

Clinical use of MRI: Virtual Dark-Lumen MR Colonography: Technique, Application and Accuracy

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الاستخدامات السريرية للتصوير بالرنين المغناطيسي

تنظير القولون باستخدام الرنين المغناطيسي وبطريقة التجويف الداكن الظاهري:

التقنية، التطبيق والدقة

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الملخص: تنظير القولون بالطريقة التقليدية بواسطة المنظار هو الطريقة المتعارف عليها عالميا والاكثر دقة للكشف عن أمراض القولون. نظرا لان هذه الطريقة تداخلية وتؤدي في بعض الاحيان الى عدم ارتياح المرضى, انعكس ذلك سلبا على تقبلها لدى عدد كبير من المرضى المزمع اجرائها لديهم. في السنوات القليلة الماضية تبين أن استخدام الرنين المغناطيسي لتنظير القولون اصبح أداة مناسبة لكشف و تشخيص أمراض القولون. لقد تم استخدام تقنيه جديده لتنظير القولون بواسطة الرنين المغناطيسي تسمى التجويف الداكن الظاهري حيث تعتمد هذه الطريقة على تصوير القولون بعد ملئه بالماء الفاتر بواسطة حقنة شرحية وبعد اعطاء ماده ملونه عن طريق الوريد. هذه المقالة تستعرض التقنية الجديدة لتنظير القولون بطريقة التجويف الداكن الظاهري من حيث طريقة عملها, طريقة الحصول على الصور و تحليلها. بالاضافه الى ذلك يبين هذا المقال كيفية تطبيق هذه الطريقة و دقتها. علاوه على ذلك يشير هذا المقال إلى مزايا هذه الطريقة بالمقارنة مع تنظير القولون بالطريقة التقليدية. كما يناقش هذا المقال تقنيات جديدة لتحسين قبول المريض لهذه الطريقة و لزيادة دقة التشخيص.

مفتاح الكلمات: تنظير القولون بالطريقة التقليدية، تنظير القولون الظاهري، تنظير القولون بالرنين المغناطيسي و بطريقة التجويف الداكن الظاهري, ماده الملونه, امراض القولون و المستقيم.

ABSTRACT: Conventional colonoscopy represents the gold standard for the detection of colorectal pathologies. However, due to its invasiveness and procedure-related discomfort, patient acceptance is sometimes poor. In the last few years, the use of MR Colonography has been shown to be an appropriate diagnostic tool for the detection of colorectal pathologies. Dark-lumen MR Colonography has been introduced. This technique is based on the acquisition of a T1-weighted sequence following the administration of a water-enema and the intravenous administration of paramagnetic contrast.

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This review article describes the underlying technique of dark-lumen MR Colonography, the process of data acquisition, image interpretation, as well as application and accuracy. Additionally, the benefits of this approach compared to conventional colonoscopy, new techniques to improve patient acceptance and diagnostic accuracy will be reviewed.

Keywords: Conventional colonoscopy, virtual colonoscopy, virtual dark-lumen MR Colonography, contrast agent, colorectal pathologies

COLORECTAL PATHOLOGIES:

Colorectal cancer is one of the most prevalent cancers worldwide (1-4) and it is the third most common type of non-skin cancer in men (after prostate cancer and lung cancer) and in women (after breast cancer and lung cancer). Despite the availability of several screening options, colorectal cancer is still the second leading cause of cancer death after lung cancer. The incidence of Inflammatory diseases of the large bowel, such as Crohn's disease, ulcerative colitis or diverticulitis, has sharply increased since the last few decades. The ileocolic region and the Rectosigmoid are most commonly affected. The clinical course of colorectal diseases is highly variable and starting symptoms range from vague, non specific symptoms such as diffuse abdominal pain, altered bowel habits and changes in the shape of stools, to the more spectacular symptom of rectal bleeding (5,6), which should activate alarm signals for both patient and physician. The prognosis of patients with colorectal pathologies including cancer and inflammation have hardly changed in the past few decades (7-9) due to considerable advances made in diagnostic tests and treatment. It has been unanimously admitted that the main prognostic factor for these diseases is its stage at initial diagnosis (9) which has been confirmed through several studies.

Conventional colonoscopy with possible biopsy is considered the gold standard for the detection of colorectal pathologies (10-11). Invasiveness, procedure-related discomfort, risk of perforation and poor patient acceptance have driven the exploration

of alternatives to endoscopy for diagnosing and characterizing colorectal diseases (12-13). Thus, the use of barium enema under fluoroscopy, leukocyte scintigraphy, and computed tomography (CT), especially virtual CT Colonography, for these purposes have been well described (14-20). Beyond lack of diagnostic accuracy, exposure to ionising radiation casts a shadow over the future of all three alternatives as a primary means to gauge diseases of large bowel, particularly in view of the patients' young age or follow-up (21-22). A real successful strategy has to overcome poor patient acceptance by making the examinations comfortable and non-invasive, reduce ionising radiation and show high accuracy. Hence, efforts have been focussed on MR imaging (MRI). Virtual dark-lumen MR Colonography (MRC) has the potential to be implemented as such a diagnostic tool. Due to its non-invasive character, it is well accepted by patients and it is highly accurate for the detection of colorectal pathologies (23-28).

The aim of this review article is to describe one of the applications of MRI, namely virtual dark-lumen MR Colonography (MRC), its technique, application and accuracy based on our 11 years experience on MRI (from 2000 to 2012). In addition, new techniques of MRC to improve patient acceptance will be discussed.

ADVANTGES OF MAGNETIC RESONANCE IMAGING:

Magnetic resonance imaging (MRI) as a non-invasive technique without radiation exposure, has been shown to be an appropriate diagnostic tool for

the detection of almost all pathologies of the human body including the hollow organs. The excellent contrast of MRI provides a good tool to differentiate between the different tissues of the body and makes it especially useful to identify healthy tissues from tumoral or inflammatory tissues compared with others medical imaging techniques based on Roentgen radiation or endoscopy.

MR SCANNER FOR DARK-LUMEN MRC:

Virtual Dark-Lumen MRC should be performed using a MR scanner with minimal field strength of 1.5 Tesla and multi receiver channels and high-performance gradients characterized by an amplitude of circa 40 mT/m and a slew rate of circa 200 mT/m/msec. Employing the newest and strong gradient systems led to shortening of the breath holding time. The examination can be performed within one breath and in just 22 seconds. We recommend a 1.5 Tesla MR scanner due to the large field of view and the availability in almost all radiological departments. The gradient system should be strong enough to enable switching of the highest possible gradient amplitudes in the shortest possible time with the aim to deliver the shortest possible repetition times (TR) and the shortest possible echo times (TE). The MR scanner should have a moving table to localize the patient in the center of magnet. An automatically contrast agent injector should be available.

PATIENT PREPARATION FOR MR COLONOGRAPHY:

Since residual stool impedes an appropriate evaluation of the large bowel, patients need to undergo bowel preparation in a manner similar to that required for conventional colonoscopy (CC). There are many commercially available laxatives worldwide. A few days before Dark-Lumen MRC patients are asked to consume a diet low in fiber and grain content to achieve an excellent bowel cleanse. The patient preparation—starts the night

before the MRC examination. In our studies, a standardized bowel cleansing procedure (26-28) with 3000 ml of a polyethylene glycol solution (e.g. Golytely®; Braintree Laboratories, Braintree, Massachusetts, USA) was used. This technique has shown an excellent effect for the bowel cleanse (Golytely® contains the following substances: sodium chloride 1.46 g, sodium hydrogen carbonate 1.68 g, sodium sulfate 5.68 g, potassium chloride 0.75 g, polyethylene glycol 59 g). Four bags of Golytely® are mixed in 3000 ml of drinking water. 2000 ml of the solution should be ingested the night before and 1000 ml in the morning of the examination day. To limit patient discomfort related to extended fasting, MR Colonography is performed in the early morning.

CONTRAINDICATIONS OF MRI:

Prior to the examination, the patient has to be screened for contraindications to MRI such as severe claustrophobia, presence of metallic implants or cardiac pacemakers. MRI is not performed in the presence of these contraindications.

The presence of hip prostheses, which is normally not regarded as an absolute contraindication to MRI, impedes a complete analysis of the rectum and sigmoid colon. Allergy against intravenous applied drugs such as scopolamine or glucagon and gadolinium-containing contrast agent should be classified as an absolute contraindication. Shortness of breath and motion artifacts are other contraindications for MRI.

HISTORY AND TECHNIQUES OF MR COLONOGRAPHY:

Bright-lumen MR Colonography:

First approaches of MR Colonography, so called bright-lumen MRC, were based on the rectal application of water spiked with paramagnetic contrast agent (gadolinium-containing) but without the use of intravenous gadolinium-containing contrast agent (29-31). The examination is

performed during a single breath-holding of about 20 seconds. On T1-weighted 3D gradient echo (GRE) data sets, the colonic lumen containing Gadolinium-spiked water is rendered bright, whereas the colonic wall, as well as pathologies arising from it, remained dark. Differentiation between polyps or carcinomas from residual fecal material on one hand, or air bubbles on the other, can therefore prove difficult and in some cases even impossible. The technique requires data acquisition in both prone and supine patient positions to compensate for the presence of residual stool or air (fig. 1). Thus, the change of positions reduces impaired the patient acceptance for bright-lumen MRC. In addition, the assessment of inflammatory processes of the large bowel or the extra-colonic organs was impaired due to the missing use of intravenous contrast agent.

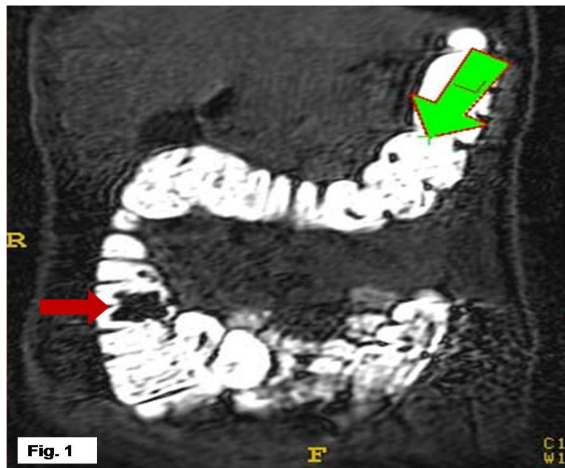


Fig. 1: Figure 1 shows bright-lumen MR Colonography after filling and distention of the colon with rectal enema. The examination is performed without the intravenous injection of gadolinium-containing contrast agent. The enema was spiked with paramagnetic contrast agent (gadolinium-containing, green arrow). The lumen appears bright on T1-weighted sequences, whereas colorectal masses and residual stool appear as filling defect in the lumen (red arrow). The differentiation between both is difficult, therefore the examination should be performed in prone and supine position in order to confirm the colorectal mass (colorectal masses stay on the same location, residual stools move and are different on both position). However, the change of position does not solve the whole problem of differentiation. In addition, inflammatory changes of the colonic wall could not be sure assessed due the missing of intravenous contrast agent and contrast uptake of the wall.

system, which is equipped with high-performance gradients. The examination itself is performed either with patients in prone or supine position. However, the use of prone position is recommended since it reduces the breathing artifacts of patients, eases the placement of the enema tube and improves the evaluation of the Rectosigmoid. A combination of two surface coils should be used for signal reception to permit coverage of the entire colon from the anus to the diaphragm (fig. 2). To minimize motion artifacts due to bowel peristalsis, a spasmolytic agent is administered intravenously (e.g. 40 mg of

Therefore, a new technique of MRC method, the Dark-Lumen MRC, was developed to reduce the limitations of bright-lumen MRC and to improve the patient acceptance for MRC. Dark-Lumen MRC is based on a different contrast mechanism (32-33, 26-27), and it has turned out to be more accurate and less time-consuming compared to bright lumen technique.

Dark-lumen MR Colonography:

Similar to contrast-enhanced 3D MR Angiography, dark-lumen MR Colonography (MRC) is based on the principles of ultra fast, T1-weighted 3D GRE acquisitions collected within the confines of a single breath hold and amounts about 22 seconds (26-27, 32-33). Thus, the patients should be examined on a 1.5 T MR scanner. This requires the use of a MR

scopolamine; Buscopan®; Boehringer Ingelheim, Germany) or 1 mg glucagon in case of contraindications to scopolamine (e.g. GlucaGen®, Novo Nordisk Pharma AG, Swiss). The main absolute contraindications for the use of scopolamine are raised intraocular pressure (Glaucoma), cardiac arrhythmias and prostatic hyperplasia and diabetes mellitus for glucagon (see package insert). In addition, spasmolytic drugs lead to a better distension of the bowel (fig. 3 a-b). Thus, colorectal lesions and inflammatory processes could be easier differentiated.



Fig. 2: The patient is lying in the prone position on 1.5 Tesla Scanner. Combination of phased-array surface coils to permit complete coverage of the entire colon and homogenous signal reception. After intravenous injection of 40 mg of scopolamine to minimize the bowel peristalsis, the rectal enema filling can be started.



Fig. 3 a-b: The left figure (3a) shows a coronal MR image of the colon after rectal enema but without an intravenous injection of spasmolytic agent like scopolamine. Consequently the bowel distension is poor. However, the bowel distension became clearly better after intravenous injection of scopolamine (3b, right).

Following the placement of a rectal enema tube (e.g. E-Z-Em, Westbury, NY, USA) and inflation of the retention balloon the colon is filled. An enema consisting of 2 - 2.5 liters of warm tap water without the mixture of gadolinium-containing contrast agent is rectally administered using hydrostatic pressure (1-1.5 m water column), in order to distend the entire colon. The filling process of the colon can be monitored using a T2-weighted non-slice select acquisition, collecting one image every three second (e.g. TrueFISP sequence, "TrueFISP stands for Fast Imaging with Steady State Precession"; with the following parameters: TR/TE 2.4/1.2 ms, flip angle 60°). After assuring adequate filling, this 2D overview allows recognition of high-grade stenosis as well as colonic spasm. Once the water enema has reached the cecum and a sufficient distension is

assured, a 3D GRE data set (pre-contrast sequence with integrated fat suppression) is collected in the coronal plane (e.g. VIBE sequence, "VIBE stands for Volumetric Interpolated Breath hold Examination"; with the following parameters: TR/TE 3.1 / 1.1 ms, flip angle 12°, field of view (FOV) 450 x 450 mm, matrix 168 x 256, and by zero filling interpolation an effective slice thickness of 1.6 to 2.0 mm is achieved depending on the thickness of the patient, so the total number of the calculated slices amount about 96). Subsequently paramagnetic contrast agent is administered intravenous at a dosage of 0.2 mmol/kg and a flow rate of 3.5 ml/s (e.g. Gadolinium-BOPTA, Multihance®, Bracco, Italy). However, the manufacturer of Gadolinium-BOPTA recommends a dosage 0.1 mmol/kg (information of the package insert). A double dosage is used in

order to get a high signal in colorectal masses and in inflammatory processes. Following a delay of 75 s, a second 3D acquisition is repeated in a portal-venous contrast phase and with identical imaging parameters (fig. 4). The 3D data are collected in breath holding in about 22 seconds. After data

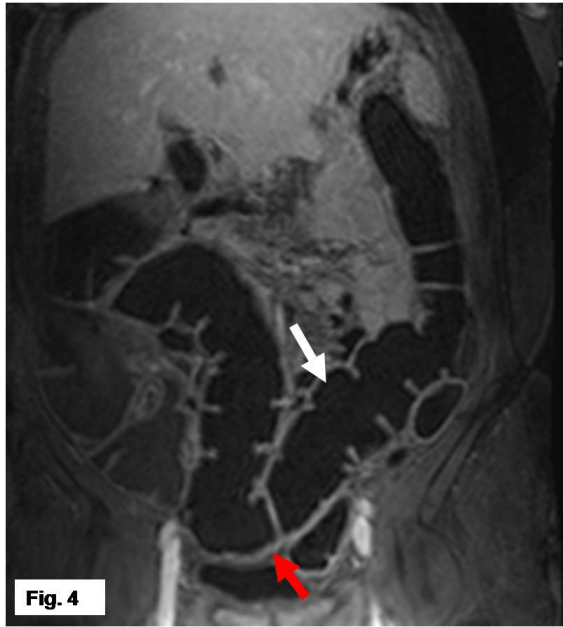


Image analysis of MRC:

For data interpretation, there are several commercially available hardware systems including post-processing workstations (e.g. Virtuoso, Siemens Medical Solutions, Erlangen, Germany). Both non-contrast and contrast-enhanced 3D data sets are transferred to a post-processing workstation, where the 3D data sets are post processed and read using a multiplanar reformation mode (MPR). This permits scrolling through the 3D data sets in all three orthogonal planes. The data sets are then assessed by experienced radiologists to avoid misinterpretations of the findings. For analysis purposes, the colon can be divided into six segments (rectum, sigmoid colon, descending colon, transverse colon, ascending colon and cecum). The diagnostic work-up interprets the contrast-enhanced data. Whenever a mass protruding from the colonic wall is detected, the identical part of the colon should be analyzed on the pre-contrast data. By measuring signal intensities of the mass in non-

acquisition, the enema bag is placed on the floor for facilitated emptying of the colon. Using this protocol, the examination is completed with an in-room time of 20 minutes.

Fig. 4: Figure 4 shows dark-lumen MR Colonography after filling and distention of the colon with rectal enema. The examination is performed in prone position and after intravenous injection of gadolinium-containing contrast agent. On T1-weighted sequence, the colonic lumen appears dark (white arrow) and the colonic wall appears white due to contrast uptake (red arrow).

contrast and post-contrast data, a contrast enhancement value can be determined. Hence, the differentiation between small residual stool particles and colorectal lesions is simple: residual stool does not show any contrast enhancement (fig. 5 a-b) and appears hyper-intense in both data sets, whereas colorectal lesions always do and appear hypo-intense in the non-contrast data and hyper-intense in the post-contrast data (fig. 6 a-b).

Through an additional step, the data can be assessed on virtual endoscopic renderings displaying the inside of the colonic lumen (fig. 7 a-b). A virtual endoscopic fly-through enables the radiologist to concentrate on the colon facilitating the depiction of small structures protruding into the colonic lumen. The three-dimensional depth perception allows the discrimination between polyps and haustra. To assure complete visualization of both sides of haustral folds, the virtual fly-through should be performed in an antegrade as well as retrograde direction. As for the detection of

colorectal masses, virtual endoscopic viewing renders improved sensitivity and specificity values

compared with the individual inspection of the cross-sectional images alone.

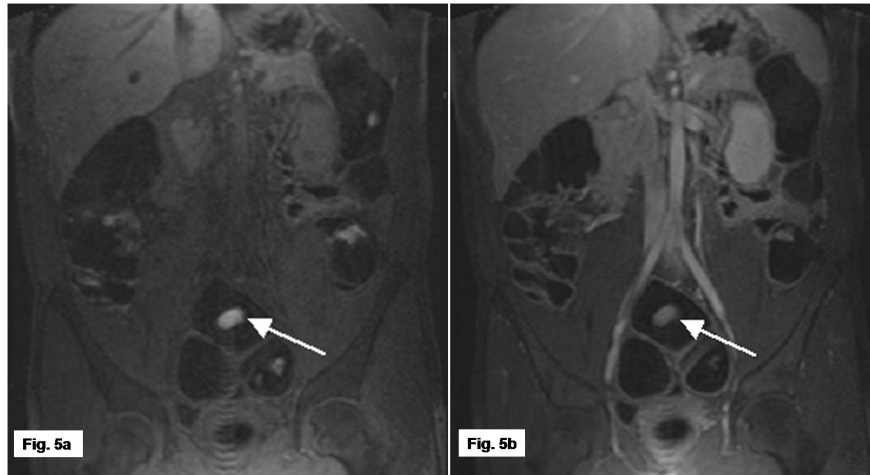


Fig. 5 a-b: Dark-lumen MR Colonography without (5a) and with (5b) intravenous injection of gadolinium-containing contrast agent. Residual stool (arrows) appears bright on the pre- and post-contrast T1-weighted sequence and does not show any contrast uptake.

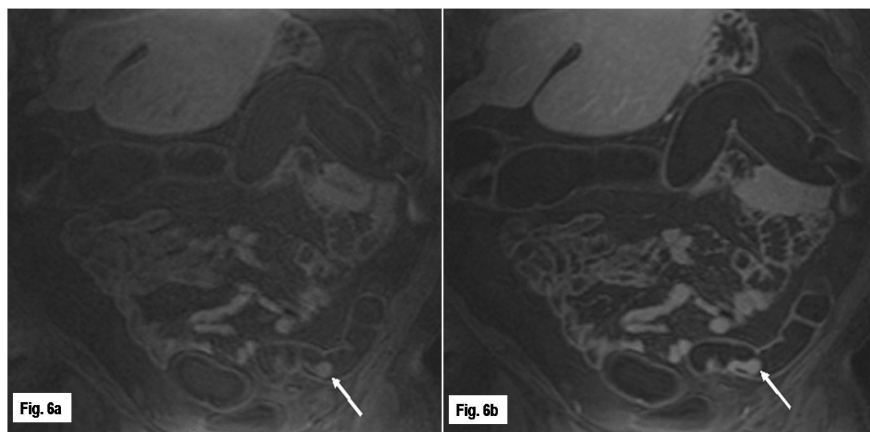


fig. 6 a-b: Dark-lumen MR Colonography without (6a) and with (6b) intravenous injection of gadolinium-containing contrast agent. Colorectal mass (arrows) appears dark on the pre-contrast T1-weighted sequence and bright on post-contrast T1-weighted sequence due to contrast uptake.

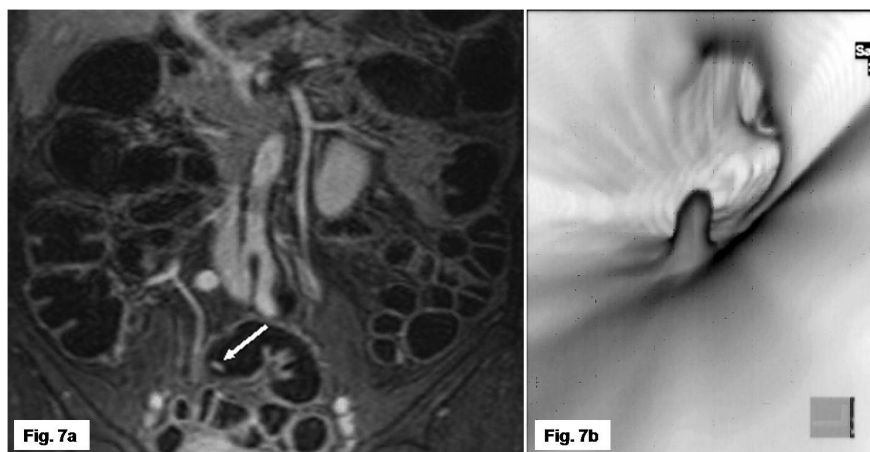


Fig. 7 a-b: Dark-lumen MR Colonography after intravenous injection of contrast agent. A small lesion (polyp) was found on the wall of the sigmoid colon (7a, arrow) and appears bright due to gadolinium uptake on the T1-weighted sequence. Virtual MR Colonography presents the small lesion (7b).

In case of inflammatory processes of the colon, the intestinal wall shows an edematous swelling and thickening and loss of haustra in both non-contrast and post-contrast data sets. However, the colonic wall appears just hyper-intense in the post-contrast

data due to the contrast uptake (fig. 8). Similar appearance of the colonic wall is apparent in stenotic processes of the intestinal lumen. Finally, the extra-colonic structures including lymph nodes, abdominal and pelvic organs, bones and vessels could and should be assessed.

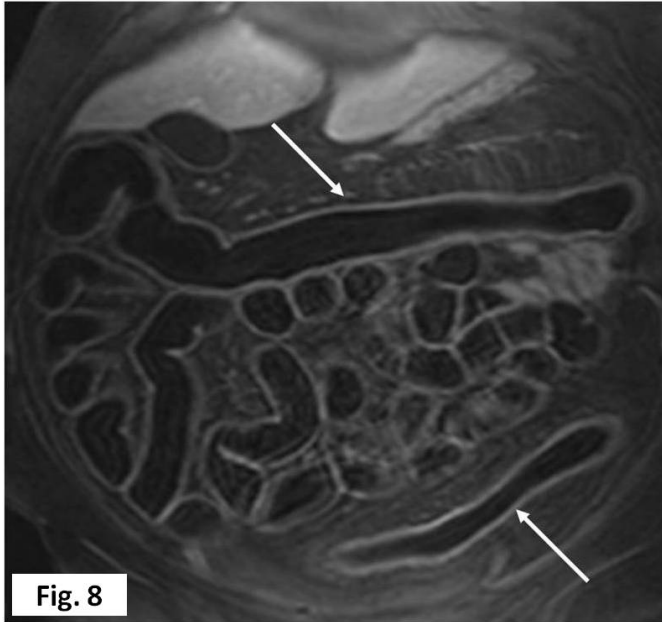


Fig. 8: Dark-lumen MR Colonography of a patient with inflammatory bowel disease (ulcerative colitis). Thickening of the colonic wall, loss of haustra and contrast uptake are typical signs of colitis (arrows). Therefore, Dark Lumen MRC appears superior to bright-lumen MRC for the detection of inflammatory disease due to the intravenously injected contrast agent and the consequent signal enhancement.

DIAGNOSTIC ACCURACY OF MRC:

MRC for the assessment of colorectal masses:

Colorectal cancer is an important cause of morbidity and mortality worldwide. The incidence of colorectal cancer (CRC) in the USA amounts to 130,000 per year with 50,000 cases of death (34). Colorectal cancer has now become the second most common cancer in both sexes in the western world. Colonic polyps are common in 10% of adults (34-35), and have become more frequent in older adults with a prevalence of 20% in the age group > 60 years. Up to 90% of colorectal cancers originate from benign adenomas through a series of genetic alterations: the adenoma-carcinoma sequence. Hence, the incidence of CRC can be considerably reduced by more than 80% if polyps were detected and

eliminated prior to their malignant transformation. Main reason is related to poor patient acceptance in current screening programs including the conventional colonoscopy as the standard examination for the detection of colorectal masses. Virtual Dark-Lumen MRC offers an alternative for CC due to good patient acceptance and high sensitivity and specificity. In a large study Ajaj et al. examined 122 patients with different colorectal masses to assess the accuracy of MRC compared to CC. Those patients underwent MRC after colonic cleansing and prior to CC. A high accuracy for MRC has been reported in the detection of colonic masses exceeding 5 mm in diameter, with sensitivity and specificity values amounting to 93% and 100% compared to CC (fig. 9 a-b). However, none of the polyps measuring < 5 mm identified by CC could be detected based on MRC images (26).

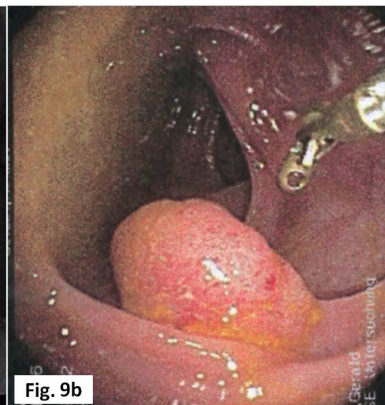


Fig. 9 a-b: Dark-lumen MR Colonography of a patient with a big mass in the rectum. On the post-contrast T1-weighted sequence, the mass demonstrates a high-contrast enhancement and infiltrates the wall (9a, arrow). Conventional endoscopy and the histopathologic result confirmed the presence of a rectal cancer in the rectum (9b).

MRC for the assessment of inflammatory bowel diseases:

Crohn's disease and ulcerative colitis are the most frequent specific inflammatory bowel diseases (IBD) with a prevalence of approximately one in 500 (36-38). Features indicating colitis include mural thickening exceeding 3 mm, submucosal edema, mesenteric fat stranding, mesenteric hypervascularity and fibro-fatty proliferation. Diagnostic procedures in IBD serve to validate the diagnosis and optimize treatment. In addition to endoscopic biopsy fluoroscopy, leukocyte scintigraphy, and computed tomography (CT) are considered the gold standard for the detection and quantification of IBD. Due to its non-invasiveness, good patient acceptance, high diagnostic accuracy and lack of exposure to ionising radiation, MRC plays a prominent role in the diagnosis and classification of IBD of the colon, especially in young patients. Ajaj et al. examined 23 patients with suspected IBD of the large bowel, to compare the detection and quantification of IBD using MRC and CC (28). Endoscopically obtained histopathology specimens were used as the standard of reference. In this MRC study the colon was divided into six segments. The presence of inflammatory changes on MRC was documented based on bowel wall contrast enhancement, bowel wall thickness, presence of perifocal lymph nodes

and loss of haustral folds. For these purposes, a point score from 0 to 3 was used (0 means no and 3 means severe). For each abnormal segment all criteria were quantified and summarized in a single score. An inflammatory score based on the sum of the four outlined inflammatory parameters was determined and the inflammation was subdivided into mild, moderate and severe lesions. It was classified as follows: ≤ 4 points = slight inflammation; 5 – 8 points = moderate inflammation; > 8 points = severe inflammation. The accuracy of the inflammatory scores determined by MRC was assessed by calculating point estimates for sensitivity and specificity using the histopathology data as the standard reference. The study results indicated that when diagnostic guidelines are followed and adequate clinical information is available, IBD is correctly detected and classified in 80 to 90% of cases using MRC. MRC correctly identified 68 of 73 bowel segments with proven IBD changes by histopathology (fig. 10 a-b). All severely inflamed segments were correctly identified as such and there were no false positive findings. Based on the proposed composite inflammatory point score, MRC detected and characterized clinically relevant IBD of the large bowel with sensitivity and specificity values of 87% for all investigated colonic segments.

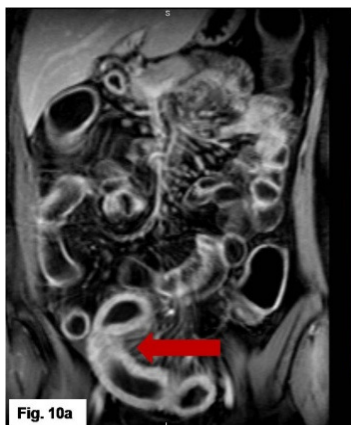


Fig. 10 a-b: Dark-lumen MR Colonography of a patient with colitis in the sigmoid colon. On the post-contrast T1-weighted sequence, the sigmoid wall appears thick and shows a high-contrast uptake (10a, arrow). Conventional endoscopy and the histopathologic result confirmed the presence of ulcerative colitis (10b).

MRC in case of incomplete conventional colonoscopy:

The value of standard CC is predicated upon the ability to reach the cecum. Unfortunately, failure to complete conventional colonoscopy is not a rare event. Rather it is observed in 5-26% of colonoscopic examinations performed by experienced endoscopists. There are many causes for failing to complete CC (39-40). The most common cause is severe procedure-related abdominal discomfort, often in combination with technical challenges associated with elongation of the sigmoid colon, as well as operator difficulties to reach the right colonic flexure and the cecum. The presence of intraluminal stenosis represents another hindrance. The failure rate of CC increases up to 50% in patients with known inflammatory bowel disease, as well as in the presence of colorectal carcinoma. Therefore, colonic segments inaccessible by conventional colonoscopy can be depicted with various imaging techniques including Dark-Lumen MRC. In order to assess the utility of MRC in patients with an incomplete CC 37, patients underwent MRC for the completion of large bowel segments that have not been endoscoped (41). For analysis purposes, the colon of each patient was divided into six segments (cecum, ascending,

transverse, descending, sigmoid colon and rectum, altogether were 214 pre- and post-stenotic segments in 37 patients). Conventional colonoscopy was able to assess all post-stenotic segments of the colon in all patients but failed to assess all pre-stenotic segments. However, Dark-Lumen MRC assessed all pre-stenotic segments of the colon in all patients and almost all post-stenotic segments. CC failed to assess 127 pre-stenotic potentially visible colonic segments in the 37 patients. MRC permitted assessment in 119 of these 127 segments (fig. 11). Non-diagnostic MR image quality in eight segments was attributed to inadequate distension of pre-stenotic colonic segments due to high grade tumour stenosis. All inflammation- and tumour-induced stenosis as well as all five polyps, identified by CC in post-stenotic segments, were correctly detected on MRC. MR-based assessment of pre-stenotic segments additionally revealed two carcinoma-suspected lesions, five polyps, and four colitis-affected segments. Thus, Dark-Lumen MRC proved reliable in evaluating the majority of colonic segments inaccessible with conventional colonoscopy. The identification of additional disease on MRC underscores the need for a second diagnostic step in the setting of incomplete conventional colonoscopy.

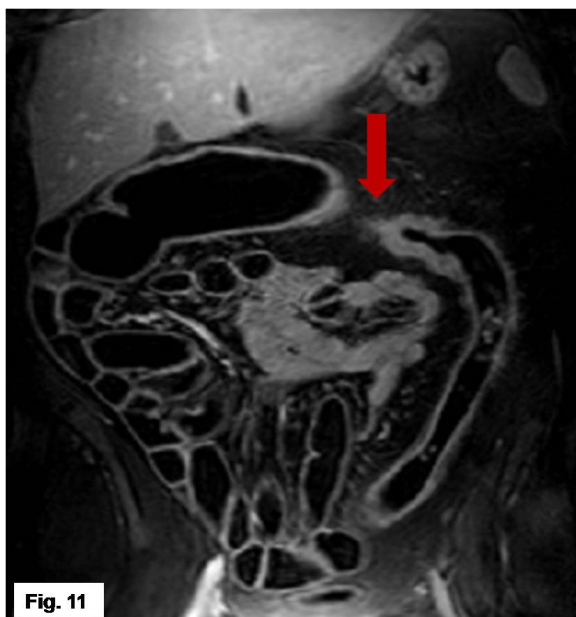


Fig. 11: Coronal T1-weighted image of dark-lumen MR Colonography after intravenous injection of contrast agent. A 37-year-old woman with ulcerative colitis underwent MRC after conventional colonoscopy. The conventional colonoscopy was incomplete because of high-grade stenosis in the descending colon. MRC permitted assessment of segments proximal to the site of stenosis (arrow) and revealed inflammatory changes affecting the transverse colon, as evidenced by loss of colonic folds and increased contrast agent uptake in the colonic wall.

MRC for the detection of diverticulitis:

A true diverticulum is defined as a herniation of the mucous membrane of the colonic wall including mucosa, muscularis mucosae and submucosa through the circular muscularis propria, and it is mainly located in the central portion of the interhaustral segments (42-46). The hypotheses on the etiology of colonic diverticulosis are variant including high age, high pressure within the large bowel, prolonged gastrointestinal transit time, fibre-deficient diet and hereditary diseases. Diverticular disease (DD) involving the left colon is a common condition in Western countries affecting 30-50 % of adults 60 years and older. The incidence of DD is increasing because of nutritional habits and an aging population. DD predominantly involves the sigmoid colon. However, most patients with diverticulosis are asymptomatic without evidence of complications. Only 10-30% of the age group over 60 years develop acute diverticulitis. Other

complications of DD include stricture, peri-colic abscess, bleeding and perforation. In a study by Ajaj et al., 40 patients with suspected sigmoid diverticulitis underwent Dark-Lumen MRC within 72 hours prior to CC (47). Dark-Lumen MRC classified 17 of the 40 patients as normal with regard to sigmoid diverticulitis. However, CC confirmed the presence of light inflammatory signs in 4 patients which were missed in MRC. MRC correctly identified wall thickness and contrast uptake of the sigmoid colon in the other 23 patients (fig. 12 a-b). In three cases, false positive findings were observed and Dark-Lumen MRC classified the inflammation of the sigmoid colon as diverticulitis, whereas CC and histopathology confirmed invasive carcinoma. Additionally, Dark-Lumen MRC detected relevant pathologies of the entire colon and could be successfully performed in 4 cases where CC was incomplete.

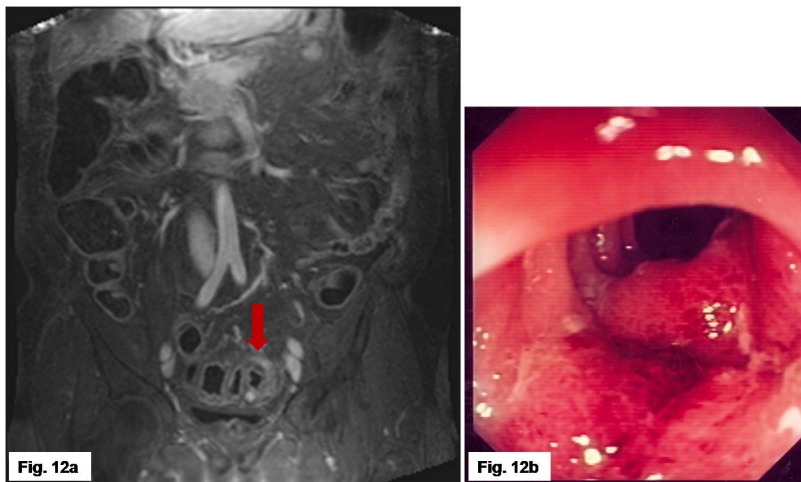


Fig. 12 a-b: Coronal image of dark-lumen MR Colonography from a 66-year-old woman with known diverticulosis of the sigmoid colon. The patient was transferred to the department of gastroenterology because of acute abdominal pain. On the post-contrast T1-weighted sequence, thickening and an increased contrast uptake of the sigmoid bowel wall could be seen (12a, arrow), and the patient was diagnosed with diverticulitis. This suspicion was subsequently confirmed by endoscopy (12b).

MRC for the assessment of colonic anastomoses:

Colonic resection with end-to-end-anastomosis is a common procedure in colorectal surgery for patients with colorectal malignancy or chronic inflammatory bowel diseases (48-51). However, postoperative recurrences at the anastomosis with consecutive stricture are frequent. Even after second or third resection, the perianastomotic area remains the most frequent site of disease recurrence (51-55). In

a study by Ajaj et al. (56) to assess the diagnostic accuracy of MRC for the evaluation of colonic anastomosis, 39 patients with previous colonic resection and end-to-end-anastomosis underwent Dark-Lumen MRC. In this study, the anastomosis was rated to be normal by means of MRC in 23 patients (CC: 20 patients). In 3 patients CC revealed a slight inflammation of the anastomosis, which were missed by Dark-Lumen MRC. A moderate

stenosis of the anastomosis without inflammation was detected by Dark-Lumen MRC in 5 patients, and confirmed by CC. In the remaining 11 patients, a relevant pathology of the anastomosis was diagnosed by both MRC and CC (fig. 13). In two patients with history of colorectal carcinoma, a recurrent tumor was diagnosed. In the other 9 patients, an inflammation of the anastomosis was seen in 7 cases with Crohn's disease and in 2 cases with ulcerative colitis. Dark-Lumen MRC did not show any false positive findings resulting in an overall sensitivity/specificity for the assessment of the anastomosis of 84%/100% (56).

Combined hydro-MRI of the small bowel and Dark-Lumen MRC:

It is known that Crohn's disease mostly affects the terminal ileum and/or the ileocecal region. Crohn's

disease predominantly involves the distal bowel (20%), the colon (30%) or the small and large bowel (50%). Therefore, a good distension of the terminal ileum and ileocecal region is necessary to detect inflammations in these regions. In patients with IBD, assessment of the terminal ileum and colonic segments is important for monitoring and therapy. In a study by Ajaj et al. (57), 40 patients with known Crohn's disease underwent hydro-MRI of the small bowel after ingestion of 1.5 liter of hydro-solution containing 0.2% locust bean gum (LBG) and 2.5% mannitol. 20 of these patients additionally underwent Dark-Lumen MRC after rectal water enema, but without large bowel cleansing. The additional time needed for the enema administration was minimal (57). Patients were divided into groups, namely non-enema group and enema-group.

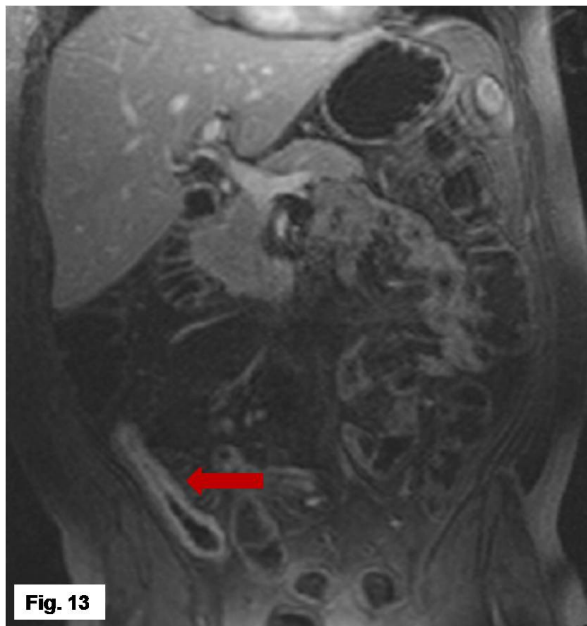


Fig. 13: Contrast-enhanced coronal VIBE image of dark-lumen MR Colonography 75 seconds after intravenous injection of contrast agent in a patient with Crohn's Disease and a history of ileoascendostomy. Increased contrast uptake of the distal ileum close to the anastomosis confirmed the recurrence of inflammatory disease (arrow).

The latter resulted in a statically significant difference between both groups in favor of the enema group in regards to the distension of all colonic segments and terminal ileum, the presence of artifacts, the diagnosis of a terminal ileitis, and the diagnostic confidence not only in the colon, but also in the terminal ileum, which lead to a higher diagnostic accuracy.. No false positive results were encountered in the enema group, whereas in the

non-enema group there were 3 false negatives alone for the terminal ileum. This enhances the impact of sufficient terminal ileum distension and can be achieved through an additional rectal enema. The study showed that the additional administration of a rectal enema is useful in small bowel MRI for the visualization of the terminal ileum (fig. 14). Thus, small and large bowel pathologies could be diagnosed with high accuracy.

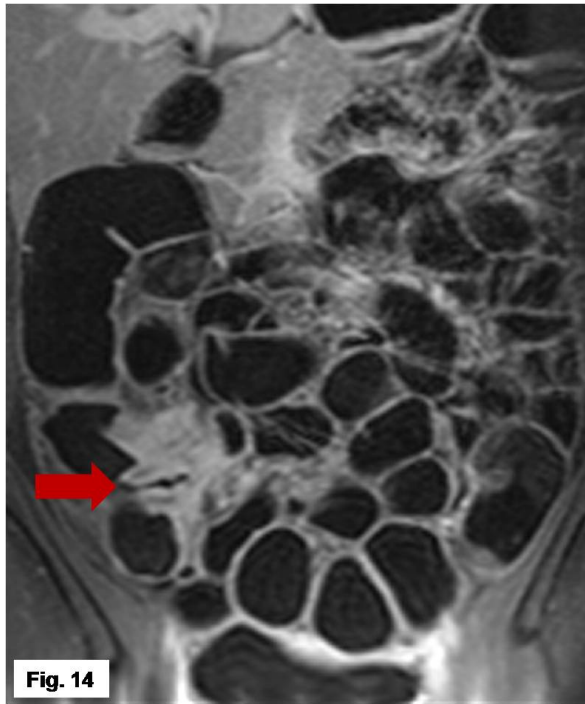


Fig. 14: Coronal image of combined dark-lumen MR Colonography and hydro-MRI of the small bowel after oral ingestion of a solution containing 0.2% locust bean gum (LBG) and 2.5% mannitol. The additional rectal enema in hydro-MRI of a 31-year-old female patient with known Crohn's disease shows a sufficient distension of the colonic segments. The thickened wall of the terminal ileum shows an increased contrast uptake (arrow). Subsequent endoscopy and biopsy confirmed the presence of an acute inflammation of the terminal ileum.

Assessment of the extraintestinal organs using Dark-Lumen MRC:

Using CC limits the view of the endoscopist to assess the colonic lumen, preventing the evaluation and assessment of the extra-colonic organs. The presence or absence of pathologic findings of the extra-colonic organs might be important for further patient management. The evaluation of the extra-colonic organs can be conducted using additional imaging techniques, which adds additional cost and possible waiting times for the examination. These limitations can be overcome through the use of virtual colonoscopy. Dark-Lumen MRC offers an additional viewing of the extra-intestinal organs, compared to CC, and it has no viewing limitations. Analysis of the 3 data sets of Dark-Lumen MRC is especially important in colorectal tumor suspects, in order to assess the presence of metastases in organs such as the liver or the lymph nodes where the choice of therapy is critical. In addition, patients with IBD or diverticulitis

could benefit from MRC through evidence or exclusion of complications like fistulae and abscesses which are often missed using CC and cannot be confirmed through conventional methods. In a large study Ajaj et al. (58) investigated 375 patients with suspected colonic diseases to evaluate the assessment of extra-intestinal organs using Dark-Lumen MRC. In total 510 extra-colonic findings were found in 260 (69%) of the 375 patients. Known extra-colonic findings were seen in 140 patients (54%) and unknown findings in 120 patients (46%). 31 (12%) of the 260 patients had therapeutically relevant findings (45 findings), 229 patients (88%) had irrelevant findings (465 findings). This indicates that Dark-Lumen MRC is a useful tool not only for the assessment of the entire colonic lumen, but also for the evaluation of extra-colonic organs (fig. 15). Thus, intra- and extra-colonic pathologies can be diagnosed within the same examination (58).

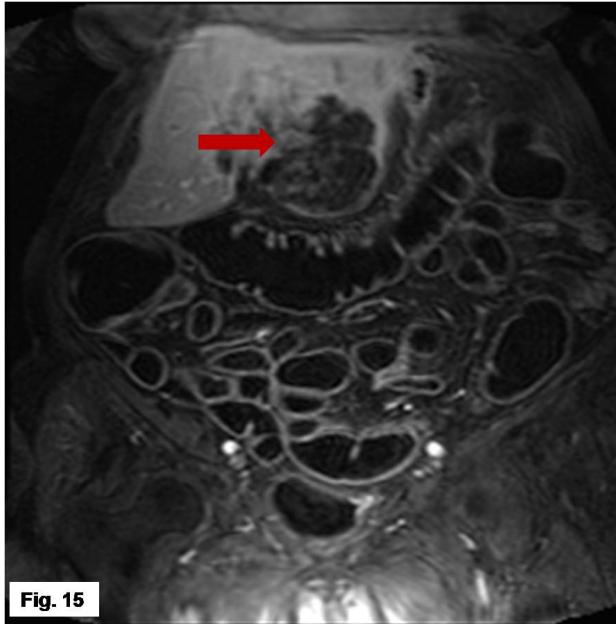


Fig. 15: Contrast-enhanced coronal 3D VIBE sequence of a 76 year-old female patient who underwent dark-lumen MR Colonography due to abdominal pain and slight icterus. The MRC did not show any colonic pathology. However, in the left segment of the liver, a great hypointense lesion with stasis of the bile ducts was detected (arrow). The biopsy of this lesion confirmed the suspected diagnosis of cholangiocellular carcinoma.

OTHER TECHNIQUES OF DARK-LUMEN MRC:

Air-based distension of the colon in Dark-Lumen MRC

Reliable assessment of the colon by means of MRC is predicated upon the fulfilment of two requirements: sufficient distension of the colonic lumen, and sufficient contrast between the colonic lumen and pathologies arising from the colonic wall. While initial experiences with MRC was based on two techniques: rendering of the colonic lumen bright after filling with enema spiked with paramagnetic contrast agent (bright-lumen MRC), and dark after filling the colonic lumen with water enema without the addition of paramagnetic contrast (Dark-Lumen MRC). Dark-Lumen MRC has been found to be advantageous (26, 28). Hence, the cleansed colon is filled either with liquid such as tap water, (26, 28) or with gaseous agents such as room air, CO₂ and hyperpolarized Helium (59-61). Better density properties and the assumption that air provides less discomfort compared to water has resulted in the predominant use of gaseous agents for CT Colonography. Although similar to water in terms of MR signal properties on T1-weighted images, the fear of susceptibility artifacts rendered the use of air or

other gases as less intuitive for MRC. The feasibility of air-distended MRC has been proved. Five volunteers and fifty patients, who had been referred to colonoscopy for a suspected colorectal pathology, were randomised into water-distension and air-distension groups (62). MRC was performed in both groups. Comparative analysis was based on qualitative ratings of image quality and bowel distension as well as Contrast-Noise-Ratio (CNR) measurements for the colonic wall with respect to the colonic lumen. In addition, patient acceptance was evaluated. No significant differences were found between air- and water-distension regarding discomfort levels and image quality. The presence of air in the colonic lumen was not associated with susceptibility artifacts. CNR of the contrast-enhanced colonic wall as well as bowel distension were superior on air-distended 3D data sets. Dark-Lumen MRC can be performed using either water or air for colonic distension. Both techniques permit assessment of the colonic wall and identification of colorectal masses (fig. 16). While discomfort levels were similar for both agents, MRC with air provided higher CNR and better colonic distension (62).



Fig. 16: Coronal image of T1-weighted VIBE sequence of a 65-year old patient undergoing dark-lumen MR Colonography in conjunction with rectal application of room air and intravenous injection of gadolinium-containing contrast agent. A large lesion with irregular borders and contrast uptake was found in the descending colon (arrow), which turned out to be a 22 mm carcinoma and was confirmed in conventional colonoscopy.

Dark-Lumen MRC without bowel cleansing: Future development

As stated, virtual MRC still mandates bowel purgation, which negatively impacts patient acceptance. If bowel cleansing can be avoided, patient acceptance of MRC could be considerably increased. This can be accomplished by modulating the signal characteristics of the fecal material and increasing the signal intensity of the stool on the T1-weighted sequence. To date there are two concepts: fecal tagging and fecal cracking.

Dark-Lumen MRC with Fecal tagging

Fecal tagging is a concept based on altering the signal intensity of stool by adding contrast modifying substances to regular meals such as barium sulfate-containing contrast agent (33, 63-64). This has been shown to decrease the signal intensity of stool in T1-weighted images because of the extended relaxation time. Thus, fecal tagging may render stool virtually indistinguishable from the distending rectal enema on MR images. The fecal tagging based MRC was applied successfully in a volunteer study (63). However it has shown a poor diagnostic accuracy and poor acceptance in a patient study (64). In a study by Goehde et al. (64) 42 patients

underwent fecal tagging based Dark-Lumen MRC after ingestion of 150 ml of 100% barium at each of 6 main meals prior CC. On a lesion-by-lesion basis, the sensitivity for polyp detection was 100% for polyps exceeding 20 mm, a sensitivity of 40% for polyps of 10 – 19 mm, 16.7% for polyps of 6 – 9 mm, and 9.1% for polyps smaller than 6 mm. High stool signal in the colon (fig. 17), which impeded a reliable in- or exclusion of polyps, and barium preparation, rated worse than the bowel cleansing procedure for CC, can explain such results. Therefore, fecal tagging MRC must be further optimized and other strategies, such as raising the hydration of stool, must be develop.

Dark-Lumen with Fecal cracking

Fecal cracking concept is based on the administration of oral and rectal stool softener used for stool hydration to increase the stool's signal intensity on the T1-weighted sequence (65). The effect of oral and rectal softener on the signal intensity of stool was assessed in a voluntary study by Ajaj et al. (65). 10 volunteers underwent fecal cracking based Dark-Lumen MRC repeated at four different times (65).



Fig. 17: Fig. 17 shows dark-lumen MR Colonography based on fecal tagging after filling and distention of the colon with rectal enema. The MRC examination was done after oral ingestion of 150 ml of 100% barium sulfate at each of 6 main meals. Thus, the stool in the whole entire colon appears dark on the T1-weighted sequence (arrow) and colorectal lesions appear bright after intravenous injection of contrast agent and contrast enhancement. Therefore, colorectal lesions arising from the colonic wall could be easily detected on the post-contrast sequence.

A baseline examination was performed without oral or rectal administration of stool softeners. In a second examination, volunteers ingested 60 ml of lactulose 24-hours prior to MRC and in the third examination, water as a rectal enema was replaced by a solution of 0.5%-docusate sodium (DS). A fourth MR-examination was performed both in conjunction with oral administration of lactulose and rectal application of docusate sodium. Without oral

ingestion of lactulose or rectal enema with docusate sodium, stool intensity was high and did not decrease over time. However, lactulose and docusate sodium together caused a statistically significant decrease of stool intensity over time. Thus, feces hardly could be distinguished from dark rectal enema allowing for the assessment of the colonic wall (fig. 18).



Fig. 18: The figure shows coronal image of dark-lumen MR Colonography based on fecal cracking. A volunteer underwent MRC after oral ingestion of 60 ml lactulose 24 hours prior to the examination and after filling the colon with a solution of 0.5%-docusate sodium (DS). Both substances have softening effect. 10 minutes after rectal enema the stool intensity decreases (arrow) by soaking and cracking the stool and appears dark on the T1-weighted sequence. After intravenous injection of gadolinium-containing contrast agent the bright colonic wall can be more easily delineated from the dark colonic lumen. Thus, colorectal lesions and inflammatory processes could be easily detected.

CONCLUSION:

Dark-Lumen MRC based on colonic cleansing shows in many published studies as a high sensitivity and specificity method. It is indeed a

promising alternative method to conventional colonoscopy for the detection of almost all colorectal diseases, and the assessment of extra-luminal organs. Future techniques to avoid colonic cleansing

and to improve patient acceptance should be more optimized and should be performed in large scale studies before they can be clinically applied. In

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