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Dark-lumen magnetic resonance colonography

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With an incidence of 130,000 per year and 50,000 cases of death in the United States alone, colorectal cancer (CRC) has matured into the second most common cancer in both sexes in the Western world.[1] Up to 90% of CRC-cases originate from benign adenomas. Hence, the incidence of CRC could be considerably reduced by more than 80% if polyps were detected and eliminated before their malignant transformation. Despite the availability of several screening options, CRC remains a considerable cause of morbidity and mortality. The main reason is related to poor patient acceptance in current screening programs. Therefore, a real successful strategy has to overcome poor patient acceptance in the future by making the examinations comfortable and noninvasive. Magnetic resonance colonography (MRC) has the potential to be implemented as such a screening tool. Due to its noninvasive character, it is well accepted by patients. Moreover, it is highly accurate for the detection of colorectal polyps.

Similar to contrast-enhanced 3D MR angiography, MRC is based on the principles of ultrafast, T1-weighted 3D gradient-echo acquisitions collected within the confines of a single breath-hold. This requires the use of an MR system equipped with high-performance gradients. Initial approaches of MRC were based on the rectal application of water spiked with paramagnetic contrast. On T1-weighted data sets, the paramagnetic contrast renders the colonic lumen bright. Hence, polypoid colonic masses appear as dark filling defects within the bright colonic lumen. This appearance may make the differentiation of polyps from residual fecal material or small pockets of air difficult. Furthermore, the technique requires data acquisition in prone and supine patient positions to compensate for the presence of residual air. A recently introduced method of MRC is based on a different contrast mechanism and is referred as dark-lumen MRC.[2] It has turned out to be more accurate and less time consuming than bright-lumen techniques.

Before the examination, the patient has to be screened for contraindications to MR imaging (MRI) such as severe claustrophobia or the presence of metallic implants or cardiac pacemakers. The presence of hip prostheses, which normally is not regarded a contraindication to MRI, impedes complete analysis of the rectum and sigmoid colon. Therefore, these patients should not be examined. As residual stool impedes appropriate evaluation of the large bowel, patients need to undergo bowel preparation in a manner similar to that required for conventional colonoscopy. To limit patient discomfort related to extended fasting, MRC should be performed in the early morning. Patients should be examined on a 1.5 Tesla or 3 Tesla MR scanner equipped with strong gradient systems. Thus, data acquisition is to be confined to one breath-hold. The examination itself is performed in patients in the prone or supine position. A combination of 2 surface coils should be used for signal reception to permit coverage of the entire colon. To minimize motion artefacts due to bowel peristalsis, a spasmolytic agent is administered intravenously (for example, scopolamine or glucagon). A contrast enema consisting of 2-2.5 L of warm tap water is rectally administered using hydrostatic pressure (1-1.5-m water column). The filling process of the colon can be monitored by using a T2-weighted non-slice select acquisition that collects one image every 3 seconds (for example, TrueFISP; repetition time/echo time, 2.4/1.2 ms; flip angle 60 degrees). Beyond assuring adequate filling, this 2-dimensional overview allows recognition of high-grade stenoses and colonic spasm. Once the water enema has reached the cecum and a sufficient distension is assured, a 3D gradient-echo data set is collected repetition time/echo time, 3.1/1.1 ms; flip angle, 12 degrees; field of view, 450 x 450 mm; matrix, 168 x 256; and effective slice thickness, 4 mm). Subsequently, paramagnetic contrast is administered intravenously at a dosage of 0.2 mmol/kg body weight and a flow rate of 3.5 mL/s. A second 3D acquisition is acquired in a portal-venous contrast

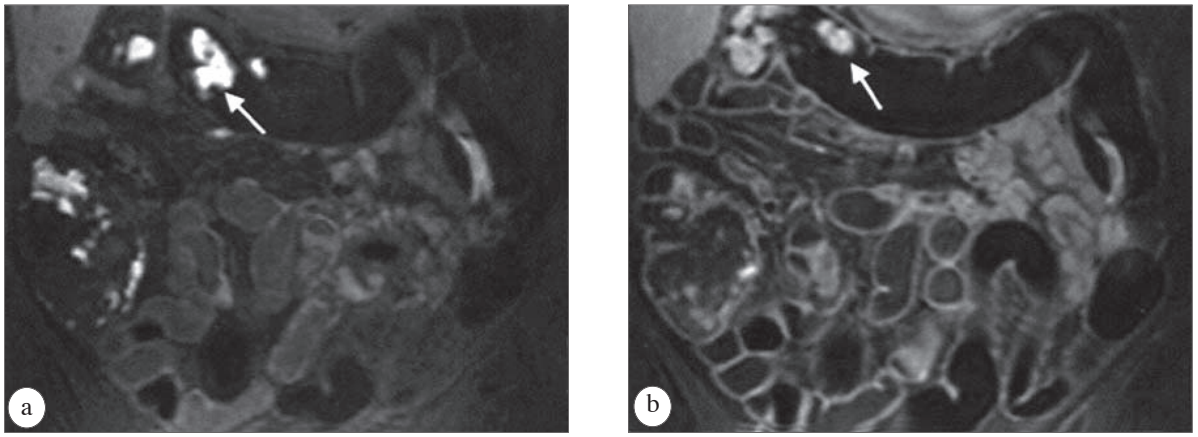

Figure 1 - Dark-lumen magnetic resonance colonography. Tap water is used for bowel distension. **a)** A native coronal T1-weighted 3D VIBE sequence. **b)** The bowel wall is bright due to intravenous application of paramagnetic contrast. Residual stool (arrow) appears bright on pre- and post-contrast phases, and shows no contrast enhancement.

phase. After data acquisition, the enema bag is placed on the floor for facilitated emptying of the colon. This protocol allows completing the examination with an in-room time of 20 minutes.

For data interpretation, the 3D data sets should be post-processed and read in multiplanar reformation mode (MPR). This permits scrolling through the 3D data sets in all 3 orthogonal planes. The diagnostic work-up should start interpreting 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 scan. By measuring signal intensities of the mass in the native and post-contrast scans, a contrast enhancement value can be determined. Hence, the differentiation between small residual stool particles and colorectal lesions is simple: the residual stool does not show contrast enhancement (**Figures 1a & 1b**) whereas colorectal lesions always do. In a second step, the data should be assessed based on virtual endoscopic renderings displaying the inside of the colonic lumen. A virtual endoscopic fly-through enables the radiologist to concentrate on the colon by facilitating the depiction of small structures protruding into the colonic lumen. Furthermore, the 3D depth perception allows discrimination between polyps and haustra. To assure complete visualization of both sides of the haustral folds, the virtual fly-through should be performed in antegrade and retrograde directions with regard to the detection of polyps, virtual endoscopic viewing renders improved sensitivity and specificity values as compared with inspection of the individual cross-sectional images alone.

Dark-lumen MRC was first introduced and evaluated in 2001.[2] Twelve patients with suspected colorectal lesions were examined. In addition to dark-lumen MRC, all patients underwent conventional colonoscopy performed within 5-14 days. Five polyps ranging in diameter from 7-12 mm were detected. All lesions were confirmed by conventional colonoscopy and subsequent polypectomy was performed. There were no false negative findings. The intravenous administration of paramagnetic contrast resulted in an average signal-to-noise ratio increase within the colonic wall of 170% from 9.2 to 24.8 ± 2.6. This difference was statistically significant ($p<0.001$). Polyps showed even more enhancement with signal intensities increasing by 306% from 8.9 ± 1.6 to 36.1 ± 3.9. Lack of contrast enhancement correctly identified 3 bright "lesions" as residual stool. In addition, dark-lumen contrast-enhanced MRC depicted 4 extra-intestinal lesions: 2 renal cysts in 2 patients, one hepatic hemangioma in one patient, and one aortic abdominal aneurysm measuring 4 cm in diameter in another patient.

A recent study used a larger patient cohort[3] of 122 patients undergoing dark-lumen MRC and subsequent conventional colonoscopy. The MRC did not detect lesions smaller than 5 mm. For lesions between 5-10 mm, MRC correctly detected 16 of 18 lesions. Nine of 9 CRCs with lesions larger than 10 mm were seen on MRC images. In addition, conventional endoscopy documented inflammatory wall alterations (Crohn's disease and ulcerative colitis) in 28 patients. The MRC correctly diagnosed inflammatory changes

in 25 patients. In 3 patients with Crohn's disease, inter-intestinal fistulae were detected with MRC and conventional colonography. There were no false positive readings based on the MRC data sets. In addition, dark-lumen MRC permitted the reliable assessment of extra-intestinal organs. Thus, a variety of therapy-relevant and irrelevant pathologies were identified. Hepatic metastases were observed in 4 patients, and the bone metastases were seen in 7 patients. Both studies emphasize that dark-lumen MRC may overcome several limitations inherent to bright-lumen MRI techniques. The intravenous application of paramagnetic contrast technique allows the direct depiction of the colorectal wall. Thus, the bright colonic wall can be easily discriminated from the dark, water-filled colonic lumen. This form of direct visualization of all colorectal pathologies reduces the incidence of false positive findings: residual stool or air bubbles, which might mimic small polyps in the bright-lumen technique, remain dark. Hence, lack of contrast enhancement between the pre- and post-contrast scans to rule out the presence of a colorectal mass. Beyond the identification of colorectal lesions, dark-lumen MRC permits the detection and characterization of colonic wall inflammation. Based on the assessment of bowel wall thickness and bowel wall contrast the enhancement, diverticulitis, Crohn's disease, and ulcerative colitis can be diagnosed with great accuracy. Common to all 3 entities, the colonic wall is thickened and characterized by increased contrast uptake.

Virtual colonography still mandates bowel purgation. As more than 50% of patients undergoing bowel preparation complain regarding negative side effects, patient compliance is negatively affected. If bowel cleansing were avoided, patient acceptance of MRC could be considerably increased. This can be accomplished by fecal tagging; a concept based on altering the signal intensity of stool by adding contrast-modifying substances to regular meals. Thus, fecal tagging may render stool virtually indistinguishable from the distending rectal enema on MR images. In an initial study, barium sulfate was evaluated as a tagging agent in conjunction with dark-lumen MRC.[4] Two hundred milliliters of a barium sulfate containing contrast agent was ingested with each of 4 principal low-fiber meals. Barium proved to be a safe and inexpensive tagging agent rendering the stool homogeneously dark and permitting the selective depiction of the contrast-enhancing colonic wall. Due to the low signal intensity of barium-tagged stool, signal differences between the colonic lumen and the colonic wall were high throughout the entire large bowel. However, further studies need to be performed to evaluate to value of barium-based fecal tagging with respect to patient acceptance and diagnostic accuracy.

To date distension of the colonic lumen for MRC has been accomplished predominantly with water or water-based contrast media. Better density properties and the assumption that air provides less discomfort than water has resulted in the predominant use of gaseous agents for CT colonography. Although similar to water with regard to MR signal properties on T1-weighted images, the fear of susceptibility artefacts rendered the use of air or other gases much less intuitive for MRC. Recently, the feasibility of air-distended dark-lumen MRC has been proved.[5] Fifty patients who had been referred to colonoscopy for suspected colorectal pathology were randomized into water-distension and air-distension groups. Dark-lumen MRC was performed in both groups. Comparative analysis was based on qualitative ratings of image quality and bowel distension and on contrast-to-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 with respect to discomfort levels and image quality. The presence of air in the colonic lumen was not associated with susceptibility artefacts. The CNR of the contrast-enhanced colonic wall and bowel distension were superior on air-distended 3D data sets. Hence, dark-lumen MRC can be performed with water or air for colonic distension. Both techniques permit assessment of the colonic wall and identification of colorectal masses.

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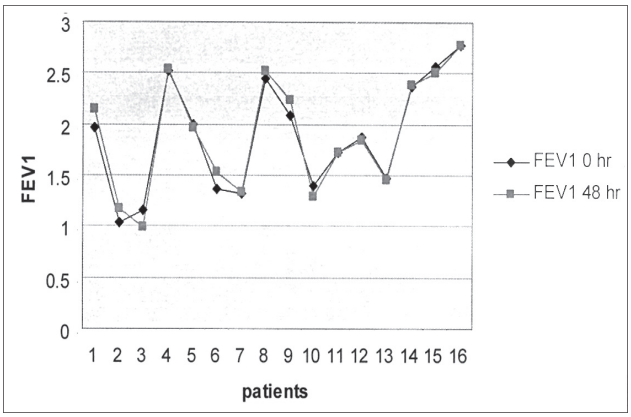

Figure 1 - Comparison of forced expiratory volume (FEV)1 at study entry and on subsequent follow-up of pulmonary function test.

The use of etoricoxib in patients with bronchial asthma associated with aspirin sensitivity

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Patients with sensitivity to aspirin (ASA) or non-steroidal anti-inflammatory drugs (NSAIDs), may develop an acute asthma attack, thus, limiting the use of such agents. Sensitivity to aspirin may occur in up to 20% of patients with bronchial asthma.[1] Aspirin induced asthma (AIA) usually presents for the first time in the third or fourth decades of life.[2] The reaction is usually slow in onset, 30-60 minutes following ingestion, manifesting as bronchospasm with profound nasal symptoms, including nasal congestion, rhinorrhea, and tearing. Facial flushing, angioedema, and gastrointestinal symptoms can also occur. This complex reaction is slow to resolve, and often severe and may be life threatening. Furthermore, AIA can be sometimes difficult to treat. Such patients are proven to have airway inflammation, which is resistant to corticosteroids and may require leukotriene receptor antagonists as therapy.[2] These patients sometimes have associated nasal polyposis or chronic urticaria.[2] Patients with AIA can react to NSAIDs, which differ in structure from aspirin, therefore, suggesting a non immunological mechanism involved in this disease state.[1] The reason why ASA sensitivity does occur in bronchial asthma is not clear. Two theories were proposed to explain AIA. The first theory suggests that asthma may develop through inhibition of cyclooxygenase 1 (COX-1) resulting in decreased production of prostaglandin E2, which is important in maintaining bronchodilation.[2] The second theory suggests an overexpression of leukotriene C4 synthetase, from blockage of COX by ASA or NSAIDs. The arachidonic acid precursors are shunted down the leukotrienes pathway resulting in excessive production of leukotrienes C, D, E, which can act as potent bronchoconstrictors.[2] Recently, 2 isoforms of COX have been found, namely, COX-1 and COX-2. Both enzymes catalyze the transformation of arachidonic acid to prostaglandins and thromboxanes. The COX-1 enzyme is expressed constitutively in many healthy tissues of the body where prostaglandins have physiologic effects, including the gastrointestinal tract, kidneys, and platelet, whereas COX-2 enzyme is induced at sites of inflammation.[3] The inhibition of COX-1 has been related to the adverse effects of NSAIDs.[3] Non-steroidal anti-inflammatory drugs that selectively inhibit COX-2 enzyme (selective COX-2 inhibitors) has been recently developed. These drugs were shown to have a comparable efficacy to traditional NSAIDs and are better tolerated. They have become widely available in the market for the management of a variety of musculoskeletal disorders. Little is known regarding the safety of selective COX-2 inhibitors in patients with AIA. A few recent trials have found some selective COX-2 inhibitors to be safe in patients with AIA.[4-5] Of these drugs, celecoxib was the first generation selective COX-2 inhibitors that were developed. Par Gyllfors et al,[4] assessed 33 aspirin sensitive asthmatics, challenged on 2 occasions, one week apart, with increasing doses of celecoxib (total