

Magnetic Resonance Imaging of the Bowel: Today and Tomorrow

Magnetresonanztomografie des Darms: Altbewährtes und Innovatives

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Abstract

Magnetic resonance imaging of the small bowel has been feasible for more than 15 years. This review is meant to give an overview of typical techniques, sequences and indications. Furthermore, newly evaluated promising techniques are presented, which have an impact on the advance of MR imaging of the small and large bowel.

Key Points:

- ▶ T2-weighted sequences both with and without fat saturation and T1-weighted fat saturated sequences prior to and following intravenous injection of a gadolinium-based contrast medium constitute the basics for bowel MR imaging.
- ▶ Newer MR applications, such as diffusion-weighted imaging or contrast-enhanced dynamic sequences supply additional information; they should thus be integrated in a regular sequence protocol for bowel MRI.
- ▶ Additional new modalities like motility imaging and PET/MRI have to be evaluated in future studies.

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Zusammenfassung

Die Möglichkeit zur Darstellung des Darmtrakts mittels Magnetresonanztomografie besteht bereits seit mehr als 15 Jahren. Dieser Übersichtsartikel soll einen Überblick über die typischen Techniken, Sequenzen und Indikationen geben. Zudem werden in den letzten Jahren neu evaluierte vielversprechende Techniken dargestellt, die einen

weiteren Fortschritt in der MRT-Bildgebung des Dünn- und Dickdarms bieten.

Introduction

Magnetic resonance imaging (MRI) has been used for examining the small and large intestines for over 15 years [1, 2]. During this period, new techniques and sequences have provided imaging with consistency and have ensured ongoing improvement and innovation.

This survey article provides a summary of time-tested principles of imaging and sequence protocols and the known and typical indications. It also presents new and future applications and techniques.

Time-tested

Indications

The typical indications for magnetic resonance imaging (MRI) of the bowel are inflammatory or tumorous changes [3]. MRI of the bowel, in particular the large intestine, was and is still discussed as a screening method for colorectal cancers, which are frequently treatable and even curable if detected at an early stage [4, 5]. An article recently published by Graser et al. demonstrates that MR colonography at 3 Tesla detects colorectal adenomas ≥ 6 mm and advanced neoplasia with greater sensitivity and specificity, yet still remains inferior to colonoscopy when it comes to colorectal neoplasia [6].

A suspected diagnosis in the large intestine can be routinely confirmed through endoscopy and histological study. In cases of incomplete colonoscopy, e.g. when there are stenotic colon tumors or unfavorable anatomy as

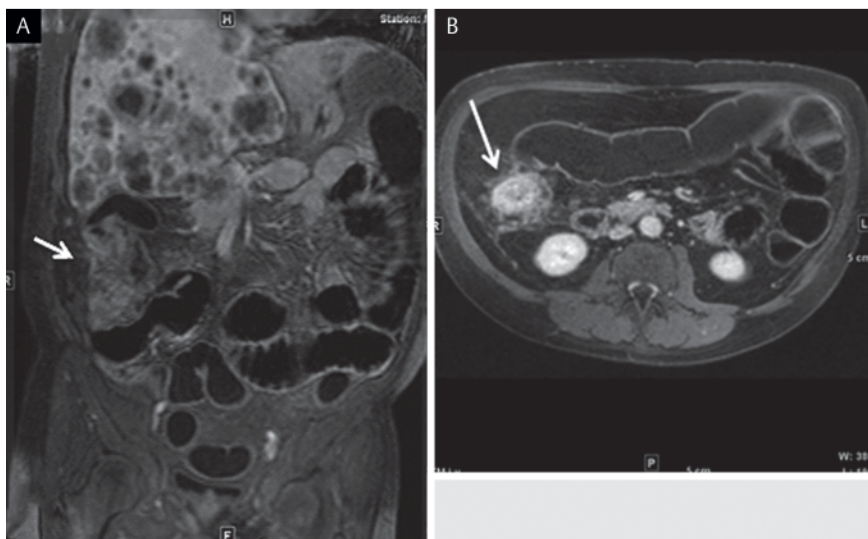


Fig. 1 66 year old male patient with histopathological confirmed diagnosis of a colonic cancer in the ascending colon (arrow in **A** coronal fat saturated VIBE sequence in arterial phase). MR colonography shows liver metastases in addition to the primary cancer and locoregional lymphangiosis (arrow in **B** fat saturated T1 TSE axial after contrast).

well as following infections, MRI makes it possible to evaluate sections of the colon more proximal [7]. For diseases of the small intestine, capsule endoscopy currently provides image-based morphological confirmation of a diagnosis, yet is still used on a limited basis because of its costliness. MRI of the small bowel constitutes a more cost-effective and very good diagnostic method for confirming or excluding diseases in this section of the bowel. MRI of the small intestine is performed primarily in cases of chronic inflammatory bowel disease in children and adults [8, 9]. The advantage of MRI over computed tomography is that it involves no exposure to radiation, which is particularly important given the young patient age and the necessity of repeated examinations for monitoring therapy. MRI has the advantage over endoscopy in that it can also examine extra-intestinal areas, which is especially important when dealing with transmural inflammatory diseases such as Crohn's disease and when assessing local and remote metastases of intestinal tumors (• **Fig. 1**). In addition, MRI of the small intestine is an observer-independent method as Schleder et al. demonstrated in an analysis of MR enterographies performed on patients with Crohn's disease [10].

Examination prerequisites, protocol and sequences

To achieve diagnostic image quality and to facilitate performing the selected sequences within one breathhold, the bowel should be examined at least on a 1.5 Tesla MRI machine. Thus far, higher field strengths have not been found to be superior in detecting polyps when used in MR colonography [11, 12] and have exhibited only minor advantages in diagnosing mucosal ulcerations in Crohn's patients [13]. Therefore, 1.5-Tesla scanners, which are the most commonly available in clinical settings, continue to be the standard for imaging. The distension of the cleansed and evacuated bowel is another prerequisite for optimal imaging. In recent years, various iso- and hyperosmolar liquids have been tested for use in distending the small intestine [14]. At our clinical practice, we use a mannitol and locus bean gum solution [15] prepared by our in-house pharmacy that is on par with other commercially available liquids [16–18]. While the question whether the contrast medium should be delivered to the intestinal tract orally (MR enterography) or via

an already in place nasojejunal probe (MR enteroclysis) is widely debated, it has been the subject of only a few comparative studies. In their respective comparative studies, Masselli et al. and Negaard et al. found that significantly better distension was achieved with MR enteroclysis than with MR enterography [19, 20]. However, Negaard et al. were able to detect Crohn's-typical changes with high diagnostic accuracy and reproducibility using either method [20]. In their intraindividual comparison of MR enteroclysis and MR enterography, Schreyer et al. demonstrated that all pathologies were correctly detected with both MR methods [21]. They thus concluded already in 2004 that patient-friendly MR enterography has the potential to replace the conventional enteroclysis. Today, MR enterography is the preferred method at many centers given its greater simplicity, practicality and non-invasiveness, and in view of the radiation involved when inserting the nasojejunal probe for MR enteroclysis [22]. MRI of the bowel is initiated after approximately 1500 ml of iso- to hyperosmolar fluid is ingested over approximately 45 minutes. At many centers, metoclopramide is used to promote gastric peristalsis and emptying. The colon is filled rectally with conventional tap water to provide contrast [23]. If rectal filling is not desired or necessary (e.g. if the primary focus is on imaging the small intestine) the colon can be sufficiently filled with the oral contrast medium by allowing a somewhat longer waiting time or by having the patient drink the liquid in intervals. In a comparative study of MR enterographies on patients with Crohn's disease, Friedrich et al. showed that the additional rectal contrast by means of water enema facilitated greater sensitivity and specificity particularly in the terminal ileum, ascending colon and rectum [24]. The classic examination protocol for examining the large and small intestine includes axial and coronal T1- and T2-weighted sequences as well as the acquisition of dynamic contrast enhanced T1-weighted sequences [25]. To keep the motion-related artefacts to a minimum, the examination should be performed with the patient lying prone, since this reduces respiratory excursion, and an antispasmodic should be administered to suspend or significantly reduce intestinal motility. The appropriate antispasmodics are hyoscine butylbromide, (Buscopan, Boehringer Ingel-

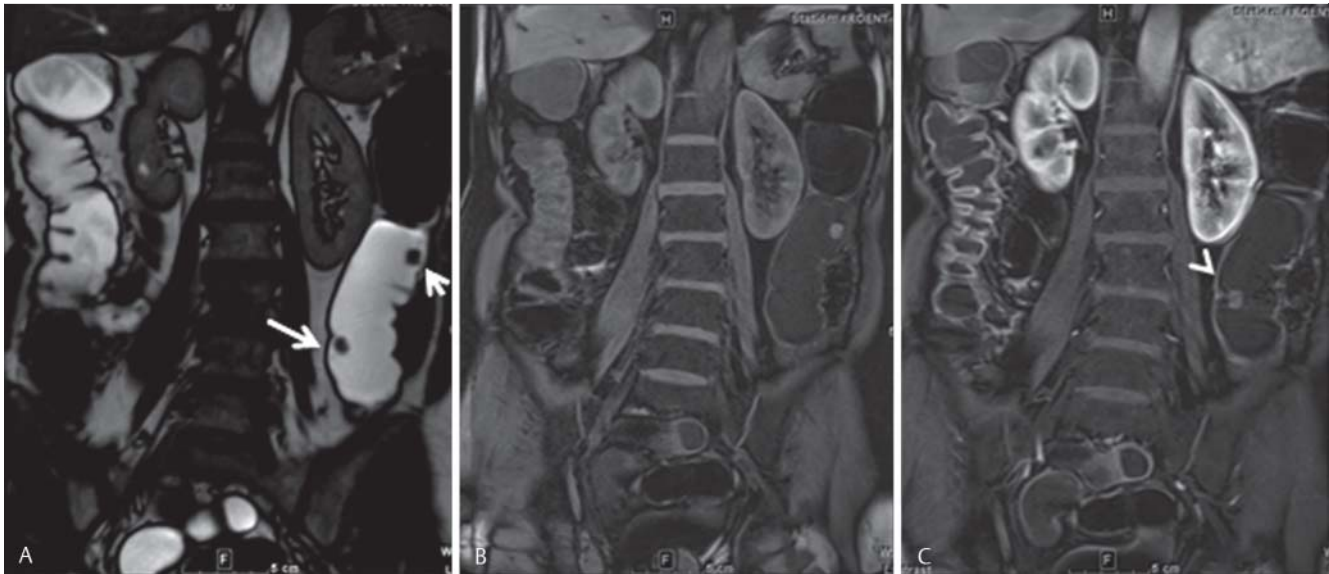


Fig. 2 MR colonography in a 46 year old female patient with anemia due to iron deficiency. Two lesions can be depicted in the TrueFISP images **A** in the descending colon (arrows). The proximal lesion is hyperintense in an unenhanced T1-weighted sequence **A** and cannot be depicted after con-

trast **C** leading to the diagnosis of residual stool. The second lesion is only visible after contrast (arrow head): Subsequent colonoscopy confirmed a polyp.

heim Pharma GmbH & Co KG, Germany) and glucagon, with studies showing glucagon to induce a longer period of spasmolysis [26]. Intravenous administration results in a faster and more reliable onset of effect [27].

One of the relevant sequences is an axial or coronal T2-weighted sequence (half-fourier single-shot turbo spin echo, HASTE with Siemens; single-shot fast spin echo, SSFSE with General Electric or ultra-fast spin echo, UFSE with Philips), which offers a good overview of the wall thickness of the intestinal segments as well as of any existing edema. A balanced Steady State Free Precession (bSSFP) sequence (True fast imaging with steady state precession, TrueFISP with Siemens; Fast Imaging Employing Steady-state Acquisition, FIESTA with General Electric or Balanced Fast Field Echo, b-FFE with Philips) in coronal acquisition facilitates good clarification of mural pathologies such as ulcerations as well as extraintestinal changes such as mesenteric lymph nodes or vascular injections (comb signs) as signs of inflammatory changes. This sequence is not sensitive to movements and can thus be used as a basic sequence on patients with reduced compliance. In addition, coronal T1-weighted, fat-saturated rapid gradient echo sequences are performed for dynamic contrast-enhanced acquisition (volume-interpolated breath hold examination, VIBE with Siemens, liver acquisition with volume acquisition, LAVA with General Electric, enhanced T1 High Resolution Isotropic Volume Excitation, eTHRIVE with Philips). Finally, a fat-saturated T1 Turbo Spin Echo (TSE) sequence is performed in axial and coronal acquisition during the late phase following administration of contrast medium to allow the surrounding organs and soft tissues to be examined for pathologies once again. In their evaluation of the specified sequences, Schleder et al. concluded that a non-contrast T1-weighted sequences can be omitted from the MRI-supported diagnostic investigation of Crohn's disease [28]. However, this type of sequence plays an important role in the diagnostic investigation of the large intestine

since it allows possible contrast-enhanced polyps to be differentiated from stool residue, which is already hyperintense in non-contrast sequences [29] as **Fig. 2** shows. By prompting subsequent endoscopic removal, polyp detection is important, since a polyp may result in a later intestinal tumor in the course of an adenoma-carcinoma sequence (see also **Fig. 1**). Non-enhanced T1-sequences should therefore be part of a conclusive bowel protocol. **Fig. 3** provides an overview of a typical basic protocol for bowel diagnostics.

Innovative



Diffusion-weighted imaging

Diffusion-weighted sequences were first used in the neuroradiological MR diagnostic investigation of strokes [30] as well as in the differentiation of brain tumors [31]. In the meantime, this technique has also been used for full body diagnostics, in particular to answer oncological clinical requests [32, 33]. Diffusion weighted imaging (DWI) essentially takes advantage of the limited diffusion (random thermal motion of the water molecules / Brownian molecular motion) caused by, for example, damaged membranes in infarcted areas. Limited diffusion is also present in inflamed or tumorous tissue. In tumors, the cells are more densely packed, resulting in less extracellular space and thus limited diffusion. Active inflammatory processes exhibit swelling or edematous changes in the cellular structure and likewise bring about a reduction in normal diffusion. Bowel imaging has also taken advantage of this. Initial examinations in patients with chronic inflammatory bowel diseases were able to differentiate healthy segments of the bowel and grade the severity of the disease on the basis of apparent diffusion coefficients (ADC) using DWI [34–36] (**Fig. 4**). It was also shown that adding diffusion-weighted sequences to the clinical examination protocol improved diagnostic certainty

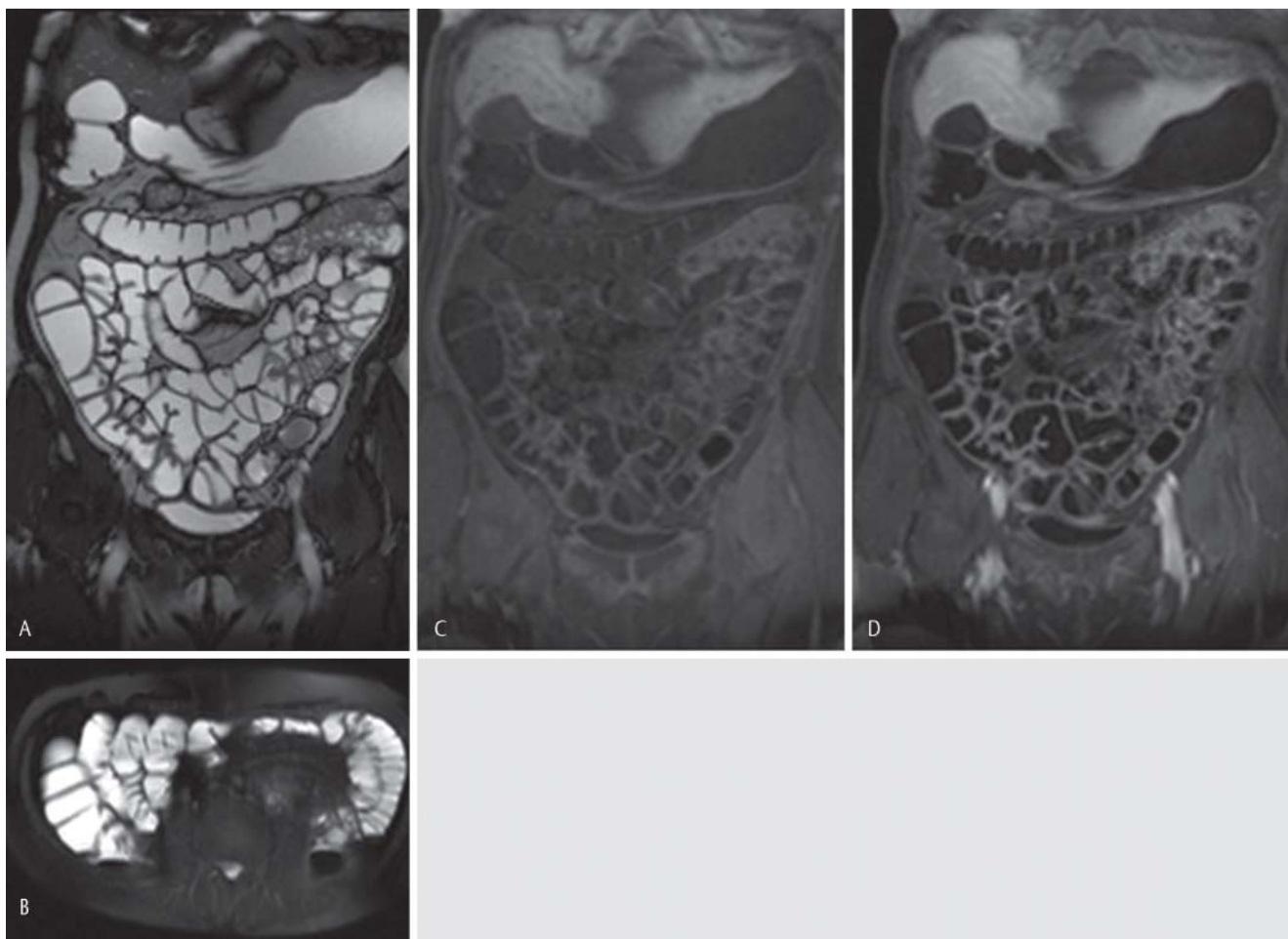


Fig. 3 A MR bowel protocol should include TrueFISP images **A** in coronal acquisition, T2 HASTE in axial or coronal acquisition **B** as well as dynamic fat saturated T1 weighted gradient echo sequences (VIBE, **C**, **D**) in coronal acquisition.

[37]. Both small and large intestine examinations were included in different clinical requests, reflecting the reality of clinical examinations. Diagnostic certainty was improved not only for inflammatory but also for tumorous lesions. Kilkickesmez et al. showed that for examining the rectosigmoid colon of patients with inflammatory and neoplastic changes, DWI is able to differentiate normal from pathologically changed findings and could thus facilitate differentiating inflammation from tumor growth [38]. Schmid-Tannwald et al. discovered additional benefits of DWI for differentiating fistulas [39]. In their publication, these authors discussed the use of DWI on patients with contraindications for contrast medium (e.g. renal failure). An already published study as well as additional current studies compare the diagnostic accuracy of DWI with that of conventional contrast-enhanced bowel imaging in patients with chronic inflammatory bowel diseases [40]. As mentioned above, the fact that DWI makes it possible to omit the use of contrast medium would be beneficial not only in cases of kidney dysfunctions but also when repeated examinations are required in pediatric diagnostics.

Diffusion-weighted imaging allows the detection of accessory inflammatory or tumorous lesions, while increasing diagnostic certainty. Because it does not require the use of contrast medium, it can additionally be used particularly

for examining patients with impaired kidney function and, because of the brief examination time involved, it can be used on pediatric patients, e.g. for evaluating response to therapy.

MRI of bowel motility

Because intestinal peristalsis is typically antegrade, chyme is propelled forward from the oral cavity to the rectum, being intensely mixed and processed along the way. Propulsion is facilitated by a contraction of the intestinal wall musculature [41]. The presence of an intestinal disease also affecting deeper layers of the intestinal wall can be manifested in this segment by a reduction or suspension of bowel motility. More recent studies have concerned themselves with these motility examinations, which are typically performed following the overview sequences and prior to administration of an antispasmodic. A T2-weighted real-time cine sequence can be employed to generate repetitive images, thereby representing bowel motility [42]. Comparison of the motility of individual intestinal segments can expose initial pathologies, since small intestinal segments in particular normally exhibit a regular, uniform contraction. Fröhlich et al. measured the changes in intestinal segment diameter over time during this process [26]. Current software solutions make it possible to quantify the reduced or sus-

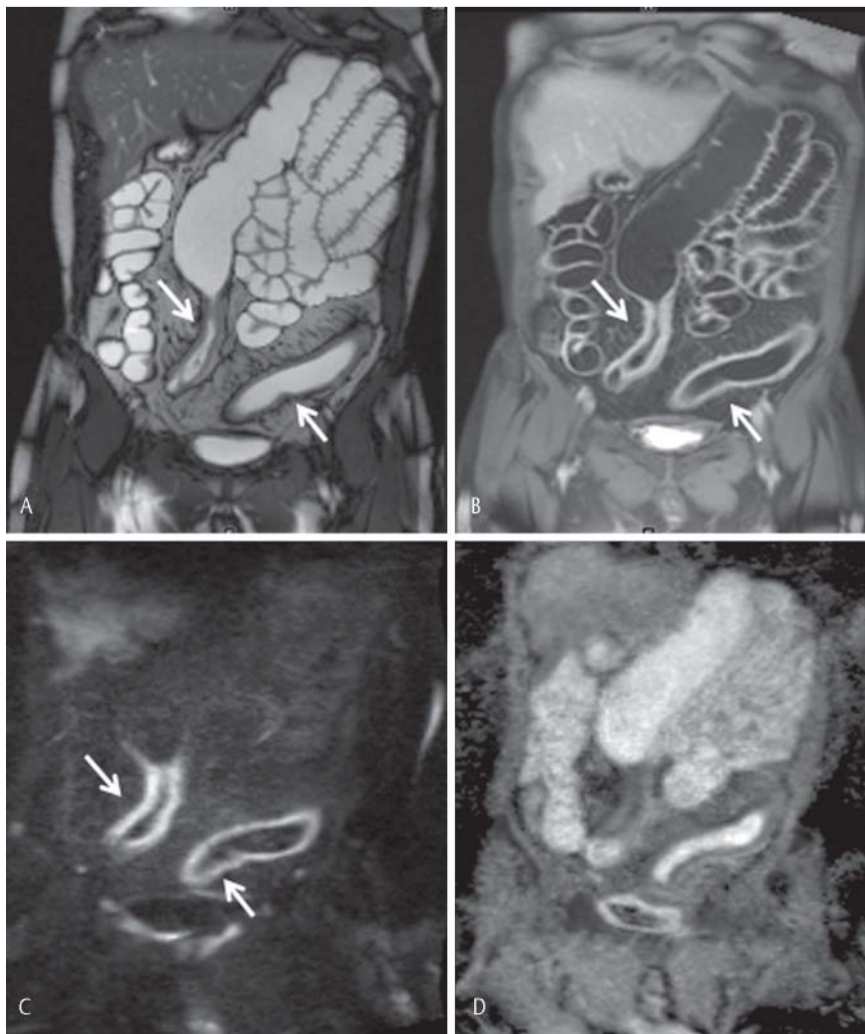


Fig. 4 54 year old patient with crohn's disease after small bowel resection and ileoascendostomy. The patient was re-evaluated because of persisting diarrhea and inflammatory markers. T2-weighted images (A coronal TrueFISP) shows mural thickening in the region of ileoascendostomy as well as in the sigmoid colon with noticeable comb sign. Distinct contrast enhancement of inflamed bowel segments (B T1 TSE after contrast). DWI shows corresponding diffusion restriction with high signal in images acquired with $b = 1000$ C as well as signal reduction in ADC (apparent diffusion coefficient) map D.

pendent bowel motility, by measuring the luminal diameter and plot it along the temporal axis [43]. Software-based measurements have proven to be highly reliable, while allowing accurate and faster measurement. Hahnemann et al. show that compared to healthy subjects, Crohn's patients exhibit reduced or even suspended bowel motility in areas exhibiting acute inflammatory changes [44] (• Fig. 5). In their retrospective study, Menys et al. presented that the motility analysis can be used to differentiate normal intestinal segments as well as those with strictures or upstream from strictures [45]. In their analysis of Crohn's disease patients, Fröhlich et al. found that additionally analyzing bowel motility significantly boosted the detection of inflammatory lesions [46]. In this way not only were more inflammatory lesions detected in the affected patients compared to standard imaging, but also more patients were found to have lesions than with standard imaging. Bickelhaupt et al. showed impaired bowel motility to be closely correlated with the inflammation markers C-reactive protein and calprotectin [47].

MR imaging of bowel motility thus enables the detection of intestinal segments with inflammatory changes that were not detectable with standard imaging and are closely correlated with inflammatory activity measured with fecal and serological inflammation markers.

Dynamic contrast enhanced (DCE) MRI

Dynamic contrast-enhanced imaging has long been employed in oncology as a non-invasive method for evaluating tumor blood perfusion [48]. The potential of DCE-MRI as a biomarker for measuring antiangiogenic effects of cancer therapy can also be used in bowel imaging for evaluating the vascularization of intestinal segments and likewise for evaluating therapy response in both chronic inflammatory bowel diseases and in tumors of the bowel [49, 50]. In a study involving 18 patients, Oto et al. showed that combining DCE-MRI with new methods of diffusion-weighted imaging (DWI) provides a good quantitative measure for differentiating acutely inflammatory changes in the small intestine from normal intestinal segments [35]. However, DWI was even superior to DCE-MRT in this endeavor. Nevertheless, the combination of ADC values and perfusion parameters makes it possible to improve specificity. In their study of children with chronic inflammatory bowel disease, Alexopoulou et al. showed that the percentage-based enhancement of the intestinal wall was significantly higher in patients with abnormal C-reactive protein (CRP) values, i. e. with acute inflammation parameters, than in patients with normal CRP values [51]. DCE-MRI requires contrast medium administration within a strictly defined timeframe to allow the quantitative and qualitative analysis of time-signal-

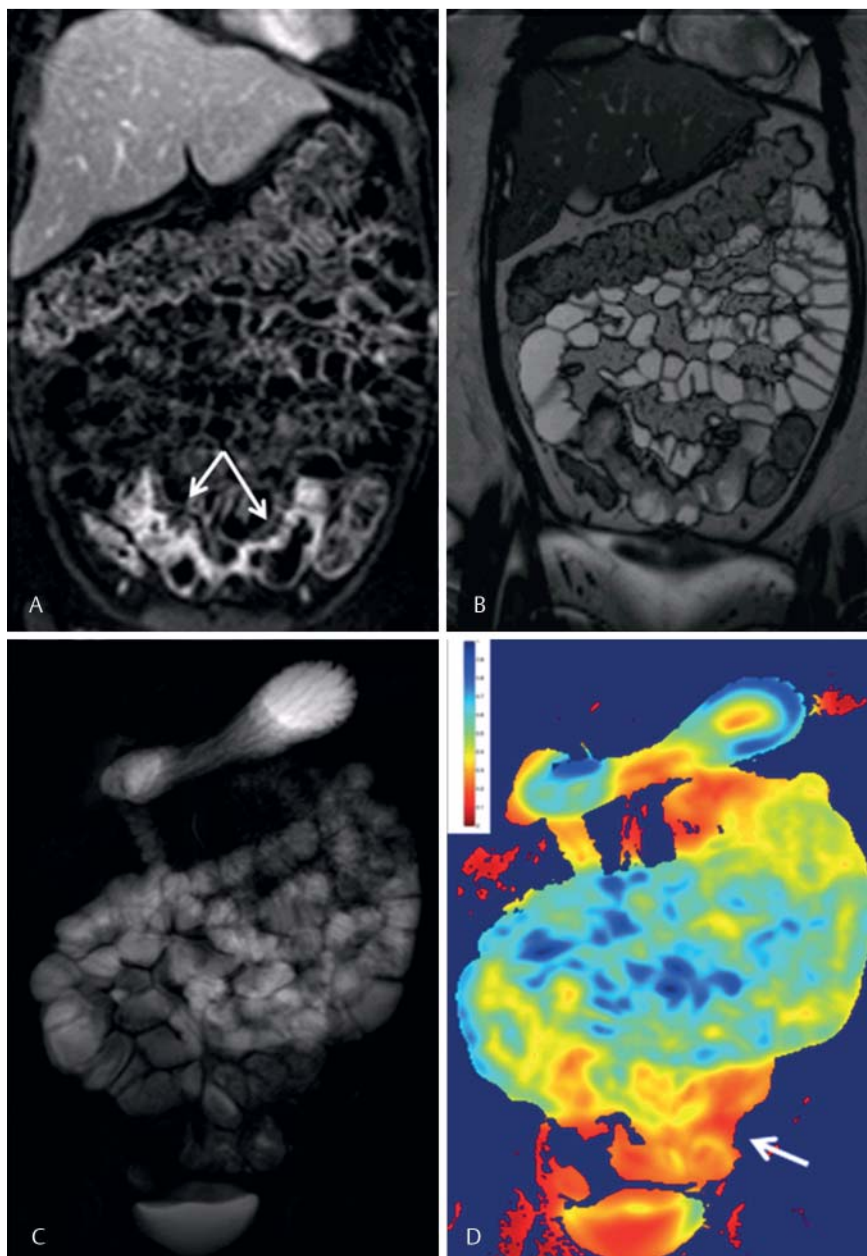


Fig. 5 15 year old female patient with known crohn's disease of the distal and terminal ileum. Distinct contrast uptake of the inflamed bowel segments are detectable on dynamic sequences **A**. TrueFISP images additionally show marked mural thickening **B**. Motility imaging (single T2 real-time image, **C**) shows reduced motility of inflamed bowel parts. Software assisted colour coding shows this reduced motility in red (arrow, **D**).

curves. In the future, 4-dimensional MR angiography sequences could also be beneficial here.

DCE-MRI is used particularly for evaluating acute inflammatory as well as tumorous processes and monitoring the response to therapy thereof. Its benefits appear to still be inferior to DWI in particular, and future studies are needed to establish its relative value.

Hybrid imaging: PET/MR

Positron emission tomography (PET) is a form of functional imaging. Using 18-F-fluorodeoxyglucose (18-F-FDG), this imaging technique takes advantage of glucose metabolism, since inflammatory and tumorous processes in the body have elevated glucose consumption and store 18-F-FDG at a greater rate. Combining computed tomography (CT) with PET/CT makes it possible to detect chronic inflammatory bowel diseases at higher sensitivity and specificity [52]. With its greater soft tissue contrast, MRI would appear to

be ideal for being combined with the metabolic information of PET and thus achieving even better results than that of PET/CT as the first images from PET/MR examination highlight (► Fig. 6). In addition, PET/MRI exposes patients to less radiation than PET/CT.

A study conducted by Lenze et al. already demonstrated that the combination of individual examinations yielded better results than 18-F-FDG PET/CT, MR enteroclysis and transabdominal ultrasound alone in the detection and differentiation of acute inflammatory changes over fibrotic strictures in Crohn's disease patients alone [53]. It is expedient for PET and MR data to be acquired simultaneously when PET/MRI is employed. This method is particularly relevant if the position of the intestinal loops shows drastic change within a brief period and offers in combination the highest accuracy for detecting pathologies. The nuclear medicine component of PET/MRI cannot rely just on 18-F-FDG as tracer. It is conceivable that additional, radiotracer-

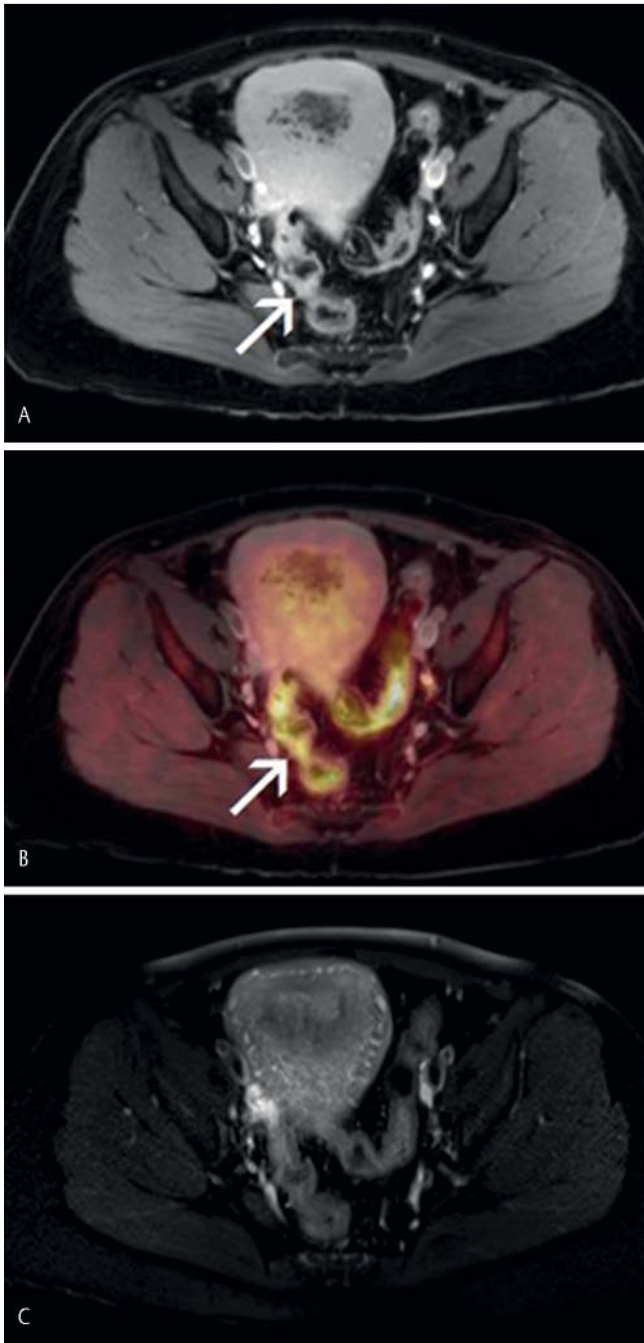


Fig. 6 28 year old female patient with initial diagnosis of breast cancer and whole-body PET MR imaging with ^{18}F -FDG for staging and known crohn's disease. Contrast enhancement and slight wall thickening can be seen in the rectosigmoid colon (**A** T1w FLASH after contrast, arrow). PET images show enhanced glucose uptake **B**. T2-weighted images of non-distended, non-prepared bowel show only slight mural edema (**C** T2 HASTE fat saturated). Imaging patients with inflammatory bowel disease therefore seems to be promising.

labelled cells or receptors can be used in the future for both inflammatory changes and tumorous processes. Future studies on both patients with chronic inflammatory bowel diseases and patients with gastrointestinal tumors are still needed to shed light on the current value of PET/MRI. In addition to the conventional morphological sequences, the other innovative sequences such as DWI and DCE-

MRI will be used as functional imaging modalities among these patients.

Conclusions

T2-weighted sequences both with and without fat saturation and T1-weighted fat saturated sequences prior to and following intravenous injection of a gadolinium-based contrast medium constitute basic diagnostic approaches in the magnetic resonance imaging of the bowel. Newer MR applications, such as diffusion-weighted imaging or contrast-enhanced dynamic sequences supply additional information in the diagnosing of chronic inflammatory bowel diseases as well as bowel tumors and should thus be integrated into the regular sequence protocol. Additional new imaging modalities such as motility imaging or the combination with PET in the form of PET/MRI must continue to be evaluated in the future and are very likely to become valuable tools in diagnosing chronic inflammatory bowel diseases. These innovative imaging modalities could provide deeper understanding of the underlying diseases and allow the possibility of functional, non-invasive therapy monitoring.

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