Original Research

Strengths and Weaknesses of Dark-Lumen MR Colonography: Clinical Relevance of Polyps Smaller Than 5 mm in Diameter at the Moment of Their Detection

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Purpose: To assess the clinical relevance of dark-lumen MR colonography (MRC) for the detection of colorectal lesions using conventional colonoscopy (CC) and histopathologic examinations as reference standard.

Materials and Methods: A total of 72 patients underwent MRC and CC. MRC was performed using a contrast-enhanced high spatial resolution T1 weighted 3D volumetric interpolated breathhold examination (VIBE)-sequence. All removed colorectal lesions were evaluated by an experienced pathologist.

Results: CC confirmed 65 polyps less than 5 mm in diameter. Non of those lesions could be detected using MRC. Just two (4%) of the 49 removed lesions smaller than 5 mm showed signs of dysplasia. Additionally, CC confirmed 25 polyps between 6–15 mm in diameter (MRC 22). All those 25 lesions were removed in CC. Only four (16%) of those polyps showed signs of dysplasia and malignancy (11, 13, 13 and 15 mm).

Conclusion: Dark-lumen MRC failed to detect all polyps smaller than 5 mm in diameter which are generally not clinically relevant at the moment of their detection and thus can be kept under surveillance. However, MRC as a non-invasive imaging modality is a promising alternative to CC in the detection of clinically relevant polyps larger than 5 mm in diameter.

Key Words: MR colonography; conventional colonoscopy; polyps; lesions smaller than 5 mm; histopathology
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COLORECTAL CANCER is an important cause of morbidity and mortality in the western world and is the second most common cancer after bronchial (male) and breast cancer (female) (1,2). Colonic polyps are common in 10% of adults (3,4) 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 alteration: the adenoma-carcinoma sequence (3). The current consideration is that colorectal cancer is preventable if all adenomas are removed before they have the chance to progress to cancer (4). Thus, early detection and treatment of colonic polyps is widely considered to be crucial to prevent colon cancer.

Conventional colonoscopy (CC) is considered the reference standard for the evaluation of the colon and its pathologies (5,6). Poor patient acceptance due to invasiveness and procedure-related discomfort led to the development of non-invasive imaging modalities to visualize the colonic lumen. Computed tomography (CT) and magnetic resonance imaging (MRI) with the administration of contrast agents and post-processing software paved the way for a new area to detect colorectal masses (7–14). Virtual colonography is based on the acquisition of 3D CT or MRI data sets (8,12). Initial studies documented high diagnostic accuracies for both CT and MR colonography (7–14).

The aim of this study was to assess the clinical relevance of dark-lumen MR colonography (MRC) for the detection of colorectal lesions using CC and histopathologic examinations as the reference standard.

MATERIALS AND METHODS

The study was conducted in accordance with all guidelines set forth by the approving institutional review board (Local Ethics Committee of the University Hospital). Informed consent was obtained prior to each examination. Exclusion criteria for MR examination are presence of a pacemaker, all metallic implants including implants in the central nervous system or vessel system, claustrophobia.

Subjects

Within a 15-month period 72 patients (37 men, 35 women, mean age: 56.4 years, age range 39–71 years)

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underwent MRC within 36 hours prior to CC. All patients had been referred to CC for various indications including first colorectal screening over 50 years of age ($N = 25$), abdominal pain ($N = 13$), suspected Crohn's disease or ulcerative colitis ($N = 10$), chronic diarrhea ($N = 9$), a positive family history of colorectal cancer ($N = 8$), a positive fecal occult blood test ($N = 4$) and suspected diverticulitis ($N = 3$).

Bowel Preparation

All patients underwent a standardized bowel cleansing procedure with 3000 mL of a polyethylene glycol solution (Golytely®: sodium chloride 1.46 g, sodium hydrogencarbonate 1.68 g, sodium sulfate 5.68 g, potassium chloride 0.75 g, polyethylene glycol 4000 59 g, Braintree Laboratories, Braintree, MA, USA), of which 2000 mL were ingested the night before and 1000 mL in the morning of the examination day.

MR Imaging

MRC was performed with the patients in the prone position on a 1.5 T MR system (Magnetom Sonata®, Siemens Medical Solutions, Erlangen, Germany) equipped with a high-performance gradient system characterized by a maximum gradient amplitude of 40 mT/m and a slew rate of 200 mT/m/msec. Imaging in the prone position generally reduces bowel motion artifacts. A combination of two surface coils was used in conjunction with the built-in spine array coil for signal reception to permit coverage of the entire colon. To minimize bowel peristalsis, 40mg of scopolamine (Buscopan®; Boehringer Ingelheim, Germany) were injected intravenously prior to the enema. None of the patients revealed any contraindications for scopolamine. Following the placement of a rectal enema tube (E-Z-Em, Westbury, NY, USA), the colon was filled with approximately 2000–2500 mL of warm tap water. This enema was performed without fluoroscopic control, as the maximum amount of water that can be administered depends only on the patient's subjective feeling; also, according to our experience, the cecum is dilated in every case following this regime. Following bowel distension a pre-contrast high spatial resolution volumetric interpolated breathhold examination (VIBE) sequence with interpolation and integrated fat suppression was acquired breath-held in the coronal plane. Sequence parameters were: TR/TE 3.4/1.4 msec, flip angle 12°, field of view (FOV) 400 × 400 mm, matrix 512 × 256, and an effective slice thickness of 2.6 mm. Depending on the patient's size the number of slices amounted to 60–74 and the breath-holding period was between 18–23 seconds.

Subsequently, paramagnetic contrast agent (Gd-BOPTA, MultiHance®, Bracco, Milan, Italy) was administered intravenously at a dosage of 0.2 mmol/kg body weight and a flow rate of 3.5 mL/second. Following a delay of 100 seconds, a second high spatial resolution VIBE sequence was acquired. After the MRC-examination the water-enema was released back into the enema bag and the patients went to the bathroom.

Conventional Colonoscopy Procedure

CC was performed using standard equipment (model CFQ 140; Olympus, Tokyo, Japan). The attending gastroenterologist was unaware of the MR findings. When necessary patients obtained sedatives (2,5–5 mg Midazolam: Dormicum®, Roche, Grenzach-Wyhlen, Germany) and/or also a low dose of analgesics (Dolantin®; Hoechst, Bad Soden, Germany). The gastroenterologist was asked to remove all removable colorectal lesions. Location and size of colorectal lesions were recorded to compare them with MRC. In addition, the gastroenterologist graded the polyps in those less than 5 mm and those larger than 5 mm in diameter.

Histological Analysis of Colonic Lesions

All removed colonic polyps were sent for histological examination and each lesion was evaluated by a board-certified, experienced pathologist.

Data Analysis

For each patient, both non-contrast and contrast-enhanced 3D data sets were transferred to a post-processing workstation (Virtuoso®, Siemens Medical Solutions, Erlangen, Germany). MR data sets were analyzed in the multiplanar reformation mode, which permitted scrolling through the 3D data sets in all three orthogonal planes by two experienced radiologists (>4 years experience in abdominal MR imaging) in consensus who had no knowledge of the respective colonoscopic findings. For purposes of analysis the colon was divided into six segments: rectum, sigmoid colon, descending colon, transverse colon, ascending colon and cecum.

Assessment of Image Quality of MRC

The Image quality of the 3D contrast-enhanced datasets was assessed both qualitatively and quantitatively. Each segment was evaluated for the presence of artifacts including motions and susceptibility artifacts: 1 = no artifacts, 2 = moderate artifacts, diagnostic image quality, 3 = extensive artifacts, non-diagnostic image quality.

For the quantitative analysis contrast-to-noise ratios (CNR) were assessed for representative parts of all bowel segments. For this purpose, the coronal post-contrast high spatial resolution MR image was magnified three-fold. Regions of interest (ROI) were placed in the lumen and the adjacent wall of all segments (Fig. 1a and b). Image noise, defined as the standard deviation of signal intensities measured in an ROI placed outside the body was determined. Based on these measurements CNR was calculated: CNR = (SI (colonic wall/colonic lesion) – SI (lumen))/noise. CNR values of all colorectal masses were determined in the same manner described before.

MRC Findings

All MR data sets were assessed for the presence of colorectal lesions. Employed criteria included increased contrast agent uptake of lesions between pre- and postcontrast phase, convexity or protrusion of the lesion in the

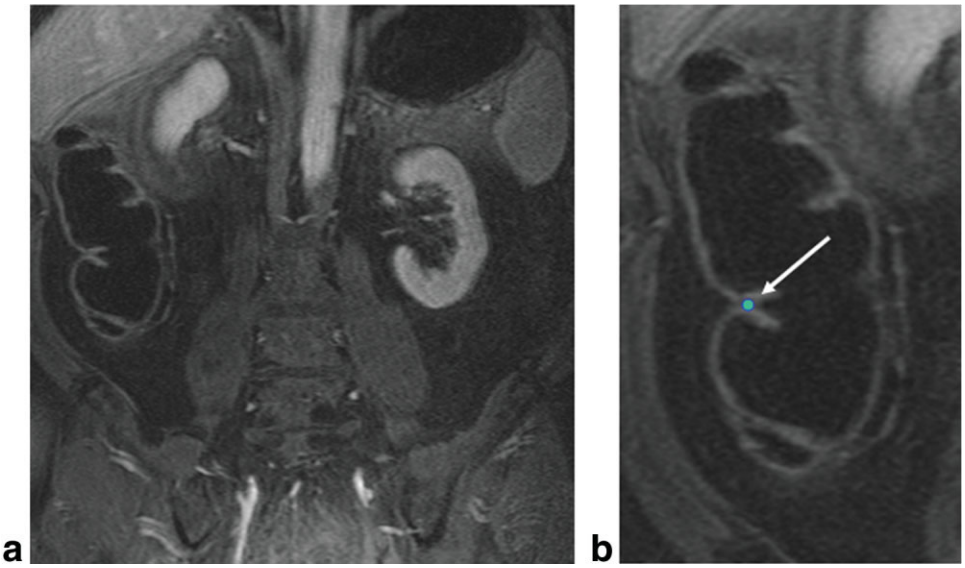

Figure 1. a: Coronal source image from T1-weighted gradient-echo 3D MR imaging data set using a high spatial resolution VIBE sequence (TR/TE = 3.4/1.4 msec, flip angle = 12°, matrix size = 512 × 256). The coronal source image was acquired after intravenous application of contrast medium. **b:** Enlargement of (a). Contrast-to-noise ratio (CNR) in the wall of all colonic segments can be easily determined (circle and arrow).

colonic lumen, the presence of polypoid handle. Finally, the lesions identified in MRC were compared with the same lesions identified in CC using their recorded and described location by the gastroenterologist.

Statistical Analysis

Ratings were compared by a Student's *t*-test using a *P*-value of <0.05 to indicate statistical significance. For the adaptation to multiple samples, a Bonferroni correction was employed. The data were carried out at our University Hospital.

RESULTS

All MRC as well as all CC examinations were tolerable and were performed without any complications.

Image Quality

The average value of image quality in the contrast-enhanced sequence was rated as 1.14 and the average value of CNR was rated as 54.0 for all colonic segments. The parameters of all colonic segments are listed in Table 1.

MR Findings

In 45 patients MRC did not show any colorectal lesions or other pathologies; thus, those examinations were classified as normal (Fig. 2). In 19 patients 22 polyps with diameters between 6–15 mm were seen (Figs. 3 and 4). In these 19 patients no further colorectal pathologies were detected. One patient revealed a sigmoid diverticulitis and in six patients with Crohn's disease and ulcerative colitis inflammatory affected colonic segments were found (Fig. 5). Additionally, in one patient with Crohn's disease a moderate stenosis of the ascending colon was seen (Fig. 6).

CC Findings

CC did not find any pathologies in 23 patients (MRC 45 patients). In the remaining 22 patients in whom MRC did not reveal any pathologic findings CC confirmed 2 polyps (7 and 9 mm in diameter) and 33 small polyps between 2–5 mm in diameter were seen. The two large polyps and just 26 of the 33 small polyps were removed. CC confirmed the 22 polyps between 6–15 mm in diameter in the 19 patients which were seen on the MRC data-sets. All those 22 polyps were removed.

Table 1
Average Values and the SD of the Clinical Data of the Patients Regarding Image Quality Based on the Presence of Artifacts and the Contrast-to-Noise-Ratio (CNR) at the Postcontrast Enhanced VIBE Sequence

	Rectum	Sigmoid colon	Descending colon	Transverse colon	Ascending colon	Cecum	Average
Artifacts high-resolution VIBE	1.10 ± 0.2	1.10 ± 0.2	1.20 ± 0.3	1.20 ± 0.2	1.20 ± 0.2	1.20 ± 0.2	1.14
CNR postcontrast high-resolution VIBE	60.0 ± 2	57.0 ± 3	51.0 ± 3	56.0 ± 2	50.0 ± 2	50.0 ± 2	54.0

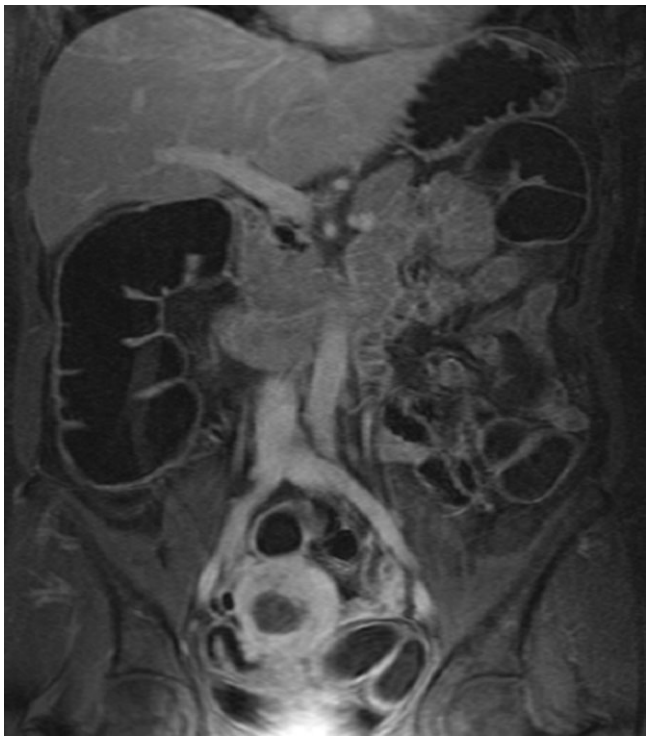

Figure 2. Contrast-enhanced high spatial resolution VIBE sequence of a 54-year-old female patient who underwent MRC as part of a screening examination. MRC classified the colon as normal. However, CC found two polyps smaller than 5 mm in diameter at the right colonic flexure.

Additionally, CC was able to detect one polyps larger than 5 mm (9 mm in diameter) and 22 small polyps in these 19 patients (2–5 mm in diameter). Those polyp and just 16 of the 22 small polyps were removed. Furthermore, in two patients with diverticulosis CC confirmed three polyps less than 5 mm in diameter which were missed in the MRC-examination. These three polyps were removed. CC confirmed the diverticulitis in one patient

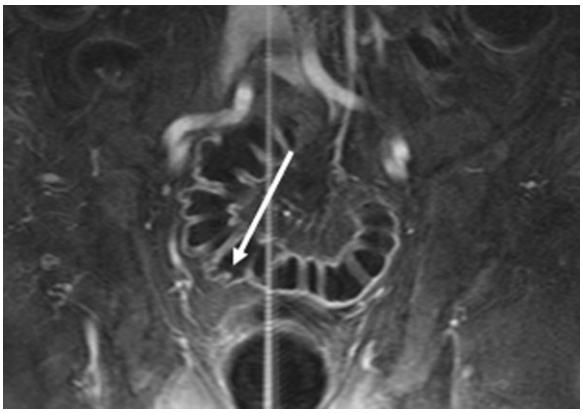

Figure 3. Contrast-enhanced high-resolution VIBE sequence of a 63-year-old female patient who underwent MRC as part of a screening examination. In MRC, a polyp 7 mm in diameter was seen in the sigmoid colon (arrow), which was confirmed and removed in CC. The histopathologist classified the polyp as tubular.

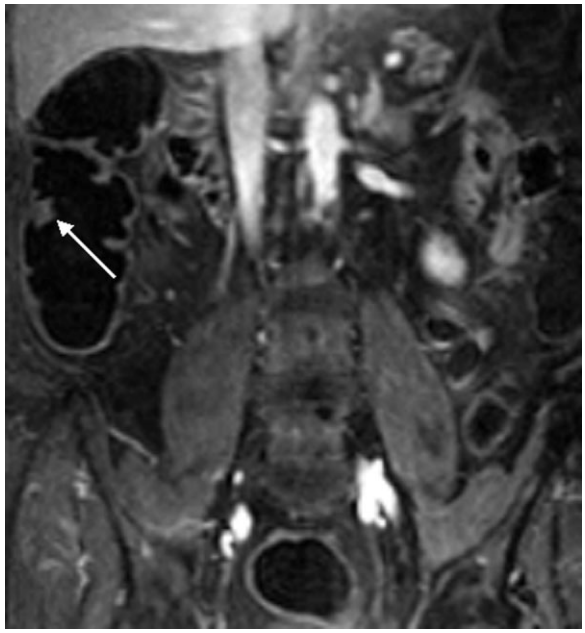

Figure 4. MRC of a 65-year-old male patient who underwent MRC due to positive fecal occult blood test. MRC shows a 13 mm polyp in the ascending colon (arrow). This polyp was confirmed and removed in CC. The histopathologist graded it as polyp with dysplasia malignancy signs.

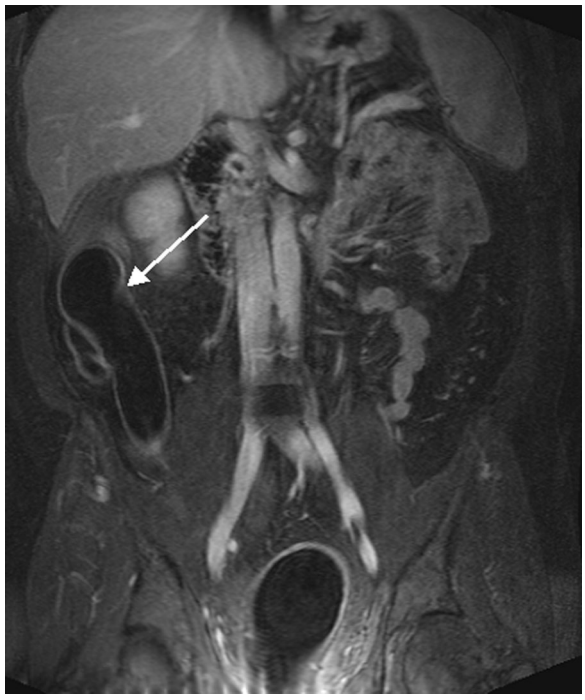

Figure 5. Contrast-enhanced coronal 3D VIBE sequence of a 40 year-old female patient with ulcerative colitis. A loss of haustral markings and light increased contrast uptake of the colonic wall can be seen in the ascending colon (arrow). CC confirmed the presence of light inflammation. Additionally, in CC a small polyp 4 mm in diameter was seen in the descending colon which MRC failed to detect. Histopathology revealed an inflammatory and hyperplastic polyp.

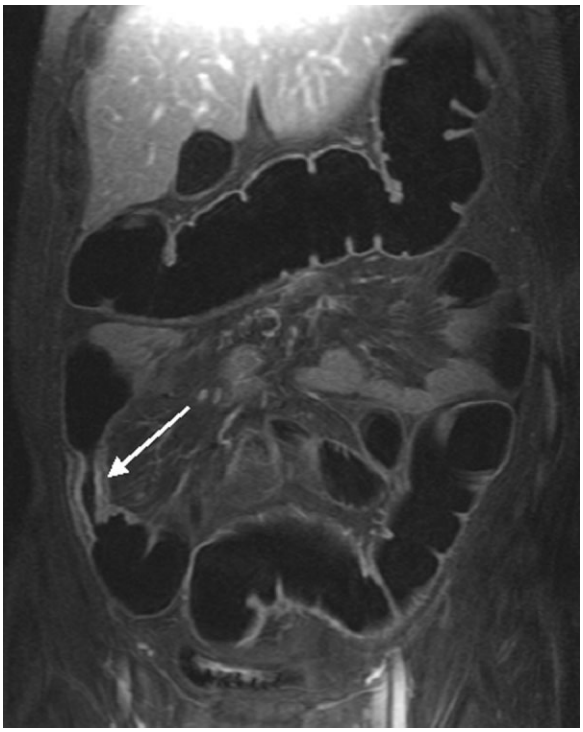

Figure 6. Coronal source image of a 37-year-old patient with Crohn's disease after intravenous administration of contrast agent. With the help of wall thickness and contrast enhancement a moderate stenosis of the ascending colon was seen (arrow), which was confirmed by means of CC. Additionally, CC found two small polyps less than 5 mm in diameter that were missed in MRC. The histopathology graded the polyps as inflammatory hyperplastic.

and no polyps in these patients were seen. In four patients CC confirmed inflammatory signs and a moderate stenosis in one patient which was seen on the MRC data-sets. Additionally, CC found seven small polyps (2–5 mm in diameter) which were missed on the MRC data sets. Four of those seven polyps were removed.

Histological Findings

The pathologist histologically examined 49 polyps with a diameter of less than 5 mm and 25 polyps larger than 5 mm in diameter. The pathologist graded the 49 polyps which were smaller than 5 mm as tubular (19 polyps), tubulovillous (nine polyps), villous (six polyps), inflammatory hyperplastic (eight polyps), juvenile (five polyps) and villous with signs of dysplasia (two polyps). In none of the 49 polyps a carcinoma or high malignancy signs were seen. In the other 25 polyps lager than 5 mm in diameter four polyps have shown dysplasia malignancy signs (11, 13, 13 and 15 mm in diameter). The remaining 21 polyps were classified as follows: nine were tubular, six tubulovillous, and six villous. All found and removed polyps are listed in Table 2.

DISCUSSION

The presented data carry three messages we believe to be important: 1) dark-lumen MRC could not detect any colorectal lesions less than 5 mm in diameter; 2) Polyps smaller than 5 mm at the time of their detection are benign and thus can be kept under surveillance; and 3) MRC turned out to be accurate regarding the detection of clinically relevant colonic lesions exceeding 5 mm in size with sensitivity and specificity values amounting to 79/100%.

Colonic cancer is an ideal disease candidate for screening and secondary prevention. Early detection of colorectal polyps leads to a decreased incidence of colorectal cancer (3,4). CC is the standard of reference to detect colonic pathologies. As many studies have shown (15), discomfort and unpleasantness of CC and low acceptance of CC decreases the screening benefit for colorectal cancer (15,16). All those facts led to the development of other methods to detect colorectal pathologies based on 3D imaging techniques.

Due to its availability CT is the most used examination for the assessment of entire colon. Using air to distend the colon, CT colonography (CTC) provides the most accurate three-dimensional depiction of colorectal masses (17). For a thorough inspection of the surrounding parenchymal organs, the intravenous administration of potentially nephrotoxic contrast agents is required. Hence, CTC has been advocated as a rapid, well-tolerated, non-invasive alternative for CC for the detection of colorectal pathologies. Especially, CTC can detect colorectal lesion smaller than 5 mm in diameter through conversion of the 3D data set in thin slices. In a study including 115 patients Vogt et al (18) have found that CTC has a sensitivity of 75% to detect polyps less than 5 mm in diameter, respectively of 91% and 100% for polyps in size 6–10 mm and lager than 10 mm in diameter. However, CTC has shown a sensitivity of only 50% for the detection of flat lesions. The presence of residual fluid does however require the acquisition of data sets in both the prone and supine patient positions (19,20). Associated doses of ionizing radiation as high as 4.7–7.2 mSv should trigger the search for an alternative, particularly in young patients (21,22).

Table 2
Histopathologic Results of All Found and Removed Polyps

	Polyps <5 mm in diameter	Polyps >5 mm in diameter
MRC	0	22
CC	65	25
Removed	49	25
Classification of histopathologic results	19 tubular, 9 tubulovillous, 6 villous, 8 inflammatory, hyperplastic, 5 juvenile, 2 villous with signs of dysplasia	4 dysplasia malignancy signs, 9 tubular, 6 tubulovillous, 6 villous

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 (10–14). Results of several preliminary studies indicate that this technique has a high sensitivity for the detection of colorectal pathologies (12,13). Dark-lumen MRC is based on the focal uptake of T1-shortening contrast material in colonic lesions which are displayed as bright areas on T1-weighted sequences (12,13), whereas the lumen is rendered totally dark due to water or water-based solutions that serve as filling material. The latter leads to uniform luminal darkening as well as sufficient distention of the colon. The diagnostic accuracy of MRC has been assessed in several studies using CC as the standard of reference (13,14). While colorectal lesions smaller than 5 mm in size were missed, all colorectal lesions exceeding 10 mm were correctly identified. Ajaj et al (13) found that dark-lumen MRC is accurate regarding the detection of colonic lesions exceeding 5 mm in size with a sensitivity and specificity values amounting to 93/100%. However, none of the colorectal lesions less than 5 mm in diameter could be detected (13,14).

Approximately 6% of the general population will develop colorectal cancer (CRC) during their lifetime (3). The disease is lethal if detected late and curable if diagnosed early. The biology of colorectal cancer, evolving from a pre-cancerous colonic polyp to carcinoma over a considerable time span (3,4), has elevated colorectal polyp screening with subsequent endoscopic polypectomy to one of the most promising preventive measures in medicine (15,16). Despite these efforts, the incidence of colorectal cancer continues to increase, with more than 130,000 newly-diagnosed patients and 50,000 deaths annually in the United States alone (4).

The size as well as the histology of detected colorectal polyps is important because large polyps are neoplastic (adenomatous or cancerous) polyps and generally considered of greater clinical importance (23–30). The adenoma-carcinoma sequence describes the potential development of colorectal cancer from polyps and increases with size and atypism of polyps (3,4). The relative risk of malignant transformation in colorectal polyps less than 5 mm in diameter is still debatable. The reason is that severe dysplasia and malignancy are rare in adenomatous polyps less than 5 mm in diameter and they do occur more in polyps larger than 5 and 10 mm in diameter (26–28).

Several studies comparing the histology of small and large colorectal adenomas have suggested that polyps smaller than 10 mm in diameter have a lower risk for subsequent malignant transformation than polyps larger than 10 mm (31,32). Other studies support the observation that polyps smaller than 5 mm in diameter are unlikely to be malignant or have a high-grade to malignant transformation (33–37).

Wallace et al (31) analyzed 4490 patients who underwent sigmoidoscopy. A neoplastic lesion was detected in just 401 patients (8.9%) and complete colonoscopy was done in 301 patients (75%). A total of 98 patients with a single or multiple distal tubular adenoma 1 mm to 5 mm in diameter had an advanced proximal polyps. However, all small polyps 1 mm to 5 mm in diameter in 106 patients were benign and no polyps had shown severe dysplasia or malignancy (31). In addition, no evidence of confounding by age or sex was found by logistic regression modeling. In contrast, 10 polyps were larger than 10 mm in diameter (range: 12–33 mm) and just two polyps showed a high-grade dysplasia and one polyp revealed an invasive carcinoma (31). Polyps with high-grade dysplasia or cancer were seen only in patients with single or multiple polyps from 6 mm to 10 mm in diameter. In a prospective study Aldridge and Simson (32) examined 445 patients who underwent conventional colonoscopy. In all patients 1228 polyps were detected and just 657 lesions were removed. In the group with polyps less than 10 mm just 11 polyps (3%) showed a severely dysplastic carcinoma although no polyp was less than 5 mm in diameter. In a study by Hofstad et al (38) the clinical relevance of polyps less than 10 mm in diameter was assessed. A total of 103 patients with known 189 colorectal polyps smaller than 10 mm in diameter were controlled by means of CC 12 months after initial detection. Only one of the 189 polyps showed an increase over 10 mm in diameter. In addition 79 small polyps (1–5 mm in diameter) in 52 patients were newly developed. Also, several other studies confirmed the harmless of polyps smaller than 5 mm in diameter.

Clearly, the present study is not without its limitations. First and foremost, we report about a rather heterogeneous patient cohort with different indications for MRC. Additionally, patient numbers are too small. However, the underlying patient selection reflects reality of the daily clinical routine for the examination of the large bowel.

In conclusion, the presented study has shown that dark-lumen MRC was not able to detect polyps smaller than 5 mm in diameter. However, this study confirmed a high potential of MRC to detect in the size clinically relevant colorectal masses. The results indicate that smaller polyps of less than 5 mm in diameter may not be clinically relevant at the moment of their detection and they could be kept under surveillance. However, large studies to support our results are required.

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