Magnetic resonance imaging in Crohn's disease

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CHAPTER 2

Inflammatory Bowel Disease Diagnosed with US, MR, Scintigraphy, and CT: Meta-analysis of Prospective Studies

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ABSTRACT

Purpose: To compare, by performing a meta-analysis, the accuracies of ultrasonography (US), magnetic resonance (MR) imaging, scintigraphy, computed tomography (CT), and positron emission tomography (PET) in the diagnosis of inflammatory bowel disease (IBD).

Materials and Methods: MEDLINE, EMBASE, CINAHL, and Cochrane databases were searched for studies on the accuracy of US, MR imaging, scintigraphy, CT, and PET, as compared with a predefined reference standard, in the diagnosis of IBD. Sensitivity and specificity estimates were calculated on per-patient and per-bowel-segment bases by using a bivariate random-effects model.

Results: Thirty-three studies, from a search that yielded 1406 articles, were included in the final analysis. Mean sensitivity estimates for the diagnosis of IBD on a per-patient basis were high and not significantly different among the imaging modalities (89.7%, 93.0%, 87.8%, and 84.3% for US, MR imaging, scintigraphy, and CT, respectively). Mean per-patient specificity estimates were 95.6% for US, 92.8% for MR imaging, 84.5% for scintigraphy, and 95.1% for CT; the only significant difference in values was that between scintigraphy and US (P = .009). Mean per-bowel-segment sensitivity estimates were lower: 73.5% for US, 70.4% for MR imaging, 77.3% for scintigraphy, and 67.4% for CT. Mean per-bowel-segment specificity estimates were 92.9% for US, 94.0% for MR imaging, 90.3% for scintigraphy, and 90.2% for CT. CT proved to be significantly less sensitive and specific compared with scintigraphy (P = .006) and MR imaging (P = .037)

Conclusion: No significant differences in diagnostic accuracy among the imaging techniques were observed. Because patients with IBD often need frequent reevaluation of disease status, use of a diagnostic modality that does not involve the use of ionizing radiation is preferable.

INTRODUCTION

Ulcerative colitis (UC) and Crohn's disease (CD) are the two main subtypes of chronic inflammatory bowel disease (IBD). Both diseases typically have a relapsing and remitting course. UC solely affects the colon, with disease spreading in a contiguous manner from the rectum proximally. Conversely, CD can affect any part of the gastrointestinal tract, from the mouth to the anus. In 30%–40% of patients, the small bowel is affected, whereas in 40%–55% of patients, ileocolonic disease is present. Involvement of the terminal ileum is observed in 90% of patients with small-intestine CD. In a minority of patients (15%–25%), CD is confined to the colon (1).

Although there is increasing interest in determining the degree of inflammatory activity, the clinically most important factor for patients suspected of having IBD is whether disease is present. For symptomatic patients known to have IBD, meanwhile, it is important to determine whether the symptoms are functional or are due to inflammatory activity or residual fibrotic stenosis.

Ileocolonoscopy with tissue sampling generally has been considered the most valuable tool for diagnosing disease in the colon and terminal ileum (2, 3). For years, the reference standard for involvement of the small bowel in CD has been small-bowel barium examination performed by using an enteroclysis technique or small-bowel follow-through (3, 4). Both ileocolonoscopy and small-bowel barium examination have the advantage of enabling the detection of disease at an early stage owing to their capability to depict the mucosal surface. However, both procedures are time-consuming, and patient tolerance of ileocolonoscopy is low because of the extensive bowel preparation necessary and the discomfort experienced during the procedure (5). Ionizing radiation and extensive bowel preparation are additional drawbacks of small-bowel barium examinations. Moreover, in patients with severe UC, ileocolonoscopy is relatively contraindicated because of the increased risk of perforation.

In recent years, many studies have been performed to investigate the diagnostic potential of less-invasive and more patient-friendly imaging modalities—namely, ultrasonography (US), magnetic resonance (MR) imaging, scintigraphy (both planar and single photon emission computed tomography [SPECT]), computed tomography (CT), and to a lesser extent positron emission tomography (PET). However, published studies vary widely in terms of the reported sensitivities and specificities, from those in which the reported diagnostic capacity approaches that of ileocolonoscopy or small-bowel barium examination (6-10) to those yielding considerable underestimations or overestimations of disease (11-18). To our knowledge, only one meta-analysis focused on imaging IBD has been published to date (19); however, only the role of US in the detection of CD was investigated. Thus, the purpose of our study was to compare, by performing a meta-analysis, the accuracies of US, MR imaging, scintigraphy, CT, and PET in the diagnosis of IBD.

MATERIALS AND METHODS

Search strategy and study eligibility

We performed a computer-assisted search of the MEDLINE, EMBASE, CINAHL, and Cochrane databases for literature on the accuracies of US, MR imaging, scintigraphy, CT, and PET in the diagnosis of IBD (Appendix 1). The search period was January 1993 through February 2006. No patient age limits or language restrictions were applied.

The title and/or abstract of all retrieved articles was assessed by one observer (K.H.) to determine the eligibility of the articles for inclusion. The reference lists of the review articles and eligible studies were checked manually to identify other relevant articles. Hand searching of major journals was not performed. Only data that were presented as full-text articles were eligible for inclusion. If from reading the abstract it became evident that the article did not describe a prospective study, described a study involving MR imaging at a field strength of 0.5 T or lower, and/or described a study involving fewer than 15 patients, the article was considered ineligible. Although we would have preferred to include only large studies to increase the statistical power of the analyses, a minimal sample size of 15 patients was chosen because most studies involving patients with IBD have small samples. All other eligible articles were retrieved as full-text articles.

Study Selection

Two reviewers (K.H., S.B.) independently checked all retrieved articles to determine whether they satisfied the following criteria: *(a)* 15 or more patients were involved; *(b)* the study design was prospective; *(c)* US, MR imaging, scintigraphy, CT, or PET was used to diagnose IBD; *(d)* the patient population comprised patients suspected of having IBD, both patients suspected of having IBD and patients known to have IBD, or patients known to have IBD but suspected of having recurrence; *(e)* histopathologic, ileocolonoscopic, and/or intraoperative findings were used as the reference standard for examination of the colon and terminal ileum, and histopathologic, small-bowel barium examination, and/or intraoperative findings were used as the reference standard for examination of the small bowel; *(f)* the criteria for positive US, MR, scintigraphy, CT, or PET findings were defined; and *(g)* the data necessary to calculate 2 x 2 contingency tables were reported. If all criteria were met, the article was included in the study. Disagreements between the two reviewers regarding study inclusion were resolved by consensus. Authors of the primary research were not approached for additional information.

Study Characteristics

Both reviewers independently assessed study characteristics and extracted relevant data (described in detail in the following paragraphs) by using a standardized form. The reviewers were not blinded to the authors' information (e.g., authors' affiliation) or the journal title. Inconsistencies in assessment between the reviewers were resolved by consensus.

Patient characteristics.—The following patient characteristics were recorded: *(a)* number of patients, *(b)* numbers of male and female patients, *(c)* mean patient age and patient age range, *(d)* prevalence of IBD (CD and UC), and *(e)* inclusion criteria used (e.g., based on medical history, physical examination, and laboratory findings) to select patients for the study.

Study quality assessment.—To assess study quality characteristics, the QUADAS (quality assessment of diagnostic accuracy studies) tool was used as a guideline. The QUADAS tool enables reviewers to evaluate the quality of studies, especially investigations of diagnostic accuracy (20, 21). The following characteristics were assessed: *(a)* whether the index test (i.e., the radiologic examination being evaluated) was assessed without knowledge of the reference-standard test results, *(b)* whether the index test findings were interpreted without clinical information, *(c)* whether the criteria used to diagnose IBD with the index test were clearly described, *(d)* the time interval between the index test and the reference-standard examination, *(e)* whether the reference-standard examination findings were interpreted without index test information and results, and *(f)* whether the reference-standard examination was described correctly.

Imaging features.—The following US features were recorded, if available: *(a)* type (linear or curved) and frequency of probe(s) used; *(b)* use of bowel preparation and, if so, type of bowel preparation (bowel cleansing, fasting, and/or diet); *(c)* type of scanning (conventional gray scale, pulsed, color, or power Doppler); and *(d)* amount and type of luminal contrast medium (enteroclysis, oral, and/or rectal), if administered.

The following MR imaging features were recorded, if available: *(a)* magnetic field strength; *(b)* type of coil used (body or surface); *(c)* use of bowel preparation and, if so, type of bowel preparation (bowel cleansing, fasting, and/or diet); and *(d)* amount and type of intravenous and/or luminal contrast medium (enteroclysis, oral, and/or rectal), if administered.

The following radionuclide imaging features were recorded, if available: *(a)* whether leukocytes were labeled in vitro or intravenously injected labeled antigranulocyte antibodies were used, *(b)* type and dose of labeling agent, *(c)* timing of scanning, and *(d)* scanning technique (SPECT or planar).

The following CT imaging features were recorded, if available: *(a)* type of scanner (single-section helical, multisection helical, or nonhelical); *(b)* use of bowel preparation and, if so, type of bowel preparation (bowel cleansing, fasting, and/or diet); and *(c)* amount and type of intravenous and/or luminal contrast medium (enteroclysis, oral, and/or rectal), if administered.

The following PET imaging features were recorded, if available: *(a)* type of scanner (dedicated full-ring or other), *(b)* type and amount of tracer, and *(c)* timing of scanning.

Imaging criteria and reference standard.—For each study, the imaging criteria (e.g., abnormal bowel wall thickening) used to diagnose IBD with the given imaging test were noted. The reference-standard examination used to verify the imaging findings (i.e., surgery, histopathology, ileocolonoscopy, or small-bowel barium examination) was also recorded for each study.

Data Synthesis and Analysis

For each study, 2 x 2 contingency tables consisting of true-positive, false-positive, false-negative, and true-negative results were constructed.

Sensitivity and specificity estimates.—Summary sensitivity and specificity estimates were calculated on a per-patient and/or per-segment basis, depending on the way the data were presented: In some studies, patient-based data were reported, whereas in others, segmental data were provided without the possibility of adapting the data to calculate patient-based accuracy values. To calculate summary sensitivity and specificity values, a bivariate approach was used. With this approach, it is assumed that the true values of logit-transformed sensitivity and logit-transformed specificity of the included studies follow an approximately bivariate normal distribution. Mean logit-transformed sensitivity and specificity values, with corresponding standard errors, were calculated by using random-effects and/or fixed-effects (mixed) models, depending on the best fit. After the antilogit transformation of the mean logit-transformed sensitivity and specificity, sensitivity and specificity estimates, with corresponding 95% confidence intervals, were obtained. This bivariate model was analyzed by using linear and nonlinear mixed-model techniques (SAS proc Nlmixed; SAS Institute, Cary, NC).

Subgroup analyses.—To determine possible explanations for the heterogeneity in diagnostic accuracy, a subgroup analysis of predefined factors was performed. The predefined factors regarding patient characteristics were disease type (CD, UC, or both), patient age (patients younger than 18 years vs adult patients), and disease location (small bowel, colon, or both). In addition, a subgroup analysis of the imaging features and imaging criteria used to diagnose IBD was performed. Subgroup analyses were performed on a per-patient basis and only when enough data were available (i.e., three or more studies per subgroup).

A *z* test for unpaired groups was performed to evaluate differences between the imaging modalities and between the subgroups; $P < .05$ was considered to indicate a significant difference. Microsoft Excel 5.0 (Microsoft, Redmond, Wash), SPSS 12.0 (SPSS, Chicago, Ill), and SAS 9.1 (SAS Institute) were used to perform the statistical analyses.

RESULTS

Search strategy and study selection

The search yielded a total of 1406 articles. After the abstracts were read, 166 articles were found to be eligible and were retrieved as full-text articles for further analysis. One hundred thirty-three of these articles were excluded (Fig 1, Appendix 2). The remaining 33 articles fulfilled all inclusion criteria and were used for data extraction and analysis. The two cases of disagreement between the two reviewers regarding study inclusion were

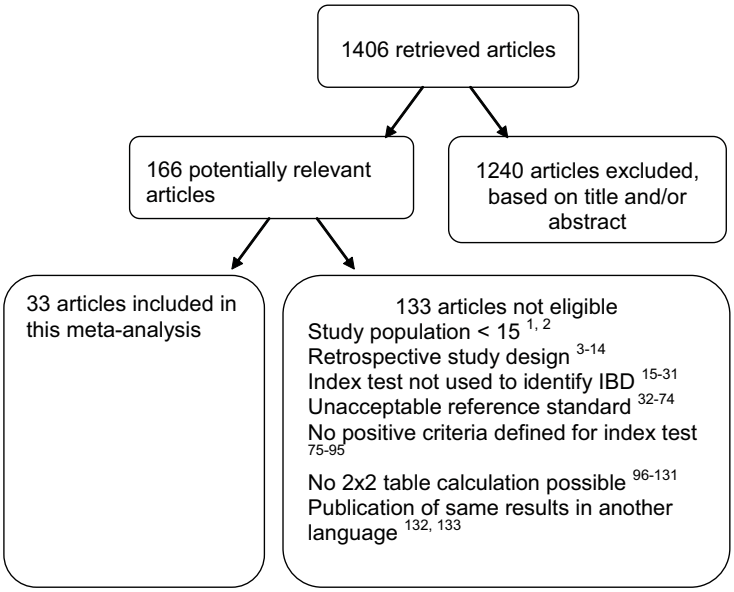

Figure 1. Number of articles identified and evaluated in this meta-analysis.

resolved by consensus.

US was evaluated in 11 studies (18, 22-31), MR imaging in 11 (6, 8, 9, 11, 12, 30, 32-36), scintigraphy in 9 (13, 15, 17, 29, 37-41) and CT in 7 studies (13, 36, 39, 42-45). No studies in which the accuracy of PET for the diagnosis of IBD was assessed, were selected.

Study and Patient Characteristics

The three cases of inconsistency in the reviewers' assessments of the included studies were resolved by consensus. Only one of the 33 included studies solely involved patients with UC; in the remaining 32 studies, patients with CD (*n* = 20) or both patients with CD and patients with UC (*n* = 12) were included (Table 1). In 11 of the 33 included studies, no criteria for inclusion were described, whereas in five studies, no clear-cut criteria were given.

Study Design Characteristics

In 17 of the included studies, it was not clear whether clinical information was available during the interpretation of imaging findings (Table 2). In seven studies, it was not clear whether the imaging test was evaluated without the reference-standard examination results, whereas in the other studies, it was clear that this evaluation was performed independently. Verification of the index test results was complete in all except seven studies, but in more than half the studies (*n* = 18), more than one reference-standard examination was used, without the possibility of separately analyzing results according to reference-standard findings. The criteria used to determine the presence of IBD with the

reference-standard examination were not uniformly described. Information as to whether the reference-standard examination was evaluated independently from the index test findings was available for only 11 studies.

Imaging Features and Criteria Used for Diagnosis

The one criterion considered indicative of disease in all except one of the cross-sectional studies (i.e., US, MR imaging, and CT) was wall thickening, although the wall thickness cutoff values used to differentiate a normal from an abnormally thickened bowel wall varied between 3 mm and 1 cm (Tables 3–6). Other imaging criteria were inconsistently used.

Data Synthesis and Analysis

Sensitivity and specificity estimates.—On a per-patient basis, sensitivity and specificity values (Tables 7, 8) did not differ significantly between modalities, with the exception that the specificity of scintigraphy was significantly lower than that of US ($P = .009$) (Fig 2). Mean per-bowel-segment sensitivity values were lower, but mean per-bowel-segment specificity remained high. CT proved to be the least sensitive and least specific on a segmental basis, with the sensitivity of scintigraphy being significantly higher than that of CT ($P = .006$) and the specificity of MR imaging being significantly higher than that of CT ($P = .037$) (Fig 3).

Subgroup analysis.—Enough data on patient characteristics were available to perform subgroup analysis of MR imaging (patient age, disease location) and US (disease location). Although no significant differences in the accuracy of MR imaging based on disease location were observed, the specificity of US was significantly lower when only the small bowel was assessed than when the colon and the small bowel were assessed ($P < .001$). In terms of patient age, MR imaging proved to have higher sensitivity in adult patients ($P = .042$) but higher specificity in pediatric patients ($P = .024$) (Fig 4).

Enough data on imaging features were available to calculate differences in accuracy between MR enterography and MR enteroclysis. The sensitivity of MR enterography for diagnosing IBD was significantly lower than the sensitivity of MR enteroclysis ($P = .046$), whereas specificity values were comparable (Fig 5).

Regarding the US criteria used to diagnose IBD, a comparison between studies involving a wall thickness cutoff value of 3 mm and those involving a cutoff value of 4 mm or greater (including studies in which the cutoff value was 5 mm) could be performed. No significant differences were observed (Fig 5). When subgroups were defined according to the exact cutoff value provided (i.e., 3, 4, or 5 mm), sensitivity was lowest with a threshold of 5 mm (79.5%) compared with the sensitivities calculated with thresholds of 3 mm (91.0%) and 4 mm (94.1%). For CT and scintigraphy, insufficient data were available to perform subgroup analysis of the patient characteristics or the test features and imaging criteria used.

DISCUSSION

Mean per-patient sensitivity (84.3%–93.0%) and specificity (84.5%–95.6%) values for the diagnosis of IBD were high with US, MR imaging, scintigraphy, and CT. At segmental analysis, mean sensitivity values were lower (67.4%–77.3%) but mean specificity remained high (90.2%–94.0%). CT proved to be the least sensitive and specific on a segmental basis, whereas scintigraphy was slightly less specific on a per-patient basis.

MR imaging performed better when bowel filling was performed by using an enteroclysis technique than when contrast medium was administered orally. On a per-patient basis, US performed better in the prediction of IBD absence when both the small bowel and the colon were examined than when only the small bowel was evaluated.

We believe there were advantages to our meta-analysis: Only prospective studies involving the specific patient population of interest were included, and data analysis was performed on both per-patient and per-segment bases. We chose to include both studies with accuracy values reported on a per-patient basis and those with accuracy values reported on a per-bowel-segment basis, because information about the capability of a given test in localizing disease and determining the extent of disease, in addition to its capability in diagnosing disease, can be obtained from segmental data. Analysis on a per-patient basis probably leads to overestimation of sensitivity values, because any patient with disease is considered to have true-positive findings without consideration of whether the localization of disease is correct or not. However, the analyses in our study were restricted to a dichotomous diagnostic level (i.e., disease present or absent), meaning that no conclusions regarding the capability of the imaging modalities in determining the degree of disease activity could be drawn from our data.

An important potential bias of our study was that both patients suspected of having disease and those known to have disease were included, although these two populations have inherently different thresholds for the diagnosis of abnormality. In a patient known to have IBD, the threshold for diagnosing disease probably would be lower owing to a higher index of suspicion. Although this bias probably influenced our study results, we tried to limit this influence by using mixed models for data analysis, which accounts for the heterogeneity between studies caused by different threshold settings or other forms of residual heterogeneity.

An important source of heterogeneity across studies was formed by the imaging criteria used to diagnose IBD. Although subgroup analysis could have provided some guidance as to which criteria should have been used for diagnosis, owing to the scarce data available and the fact that precise definitions of parameters were often lacking, analysis of only one parameter—bowel wall thickening—and for only one modality—US—could be performed.

Cutoff values to differentiate a normal from a thickened bowel wall varied between 3 and 5 mm in the US studies included in our meta-analysis. Although both the sensitivity and the specificity for diagnosing IBD were highest with use of a cutoff value of 4 mm, the limited amount of data prevented us from investigating whether accuracy estimates differed

significantly between the different cutoff values. However, the sensitivity achieved with use of the 5-mm threshold was clearly lower than the sensitivity estimates achieved with lower thresholds. In the meta-analysis of US performed by Fraquelli et al (19), different sensitivity and specificity estimates were also seen, depending on the chosen bowel wall thickness threshold: Sensitivity decreased and specificity increased when the threshold changed from 3 to 4 mm. However, as was the case in our study, no test was performed to determine if this difference was significant.

It would have been interesting to determine the diagnostic performance of US and MR imaging in the diagnosis of UC and CD separately. However, in only three of the seven MR imaging and US studies involving both patients with CD and patients with UC was an attempt made to differentiate between these two disease subtypes (8, 27, 34). In the other studies, accuracy values could not be calculated for the diagnosis of CD and UC individually, because separating the data was not possible. Because the inflammation with UC is exclusively mucosal whereas transmural inflammation is seen with CD, theoretically, more bowel wall thickening should be expected with CD than with UC, while other wall features also can differ (47). Thus, combined analysis of the findings in patients with CD and those in patients with UC with use of identical radiologic criteria does not necessarily reflect with total correctness the accuracy of MR imaging and US in the diagnosis of IBD.

An important limitation of our meta-analysis was the heterogeneity in the reference-standard examinations used to compare the imaging tests. However, only those modalities that are widely accepted as adequate and objective in the diagnosis of IBD were included. Although one might argue that small-bowel barium examination is increasingly being found to be an imperfect reference standard, established superior reference tests for evaluation of the small bowel, such as double-balloon endoscopy (48, 49) and video capsule endoscopy (50, 51), were not commercially available until recently and at present have limited availability, which precluded the inclusion of these techniques as reference standards in this meta-analysis.

Heterogeneity in the different features of each imaging technique was also seen. Subgroup analysis of the imaging features could be performed only for the different bowel-filling methods used in MR imaging. Oral contrast medium intake was associated with lower sensitivity compared with contrast medium administration by means of enteroclysis. A collapsed bowel can hide lesions or mimic disease by suggesting an abnormally thickened and/or enhancing bowel wall (52–55). The fact that the bowel distention achieved with oral contrast medium can be inadequate in portions of the small bowel might explain the lower sensitivity of MR imaging with oral contrast medium. However, a side-by-side comparison of accuracy between MR enterography and MR enteroclysis was performed in a small prospective study, and no significant differences between the two methods of luminal contrast medium administration were observed (56). It might be advisable to perform a side-by-side comparison of these two methods in a large population to determine which one to use for the diagnosis of IBD.

Finally, heterogeneity in the study design characteristics was also observed. Because the study design can influence the reporting of diagnostic test accuracy and limit the (internal) validity of study results (57, 58), it is important to evaluate study quality when reviewing articles. Although patient and study design characteristics were assessed in this meta-analysis, the effects of these factors could not be examined because of incomplete data reporting. Although we attempted to analyze these heterogeneous data by using appropriate analytic approaches, publication bias remained an issue. We did not study publication bias for the following reasons: *(a)* A recent study (59) in which different statistical methods (60–62) of detecting publication bias were compared revealed that the methods were diverse and, when compared with one another, yielded different estimates; *(b)* to our knowledge, no registry of diagnostic accuracy studies as opposed to clinical trials exists; and *(c)* all of the studies had small samples, so it was impossible to determine whether there was an association between sample size and diagnostic performance.

Because the accuracy values for US, MR imaging, scintigraphy, and CT were comparable in this meta-analysis, it might be justified to make a well-considered choice for either of these techniques based on their specific advantages and disadvantages. Because of the relapsing nature of IBD and the young age at which it usually develops, frequent reevaluation of disease is necessary in many patients. Therefore, it might be preferable to use a technique that does not involve ionizing radiation, and the patient-friendliness of the modality also should be considered for this specific patient population. Although the costs of the respective examinations are not to be neglected in a cost-benefit analysis, these have not been taken into account here.

The ionizing radiation used and the long duration of the examination are drawbacks of scintigraphy. Non-invasiveness, low cost, and widespread availability make US a useful modality for imaging IBD. However, US has limitations: The effectiveness of this technique depends on the experience of the operator performing the examination, and the gastrointestinal tract cannot be visualized in its entirety. It would have been valuable to study the effect of operator experience on diagnostic performance. However, exact data on observer experience were available in only one article (23). The advantages of MR imaging include the possibility for cross-sectional imaging in any plane, the absence of ionizing radiation, and the easier follow-up of disease status with MR images than with US images because with US, only selected images from an essentially dynamic examination are available at a later time, while MR examinations are completely standardized and all data can be fully saved.

Although CT is widely used to evaluate IBD, the findings of our meta-analysis, as well as the relatively large radiation dose and the intravenous iodine-based contrast medium needed for CT, favor the use of US or MR imaging. However, a critical point is that although US and MR imaging are often used to evaluate the abdomen in Europe, in the United States, CT is more often used for this purpose. This inclination is reflected by the fact that all of the US studies included in this meta-analysis and the majority of the MR imaging studies included were conducted in Europe. Thus, for radiologists in the United States, the accuracy of US

and MR imaging in the diagnosis of IBD might be lower because these techniques are less frequently used, just as the accuracy of CT in the diagnosis of IBD might be lower in Europe owing to less frequent use.
Nevertheless, before any of these imaging tests can have a large role in the diagnosis of IBD, the imaging criteria that are consistent with CD and UC should be clearly established. If standardized criteria were available internationally, larger trials would be possible and comparisons between studies would be simplified. For these purposes, a more standardized technical imaging approach also would be advisable. Therefore, future research should be focused on standardization of the preparation, imaging technique, and imaging criteria used to diagnose IBD, besides including larger numbers of patients. In conclusion, we propose US or MR imaging as the imaging modality of first choice for the diagnosis of IBD; however, more research is needed to improve the accuracy of these techniques.

APPENDIX 1

Search strategy

Cochrane: Limit: 1993 - 2006
Inflammatory Bowel Diseases [MeSH] AND Diagnostic Techniques and Procedures [MeSH]

PubMed: Limit: 1993 - 2006
"Inflammatory Bowel Diseases"[MeSH] AND (("Magnetic Resonance Imaging"[MeSH] OR "Ultrasonography"[MeSH] OR "ultrasonography (subheading) OR "Radionuclide Imaging"[MeSH] OR "Radionuclide Imaging" (subheading) OR "Tomography, X-Ray Computed"[MeSH] OR "Tomography Scanners, X-Ray Computed"[MeSH] OR "Tomography, Spiral Computed"[MeSH] OR "Tomography, Emission-Computed"[MeSH] OR "Tomography, Emission-Computed, Single-Photon"[MeSH]))

Embase/Cinahl: Limit: 1993 - 2006
(Crohn Disease OR Ulcerative Colitis) AND (Nuclear Magnetic Resonance Imaging OR Echography OR Computer Assisted Tomography OR Scintigraphy OR Positron Emission Tomography) AND sensitivity OR specificity OR accuracy OR false negatives OR false positives

APPENDIX 2

Excluded articles

Study evaluated < 15 patients (n=2)

1) Durno CA, Sherman P, Williams T, Shuckett B, Dupuis A, Griffiths AM. Magnetic resonance imaging to distinguish the type and severity of pediatric inflammatory bowel diseases. J Pediatr Gastroenterol Nutr 2000;30:170-174.
2) Biancone L, Scopinaro F, Ierardi M, et al. ^{99m}Tc-HMPAO granulocyte scintigraphy in the early detection of postoperative asymptomatic recurrence in Crohn's disease. Dig Dis Sci 1997;42:1549-1556.

Retrospective study design (n=12)

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11) Makó EK, Mester ÁR, Tarján Zs, Karlinger K, Tóth G. Enteroclysis and spiral CT examination in diagnosis and evaluation of small bowel Crohn's disease. Eur J Radiol 2000;35:168-175.
12) Charron M, Di Lorenzo C, Kocoshis S. CT and 99mTc-WBC vs colonoscopy in the evaluation of inflammation and complications of inflammatory bowel diseases. J Gastroenterol 2002;37:23-28.
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14) Ota Y, Matsui T, Ono H, et al. Value of virtual computed tomographic colonography for Crohn's colitis: comparison with endoscopy and barium enema. Abdom Imaging 2003;28:778-783.

US, MR imaging, radionuclide imaging, CT or FDG-PET not used to identify IBD (n=17)

15) Bozkurt T, Richter F, Lux G. Ultrasonography as a primary diagnostic tool in patients with inflammatory disease and tumors of the small intestine and large bowel. J Clin Ultrasound 1994;22:85-91.

16) Elewaut AE, Afschrift M. Hydrocolonic sonography: a novel screening method for the detection of colon disease? Bildgebung 1995;62:230-234.

17) Dux M, Roeren T, Kuntz C, Richter GM, Kauffmann GW. Colorectal hydrosonography for evaluation of neoplastic and inflammatory large bowel disease. *Article in German*. Ultraschall Med 1996;17:266-273.

18) Signore A, Picarelli A, Chianelli M, et al. ^{123} I-interleukin-2 scintigraphy: a new approach to assess disease activity in autoimmunity. J Pediatr Endocrinol Metab 1996;9:139-144.

19) Biancone L, Fiori R, Tosti C, et al. Virtual colonoscopy compared with conventional colonoscopy for stricturing postoperative recurrence in Crohn's disease. Inflamm Bowel Dis 2003;9:343-350.

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Table 1: Patient characteristics in 33 included studies

Study	Year of publication	Patient spectrum	Selection criteria	No of patients	CD (n)	UC (n)
Heresbach et al (40)	1993	Known CD	Admitted for acute exacerbation	19	19	0
Sheridan et al (22)	1993	CD known or suspected	Referred for small bowel barium studies for either suspected small bowel CD or known CD with possible recurrence	127	41	0
Limberg and Osswald (27)	1994	Suspected IBD	Abdominal pain, diarrhea, weight loss or positive FOBT	440	41	36
Shoenut et al (8)	1994	Suspected IBD	Symptoms consistent with IBD	20	12	6
Dhôte et al (41)	1995	Known CD	NA	20	20	0
Middleton et al (37)l	1995	Known UC	Mild to moderately severe disease	15	0	15
Solvig et al (26)	1995	Known or suspected CD	Referred for barium examination (because of suspected CD, or suspicion of recurrence after resection	59	19	0
Kolkman et al (39)	1996	Known IBD	Exacerbation: CDAI > 150(CD) or Sutherland score > 6 (UC) and requiring admission or severe first attack or suspected abdominal complication	32	17	15
Papos et al (38)	1996	Known IBD	NA	24	11	13
Pradel et al (18)	1997	Known or suspected IBD	NA	30	17	5
Stahlberg et al (15)	1997	Known IBD	Severe or moderately severe attack of colonic IBD	21	7	14
Andreoli et al (23)	1998	Known CD	Intestinal resection with ileocolonic anastomosis	41	41	0
Cucchiara et al (17)	1999	Suspected IBD	NA	48	13	5
Reimund et al (24)	1999	Known and suspected IBD	NA	118	48	23

Other diagnosis/ No disease	Male: female ratio	Age (y) *
0	7:12	37±19†
14 patients with inactive CD; 72 with no disease	NA	21-84‡
NA	43:34§	56±12†§
2 indeterminate colitis	12:8	42.6 (20-70)
0	8:12	47±16†
0	7:8	21-70‡
39 no disease; 1 Yersinia	27:32	38 (15-74)
0	12:20	17-65‡
0	9:15	42.5 (23-65)
7 indeterminate ileitis and/or colitis; 1 Yersinia colitis	19:11	34 (17-58)
0	12:9	46 (17-82)
0	26:15	42.4 (20-86)
3 indeterminate colitis; 9 non-specific colitis; 6 lymphoid hyperplasia; 12 spondylarthropathy and colitis	26:22	10 (2-17)
3 indeterminate colitis; 21 inflammatory controls; 23 non-inflammatory controls	50:68	17-86‡

Study	Year of publication	Patient spectrum	Selection criteria	No of patients	CD (n)	UC (n)
Low et al (36)	2000	Known or suspected CD	Symptomatic	26	26	0
Rieber et al (33)	2000	Suspected IBD of the small bowel	NA	50	27	0
Tarjan et al (28)	2000	Suspected CD	Consecutive patients referred for enteroclysis with suspected CD	73	47	NA
Koh et al (32)	2001	Known CD	Clinically symptomatic	30	30	0
Mazzeo et al (43)	2001	Known or suspected CD of the small bowel	NA	33	14	0
Molnar et al (13)	2001	Known CD	Acute relapse or severe first attack	28	28	0
Miao et al (30)	2002	Known CD	Clinical symptoms, recently undergone colonoscopy and/or barium studies	30	30	0
Hassan et al (42)	2003	Known or suspected CD	Needing both endoscopic and radiological assessment	39	30	0
Jamieson et al (44)	2003	Suspected IBD	Clinically suspected but untreated IBD	18	12	2
Laghi et al (6)	2003	Suspected CD	NA	75	26	18
Wold et al (45)	2003	Known or suspected CD	Previously scheduled small-bowel follow-through Age ≥18 yrs	23	20	2
Darbari et al (34)	2004	Suspected IBD	NA	58	21	7
Neye et al (31)	2004	Known CD	NA	22	22	0
Ochsenkuhn et al (9)	2004	Known CD	CDAI < 200; stable medication ≥ 3 months, episodes of abdominal pain; without previously known inflammation of the small bowel proximal to the terminal ileum	29	29	0
Ajaj et al (35)	2005	Known IBD	Clinical symptoms; leucocytosis > 13.000/nl and/or CRP > 1.5 mg/dl	23	7	16
Calabrese et al (25)	2005	Known CD	Routine follow-up assessment of disease lesions; signs and symptoms indicating recurrent CD	28	28	0
Rispo et al (29)	2005	Known or suspected CD of the small bowel	NA	84	54	6

Other diagnosis/ No disease	Male: female ratio	Age (y) *
0	11:15	43 (22-58)
2 small-bowel tumours; 21 no IBD	21:29	38.6 (19-81)
NA	34:39	27 (10-57)
0	14:16	37.6 (18-58)
16 no disease; 1 cancer ileocecal valve; 1 carcinosis of mesenteric root; 1 intestinal lymphangiectasia	15:18	18-71‡
0	13:15	32.5 (18-59)
0	11:19	36 (17-78)
9 no disease	21:18	21-73‡
1 indeterminate IBD; 1 juvenile polyposis; 1 non-specific microscopic colitis; 1 no disease	12:6	12 (7-16)
11 indeterminate colitis; 20 no disease	NA.	13.6 (8-17)
1 abdominal pain e.c.i.	11:12	22-55‡
17 indeterminate colitis; 13 no disease	33:25	13.2 ± 3.8†
0	9:13	33.7 (16-56)
0	15:14	32 (19-58)
0	9:14	37.2 (27-60)
0	16:12	NA
8 IBS; 2 colon cancer; 2 celiac disease; 1 adhesions; 3 lymphoma; 1 appendicitis; 1 collagenous colitis; 1 ischemic colitis; 1 postactinic enteritis; 1 chronic granulomatous disease; 1 sclerosing mesenteritis; 2 inactive CD	27:23 II	31.8 (15-57)II

Study	Year of publication	Patient spectrum	Selection criteria	No of patients	CD (n)	UC (n)
Schreyer et al (11)	2005	Highly suspected or known IBD	Consecutive patients scheduled for a conventional CS to assess disease activity or pathological changes of the colon	22	12	8
Schreyer et al (12)	2005	Known CD	Consecutive patients assigned to a routine MRE of the small bowel	30	30	0

Note.—CRP = C-reactive protein, FOBT = fecal occult blood test, IBS = irritable bowel syndrome, NA = not available.

* Unless otherwise noted, data are the mean age, with the age range in parentheses.

†Mean age ± standard deviation.

‡Age range.

§ Characteristics available for only the 77 patients with IBD.

II Characteristics available for only the 50 patients with CD.

	Other diagnosis/ No disease	Male: female ratio	Age (y) *
	1 unspecific colitis; 1 infectious colitis	11:11	38 (19-71)
	0	8:22	29 (18-65)

Table 2: Study design characteristics of the 33 included studies

Study	Year of publication	Clinical information available *	Time interval †	Verification ‡
Heresbach et al (40)	1993	No	Mean 2.9.days	Complete
Sheridan et al (22)	1993	NA	Same day	Complete
Limberg and Osswald (27)	1994	No	Same day	Complete
Shoenut et al (8)	1994	NA	Within 3 days	Complete
Dhôte et al (41)	1995	NA	Within 4 days	Incomplete (44/120)
Middleton et al (37)	1995	No	Within 5 days	Complete
Solvig et al (26)	1995	NA	Same day	Complete
Kolkman et al (39)	1996	No	CS: 2 weeks Surgery: 1-50 days	Complete
Papos et al (38)	1996	No	Within 2 weeks	Complete
Pradel et al (18)	1997	No	Within 8 days	Complete
Stahlberg et al (15)	1997	No	Within 24 hours	Complete
Andreoli et al (23)	1998	No	Within 2 weeks	Incomplete (41/47)
Cucchiara et al (17)	1999	NA	NA	Complete
Reimund et al (24)	1999	No	NA	Complete
Low et al (36)	2000	NA	NA	Incomplete (26/33)
Rieber et al (33)	2000	NA	Same day	Complete
Tarjan et al (28)	2000	NA	NA	Complete
Koh et al (32)	2001	No	Median 21 days	Complete
Mazzeo et al (43)	2001	NA	Same day	Complete
Molnar et al (13)	2001	No	Within 7 days	Complete
Miao et al (30)	2002	No	Median 29 days (range 0-102 days)	Incomplete
Hassan et al (42)	2003	NA	NA	Incomplete (39/46)
Jamieson et al (44)	2003	NA	Within 3 days	Incomplete (16/18)
Laghi et al (6)	2003	NA	NA	Complete

	Execution index test §	Evaluation index test II	Reference standard	Reference test criteria ¶	Evaluation of reference test #
	Yes	Yes	CS	Yes	NA
	Yes	Yes	SBE	No	Yes
	Yes	Yes	CS	No	NA
	No	NA	CS HA	Yes	NA
	Yes	NA	CS SBE	Yes (CS) No(SBE)	NA
	Yes	Yes	HA	Yes	Yes
	Yes	Yes	CS	No	NA
	Yes (Scintigraphy) No (CT)	No	CS Surgery	Yes	NA
	Yes	NA	SBE HA	No	NA
	Yes	Yes	CS SBE	Yes	NA
	Yes	Yes	CS HA	Yes	NA (CS) Yes (HA)
	Yes	Yes	SBE	No	Yes
	Yes	Yes	CS HA	Yes	NA
	Yes	Yes	CS SBE	No	NA
	Yes (MRI/CT)	Yes (MRI/CT)	SBFT CS Surgery	No	NA
	Yes	Yes	SBE	No	Yes
	No	Yes	SBE	Yes	Yes
	No	Yes	CS Surgery	No	NA
	Yes	NA	SBE (all pts) CS: 8 pts Surgery: 4 pts	No	NA
	Yes (scintigraphy) No (CT)	NA	SBE CS	Yes	NA
	Yes (MRI/US)	NA (MRI/US)	SBFT CS Surgery	Yes	NA
	No	Yes	CS	NA	NA
	No	Yes	SBE	No	Yes
	Yes	Yes	CS HA	Yes	NA

Study	Year of publication	Clinical information available *	Time interval †	Verification ‡
Wold et al (45)	2003	NA	Mean 5.3days (0-34)	Complete
Darbari et al (34)	2004	NA	NA	Complete
Neye et al (31)	2004	No	Within 3 days	Complete
Ochsenkuhn et al (9)	2004	No	SBE on the same day; CS/PA 10 weeks (3-13)	Complete
Ajaj et al (35)	2005	NA	Within 24 hours	Incomplete
Calabrese et al (25)	2005	Yes	Within 1 week	Complete
Rispo et al (29)	2005	No	Within 10 days	Complete
Schreyer et al (11)	2005	NA	Same day	Complete
Schreyer et al (12)	2005	NA	Within 1 week	Complete

Note.—CS =colonoscopy, HA = histopathologic analysis, SBE = small-bowel barium enteroclysis, SBFT = small-bowel follow-through.

* Clinical information available during image interpretation. NA: Not described in the study

† Time interval between imaging and reference-standard examination

‡ Complete or incomplete verification of index test results in the included patients with reference-standard examination

§ Execution of the imaging test described sufficiently, that is, with the magnetic field, bowel preparation, and luminal and/or intravenous contrast medium described for MR imaging; with the bowel preparation and transducer frequency described for US; with the labeling, type and dose of labeling agent, and timing of scanning described for scintigraphy; and with the scanner type, bowel preparation, and luminal and/or intravenous contrast medium described for CT. NA = only a reference mentioned (execution of imaging test not described sufficiently)

II Mention or no mention of the imaging test being evaluated with blinding to the reference-standard examination results. NA = information concerning blinding not available.

¶ Reference-standard criteria defined or not defined in the study. NA = only reference mentioned (execution of imaging test not described sufficiently)

Mention or no mention of the reference-standard examination being evaluated with blinding to the index test results. NA = information concerning blinding not available.

	Execution index test §	Evaluation index test II	Reference standard	Reference test criteria ¶	Evaluation of reference test #
	No	Yes	CS HA	No	NA
	NA	Yes	HA	Yes	Yes
	No	Yes	CS	Yes	Yes
	Yes	Yes	CS HA SBE	No (CS/HA) Yes (SBE)	Yes
	Yes	NA	CS HA	No	NA
	Yes	Yes	SBE	Yes	NA
	Yes	Yes	CS HA SBE	No (CS) Yes (SBE)	Yes
	Yes	yes	CS	Yes	NA
	Yes	Yes	CS	Yes	NA

Table 3:

US imaging features					
Study	**Year of publication**	**Transducer**	**Bowel preparation**	**Luminal contrast medium**	**Criteria used for diagnosis**
Sheridan et al (22)	1993	3.5/5 MHz	1 sachet of sodium picosulphate/ magnesium citrate, low-residue diet	NA	Wall thickness
Limberg and Osswald (27)	1994	3.5/5.0/7.5 MHz	Laxative intestinal lavage 20 mg hyposcine b utylbromide	1500 ml water administered rectally	Wall thickness, wall stratification
Solvig et al (26)	1995	3.5/5 MHz	Overnight fasting	Not administered	Wall thickness, peristalsis
Pradel et al (18)	1997	Linear 5/10 MHz	6 hrs fasting	NA	Wall thickness
Andreoli et al (23)	1998	Linear 7.5 MHz Convex 5 MHz	Overnight fasting	NA	Wall thickness, extraluminal findings
Reimund et al (24)	1999	Linear 7.5MHz	NA	Not administered	Wall thickness, bowel motility, extraluminal findings
Tarjan et al (28)	2000	NA	Overnight fasting	NA	Wall thickness, stenosis, extraluminal findings
Miao et al (30)	2001	3.5/7.5 MHz	6 hrs fasting	NA	Wall thickness
Neye et al (31)	2004	Linear 5/12 MHz Dynamic 4/7 MHz + Power Doppler	NA	NA	Wall thickness, vascularization pattern
Calabrese et al (25)	2005	Convex 3.5/5 MHz	Overnight fasting	Luminal contrast administrated. Data for contrast-enhanced US not complete	Wall thickness, peristalsis, bowel compressibility, extraluminal findings
Rispo et al (29)	2005	Linear and convex: 5-7.5 MHz	Overnight fasting	NA	Wall thickness

Table 4:

			MR Imaging features	
Study	**Year of publication**	**Magnetic field**	**Bowel preparation**	**Luminal contrast medium**
Shoenut et al (8)	1994	1.5 T	NA	NA
Low et al (36)	2000	1.5 T	3 hrs fasting, 1 mg Glucagon	1350 ml 2% Barium Sulfate (oral), 500-1000 ml water (rectal)
Rieber et al (33)	2000	1.5 T	20 mg Hyoscine butylbromide	Enteroclysis
Koh et al (32)	2001	1.0 T	1 mg Glucagon	600 ml water (oral)
Miao et al (30)	2002	1.0 T	Overnight fasting, 1 mg Glucagon	600 ml water (oral)
Laghi et al (6)	2003	1.5 T	Overnight fasting	10 ml/kg polyethylene glycol electrolyte solution (oral)
Darbari et al (34)	2004	NA	NA	NA
Ochsenkuhn et al (9)	2004	1.5 T	30-60 mg Hyoscine butylbromide	400 ml barium suspension 1.5-2L ferristene (enteroclysis)
Ajaj et al (35)	2005	1.5 T	3 L polyethylene glycol electrolyte solution, 40 mg Hyoscine butylbromide	1500-2000 ml warm water (rectal)
Schreyer et al (11)	2005	1.5 T	Klean prep 40 mg Hyoscine butylbromide	1.5 L gadopentetate dimeglumine in water (5mmol/L)
Schreyer et al (12)	2005	1.5 T	12 hrs fasting 40 mg Buscopan	2L water (oral), 700 ml 0.9%NaCl (rectal)

	Intravenous contrast medium	Coil	Criteria used for disease assessment
	0.1 mmol/kg Gd-DTPA	NA	Enhancement, wall thickness, length of diseased segment
	0.1 mmol/kg Gd-DTPA	Body	Enhancement, wall thickness
	0.1 mmol/kg Gd-DTPA	Surface	Wall thickness, stenosis
	0.1mmol/kh Gd-DTPA	NA	Enhancement, wall thickness, lymphadenopathy, comb sign
	0.1mmol/kg Gd-DTPA	NA	Enhancement, wall thickness, lymphadenopathy, comb sign
	0.1 mmol/kg Gd-DTPA	Surface	Enhancement, wall thickness
	NA	Surface	Enhancement, wall thickness
	0.1 mmol/kg Gd-DTPA	NA	Enhancement, wall thickness, stenosis
	0.2 mmol/kg Gd-BOPTA	Surface	Enhancement, wall thickness, haustration, lymphadenopathy
	0.1mmol/kg Gd-DTPA	Surface	Enhancement, wall thickness, comb sign, lymphadenopathy
	0.2 mmol/kg Gd-DTPA	Surface	Enhancement , wall thickness, comb sign, lymphadenopathy, stenosis

Table 5:

			Scintigraphic Imaging features	
Study	**Year of publication**	**Labeled structure**	**Labeling agent Dose**	**Imaging duration**
Heresbach et al (40)	1993	Leucocytes	3.7-5.5MBq	3 hrs, 24 hrs
Dhôte et al (41)	1995	Leucocytes	296-740 MBq	30 min, 2 hrs
Middleton et al (37)	1995	Leucocytes	200-300 MBq	1.5-3 hrs
Kolkman et al (39)	1996	Leucocytes	370 MBq	1 hr, 4 hrs
Papos et al (38)	1996	Leucocytes Antigranulocytes	182-370 MBq, 495-635 MBq	For leukocytes: 30 min, 2hrs, 4 hrs; for antigranulocytes: 2 hrs, 6 hrs, 20-24 hrs
Stahlberg et al (15)	1997	Leucocytes	185±20 MBq ‡	10-30 min, 3 hrs
Cucchiara et al (17)	1999	Leucocytes	185±74 MBq ‡	30 min, 1 hr, 2 hrs, 3 hrs
Molnar et al (13)	2001	Leucocytes	208-614 MBq	30 min, 2 hrs
Rispo et al (29)	2005	Leucocytes	185±74 MBq ‡	30 min, 1 hr, 2 hrs, 3 hrs

* The labeling agent used was technetium 99m in all studies except in the study by Heresbach et al, in which Indium 111 was used for labeling
† Scoring system based on that used by Saverymuttu et al (46).
‡ Mean dose ± standard deviation

	Scanning technique	Criteria used for disease assessment
	Planar	Decreased splenic activity †
	Planar	Intestinal uptake of tracer compared with bone marrow uptake
	Planar	Intestinal uptake of tracer compared with bone marrow and internal organ (spleen) uptake
	Planar	Intestinal uptake of tracer compared with bone marrow and liver uptake
	Planar	Intestinal uptake of tracer compared with bone marrow uptake
	Planar	Intestinal uptake of tracer compared with bone marrow and liver uptake
	Planar	Intestinal uptake of tracer compared with bone marrow and internal organ (liver) uptake
	Planar	Intestinal uptake of tracer compared with bone marrow uptake
	Planar	Uptake within 1 hr

Table 6:

				CT Imaging features
Study	**Year of publication**	**Type of scanner**	**Bowel preparation**	**Luminal contrast**
Kolkman et al (39)	1996	NA	NA	15 ml meglumine ioglicate in 500 ml water (oral) + 15 ml meglumine ioglicate in 1000 ml water (rectal)
Low et al (36)	2000	Helical CT	3 hrs fasting, 1 mg Glucagon	1.8 L barium sulphate (oral) + 500-1000 ml water (rectal), 2-3- L water (oral) + 500-1000 ml water (rectal)
Mazzeo et al (43)	2001	Helical CT	20 mg Hyoscine butylbromide	2 l polyethylene glycol solution (oral)
Molnar et al (13)	2001	Multislice (4 detector rings)	NA	2 L diluted sodium amidotrizoate (oral)
Hassan et al (42)	2003	Helical CT	NA	Minimum of 1 L 0.5% methylcellulose for enteroclysis
Jamieson et al (44)	2003	Multislice (4 detector rings)	NA	200-500 ml water or clear juice
Wold et al (45)	2003	NA	10 mg Metoclopramide, 1 mg Glucagon	1.8 L methylcellulose for enteroclysis, 1.8 L water (oral)

	Intravenous contrast	Criteria used for disease assessment
	NA	Enhancement, double-halo sign, wall thickness, ulcerations, extraluminal findings
	125 ml iohexol	Enhancement, wall thickness, extraluminal findings
	110-130 ml iodixanol	Wall thickness, extraluminal findings
	100 ml Iopromide	Enhancement, double-halo sign, wall thickness, ulcerations, extraluminal findings
	Iopamiro n	Enhancement, wall thickness, extraluminal findings
	Iohexol, 300 mg iron per milliliter (2 ml/kg)	Enhancement, wall thickness, extraluminal findings
	Iopamidol	Enhancement, mural stratification, mesenteric fat stranding

Table 7: Per patient sensitivity and specificity values

US						
Study	**Patients with IBD**		**Patients without IBD**		**Sensitivity (%)**	**Specificity (%)**
	TP	**FN**	**FP**	**TN**		
Sheridan 1993	32	9	8	78	78.0	90.7
Limberg 1994	72	5	3	360	93.5	99.2
Solvig 1995	18	2	2	37	90.0	94.9
Andreoli 1998	26	6	1	8	81.2	88.9
Reimund 1999	81	6	2	29	93.1	93.5
Tarjan 2000	38	5	2	28	88.4	93.3
Miao 2001	20	3	0	7	87.0	100.0
Calabrese 2005	24	1	1	2	96.0	66.7
Rispo 2005	46	4	1	29	92.0	96.7
MRI						
Study	**Patients with IBD**		**Patients without IBD**		**Sensitivity (%)**	**Specificity (%)**
	TP	**FN**	**FP**	**TN**		
Shoenut 1994 *	20	0	0	0	100.0	
Rieber 2000 ¶	27	0	0	21	100.0	100.0
Koh 2001	21	2	2	5	91.3	71.4
Miao 2002	20	3	2	5	87.0	71.4
Laghi 2003 §	36	8	0	31	81.8	100.0
Laghi 2003 II	36	9	0	30	90.0	100.0
Darbari 2004 #	43	2	1	12	95.6	92.3
Ochsenkuhn 2004 †	16	2	1	6	88.9	85.7
Ochsenkuhn 2004 ‡	4	0	9	12	100.0	57.1
Scintigraphy						
Study	**Patients with IBD**		**Patients without IBD**		**Sensitivity (%)**	**Specificity (%)**
	TP	**FN**	**FP**	**TN**		
Dhôte 1995	18	1	1	0	94.7	0
Cucchiara 1999	16	5	6	21	76.2	77.8
Rispo 2005	45	5	2	28	90.0	93.3
CT						
Study	**Patients with IBD**		**Patients without IBD**		**Sensitivity (%)**	**Specificity (%)**
	TP	**FN**	**FP**	**TN**		
Mazzeo 2001	12	2	0	19	85.7	100.0
Hassan 2003	26	4	0	9	86.7	100.0
Jamieson 2003	11	2	1	2	84.6	66.7
Wold 2003	10	3	1	9	76.9	90.0

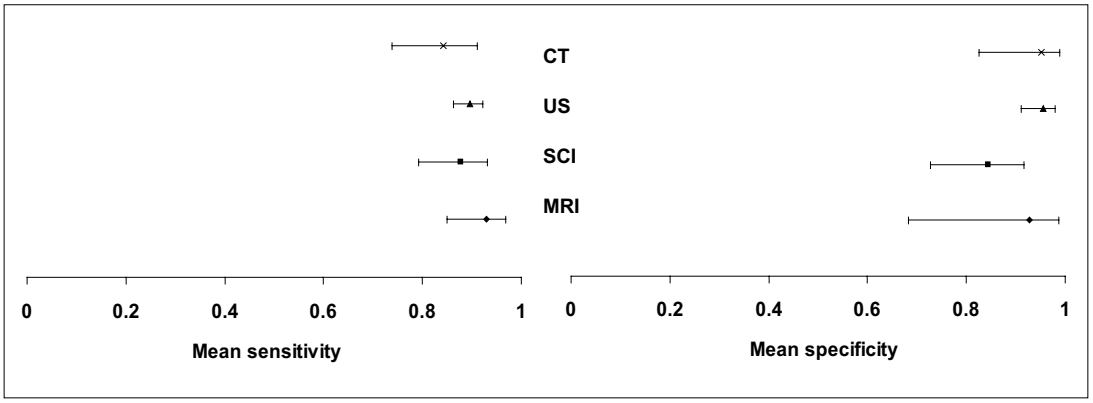
* Including two patients with indeterminate colitis
¶ Two patients with tumor excluded (verification not possible)
§ MRI findings compared to colonoscopy
II MRI findings compared to pathology
including 17 patients with inderminate colitis
† MRI findings in the terminal ileum compared to colonoscopy and histology
‡ MRI findings in the small bowel proximally of terminal ileum, compared with barium enteroclysis

Table 8: Per segment sensitivity and specificity values

Study	Patients with IBD		Patients without IBD		Sensitivity (%)	Specificity (%)
	TP	FN	FP	TN		
US						
Pradel 1997	61	26	6	76	70.1	92.7
Neye 2004	53	15	4	54	77.9	93.1
MRI						
Low 2000 α	55	10	11	117	84.6	91.4
Low 2000 β	52	13	11	117	80.0	91.4
Koh 2001	24	17	6	77	58.5	92.8
Ajaj 2005 *	68	5	0	19	93.2	100
Schreyer 2005 †	32	40	3	77	44.4	96.3
Schreyer 2005 ‡	28	24	2	107	59.7	98.2
Scintigraphy						
Heresbach 1993	51	19	1	15	72.9	93.8
Middleton 1995	31	9	3	30	77.5	90.9
Kolkman 1996 §	29	7	1	6	80.6	85.7
Papos 1996 #	33	5	2	24	86.8	92.3
Papos 1996 ##	24	14	1	25	63.2	96.2
Stahlberg 1997	74	16	5	16	82.2	76.2
Molnar 2001	54	17	6	61	76.1	91.0
CT						
Kolkman 1996	42	15	3	53	73.7	94.6
Low 2000 α	39	26	13	115	60.0	89.8
Low 2000 β	42	23	10	118	64.6	92.2
Molnar 2001	51	20	11	56	71.8	83.6

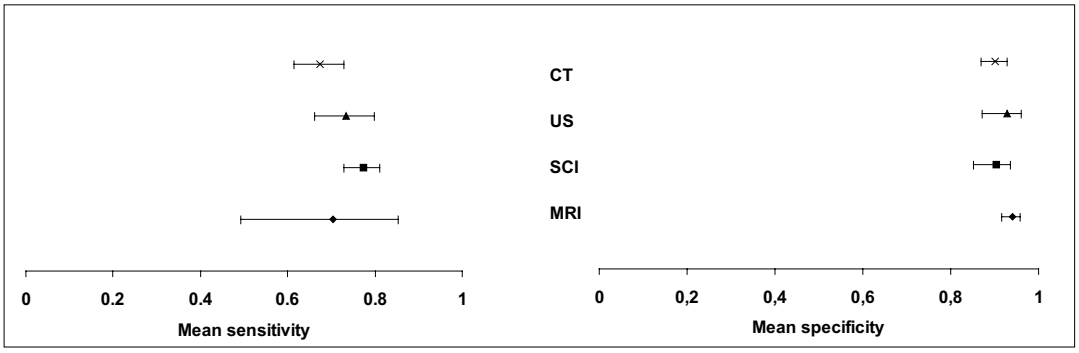
α data reported for observer 1
β data reported for observer 2
*92/138 segments verified with reference standard
† (Gut)
‡ (Inflamm Bowel Dis) only patients who had undergone complete ileocolonoscopy (n=23) were included for analysis by the authors of the study
§ Only UC patients, incomplete data reported for CD patients for scintigraphy
# leucocyte scintigraphy
antigranulocyte-immunoscintigraphy

Figure 2: Accuracy estimates (with confidence intervals) for diagnosis of IBD on a per-patient basis



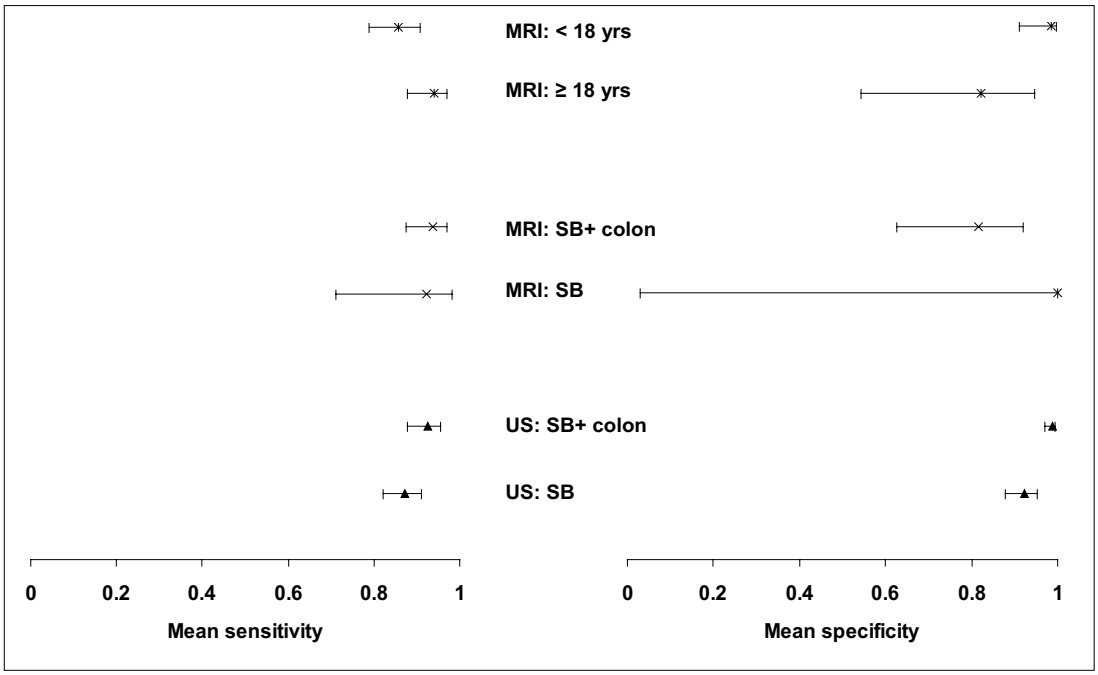
SCI= scintigraphy

Figure 3: Accuracy estimates (with confidence intervals) for diagnosis of IBD on a per-segment basis



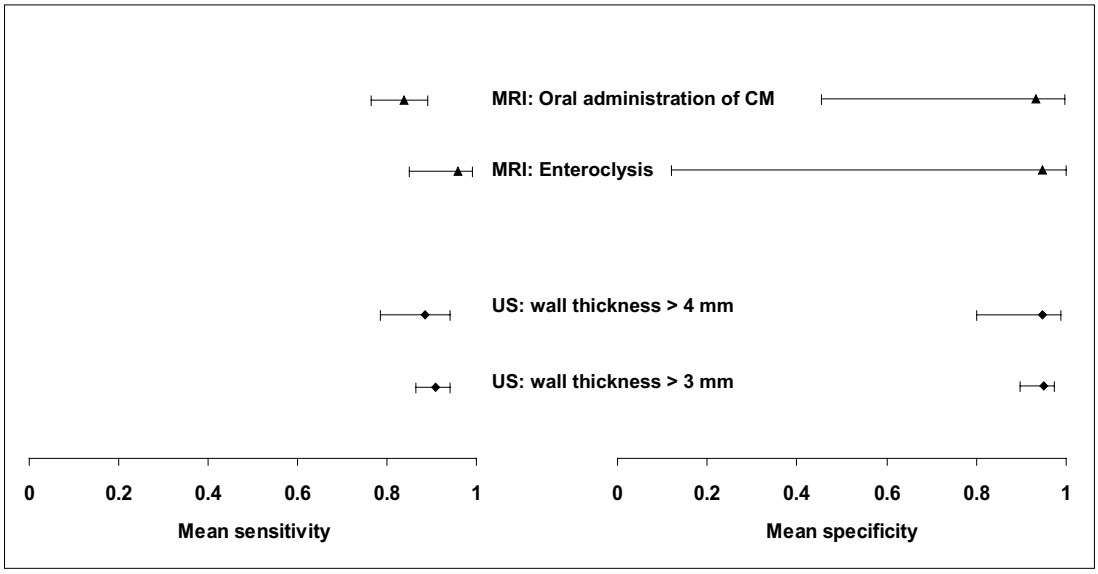
SCI=scintigraphy

Figure 4: Accuracy estimates (with confidence intervals) for subgroup analysis: patient characteristics.



SB = small bowel.

Figure 5: Accuracy estimates (with confidence intervals) for subgroup analysis: imaging test features and imaging criteria.



CM= contrast medium