Minimally-invasive imaging of the small intestine

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Chapter 3

MR enteroclysis in the diagnosis of small-bowel neoplasms

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Abstract

Purpose

To evaluate the diagnostic accuracy and interobserver variance of magnetic resonance (MR) enteroclysis in the diagnosis of small-bowel neoplasms, with small-bowel endoscopy, surgery, histopathologic analysis and follow-up serving as standards of reference, and to identify MR enteroclysis characteristics capable of enabling discrimination between benign and malignant small-bowel neoplasms.

Materials and Methods

This study was performed in accordance with the guidelines of the institutional review board, and the requirement for informed consent was waived. MR enteroclysis studies of 91 patients (43 women, 48 men; age range 18–83 years) were retrospectively evaluated by two radiologists blinded to clinical details. Only studies explicitly performed to investigate or exclude the presence of small-bowel neoplasms were included. Radiologic findings were compared with findings of double-balloon endoscopy (n = 45), surgery (n = 18), oesophagogastroduodenoscopy (n = 3), ileocolonoscopy (n = 2), autopsy (n = 2), and clinical follow-up for more than 18 months (n = 21). Efficacy parameters were calculated with 95% confidence intervals. Tumour characteristics were compared with the Student t test and the Fisher exact test.

Results

Readers 1 and 2 interpreted 31 and 33 studies, respectively, as depicting a small-bowel neoplasm and 19 and 17 studies, respectively, as depicting small-bowel malignancy. In 32 patients, the presence of small-bowel neoplasm was confirmed. In 19 of these patients, the neoplasm was malignant. Sensitivity and specificity in the diagnosis of small-bowel neoplasms was 0.91 and 0.97, respectively, for reader 1 and 0.94 and 0.95, respectively, for reader 2; the κ value was 0.95. Factors associated with malignancy were the presence of longer solitary nonpedunculated lesions, mesenteric fat infiltration, and enlarged mesenteric lymph nodes.

Conclusion

Eighty-six of 91 studies were correctly interpreted, resulting in an overall diagnostic accuracy of 0.95 for MR enteroclysis in the detection of small-bowel neoplasms.

Introduction

Small-bowel neoplasms are rare entities and often pose a challenge to radiologists, gastroenterologists and oncologists. The annual age-adjusted incidence of primary small-bowel malignancy is estimated at 17 cases per million individuals.[1] A median delay in diagnosis of twelve months, attributable to radiologic studies failing to depict neoplasms has been reported.[2]

Several modalities are available with which to investigate suspected small-bowel masses. Small-bowel enteroclysis has better accuracy than conventional small-bowel follow through (SBFT).[3, 4] Multidetector computed tomography (CT) enteroclysis has the advantage of depicting transmural and extramural abnormalities, and researchers reported an accuracy of 0.85 for small-bowel neoplasms.[5] Video capsule endoscopy and double-balloon endoscopy (DBE) are new endoscopic techniques that are used to examine the small bowel.[6-8] Both video capsule endoscopy and DBE enable optical depiction of tumours.[9-13] A major limitation of video capsule endoscopy is the fact that it does not depict the complete small bowel in up to 34% of studied patients.[14] DBE facilitates histologic sampling of suspicious lesions. Although the role of DBE in the diagnosis of small-bowel neoplasms is not yet clear, it seems reasonable to assume that histologic samples of abnormalities encountered during DBE can be considered a standard of reference. DBE is time consuming, and invasive, and it usually requires two sessions to depict the entire small bowel.[15] Furthermore, the complication rate of DBE is 1.2–3.6%.[16-18] Therefore, a reliable non-invasive modality might be useful in the identification of patients in whom more invasive diagnostic methods are warranted.

Magnetic resonance (MR) enteroclysis is an emerging technique with which to diagnose small-bowel disease. Potential benefits of MR enteroclysis include direct acquisition of coronal plane images and high intrinsic soft-tissue contrast resolution, as well as the absence of exposure to ionizing radiation.[19] An additional benefit of MR enteroclysis when compared to SBFT, small-bowel enteroclysis, video capsule endoscopy or DBE is the ability to depict extraintestinal involvement. A recent study showed the sensitivity and specificity of MR enteroclysis in the diagnosis of small-bowel neoplasms to be 0.86 and 0.98 respectively.[20]

The aims of our study were evaluate the diagnostic accuracy and interobserver variance of MR enteroclysis in the diagnosis of small-bowel neoplasms, with small-bowel endoscopy, surgery, histopathologic analysis and follow-up serving as standards of reference, and to identify MR enteroclysis characteristics capable of enabling discrimination between benign and malignant small-bowel neoplasms.

Methods

Study population

This retrospective study was approved by our institutional review board, and the requirement for informed consent was waived. From September 2004 to July 2007 MR enteroclysis studies were performed in 297 patients who were clinically suspected or

known to have small-bowel disease, for which our centre is a tertiary referral centre. Informed consent for the MR enteroclysis examinations had been obtained in all patients.

We included only those studies performed in patients who were suspected of having a small-bowel neoplasm or in whom the physician responsible for patient care explicitly ordered the MR enteroclysis study to exclude the presence of a small-bowel neoplasm. Studies performed in patients with known coeliac disease were excluded. Investigations performed in patients younger than 18 years or in patients who underwent only clinical follow-up for less than 18 months were not included. A flow chart showing the progress of subjects through the study is presented in ***figure 3.1***.

The study group comprised 91 patients (age range 18–83 years; mean 53.1 years). There were 43 female patients (age range 26–82 years; mean 51.5 years) and 48 male patients (age range 18–83 years; mean 54.5 years). MR enteroclysis studies were performed to investigate or to exclude the presence of small-bowel neoplasms in patients with iron-deficiency anaemia (n = 25), low grade small-bowel obstruction (n = 21), known polyposis syndrome (n = 12), persistent abdominal pain (n = 11), midgastrointestinal bleeding (defined by either melaena or haematochezia with negative oesophagogastroduodenoscopy and colonoscopy) (n = 5), history of solitary small-bowel adenoma (n = 4), weight loss (n = 3), suspected small-bowel fistula in the absence of Crohn's disease (n = 3), adenocarcinoma with unknown primary origin (n = 2), diarrhoea (n = 2), protein-losing enteropathy (n = 1), ileostomal dysfunction (n = 1), and suspected afferent loop syndrome (n = 1).

Twenty-eight patients (31%) underwent MR enteroclysis after an invasive small-bowel investigation had been performed. In 14 of these patients MR enteroclysis was performed to confirm negative DBE findings. In the remaining fourteen patients MR enteroclysis was performed after DBE had revealed a small-bowel neoplasm, but failed to depict the complete small bowel. Reasons for incomplete DBE in these patients were small-bowel stenosis that could not be passed with the endoscope (n = 6), suboptimal progression of the endoscopy in the absence of stenosis (n = 6), and decreased tolerance to the DBE-procedure (n = 2).

MR enteroclysis protocol

After an overnight fast, a nasojejunal tube (duodenal set with Teflon guide wire, outer diameter 3.1 mm, inner diameter 2.1 mm, total length 150 cm, Hospimed International, Zwolle, The Netherlands) was positioned distal to the duodenojejunal junction under fluoroscopic guidance. Next, during MR imaging, a minimum of 2000 ml 0.5% methylcellulose solution in water was infused through the tube, at a flow rate of 80–100 mL/min, using an infusion pump system (Watson Marlow, Falmouth, England).

We performed 1.5T MR Imaging (Sonata, Siemens Medical Systems, Erlangen, Germany) with use of a 16-element phased-array surface coil during infusion. The imaging protocol included multiple axial and coronal breath-hold true fast imaging with steady-state precession (FISP) sequences (repetition time msec/echo time msec, 4.3/2.2; field of view, 320–400 (depending on the size of the patient); matrix, 288 × 512; flip angle; 70°;

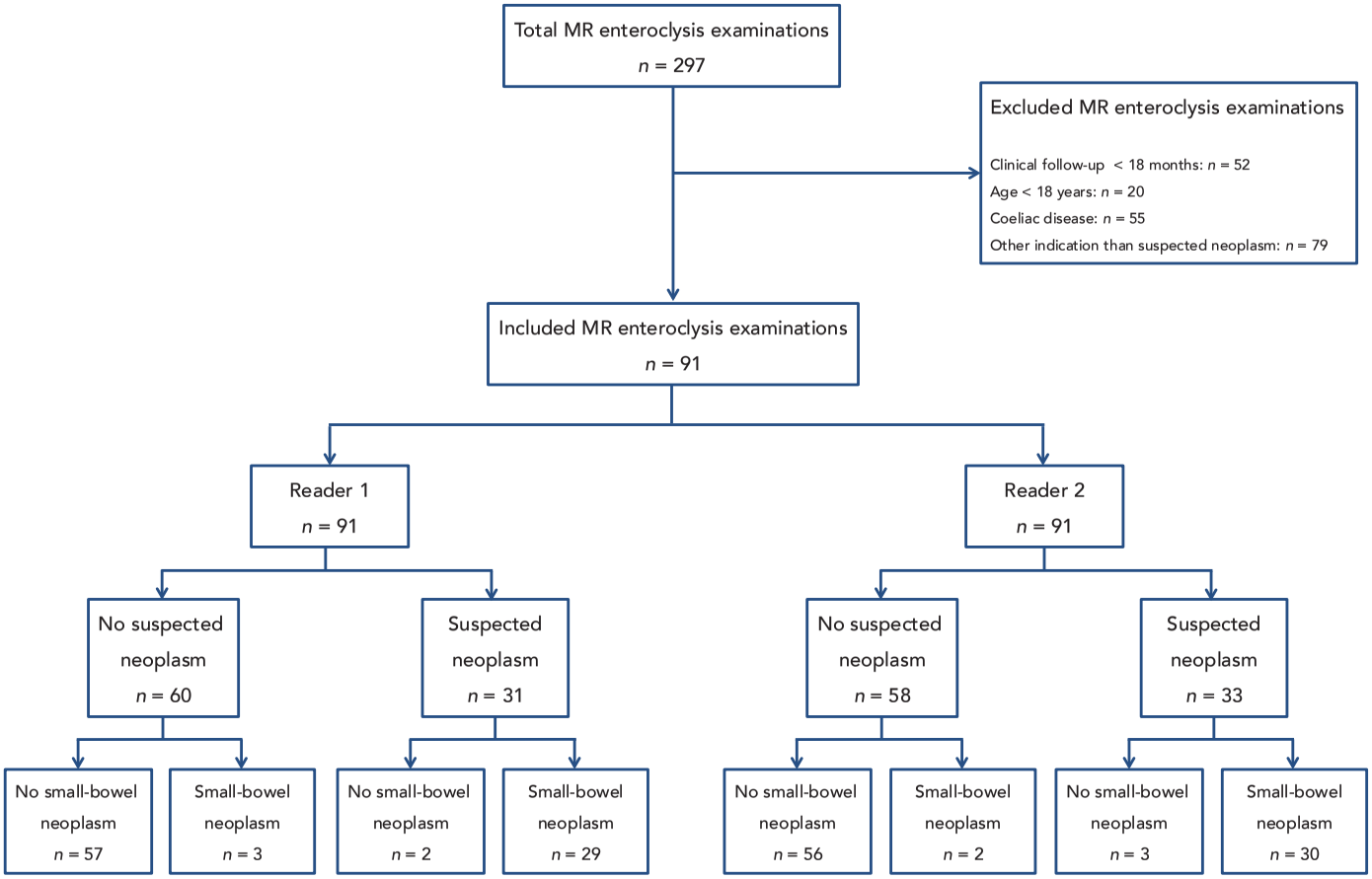

Figure 3.1: Flowchart shows the progress of patients who underwent MR enteroclysis studies as they passed through the study protocol.

one signal acquired; slice thickness, 4 mm; intersection gap, 0.8 mm), in multiple breath-hold series repeated at least five times in a row. Images were acquired with patients in prone position. Acquisition time per sequence was 20–25 sec; the total imaging time per patient was approximately 30 minutes. In between the true FISP sequences, a heavily T2-weighted half-Fourier acquisition single-shot fast spin-echo (HASTE) sequence (1000/90, field of view. 320–400 depending on the size of the patient; matrix. 388 × 512; flip angle, 150°; one signal acquired; echo train length, 224; section thickness, 6mm; intersection gap, 3 mm) was performed three times with full abdominal coverage. Imaging was stopped when optimal distension of the full small bowel and caecum was obtained. No intravenous contrast material was used. True FISP images were used for diagnostic analysis, while HASTE sequences were used to follow the infusion of the oral contrast agent.

No major complications occurred during the studies. One patient (1%) did not tolerate the nasojejunal catheter. In seven patients (8%), the MR enteroclysis procedure was temporary stopped because of vomiting at the end of image acquisition. Four patients (4%) experienced faecal incontinence during the procedure.

Image analysis

Two gastrointestinal radiologists (J. H. T. M. v. W. and M. R. M.); 6 and 2 years of experience in MR enteroclysis, reviewed the images independently for the presence of small-intestinal neoplasms. Both reviewers were blinded to clinical details, results of previous investigations and the final diagnosis. In all cases in which a neoplasm was suspected on the basis of imaging study results, the case was scored as a suspected benign or malignant finding. In a second session, reader 1 reviewed all images of patients with positive MR enteroclysis findings (defined as neoplasm identified by at least one reader) and histological proven neoplasms, to identify MR enteroclysis characteristics associated with either benign or malignant neoplasms. The following MR enteroclysis features were examined: size, location, shape (sessile or pedunculated), and number of masses; prestenotic dilatation; mesenteric fat infiltration; and size of mesenteric lymph nodes. Small-bowel masses were defined as intraluminal structures present on at least two planes. If more than one neoplasm was present, the size of the largest neoplasm was included for this analysis. Prestenotic dilatation was considered to be present if the diameter of a bowel loop proximal to a neoplasm was at least 3 cm in diameter on transverse images.[21] Mesenteric fat infiltration was defined as a decrease of signal intensity of the mesentery surrounding mesenteric vessels. Lymph nodes larger than 1 cm in diameter in their shortest axis were considered enlarged.[22]

Standard of reference

As a standard of reference for the presence of neoplasms, we used histopathologic findings of biopsy specimens obtained in (a) biopsy specimens that where obtained during either DBE (n = 21) or oesophagogastroduodenoscopy (n = 1) or (b) surgical resection specimens

(*n* = 10). In case of an absence of histologic confirmation of suspected neoplasms, the case was considered false positive. The absence of small-bowel neoplasms was confirmed with DBE (*n* = 24), surgery (*n* = 8), oesophagogastroduodenoscopy (*n* = 2), ileocolonoscopy (*n* = 2), autopsy (*n* = 2), and clinical follow-up lasting at least 18 months (*n* = 21; mean follow-up duration, 32 months; range 18–52 months). DBE was performed according to the method described in detail by Yamamoto and co-workers.[23]

Statistical analysis

Performance characteristics for MR enteroclysis in the diagnosis of any small-bowel neoplasm (either benign or malignant) were calculated for both readers and included sensitivity, specificity, negative and positive predictive values, overall accuracy and Youden index.[24, 25] Efficacy parameters were also calculated in subgroups consisting of (a) patients without known polyposis syndromes (*n* = 79); (b) patients in whom endoscopy, surgery or autopsy served as the standard of reference (*n* = 70); and (c) patients who underwent MR enteroclysis before they underwent an invasive small-bowel investigation (*n* = 63). Interobserver agreement was assessed with κ statistics. A κ value greater than or equal to 0.75 was considered to represent excellent agreement. In the comparison of MR enteroclysis characteristics of benign neoplasms with those of malignant neoplasms, continuous variables were tested with the Student *t* test, whereas categorical variables were tested with the Fisher exact test.

Results

MR enteroclysis findings

The number of MR enteroclysis studies interpreted as depicting a small-bowel neoplasm was 31 (reader 1) and 33 (reader 2) (***table 3.1***). The number of MR enteroclysis studies interpreted as depicting small-bowel malignancy was 19 (reader 1) and 17 (reader 2). In 32 patients, the presence of a small-bowel neoplasm was histopathologically proven after surgery or endoscopy. In 19 of these patients, the neoplasm was malignant. Histopathologic diagnoses were as follows: lymphoma (*n* = 7), primary small-bowel adenocarcinoma (*n* = 6), small-bowel metastasis (*n* = 4), neuroendocrine tumour (*n* = 2), hamartomatous polyps (*n* = 9), adenoma (*n* = 2), and inflammatory fibroid polyp (*n* = 2). In all confirmed neoplasms, the location suggested by MR enteroclysis was confirmed either surgically or endoscopically.

Sensitivity of MR enteroclysis in the diagnosis of small-bowel neoplasms was 0.91and 0.94 for readers 1 and 2, respectively, while specificity was 0.97 and 0.95, for readers 1 and 2, respectively (***table 3.2***). Reader 1 correctly assessed the benign or malignant nature of 29 (94%) of 31 recognized small-bowel neoplasms. Reader 2 correctly assessed the benign or malignant nature in 29 (88%) of 33 recognized small-bowel neoplasms.

There was excellent agreement between the readers, with a κ value of 0.95 for MR enteroclysis diagnosis of small-bowel neoplasm.

Table 3.1: True-negative, true-positive, false-positive and false-negative MR enteroclysis readings in the total study group and the three subgroups.

Group and Reader	No. of true-negative cases	No. of true-positive cases	No. of false-positive cases	No. of false-negative cases	Total
Total study group					
Reader 1	57 (63)	29 (32)	2 (2)	3 (3)	91
Reader 2	56 (62)	30 (33)	3 (3)	2 (2)	91
Patients without known polyposis syndrome					
Reader 1	55 (70)	19 (24)	2 (3)	3 (4)	79
Reader 2	54 (68)	20 (25)	3 (4)	2 (3)	79
Patients with invasive standard of reference					
Reader 1	37 (53)	29 (41)	1 (1)	3 (4)	70
Reader 2	36 (51)	30 (43)	2 (3)	2 (3)	70
Patients without prior invasive small-bowel investigation					
Reader 1	43 (68)	16 (25)	2 (3)	2 (3)	63
Reader 2	42 (67)	16 (25)	2 (3)	3 (5)	63

Note: Data in parentheses are percentages of group.

False-negative and false-positive results

In four patients, both readers misinterpreted MR enteroclysis findings (***table 3.3***). In two patients, both readers correctly identified a tumour, but misinterpreted its origin. This resulted in one false-positive result (suspected duodenal tumour with pancreatic invasion proved to be primary pancreatic tumour with small-bowel invasion) and one false-negative result (suspected carcinoma of the caecum with ileal invasion proved to be ileal tumour with caecal invasion).

In the patient who did not tolerate the nasojejunal catheter a jejunal metastasis from non-small cell lung cancer was not identified. We suspect this was caused by insufficient distension of the region where the tumour was localized. In one patient, both readers identified a suspected jejunal malignancy, but the general condition of the patients did not allow surgical or endoscopic confirmation. This patient had bone metastases of lobular breast cancer and died after palliative treatment for small-bowel stenosis was commenced. Autopsy was declined by her relatives. Because of lack of histologic confirmation, this case was considered false positive.

One reader did not identify one inflammatory fibroid polyp, whereas one reader misinterpreted a peptic duodenal stenosis as a malignant stricture. One reader misinterpreted two studies that depicted lymphoma as showing benign neoplasms. This occurred in a patient with more than 20 nonpedunculated masses that ranged in diameter from 0.5 cm to 3.5 cm and in a patient with two nonpedunculated masses, ranging from 2.0 to 3.0 cm, one of which caused an intussusception.

Table 3.2: Efficacy parameters of MR enteroclysis in detecting small-bowel neoplasms and malignancy in the total study group and the three subgroups.

Parameter and Reader	Total study group (n = 91)	Patients without known polyposis syndromes (n = 79)	Patients with invasive standard of reference (n = 70)	Patients without prior invasive small bowel-investigation (n = 63)
Sensitivity				
Reader 1	0.91 (0.74–0.98)	0.86 (0.64–0.96)	0.91 (0.74–0.98)	0.89 (0.64–0.98)
Reader 2	0.94 (0.78–0.99)	0.91 (0.69–0.98)	0.94 (0.78–0.99)	0.84 (0.60–0.96)
Specificity				
Reader 1	0.97 (0.87–0.99)	0.96 (0.87–0.99)	0.97 (0.85–1.00)	0.96 (0.84–0.99)
Reader 2	0.95 (0.85–0.99)	0.95 (0.84–0.99)	0.95 (0.81–0.99)	0.95 (0.83–0.99)
Positive predictive value				
Reader 1	0.94 (0.77–0.99)	0.90 (0.68–0.98)	0.97 (0.81–1.00)	0.89 (0.64–0.98)
Reader 2	0.91 (0.75–0.98)	0.87 (0.65–0.97)	0.94 (0.78–0.99)	0.89 (0.64– 0.98)
Negative predictive value				
Reader 1	0.95 (0.85–0.99)	0.95 (0.85–0.99)	0.93 (0.79–0.98)	0.96 (0.84–0.99)
Reader 2	0.97 (0.87–0.99)	0.96 (0.87–0.99)	0.95 (0.81–0.99)	0.93 (0.81–0.98)
Accuracy				
Reader 1	0.95 (0.88–0.97)	0.94 (0.86–0.97)	0.94 (0.86–0.97)	0.94 (0.85–0.98)
Reader 2	0.95 (0.88–0.97)	0.94 (0.86–0.97)	0.94 (0.86–0.98)	0.92 (0.83–0.96)
Youden index				
Reader 1	0.87 (0.73–0.94)	0.83 (0.65–0.91)	0.88 (0.72–0.93)	0.84 (0.63–0.94)
Reader 2	0.89 (0.74–0.95)	0.86 (0.67–0.94)	0.89 (0.72–0.96)	0.80 (0.58–0.90)

Note: Data in parentheses are 95%-confidence intervals. Youden index was calculated with the following equation: Youden index = (sensitivity + specificity) – 1.

Tumour characteristics on MR enteroclysis

Lymphomas detected with MR enteroclysis were diffuse large-cell B-cell lymphoma (n = 5) and follicular lymphoma (n = 2). Lymphomas were located in the jejunum (n = 3), ileum (n = 2), or both (n = 2). Mean length of lymphoma was 9.3 cm (range, 3.8–18.0 cm). Mean thickness (including bowel wall) was 2.5 cm (range, 0.9–5.8 cm). Mean lymph node short-axis diameter was 1.7 cm (range, 0.7–3.4 cm). In four patients short-axis diameter of mesenteric lymph nodes was more than 1 cm (***figure 3.2***).

Primary adenocarcinomas diagnosed with MR enteroclysis were located near the ligament of Treitz (n = 3), proximal jejunum (n = 1), and distal jejunum (n = 1). The mean length of primary adenocarcinoma was 4.8 cm (range, 3.5–6.5 cm). Mean thickness (including bowel wall) was 1.4 cm (range, 1.0–2.1 cm). Mesenteric lymph nodes with short-axis diameter of more than 1 cm were present in one patient, but histopathologic examination of 18 lymph nodes in the resection specimen revealed no metastases. The growth pattern of adenocarcinomas was predominantly intraluminal (***figure 3.3***). One

Table 3.3: Cases in which interpretation of one or both readers did not match histologic diagnosis.

Sex/Age	Reader 1	Reader 2	Incorrect MR enteroclysis diagnosis	Final diagnosis	Comment
F/67	FN	FN	Primary caecal carcinoma with ileal invasion	Primary ileal adenocarcinoma with caecal invasion	—
F/65	FN	FN	No evident abnormalities	Metastasis of non-small cell lung cancer.	Suboptimal bowel distension, no nasojejunal catheter after vomiting.
M/42	FN	Correct	Invagination without neoplasm	Inflammatory fibroid polyp	—
F/62	FP	FP	Primary distal duodenal tumour with pancreatic invasion	Duodenal invasion of pancreatic neuroendocrine tumour	—
F/69	FP	FP	Focal bowel-wall thickening jejunum suspected of malignancy	Tumour not confirmed	Suspected metastasis of lobular breast cancer. No endoscopy or surgery was performed due to terminal condition.
F/73	Correct	FP	Malignant stenosis proximal duodenum	Peptic bulbar stenosis, confirmed with oesophagogastroduodenoscopy	Movement artefacts
F/68	Correct	FN for malignancy	Benign neoplasm proximal ileum	Small-bowel lymphoma proximal ileum	Neoplasm recognized, but regarded benign
F/61	Correct	FN for malignancy	Benign neoplasms, multiple locations	Small-bowel lymphoma, multiple locations	Neoplasm recognized, but regarded benign

Note: F= female; M = male; FN = false negative; FP = false positive.

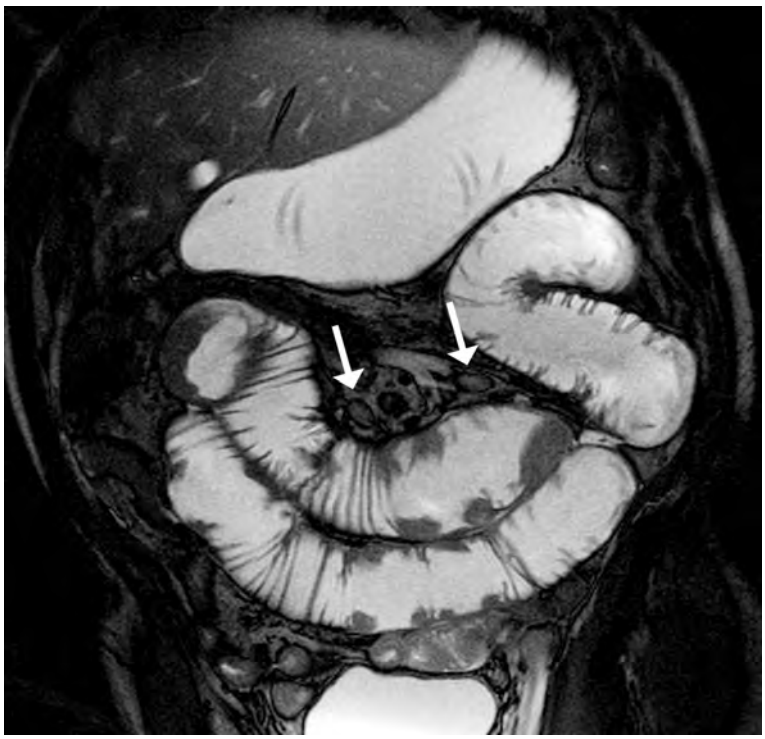

Figure 3.2: Coronal true FISP image (4.3/2.2, 67° flip angle) obtained in a 61-year-old man with low-grade small-bowel obstruction caused by multiple jejunal lymphoma shows multiple sites with eccentric irregular thickening of the jejunal wall. Enlarged mesenteric lymph nodes are visible (arrows).

ileal adenocarcinoma was not identified by any reader as being of small-intestinal origin and therefore not included in this analysis.

Small-bowel metastases diagnosed by MR enteroclysis were from patients with non-small cell lung cancer (n = 2) and colorectal carcinoma (n = 1). Solitary metastases were located in the proximal jejunum (n = 1) and distal ileum (n = 1). One patient had two metastases, located in the midjejunum and distal ileum. In one patient a metastasis of non-small cell lung cancer was not identified and therefore not included in the analysis of MR enteroclysis features associated with malignancy (***figure 3.4***).

In one patient, a solitary 8-cm-diameter neuroendocrine tumour was located in the midileum. In one patient two lesions were located in the proximal ileum, with a large lymph node in the adjacent mesentery (***figure 3.5***).

Thirteen patients had benign small-bowel neoplasms. Nine patients had hamartomatous polyps. Two of these patients had more than twenty hamartomatous polyps detected by MR enteroclysis (***figure 3.6***). Six patients had duodenal and jejunal hamartomatous polyps. Three patients had duodenal, jejunal and proximal ileal hamartomatous polyps. Mean polyp size was 17 × 24 mm (range, 3 × 3 mm to 32 × 39 mm).

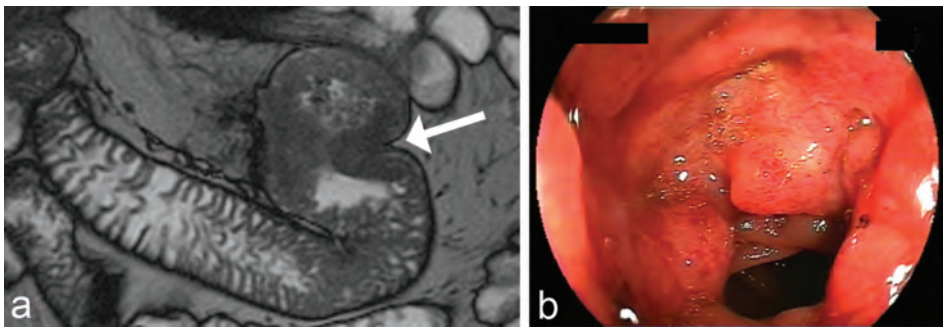

Figure 3.3: Images in a 59-year-old man with iron-deficiency anaemia caused by adenocarcinoma near the ligament of Treitz. (a) Coronal true FISP image (4.5/2.2, 70° flip angle) shows irregular circumferential thickening of the proximal jejunum (arrow) and infiltration of the surrounding mesenteric fat. (b) Endoscopic image of the circumferential tumour. A histopathologic examination revealed the lesion was an adenocarcinoma.

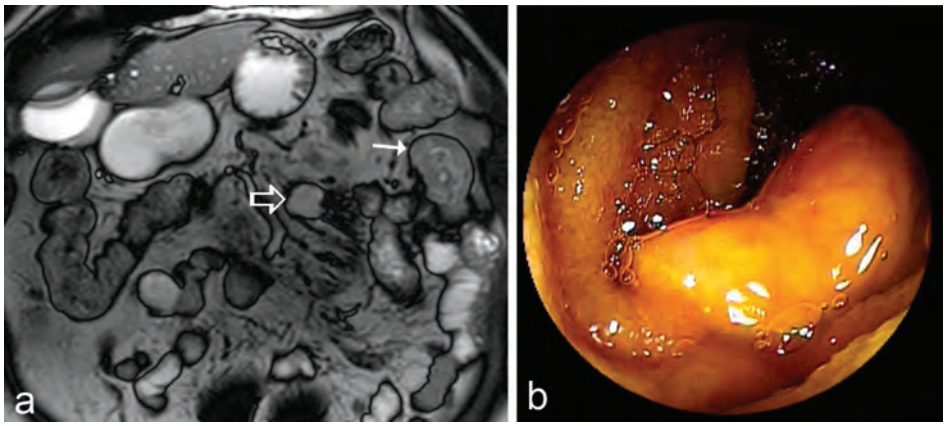

Figure 3.4: Images in a 65-year-old woman with iron-deficiency anaemia caused by jejunal non-small cell lung cancer metastasis. (a) Coronal true FISP image (3.8/2.1, 58° flip angle) acquired without jejunal fluid delivery, shows the absence of small-bowel distension. In the blinded readings both reviewers missed a metastasis of non-small cell lung cancer. In the diagnostic reading a lesion was suspected in the proximal jejunum (arrow). Additionally, an enlarged lymph node is visible (open arrow). (b) Endoscopic image of the tumour in the proximal jejunum. Histopathologic examination revealed the lesion was a metastasis of non-small cell lung cancer.

Two patients had small-bowel adenoma. One patient had five duodenal lesions that ranged in size from 5 × 8 mm to 14 × 11 mm. The other patient had three lesions that ranged in size from 7 × 4 mm to 10 × 15 mm. Sizes of the inflammatory fibroid polyps detected in two patients were 17 × 42 mm and 50 × 55 mm (***figure 3.7***). All adenomatous and inflammatory fibroid polyps, as well as all hamartomatous polyps larger than 1 cm, were endoscopically resected and proved to be benign after histopathologic examination.

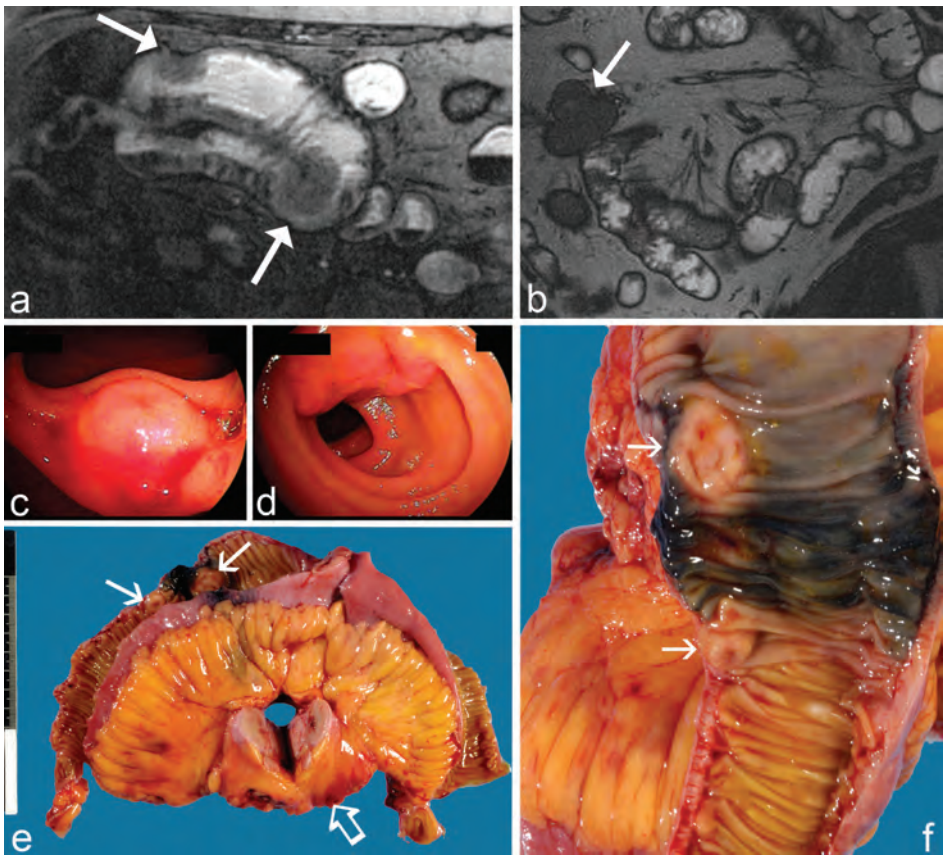

Figure 3.5: Images in a 60-year-old man with persistent abdominal pain caused by neuroendocrine tumours. (a) Axial true FISP image (4.3/2.1, 69° flip angle) shows two intraluminal masses in the proximal ileum (arrows). (b) Coronal true FISP image (4.3/2.1, 69° flip angle) shows an enlarged adjacent lymph node (arrow). (c) Endoscopic image of the proximal, smaller tumour in the proximal ileum, corresponding to the tumour seen on the left in figure a. (d) Endoscopic image of the distal, larger tumour in the proximal ileum, corresponding to the tumour seen on the right in figure a. Histopathologic examination revealed both masses were neuroendocrine tumours. (e) Overview of the laparoscopically resected part of the ileum. The two neuroendocrine tumours can be seen in the upper part of the image (arrows). The enlarged lymph node is included in the resection specimen (open arrow) and transected. Histopathologic examination revealed the lymph node was metastatic. The large stripes on the scale represent centimetres. (f) Detail of the laparoscopically resected part of the ileum. Both neuroendocrine tumours are visible (arrows). The blue discolouration between the tumours is caused by the endoscopic tattoo that was placed to guide surgical resection.

Table 3.4 shows the comparison of selected MR enteroclysis characteristics with regard to the final histologic assessment (benign or malignant) of all studies in which histopathologically confirmed neoplasms were identified.

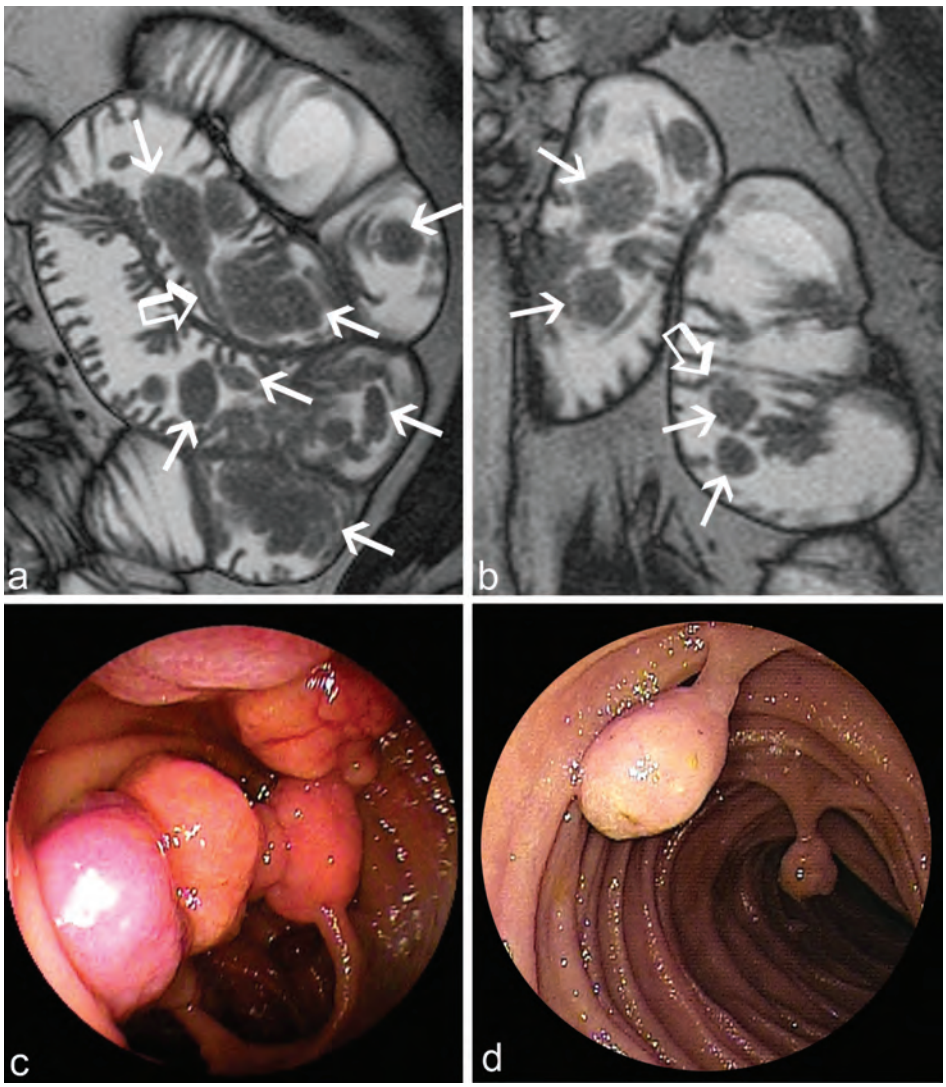

Figure 3.6: Images in a 40-year-old man with Peutz-Jeghers syndrome. (a) and (b) Coronal true FISP images (4.3/2.1, 70° flip angle) of the proximal jejunum show multiple masses (arrows), some stalks are clearly visible (open arrows). (c) Endoscopic image of a conglomerate of jejunal hamartomatous polyps. (d) Endoscopic image of two pedunculated jejunal hamartomatous polyps.

Discussion

Our study results confirm that MR enteroclysis is an accurate modality with which to diagnose or exclude small-bowel neoplasms. The performance of MR enteroclysis in detection of small-bowel neoplasms was comparable to that described recently by Masselli and co-workers.[20] The interobserver agreement was interpreted as excellent ($\kappa = 0.95$). In

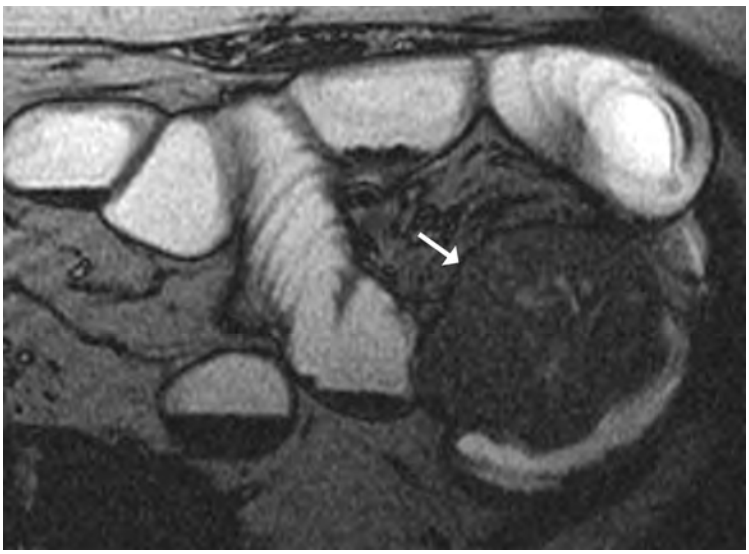

Figure 3.7: Axial true FISP image (4.3/2.2, 68° flip angle) in a 57-year-old female with iron-deficiency anaemia shows a 50 × 55 mm large mass in the proximal ileum (arrow). Histopathologic examination revealed the mass was an inflammatory fibroid polyp.

addition, we identified several MR enteroclysis characteristics that helped us differentiate between benign and malignant neoplasms.

Although conventional CT has high diagnostic accuracy in the identification of high-grade small-bowel obstruction, its usefulness in the identification of low-grade small-bowel obstruction is disappointing.[26] It is difficult to compare our findings with the findings of studies on video capsule endoscopy in the diagnosis of small-bowel tumours. Most studies on video capsule endoscopy in small-bowel neoplasms do not include calculations of sensitivity or specificity because they lack a standard of reference for negative findings. Van Tuyl and co-workers found video capsule endoscopy superior to radiologic methods in the detection of small-bowel neuroendocrine tumours.[27] Comparison was with plain abdominal CT and conventional enteroclysis, and not with cross-sectional enteroclysis modalities. Video capsule endoscopy often does not depict the total small bowel, thereby limiting its use as a screening tool.[14] Although enteroscopy is the only nonsurgical method used to obtain tissue samples, its use as a screening tool is limited by its invasive and time-consuming nature. Moreover, because failure to intubate the terminal ileum has been reported to occur in up to 21% of investigated patients, investigation of the total small bowel is not always achieved.[28]

In our study we planned to perform all MR enteroclysis studies with use of a nasojejunal catheter to obtain small-bowel distension. Although this was not tolerated by one patient, we think optimal bowel distension is an important contributor to the accuracy of MR enteroclysis, especially in patients without high-grade bowel obstruction, as has been shown in studies on CT enteroclysis.[29, 30]

Table 3.4: Comparison of selected MR characteristics in relation to final histologic assessment of 30 studies with histopathologically confirmed neoplasms diagnosed with MR enteroclysis.

Parameter	Benign neoplasms (*n* = 13)	Malignant neoplasms (*n* = 17)	*P* value
Tumour length (mm)*	24 ± 14	65 ± 50	0.008
Tumour depth (mm)*	26 ± 19	23 ± 18	0.577
Presence of more than one neoplasm			0.025
Positive	9 (69)	4 (24)	
Negative	4 (31)	13 (76)	
Presence of stalked neoplasms†			< 0.001
Positive	12 (92)	0 (0)	
Negative	1 (8)	17 (100)	
Presence of enlarged mesenteric lymph nodes‡			0.003
Positive	0 (0)	9 (53)	
Negative	13 (100)	8 (47)	
Prestenotic dilatation			0.711
Present	7 (54)	11 (65)	
Absent	6 (46)	6 (35)	
Mesenteric fat infiltration			< 0.001
Positive	0 (0)	15 (88)	
Negative	13 (100)	2 (12)	

Note: Unless otherwise indicated, data are number of patients and data between parentheses are percentages.
* Data are means ± standard deviations. If more than one neoplasm was present, the size of the largest neoplasm was included for this analysis.
† At least one pedunculated neoplasm had to be present.
‡ Short axis diameter was at least 1 cm.

When compared with large studies on the histological nature of small-bowel malignancy, lymphoma seems to be overrepresented in our study population, whereas neuroendocrine tumours seem to be underrepresented.[31] This is most likely caused by the relatively small size of our cohort.

The retrospective nature of data gathering, the high prevalence of small-bowel neoplasms and the small number of patients studied were major limitations of our study. MR enteroclysis was only performed in symptomatic patients with suspected or established small-bowel disease. Therefore, an inclusion bias was inevitably present. This is represented by the difference between the incidence of histologically proven small-bowel neoplasm (35%) and small-bowel malignancy (20.9%) in our study group and the low incidence of small-bowel tumours in the general population. Therefore, our results cannot be directly translated to the general population. There are several factors that contributed to the high prevalence of small-bowel neoplasms in our study group. First, we only included MR enteroclysis studies performed in patients who were specifically

suspected of having a small-bowel neoplasm or in whom MR enteroclysis was performed to exclude the presence of a small-bowel neoplasm. In general, such a suspicion is based on a combination of sometimes nonspecific signs and symptoms, as well as on negative findings of conventional radiologic or endoscopic modalities. This results in a highly selected study population, which is not unusual in a tertiary referral centre such as ours. Second, 31% of all MR enteroclysis studies were performed after an invasive small-bowel investigation. Subgroup analysis showed that inclusion of these patients did not change the efficacy parameters significantly. Third, we included patients with known small-bowel polyposis syndromes. As is shown in the subgroup analysis, the inclusion of these patients did not alter the efficacy parameters significantly.

Seventy (77%) of the patients underwent an invasive method of small-bowel investigation. Patients with abnormal MR enteroclysis findings underwent an invasive small-bowel investigation more frequently than did patients with MR enteroclysis findings that were not suggestive of small-bowel neoplasm. This could have resulted in a verification bias. In addition, underdiagnosis of slow-growing small-bowel tumours and, therefore, overestimation of the accuracy of MR enteroclysis, could have occurred in the group of patients with only clinical follow-up as the reference standard. However, comparison of efficacy parameters of the total study group and the subgroup of patients who underwent an invasive procedure as the standard of reference did not reveal a significant difference.

In conclusion, our results confirm MR enteroclysis to be a promising modality in the diagnosis of both malignant as benign small-bowel neoplasms. The overall diagnostic accuracy of MR enteroclysis in the detection of small-bowel neoplasms was 0.95 in a highly selected patient population. Tumour characteristics associated with a malignant nature were solitary lesions, nonpedunculated lesions, longer lesions, the presence of mesenteric fat infiltration, and the presence of enlarged mesenteric lymph nodes. MR enteroclysis might allow clinicians to select patients in whom invasive diagnostic methods are indicated.

References

1 Haselkorn T, Whittemore AS, Lilienfeld DE. Incidence of small bowel cancer in the United States and worldwide: geographic, temporal, and racial differences. Cancer Causes Control. 2005;16(7):781-7.

2 Maglinte DD, O'Connor K, Bessette J, Chernish SM, Kelvin FM. The role of the physician in the late diagnosis of primary malignant tumors of the small intestine. Am J Gastroenterol. 1991;86(3):304-8.

3 Bessette JR, Maglinte DD, Kelvin FM, Chernish SM. Primary malignant tumors in the small bowel: a comparison of the small-bowel enema and conventional follow-through examination. AJR Am J Roentgenol. 1989;153(4):741-4.

4 Maglinte DD, Burney BT, Miller RE. Lesions missed on small-bowel follow-through: analysis and recommendations. Radiology. 1982;144(4):737-9.

5 Pilleul F, Penigaud M, Milot L, Saurin JC, Chayvialle JA, Valette PJ. Possible small-bowel neoplasms: contrast-enhanced and water-enhanced multidetector CT enteroclysis. Radiology. 2006;241(3):796-801.

6 Heine GD, Al-Toma A, Mulder CJ, Jacobs MA. Milestone in gastrointestinal endoscopy: double-balloon enteroscopy of the small bowel. Scand J Gastroenterol Suppl. 2006(243):32-8.

7 Tanaka S, Mitsui K, Tatsuguchi A, Kobayashi T, Ehara A, Gudis K, et al. Current status of double balloon endoscopy--indications, insertion route, sedation, complications, technical matters. Gastrointest Endosc. 2007;66(3 Suppl):S30-3.

8 Rondonotti E, Villa F, Mulder CJ, Jacobs MA, de Franchis R. Small bowel capsule endoscopy in 2007: indications, risks and limitations. World J Gastroenterol. 2007;13(46):6140-9.

9 Hadithi M, Akol H, Al-Toma A, Jacobs M, Mulder CJ. Indigo carmine chromoendoscopic appearances of enteropathy-associated T-cell lymphoma during double-balloon endoscopy in a patient with celiac disease. Endoscopy. 2007;39 Suppl 1:E212-3.

10 Monkemuller K, Fry LC, Ebert M, Bellutti M, Venerito M, Knippig C, et al. Feasibility of double-balloon enteroscopy-assisted chromoendoscopy of the small bowel in patients with familial adenomatous polyposis. Endoscopy. 2007;39(1):52-7.

11 Scherubl H, Faiss S, Tschope R, Zeitz M. Double-balloon enteroscopy for the detection of midgut carcinoids. Gastrointest Endosc. 2005;62(6):994; author reply -5.

12 Spada C, Riccioni ME, Familiari P, Marchese M, Bizzotto A, Costamagna G. Video capsule endoscopy in small-bowel tumours: a single centre experience. Scand J Gastroenterol. 2008;43(4):497-505.

13 Delvaux M, Ben Soussan E, Laurent V, Lerebours E, Gay G. Clinical evaluation of the use of the M2A patency capsule system before a capsule endoscopy procedure, in patients with known or suspected intestinal stenosis. Endoscopy. 2005;37(9):801-7.

14 Endo H, Kondo Y, Inamori M, Ohya TR, Yanagawa T, Asayama M, et al. Ingesting 500 ml of Polyethylene Glycol Solution During Capsule Endoscopy Improves the Image Quality and Completion Rate to the Cecum. Dig Dis Sci. 2008.

15 May A, Nachbar L, Ell C. Double-balloon enteroscopy (push-and-pull enteroscopy) of the small bowel: feasibility and diagnostic and therapeutic yield in patients with suspected small bowel disease. Gastrointest Endosc. 2005;62(1):62-70.

16 Jarbandhan SV, van Weyenberg SJ, van der Veer WM, Heine DG, Mulder CJ, Jacobs MA. Double balloon endoscopy associated pancreatitis: a description of six cases. World J Gastroenterol. 2008;14(5):720-4.

17 Mensink PB, Haringsma J, Kucharzik T, Cellier C, Perez-Cuadrado E, Monkemuller K, et al. Complications of double balloon enteroscopy: a multicenter survey. Endoscopy. 2007;39(7):613-5.

18 Moschler O, May AD, Muller MK, Ell C. [Complications in double-balloon-enteroscopy: results of the German DBE register]. Z Gastroenterol. 2008;46(3):266-70.

19 Maglinte DD, Siegelman ES, Kelvin FM. MR enteroclysis: the future of small-bowel imaging? Radiology. 2000;215(3):639-41.

20 Masselli G, Polettini E, Casciani E, Bertini L, Vecchioli A, Gualdi G. Small-bowel neoplasms: prospective evaluation of MR enteroclysis. Radiology. 2009;251(3):743-50.

21 Frager D. Intestinal obstruction role of CT. Gastroenterol Clin North Am. 2002;31(3):777-99.

22 Dorfman RE, Alpern MB, Gross BH, Sandler MA. Upper abdominal lymph nodes: criteria for normal size determined with CT. Radiology. 1991;180(2):319-22.

23 Yamamoto H, Yano T, Kita H, Sunada K, Ido K, Sugano K. New system of double-balloon enteroscopy for diagnosis and treatment of small intestinal disorders. Gastroenterology. 2003;125(5):1556; author reply -7.

24 Youden WJ. Index for rating diagnostic tests. Cancer. 1950;3(1):32-5.

25 Jaeschke R, Guyatt GH, Sackett DL. Users' guides to the medical literature. III. How to use an article about a diagnostic test. B. What are the results and will they help me in caring for my patients? The Evidence-Based Medicine Working Group. Jama. 1994;271(9):703-7.

26 Maglinte DD, Gage SN, Harmon BH, Kelvin FM, Hage JP, Chua GT, et al. Obstruction of the small intestine: accuracy and role of CT in diagnosis. Radiology. 1993;188(1):61-4.

27 van Tuyl SA, van Noorden JT, Timmer R, Stolk MF, Kuipers EJ, Taal BG. Detection of small-bowel neuroendocrine tumors by video capsule endoscopy. Gastrointest Endosc. 2006;64(1):66-72.

28 Mehdizadeh S, Ross A, Gerson L, Leighton J, Chen A, Schembre D, et al. What is the learning curve associated with double-balloon enteroscopy? Technical details and early experience in 6 U.S. tertiary care centers. Gastrointest Endosc. 2006;64(5):740-50.