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Chapter 5

Feasibility of Using Automated Insufflated Carbon Dioxide (CO₂) for Luminal Distension in 3.0T MR colonography.

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Abstract

Objective: Primary aim of our study was to prospectively evaluate the feasibility of automated carbon dioxide (CO₂) delivery as luminal distending agent in 3.0T MR colonography.

Material and methods: Rectally insufflated CO₂ was evaluated in four groups with different bowel preparation (A-D). Bowel preparation regimes were: gadolinium-based tagging (A), bowel purgation (B), barium-based tagging (C) and iodine-based tagging (D). Supine (3D)T1w-FFE and (2D)T2w-SSFSE series were acquired. Each colon was divided into six segments (cecum S1-rectum S6). Two observers independently assessed the presence of artefacts, diagnostic confidence and segmental colonic distension. Also characteristics of the residual stool (presence, composition and signal-intensity) were assessed per segment. Discomfort was assessed with questionnaires.

Results: Fourteen healthy subjects were included. Colonic distension by means of rectally insufflated CO₂ was not associated with susceptibility artefacts. Overall image quality was affected by the presence of bowel motion-related artefacts: none of the segments in 3DT1w-series and 10/84 (12%) colon segments in 2DT2w-series were rated artefact-free by both observers. Diagnostic confidence ratings were superior for the 2DT2w-SSFSE series. Overall bowel distension was rated adequate to optimal in 312/336 (93%) colon segments.

Conclusion: MR colonography at 3.0T using carbon dioxide (CO₂) for colonic distension is technically feasible. The presence of intraluminal CO₂ did not result in susceptibility artefacts, although overall image quality was influenced by artefacts.
Introduction

Magnetic resonance (MR) colonography has been increasingly studied as non-invasive diagnostic tool for the detection of colorectal neoplasia [1-3]. Important reason to study MR colonography is the lack of ionizing radiation exposure. Further, it has a wide spectrum of soft tissue contrast which allows for a diversity of bowel preparation methods. However, besides the limited availability and relatively higher costs, at present there is no established MR colonography method [4].

Colonic distension in MR colonography is predominantly achieved with the use of a water-based enema, although the rectal administration of water is reported as the most burdensome part of a MR colonography examination [5]. The use of carbon dioxide (CO2) or alternatively room air as luminal distending agent, as generally applied in CT-colonography, can be expected to decrease procedural discomfort. Furthermore, automated insufflation results in superior colonic distension, when compared with manual insufflation of a gaseous distending agent [6]. The potential presence of susceptibility artefacts at air /tissue interfaces is a potential disadvantage of the application of gaseous agents for luminal distension in MR colonography. However, recent developments allow data acquisition with short echo-times and therefore this limitation can be largely overcome. Still, current available studies using room-air for colonic distension in MR colonography demonstrate divergent outcomes regarding feasibility [7,8].

As high-field strength imaging is now widely available for clinical purpose, 3.0T MR imaging is used for MR colonography [9]. Several technical issues, including tissue T1 and T2 relaxation parameters, specific absorption rate (SAR), susceptibility and chemical shift effects differ distinctively from 1.5T [10] and this may affect the use of 3.0T for MR colonography. On the other hand, the gain in signal-to-noise ratio can be used to increase spatial resolution and decrease acquisition times [9].

In order to give direction towards a future more elaborate study, purpose of this study was to assess the feasibility of automated insufflated carbon dioxide as luminal distending agent in MR colonography at 3.0T, particularly regarding the presence of susceptibility artefacts. As dark-lumen MR colonography can be combined with several bowel preparation regimes, we additionally studied CO2 insufflation in four different applied bowel preparation regimes in terms of image quality and burden.
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Materials and methods

Subjects
In this prospective feasibility study, volunteers without relevant medical history were consecutively recruited by public advertisement. Whereas this comprised a feasibility study, no power analysis was performed and for practical reasons sixteen volunteers were included. Exclusion criteria for this study were an age of less than 18 years or over 75 years, the inability to hold breath for 25 seconds, any suspicion of bowel perforation or obstruction in subjects’ medical history and general contraindications to undergo MRI or bowel preparation. This study was approved by the institutional review board and all participants gave informed consent. No evaluation of colonic or extracolonic abnormalities was performed in these normal volunteers.

Bowel preparation
Each subject was randomly allocated to one of four different preparation groups: A, B, C and D (Table 1). All groups received a low-fibre diet starting three days before the MRI. In group A, subjects received 10mL Gadolinium (dimegluminegadopentetate 0.5 mmol/ml (Magnevist; Schering, Berlin, Germany)) as oral contrast agent for faecal tagging with all major meals starting two days prior to the MR colonography, together with the ingestion of 12 grams lactulose (Lactulose CF powder 6g/sachet, Centrafarm, Etten-Leur, the Netherlands), once per day. Subjects in group B received 4 L polyethylene glycol electrolyte solution (KleanPrep; Helsinn Birex Pharmaceuticals, Dublin, Ireland), starting one day prior to the examination. In group C, subjects ingested 200mL 1 g/ml bariumsulfate (Micropaque, Guerbet, Aulnay-sous-Bois, France) three days prior to MR colonography with all major meals, together with a daily 12 g lactulose (Lactulose CF powder 6g/sachet). In addition subjects in group C were asked to avoid the consumption of high concentrations of manganese (e.g. chocolate), whereas this shortens T1 relaxation time and therefore potentially outweighing the darkening effect of bariumsulfate. In group D, subjects ingested a high-osmolar ionic monomer contrast agent (meglumine-ioxithalamate, 300 mg I/ml, Telebrix Gastro; Guerbert, Cedex, France); an analogous bowel preparation regime as recently proposed for CT-colonography [11]. One day prior to MR colonography examination, 50mL Telebrix was taken with all three major meals. A final 50mL was taken 1.5h before MR colonography.
CO₂ in MR colonography

MR colonography

MR colonography in supine position was performed at 3.0T (Intera, Philips Healthcare, Best, the Netherlands). A 16-channel phased-array surface coil (SENSE-XL-Torso) for signal reception was used and data was acquired with two data-stacks using software-controlled table movement (Figure 1). The automated table movement takes less than 30 seconds. Prior to data acquisition, the colon was automatically insufflated with CO₂ gas via a balloon-tipped flexible rectal catheter (20 French Gauge) with long tubing using an automated insufflator outside the MRI suite (Bracco, PROTOCO2L insufflator, New York, USA). While currently used automated insufflators are not MRI compatible, we extended the tube to insufflate CO₂ to approximately 7m, in order to cover the distance between the automatic device and subject. The extended insufflation system was tested as a closed system, in order to test the maximum rectal pressure shutdown and to prevent for any pressure drop.

Table 1. Characteristics on bowel preparations for each of the four different MR colonography approaches. Rows describe type of bowel preparation for each approach.

<table>
<thead>
<tr>
<th>groups</th>
<th>Bowel preparation</th>
<th>Bowel distension</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (n=4)</td>
<td>Low-fibre diet</td>
<td>Lactulose</td>
</tr>
<tr>
<td>B (n=4)</td>
<td>Low-fibre diet</td>
<td>Polyethylene glycol electrolyte solution</td>
</tr>
<tr>
<td>C (n=3)</td>
<td>Low-fibre diet</td>
<td>Lactulose</td>
</tr>
<tr>
<td>D (n=3)</td>
<td>Low-fibre diet</td>
<td>Telebrix</td>
</tr>
</tbody>
</table>

Controlled insufflation was started with the subject in a right lateral position, supine position, followed by a left lateral position and the subject then gradually turned to the supine position. The automated system was left active during the total examination. Data acquisition was started when approximately 3 L of CO₂ was insufflated into the colon. The maximum insufflation pressure was set at 20 mm Hg throughout the complete procedure which was reached by gradual increase of the insufflation pressure. The pressure was decreased if subjects reported pain or felt uncomfortable.

A smooth muscle relaxant (Buscopan; Boehringer-Ingelheim, Ingelheim, Germany or when contraindicated Glucagen; Novo-Nordisk, Bagsvaerd, Denmark) was administered intravenously before insufflation and prior to the 2D/3D data acquisition, 20 mg in total. No intravenous paramagnetic contrast agent was administered. Examinations were performed in supine position.
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Three-dimensional (3D) fat suppressed fast T1-weighted spoiled gradient-echo (fast field echo (FFE)) and two-dimensional (2D) T2-weighted (single-shot fast spin echo (SSFSE)) series were acquired in the coronal plane. Scan parameters were: 3DT1w-FFE: TR/TE 2.12/1.01 ms; FA 10°; No. of slices 90; FOV 540mm x 400mm; voxel 2.00mm x 2.00mm x 2.00mm; 2DT2w-SSFSE: TR/TE 475/60 ms; FA 90°; No. of slices 45; FOV 540mm x 400mm, parallel imaging factor (SENSE) 2, voxel: 2.00mm x 2.00mm x 3.00mm; slice gap 0; interleaved scan order. Breath hold was at maximum 18 seconds per data-stack. The refocusing angle (RA) of the 2DT2w-SSFSE was adjusted to 120° in order to prevent exceeding the Specific Absorption Rate (SAR) limit at 3.0T. The examination was limited to these sequences in supine position only, as the primary aim was to evaluate the presence of susceptibility artefacts.

Figure 1. 2D-T2w Single-Shot Fast Spin Echo (SSFSE) of a 51-year old normal healthy female volunteer after the insufflation of CO2 as negative luminal distending agent showing adequate overall colonic distension. Coverage of the entire colon included the acquisition of two linked image-stacks of the upper abdomen (a) and lower abdomen (b) using software-controlled table movement. For non-diagnostic purpose, the separate stacks can be fused into one image using the MR imaging system post-processing software (MobiView, Philips Healthcare) (c).
Data analysis
All data-stacks were separately analyzed on a dedicated post-processing workstation (View Forum, Philips Healthcare) by two observers, who were instructed to critically analyze the data-stacks and were blinded for the type of applied bowel preparation. Observer 1 (SJ), an abdominal radiologist, with a prior experience of >250 CT-colonography examinations and >250 MR colonography examinations [1]. The second observer (IF), a fourth-year resident in radiology, had evaluated over >600 CT-colonography examinations with colonoscopy verification and matched >120 CT-colonography and >250 MR colonography examinations with colonoscopy in previous studies [1, 12]. For evaluation purposes the colon was divided in six colon segments: cecum (S1), ascending colon (S2), transverse colon (S3), descending colon (S4), sigmoid colon (S5) and rectum (S6).

Both observers scored image quality regarding presence of (susceptibility) artefacts (3-point scale: 1 = absent; 2 = present; 3 = present and influencing evaluation) and diagnostic confidence (3-point scale: 1 = non-diagnostic, polyps ≥ 10 mm could be missed when it would concern a symptomatic patient or screening, 2 = diagnostic, only for polyps ≥ 10 mm, 3 = diagnostic, for polyps ≥ 6 mm) of both 3DT1w and 2DT2w series. Bowel-distension (3-point scale: 1 = optimal, 2 = adequate, 3 = poor) of both series was scored and outcomes were combined. An additional assessment was performed in order to discriminate between the presence of susceptibility artefacts and other artefacts.

Although the study was not primarily intended for evaluating bowel preparation schemes, the residual stool was evaluated for presence (4-point scale: 1 = 0-25%, 2 = 25-50%, 3 = 50-75%, 4 = 75-100%), composition (3-point scale: 1=liquid, 2=combined liquid/solid, 3=solid) and signal intensity (3-point scale: 1=low, 2=intermediate, 3=high signal intensity) in both sequences.

Questionnaires
Participants were asked to complete two questionnaires (based on previous questionnaires for MR colonography [5]). Both questionnaires evaluated the discomfort (5-point Likert scale: not, mild, adequate, severe and extreme); one questionnaire prior to MR colonography evaluated the discomfort of the bowel preparation. The second questionnaire was completed after MR colonography. Additionally, subjects were asked what they considered the most burdensome aspect of the examination.
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Statistical analysis
We used descriptive statistical analysis to evaluate study group characteristics, image quality and subject acceptance. Continuous data were expressed as mean±SD, and dichotomized data as number and percentage. Ordinal data were also expressed as mean±SD. In addition, each observation (multiple ratings per observer and per sequence), was considered as independent, and therefore per-segment outcomes consist of ratings for both observers and sequences. The total included number of subjects was too small for statistical assessment of inter-group and inter-observer differences.

Results
Subjects
Between January 6, 2009, and June 6, 2009, sixteen subjects provided written informed consent. Two subjects were unable to complete the MR colonography examination, data from fourteen subjects were available for study analysis (mean age 40.1 years ± 15.5 (standard deviation), range 18.5 - 67.7 years; M:F 8:6). Total insufflated C02 volume was 5.2 (SD±1.1) L.

 Artefacts and diagnostic confidence
No susceptibility effects were identified on both sequences. 3DT1w series were substantially more prone to artefacts than the 2DT2w series and were attributed to the presence of bowel motion. Observer 1 detected artefacts which influenced evaluation in 62 / 84 (74%) of the available colon segments on 3DT1w series, and in 27 / 84 (32%) of the segments on 2DT2w series. Observer 1 rated 6 / 84 (7%) and 17 / 84 (20%) of the segments as completely artefacts-free on 3DT1w and 2DT2w series, respectively.

Similar ratings were obtained from observer 2, detecting artefacts influencing evaluation in 60/84(71%) of the available colon segments on 3DT1w series, and in 32 / 84 (38%) of the segments on corresponding 2DT2w series. No segments on 3DT1w series were rated as artifact-free by the second observer compared with 22 / 84 (26%) segments on 2DT2w series. None of the colon segments were rated artifact free on 3DT1w series, 10 / 84 (12%) of the colon segments were rated artifact free on 2DT2w series by both observers. Diagnostic confidence ratings for each of the different MR colonography approaches showed most favorable results for 2DT2w series (Figure 2).
Figure 2. Diagnostic confidence was estimated on presence of artefacts, quality of bowel distension and subjective ability to differentiate bowel wall from the colonic lumen. Ratings on diagnostic confidence regarding 3DT1w and 2DT2w series combined for both observers and are stratified for each of the four different groups and combined for all colonic segments. (3-point scale: 1= non-diagnostic; polyps ≥ 10 mm could be missed when it would concern a symptomatic patient or screening; 2= diagnostic, polyps 6 - 9mm could be missed; 3 = diagnostic, polyps ≥ 6 mm might be visible).

Bowel distension
Overall distribution of distension showed adequate to optimal distension in 312/336 (93%) of the colon segments. In 12/336 (4%) segmental distension was poor. In three subjects the rectum was insufficiently visualized for proper analysis. Mean segmental bowel distension scores were distributed as follows: 1.2 (S1); 1.3 (S2); 1.3 (S3); 1.8 (S4); 1.9 (S5) and 1.3 (S6) with lower numbers indicating better distension (1.0 is optimal).
Evaluating the individual segments, the descending colon (S4) accounted for the highest number of poorly distended segments (n=6; 50%), followed by the sigmoid colon (S5) and rectum (S6) (both n = 3, 25%). No perceptible differences were observed in distension ratings between both sequences.

Presence, composition and signal intensity of residual stool
The total amount of residual stool visible on 3DT1w series was lowest in groups B and D (1.3 and 1.2 respectively) (Table 2). Stool composition was rated as homogenously liquid in all subjects of group D (mean value of 1.0) and relatively liquid in group B (mean value of 1.5) (Figure 3). In subjects receiving a barium-
based bowel preparation, the residual stool showed relatively high signal intensity on the 3DT1w series (mean 2.6).

**Figure 3.** Coronal 3D fat suppressed T1w-FFE without susceptibility artefacts, in a subject receiving polyethylene glycol electrolyte solution for bowel preparation and CO2 for colonic distension (group B) (a). Multiplanar reconstruction (MPR) allows the reconstruction of a transverse image showing a small amount of liquid stool with a relatively high signal intensity as compared to adjacent structures (b). Subject receiving iodine-based contrast agent for bowel preparation and CO2 for colonic distension (group D) (c), showing liquid stool with intermediate signal intensity in the proximal colon on corresponding (dotted line) reconstructed transverse image (d).

**Discomfort score**

None of the participants rated the bowel preparation extremely burdensome regardless of preparation (**Figure 4**). Comparing the discomfort caused by the bowel preparation, MRI-examination including CO2 insufflation and preparation plus MRI-examination combined, the type of bowel preparation mainly determined the overall experienced burden during the MR colonography examination in all four groups. The most burdensome aspect of the complete
examination for groups A - D combined was the execution of breath-holds (4/14 participants) during the MR examination.

Figure 4. Discomfort scores sorted for each of the four different groups (A - D) regarding the burden of bowel preparation (a), of the MRI examination (b) and of both bowel preparation and MR colonography combined (c).

Discussion
In this feasibility study, evaluating the use of automated insufflation of carbon-dioxide (CO₂) for luminal distension in 3.0T MR colonography, we found no susceptibility artefacts on either 3DT1w or 2DT2w series. Overall adequate to optimal colonic distension was found. The diagnostic confidence was inferior for 3DT1w series as compared to the 2DT2w series, which was most likely related to the presence of bowel motion related artefacts.

Until now, concerns regarding the presence of susceptibility artefacts using gaseous distending media in MR colonography favoured the use of water-based distending agents. Only a few studies on a small number of patients have studied the use of gaseous agents for luminal distension in MR colonography, either by manually inflated room air [7,8,12,13,14] or by manually inflated CO₂ [15]. In a comparative study, Ajay et al. reported a higher CNR and better colonic distension using manually inflated air for colonic distension, if compared to the use of conventional water-based colonic distension in 50 patients at increased risk for CRC [7]. Importantly, the presence of air in the colonic lumen was not associated with susceptibility effects. In a comparable study design, 83 patients at increased risk for CRC underwent MR colonography using either water or air for colonic distension [8]. Air distension evidently proved inferior to water-based distension in most quality aspects. The artefacts as observed in the air-based distension group were largely attributable to susceptibility effects. The discordant findings between these two studies can be explained by the substantial difference.
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Table 2. Ratings for amount, composition and signal intensity of residual stool for each different bowel preparation (A-D) per segment (S1-S6).

<table>
<thead>
<tr>
<th></th>
<th>3D-T1w FFE</th>
<th>2D-T2w SSFSE</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S1</td>
<td>S2</td>
<td>S3</td>
</tr>
<tr>
<td><strong>Amount</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group A</td>
<td>2.0</td>
<td>1.5</td>
<td>1.3</td>
</tr>
<tr>
<td>Group B</td>
<td>1.3</td>
<td>1.4</td>
<td>1.3</td>
</tr>
<tr>
<td>Group C</td>
<td>2.0</td>
<td>1.8</td>
<td>1.7</td>
</tr>
<tr>
<td>Group D</td>
<td>1.2</td>
<td>1.6</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Composition</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group A</td>
<td>2.0</td>
<td>2.0</td>
<td>2.1</td>
</tr>
<tr>
<td>Group B</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Group C</td>
<td>2.3</td>
<td>2.3</td>
<td>2.1</td>
</tr>
<tr>
<td>Group D</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Signal Intensity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group A</td>
<td>2.9</td>
<td>2.9</td>
<td>2.8</td>
</tr>
<tr>
<td>Group B</td>
<td>2.8</td>
<td>2.7</td>
<td>2.3</td>
</tr>
<tr>
<td>Group C</td>
<td>2.7</td>
<td>2.7</td>
<td>2.7</td>
</tr>
<tr>
<td>Group D</td>
<td>2.0</td>
<td>2.5</td>
<td>2.0</td>
</tr>
</tbody>
</table>

*Unable to characterize; Mean = mean value of available segments

In applied echo sequence parameters. In our study the use of 3.0T imaging allowed the use of fast imaging sequences with a short echo-time (TE), which is a similar TE as applied by Ajaj et al. [7]. The use of such short echo-times practically excludes the presence of artefacts at the interface between luminal gas and soft tissue colonic wall.

Insufflation of CO₂ is considered preferable to room air because of the better absorption and consequently less post-procedural discomfort. Its use has been propagated in a current consensus statement of CT colonography [16]. Yet, the rapid absorption of CO₂ by the bowel wall, might lead to varying colonic distension in a prolonged data-acquisition setting like MR colonography [7]. By the use of continuous automated CO₂ insufflation, we were able to avoid a potential decrease in distension during data-acquisition. To our knowledge this is the first study which describes the use of automated insufflation of CO₂ for luminal distension in MR colonography.
CO\textsubscript{2} in MR colonography

A number of different bowel preparation methods have been proposed in MR colonography [4]. Dark lumen strategies generally use barium-based approaches as oral tagging agent, although its use in air-based distending methods is reported to result in inferior image quality [8,12]. We hypothesized that the oral ingestion of gadolinium together with the ingestion of a stool softener (group A), would result in fluid tagged stool with luminal contrast ratios similar to CT colonography. However, comparable to the barium-based approach (group C), the gadolinium-based approach resulted in relatively high-signal intense sticky residual faeces throughout the colon.

On 3DT1w series, residual stool was observed in all four bowel-preparation approaches with the smallest liquid volumes scored in groups B and D. In group D, the bowel content was liquid by the laxative effect of the iodine and rated as having slightly lower signal intensity when compared to other preparation methods. Moreover, the amount of total residual faecal material was relatively small, which is in concordance to the findings as recently reported for CT-colonography [11].

This feasibility study has recognized limitations. Firstly, the total number of included subjects was small and therefore the qualitative results are too small to study statistical significant differences between observations. Yet, the current study was primarily aimed to assess feasibility of using CO\textsubscript{2} for colonic distension in MR colonography, in order to give direction towards a future more elaborate clinical study. Thence only supine datasets were acquired as we primarily focused on technical feasibility. This will ultimately have influenced current study results since double position scanning, as routinely applied in colonography, is mandatory for sufficient distension [17]. Also, this may have ultimately influenced the burden of participants.

In dark lumen MR colonography, intravenous administration of paramagnetic contrast agent is used in order to improve the contrast between the low intense colonic lumen and colonic wall. Nonetheless, this study was performed in normal healthy volunteers and in order to prevent any gadolinium side effects, we did not use intravenous contrast agent. Consequently, the subjective image quality ratings including the diagnostic confidence, as scored by both observers, will ultimately differ when compared to a diagnostic setting with colonic wall enhancement. Among others this will differ due to post-processing automatic scaling. It also prevents a practical objective evaluation (contrast-to-noise ratio, CNR) of image quality on the T1-weighted series [7,18].
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In our study, a spasmylytic agent for both optimizing bowel distension and minimizing bowel motion was administrated intravenously in two aliquots, prior to the rectal filling process and 2D/3D data-acquisition. However, the second injection was not performed directly prior to the 3DT1w data-acquisition and in addition, 3D data-acquisition was rather lengthened with the use of software-controlled table movement. When taking into account the relatively short half-life of the administered spasmylytic agent, these issues might largely explain the presence of bowel motion artefacts as observed in the fast gradient echo series. In addition, data acquisition was performed with an active insufflation system and it is indefinable whether continuous pumping during data acquisition has been a source of the perceptible motion artefacts. Besides the injection timing, either increasing the total dosage of spasmylytic agent or the intramuscular administration of N-butylscopolamine for minimizing peristalsis can be considered [19].

In conclusion, this study demonstrates that MR colonography using automated insufflation of CO2 for colonic distension, similar as currently applied in CT colonography, is technically feasible and is not associated with susceptibility artefacts. Nonetheless, in this study image quality was substantially impaired by motion artefacts, therefore refining the protocol regarding certain essential aspects (eg. impact of spasmylytic agents) is necessary in order to make this technique applicable in a clinical setting. Future prospective clinical studies are warranted in order to determine the exact diagnostic performance and acceptance of this technique in MR colonography.
CO₂ in MR colonography

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