Magnetic resonance imaging in Crohn's disease
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CHAPTER 6

Feasibility of evaluating Crohn’s disease activity at 3.0 Tesla

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ABSTRACT

**Purpose:** To determine whether abdominal 3.0 Tesla-MRI can be used for evaluation of Crohn’s disease compared with ileocolonoscopy (CS) and to determine patient preference for MRI as opposed to CS.

**Materials and Methods:** Twenty patients scheduled for CS underwent MRI. At CS, disease severity was graded and the Crohn’s Disease Endoscopic Index of Severity (CDEIS) was determined. Radiological grading (by two observers) was compared with endoscopic grading and CDEIS. Patient experience and preference were determined.

**Results:** In respectively 10 (observer 1) and 13 patients (observer 2) exact agreement between radiological and endoscopic grading was found. In respectively 10 and 7 patients radiological and endoscopic grading differed one level. No statistically significant correlation was found between radiological grading and CDEIS. Between bowel wall thickness and CDEIS weak to moderate correlations were found, and between bowel wall enhancement and CDEIS weak correlations were found. All patients preferred MRI over CS.

**Conclusion:** It is feasible to perform abdominal 3.0 Tesla MR using orally administered contrast medium for evaluation of CD and this method can be considered a patient friendly alternative to CS.
INTRODUCTION

Crohn’s disease (CD) is a chronic bowel disease characterized by transmural inflammation that can affect the entire gastrointestinal tract, although the location of predilection is the terminal ileum. The current gold standard diagnostic test is endoscopy as with this technique even early mucosal changes can be visualized and the extent and severity of disease can be assessed accurately. Consequently, endoscopy (with mucosal biopsy sampling) is generally used to establish a diagnosis in CD and is routinely used to monitor treatment (1, 2). However, endoscopy is associated with unpleasant bowel preparation, discomfort during the endoscopic procedure, the risk of procedure-related complications, and a relatively high cost (3). Moreover, conventional upper and lower endoscopic techniques allow visualization of only esophagus, stomach and duodenum, and colon and terminal ileum, respectively, leaving the larger part of the small bowel indiscernible to the gastroenterologist.

Barium enteroclysis, which at present is the primary means of assessing the small bowel in CD (4), has a limited diagnostic yield; subtle mucosal changes as well as transmural and extraintestinal pathology are not visualized. The fact that ionizing radiation is used, is an additional disadvantage, especially since patients with CD (who are often young) have to be subjected repeatedly to bowel examinations.

As MRI is a patient-friendly imaging method that allows both transmural and extraintestinal assessment of the abdomen, many studies used MRI to evaluate CD, and proved MRI capable of detecting active disease (5-26). However, before MRI can be considered an alternative for endoscopy in CD, it should be firmly established that - in addition to detection of disease activity - MRI is capable of revealing both the severity and the exact location of disease. Few prospective studies have compared MRI with endoscopy regarding the severity of disease, whereas only the five most recent of these studies also analyzed accuracy of MRI in localizing disease (27-33). The results of these studies were conflicting; reported sensitivities and specificities varied widely from approaching endoscopic accuracy to considerable over- or underestimation of disease.

All of the aforementioned studies were performed at field strengths of 1.5 Tesla or less. Recently scanners that use higher field strength (i.e. 3.0 Tesla and more) have become commercially available. With high-field MRI a better signal-to-noise ratio (SNR) can be achieved, with the possibility of higher spatial resolution or shorter scan times. Theoretically, using these advantages image quality would improve so that even subtle abdominal pathology could be seen consistently, which potentially could improve accuracy in grading disease activity. However, in practice abdominal 3.0 Tesla-imaging is hampered by the following limitations: Due to dielectric resonance effects inhomogeneity of the B1-field is observed at 3.0 Tesla. These RF inhomogeneities and thus locally irregular flip angles lead to spatial signal intensity variations (33). Moreover, with higher field strength more chemical shift artifacts can be seen as the Larmor frequency difference between nuclei with different chemical bonds increases linearly with the applied magnetic field.
Fat suppression is a possible solution to the chemical shift problem, but fat suppression is more challenging at 3.0 Tesla. New fat suppression strategies have been implemented at 3.0 Tesla, such as SPeectrally selective Attenuated Inversion Recovery (SPAIR), which is a high-uniformity fat saturation method that uses adiabatic spectral saturation pulses, ensuring insensitivity to RF field inhomogeneity. This appears to be successful, although it causes considerable lengthening of a sequence.

To our knowledge, no clinical studies have been published regarding the feasibility of imaging of CD at 3.0 Tesla.

The aim of this prospective study was to determine the diagnostic value of 3.0 Tesla-MR for evaluation of CD compared with CS. The secondary aim was to examine differences in patient preference between MRI and CS.

MATERIALS AND METHODS

Study Population

Twenty-two consecutive patients with a proven diagnosis of CD (by endoscopy, histology or both), participated in this prospective study after having given written informed consent. Patients who were scheduled to undergo CS were asked to participate in this study. Exclusion criteria were general contraindications to MRI, pregnancy, or inability to tolerate a 20-second breath hold. The study was approved by the institutional review board.

Patient Preparation

Starting four hours prior to the MR examination the patients were administered 3.4 grams of Ispaghula Husk Anhydricum (Metamucil, Procter & Gamble Nederland B.V., Rotterdam, the Netherlands) dissolved in at least 250 ml of water, each hour. The total volume of ingested contrast medium thus amounted to at least one liter. Ispaghula forms, when mixed with water, a voluminous non-digestible hydrogel with a high water-binding capacity. This oral contrast agent was chosen for its biphasic properties; positive intraluminal contrast on T2-weighted images and negative intraluminal contrast on T1-weighted images. During this period no ingestion of food or fluids was allowed, with the exception of additional water if wished. No rectal contrast medium was administered, to minimize patient discomfort.

MR imaging was performed on a 3.0 Tesla-MRI (Intera, Philips Medical Systems, Best, the Netherlands) using a torso phased-array surface coil. Both T2-weighted 2D Turbo Spin Echo (TSE) coronal (TR 1699.9; TE 60; TSE factor 81; FOV 485; RFOV 100%); scan matrix 304 x 274; SENSE factor 2; slice thickness 5 mm; gap 0; 27-35 slices; scan duration 00:59.5 min) and axial (TR 1042.9; TE 60; TSE factor 49; FOV 455; RFOV 60%; scan matrix 304 x 243; SENSE factor 2; slice thickness 5 mm; gap 0; 72 slices; scan duration 01.15 min) respiratory triggered sequences and a breath hold coronal Balanced-Fast Field Echo (B-FFE) sequence (TR 2.8; TE 1.4; flip angle 45º; FOV 450; RFOV 70%; matrix scan 192 x 230; slice thickness
5mm (interpolated); gap 0; 10 slices per breath hold; 28-35 slices; scan duration 01.23 min) were performed.

To suppress bowel peristalsis 20 milligrams of butylscopolamine bromide (Buscopan; Boehringer Ingelheim, Germany) or 1 mg glucagon hydrochloride (Glucagen; Novo-Nordisk A/S, Bagsvaerd, Denmark), were administered intravenously prior to performing the T1-weighted sequences. Seventy seconds after intravenous administration of 0.1 ml/kg of bodyweight Gadodiamide (Omniscan 0.5 mmol/ml Gd, Amersham Health B.V., Eindhoven, the Netherlands) fat saturated 3D T1-weighted FFE coronal (TR 3.0; TE 1.5; flip angle 10°; FOV 395; RFOV 100%; matrix scan 192 x 154; SENSE factor 2; 1 stack; 80 slices/stack; slice thickness 2 mm (interpolated); SPAIR inversion delay 100ms; scan duration 00:16 min) and axial (TR 3.0; TE 1.5; flip angle 10°; FOV 395; RFOV 85%; matrix scan 192 x 154; SENSE factor 2; 2 stacks; 80 slices/stack; slice thickness 2mm (interpolated); SPAIR inversion delay 100 ms; scan duration 00:29 min) breath hold sequences were performed.

Image Reading and Interpretation

Observers

Images were independently evaluated by two observers who were blinded to clinical and endoscopic findings, on a PACS system (IMPAX, IMPAX SP4 SU4 DS3000, AGFA, Mortsel, Belgium). The first observer was an abdominal radiologist with more than 10 years’ experience in reading abdominal MRI. Previously to this study this observer had read 80 1.5 Tesla CD MR examinations, 48 of which included endoscopic feedback. The second observer was a research fellow, who prior to this study had read 35 abdominal MRI examinations for CD for training purposes and had linked results of 300 MRI examinations with endoscopic reports for studies on colonography and CD. Most examinations were performed at 1.5 Tesla MR, but 60 of these examinations were performed at 3.0 Tesla.

Images were evaluated both qualitatively and morphologically. To this end the gastrointestinal tract was divided into 8 segments; duodenum, jejunum, proximal ileum, terminal ileum, cecum and right colon, transverse colon, left colon and sigmoid, and rectum.

Image Quality

To determine image quality bowel distension, homogeneity of bowel contents and conspicuity of bowel wall were scored per bowel segment by the first observer. Bowel distension was scored as one of 4 categories (complete distension of a segment, adequate distension of the majority of the segment, poor distension of the majority of the segment, completely collapsed segment). Homogeneity of bowel contents was scored as either poor, moderate, good, very good or excellent.

For conspicuity of bowel wall 5 categories were provided: wall not seen, only portions seen, wall seen without clear delineation, wall clearly seen or excellent delineation of bowel wall.

Overall image quality (poor, moderate, good, very good or excellent) and the presence of artifacts were assessed by the second observer.
**Imaging Findings**

Morphological evaluation was done by both observers per bowel segment for the following items: on the T1-weighted fat saturated images bowel wall enhancement was scored; firstly enhancement was subjectively scored as either absent, mild, moderate or strong. Secondly, semi-objectively enhancement was scored as either less intense than spleen, as intense as spleen, as intense as liver, as intense as renal cortex or hyperintense in comparison with renal cortex.

All sequences could be used to score the remaining items; the maximum wall thickness and length of pathological bowel were measured using electronic calipers. Stenosis was recorded as either absent, low-grade stenosis, high-grade stenosis or high-grade stenosis with prestenotic dilatation. The presence or absence of ulceration and cobblestoneing was noted. The observers also recorded presence or absence of fibrofatty proliferation, increased mesenteric vascularisation (‘comb sign’), mesenteric lymphadenopathy (short axis > 1 cm), lymphadenopathy at other locations, abscess and fistula.

The severity of disease (remission, mild disease, moderate disease, severe disease) was subjectively graded (MRI\textsubscript{total}), based on the abovementioned items. However, to be able to compare radiological and endoscopic grading accurately, the observers were also asked to provide a modified grading of disease (MRI\textsubscript{CS-based}). This was done as with CS only the lumen and mucosal surface of the large bowel and terminal ileum can be visualized, while MRI allows visualization of the entire abdomen. Therefore, for MR\textsubscript{CS-based} grading only pathological findings that could also be visualized at CS could be taken into account (i.e. excluding extraintestinal findings (e.g. abscess, fibrofatty proliferation, lymphadenopathy) and bowel segments not visualized at endoscopy (e.g. ileum, jejunum)). Prior to scoring no specific instructions regarding criteria for grading disease severity were given to the observers; this subjective rating of disease severity was done as no validated definitions for different categories of disease at MRI are available at this time.

**Endoscopic Parameters**

For all patients CS was planned to take place within two weeks from the MR examination. Patients either ingested 4–6 L of polyethylene glycol electrolyte solution (KleanPrep; Helsinn Birex Pharmaceuticals, Dublin, Ireland) or 90 ml of Phosphoral (Ferring BV, Hoofddorp, the Netherlands) for bowel cleansing on the day before and/or the day of the endoscopy. CS was performed using a standard colonoscope (CF-140L; Olympus, Tokyo, Japan). During this procedure patients received sedatives (midazolam; Roche, Basel, Switzerland) and analgesics (fentanyl; Janssen Pharmaceuticals, Beerse, Belgium).

Endoscopic findings were recorded by the endoscopist in a standardized manner; the presence of CD-associated lesions (i.e. pseudopolyp, ulceration (healed, aphthoid, superficial/shallow, or deep), frank erythema, frankly swollen mucosa, stenosis (non-ulcerated or ulcerated)) and the percentage of the surface involved by the disease were recorded per bowel segment (terminal ileum, right colon, transverse colon, left colon and sigmoid, and rectum). The Crohn’s Disease Endoscopic Index of severity (CDEIS) was
calculated from these data, with scores from 0-44 (higher scores reflect more severe disease) (34). As the CDEIS score reflects the severity of disease for all evaluated bowel segments combined, a CDEIS score was also defined per bowel segment to enable comparison between MRI grading per bowel segment and CDEIS.

In addition, the endoscopist was asked to subjectively rate disease severity as either no disease, mild, moderate or severe disease. This was requested as in clinical practice endoscopists usually base their therapeutic strategy on their subjective impression of the disease severity instead of on the laborious CDEIS (which is generally not scored in daily practice).

In the week preceding the MRI, the patients kept a symptom diary to determine CDAI-scores. C-reactive protein (CRP) was determined as a biological marker of disease activity.

**Patient Questionnaires**

Patient experience was determined using standardized questionnaires. After completion of both examinations patients were asked how they had experienced the respective bowel preparations (5-point Likert scale; not/ a little/ somewhat/ rather/ severely burdensome). They were also asked how much pain, embarrassment and discomfort they had experienced (5-point Likert scale), and what they considered the most burdensome aspect of the two examination methods. Finally the patients were asked to rate on a 7-point Likert scale which technique they would prefer for their next examination, assuming both techniques would give equal information about disease severity. They were also asked to order the four aspects of this study (MRI, CS, and both bowel preparations) from the most burdening to the least burdening.

**Statistical Analysis**

Interobserver variability for radiological grading of disease was calculated using weighted kappa statistics according to the method of Fleiss and Cohen (35). Spearman correlation coefficients (two-sided) were calculated to determine interobserver correlations for maximum wall thickness and maximum bowel wall enhancement per bowel segment. For maximum bowel wall thickness, limits of agreement were calculated as well. Agreement between radiological grading of disease (MRIcs-based) and endoscopic grading of disease was determined using weighted kappa statistics. Spearman correlation coefficients were determined between MRI grading (MRIcs-based) and CDEIS, and between overall MRI grading (MRItotal) and the secondary reference parameters (CRP and CDAI). Correlation coefficients were also calculated between two independent MRI parameters (i.e. bowel wall thickness and bowel wall enhancement) and the reference parameters.

Differences in patient experience regarding both examinations were tested for statistical significance using Wilcoxon matched pairs signed rank sum test. Differences in patient preference were tested using the Fisher exact test after dichotomizing the parameter
(preference for MRI versus preference for CS). Kappa values were interpreted according to Altman (36). Correlation coefficient values were interpreted as follows: 0.0 no association, 0.2 weakly correlated, 0.5 moderately correlated, 0.8 strongly correlated and 1.0 perfectly correlated (37). P-values < 0.05 were considered statistically significant.

RESULTS

From April 1st 2004 to December 17th 2004 22 patients were included in this study. MRI examinations were carried out within a median of 5 days (range 1-48 days) of ileocolonoscopy.

One patient was excluded because the MR examination was not completed due to nausea and vomiting after administration of intravenous contrast medium. Another patient was excluded because high-dose intravenous steroids were started before the MRI had taken place. Therefore a total of 20 patients could be evaluated of whom baseline characteristics are shown in table 1.

Seven patients had previously undergone ileocecal resection; in these patients the neoterminal ileum was scored as terminal ileum. In one of these patients the ascending colon was removed as well. In six patients no complete evaluation of colon and terminal ileum was possible; in one patient the endoscope could only be introduced as far as the hepatic flexure, and in five patients the endoscope could only be introduced as far as the cecum. As a result, a total of 92 bowel segments could be evaluated endoscopically.

| Table 1: Demographic characteristics and severity indices of the study population |
|---------------------------------------------------------------|------------------|
| Number of patients                                            | 20               |
| Male/female                                                   | 7/13             |
| Mean age ± SD                                                 | 36 ± 13          |
| Range                                                        | 22-58            |
| Disease history                                               |                  |
| Surgery (ileocecal resection)                                 | 7                |
| Categories (no, mild, moderate, severe)                       | 5/ 9/ 5/ 1       |
| Mean CDEIS ± SD                                               | 3.8 ± 3.3        |
| Median                                                        | 3.4              |
| Range (IQR)                                                   | 0.11 (1.0 - 5.5) |
| Mean CDAI ± SD                                                | 161 ± 96         |
| Median                                                        | 143              |
| Range (IQR)                                                   | 14-376 (96-226)  |
| Mean CRP ± SD                                                 | 13.3 ± 19.6      |
| Median                                                        | 6.2              |
| Range (IQR)                                                   | 1.0 - 83.3 (2.2 -6.2) |
Image Quality

Theoretically, a total of 159 bowel segments could be evaluated on MRI. However, in 8 examinations the rectum was incompletely visible, leading to 151 qualitatively assessable segments.

Complete bowel distension was observed in 40 segments (26.5%), adequate distension in 47 (31%), and poor distension in 48 (32%) segments. Completely collapsed bowel was observed in 16 (10.5%) segments. Best distension of bowel was observed in the terminal ileum, ascending colon and transverse colon. Duodenum and jejunum were inadequately distended in most patients (poor distension or completely collapsed bowel in respectively 19 and 15 segments). The descending colon was poorly distended or completely collapsed in 14 patients; for the rectum this was the case in 4 patients. Homogeneity of bowel contents was scored as poor in 84 segments (56%), moderate in 38 segments (25%), good in 26 (17%) and very good in three (2%) segments.

The bowel wall could not adequately be identified in 6 segments (4%); only portions were seen in 82 (54%); in 8 segments (5%) bowel wall was seen without clear delineation; in 54 segments (36%) bowel wall could be clearly seen, while in one bowel segment (1%) bowel wall delineation was excellent.

Overall image quality was scored as moderate in 3, good in 14 and very good in 3 examinations. In seven examinations T1-weighted sequences were affected by motion artifacts (peristalsis/ breathing). In none of the examinations chemical shift artifacts, susceptibility artifacts or contrast inhomogeneity were rated as disturbing image quality.

Interobserver Variability

Interobserver agreement showed kappa values of 0.34 (95% CI 0.06 – 0.61) for MRIendoscopy based and 0.59 (95% CI 0.30 – 0.89) for MRItotal. Significant correlations were found for maximum bowel wall thickness at the proximal ileum \( r = 0.77 \) (\( p < 0.001 \)), terminal ileum \( r = 0.55 \) (\( p=0.011 \)) and transverse colon \( r = 0.57 \), \( p=0.009 \). Limits of agreement showed a mean difference of 1.6 mm (± 1.96*1.7, range 0 to 9 mm, median 1.0). In seven bowel segments measurements of maximum bowel wall thickness differed more than 5 millimeters.

For subjective bowel wall enhancement (no/mild/moderate/strong) a moderate correlation was found between the two observers \( r = 0.54 \), \( p<0.001 \). A weak to moderate correlation \( r=0.39, p < 0.001 \) between the two observers was found for bowel wall enhancement compared with enhancement of internal organs.

Agreement between MRI and reference parameters

For the first observer grading of disease severity corresponded completely with endoscopic grading in 10 patients, while in 10 patients one grade of difference was scored (weighted kappa 0.42, 95% CI 0.17 -0.67) (table 2).
For observer 2 radiological grading corresponded with endoscopic grading in 13 patients, while in 7 patients MR based grading differed 1 grade from endoscopic grading (weighted kappa 0.74, 95% CI 0.58 – 0.90) (Table 2). Comparing MRI grading (CSbased) with CDEIS no statistically significant correlation was found for either observer. However, no significant correlation was found either (r=0.390, p= 0.099) between endoscopic grading and CDEIS. Between bowel wall thickness and segmental CDEIS a weak (observer 1) to moderate (observer 2) correlation was found, while for bowel wall enhancement correlation was weak for both observers (Table 3). For both observers moderate correlations were observed between radiological grading of disease (MRItotal) and CRP whereas no significant correlations were found between CDAI and radiological grading (Table 4).

Table 2: Comparison of grading of Crohn’s disease activity by MRI and endoscopy

<table>
<thead>
<tr>
<th>MR Ileocolonoscopy</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Remission</td>
</tr>
<tr>
<td>Remission</td>
<td>0 / 4</td>
</tr>
<tr>
<td>Mild</td>
<td>5 / 1</td>
</tr>
<tr>
<td>Moderate</td>
<td>0 / 0</td>
</tr>
<tr>
<td>Severe</td>
<td>0 / 0</td>
</tr>
<tr>
<td>Total</td>
<td>5</td>
</tr>
</tbody>
</table>

Grading of the first MRI observer is shown left of the slash, of the second observer right of the slash. Exact agreement between MR grading and endoscopic grading is in bold.

Table 3: Correlation between MRI and CDEIS

<table>
<thead>
<tr>
<th>MRICSbased</th>
<th>Bowel wall thickness</th>
<th>Bowel wall enhancement</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDEIS</td>
<td>Observer 1</td>
<td>Observer 2</td>
</tr>
<tr>
<td>0.283</td>
<td>0.312</td>
<td>0.328</td>
</tr>
<tr>
<td>(p=0.240)</td>
<td>(p=0.004)</td>
<td>(p=0.008)</td>
</tr>
<tr>
<td>0.303</td>
<td>0.495</td>
<td>0.311</td>
</tr>
<tr>
<td>(p=0.207)</td>
<td>(p&lt;0.001)</td>
<td>(p=0.003)</td>
</tr>
</tbody>
</table>

Table 4: Correlation between MRI and secondary reference parameters

<table>
<thead>
<tr>
<th>MRItotal</th>
<th>Observer 1</th>
<th>Observer 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP</td>
<td>0.540</td>
<td>0.590</td>
</tr>
<tr>
<td></td>
<td>(p=0.015)</td>
<td>(p=0.007)</td>
</tr>
<tr>
<td>CDAI</td>
<td>0.222</td>
<td>0.120</td>
</tr>
<tr>
<td></td>
<td>(p=0.348)</td>
<td>(p=0.618)</td>
</tr>
</tbody>
</table>

Mural abnormalities

At endoscopy seven stenoses –all in the terminal ileum- were identified by the endoscopist (Figure 1). In two patients balloon dilatation was undertaken during the same session. In neither of these patients intubation of the terminal ileum was performed after dilatation.
which in one person was due to persisting narrowing of the anastomosis. Observer 1 correctly identified the six persisting stenoses of the terminal ileum; observer 2 correctly identified five of the six stenoses of the terminal ileum and scored the remaining stenosis as situated in the ileum proximally of the terminal ileum; observer 1 scored this stenosis as involving both terminal ileum and several centimeters beyond.

In two patients a stenosis of the terminal ileum was seen by both observers that was not confirmed by endoscopy. However, in one subsequently operated patient pathological examination of the resected bowel revealed macroscopically thickened bowel wall of the ileum with active inflammation. In the other patient endoscopy had only been performed until the hepatic flexure. At three earlier ileocolonoscopies performed in the previous 12 months a stenosis of the terminal ileum had been seen.

Additionally, both observers identified stenoses that were not observed by the endoscopist; observer 1 identified one stenosis of the terminal ileum and one in the descending colon/sigmoid. Observer 2 identified 5 additional stenoses of the terminal ileum. These stenoses were considered false-positive findings, as no verification of MR findings was performed. In none of the MRI examinations a cobblestone-pattern or deep ulcerations was apparent, while endoscopically in three patients deep ulcerations were seen.

Extraintestinal findings

Lymphadenopathy (short axis > 1 cm) was only seen in 1 patient, of whom endoscopically disease activity was graded as moderate. Presence of fibrofatty proliferation or mesenterial hypervascularity (Figure 2) was not associated with presence of active disease as graded by the endoscopist. Neither was presence of fibrofatty proliferation associated with longer duration of disease. In one patient a large abscess was seen by both observers. Observer 1 identified 3 ileo-ileal fistulas, of which none were identified by observer 2.
Patient experience

All patients completed the questionnaire. However, three patients provided incomplete information regarding the rating of the burden of the two examinations and the bowel preparation for ileocolonoscopy. Overall, patients ranked the MRI examination as least burdensome, followed by the bowel preparation with isphagula. Bowel preparation with polyethylene glycol was ranked third, while most patients considered ileocolonoscopy as the most burdensome. Patient ratings regarding the respective bowel preparations and the discomfort experienced during the examinations are shown in figure 3 and 4.

When asked whether patients would prefer MRI or ileocolonoscopy in the future, 17 patients answered they would definitely prefer MRI, the remaining 3 patients responded they most probably would prefer MRI.

Differences in experience and preference between MRI and CS were all statistically significant (p<0.01).

**Figure 2:** 22-year old female patient with CD. At ileocolonoscopy intubation of the terminal ileum was impossible due to stenosis.

a. Axial T2-weighted image shows the thickened bowel wall (arrow) of the terminal ileum. Infiltration of the surrounding mesenteric fat is seen (arrowheads).
b. Axial T1-weighted image after administration of intravenous contrast medium shows enhancement of bowel wall of the ileum with increased mesenterial vascularisation (arrowheads).
c. Endoscopic image shows the stenotic terminal ileum.

**Figure 3:** Ratings of discomfort experienced during examinations
DISCUSSION

This study demonstrates that using a field strength of 3.0 Tesla, radiological grading of disease shows moderate to good agreement with endoscopic grading of disease and moderate correlation with CDEIS. This study also shows that patients prefer MRI over CS regarding the examinations as well as their respective bowel preparations.

Agreement between radiological and endoscopic grading was moderate for observer 1, while good agreement was found for observer 2. This difference in agreement was mostly caused by observer 1 grading all patients in remission as having mildly active disease. These false positive MR results can be largely attributed to the fact that observer 1 more readily identified mesenteric hypervascularity than observer 2 and judged this to be proof of active disease in patients that the endoscopist identified as in remission. If mesenteric hypervascularization was discarded as proofing disease, better agreement between endoscopic and radiological scoring would result for observer 1.

Mesenteric hypervascularity, which in several studies has been mentioned as indicative of active disease (6, 7, 31, 32) might be more pronounced at 3.0 Tesla. It is known that flow appears brighter at 3.0 Tesla than at 1.5 Tesla, due to the longer T1 of the tissues at higher field strength. This results in enhanced contrast of tissue with inflowing blood that has not experienced the excitation pulse. This could also be true in mesenteric vessels.

This discrepant result regarding mesenteric hypervascularization can likely be explained by the fact that the first observer - although very experienced in reading abdominal MRI at 1.5 Tesla– was inexperienced at reading abdominal 3.0 Tesla MR. This serves to emphasize the importance of training abdominal radiologists when reading MR images acquired on a higher field system, as it appeared in this study that significant differences may occur between images of the bowel acquired at a lower and a higher field.

For both observers bowel wall enhancement, bowel wall thickening and mesenteric hypervascularization were key criteria for determining disease activity. However, differences in appraisal of these aspects have contributed to the low interobserver values as, besides mesenteric hypervascularization, enhancement of bowel segments was rated differently by the two observers in 75 of 151 assessable segments. In the literature contrast enhancement has been described as one of the most important parameters that indicate active disease (9, 27, 29). However, in these studies quantitative measurements of
percentage of contrast enhancement were obtained only of the most diseased segment of bowel, subsequently correlating these values with endoscopic findings. Moreover, in theory technical problems (e.g. field inhomogeneity, proximity of the studied tissue to the coil) prevent extrapolation of these quantitative data to a general population of CD patients. In a recent study by Narin et al. (29) in all segments judged as inflamed by MRI higher SNR value was seen compared with non-affected bowel. However, using this criterion as indicative of inflammation, overestimation of disease was seen in colonic segments. In another recent study (30) mean SNR of colonic bowel segments measured in healthy volunteers was found to fluctuate after administration of intravenous contrast medium, displaying highest values in the rectum and lowest in the ascending colon. Although the correlations between segmental CDEIS and respectively enhancement and bowel wall thickness indicate that these are important parameters for determining disease activity, the large inter-observer variability regarding these parameters in our study in addition to the results of the abovementioned studies, indicate that there is a need for large (multi-center) studies on MRI in CD in order to be able to determine accurate criteria for disease activity.

CDEIS scores did not show statistically significant correlation with radiological grading, as was the case for CDEIS and endoscopic grading of disease. The fact that no correlation could be established between CDEIS and MR grading can be explained by the many colonic segments wherein disease was under –or overestimated by MRI. A possible explanation for the absence of significant correlation between CDEIS and endoscopic grading is the fact that even if no active disease is seen, presence of a non-ulcerated stenosis will increase the CDEIS score by more than 3 points.

Between MRtotal and CRP moderate correlation was found for both observers. Values of CRP –an inflammatory marker- should be elevated in active inflammatory disease. When performing overall radiological grading, all manifestations of Crohn’s disease including extraintestinal ones, are taken into account. No correlation between CRP and endoscopic grading was found, while there was a moderate correlation between MRtotal and CRP indicating that MRI could be considered a suitable indicator of inflammatory activity outside endoscopic scope.

Between MRtotal and CDAI no correlation was found. A possible explanation for this is that the CDAI partly consist of subjective items (e.g. general well-being). It seems logical that a partly subjective index does not necessarily correlate with anatomy-based grading of disease activity. Our hypothesis is supported by earlier studies (2, 38), showing low correlation coefficients between CDEIS and CDAI, and between individual MR parameters and CDAI (28).

To our knowledge seven prospective studies have been performed determining accuracy of MRI in assessment of CD in an adult population using endoscopy as gold standard (27-33). However, in all but two of these studies (29, 32) both patients with ulcerative colitis and with Crohn’s disease were included. Both one radiological as well as one endoscopic scoring system of inflammatory activity (no disease, mild disease, marked disease) was
used for the two subgroups of patients. As in ulcerative colitis inflammation is exclusively mucosal while in CD transmural inflammation is seen, theoretically more enhancement should be expected in CD than in ulcerative colitis. As pathological enhancement was considered one of the major parameters indicating active disease in the abovementioned studies, combined analysis of patients with CD and UC does not necessarily accurately reflect diagnostic capacity of MRI.

In the two studies exclusively focusing on CD patients combined evaluation of the small bowel and colon was performed by both orally and rectally administered contrast medium. In the study by Schreyer et al. (32) sensitivity of 55.1% and specificity of 98.2% were achieved for correct grading of inflammatory activity. Segmental analysis showed correlation coefficients of 0.58 for the terminal ileum between radiological and endoscopic grading, which is in line with our results. However, these authors state that MRI is not suited to correctly assess mild inflammation in CD as 22 segments were falsely assessed as not inflamed on MRI while mild endoscopic activity was seen. In the study by Narin et al. (29) MRI overestimated disease in the colon. In both studies results for the terminal ileum were good, whereas for the colon lower accuracy was achieved, as was the case in our study.

Several limitations of our study must be taken into consideration when interpreting study results: The lack of training for the first observer regarding abdominal imaging at 3.0 Tesla was a serious flaw of our study. This observer did already have a considerable experience with abdominal 1.5 Tesla MRI for CD; better agreement with endoscopic results was obtained at 1.5 Tesla for this observer in an earlier study regarding abdominal MR-imaging in CD (39).

We did not compare performance of 1.5 Tesla versus 3.0 Tesla; scanning the same patients both at 1.5 T and at 3T would have improved our study design as direct comparison regarding image quality and accuracy in grading disease activity would have been possible. However, our results seem comparable to the two studies performed at 1.5 Tesla in CD patients.

Only a small number of patients was included in this study. All disease categories were represented, but only small numbers of patients were included per subgroup as the conducted study was a feasibility study. Moreover, no rectal filling of the colon was performed, hampering adequate assessment of bowel segments not filled with orally administered contrast medium. In literature false positive MR observations resulting from collapsed bowel displaying pathological enhancement have been described (23, 24, 32).

Finally, in this study we have kept our MR protocol invariant in order to obtain constant image quality, meaning that all patients were scanned with the same FOV and same image resolution. The choice of these parameters was made to provide a good SNR and good temporal resolution. However, this was achieved at the cost of spatial resolution. Theoretically, a higher spatial resolution could have aided in identifying ulceration or cobblestoning, but because of the abovementioned considerations, this was not achieved.
Before implementation of MRI can take place in the routine diagnostic care of CD patients, good radiological interobserver agreement is a prerequisite. To that end MRI parameters indicating inflammation should be well-defined regarding different degrees of disease activity as the development and validation of a standardized scoring system would probably greatly increase diagnostic reproducibility. Consequently, further studies evaluating combined small and large bowel MR imaging should be conducted in larger groups of CD patients representing the entire spectrum of disease.

In conclusion, it is feasible to perform abdominal 3.0 Tesla MR using orally administered contrast medium for evaluation of CD and this method can be considered a patient-friendly alternative to CS.

REFERENCES


