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Magnetic resonance colonography without bowel cleansing using oral and rectal stool softeners (fecal cracking)—a feasibility study

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Abstract The aim of our study was to assess the effect of oral and rectal stool softeners on dark-lumen magnetic resonance (MR) colonography without bowel cleansing. Ten volunteers underwent MR colonography without colonic cleansing. A baseline examination was performed without oral or rectal administration of stool softeners. In a second set, volunteers ingested 60 ml of lactulose 24 h prior to MR examination. In a third examination, water as a rectal enema was replaced by a solution of 0.5%-docusate sodium (DS). A fourth MR examination was performed, in conjunction with both oral administration of lactulose and rectal application of DS. A T1-weighted data set was acquired at scanning times of 0, 5 and 10 min after colonic filling. A fourth data set was acquired 75 s after i.v. injection of contrast agent. Signal intensity of stool was calculated for all colonic segments. Without oral ingestion of lactulose or rectal enema with DS stool signal intensity was high and did not decrease over time. However, lactulose and DS caused a decrease in stool signal intensity. Both substances together led to a decreasing signal intensity of feces. Combination of lactulose and DS provided the lowest signal intensity of stool. Thus, feces could hardly be distinguished from dark rectal enema allowing for the assessment of the colonic wall.

Keywords Magnetic resonance imaging · Lactulose · Docusate sodium · Stool signal intensity · Fecal cracking

Introduction

Colonic polyps are common, found in 10% of adults [1, 2], and become more frequent in older adults, with a prevalence of 20% in the age group >60 years. Up to 90% of colorectal cancers develop from benign adenomas by a series of genetic alterations: the adenoma–carcinoma sequence [3]. Colorectal cancer is an important cause of morbidity and mortality in the western world and is the second most common cancer after bronchial cancer (in men) and breast cancer (in women). The current consideration is that colorectal cancer is preventable if all ade-

nomas are removed before they have the chance to progress to cancer [3, 4].

Conventional colonoscopy (CC) is considered the reference standard for the evaluation of the colon and its pathologies [4–6]. A good preparation of the large bowel is crucial for the reliable detection of colonic pathologies [7, 8]. Virtual computed tomography (CT) and magnetic resonance (MR) colonography have shown a high diagnostic accuracy for the detection of colorectal pathologies. To date, virtual colonography mandates bowel cleansing in a manner similar to colonoscopy. Since more than half of the patients undergoing bowel preparation complain about negative side effects, patients' acceptance is negatively influenced [9, 10]. To assure high patient acceptance of MR colonography, bowel cleansing could be eliminated [8].

For MR colonography without bowel cleansing the stool needs to be made dark in order to provide contrast against polyps or masses. The aim of the study was to assess the effect of lactulose as an oral stool softener and docusate sodium (DS) as a rectal stool softener on dark-lumen magnetic resonance colonography (MRC) without prior colonic cleansing.

Materials and methods

Subjects

The study was performed according to good clinical practice (GCP) rules and was approved by the local ethics committee. Written informed consent was obtained from all volunteers, who were not charged for the examination.

Ten healthy volunteers (seven men, three women, range 27–46 years, mean age 43.6 years) without a history of colorectal pathologies underwent MRC without bowel cleansing on four separate days.

MRC examination

No specific diet was necessary. However, so that we could standardize the primary consistency of feces the volunteers were asked to eat similar meals 2 days prior to the respective MRC examinations. All examinations were performed on a 1.5-T system (Magnetom Sonata, Siemens Medical Systems, Erlangen, Germany) equipped with high-performance gradient systems characterized by a maximum gradient amplitude of 40 mT/m and a slew rate of 200 mT/m per ms. For signal reception a set of two large 'flex surface coils' was used. Each volunteer underwent four different contrast-enhanced MR protocols. There was a minimum time lag of 7 days (range 7–10 days) between two single examinations.

As a first set of experiments, a baseline examination was performed without oral or rectal administration of stool-softening agents. After the placement of a rectal tube (E-Z-Em, Westbury, N.Y., USA) 40 mg of scopolamine (Buscopan; Boehringer Ingelheim, Germany) to minimize bowel peristalsis were slowly administered intravenously through a 100 ml saline solution over 10 min. During that time the colon was filled, while the patient lay in a prone position, with 2,000–2,500 ml of tap water under hydrostatic pressure (1.0–1.5 m water column). After the enema filling of the colon a T1-weighted, 3D gradient echo, volumetric interpolated breath-hold examination (VIBE) sequence, with integrated fat suppression, was acquired in the coronal plane over 22 s in a single breath-hold at scan times of 0, 5 and 10 min. An additional data set was acquired with identical examination parameters after intravenous administration of Gd-BOPTA at a dose of 0.2 mmol/kg (MultiHance, Bracco, Milan, Italy) and a flow rate of 3 ml/s and a delay of 75 s. Sequence parameters included: TR/TE 3.1/1.1 ms, flip angle 12°, field of view (FOV) 400 mm×400 mm, matrix 168×256 pixels, and, by zero filling interpolation, a slice thickness of 1.6 mm to 2.0 mm, depending on the thickness of the volunteers, the total number of the calculated slices was 96. After MRC the enema water was led back into the enema bag and the patients went to the bathroom.

In a second set of experiments, all volunteers were asked to ingest 60 ml of lactulose (Bifiteral Sirup, Solvay Arzneimittel, Hanover, Germany, 0.5 g lactulose/ml) in a volume of 20 ml with each of three principle meals beginning 24 hours prior to MR colonography. The rectal enema (tap water) and data acquisition were performed similarly to the first examination. For the third examination the volunteers did not ingest any lactulose; however, water as a rectal enema was replaced by a solution of 0.5% docusate sodium. The data acquisition was performed similarly to the first and second examinations. Eventually, the fourth MR examination was performed in conjunction with both the oral administration of 60 ml lactulose and the rectal application of 0.5% docusate sodium solution (Table 1).

Data analysis

For each subject, native and contrast-enhanced 3D MRI data sets were transferred to a post-processing workstation (Virtuoso, Siemens Medical Solutions, Erlangen, Germany). The data sets were assessed in consensus by two board-

Table 1 The four different protocols of dark–lumen MRC

Examination no.	Oral ingestion	Rectal enema
1	Without lactulose	Water enema
2	60 ml lactulose	Water enema
3	Without lactulose	Solution of 0.5% docusate sodium
4	60 ml lactulose	Solution of 0.5% docusate sodium

certified radiologists with special training in magnetic resonance imaging in the multiplanar reformation mode, which permitted scrolling through the 3D data sets in all three orthogonal planes. For analysis the colon was divided into six segments: rectum, sigmoid colon, descending colon, transverse colon, ascending colon, and cecum.

Stool quantity

The quantity of stool visible in all colonic segments was assessed and classified as: 1=no stool, 2=little stool, 3=moderate stool, 4=severe stool.

Stool signal intensity and signal-to-noise ratio of stool

To assess the effect of both substances, stool intensity was measured for all colonic segments including cecum, ascending/transverse/descending/sigmoid colon and rectum. For this purpose, the coronal MR images were magnified three-fold. Regions of interest (ROIs) were placed in the lumen of all segments. Image noise, defined as the standard deviation (SD) of signal intensities measured in an ROI placed outside the body, was determined. Based on these measurements the signal-to-noise ratio (SNR) was calculated: SNR=[SI (colonic lumen)/SI (SD)].

Side effects

Twenty-four hours after each MR examination the volunteers were questioned regarding side effects such as diarrhea, flatulence, vomiting or abdominal spasms. For this purpose a standardized questionnaire was used, which was based on a 4-point scale (0=no side effects, 1=mild side effects, 2=moderate side effects, 3=severe side effects).

Statistical analysis

Qualitative results concerning the grade of stool quantity, as well as stool intensity, and the grades of discomforts were compared using the Wilcoxon rank test for each pair separately. For all statistical analyses, a P value <0.05 was considered to indicate a statistically significant difference.

Results

All ten volunteers tolerated the MR examination well, and no complications were observed. Good image quality was achieved in all sets of experiments.

Side effects

Neither the oral nor the rectal administration of lactulose/docusate sodium solution adversely affected the volunteers' acceptance. The highest degree of diarrhea was observed following the oral ingestion of lactulose and rectal enema containing 0.5% docusate sodium (mean value 1.6). The only ingestion of lactulose led to the lowest degree of diarrhea (mean value 1.3). The rectal enema containing 0.5% docusate sodium did not lead to abdominal spasms. No side effects concerning nausea and vomiting were observed after oral ingestion of lactulose or rectal enema containing water or 0.5% docusate sodium solution (Fig. 1).

Stool quantity

Without oral ingestion of lactulose there were no statically significant differences in any of the colonic segments; the mean value of all colonic segments amounted to 3.5. With regard to the presence of stool in all colonic segments, the

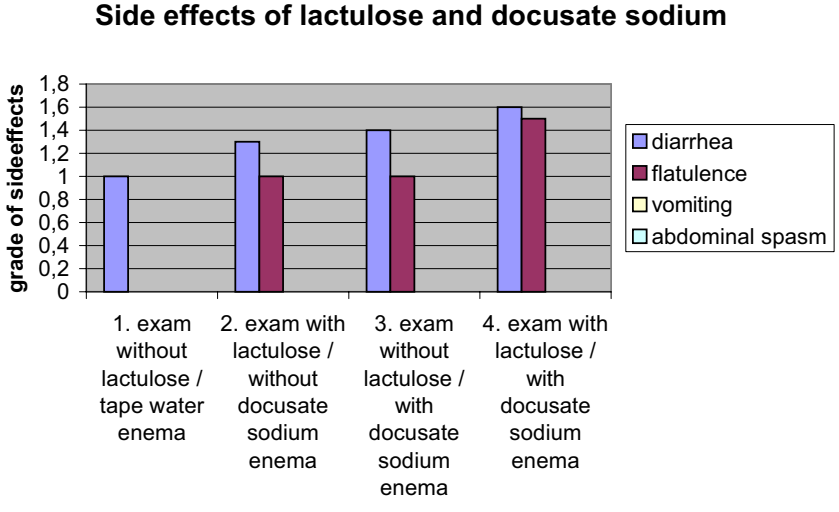

Fig. 1 Side effects of lactulose and docusate sodium as oral and rectal softeners. Primarily diarrhea and flatulence both lead to mild side effects, but no abdominal spasms were observed

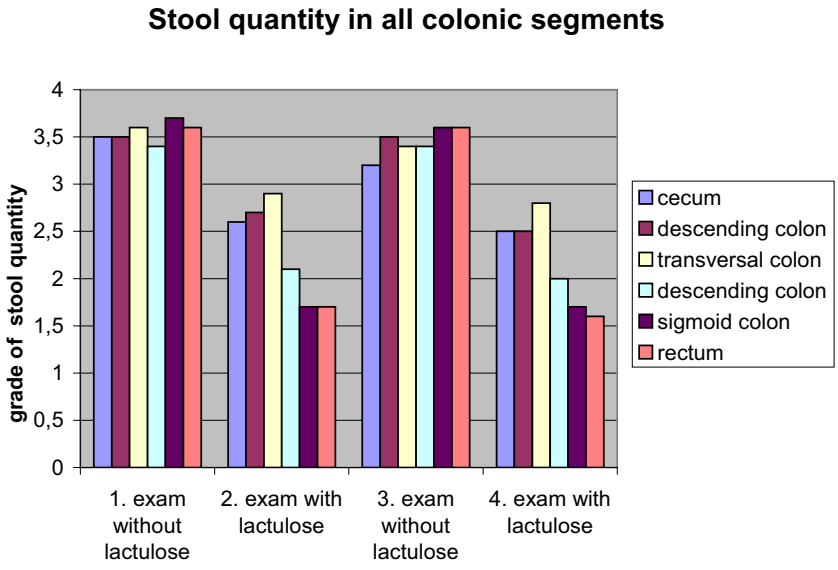

Fig. 2 The ingestion of lactulose led to a statistically significant reduction of stool quantity in all colonic segments

oral ingestion of lactulose led to statistically significant reduction of the stool quantity in all colonic segments. Best results of stool quantity after oral ingestion of lactulose were documented in the rectum and sigmoid colon, with mean values of 1.5 and 1.7. Stool quantity was poorest in the cecum and transversal colon, with a mean value of 2.2 and 2.6, respectively (Fig. 2).

Signal intensity and SNR of stool

First examination (no oral ingestion of lactulose, water rectal enema)

Without the application of lactulose the lowest SNR of stool after the water rectal enema was found in the cecum,

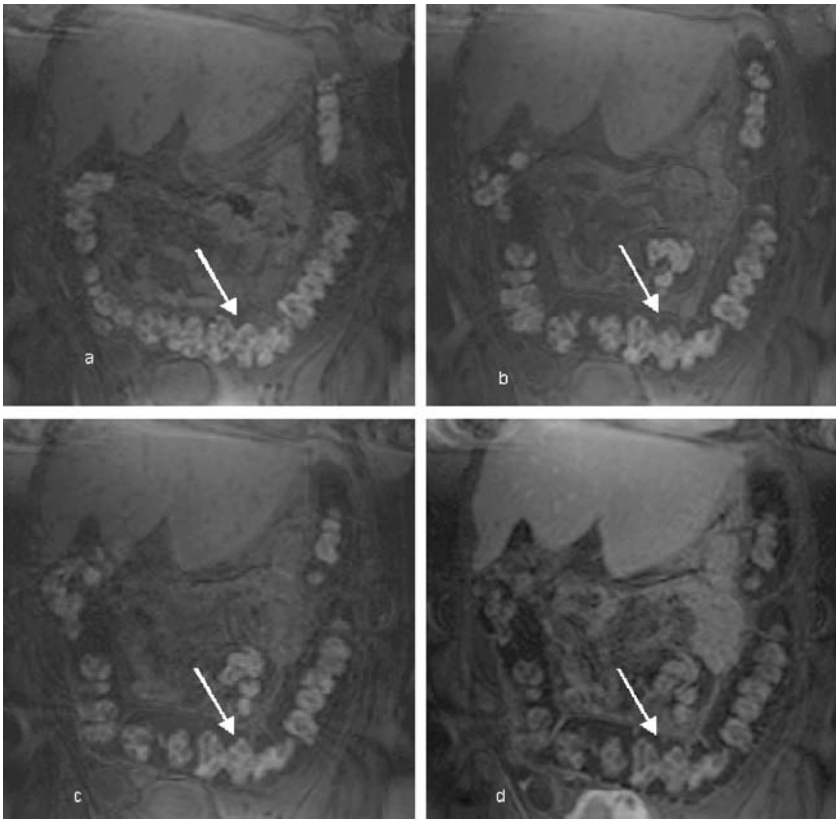

Fig. 3 Coronal source images of T1-weighted 3D GRE (TR/TE 3.1/1.1, flip 12°) scan of a 24-year-old female volunteer undergoing a, MRC examination at baseline without administration of oral or rectal stool softener in conjunction with rectal application of water. Bright colonic stool impedes the assessment of the bowel wall (*arrows*). The water enema did not lead to a decrease in signal intensity of stool over time. 0 min (**a**), 5 min (**b**) and 10 min (**c**): coronal source images of the same volunteer acquired 75 s after i.v. administration of gadolinium. The colonic wall is brightly enhanced but cannot be easily delineated from the background of a bright colonic lumen

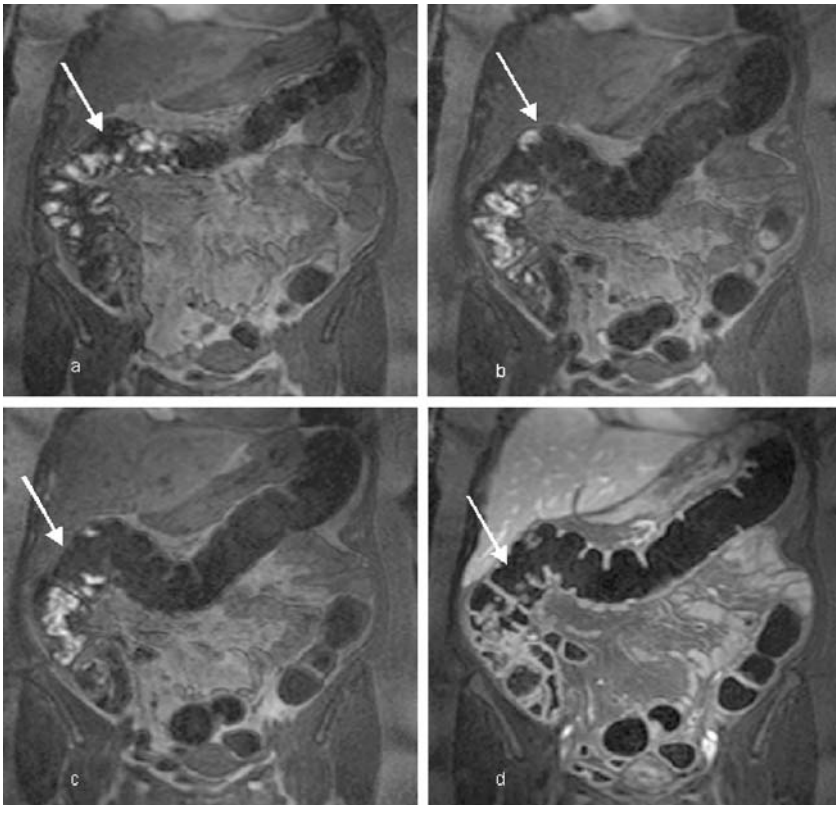

Fig. 4 Coronal images of 30-year-old male volunteer undergoing MRC after oral ingestion of 60 ml lactulose. The stool in the cecum at 0 min after rectal enema with water (**a**, *arrow*) appears bright; however, it is dark in the transverse colon. Five minutes and 10 min after the rectal enema (**b** and **c**) the stool darkening increases over time but stays bright. After i.v. injection of contrast agent the colonic wall of the cecum cannot be easily delineated from the colonic wall (**d**, *arrow*)

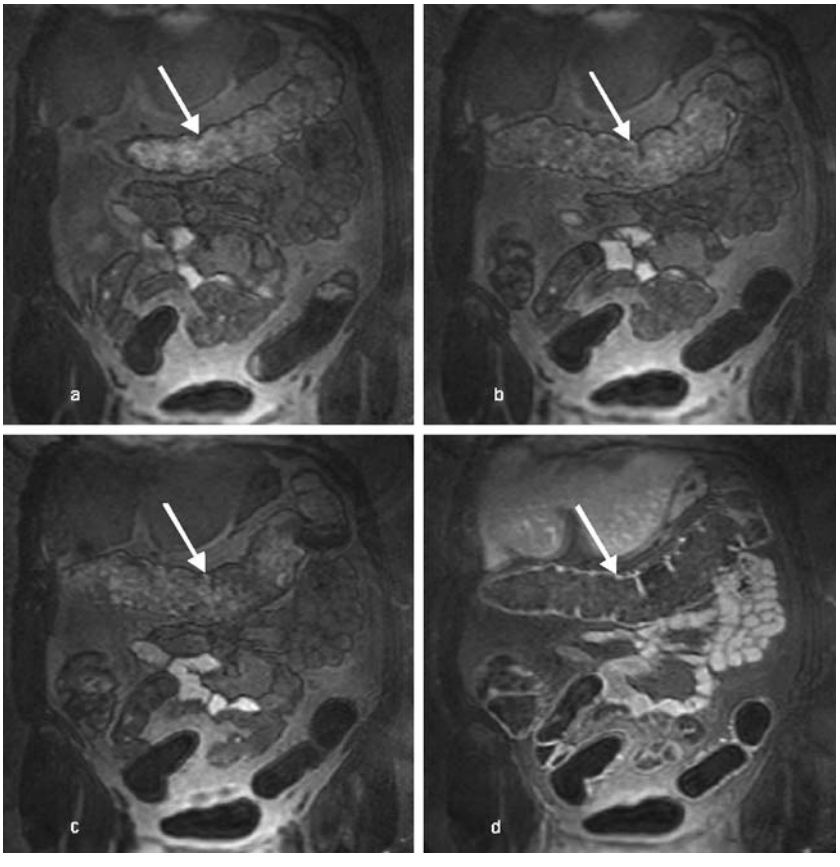

Fig. 5 Female volunteer undergoing MRC without oral ingestion of lactulose but with rectal enema containing 0.5% of docusate sodium solution. The bright stool within the transverse colon (**a**, *arrow*) decreasing in signal intensity, soaks (**b**, *arrow*) and cracks (**c**, *arrow*). On **d** after i.v. injection of contrast agents the colonic wall of can be easily delineated from the colonic lumen (*arrow*)

with a mean value of 39 at scan time 0 min decreasing to 37 at scan time 10 min after the water rectal enema. However, the highest SNR was seen in the rectum, with an average value of 54 at scan time 0 min, which decreased to 51 at scan time 10 min (Fig. 3a–d).

Second examination (oral ingestion of 60 ml lactulose, water rectal enema)

The oral ingestion of lactulose led to a reduction of SNR in all colonic segments. The highest SNR was seen in the transverse colon and amounted to 37 at scan time 0 min and decreased to 32 at scan time 10 min after rectal water enema and in the rectum from 33 to 31 (Fig. 4a–d).

Third examination (no oral ingestion of lactulose, rectal enema with 0.5% docusate sodium)

The rectal administration of 0.5% docusate sodium solution led to a decrease of SNR in the cecum from 37 at scan time 0 min to 33 at scan time 10 min after rectal enema and in the rectum from 48 to 39 (Fig. 5a–d).

Fourth examination (oral ingestion of 60 ml lactulose, rectal enema with 0.5% docusate sodium solution)

The use of both the oral and rectal stool softeners revealed the highest decrease in SNR of stool in all colonic segments. The lowest SNR of stool was found in the rectum and was 30 at scan time 0 min and decreased to 23 at scan time 10 min after rectal enema. The highest SNR in the transverse colon decreased from 33 at scan time 0 min to 25 at scan time 10 min after rectal enema (Fig. 6a–d).

The changes in SNR of stool in all colonic segments are listed in Fig. 7. In all ten healthy volunteers no pathologies of the colonic wall were seen.

Discussion

The presented data carry three messages we believe to be important: (a) oral ingestion of lactulose reduces the quantity and signal intensity of stool in all colonic segments; (b) the use of docusate sodium solution as a rectal enema reduces the signal intensity of stool in all colonic segments; (c) the signal intensity of fecal material in the colon can be significantly decreased by both the oral administration of lactulose and the use of a rectal enema consisting of a docusate sodium solution.

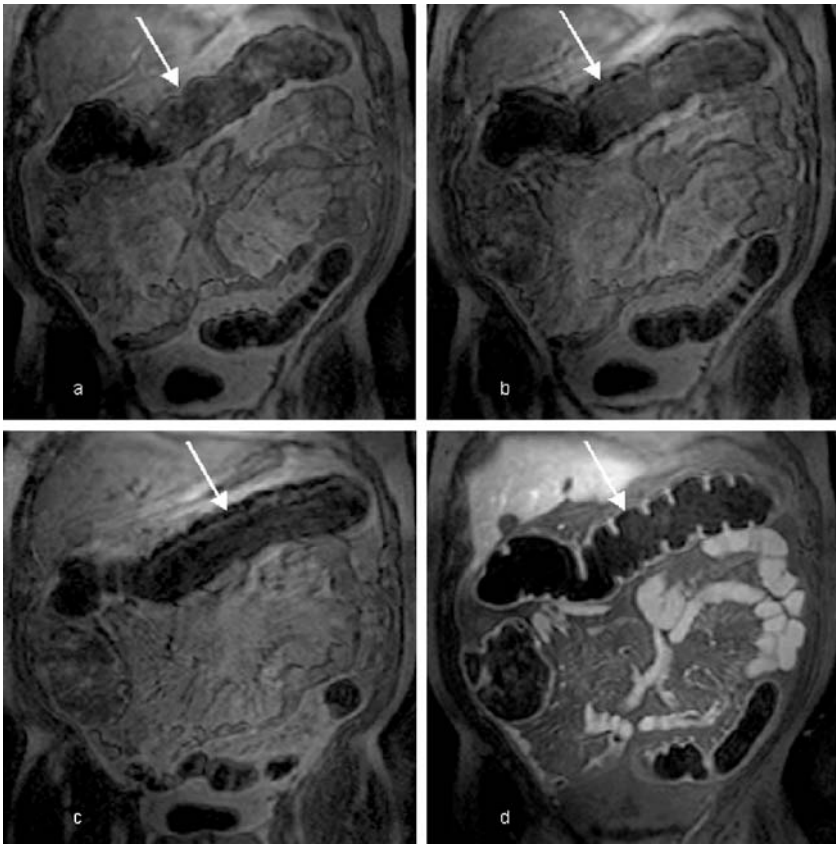

Fig. 6 Volunteer undergoing MRC after oral ingestion of 60 ml lactulose and rectal enema with docusate sodium. The stool is already dark on the T1-weighted sequence at scan time 0 min after the rectal enema (**a**, *arrow*). Over time (5 min, **b** and 10 min, **c**) the stool intensity decreases by soaking and cracking of the stool (*arrows*). Seventy-five seconds after i.v. injection of contrast agents (**d**) the colonic wall can be more easily delineated from the dark colonic lumen (*arrow*)

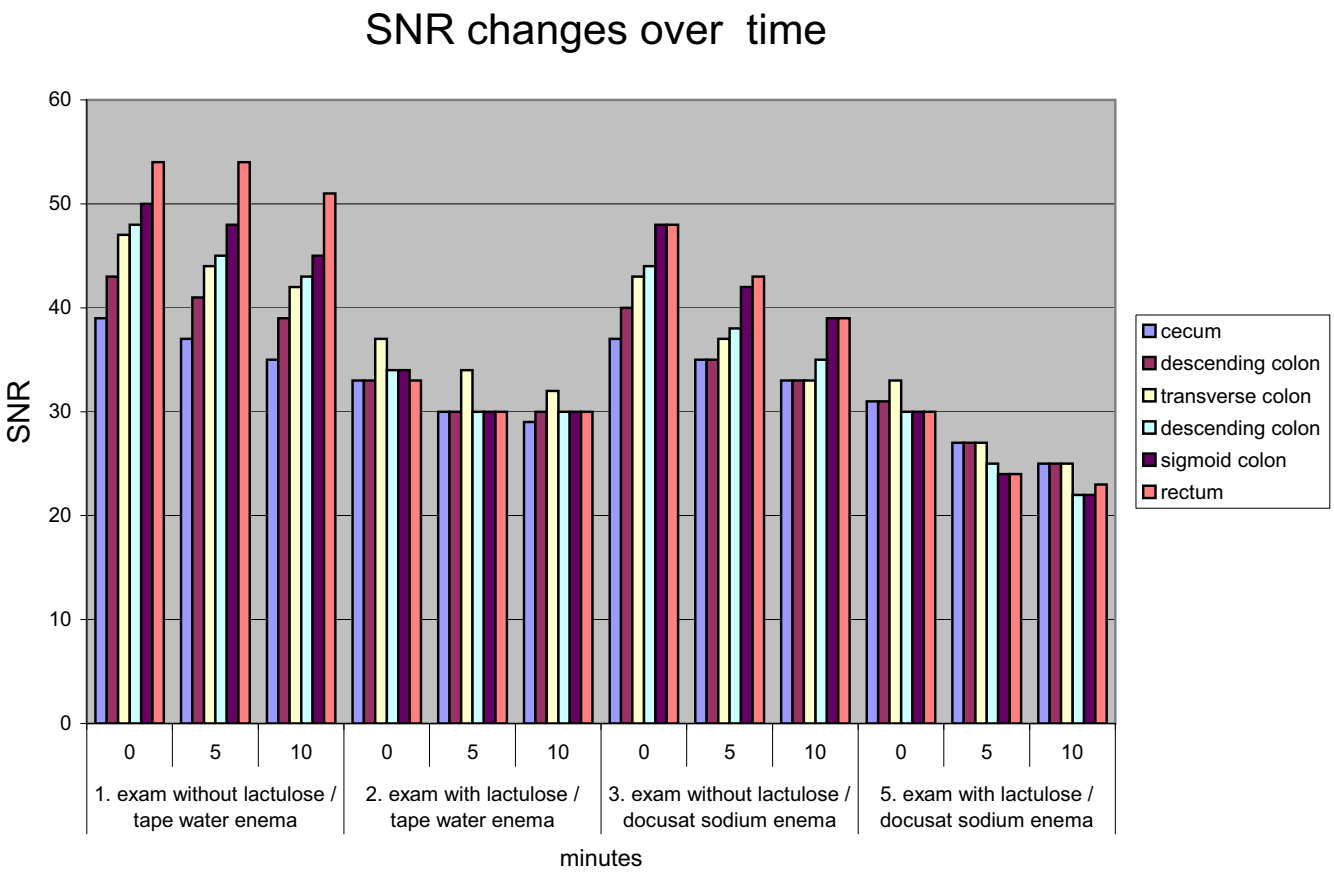

Fig. 7 Both substances together decreasing the stool signal intensity by entrance of water in the stool, which has a positive effect on T1-weighted MRI

Conventional colonoscopy is considered the gold standard for the detection of colorectal pathologies [4–6]. Invasiveness, procedure-related discomfort, bowel cleansing and poor patient acceptance have driven the exploration of alternatives to endoscopy for diagnosing colorectal pathologies. Thus, the use of endoluminal sonography, virtual CT and magnetic resonance tomography for these purposes have been well described [7, 8, 11, 12]. However, similarly to conventional colonoscopy, bowel cleansing is necessary to assess the colonic wall and its pathologies. With regard to bowel preparation, the patient's acceptance is negatively affected due to many symptoms, ranging from persistent diarrhea, to feeling unwell, to inability to sleep. To assure high patient acceptance for virtual colonography, bowel preparation needs to be eliminated. Thus, new concepts based on fecal tagging were developed for virtual colonography in computed tomography and magnetic resonance tomography [13–16]. CT colonography has some advantages regarding spatial resolution, examination costs and scanner availability. However, exposure to the ionizing radiation of CT colonography (CTC) casts a shadow, particularly in view of the patients' young age [17–19]. Hence, efforts have been focused on MR colonography [8]. The concept of fecal tagging is based on the oral ingestion of barium sulphate over 2 days at a dosage of 200 ml per meal for the six principle meals [13, 14]. This leads to homogeneous distribution of barium sulphate in the stool. In addition, unsurpassed soft tissue contrast renders MRI attractive as a possible alternative imaging modality for colorectal screening.

Dark-lumen MRC, combining an aqueous enema with intravenous administration of gadolinium-based contrast agents, is a rapidly evolving, almost non-invasive method for the evaluation of the entire colon. Results of several preliminary studies indicate that this technique has a high sensitivity for the detection of colorectal pathologies [8]. Dark-lumen MRC is based on focal uptake of T1-shortening contrast material in colonic lesions, which are displayed as bright areas on T1-weighted sequences, whereas the lumen is rendered totally dark due to material with long T1 relaxation times, such as water or oral barium or gastrografin [20, 21]. Thus, gadolinium-enhanced MRI of the bowel has been shown to be more accurate than unenhanced MRI and has also advantages over T2-weighted MRI [22].

According to our results, a restricted diet strategy to reduce fecal signal for dark-lumen MRC is unlikely to be successful. Moreover, reduction of the signal of the stool

can be achieved by an increase of the water content of stool. This can be achieved in two ways: (a) the oral ingestion of stool softeners such as lactulose, (b) the application of rectal stool softener such as docusate sodium.

The choice of lactulose and docusate sodium was based on previous studies [23–27]: laxative treatments in constipation are associated with increases in bowel movement frequency and improvement of stool consistency. Laxatives with softening action appear to be more active than bulk laxative in stool frequency and stool consistency.

Lactulose is a disaccharide and is fabricated from lactose. Lactulose is used as an oral laxative in constipation to soften the stool and is given over the day with the principal meals. The maximum daily dose of lactulose is 30 g/day. In high doses lactulose exhibits laxative properties. The 60 ml lactulose syrup in our study contained 30 g lactulose [28]. Lactulose is a laxative with microbiological effects and reaches the colon unmetabolized where it is metabolized by the bowel flora to acetic acid and lactate, which affect osmosis and stimulate bowel peristalsis. This enhances the secretion of water from the colonic wall in the colonic lumen [23–25]. The increased water in the colonic lumen makes the stool more liquid and voluminous [28]. This does not cause diarrhea. Thus, the water content of stool increases, which leads to positive effects on T1-weighted MRI.

Docusate sodium (sodium 1,4-to (2-ethylhexyl)-1,4-dioxobutan-2-sulfate, dioctyl sodium sulfosuccinate) is a detergent agent [26, 27] used as drug in gastroenterology and otorhinolaryngology. It is used as a rectal stool softener, with a fast effect within 10 min, and is given usually as an enema combined with glycerol (Norgalax Miniklistier, Norgine GmbH, Marburg, Germany). Glycerol as a lubricant and bowel stimulant accelerates defecation. Thus, the stool can be more easily pushed out from the large bowel. In our study we did not aim to cause defecation so we just used the docusate sodium solution. Docusate sodium has a soapy effect and reduces the surface tension of the stool. Thus, it facilitates the entry of water into the stool, which soaks and than cracks. In addition, docusate sodium is used as ear drops to dissolve cerumen (Otitex, Suedemedica GmbH, Munich, Germany).

Without the application of lactulose or docusate sodium the mean SNR of feces in the rectum was 54 on the first data set and 51 after a 10-min delay. The sole oral administration of lactulose led to a decrease of SNR in the rectum to 33 (31 after a 10-min delay). The sole rectal administration of docusate sodium resulted in a mean SNR of stool in the rectum of 48 (39 after a 10-min delay). The use of both oral and rectal stool softeners revealed the highest loss of SNR, with average values of 33 (25 after a 10-min delay), thereby allowing reliable discrimination between the colonic lumen and the colonic wall.

In conclusion, the signal intensity of fecal material in the colon can be significantly decreased by the combination of an oral administration of lactulose and the use of a rectal enema consisting of a docusate sodium solution. The administration of both substances was well accepted and did not lead to any harmful side effects. Following the rectal enema, consisting of docusate sodium, a delay of 10 min before the start of data acquisition is useful in order to obtain the best results. Owing to the simple examination protocol, a high patient acceptance can be achieved for MRC without the need for bowel cleansing. Further studies are needed to prove the clinical usefulness of this new technique in patients with colonic pathologies.

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