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New Imaging Techniques in the Diagnosis of Inflammatory Bowel Diseases

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Keywords
MRI · Crohn's disease · IBD

Summary
Background: Cross-sectional imaging modalities are fundamental in the management of patients with inflammatory bowel disease (IBD) from the first diagnosis and throughout the entire course of the disease. Over the past few years, the use of magnetic resonance (MR) imaging (MRI) has considerably increased, and no other imaging modality has experienced as advanced a development as MRI. **Methods:** A comprehensive literature search (PubMed/Medline) using keywords such as 'MR enterography', 'imaging modalities', 'IBD', and 'Crohn's disease' was performed. 48 articles published between 1999 and 2015 were systematically reviewed. In this article, besides the current standard MRI techniques, we review novel and implementable for routine use MR techniques. The use of positron emission tomography/computed tomography (PET/CT) and hybrid imaging such as PET/MRI with enormous potential will also be briefly discussed. **Results:** New imaging techniques such as diffusion-weighted imaging, dynamic contrast-enhanced MR perfusion, and MR motility imaging yield advanced findings about changes in the microenvironment and alterations in motility of the affected bowel segment, and are proven to improve the diagnostic accuracy in assessing the scale, activity level, and severity of the IBD. Novel magnetization transfer imaging allows direct visualization of fibrosis in the bowel wall. **Conclusion:** Diffusion-weighted imaging can be easily implemented in standard MRI for routine use to further enhance the diagnostic accuracy in disease assessment. For validation of magnetization transfer imaging, larger studies are warranted.

Introduction

The diagnosis of inflammatory bowel disease (IBD) is based on a combination of endoscopic, histological, radiological, and/or biochemical investigations [1]. Ileocolonoscopy and biopsies of the terminal ileum and colonic segments are the first-line procedures to establish the diagnosis, while radiological imaging techniques, especially cross-sectional imaging, are complementary to endoscopic assessment [1, 2]. Cross-sectional imaging techniques such as magnetic resonance (MR) imaging (MRI), computed tomography (CT), as well as ultrasound do not only enable visualization of the entire bowel but also allow detailed evaluation of the bowel wall and of adjacent extramural changes including complications (i.e. fistula, abscess etc.) in the affected bowel segments. Hence, they are fundamental in the management of IBD patients from the first diagnosis and throughout the entire course of the disease [2].

Due to significant advantages such as superior tissue contrast and lack of ionizing radiation, the use of MRI in the diagnostic workup of IBD has increased considerably over the past few years, particularly in pediatric patients [3, 4]. MR enterography, enteroclysis, and colonography are well established imaging modalities with high diagnostic accuracy in assessing the scale, activity level, and severity of IBD lesions, as well as detecting complications [3–10]. Recently, novel MR techniques such as diffusion-weighted imaging (DWI), dynamic contrast-enhanced (DCE)-MR perfusion, and MR motility imaging yield advanced findings about pathologic changes in the microenvironment and motility alterations in the setting of IBD. Along with these functional parameters, which serving as semi-quantitative or quantitative analysis could further enhance the diagnostic confidence and accuracy, MRI is playing an ever evolving role in the evaluation of IBD [6, 11, 12]. In this article, besides the currently recommended standard MRI, we review novel and clinically implementable MR techniques and briefly highlight latest technical developments such as MR magnetization transfer (MT). The use of positron emission tomography (PET) or PET/CT and hybrid imaging such as PET/MRI which has enormous potential will also be briefly discussed.

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For optimal evaluation of the bowel wall, proper bowel distension is a prerequisite, and currently 2 techniques, namely MR enterography and MR enteroclysis, are used for small bowel investigation. Many institutions favor MR enterography over MR enteroclysis because of better patient comfort by means of oral contrast agent intake and the simplicity of preparation about 1 h prior to scanning, whereas MR enteroclysis requires the placement of a nasojejunal tube under fluoroscopy and continuous monitoring of the filling status during steady infusion in the MR scanner using fast sequences e.g. thick-slab half-Fourier acquisition single-shot turbo spin-echo (HASTE). An interesting and practically relevant debate concerning the first-line investigation method (MR enterography vs. MR enteroclysis) in the small bowel was published in the February 2013 issue of *Radiology* [13, 14]. MR enteroclysis allows better and consistent bowel distension especially in the jejunal loop; however, no significant difference in the diagnostic accuracy for Crohn's disease (CD) could be demonstrated in a prospective study involving 40 patients by Negaard et al. [15]. Hence, MR enterography serves as primary diagnostic technique at our institution, and MR enteroclysis is reserved for cases of significant discrepancy between the MR enterography results and other clinical parameters. The MR colonography technique for the specific evaluation of the large bowel in IBD patients permits visualization of entire colonic segments in the case of incomplete colonoscopy and detection of extracolonic complications, but not the identification of affected segments with mild activity [16].

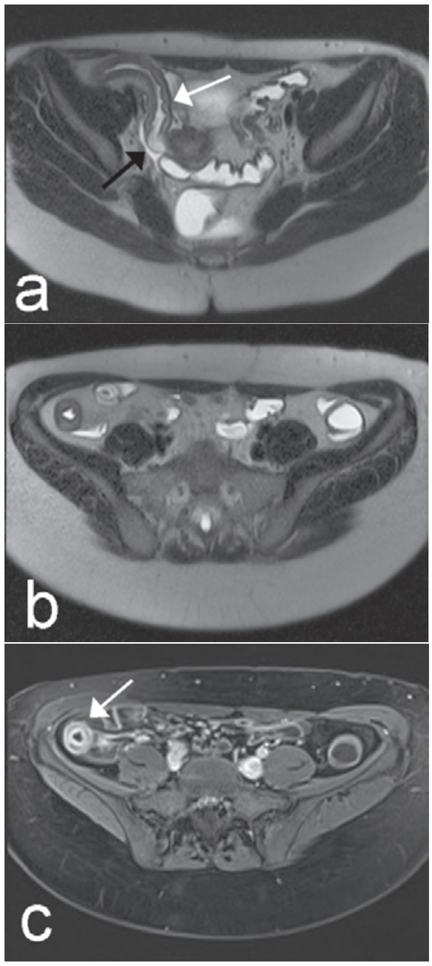

Fig. 1. 28-year-old woman with known Crohn's disease. **a, b** Axial HASTE images show an inflamed bowel wall of the terminal ileum with wall thickening and intramural edema. Notice the perienteric fluid (black arrow in **a**) and the irregular mucosal lining (white arrow in **a**) that indicates presence of fissuring ulcers. **c** Post-contrast and fat-suppressed T1-weighted (3D VIBE) image shows a layered pattern of bowel wall enhancement.

Current Standard MR Enterography Techniques

None of the published MR enterography protocols differ substantially [3, 5, 9, 10, 16]. Generally, a biphasic contrast medium (usually low signal intensity in T1 and high in T2) consisting of a mixture of osmotic materials and water (1–2 l) should be steadily ingested by the patient approximately 1 h before the MRI scan. The choice of supine versus prone position is patient- and institution-dependent. For better separation of the bowel loops and potentially reduced motion artifacts and shortened anterior-posterior range, we generally choose the prone position at the cost of patient comfort. A spasmolytic is recommended for reducing bowel motility, administered either as a single or split dose and intravenously or intramuscularly.

The basic MR pulse sequences include fast T2-weighted images and pre-/post-contrast T1-weighted images. The fast T2-weighted imaging consists of 2 complementary sequences known as balanced steady-state free precession (BSSFP; e.g. TrueFISP, Siemens, Erlangen, Germany) and HASTE. To improve the visibility of edema in the bowel wall and perienteric inflammatory changes, but also to distinguish the submucosal fat deposits in the chronic inflammatory phase from edema in the acute stage, fat suppression is needed, and fat-suppressed BSSFP depicts the bowel wall better than HASTE [5]. Most institutions perform ultrafast 2- or 3-dimension T1-weighted gradient echo sequences such as fat-suppressed 3-dimension volumetric interpolated breath-hold examination (3D VIBE) sequences for analyzing the enhancement pattern of the bowel wall and other corresponding extramural pathologies. Sinha et al. [17] demonstrated increased diagnostic confidence by applying high-resolution (HR) MRI techniques (fat-suppressed and contiguous thin-slap BSSFP/TrueFISP with small field-of-view) in detecting aphthous ulcers and transmural and mesenteric changes, and they emphasized the importance of using adequately aligned thin-slap images to detect incipient fistulas, mural abscesses, and sinuses. Again, in a recent study by the same authors, the significantly greater diagnostic accuracy of HR sequences as compared to basic pulse sequences in the diagnosis of bowel ulceration, fistulae, and abscesses was revealed taking surgical and histological results as references [18]. Thus, HR sequences are steadily integrated into the standard sequence protocols in addition to basic ones in many institutions. Another trend is the increasing use of 3-Tesla MRI scanners. The diagnostic accuracy of 3-Tesla MRI in the diagnosis of IBD was proven to be equivalent to that of 1.5-Tesla MRI, but not superior except for detecting mucosal ulcers [19, 20]. An adaptation of the sequence protocols of 1.5-Tesla MRI scanners to the 3-Tesla field remains challenging particularly in the case of BSSFP [3, 6].

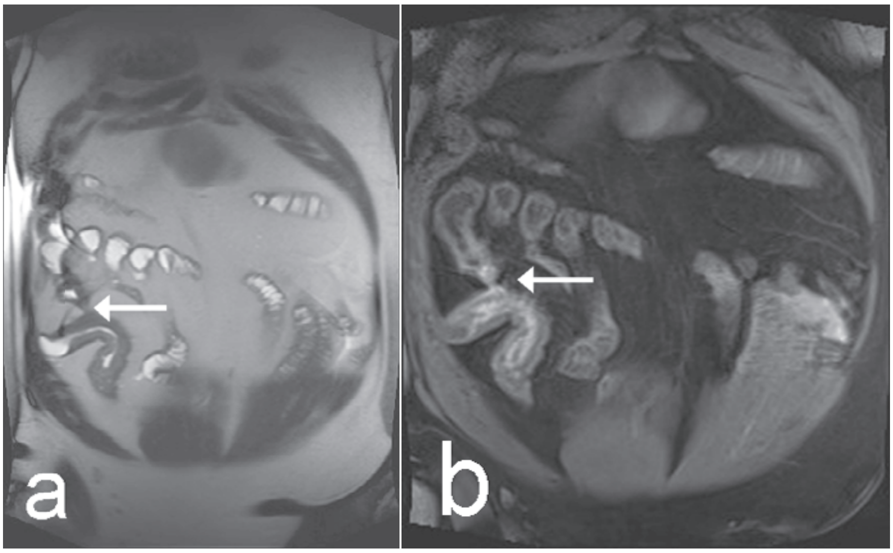

Fig. 2. 60-year-old man with proven Crohn's disease. MRI showed not only irregular wall thickening and pathologic wall hyperenhancement but also an interenteric fistula (white arrow) in the affected ileum loop. **a** Coronal HASTE, **b** post-contrast and fat-suppressed T1-weighted 3D VIBE.

Based on the currently recommended standard MRI protocols, the pathologic findings of IBD, which refer to a broad range of morphologic evaluations from the mucosal surface to adjacent mesenteric changes including complications as well as mural/extramural enhancement patterns (both qualitative and semi-quantitative, e.g. calculated post-/pre-enhancement ratio), correlate well with other diagnosing parameters [7, 8, 18]. The interpretation of these MRI findings in the settings of IBD is well documented in the literature [3–5, 10, 17, 21] and will not be further discussed in this article. Typical morphologic MRI findings based on standard protocols are shown in figures 1 and 2.

Novel and Clinically Implementable MR Techniques

Diffusion-Weighted Imaging

DWI is a well-established and fundamental MR sequence in neuroimaging and oncology. In recent times, the range of its application has explosively widened, and it has become a promising and standard tool in abdominal imaging. With DWI, the motility of water molecules, which depends on many cellular and extracellular factors and thus provides functional parameters about the microenvironment of the tissue, can be visualized and quantitatively measured. For colorectal cancer, DWI has become a promising and regular sequence not only in pre-operative staging but also in predicting therapy response [22, 23]. Oto et al. [24] evaluated DWI in the detection of bowel inflammation in a small number of patients with CD using endoscopy and surgical specimens as reference. The authors were able to show a decrease in the apparent diffusion coefficient (ADC) value in the inflamed segment as compared with that in the normal segment ($0.47–2.60 \times 10^{-3}$ and $1.39–4.03 \times 10^{-3}$ mm^2/s, respectively). They speculated that restricted water diffusion as a result of increased cell density and narrowed extracellular space may be a pathogenic mechanism in bowel wall inflammation. In a retrospective study of 33 pediatric patients with CD, the mean ADC value in the inflamed bowel wall was approximately 1.2×10^{-3} mm^2/s [25]. Lower ADC values in disease-active bowel segments compared with disease-inactive segments ($1.57 \times 10^{-3} \pm 0.44 \times 10^{-3}$ mm^2/s vs. $2.38 \times 10^{-3} \pm 0.58 \times 10^{-3}$ mm^2/s) were confirmed by another group [26].

The use of a high b value of 800 s/mm^2 was proven to be capable of suppressing background signals arising from non-inflamed tissue or body fluids and to make the inflamed bowel segments stand out with high signal intensity. In a recent study, the use of a high b value of 800 s/mm^2 not only demonstrated the best signal-to-noise and contrast-to-noise ratios but also the highest diagnostic sensitivity for assessing active CD lesions compared with b values of 1,500–2,500 s/mm^2 [27]. The MR images generated with b values of 800 s/mm^2 are similar to fat-suppressed T2-weighted images but without requiring oral contrast agent, and allow direct visualization of the affected segments. The reported overall sensitivity, specificity, and accuracy in CD patients were 86.0, 81.4, and 82.4%, respectively [26].

However, one should be aware that increased fibrosis (e.g. liver fibrosis) also causes a decrease in ADC values [28]. Tielbeek et al. [29] demonstrated that a decrease in ADC values correlated significantly with fibrosis while no significant correlation was observed between ADC values and histopathological grading of inflammation, although the ADC values decreased in affected segments with a higher inflammatory score, suggesting that inflammation and fibrosis are not binary processes. Furthermore, the authors found that other MR parameters such as the mural T2-weighted signal intensity/cerebral spinal fluid ratio might help to discriminate between inflammation and fibrosis.

Susceptibility to artifacts and limited spatial resolution are the main disadvantages of DWI. We are in agreement with Neubauer et al. [25] that reliable DWI requires proper bowel distention; otherwise it might lead to false-positive results. To overcome the limited spatial resolution, the combination of DWI and conventional MR sequences provides the highest diagnostic accuracy compared to DWI or conventional sequences alone [27]. Figure 3 demonstrates restricted diffusion of an inflamed bowel segment in a young patient with CD.

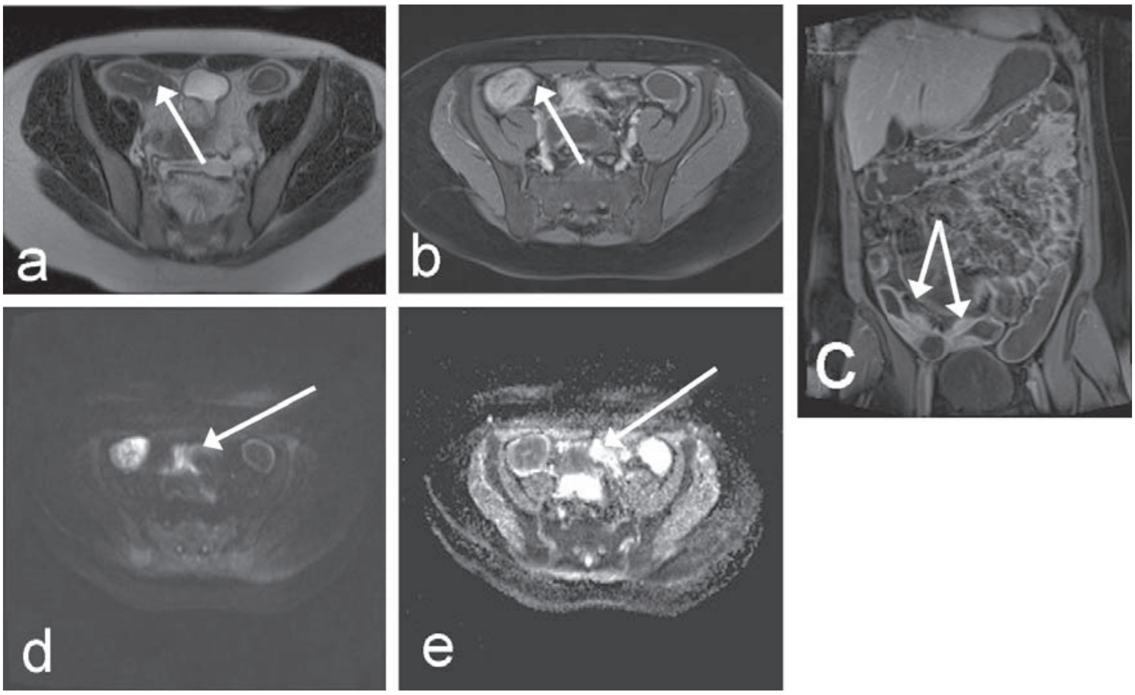

Fig. 3. 27-year-old woman with proven Crohn's disease. **a** The wall of the terminal ileum is markedly thickened with a mural ulcer (white arrow), and **b** shows homogenous mural hyperenhancement. The DWI images clearly demonstrate the corresponding restricted diffusion in the severely inflamed bowel wall with **d** increased signal intensity (b = 800 s/mm^2) and **e** reduced ADC value (0.876×10^{-3} mm^2/s). Notice the typical skip lesion in the proximal side, which is sensitively detected in the DWI (white arrow in **d** and **e**) and also reliably shown in the coronal post-contrast and fat-suppressed T1-weighted 3D VIBE (white arrow in **c**).

Dynamic Contrast-Enhanced MR Perfusion

The importance of conventional post-contrast T1-weighted images in the detection and grading of active lesions in IBD patients is well established [7, 8, 17, 25, 29]. Images are generated as a snapshot, and the analysis of mural enhancement in the diseased bowel wall depends either on subjective visual assessment or quantitative calculation of the post-/pre-enhancement ratio. There was no advantage to the use of region of interest (ROI)-based measurement over subjective assessment according to a study by Ziech et al. [30] on the correlation of MR findings with Crohn's disease endoscopic index of severity (CDEIS).

DCE-MR imaging, based on the acquisition of serial fast T1-weighted images before, during, and after application of contrast agent, provides functional parameters about the perfusion of the bowel wall, which may further characterize the activity status of a patient's IBD. After ROI placement in the bowel wall, the signal intensity-time curve can be calculated, and slope of enhancement, time to peak, as well as the enhancement ratio are extracted as semi-quantitative parameters. In comparison to the normal bowel wall, in the diseased bowel of patients with CD the initial slope of increase and enhancement ratio were higher [31–34]. However, no correlation between time to peak and the histopathological grading of active inflammation or fibrosis could be shown [29]. Pupillo et al. [32] demonstrated a statistically significant correlation between relative maximum enhancement in the inflamed bowel wall and the Crohn's disease activity index (CDAI), which could not be confirmed by other groups [30, 33].

The aforementioned semi-quantitative parameters are easier and faster to calculate; however, they are not of direct physiologic meaning. Quantitative parameters such as V_e (volume of extravascular-extracellular space per unit volume of tissue) and K^{trans} (volume transfer constant between intravascular space and extravascular-extracellular space in min^{-1}) are derived from a simple 2-compartmental model published by Tofts et al. [35]. These parameters refer to the pharmacokinetics of contrast agent moving from the intravascular space after injection into the extravascular-extracellular space. In a review of 18 patients with known CD, the K^{trans} and V_e were significantly higher in the actively inflamed terminal ileum compared with normal ileal loop (0.92 min^{-1} vs. 0.36 min^{-1}; 0.31 vs. 0.15), indicating increased blood perfusion and permeability in active inflammation [36]. In 2 studies, the enhancement ratio and relative maximum enhancement were both found to correlate significantly with disease chronicity, but the underlying hypotheses were totally different [30, 33]. Therefore, larger studies are required to establish the feasibility of DCE-MR perfusion imaging in routine clinical practice. The motion artifacts of the bowel wall and the weak reproducibility of signal measurement between different observers are the main limitations of DCE-MR imaging.

MR Motility Imaging

It is of increasing interest to investigate alterations in small bowel motility in patients with CD. Fast T2-weighted MR cine sequences such as BSSFP (e.g. TrueFISP), performed under the same conditions as required in standard MR enterography but without a spasmolytic, permit repeated acquisition of images on the same plane within a single breath hold, resulting in high temporal resolution of bowel motility. With this additional motility parameter, more CD-specific findings could be detected and significantly more patients with CD-relevant MR findings identified than with standard sequences alone [37] where only visual assessment of the cine sequence was used. Recently, a new software was introduced which allows analysis of bowel motility by plotting the luminal diameter over time [38]. With the help of such semi-automatic software, Cullmann et al. [39] tried to correlate the motility changes with endoscopic histopathological findings of the terminal ileum. As a result, they found that the severity of CD correlated significantly with the grade of motility impairment. Motility differed significantly in patients with active or chronic CD compared with patients without disease, but a differentiation between active and chronic disease was not possible. It was shown that the motility index of non-inflamed terminal ileum was significantly greater than that of actively inflamed sections, and there was a significant negative correlation between motility index and both endoscopic histopathological acute inflammation score (eAIS) and activity score based on standard MR enterography sequence [40]. Not only the histopathological findings but also laboratory parameters reflecting disease activity, such as C-reactive protein and calprotectin, were shown to correlate with motility impairment [41]. Further investigations are necessary for the evaluation of the diagnostic feasibility of this quantitative parameter.

Magnetization Transfer MRI

The accurate etiologic distinction of acute inflammation and fibrosis in the case of intestinal stricture is quite important for therapy planning in CD patients, since fibrosis-induced stenosis needs surgical or endoscopic treatment while acute inflammation benefits mainly from anti-inflammatory drugs. Currently, the available radiological modalities cannot reliably and accurately distinguish fibrosis from acute inflammation. MT MR imaging is a novel and promising technique that establishes image contrast based on interactions between protons of mobile free water and those of large immobile macromolecules such as collagen [42]. In a ground-breaking study, Adler et al. [43] using a rat model showed that the MT ratio of bowel wall affected by fibrosis was higher than that in the control group as well as that of bowel wall affected by acute inflammation but not fibrosis. Therefore, they demonstrated clearly that MT MR imaging was sensitive to fibrotic changes and relatively non-sensitive to inflammation. In another recently published study also based on an animal model, Dillmann et al. [44] showed that both MT ratio and T2-weighted ratio (compared with paraspinous muscle) allowed the detection of fibrosis in the setting of superimposed inflammation, and a novel parameter – T2-weighted ratio divided by normalized MT ratio – offered excellent diagnostic performance over MT or T2-weighted ratio alone. Pazahr et al. [45] demonstrated the feasibility of implementation of MT MR imaging in CD patients, with convincing image quality and diagnostic performance for quantitative assessment in only a few minutes. However, to date there are only few reports on the clinical use of MT MR imaging in IBD patients; hence, additional studies are needed to optimize the technique and evaluate the diagnostic performance.

PET/CT Imaging of the Bowel

Recently, there have been an increasing number of reports on the use of F-18-fluorodeoxyglucose (FDG)-PET and FDG-PET/CT for the localization and quantification of inflammation in both pediatric and adult IBD patients. Standardized uptake value is an objective quantitative parameter that was shown to correlate well with other radiological, chemical, and histopathological parameters in the inflamed segment, and the overall reported diagnostic accuracy was high [46]. In a prospective study with 43 CD patients, sensitivity and specificity of FDG-PET were reported to be as high as 90 and 92.6%, respectively, compared to those of hydro-MRI (66.3 and 99.4%, respectively) [47]. Ionization exposure and high costs are the main limitations of PET/CT, although non-invasive assessment and high diagnostic performance make FDG-PET and FDG-PET/CT attractive and promising tools. However, according to the evidence-based consensus guidelines published in 2013 by the European Crohn's and Colitis Organisation (ECCO) and European Society of Gastrointestinal and Abdominal Radiology (ESGAR), the role of PET/CT with FDG in the management of IBD patients is defined as unclear [2].

Hybrid PET/MRI

Operational hybrid PET/MRI scanners are available worldwide for clinical use, mainly in oncological imaging. It is commonly agreed that the combination of specific MRI features including high soft tissue contrast, multifunctional parameters like diffusion and dynamic perfusion as well as spectroscopy and other specific sequences with metabolic functions provided by PET makes PET/MRI a striking hybrid imaging modality in various clinical settings [48]. One may expect that the use of PET/MRI in the setting of IBD might lead to better diagnostic performance than can be achieved with PET or MRI alone; however, it is uncertain whether simultaneous PET/MRI is of competitive advantage over separate imaging examinations [48]. Nevertheless, ionization exposure could be further reduced by PET/MRI as compared with PET/CT, which makes PET/MR the best suited modality for pediatric IBD patients that undergo repeated diagnostic imaging sessions throughout the course of disease.

Conclusion

Due to the excellent diagnostic performance (table 1) and lack of ionizing radiation, MRI has become the standard assessment modality in the management of IBD patients. In the pelvic space and perineal region, MRI is proven to be the first-line imaging method, especially in the diagnosis of extramural complications such as perianal fistula and abscess. New innovative and clinically implementable imaging techniques such as DWI, DCE-MR perfusion, and cine MR motility sequence analysis provide important quantitative parameters that can further improve diagnostic per-

Table 1. Diagnostic accuracy of MR imaging in detecting active inflamed bowel segment

Author	Technique and sequences	Number of patients / disease	Reference	Sensitivity, %	Specificity, %
Oto et al., 2009 [24]	MR enterography, DWI	11/CD	endoscopy and surgery	94.7	84.2
Kiryu et al., 2009 [26]	MR conventional, DWI	31/CD	barium study or surgery	86.0	81.4
Neubauer et al., 2013 [25]	MR enterography, DWI	60/CD	endoscopy	*98*[a]	
Jiang et al., 2014 [20]	MR enterography, T2 + T1 pre-/postcontrast	88/IBD	endoscopy	92.1[b] 79.1[c]	72.0[b] 93.6[c]
Qi et al., 2015 [27]	MR enterography, DWI + T2 + T1 pre-/postcontrast	36/CD	endoscopy	93.55	89.47

[a]Diagnostic accuracy.
[b]Per patient basis.
[c]Per segment basis.

formance. From our institutional experience, the additional use of DWI can increase the diagnostic confidence with respect to imaging interpretation and also enhance diagnostic accuracy in the detection of extramural complications. Novel MT MR imaging seems to be a striking new tool for the discrimination between fibrosis and inflammation and is already proven to be feasible in routine use; however, further studies are needed for validation. Despite their non-invasiveness and proven potential usefulness, FDG-PET and FDG-PET/CT are still underutilized, and their role in IBD patient management remains unclear according to the 2013 consensus guidelines of ECCO and ESGAR. The current experimental and clinical use of PET/MRI is focused mainly on oncology; however, in the near future, for specific clinical indications and with an optimized workflow, PET/MRI might become a powerful tool in the assessment of IBD patients.

Disclosure Statement

The authors declare no conflicts of interest.

References

1 Van Assche G, Dignass A, Panes J, et al: The second European evidence-based consensus on the diagnosis and management of Crohn's disease: definitions and diagnosis. J Crohns Colitis 2010;4:7–27.
2 Panes J, Bouhnik Y, Reinisch W, et al: Imaging techniques for assessment of inflammatory bowel disease: joint ECCO and ESGAR evidence-based consensus guidelines. J Crohns Colitis 2013;7:556–585.
3 Mollard BJ, Smith EA, Dillman JR: Pediatric MR enterography: technique and approach to interpretation – how we do it. Radiology 2015;274:29–43.
4 Mentzel HJ, Reinsch S, Kurzai M, Stenzel M: Magnetic resonance imaging in children and adolescents with chronic inflammatory bowel disease. World J Gastroenterol 2014;20:1180–1191.
5 Fidler JL, Guimaraes L, Einstein DM: MR imaging of the small bowel. Radiographics 2009;29:1811–1825.
6 Yacoub JH, Obara P, Oto A: Evolving role of MRI in Crohn's disease. J Magn Reson Imaging 2013;37:1277–1289.
7 Ordas I, Rimola J, Garcia-Bosch O, et al: Diagnostic accuracy of magnetic resonance colonography for the evaluation of disease activity and severity in ulcerative colitis: a prospective study. Gut 2013;62:1566–1572.
8 Rimola J, Ordas I, Rodriguez S, et al: Magnetic resonance imaging for evaluation of Crohn's disease: validation of parameters of severity and quantitative index of activity. Inflamm Bowel Dis 2011;17:1759–1768.
9 Sinha R, Verma R, Verma S, Rajesh A: MR enterography of Crohn disease: part 1, rationale, technique, and pitfalls. AJR Am J Roentgenol 2011;197:76–79.
10 Sinha R, Verma R, Verma S, Rajesh A: MR enterography of Crohn disease: part 2, imaging and pathologic findings. AJR Am J Roentgenol 2011;197:80–85.
11 Maccioni F, Patak MA, Signore A, Laghi A: New frontiers of MRI in Crohn's disease: motility imaging, diffusion-weighted imaging, perfusion MRI, MR spectroscopy, molecular imaging, and hybrid imaging (PET/MRI). Abdom Imaging 2012;37:974–982.
12 Yoon K, Chang K-T, Lee HJ: MRI for Crohn's disease: present and future. Biomed Res Int 2014;article ID 786802 (in press).
13 Arrivé L, El Mouhadi S: MR enterography versus MR enteroclysis. Radiology 2013;266:688.
14 Sinha R, Rajesh A: MR imaging of the small bowel: is MR enteroclysis the only valid first-line investigation? Radiology 2013;266:689–690.
15 Negaard A, Paulsen V, Sandvik L, et al: A prospective randomized comparison between two MRI studies of the small bowel in Crohn's disease, the oral contrast method and MR enteroclysis. Eur Radiol 2007;17:2294–2301.
16 Rimola J, Rodriguez S, Garcia-Bosch O, et al: Role of 3.0-T MR colonography in the evaluation of inflammatory bowel disease. Radiographics 2009;29:701–719.
17 Sinha R, Rajiah P, Murphy P, et al: Utility of high-resolution MR imaging in demonstrating transmural pathologic changes in Crohn disease. Radiographics 2009;29:1847–1867.
18 Sinha R, Murphy P, Sanders S, et al: Diagnostic accuracy of high-resolution MR enterography in Crohn's disease: comparison with surgical and pathological specimen. Clin Radiol 2013;68:917–927.
19 Fiorino G, Bonifacio C, Padrenostro M, et al: Comparison between 1.5 and 3.0 Tesla magnetic resonance enterography for the assessment of disease activity and complications in ileo-colonic Crohn's disease. Dig Dis Sci 2013;58:3246–3255.
20 Jiang X, Asbach P, Hamm B, et al: MR imaging of distal ileal and colorectal chronic inflammatory bowel disease – diagnostic accuracy of 1.5 T and 3 T MRI compared to colonoscopy. Int J Colorect Dis 2014;29:1541–1550.
21 Grand DJ, Guglielmo FF, Al-Hawary MM: MR enterography in Crohn's disease: current consensus on optimal imaging technique and future advances from the SAR Crohn's disease-focused panel. Abdom Imaging 2015;40:953–964.
22 Ichikawa T, Erturk SM, Motosugi U, et al: High-B-value diffusion-weighted MRI in colorectal cancer. AJR Am J Roentgenol 2006;187:181–184.
23 Sassen S, de Booij M, Sosef M, et al: Locally advanced rectal cancer: is diffusion weighted MRI helpful for the identification of complete responders (ypT0N0) after neoadjuvant chemoradiation therapy? Eur Radiol 2013;23:3440–3449.
24 Oto A, Zhu F, Kulkarni K, et al: Evaluation of diffusion-weighted MR imaging for detection of bowel inflammation in patients with Crohn's disease. Acad Radiol 2009;16:597–603.
25 Neubauer H, Pabst T, Dick A, et al: Small-bowel MRI in children and young adults with Crohn disease: retrospective head-to-head comparison of contrast-enhanced and diffusion-weighted MRI. Pediatr Radiol 2013;43:103–114.
26 Kiryu S, Dodanuki K, Takao H, et al: Free-breathing diffusion-weighted imaging for the assessment of inflammatory activity in Crohn's disease. J Magn Reson Imaging 2009;29:880–886.
27 Qi F, Jun S, Qi QY, et al: Utility of the diffusion-weighted imaging for activity evaluation in Crohn's disease patients underwent magnetic resonance enterography. BMC Gastroenterol 2015;15:12.

28 Taouli B, Tolia AJ, Losada M, et al: Diffusion-weighted MRI for quantification of liver fibrosis: preliminary experience. AJR Am J Roentgenol 2007;189:799–806.

29 Tielbeek JA, Ziech ML, Li Z, et al: Evaluation of conventional, dynamic contrast enhanced and diffusion weighted MRI for quantitative Crohn's disease assessment with histopathology of surgical specimens. Eur Radiol 2014;24:619–629.

30 Ziech ML, Lavini C, Caan MW, et al: Dynamic contrast-enhanced MRI in patients with luminal Crohn's disease. Eur J Radiol 2012;81:3019–3027.

31 Giusti S, Faggioni L, Neri E, et al: Dynamic MRI of the small bowel: usefulness of quantitative contrast-enhancement parameters and time-signal intensity curves for differentiating between active and inactive Crohn's disease. Abdom Imaging 2010;35:646–653.

32 Pupillo VA, Di Cesare E, Frieri G, et al: Assessment of inflammatory activity in Crohn's disease by means of dynamic contrast-enhanced MRI. Radiol Med 2007; 112:798–809.

33 Taylor SA, Punwani S, Rodriguez-Justo M, et al: Mural Crohn disease: correlation of dynamic contrast-enhanced MR imaging findings with angiogenesis and inflammation at histologic examination – pilot study. Radiology 2009;251:369–379.

34 Oommen J, Oto A: Contrast-enhanced MRI of the small bowel in Crohn's disease. Abdom Imaging 2011; 36:134–141.

35 Tofts PS, Brix G, Buckley DL, et al: Estimating kinetic parameters from dynamic contrast-enhanced T(1)-weighted MRI of a diffusable tracer: standardized quantities and symbols. J Magn Reson Imaging 1999; 10:223–232.

36 Oto A, Kayhan A, Williams JT, et al: Active Crohn's disease in the small bowel: evaluation by diffusion weighted imaging and quantitative dynamic contrast enhanced MR imaging. J Magn Reson Imaging 2011; 33:615–624.

37 Froehlich JM, Waldherr C, Stoupis C, et al: MR motility imaging in Crohn's disease improves lesion detection compared with standard MR imaging. Eur Radiol 2010;20:1945–1951.

38 Bickelhaupt S, Froehlich JM, Cattin R, et al: Software-assisted small bowel motility analysis using free-breathing MRI: feasibility study. J Magn Reson Imaging 2014;39:17–23.

39 Cullmann JL, Bickelhaupt S, Froehlich JM, et al: MR imaging in Crohn's disease: correlation of MR motility measurement with histopathology in the terminal ileum. Neurogastroenterol Motil 2013;25:749–e577.

40 Menys A, Atkinson D, Odille F, et al: Quantified terminal ileal motility during MR enterography as a potential biomarker of Crohn's disease activity: a preliminary study. Eur Radiol 2012;22:2494–2501.

41 Bickelhaupt S, Pazahr S, Chuck N, et al: Crohn's disease: small bowel motility impairment correlates with inflammatory-related markers C-reactive protein and calprotectin. Neurogastroenterol Motil 2013;25:467–473.

42 Henkelman RM, Stanisz GJ, Graham SJ: Magnetization transfer in MRI: a review. NMR Biomed 2001;14:57–64.

43 Adler J, Swanson SD, Schmiedlin-Ren P, et al: Magnetization transfer helps detect intestinal fibrosis in an animal model of Crohn disease. Radiology 2011;259: 127–135.

44 Dillman JR, Swanson SD, Johnson LA, et al: Comparison of noncontrast MRI magnetization transfer and T-weighted signal intensity ratios for detection of bowel wall fibrosis in a Crohn's disease animal model. J Magn Reson Imaging 2014; DOI: 10.1002/jmri.24815.

45 Pazahr S, Blume I, Frei P, et al: Magnetization transfer for the assessment of bowel fibrosis in patients with Crohn's disease: initial experience. MAGMA 2013;26: 291–301.

46 Perlman SB, Hall BS, Reichelderfer M: PET/CT imaging of inflammatory bowel disease. Semin Nucl Med 2013;43:420–426.

47 Holtmann MH, Uenzen M, Helisch A, et al: 18F-Fluorodeoxyglucose positron-emission tomography (PET) can be used to assess inflammation non-invasively in Crohn's disease. Dig Dis Sci 2012;57:2658–2668.

48 Jadvar H, Colletti PM: Competitive advantage of PET/MRI. Eur J Radiol 2014;83:84–94.