparing the use of VCE and small-bowel radiology as well.

Suspected Crohn's disease

Crohn's disease can be located throughout the complete gastrointestinal tract, but ileocolonic localisation is the most prevalent. A recent study among 2105 patient with Crohn's disease, showed that 16% of these patients had involvement of the gastrointestinal tract proximal to the terminal ileum.²³ Most of these patients also had ileocolonic involvement, and

Table 2.2: Overview of radiation exposure from environmental factors and abdominal medical imaging tests.

Environmental factor	Radiation dose (mSv)
Transatlantic flight	0.07
Annual background radiation dose	2.7
Imaging test	
Fluoroscopic placement of an enteroclysis catheter	0.2
Plain abdominal X-ray	0.7
Endoscopic retrograde cholelchopancreaticography	4.0
Small bowel follow through	5.0
Conventional small bowel enteroclysis	8.0
Computed tomography abdomen and pelvis	8.0
Computed tomography virtual colonoscopy	10.0
Multiphase computed tomography abdomen and pelvis	31.0

Note: mSv = milliSievert

Adapted from: Puustinen L, Numminen K, Uusi-Simola J, Sipponen T. Radiation exposure during nasojejunal intubation for MRI enteroclysis. *Scandinavian journal of gastroenterology*. 2012;47(6):658-61; Lin EC. Radiation risk from medical imaging. *Mayo Clin Proc*. 2010;85(12):1142-6; Mettler FA, Jr., Huda W, Yoshizumi TT, Mahesh M. Effective doses in radiology and diagnostic nuclear medicine: a catalog. *Radiology*. 2008;248(1):254-63.

overall, only 25 (1.1%) patients had involvement of the gastrointestinal tract proximal to the terminal ileum without ileocolonic disease manifestation being present. Although the study design could have resulted in some underestimation of the presence of proximal small-bowel Crohn's disease, these data confirm that ileocolonoscopy is the most reliable first diagnostic modality to be considered in patients suspected of having Crohn's disease. An additional benefit is that during ileocolonoscopy tissue samples can be obtained. Moreover, in a patient suspected to have Crohn's disease, important alternative diagnoses like ulcerative colitis or colon cancer can be excluded during the same investigation. In some instances small-bowel radiology or small-bowel endoscopy may have a role in the diagnosis of Crohn's disease. First, there is a small, but not negligible chance that a patient with a normal ileocolonoscopy does suffer from Crohn's disease. Therefore, in case of persistent suspicion of Crohn's disease despite normal ileocolonoscopy, small-bowel investigations could be considered. Second, in some patients intubation of the ileum is not successful during ileocolonoscopy. Third, in a minority of patients it is difficult to discriminate between ulcerative colitis and Crohn's disease.

When the results of ileocolonoscopy and oesophagogastroduodenoscopy are normal but a high suspicion of Crohn's disease is still present, several modalities can be used to examine the small bowel. There is much debate about the best modality to use in such situations, because (wireless) endoscopic examinations, like radiological studies, have their advantages and disadvantages. In our view, histologic confirmation of suspected lesions (either visualized with VCE or radiological imaging) should be pursued. It is difficult to compare the diagnostic accuracy of VCE with that of radiological methods, because most studies comparing VCE with small-bowel radiology in patients with Crohn's disease do not relate VCE or radiology findings to an accepted reference standard. Therefore, usually the "diagnostic yield" is reported, which includes all abnormalities encountered during VCE examination, without histologic proof or other findings congruent with the diagnosis of Crohn's disease being present. Therefore, often only the sensitivity of these methods can be assessed.

In studies on patients suspected of having Crohn's disease but in whom ileocolonoscopy showed no abnormalities, Crohn's disease could be diagnosed in 26–71% of cases.²⁴ In a study involving 102 patients suspected of having Crohn's disease, but in whom ileocolonoscopy was normal, the prevalence rate of Crohn's disease after 12 months of follow-up was 13%.²⁵ Using the presence of more than 3 small-intestinal ulcers as the criterion for an abnormal VCE study, the positive predictive value was 50%, and the negative predictive value was 96%. In view of the very low prevalence of isolated upper-intestinal Crohn's disease, one should be very careful to label a patient as having Crohn's disease, based on VCE findings alone.

Although the risk of capsule retention in patients with suspected Crohn's disease seems low, some gastroenterologists prefer to perform radiological evaluation of the small bowel before VCE to exclude the presence of small-bowel stenosis.^{26, 27} A meta-analysis comparing the yield of radiological imaging and VCE included 6 studies comparing

small-bowel radiographs (either SBFT or conventional enteroclysis) in patients with suspected Crohn's disease. The total yield for the radiological studies was 13%, whereas the yield for VCE was 43%, a difference that failed to reach statistical significance.²⁸ In addition, patients with radiological evidence of stenotic disease were excluded in several of the studies and the inclusion criteria varied widely between the studies.

Conventional enteroclysis and SBFT are the traditional modalities to examine the small bowel in patients with suspected Crohn's disease, and are still used as the standard of reference in many studies comparing radiological modalities (*figure 2.4*). The sensitivity and specificity of state-of-the-art conventional enteroclysis performed by experts have been reported to be 100% and 98.3%, respectively.²⁹ In comparison with double-contrast enteroclysis, the sensitivity, specificity, and diagnostic accuracy of multidetector CT enteroclysis are 92%, 83%, and 90%, respectively.³⁰ Mazzeo and co-workers reported a sensitivity and specificity of CT for the diagnosis of Crohn's disease of 86% and 100% respectively.³¹ Another recent comparison between conventional enteroclysis and CT enteroclysis in 50 patients with histologically proven Crohn's disease, conventional enteroclysis showed normal findings in 42 patients, whereas CT enteroclysis showed abnormalities in 44 patients. No differences between conventional enteroclysis and CT enteroclysis were found for mucosal changes, stenosis, and prestenotic dilatation. However, CT was able to depict extraluminal complications like fistula, abscesses, and lymphadenopathy better than conventional enteroclysis. CT enteroclysis was also superior in detecting skip lesions.³²

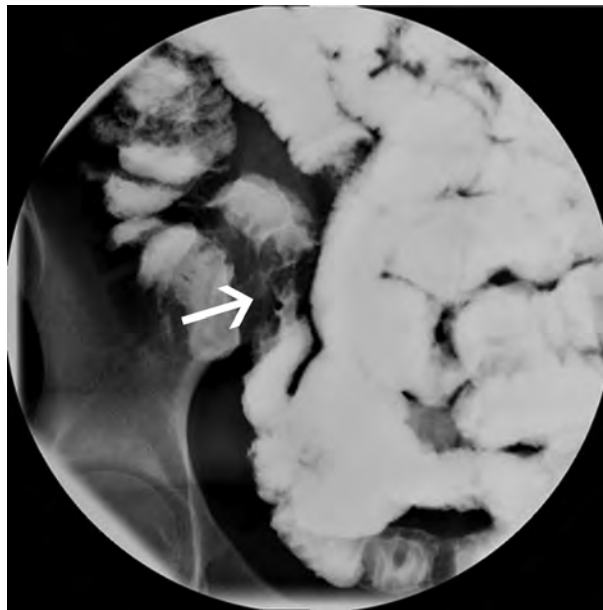


Figure 2.4: Conventional enteroclysis image, obtained in a 34-year-old female patient with Crohn's disease, shows narrowing of the lumen of the terminal ileum, with linear ulceration (arrow).

When comparing the amount of exposure to radiation, multidetector CT is less attractive; the mean effective dose of multidetector CT has been reported to be 16.1 mSv, whereas the effective doses for SBFT were 1.4 mSv (right lower quadrant), 2.0 mSv (central abdomen) and 3.8 mSv (pelvis).³³ To avoid these amounts of radiation exposure, reliable alternatives for SBFT, conventional enteroclysis, and CT examinations of the small bowel are needed.

One meta-analysis of studies on the use of ultrasound to diagnose Crohn's disease reported sensitivity and specificity between 75–94% and 67–100%, respectively.³⁴ A more recent systematic review found the sensitivity and specificity of ultrasound for the diagnosis of Crohn's disease were 85% and 98%, respectively.³⁵ Compared with a reference standard consisting of a combination of clinical and conventional enteroclysis findings, the specificity and sensitivity of ultrasound in the diagnosis of Crohn's disease have been reported to be 88% and 93%, respectively.³⁶ However, ultrasound was less reliable in patients with early stage Crohn's disease of the small bowel (sensitivity 67%). Therefore, if ultrasound is used as the initial modality to examine the small bowel in patients with suspected Crohn's disease, a negative result warrants further evaluation.

A recent systematic review found the sensitivity and specificity of MR imaging for the diagnosis of Crohn's disease (including all locations), were 78% and 85%, respectively.³⁵ The authors concluded that for the assessment of jejunal and ileal lesions MR imaging was preferred over ultrasound, for its higher sensitivity particularly for jejunal lesions, but that assessment of disease extension in the colon and terminal ileum should be based on endoscopy.³⁵ Many features of Crohn's disease can be observed with MR imaging (**box 2.1**). Compared with conventional enteroclysis, MR enteroclysis might be less sensitive in detecting superficial ulceration, fold distortion, and fold thickening.³⁷ No difference was found in the sensitivity of MR imaging for the detection of deep ulcers, cobblestoning pattern, stenosis, and prestenotic dilatation. However, additional information provided by MR imaging includes fibrofatty proliferation and mesenteric lymphadenopathy (**figure 2.5**).³⁸ It is not clear whether MR investigations in patients with suspected Crohn's disease should be performed with oral contrast, or with contrast delivered by a nasojejunal catheter. It is clear that patients prefer MR investigation

Box 2.1: Features of Crohn's disease using MR imaging.

Luminal and mural findings	Extraluminal findings	Markers of disease activity
Ulceration	Fibrofatty proliferation in the mesentery	Mucosal hyperaemia
Cobblestoning	Fistula	Intramural oedema
Wall thickening	Abscesses	Transmural ulceration
Stenosis	Phlegmons	Wall thickening and enhancement
Fold thickening*	Mesenteric lymphadenopathy	Vascular engorgement (comb sign)
Distortion of the valvulae conniventes*		Enhancement of mesenteric lymph nodes
Mucosal nodularity*		

Adapted from Gourtsoyiannis NC, Papanikolaou N, Karantanis A. Magnetic resonance imaging evaluation of small intestinal Crohn's disease. *Best Pract Res Clin Gastroenterol.* 2006;20(1):137-56.

* Probably best visualized with conventional enteroclysis



Figure 2.5: MR enteroclysis image obtained in a 17-year-old woman with Crohn's disease. Note the irregular thickening of the wall of the terminal ileum (arrows). Additionally, mild hyperaemia of the surrounding mesenteric fat can be observed.

without a nasojejunal catheter.³⁹ In one study, MR enteroclysis, when compared with MR enterography, was better for visualizing superficial abnormalities, whereas no differences were found in depicting mural stenosis or fistulae, which suggests that MR enteroclysis could be superior to MR enterography in patients with suspected Crohn's disease.⁴⁰

The first study in which DBE was compared to radiological examination of the small bowel in patients with suspected small-bowel Crohn's disease appeared in 2007.⁴¹ Antegrade DBE revealed pathologic results in five patients. MR enteroclysis and DBE agreed for 75% of all lesions found. Nowadays, flexible enteroscopy is usually being reserved for patients with fibrotic strictures that require endoscopic balloon dilatation. Short-term success rates of 72% have been reported.⁴²

In conclusion, the lack of exposure to ionizing radiation and the possibility of detecting extraluminal abnormalities all favour MR or ultrasound as the initial radiological

investigation in suspected small-intestinal Crohn's disease. However, conventional enteroclysis has probably still the best accuracy in detecting early stage small-bowel Crohn's disease. In our view, VCE is more reliable than radiology to investigate suspected Crohn's disease, in the absence of symptoms suggestive of stenotic disease. However, in view of the major impact the diagnosis of Crohn's disease might have, histologic confirmation by enteroscopy should be considered.

Monitoring established Crohn's disease and post-operative recurrence

In patients with established Crohn's disease, VCE and radiology could be of use to monitor (ileocolonic) disease activity, post-operative recurrence, or to discriminate between symptoms caused by active inflammation, fibrostenotic lesions without active inflammation, or by conditions not primarily related to Crohn's disease.

In patients with established Crohn's disease, the risk of video capsule retention has been reported to be as high as 13%, even in the absence of clinical symptoms suggestive of small-bowel stenosis.²⁶ Small-bowel series were performed previous to VCE in all patients. No significant small-bowel stenoses were reported and small bowel series were reported to be normal in 82% of these patients. A study from the Netherlands found that in 34% of patients with Crohn's disease and suspected proximal small-bowel involvement, a high-grade stenosis was present on MR enteroclysis examinations. In these cases the authors refrained from performing capsule endoscopy. Despite this precaution, capsule retention occurred in 1/38 patients studied.⁴³ Because normal findings during small-bowel radiology do not prevent capsule retention, established Crohn's disease is considered by some to be a contraindication for VCE.

In addition, to monitor the effect of medical therapy, which is often expensive and associated with major side-effects, one can argue that nonspecific capsule and radiological findings are sometimes not sufficient, and histologic proof (obtained by means of enteroscopy) of the effectiveness of medical therapy is mandatory. In order to allow for a more reliable assessment of disease activity with VCE, a scoring system has been developed, the capsule endoscopy Crohn's disease activity index (CECDAI), that has been validated for use in patients with established Crohn's disease (**box 2.2**).⁴⁴ To date, the clinical relevance of this scoring system had not been clearly established. Triester and colleagues reported a higher yield for VCE capsule compared with conventional enteroclysis (78% *vs* 32%), and CT enterography (68% *vs* 38%).²⁸ However, patients with radiological evidence of small-bowel stenosis were excluded. Therefore, these results are only valid for patients with proven nonstricturing small-bowel Crohn's disease.

An extensive evaluation of the literature regarding radiology and ileocolonoscopy in the monitoring of ileocolonic Crohn's disease is beyond the scope of this overview. In general, both MR imaging and ultrasound are reliable alternatives to ileocolonoscopy to assess disease activity in the terminal ileum and colon.³⁵ Radiologic modalities, and especially cross-sectional modalities like CT enterography/enteroclysis and MR enterography/enteroclysis, are frequently being used to estimate disease activity in patients with Crohn's disease.

Box 2.2: Capsule endoscopy Crohn's disease activity index (CECDAI).

A. Inflammation score	B. Extent of disease score	C. Narrowing (stricture)
0 = none	0 = none	0 = none
1 = mild to moderate oedema hyperaemia/denuadation	1 = focal disease (single segment)	1 = single-passed
2 = severe oedema hyperaemia/denuadation	2 = patchy disease (multiple segments)	2 = multiple-passed
3 = bleeding, exudate, aphthae, erosion, small ulcer (≤ 0.5 cm)	3 = diffuse disease	3 = obstruction
4 = moderate ulcer (0.5–2 cm), pseudopolyp		
5 = large ulcer (>2 cm)		

Note: The CECDAI is calculated for the proximal small bowel (first 50% of small-bowel transit time) the distal small bowel (last 50% of small-bowel transit time). Proximal score = $(A_{\text{prox}} \times B_{\text{prox}}) + C_{\text{prox}}$. Distal score is $(A_{\text{dist}} \times B_{\text{dist}}) + C_{\text{dist}}$. The total CECDAI is calculated by adding the proximal and distal score. Adapted from Gal E, Geller A, Fraser G, Levi Z, Niv Y. Assessment and validation of the new capsule endoscopy Crohn's disease activity index (CECDAI). *Dig Dis Sci.* 2008;53:1933-7.

Amongst other parameters, mural enhancement after intravenous administration of contrast agents and wall thickening seem to correlate with endoscopic and clinical scoring systems for disease activity.⁴⁵⁻⁴⁸ However, most studies on this subject focus on Crohn's disease of the terminal ileum. Little is known on CT and MR imaging to evaluate disease activity in the more proximal small bowel, not accessible during conventional ileocolonoscopy.

In our view conventional enteroclysis is not informative enough to monitor therapy in patients with Crohn's disease, because Crohn's disease-related complications, such as fistula and abscesses, cannot be depicted reliably. CT is not preferred because it exposes patients to ionizing radiation, which is especially of concern in young patients in whom repeated examinations are needed.⁴⁹ The reported sensitivities and specificities of CT enterography and CT enteroclysis are 73–82% and 70–98%, respectively, and these techniques are superior to conventional enteroclysis for mural, serosal, and mesenteric abnormalities such as bowel wall thickening, fibrofatty proliferation of mesenteric fat, mesenteric abscess, and mesenteric lymphadenopathy. Such information is important for monitoring disease activity.⁵⁰ A recent study of 41 patients with known Crohn's disease showed CT enterography to have the same accuracy for mural disease as conventional enteroclysis.⁵¹ However, CT enterography provided additional information on colonic involvement, mesenteric involvement, and extraintestinal complications.

The sensitivity and specificity of MR imaging (enterography or enteroclysis) are comparable with those of conventional enteroclysis for diagnosing advanced small-bowel Crohn's disease.⁵² Inter- and intraobserver agreement is good or excellent for most pathologic signs. A systematic review on the accuracy of MR to stage disease showed MR correctly graded 91% of patients with frank disease, 62% of patients with mild disease and 62% of patients in remission.⁵³ In all, the authors concluded that MR more often overstaged than understaged disease activity.

Small-bowel tumours and small-bowel polyposis syndromes

Small-bowel cancers are rare. They include primary 'solid' lesions like adenocarcinoma, lymphoma, and metastasis. The annual incidence of primary small-intestinal adenocarcinoma is around 7 per million.⁵⁴ They comprise approximately one third of all malignancies encountered in the small intestine.⁵⁴ The risk of adenocarcinoma of the small bowel is increased in patients with Crohn's disease, coeliac disease, and small-bowel polyposis syndromes (*figure 2.6*).⁵⁵ Circumstantial evidence suggests an adenoma–carcinoma sequence.⁵⁶

Gastrointestinal stromal tumours (GISTs) are small, well-circumscribed lesions, usually with central ulceration or umbilication, originating from the cells of Cajal.⁵⁷ They account for less than 10% of all small-intestinal malignancies.⁵⁵ Tumours arising in the small bowel have worse prognosis than those of comparable size and mitotic count arising in other organs.⁵⁷

Neuroendocrine tumours are the only tumours that occur predominantly in the small intestine. In all, approximately 44% of all small-bowel malignancies are of neuroendocrine origin.⁵⁴ They are more likely to occur in the ileum than in the jejunum (*figure 2.7*)

Around 15% of all small-intestinal malignancies are small-bowel lymphoma, and approximately one third of all gastrointestinal lymphoma occur in the small bowel.^{54,58} Four



Figure 2.6: MR enteroclysis image obtained in an 88-year-old man with small-bowel obstruction shows a stenotic segment with an apple-core appearance (arrow). Histopathologic analysis showed this lesion to be adenocarcinoma.

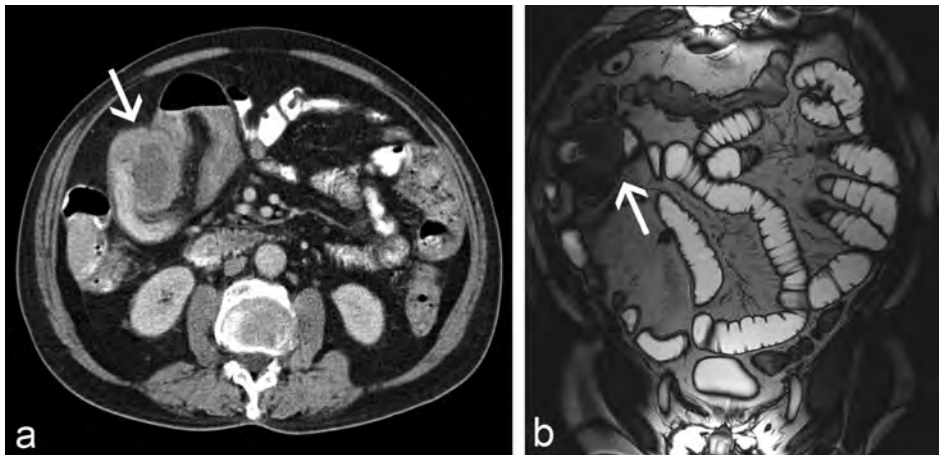


Figure 2.7: Images obtained in a 68-year-old man with a neuroendocrine tumour of the ileum. (a) Abdominal CT image shows a mass in the right lower quadrant of the abdomen (arrow), probably originating from an adjacent ileal loop. (b) MR enteroclysis clearly shows the relation between the ileum and the mass (arrow).

major forms of small-bowel involvement can be seen: primary small-bowel lymphoma, enteropathy-associated T cell lymphoma, mesenteric nodal lymphoma, and disseminated lymphoma.⁴⁹ Several radiographic patterns can be observed: a polypoid form, multiple nodules, an infiltrating form, an endoexoenteric form with excavation and formation of fistula, and a mesenteric invasive form with extraluminal masses. However, the correlation between radiological appearance and histology is poor.⁵⁸

In a review of 55 cases of small-bowel metastasis, metastases from lobular breast cancer (47.2%), lung cancer (11.1%), and malignant melanoma (8.3%) were most frequent.⁵⁹ Small-intestinal metastases should be considered in patients with known malignancies who experience small-bowel obstruction, gastrointestinal blood loss, or abdominal pain (*figure 2.8*).

Due to the rarity of small-bowel tumours, primary and metastatic, information on the diagnostic accuracy of radiological and endoscopic techniques is limited. The diagnostic accuracy of SBFT in the diagnosis of small-intestinal malignancies has been reported to be around 60%, whereas that of conventional enteroclysis has been reported to be as high as 95% if performed by experts.^{60, 61} Contrast and water-enhanced multidetector CT enterography has a reported sensitivity and specificity of 85% and 97%, respectively, in the detection of malignant and benign small-intestinal tumours.⁶² Negative results of transabdominal ultrasound in patients with suspected small-bowel tumours warrant further examination, because the reported sensitivity is only 26%. However, the 99% specificity of transabdominal ultrasound for the detection of small-bowel tumours might allow ultrasound to be considered as the first screening modality, because of its low invasiveness and low cost.⁶³

A study performed in the VU University Medical Centre on the diagnostic accuracy of MR enteroclysis shows even more promising results: The overall sensitivity and specificity of MR

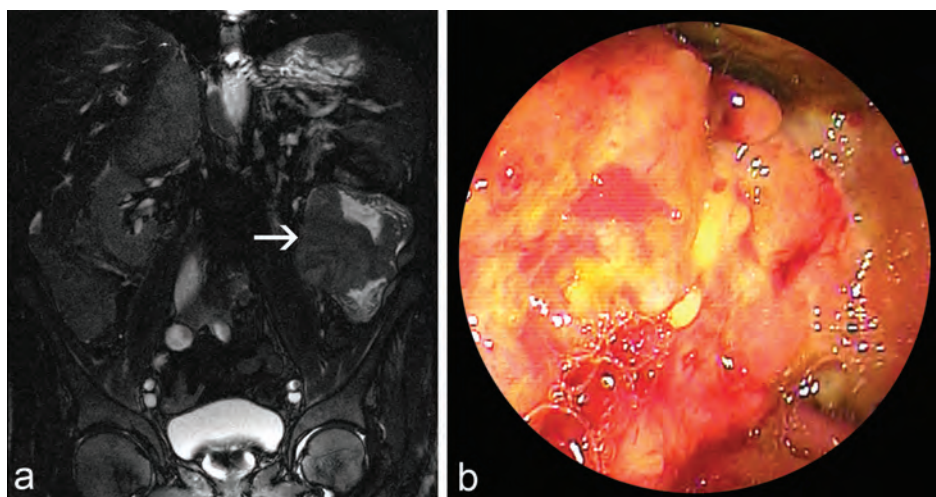


Figure 2.8: Images obtained in a 69-year-old male patient with jejunal metastasis of non-small-cell lung cancer. (a) MR enteroclysis shows an irregular stenotic tumour in the jejunum. (b) Corresponding DBE image.

enteroclysis in the detection of small-bowel tumours was 91–94% and 95–97%, respectively.¹⁶ In this study, 12 patients with known small-bowel polyposis syndromes (mostly Peutz-Jeghers syndrome) were included, which might have led to overestimation of diagnostic accuracy. However, when these patients were excluded in a subgroup analysis, the diagnostic accuracy remained high (94%). Interobserver agreement was excellent, with a kappa value of 93%.

Although the potential negative effect of exposure to ionizing radiation is probably of little relevance in patients who need to undergo small-bowel imaging only once to exclude or investigate suspected small-bowel malignancies, it might be of importance in patients who need to undergo repeated examinations in the follow-up of small bowel polyposis syndromes.

The diagnostic accuracy of CT and MR enteroclysis in the detection of small-intestinal neoplasms is high, and additional benefits include depiction of extra-intestinal abnormalities, such as enlarged lymph nodes.^{16, 17, 62} Therefore, in centres with experience in cross-sectional enteroclysis, such studies are considered the first option in patients with suspected small-intestinal cancer. This is also because there are some studies describing small-bowel tumours being missed on capsule studies but identified with cross-sectional enteroclysis.^{12, 64} This could be because of motion artefacts, lack of bowel distension during VCE, the unidirectional capsule view, or incompleteness of capsule studies. Therefore, in patients suspected of having a small-bowel tumour, but in whom VCE is normal, MR or CT enteroclysis should be considered. Even if radiological or wireless capsule examination shows a clear tumour, enteroscopy remains mandatory. Not only does enteroscopy facilitate histologic analysis of the tumour, it also is useful to tattoo a lesion to guide surgical resection, if indicated.

In patients with familial adenomatous polyposis syndrome, DBE and VCE have been proposed as tools to investigate the presence of small-bowel adenoma.⁶⁵ VCE seems less reliable in detecting duodenal adenoma.^{66, 67} There is limited experience with CT enterography as a tool to examine the duodenum of patients with FAP.^{68, 69} However, this seems less reliable than oesophagogastroduodenoscopy, especially in defining the number of polyps, because fine carpeting of miniscule duodenal polyps is poorly visualized with CT. VCE is probably superior to conventional enteroclysis in detecting small adenoma or hamartoma distal to the duodenum.⁷⁰ However, the clinical relevance of these small polyps is uncertain. A small study on Peutz-Jeghers syndrome suggests VCE is superior to conventional enteroclysis.⁷¹ In another study on patients with Peutz-Jeghers syndrome, 19 underwent both VCE and MR enterography. Although in general diagnostic accuracy was similar, in three patients, large polyps (>15 mm) were not detected on capsule endoscopy. Additionally, interobserver agreement was high for MR enterography but was only fair for capsule endoscopy ($\kappa = 0.81$ and 0.27 , respectively).⁷²

In patients with suspected small-bowel tumours MR enteroclysis might be used as the first modality of choice. If the presence of a tumour is confirmed, DBE is used to allow histological determination. In addition, MR enteroclysis helps in the choice of the preferred route of insertion of the DBE endoscope. In patients with small-bowel polyposis syndromes, MR enteroclysis is used to estimate the number, location, and size of small-bowel polyps. In patients with Peutz-Jeghers syndrome, we only perform DBE if polyps larger than 2 cm are present or if the patient experiences symptoms suggestive of (intermittent) small-bowel obstruction (*figure 2.9*). These polyps are then removed using snare coagulation.

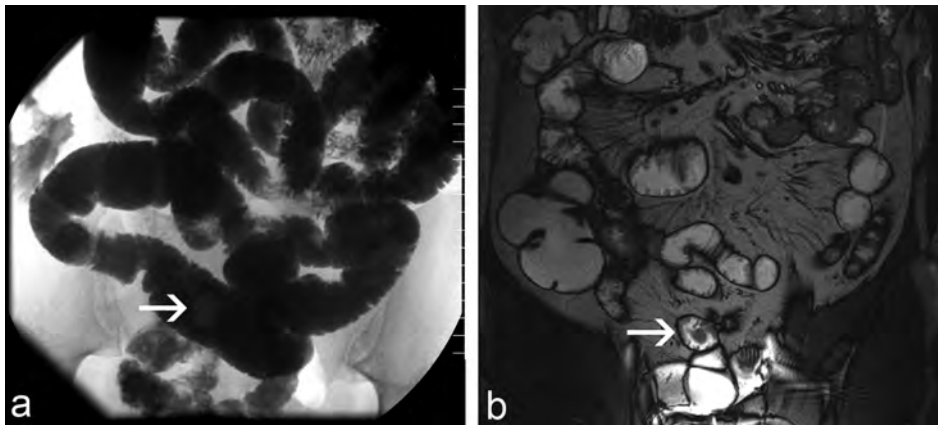


Figure 2.9: Images obtained in a 20-year-old man with Peutz-Jeghers syndrome. (a) Conventional enteroclysis revealed a polyp in the proximal ileum (arrow). (b) Corresponding MR enteroclysis image of the polyp (arrow).

Coeliac disease

The sensitivity and specificity of serologic tests (anti-tissue transglutaminase and anti-endomysial antibodies) and histologic examination of biopsies obtained in the duodenum are high.⁷³ Therefore, small-bowel imaging is not likely to have additional value in a novel diagnosis of coeliac disease. However, several radiological abnormalities can be encountered (*box 2.3, figures 2.10 and 2.11*).⁷⁴

In patients who do not respond well to a gluten-free diet, refractory coeliac disease should be suspected. This condition warrants a more aggressive diagnostic pathway, because one subtype (type II) is associated with high mortality, mainly due to its association with ulcerative jejunitis and enteropathy-associated T cell lymphoma (EATL).^{75, 76} These entities often present in regions of the small bowel that are not within reach of a conventional gastroscope. SBFT, conventional enteroclysis, and ultrasound have not been studied in patients with refractory coeliac disease. A study on the use of CT with oral contrast in patients with suspected refractory coeliac disease showed more bowel wall

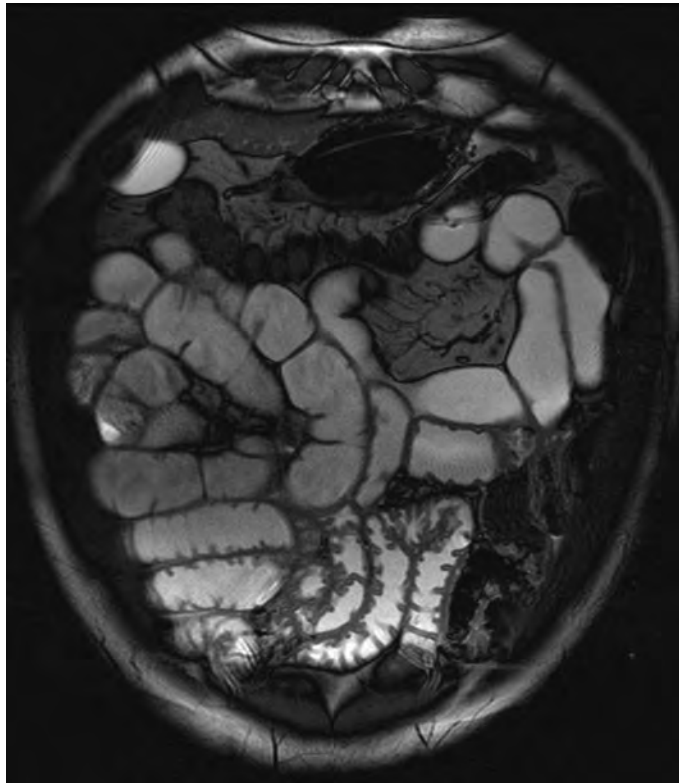


Figure 2.10: MR enteroclysis image obtained in a 66-year-old male patient with refractory coeliac disease. The decrease of jejunal folds (left upper abdominal quadrant) and the increase of ileal folds (right lower abdominal quadrant) results in jejunioileal fold pattern reversal.

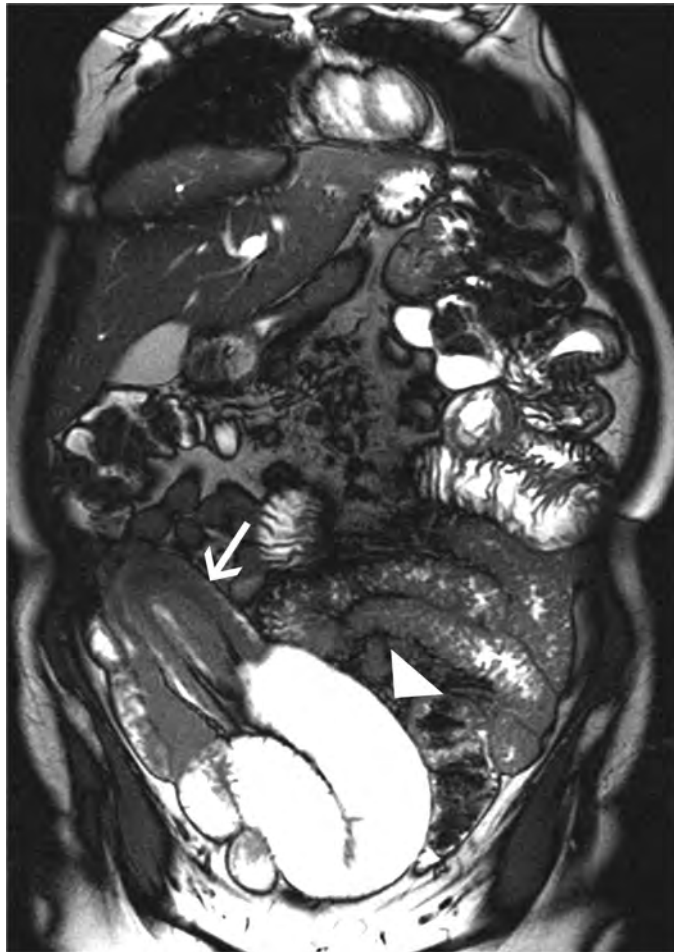


Figure 2.11: MR enteroclysis image of a patient with intussusception. The bowel-in-bowel appearance with proximal dilation is clearly visible (arrow) as is the prestenotic bowel dilatation (arrowhead).

Box 2.3: Radiological features of coeliac disease.

Luminal findings	Extraluminal findings
Bowel dilatation and small bowel atonia	Mesenteric lymphadenopathy
Increased number of ileal folds*	Mesenteric vascular engorgement
Decreased number of jejunal folds*	Small spleen
Small intestinal wall thickening	Ascites
Intussusception	
Stenosis and prestenotic dilatation†	
Small intestinal masses†	

Adapted from: Paolantonio P, Tomei E, Rengo M, Ferrari R, Lucchesi P, Laghi A. Adult celiac disease: MRI findings. *Abdom imaging.* 2007;32(4):433-40.

* If both are present, this is referred to as jejunoileal fold pattern reversal.

† Might indicate refractory coeliac disease or enteropathy associated T-cell lymphoma.

thickening, lymphadenopathy, and intussusception, less increase in the number of small mesenteric vessels and a smaller splenic volume in patients with refractory coeliac disease type II or EATL compared with patients with uncomplicated coeliac disease or refractory coeliac disease type I. No discrimination between uncomplicated coeliac disease and refractory coeliac disease type I was possible.⁷⁷ The use of MR enteroclysis in patients with suspected refractory coeliac disease has not yet been clarified. However, results from the VU University Medical Centre show that the presence of less than 10 jejunal folds per 5 cm and bowel wall thickness of 4 mm or greater were associated with the presence of refractory coeliac disease type II.⁷⁸ In addition, factors possibly associated with the development of ulcerative jejunitis and lymphoma, such as small splenic volume and infiltration of the mesenteric fat, can be assessed.

Because small-bowel histology is mandatory in patients with suspected refractory disease, DBE should always be performed to assess the presence of ulcerative jejunitis. MR might be helpful in assessing extraintestinal complications of refractory coeliac disease. However, DBE will always be a more reliable tool to diagnose ulcerative jejunitis and nonprotruding lymphoma.⁷³

Small-bowel diverticular disease, including Meckel's diverticulum

The incidence of diverticula in the small intestine distal to the duodenum is reported to be 0.06–2.3%.^{79, 80} Usually, these diverticula are asymptomatic. Complications include bacterial overgrowth, bleeding, and inflammation. Several radiological imaging methods have been described for the diagnosis of small-bowel diverticulitis.⁸¹ Plain abdominal radiography is usually not helpful, although small-bowel diverticula may be visible as air-filled pockets and intraperitoneal air can be identified. SBFT or conventional enteroclysis can depict small-bowel diverticula, but usually does not provide information on mural, serosal, or mesenteric involvement.⁸² Although abdominal ultrasound is able to depict extraluminal air and hyperechoic fat, it does not inform about the extent of small-bowel diverticula.^{83, 84} Abdominal CT might allow a specific diagnosis of small-bowel diverticulitis, however in the absence of clearly depicted small-bowel diverticula, inflammation in and around small-bowel loops cannot be distinguished from other conditions such as small-bowel Crohn's disease and small-bowel malignancies. MR and CT enteroclysis have the benefit of being able to depict small-bowel diverticula (because distension of the small bowel prevents collapse of diverticular segments) and the extraluminal abnormalities encountered with inflammation (*figure 2.12*).

Meckel's diverticula result from failure of the omphalomesenteric duct to regress and occur in approximately 2% of all adults. Complications include bleeding and intussusception.⁸⁵ In our experience, VCE is a disappointing modality to investigate the small bowel for Meckel's diverticulum. Although we have seen clear images of a Meckel's diverticulum occasionally, the absence of bowel distension prevents a clear depiction of Meckel's diverticula in most patients. Meckel's diverticula are usually not seen with SBFT or conventional enteroclysis, although the latter seems a little more sensitive.⁸⁶ On ultrasound

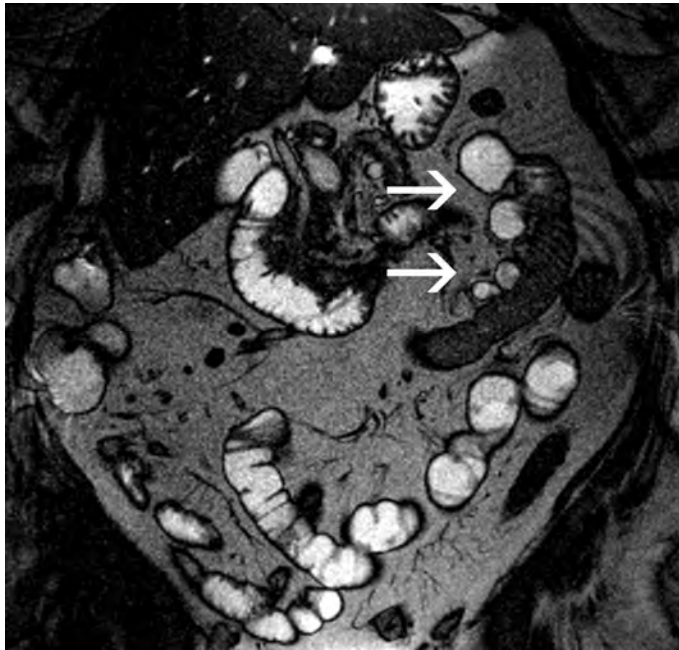


Figure 2.12: MR enteroclysis image obtained in a 68-year-old patient with small-bowel diverticulosis, several weeks after she presented with signs of diverticulitis. Several jejunal diverticula can be observed (arrows).

or cross-sectional imaging, Meckel's diverticula are frequently difficult to discriminate from normal small-bowel loops.⁸⁵ Scintigraphy with [^{99m}Tc]Na-pertechnetate has limited sensitivity in adults, but might be more reliable in children.⁸⁷ Retrograde DBE has been described as a tool to depict Meckel's diverticula and its complications.⁸⁸ In addition, haemostatic procedures can be performed in case of bleeding. Although no studies comparing radiological imaging with DBE have been performed, DBE does seem more reliable. Therefore, with obscure gastrointestinal blood loss, retrograde DBE should be considered early in the diagnostic pathway, especially in young adults.

Part III: Enteroscopy and radiological imaging: complementary techniques

Small-bowel endoscopy and radiological imaging of the small bowel are supplementary techniques. One of the drawbacks of radiological imaging is that it is usually not informative on flat mucosal lesions, as most vascular lesions are. Therefore its role as a primary investigation in patients with MGIB is limited, because VCE is more informative for vascular lesions. The major advantage of radiological examination, especially cross-sectional techniques, is its ability to demonstrate mural and extramural abnormalities.

It is difficult to suggest standardized diagnostic protocols for evaluating suspected small-bowel diseases, because there are many factors to be considered when choosing the optimal sequence of diagnostic tests. Several strategies can be followed. In general, in acute MGIB, we refrain from VCE and proceed directly to DBE because the need for endoscopic intervention is high in these patients. Usually, we start with the antegrade approach, because active bleeding might interfere with endoscopic progress during the retrograde approach. However, in young patients with acute MGIB, the retrograde approach might be preferable given the high likelihood of a Meckel's diverticulum. In patients with chronic MGIB, some centres prefer to plan antegrade DBE followed by retrograde DBE to achieve total enteroscopy, whereas other centres prefer VCE to be able to choose the optimal route of insertion to avoid 2 enteroscopy sessions. Usually, in MGIB the role of radiology is limited to patients with additional symptoms suggesting small-bowel obstruction, or a history of cancer. Radiology findings might indicate lesions that allow gastroenterologists to perform a targeted enteroscopy. The optimal strategy depends on the endoscopic skills of the gastroenterologist, the experience of the radiology department in small-bowel imaging and on reimbursement of the various examinations by local health care authorities.

Only one study has been performed to investigate the effect of small-bowel imaging on the yield of DBE.⁸⁹ In this retrospective study of 124 patients undergoing DBE, conventional enteroclysis was performed in 76 patients and was abnormal in 45 patients. Positive DBE findings were more likely to occur in patients who had abnormal enteroclysis than in patients with normal enteroclysis results or in whom enteroclysis was performed. Although the retrospective nature of this study made it prone to inclusion and confirmation bias, it is clear that pre-DBE small-intestinal imaging might be useful to select patients for DBE. However, only 1 of 16 patients with vascular lesions as the final diagnosis had abnormal enteroclysis results. This finding emphasizes the limited value of radiological modalities in patients with MGIB. In our view, negative radiological results should lead to referral for VCE or DBE.

In conclusion, similar to the major developments that have been achieved in small bowel endoscopy, small-bowel radiology is a rapid changing field. Although the already high diagnostic accuracy of advanced cross-sectional small-bowel imaging will probably increase even more, endoscopic methods will remain indispensable for diagnosing nonprotruding mucosal lesions and obtaining histologic confirmation of suspected small-bowel lesions. Solid prospective studies comparing radiological methods with VCE and enteroscopy, using either enteroscopy or operative findings as the standard of reference, are needed. To design and interpret such studies, it is important for gastroenterologists to be able to speak the same language as radiologists, and vice versa. It is of the utmost importance for physicians interested in small-intestinal diseases to realize that there is no need for competitive comparison between radiological imaging, VCE, and DBE. The combination of endoscopic, radiological, and surgical knowledge, will lead to new developments in all medical disciplines involved in the care for patients with small-intestinal diseases.

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