Radiol med (2016) 121:362–377
DOI 10.1007/s11547-015-0613-2

PAEDIATRIC RADIOLOGY

Features and perspectives of MR enterography for pediatric Crohn disease assessment

Noemi Maria Giovanna Ognibene[1] · Massimo Basile[2] · Marco Di Maurizio[2] · Giuseppe Petrillo[1] · Claudio De Filippi[2]

Received: 9 October 2015 / Accepted: 1 December 2015 / Published online: 2 February 2016

Abstract The aim of this paper is to provide indications for performing magnetic resonance enterography (MRE) in Crohn's disease (CD), the essential technical elements of MRE techniques and typical findings in patients with CD. Patients suffering from CD frequently require cross-sectional imaging. By performing MRE, it is possible to obtain results comparable to those obtained with endoscopy in terms of identifying and assessing disease activity and better than other cross-sectional imaging techniques, such as CT, in the evaluation of the fibrosis and complications of disease. The MR imaging of diffusion MR is a technique which enables medical staff to add important additional information and which may replace the use of intravenous contrast agents in the near future. Magnetic resonance enterography is an accurate tool for assessing bowel disease and the various complications associated with CD. The lack of exposure to non-ionizing radiation is an important advantage of this imaging technique, especially in the case of pediatric patients. Familiarity with common and pathognomonic imaging features of CD is essential for every clinician involved in the treatment of inflammatory bowel disease and the care of patients.

Keywords Crohn's disease · Pediatric radiology · MR enterography · Perianal fistula · Diffusion-weighted MRI

Introduction

There has recently been a significant incidence rise of Crohn's disease (CD), particularly in pediatric patients.

The typical lesions of the disease that affect the whole gastrointestinal tract may extend to extra-luminal and join fistulae, abscesses and lymphadenopathy.

The gold standard for the diagnosis and follow-up of CD is an endoscopic evaluation of the colon and the terminal ileum; however, MRI is a non-invasive test that does not entail exposure to ionizing radiation, allows for an accurate study of intra- and extra-luminal of the whole gastro-intestinal tract characterized by a multiparametric and multiplanar approach and high spatial and contrast resolution.

An ever growing number of studies shows that MR enterography (MRE) is the optimal technique of cross-sectional imaging for the diagnosis and evaluation of CD activity.

DWI has recently been associated with MRE for studying CD, with a good degree of correlation between the restriction of diffusion parietal and MRI findings specifically associated with disease activity.

The purpose of MRE with DWI is to avoid using paramagnetic contrast for identifying and assessing disease activity.

✉ Claudio De Filippi
defilippiditorino@hotmail.com

Noemi Maria Giovanna Ognibene
noeminox@hotmail.com

Massimo Basile
massimo.basile@meyer.it

Marco Di Maurizio
marco.dimaurizio@meyer.it

Giuseppe Petrillo
g.petrillo@unict.it

[1] Radiodiagnostic and Oncological Radiotherapy Unit, University Hospital "Policlinico-Vittorio Emanuele", Catania, Italy

[2] Pediatric Radiology, Meyer Children's University Hospital, Florence, Italy

MRI represents the gold standard technique for studying the pelvis and perineum, and has proved to be a highly effective means of identifying fistula perianal complications related to CD, both in adults and children.

The disease appears to be more aggressive in children over 8 years of age. The most recent studies have found significant differences between adults and children with regard to the stenotic complications that arise in 13 % of the cases involving children compared to 4 % of adult cases 4 years after the diagnosis of the disease. Similar percentages have been observed for fistula complications (4 % in adults compared to 11 % in children). These differences are of particular diagnostic and therapeutic interest [1].

Epidemiological aspect

CD is a granulomatous inflammatory bowel disease [2–6] characterized by high morbidity and mortality [7], which, together with ulcerative colitis and indeterminate colitis, are included in the spectrum of inflammatory bowel disease (IBD).

Little is known of the causes although it is thought that it derives from a combination of environmental and genetic factors related to intestinal flora [5, 8].

Diagnosis is based on clinical evidence, laboratory tests, radiological and endoscopic investigations and histological evaluation.

The incidence of CD has increased worldwide and has doubled in the pediatric population over the past 12 years [9].

There is a peak in incidence in late teenagers or young adults (up to 25 years of age), while the rate of growth appears to be more rapid in children under 10 years, which may be due to early onset or earlier diagnosis [9–11].

Phenotype

Ileum-colic localization is the most common site of disease [12–18], yet the CD phenotype differs according to the age of the patient at the onset of the disease.

Mamula et al. [19] observed that while 59 % of individuals suffering from CD aged <18 years are affected in both the small and large intestines, 89 % of children under the age of 10 are only affected in the large intestine.

Based on these observations, the classification of Paris (2009) re-examines the classification of Montreal (2005). The Very Early Onset Inflammatory Bowel Disease (VEO-IBD) is considered a form of its own and patients aged <10 years at disease onset (A1a) are classified differently from those aged >10 years (A1b) [20].

Children aged under two at diagnosis are more likely to suffer from a more aggressive phenotype [21–23] and have a clear genetic predisposition to immune deficiency.

Finally, the timeliness with which immunosuppressive therapy is carried out has a significant effect on the development of complications [12].

Clinical aspects

Abdominal pain, fever and weight loss are common symptoms of juvenile CD onset (<16 years). The main complications are intestinal perforation, progressive stricture and subsequent intestinal obstruction.

Nutritional deficiencies, stunted growth and delayed puberty occur in percentages ranging between 65 and 85 % of patients with childhood CD onset.

15–40 % of these patients continue to suffer from stunted growth throughout the course of the disease [24–26].

It is also noted a high prevalence of oral manifestations, attributable to bad absorption [12], a greater involvement of the upper gastrointestinal tract [12, 27] and a higher incidence of perianal lesions [12, 14, 27, 28]. Perianal involvement in children is observed in 25–38 % of cases [2–6, 29, 30]; it affects males four times more frequently than females [4, 30, 31] and begins with a fistula in over a third of cases. One child in 20 with CD has an isolated fistulous disease [2, 5, 6, 32].

MR imaging

MR imaging plays an important role in the evaluation of patients with MC at diagnosis whether symptomatic or asymptomatic, in the spread of the disease, in the assessment of the degree of activity and severity of the disease, and finally for identifying the complications during follow-up and evaluating treatment response [33, 34].

When treating pediatric patients, methods that use ionizing radiation should be avoided since children are much more sensitive to radiation than the adult population [35, 36].

MR enterography in gastro-intestinal disease assessment

Procedural details

It is not easy to investigate the intestinal wall with RM.

The thinness, the movement and the presence of the intra-luminal contents, especially gases, are responsible for conditions that hamper the study.

However, the use of faster, free-motion and high-resolution sequences in breath hold, together with the administration of antiperistaltic drugs has significantly improved the situation [37].

Table 1 MR enterography imaging protocol for pediatric Crohn disease performed with a body coil in 1.5 and 3 T magnet

Sequence	Plane	Reconstruction matrix (mm)	FOV (mm)	Thickness (mm)
Balanced gradient echo	Axial e coronal	528 × 528	Suitable for the patient's size	4
Dynamic scan (cine)	Coronal	15 dynamic scans each lasting 15 s	Suitable for the patient's size	10
T2 turbo spin echo with fat saturation	Axial	480 × 480	Suitable for the patient's size	4
T2 single-shot with fat saturation	Coronal	480 × 480	Suitable for the patient's size	4
T2 turbo spin echo	Axial	380 × 380	Suitable for the patient's size	4
DWI (0,500, 1000 *b* value)	Axial	256 × 256	Suitable for the patient's size	5
THRIVE 3D with fat saturation pre-and post-mdc[a]	Coronal	352 × 352	Suitable for the patient's size	3
T1 TFE with fat saturation dopo mdc	Axial	480 × 480	Suitable for the patient's size	4

[a] 10 dynamic scans, each lasting 18 s

A basic requirement for obtaining a good quality MRI is to distend the intestinal loops that can be achieved by administering mdc per os (MR enterography) or via naso-duodenal catheter (MR enteroclysis).

We only used oral administration, since it is more suitable for pediatric patients.

Moreover, placing a naso-duodenal catheter under fluoroscopic guidance results in limited exposure to ionizing radiation.

The enteroclysis allows for a greater degree of bowel distension, but this does not significantly improve the clinical value of the study [38–41].

Positive, negative or biphasic oral contrast material (contrast medium) can be used depending on the characteristics of the signal in the various MR sequences [41–43].

One hour before examination, we administrated between 1000 and 1500 ml (depending on the patient's age) of an aqueous solution of 70 % sorbitol, divided into 3–4 doses, each to be taken within 15–20 min. Biphasic contrast medium enables us to obtain an excellent morphological evaluation of the small intestine in T2 sequences and a better characterization of inflammatory activity in the T1 sequences together with the suppression technique of the adipose signal.

It is preferable to place the patient in the prone position to reduce the movement caused by breathing and ensure better abdominal compression and more safety in the event of vomiting. Abdominal compression favors the distension of the intestinal loops and enables us to decrease the number of slices, thus reducing examination time thanks to the reduction in the thickness.

However, in the presence of abundant intraluminal gas magnetic susceptibility artefacts may occur at epigastric and peri-umbilical level.

We used *N*-butylbromidehyoscine (Buscopan) as anti-peristaltic drug. 0.25 mg/kg of this drug is administered intravenously to patients weighing <20 kg and from 0.5 mg/kg to a maximum of 20 mg, into patients weighing more. The dose is divided into two administrations, one after the initial dynamic cine evaluation and the other one before injecting gadolinium intravenously.

The paramagnetic contrast agent is administered in doses of 0.1 mg/kg.

MR imaging protocol

The MR enterography examinations are performed with a body coil in 1.5 T (Philips Achieva, Nova Qasar) and 3 T (Philips Ingenia 3 T) magnet, according to the protocol described in the table (Table 1).

Firstly, we assess the degree of bowel distension by means of very thick single-shot fast spin echo sequences, with "fluoroscopic" effect. If the intestinal distension is not sufficient, we administrate an additional dose of sorbitol solution.

Dynamic assessment of intestinal peristalsis by cine imaging is an integral part of the protocol, because it allows for a better identification of pathological features.

It is possible to identify the bowel segments affected by active inflammation, characterized by a reduced or absent motility as well as the fibro-stenotic segments that appear aperistaltic with pre-stenotic dilatation and the upper portion which is hypo-peristaltic. The cine-MRI sequences provide us with useful information even in the presence of an insufficiently relaxed intestine, since they enable us to appreciate the distension of a normal loop even if this is initially collapsed.

Correlation with some inflammatory markers such as C-reactive protein is good [44–46].

Sequences of diffusion (DWI) are very quick and can be carried out in free breathing or in breath hold and constitute a source of alternative contrast compared to the relaxation time.

Recent studies have shown reduced diffusivity in intestinal segments affected by CD.

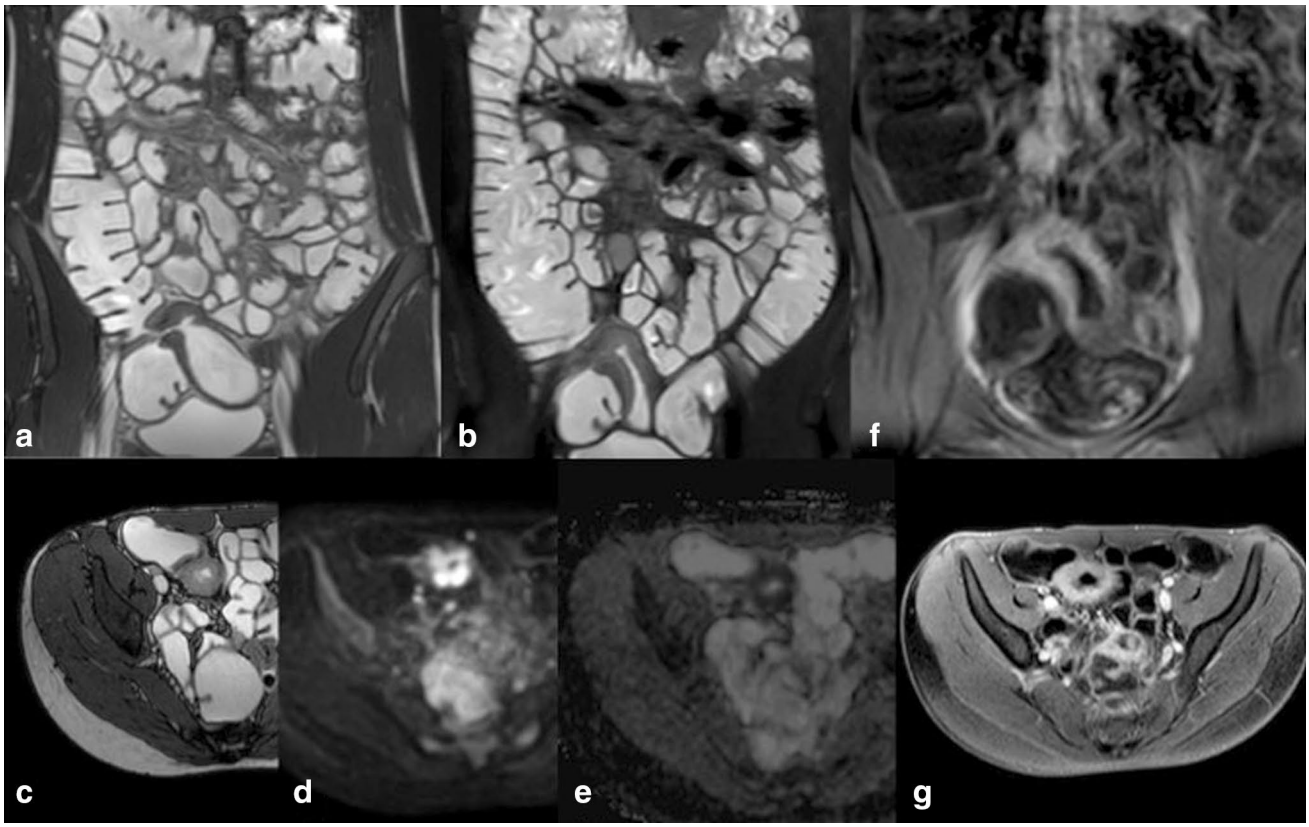

Fig. 1 An 8-year-old boy with Crohn's disease (CD). Coronal balanced FFE (BTFE) images (**a**, **b**) show concentric wall thickening of the terminal ileum with hypersignal and substenosis which determines prestenotic dilatation. The axial BTFE image (**c**) shows wall thickening, which appears hyperintense on diffusion-weighted image (DWI) (**d**) and shows restricted diffusion on ADC map (**e**). Coronal volume interpolated GRE (THRIVE) image (**f**) and axial contrast-enhanced T1-weighted with fat suppression image (**g**) show intense enhancement parietal with layered appearance

The mechanism according to which this kind of phenomenon occurs is not known with certainty [47–49].

It is assumed that the infiltration of inflammatory cells, in particular of the aggregates of lymphocytes, lymphatic dilatation and the development of granulomas lead to a reduction in the extracellular space, thus restricting the mobility of water molecules [48].

The reduced diffusion may represent a new radiological non-invasive bio-marker of CD activity. Although characterized by a low spatial and contrast resolution, the diffusion sequences are able to identify the bowel segments affected by the inflammatory process, the lymph nodes and any complications such as fistulas or abscesses [50] (Fig. 1).

Recent studies show a significant correlation between bowel wall minimum ADC value and some MRI markers of disease activity, including:

- degree of bowel wall thickening;
- striated pattern and degree of arterial enhancement;
- degree of delayed enhancement;
- quality of mesenteric inflammatory changes;
- presence of stricture.
- There is a rather poor correlation concerning other modifications, such as
- bowel wall T2-weighted signal intensity normalized to either spleen or paraspinal musculature;
- length of intestinal segment affected;
- fibrofatty proliferation of the mesentery.

If the value of positivity in DWI is confirmed and ADC cutoff values were identified, this imaging technique could prove to be a useful tool for evaluating inflammatory activity. Potentially, ADC values may make the use of intravenous gadolinium-based contrast unnecessary.

In our experience, it was possible to differentiate in the same patient intestinal tracts with active inflammation from fibro-stenotic tracts, according to ADC parameters and their correlation with the type of enhancement in the various phases of the dynamic study (Fig. 2c–f).

Submucosal edema is present in the course of active inflammation, and also in the presence of

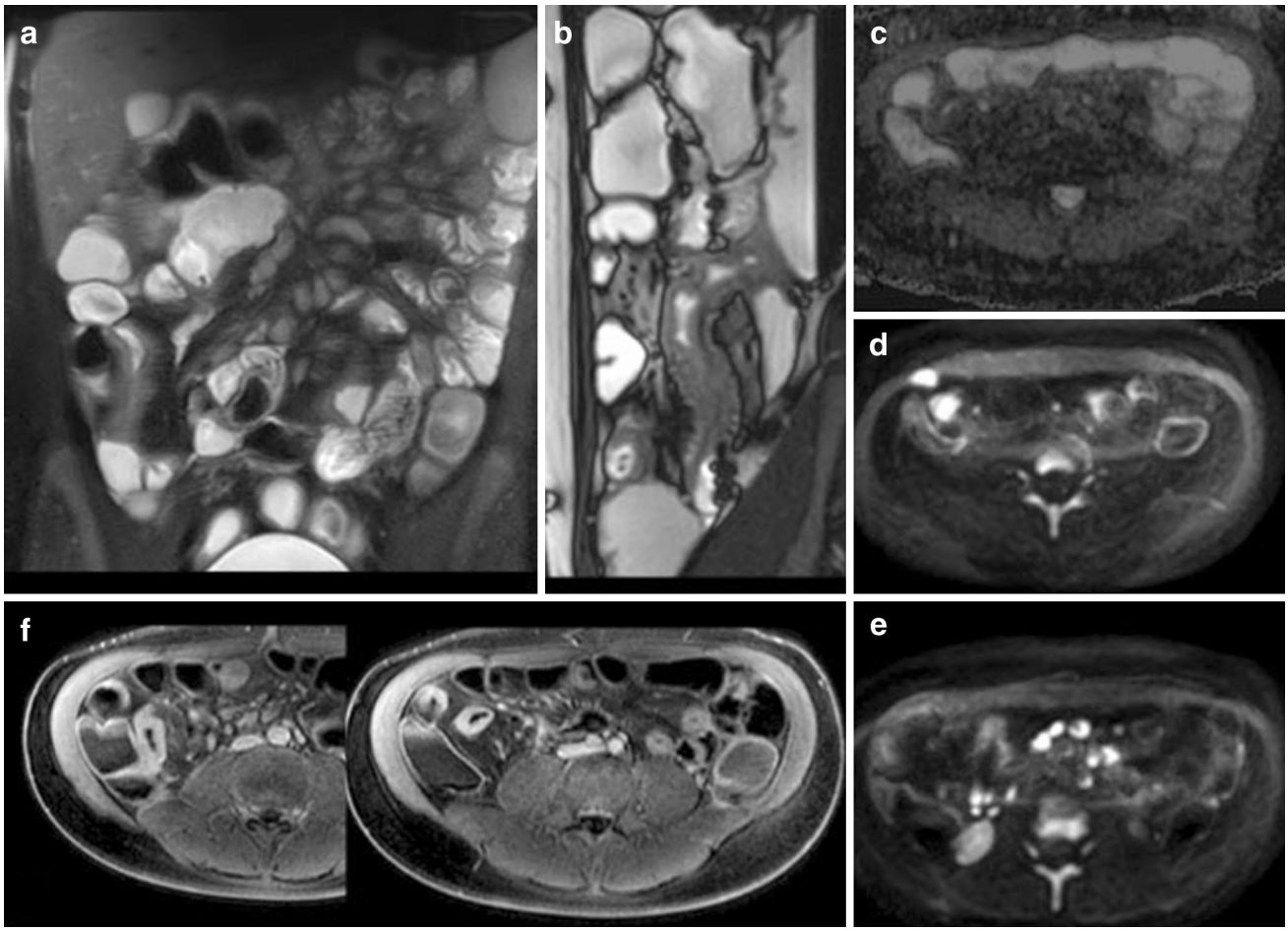

Fig. 2 A 13-year-old boy with re-active Crohn's disease (CD). Coronal (**a**) and sagittal (**b**) SSTSE T2-weighted with fat suppression images show significant pathological ileal involvement with multiple enlarged mesenterial lymph nodes. ADC map (**c**) and DWI image (**d**, **e**) show parietal restriction of diffusivity in the *right* pathological ileal loops and lower positivity in those in *left* quadrants with positive lymph node (**e**). These findings express the various degrees of disease activity in different pathological traits with coexistence both of acute inflammation and fibrosis, as confirmed by the different degree of enhancement on axial contrast-enhanced T1-weighted with fat suppression image (**f**)

stenotic sections due to fibro-adipose involution or in sections with mural fibrosis and superimposed active inflammation.

The imaging of diffusion must be integrated with other morphological and cine sequences and with the type and degree of enhancement.

Finally, it is possible to provide documentary evidence of a reduction in diffusivity even in not dilated or collapsed loops, in which there are also aspects of wall thickening and enhancement which do not correspond to the actual situation.

Imaging diffusion must still be an integral part of MRE because of the amount of information that it provides concerning CD patients.

The speed of execution is also essential in the case of younger patients who are generally more intolerant.

Imaging findings

Some authors simply distinguish between active disease and chronic illness [41, 43].

We prefer to distinguish three main forms of CD:

- uncomplicated active inflammatory disease (no fistulas or strictures);
- penetrating disease (deep ulcers, fistulas or abscesses);
- fibrostenosing disease.

This type of classification better answers the clinical needs and helps to direct clinicians toward a more or less intensified medical therapy or surgery [51].

Erythema and superficial aphthous ulcers are the earliest macroscopic lesions in active CD [52].

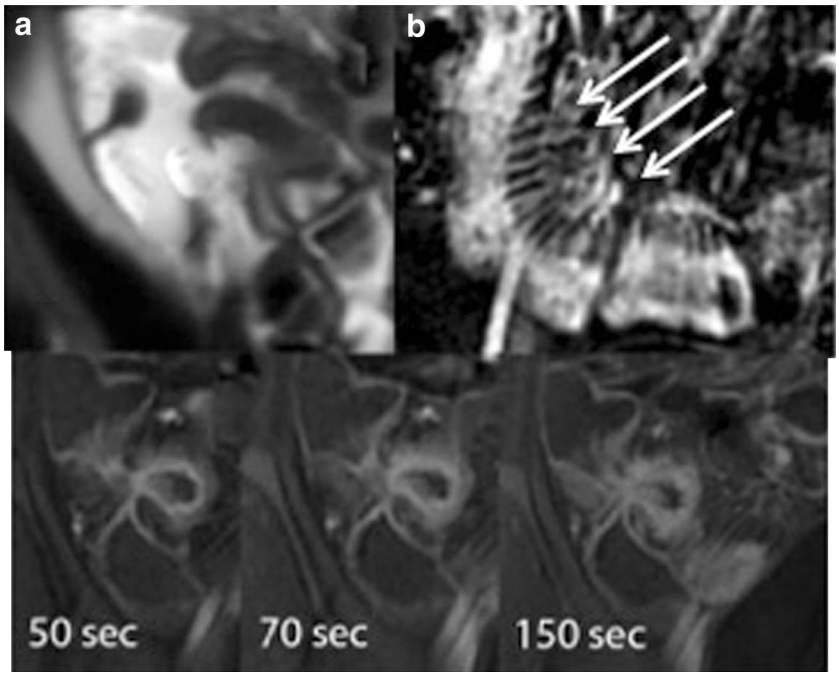

Fig. 3 Coronal BTFE image (**a**) shows wall thickening of the terminal ileum with hypersignal compared to the psoas muscle (not shown). Coronal contrast-enhanced T1-weighted with fat suppression image (**b**) shows (*arrow*) ectasia of vasarecta from active inflammation with characteristic "comb sign". Coronal THRIVE images show progressive parietal enhancement and an early involvement of the mucous layer (50 s) which spreads to transmural in the later stages 70 and 150 s)

The spatial resolution of MRI is not yet able to detect all superficial mucosal abnormalities even if the use of high-field MR may help to overcome this limitation.

Enlarged mucosal enhancement with respect to the adjacent loops with a similar degree of distension is one of the earliest signs of inflammatory activity. This is caused by hyperemia and histologically corresponds to submucosal edema and an increased number of dilated submucosal capillaries (Fig. 3b).

The stratified enhancement produced by alternating intense enhancement of the mucous layer and muscle/serous with an intermediate enhancement of the edematous submucosal produces the "target sign" characteristic in post-contrast T1-weighted sequences.

The thickening of the intestinal wall is another important manifestation of active CD. Bowel wall thicknesses of more than 3 mm should considered pathologic [53]. However, it is important to note that at fasting level, wall thicknesses of 3 mm measured following oral administration of the contrast agent should be considered to be standard, in relation to anatomical peculiarities and the non-optimal distension levels obtained with this technique with respect to MR enteroclysis.

The degree of wall thickening is related to the endoscopic and histological severity indexes of the disease.

However, wall thickening is not always associated with fibrosis and, therefore, does not necessarily lead to a terminal stage of the disease [54–56].

In fact in the early stages, thickening is secondary to the presence of submucosal edema.

Since only moderate or severe edema constantly produces intramural high signal intensity in T2-weighted sequences, the absence of this does not necessarily exclude active disease.

Sensitivity towards wall edema and small fluid perienteric collections can be increased with T2-weighted fat-suppressed sequences [57].

The fibrofatty proliferation of the mesentery, detectable in relation to the neat separation of bowel loops, is considered a specific finding of MC but not correlated with disease activity (Fig. 4a, b).

The vascular engorgement of the vasa recta on the mesenteric side of the bowel wall (comb sign), which is more evident on post-contrast T1-weighted fat-suppressed sequences following mdc (comb sign), is an indicator of disease activity (Fig. 3).

The increase in number and enhancing lymph nodes are not specific, but are generally associated with a state of inflammatory activity of the ascending colon and terminal ileum (Fig. 2a–e).

The "cobblestone effect" is easily identifiable with RM, as long as an adequate level of distension of the intestinal lumen is achieved. It is characterized by the presence of inflammatory mucosal pseudo-polyps delimited by ulcerative lesions in transverse and longitudinal course (Fig. 1).

The mucosal islands are characterized by a significant enhancement of the T1 signal following intravenous administration of the contrast medium.

Besides helping to confirm the diagnosis in an appropriate clinical setting, this nodular pattern is an indicator of

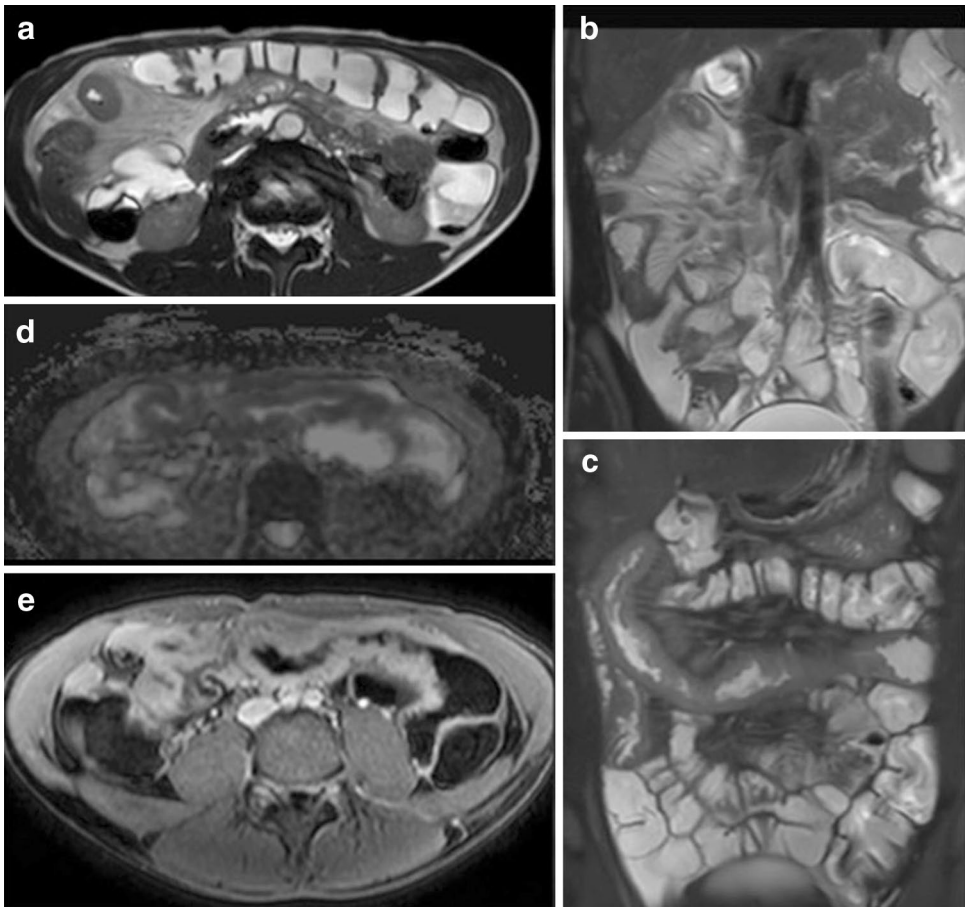

Fig. 4 A 15-year-old boy with Crohn's disease (CD) with extensive ileal and colic involvement. Axial turbo spin echo (TSE) T2-weighted image (**a**) and coronal SSTSE (single-shot turbo spin echo) T2-weighted image (**b**) show significant wall thickening of the ascending colon with fibro-fatty proliferation. Coronal SSTSE T2-weighted with fat suppression image (**c**) shows extensive ileal involvement with characteristic "cobble stoning" with prestenotic dilatation. Apparent diffusion coefficient (ADC) map (**d**) indicates a clear restricted diffusion of involved ileal tract shown in **c**. Axial contrast-enhanced T1-weighted with fat suppression (**e**) shows intense enhancement of the involved ileal tract

the severity of the disease which orientates us towards an intensification of the treatment [58].

Deep ulcers and intestinal fistulae are of fundamental prognostic significance with implications towards possible surgical therapeutic planning.

The extension of the intra-parietal ulcerative process (sinus tract) and the extra and inter-parietal fistulizing, both activity index of severe disease, are well detectable on post-contrast T1-weighted sequences and sometimes, in the presence of fluid content, even in the images T2w.

The accuracy of the MR enterography for detecting fistulas is 71–100 % with specificity ranging between 93 and 100 % [59–63].

Fistulas may form abscesses and phlegmons or cause fibrous adhesive processes between adjacent intestinal segments.

Phlegmons appear as extra-intestinal masses with moderate hyperintensity in T2 and T1-weighted sequences following mdc intravenous administration.

Abscesses are represented by fluid collections, possibly containing gas (with strong parietal enhancement on post-contrast T1-weighted fat-suppressed sequences).

The restriction of the diffusion documented in DWI may be useful for differentiating small abscesses from loops filled with fluid or pseudo-collection.

Fibro-stenotic lesions are indicative of chronic disease, which occur after recurrent episodes of inflammatory activity alternated with granulomatous reaction and deposition of reparative fibrotic tissue and result in progressive stricture of the intestinal segment, stenosis and pre-stenotic dilation.

The sensitivity of MRI for detecting stenosis ranges between 75 and 100 % with a specificity of 91–100 % [64].

As a loop affected by a severe inflammatory process may become stenotic, the differentiation between inflammatory stenosis and fibro-stenotic lesion significantly influences the choice of treatment.

Usually bowel wall thickening in fibrostenosing disease is less pronounced and enhancement is more homogeneous and unstratified.

Fat-saturated and non-fat-saturated T2w sequences enable us to distinguish between edema and fat deposition at submucosal level. Submusal fat infiltration causes the separation of the collagen fibers that, with an orientation parallel to the surface, create a characteristic layering effect

known as “halo sign” that must be distinguished from the so-called “target sign” of the submucosal edema [57].

The cine imaging completes the study showing a marked reduction or even the disappearance of peristaltic activity at the stricture.

The reliability of imaging criteria alone is not absolutely certain, since there are often both inflammatory and fibrotic changes in the same intestinal segment.

Comparison with histological standards confirms a high level of accuracy (87 %) of the MRE in the identification of disease and it is significantly lower in the evaluation of mural fibrosis [43].

The regenerative processes cause mucosal atrophy associated with the emergence of regenerative polyps.

In these cases, there is neither a significant thickening of the wall nor a significant increase of enhancement and unlike what occurs in chronic disease, stenosis and prestenotic dilation are not characteristic findings.

Pelvic MR in perianal disease assessment

In radiological imaging, the correct interpretation of perianal disease is based on pelvic anatomy evaluation, pathophysiology aspects and the correct classification of the various types of fistula [65]. In children inadequate treatment, following a wrong diagnostic classification, almost always leads to a significant increase in morbidity, thus causing deep extension of the pathological process that affects the pelvic muscles and perianal areas. In children, the presence of fistulas and/or perianal abscesses is one of the main causes of incomplete response to medical or surgical treatment and relapse.

Anatomy of the anal canal [66]

The anal sphincter is composed of two types of muscles: the external voluntary anal sphincter (ES) and that internal involuntary anal sphincter (IS).

Between the ES and the IS lies the inter-sphincteric space (ISS), consisting in a thin layer of mainly adipose connective tissue. The ES merges anteriorly with the perineal body and above with the puborectalis muscle (PR), the latter continuing posteriorly with the levator ani muscle (LA).

The IS extends from the ano-rectal junction up to 1–1.5 cm below the dentate line and is an offshoot of the circular musculature of the rectum.

The ES is the medial edge of the ischio-anal fossae (IAF) or ischio-rectal fossae (IRF), composed of loose and fibrous connective tissue, vessels and some nerves (inferior rectal and perineal branch of the fourth sacral nerve).

The lateral border of IAF is represented by the internal obturator muscle (IO), while the superior border is represented by the LA; the posterior border is formed by the sacrotuberous ligament and gluteus maximus muscle (GM), while anteriorly it is delimited by the superficial and deep transverse muscles.

Between the LA and the ano-coccygeal ligament, there is a horseshoe connection that links the ischioanal space and deep post-anal space.

MR anatomical landmarks [2, 67]

The axial and coronal planes are oriented at right angles and parallel to the anal sphincter, respectively, to allow for an accurate definition of the anatomical structures of reference.

The T2-weighted images enable us to distinguish the various components of the sphincter in relation to the characteristics of the signal, which is relatively hyperintense at IS level compared to ES. IS, ES, LA and the IAF are well visualized in T1w unenhanced sequences and post-contrast medium acquisitions and define the relationships with abscess vehicles, especially on the coronal plane which is the main anatomic reference.

The IS also shows a normal homogeneous signal enhancement on post-contrastographic T1w sequence.

The ISS shows a fat-type signal in all sequences, therefore on T2w sequences with suppression of fat signal it differs greatly from IS.

The main fistulae, their secondary branches and abscesses appear hyperintense on long TR sequences, which allow for a good differentiation of the muscles and the sphincter.

The course and relationships of fistulae and abscesses are best evaluated on post-intravenous contrast agents T1w sequences, particularly in the coronal plane, which is the main anatomical reference.

MRI technique

Let us outline the fields of application of the MR in the diagnostic and treatment procedure of perianal disease in CD:

- diagnosis and classification of fistulas (disease status),
- planning, pre-surgical treatment and
- follow-up.

Unlike what occurs for MRE, pelvic MR does not require specific preparation and is, therefore, well tolerated by young patients. The study of the pelvis can be integrated with MRE which completes the evaluation of the status of the disease (in particular at diagnosis of CD).

The study of perianal disease by means of MRI on supine patient with pelvic body coil is essentially based on axial and coronal T2w sequences with and without fat saturation sequences, axial/coronal T1w unenhanced sequences and dynamic post-contrastographic T1w sequences.

Our standard protocol, applied with MRI 1.5 T (Philips Achieva, Nova Qasar) [68, 69] and 3 T (Philips Ingenia) systems, foresees [70, 71]:

- T2-weighted TSE sequences (single-shot) and T1 Fat Sat SPIR on axial and coronal planes, with sagittal optional with respect to number and location of the fistula;
- STIR/SPAIR sequences on multiple scanning planes;
- DWIBS (*b* value 1000) with axial acquisition and MPR reconstruction;
- T1 TSE Fat Sat SPIR sequence on coronal plane pre- and post-contrastographic and subtraction of images;
- Axial T1 FS THRIVE volumetric and dynamic contrast-enhanced (DOTAREM 0.2 mg/kg).

Optional GE (BTFE) sequences on axial/coronal plane can be carried out to improve the definition of the anatomic relationships of the lesion against IS and ES, using the distinctive "edge effect". The DWIBS sequence acquired in free breathing (Diffusion-Weighted Imaging with background body subtraction, TR >5000 MS, TE shortest ≈70 ms, 180 ms TI, EPI factor 47, *B*-factor 1000 s/mm^2) represents something of a compromise between DWI and STIR; it suppresses the normal tissues and organs and it enhanced through a strong hyperintense signal pathological tissues, providing striking images-like PET [72, 73].

Pathophysiology and epidemiology of perianal fistulas

At present, the "crypto-glandular" etiopathogenetic hypothesis is the most accepted even if controversial [8, 74]. The anal glands, located on the same level as the dentate line between the columns of Morgagni, are involved in the lubrication process of the anus through the secretion of mucus in the anal crypts. The alteration or obstruction of the drainage of crypts is probably at the origin of a local inflammatory/infectious process that results in an abscess which may resolve itself spontaneously due to direct drainage into the anal canal or lead to the formation of fistulas [75].

Abscess and fistula would then be acute or chronic manifestations of a single disease process, since 87 % of the patients develop fistulas following an acute perianal abscess [67].

Other causes of perianal fistula, less significant in statistical terms than CD, are tuberculosis, diverticulitis, pelvic infections, trauma and complications of surgery [76, 77]. There is perianal involvement in patients with more than 38 % CD with a ratio of four males to one female (due to the fact that males have more anal glands than females). More than 30 % of pediatric patients with CD develop a perianal inflammation that will lead to the formation of a fistula in a high percentage of cases. For over 5 % of pediatric patients, the perianal fistula is the expression of onset of CD in the absence of intestinal involvement at diagnosis [76, 77].

Classification of fistulas

Parks's classification (1976) is the first and main classification of perianal fistulas; it is based on principles of surgical anatomy [78, 79] and classifies the various types of fistulas according to their course and relationship with the ES.

Parks's classification identifies four types of fistula: inter-sphincteric, trans-sphincteric, supra-sphincter and extra-sphincter according to the relationship of the sphincter complex in the coronal plane of the anal canal.

St. James' University Hospital Classification (Morris et al.) is an adaptation of Park's classification of diagnostic imaging [31].

In this classification, the categories identified by Park are maintained, while the surgical references are replaced with radiologic anatomy on pelvic MRI and additional parameters are introduced, such as the presence of secondary sinus tract and/or abscess formation.

According to Morris's classification, there are five different types or degrees of perianal fistulas:

1. Simple linear intersphincteric fistula (grade 1) that penetrates the IS and ISS runs through it to the skin in the absence of secondary tracts, abscesses or extensions to the LA (Fig. 5);
2. Intersphincter fistula with intersphincteric abscess or secondary fistulous tract (grade 2) consists of an intersphincteric fistula associated with an abscess or a secondary tract that lies within the ISS. When process extends to the opposite side, spreading partially circumferentially around the IS, it is termed a horseshoe fistula. The profile of ES is always intact (Fig. 6);
3. Simple transphincteric fistula (grade 3), which penetrates both the IS and the ES and penetrates the IRF or the IAF down to the skin. There are no secondary tracts, abscesses or signs of involvement of the LA (Fig. 7);
4. Complex transphincteric fistula with abscess or secondary fistulous tract within the IAF or IRF (grade 4) that has similar characteristics to simple trans-sphincteric fistula, but it is complicated by secondary tracts or abscesses. There is no involvement of the LA (Fig. 8);
5. Supra- and extra-sphincteric fistula that forms complex fistulas (grade 5): supra-sphincter fistula exits the ISS

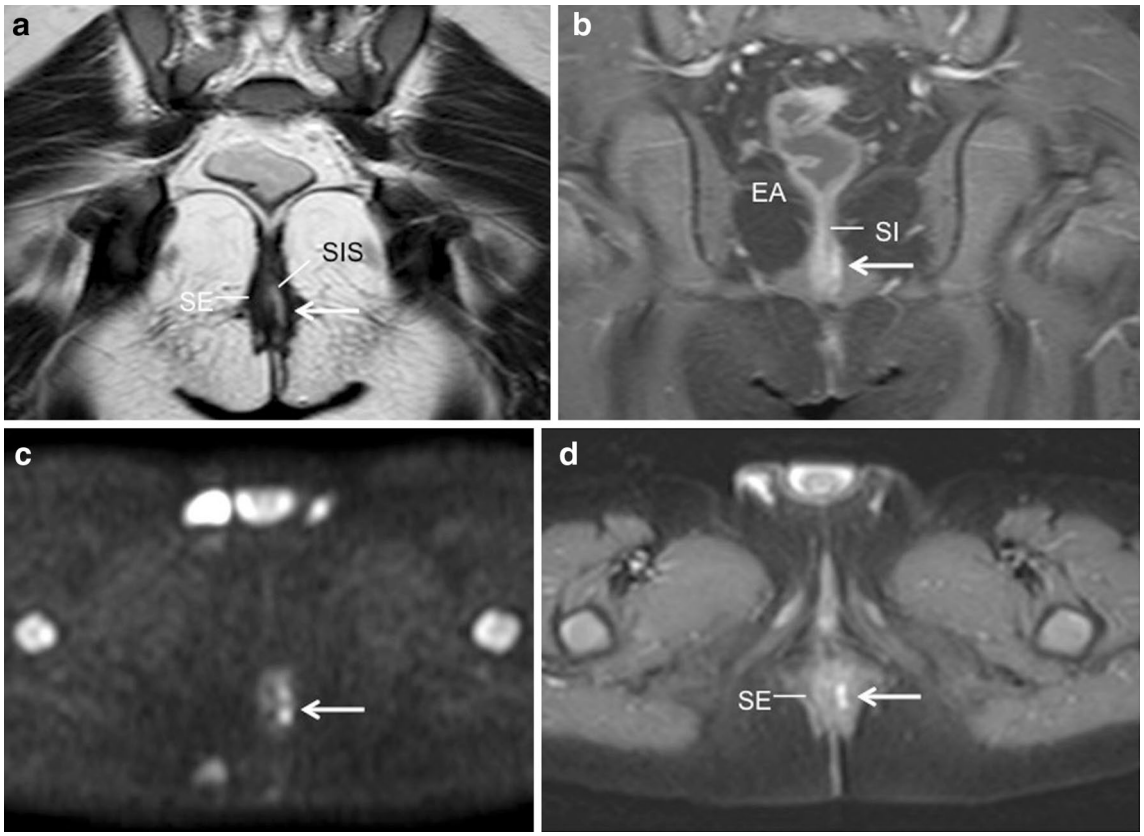

Fig. 5 Grade 1 (Morris's) simple intersphincteric fistula which passes through the intersphincteric space (ISS). The fistula tract does not involve the external sphincter (SE) as evident in coronal T2-weighted image (**a**) and coronal short T1 inversion recovery (STIR) image (**b**). Axial diffusion-weighted whole-body imaging with background body signal suppression (DWIBS) image (**c**) shows a high signal tract which matches with intense enhancement shown on axial contrast-enhanced T1-weighted with fat suppression image (**d**) consistent with active disease. *SIS* intersphincteric space, *EA* levator ani, *SI* internal sphincter

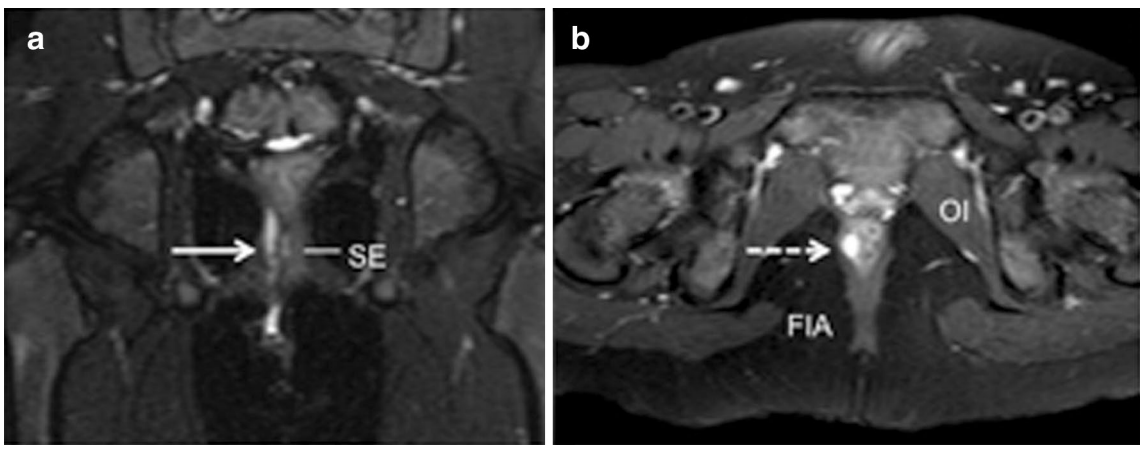

Fig. 6 Grade 2 (Morris's) intersphincter fistula (**a**, *arrow*) which is limited by the external sphincter (SE) with cryptoglandular abscess (**b**, *dashed arrow*). *OI* internal obturator muscle, *FIA* ischioanal fossae

above the puborectalis muscle and penetrates the LA before passing through the IRF towards the skin. Extrasphincter fistulas are independent of pathologic entities, since there is no involvement of the sphincter complex and they pass caudally through the plane of the LA through the IRF until they reach the skin (Fig. 9).

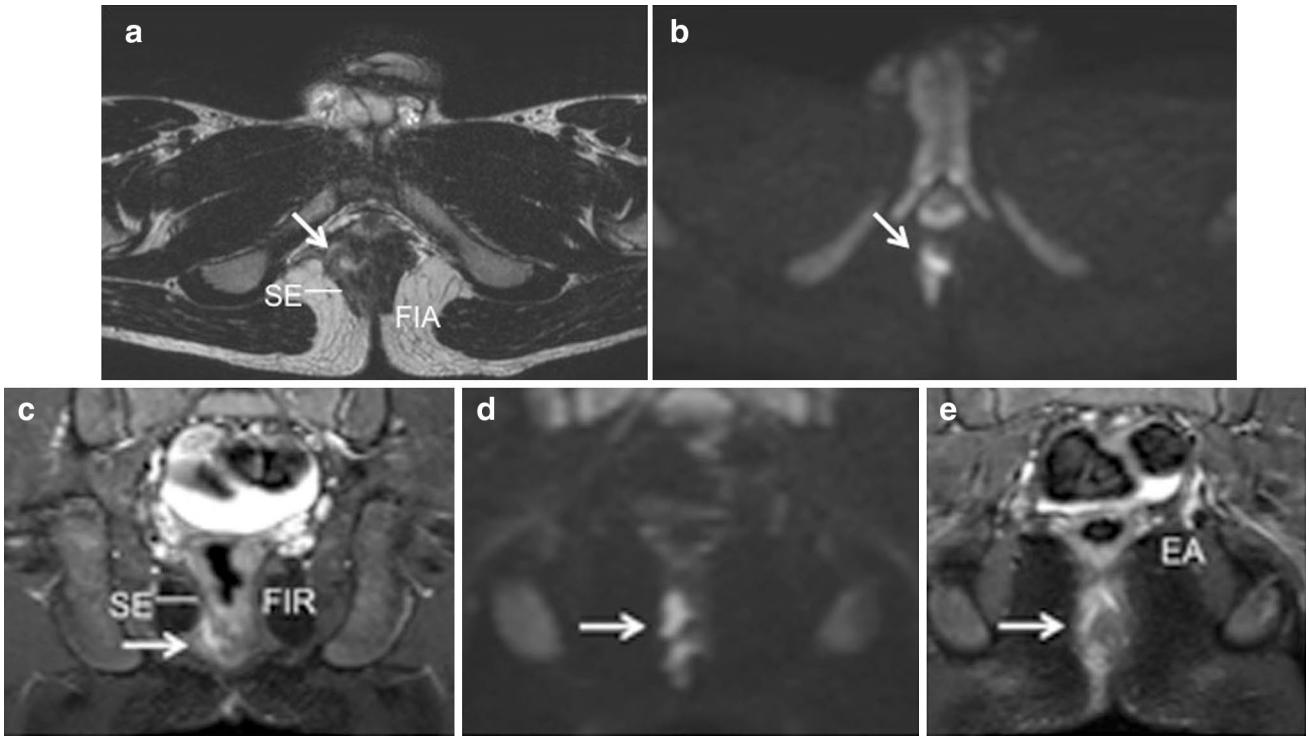

Fig. 7 Grade 3 (Morris's) transphincteric fistula with an internal opening at 9–10 o'clock and which penetrates the sphincterial complex and in particular the external anal sphincter (SE) as shown on axial T2-weighted image (**a**) and on the corresponding axial DWIBs image (**b**). Coronal STIR image (**c**), coronal DWIBs image (**d**) and coronal contrast-enhanced T1-weighted with fat suppression image (**e**) show penetration through the ischio-rectal fossae (FIR). *EA* levator ani

Although the classification of St. James 'University Hospital is more descriptive and is based on MR anatomy, Park's classification is preferable in pediatrics as it is based on the coronal plane rather than the axial plane. In fact in children, the anal canal is much shorter than in adults, for which it is particularly difficult to classify a type of fistula on the axial plane correctly.

Therefore, the description of secondary vehicles and the associated abscesses must be included in the radiological reports when referring to Park's classification as they are the main causes of inadequate response to treatment (medical or surgical) and relapse in children.

For descriptive purposes when reporting MR, the so-called "anal clock" [80] of the surgical field is generally used to locate the origin of the fistula with respect to the anal canal exactly. The "anal clock" is an axial section comparable to a clock face in which the pubic symphysis indicates 12 o'clock, the buttock crease 6 o'clock, and the right and left buttocks 9 and 3 o'clock, respectively.

Imaging findings

The first element to be assessed is whether there is a main tract or not and the total number of fistulas present [32, 81].

In the structure of the sphincter complex and pelvic muscles, a fistula is distinguished as a hypointense linear structure on T1-weighted sequences and hyperintense on T2w and T1-weighted sequences (especially with fat saturation). The intrinsic characteristics of the MRI method, based on multiparametricity, enable us to assess the degree of activity of perianal disease. Active fistula or abscesses are characterized by a marked positivity on DWIBS images and a corresponding enhancement on T1 post-contrastographic sequences.

A loss of T2-weighted imaging hyperintense signal or lack of enhancement on T1-weighted post-contrastographic sequences correlated with a progressive inactivation of the disease process [82]. These changes are reliable predictors and make the MR study particularly useful in the follow-up of peri-anal disease, especially as an instrumental assessment of the response to treatment [4, 83, 84].

Equally important is the contribution provided by MRI in the evaluation of deep tissue, peripheral to the fistula, with particular regard to the IRF or IAF. Edema, signal and structural distortion of fibro-adipose components and post-contrast-enhancement of the signal indicate deep and persistent inflammation in the tissue.

The fistula must be characterized and classified according to its course and its relationship with the sphincter

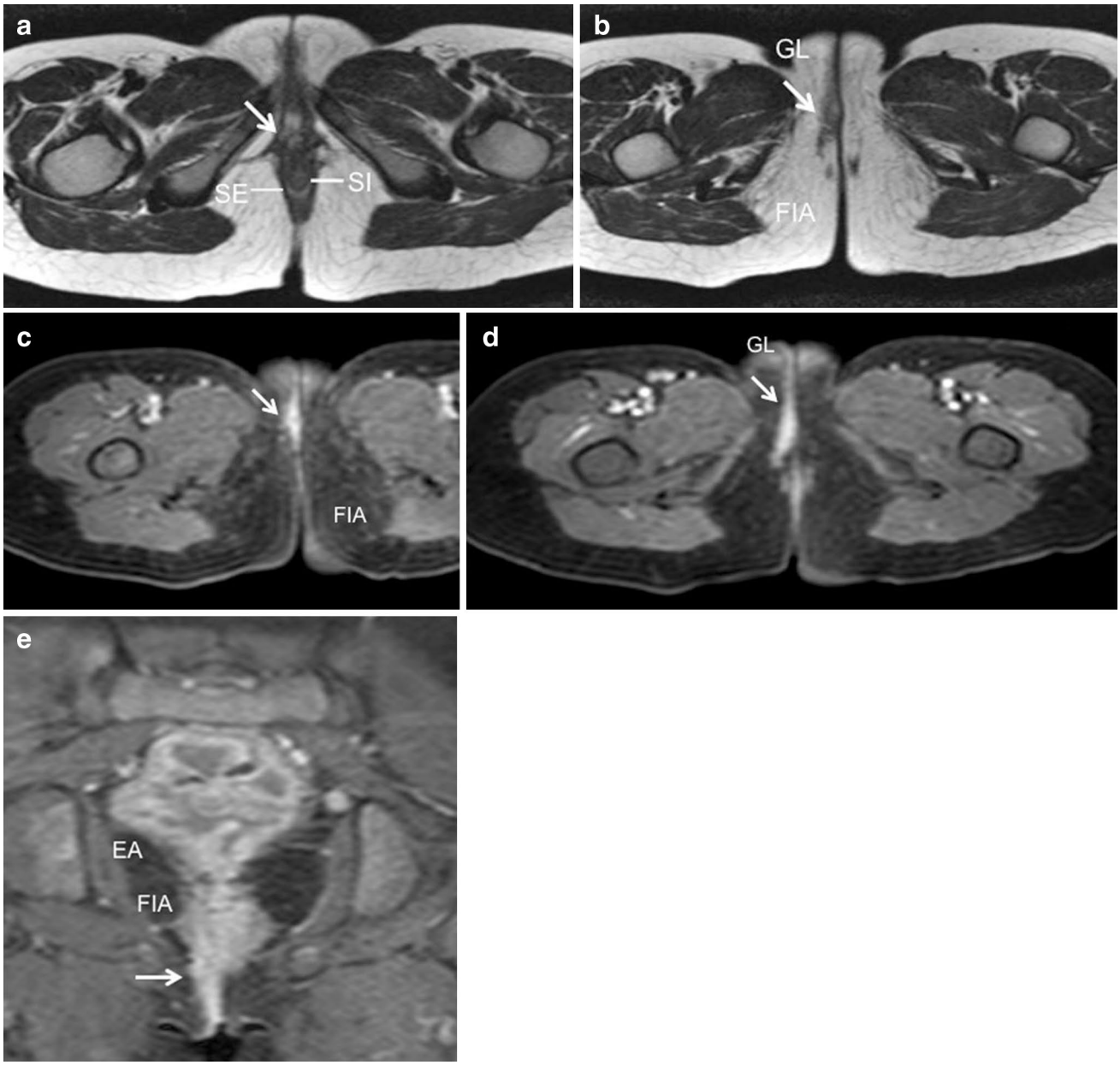

Fig. 8 Grade 4 (Morris's) transphincteric fistula: it combines a transphincteric fistula (as Fig. 7) with a secondary tract (**a**, **b**) that extends caudally to the *right* large lip (GL) with marked enhancement(**c**–**e**). *EA* levator ani muscle, unscathed, *FIA* ischio-anal fossa, *SE* external anal sphincter, *SI* internal anal sphincter

complex. Most fistulas are of posterior origin and must be localized according to the "anal clock" [85].

Therefore, the description of secondary tracts and the associated abscesses must be included in the radiological reports when referring to Park's classification as they are the main causes of inadequate response to treatment (medical or surgical) and relapse in children. The secondary tracts are identified separately and described according to their relationships with the main fistula, localizing them with respect to the anal sphincter, the LA and any skin outlet skin, if independent. The perianal abscesses tend to show high signal intensity on T2-weighted sequences as fistulas, but may appear uneven and hyper intense in T1-weighted baseline sequences with peripheral characteristic peripheral enhancement in post-contrastographic sequences. MR images enable us to view and correctly assess post-surgical findings, particularly in the presence of setons [86, 87].

The identification of collateral findings is particularly important in children, especially in pelvic MRI. Here, are

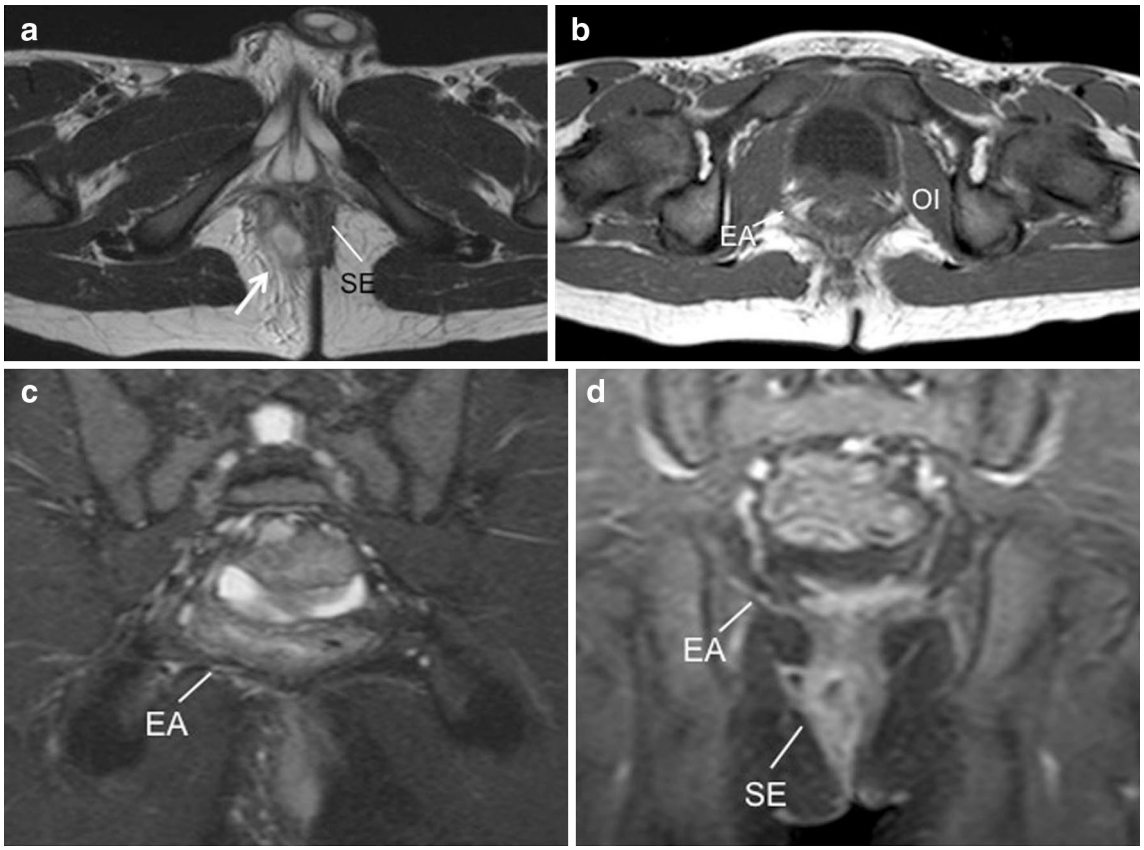

Fig. 9 Grade 5 (Morris's) supralevator fistula with abscess: right supralevator fistula that penetrates levator ani (EA) above the puborectal muscle which shows an anomalous signal on axial T2-weighted image (**a**) and on axial T1-weighted image (**b**), hyperintense and discontinued signal on coronal STIR image (**c**) and abnormal enhancement on T1-weighted image with fat suppression following contrast agent administration (**d**). *SE* external sphincter, *OI* internal obturator muscle

some extra-anal and extra-sphincter findings that frequently affect the clinical development of the disease in children:

- sacroiliitis or hip joint articular involvement;
- enterocolitis;
- abdominal or pelvic fluid collection;
- lymphadenopathy;
- post-medical or surgical complications.

Conclusions

The MRE is a highly sensitive and specific method that is preferable for evaluating pediatric patients suffering from Crohn's disease.

The MRE provides us with results comparable to those obtained with endoscopy for the identification and assessment of disease activity and is better than other cross-sectional imaging techniques, such as CT, for evaluating the degree of fibrosis and complications of disease.

MR Diffusion Imaging is a technique that enables us to add important additional information and which may replace the use of intravenous contrast agents.

Although perianal fistulas can be identified with high sensitivity and specificity during a pelvic MR examination, a pelvic MR is optimal and can provide all the necessary information for a correct diagnostic and therapeutic management of disease.

In children, pelvic MRI reaches specificity levels above 81 % that can reach 100 % and can easily be integrated with MRE, while causing a relative increase of the duration of the examination.

Pelvic MRI also helps to identify extra-anal and extra-sphincteric complications included in the field of view acquired and above all to detect, assess and classify secondary fistulas that are often responsible for complications and recurrences [88, 89].

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964

Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Lovasz BD, Lakatos L, Horvath A et al (2013) Evolution of disease phenotype in adult and pediatric onset Crohn's disease in a population-based cohort. World J Gastroenterol WJG. 19(14):2217–2226. doi:10.3748/wjg.v19.i14.2217
2. Essary B, Kim J, Anupindi S, Katz JA, Nimkin K (2007) Pelvic MRI in children with Crohn disease and suspected perianal involvement. Pediatr Radiol 37(2):201–208 **(Epub 2006 Dec 16, review PubMed PMID 17180366)**
3. Haggett PJP, Moore NRN, Shearman JDJ et al (1995) Pelvic and perineal complications of Crohn's disease: assessment using magnetic resonance imaging. Gut 36:407–410
4. Horsthuis K, Stoker J (2004) MRI of perianal Crohn's disease. AJR Am J Roentgenol 183:1309–1315
5. Hildebrand H, Finkel Y, Grahnquist L et al (2003) Changing pattern of paediatric inflammatory bowel disease in northern Stockholm 1990–2001. Gut 52:1432–1434
6. Bernstein CN, Wajda A, Svenson LW et al (2006) The epidemiology of inflammatory bowel disease in Canada: a population-based study. Am J Gastroenterol 101:1559–1568
7. Kim H, Lim JS, Choi JY et al (2010) Rectal cancer: comparison of accuracy of local-regional staging with two- and three-dimensional preoperative 3-T MR imaging. Radiology 254:485–492
8. Hendrickson BA, Gokhale R, Cho JH (2002) Clinical aspects and pathophysiology of inflammatory bowel disease. Clin Microbiol Rev 15:79–94
9. Malaty HM, Fan X, Opekun AR et al (2010) Rising incidence of inflammatory bowel disease among children: a 12-year study. J Pediatr Gastroenterol Nutr 50:27–31
10. Benchimol EI, Mack DR, Nguyen GC et al (2014) Incidence, outcomes, and health services burden of very early onset inflammatory bowel disease. Gastroenterology 147:803–813
11. Chouraki V, Savoye G, Dauchet L et al (2011) The changing pattern of Crohn's disease incidence in northern France: a continuing increase in the 10- to 19-year-old age bracket (1988–2007). Aliment Pharmacol Ther 33:1133–1142
12. Law ST, Li KK (2013) Age-related differences in the clinical course of Crohns disease in an Asian population: a retrospective cohort review. Indian Pediatr 50(12):1148–1152 **(Epub 2013 Jul 5)**
13. Sauer CG, Kugathasan S (2009) Pediatric inflammatory bowel disease: highlighting pediatric differences in IBD. Gastroenterol Clin N Am 38:611–628
14. Ishige T, Tomomasa T, Takebayashi T, Asakura K, Watanabe M, Suzuki T et al (2010) Inflammatory bowel disease in children: epidemiological analysis of the nationwide IBD registry in Japan. J Gastroenterol 45:911–917
15. Su CG, Judge TA, Lichtenstein GR (2002) Extraintestinal manifestations of inflammatory bowel disease. Gastroenterol Clin N Am 31:307–327
16. Shin DH, Sinn DH, Kim YH, Kim JY, Chang DK, Kim EJ et al (2011) Increasing incidence of inflammatory bowel disease among young men in Korea between 2003 and 2008. Dig Dis Sci 56:1154–1159
17. Song XM, Gao X, Li MZ, Chen ZH, Chen SC, Hu PJ et al (2011) Clinical features and risk factors for primary surgery in 205 patients with Crohn's disease: analysis of a South China cohort. Dis Colon Rectum 54:1147–1154
18. Chow DK, Leong RW, Lai LH, Wong GL, Leung WK, Chan FK et al (2008) Changes in Crohn's disease phenotype over time in the Chinese population: validation of the Montreal classification system. Inflamm Bowel Dis 14:536–541
19. Mamula P, Telega GW, Markowitz JE et al (2002) Inflammatory bowel disease in children 5 years of age and younger. Am J Gastroenterol 97:2005–2010
20. Levine A, Griffiths A, Markowitz J et al (2011) Pediatric modification of the Montreal classification for inflammatory bowel disease: the Paris classification. Inflamm Bowel Dis 17:1314–1321
21. Cannioto Z, Berti I, Martelossi S et al (2009) IBD and IBD mimicking enterocolitis in children younger than 2 years of age. Eur J Pediatr 168:149–155
22. Mamula P, Markowitz JE, Piccoli DA et al (2007) Immune response to influenza vaccine in pediatric patients with inflammatory bowel disease. Clin Gastroenterol Hepatol 5:851–856
23. Ruemmele FM, El Khoury MG, Talbotec C et al (2004) Characteristics of inflammatory bowel disease with onset during the first year of life. J Pediatr Gastroenterol Nutr 43:603–609
24. Gasparetto M, Guariso G (2014) Crohn's disease and growth deficiency in children and adolescents. World J Gastroenterol 20(37):13219–13233. doi:10.3748/wjg.v20.i37.13219 **(Review PubMed PMID 25309059; PubMed Central PMCID PMC4188880)**
25. Alhagamhmad MH, Day AS, Lemberg DA, Leach ST (2012) An update of the role of nutritional therapy in the management of Crohn's disease. J Gastroenterol 47: 872–882. doi:10.1007/s00535-012-0617-9 **(PMID 22699323)**
26. Shamir R (2009) Nutritional aspects in inflammatory bowel disease. J Pediatr Gastroenterol Nutr 48(Suppl 2):S86–S88. doi:10.1097/MPG.0b013e3181a15ca0
27. Chow DK, Sung JJ, Wu JC, Tsoi KK, Leong RW, Chan FK (2009) Upper gastrointestinal tract phenotype of Crohn's disease is associated with early surgery and further hospitalization. Inflamm Bowel Dis 15:551–557
28. Kim BJ, Song SM, Kim KM, Lee YJ, Rhee KW, Jang JY et al (2010) Characteristics and trends in the incidence of inflammatory bowel disease in Korean children: a single center experience. Dig Dis Sci 55:1989–1995
29. Duigenan S, Gee MS (2012) Imaging of pediatric patients with inflammatory bowel disease. AJR Am J Roentgenol 199:907–915
30. Toma P, Granata C, Magnano G et al (2007) CT and MRI of paediatric Crohn disease. Pediatr Radiol 37:1083–1092
31. Morris J, Spencer JA, Ambrose NS (2012) MR imaging classification of perianal fistulas and its implications for patient management. Radiographics 20:623–635 **(Discussion 635–637)**
32. Halligan S, Stoker J (2006) Imaging of fistula in ano. Radiology 239:18–33
33. Patak MA, Mortele KJ, Ros PR (2005) Multidetector row CT of the small bowel. Radiol Clin N Am 43:1063–1077
34. Mackalski BA, Bernstein CN (2006). New diagnostic imaging tools for inflammatory bowel disease. Gut 55:733–741
35. Brenner DJ, Elliston CD, Hall EJ, Berdon WE (2001) Estimates of the cancer risks from pediatric CT radiation are not merely theoretical: comment on "point/counterpoint: in X-ray computed tomography, technique factors should be selected appropriate to patient size—against the proposition". Med Phys 28:2387–2388
36. Rice HE, Frush DP, Farmer D, Waldhausen JH (2007) Review of radiation risks from computed tomography: essentials for the pediatric surgeon. J Pediatr Surg 42:603–607
37. Furukawa A, Saotome T, Yamasaki M et al (2004) Cross-sectional imaging in Crohn disease. Radiographics 24:689–702

38. Solem CA, Loftus EV Jr, Fletcher JG et al (2008) Small bowel imaging in Crohn's disease: a prospective, blinded, 4-way comparison trial. Gatrointest Endosc 68:255–266
39. Negaard A, Paulsen V, Sandvik L et al (2007) 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 17:2294–2301
40. Masselli G, Casciani E, Polettini E, Gualdi G (2008) Comparison of MR enteroclysis with MR enterography and conventional enteroclysis in patients with Crohn's disease. Eur Radiol 18:438–447
41. Tolan DJ, Greenhalgh R, Zealley IA, Halligan S, Taylor SA (2010) MR enterographic manifestation of small bowel Crohn disease. Radiographics 30:367–384
42. Absah I, Bruining DH, Matsumoto JM et al (2012) MR enterography in pediatric inflammatory bowel disease: retrospective assessment of patient tolerance, image quality, and initial performance estimates. AJR Am J Roentgenol 199:W367–W375
43. Gee MS, Nimkin K, Hsu M, Israel EJ et al (2011) Prospective evaluation of MR enterography as the primary imaging modality for pediatric Crohn disease assessment. AJR Am J Roentgenol 197:224–231
44. Froehlich JM, Waldherr C, Erturk SM, Patak MA (2010) MR motility imaging in Crohn's disease improves lesion detection compared with standard MR imaging. Eur Radiol 20:1945–1951
45. Bickelhaupt S, Pazahr S, Chuck N, Blume I, Froehlich JM, Cattin R, Raible S, Bouquet H, Bill U, Rogler G, Frei P, Boss A, Patak MA (2013) Crohn's disease: small bowel motility impairment correlates with inflammatory-related markers C-reactive protein and calprotectin. Neurogastroenterol Motil 25(6):467–473. doi:10.1111/nmo.12088 **(Epub 2013 Mar 18)**
46. Menys A, Atkinson D, Odille F et al (2012) Quantified terminal ileal motility during MR enterography as a potential biomarker of Crohn's disease activity: a preliminary study. Eur Radiol 22:2494–2501
47. Kiryu S, Dodanuki K, Takao H, Watanabe M, Inoue Y, Takazoe M et al (2009) Free-breathing diffusion-weighted imaging for the assessment of inflammatory activity in Crohn's disease. J Magn Reson Imaging 29:880–886
48. Oto A, Zhu F, Kulkarni K, Karczmar GS, Turner JR, Rubin D (2009) Evaluation of diffusion-weighted MR imaging for detection of bowel inflammation in patients with Crohn's disease. Acad Radiol. 16:597–603
49. Neubauer H, Pabst T, Dick A, Machann W, Evangelista L, Wirth C et al (2013) 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 43:103–114
50. Schmid-Tannwald C, Agrawal G, Dahi F, Sethi I, Oto A (2012) Diffusion-weighted MRI: role in detecting abdominopelvic internal fistulas and sinus tracts. J Magn Reson Imaging 131:125–131
51. Leyendecker JR, Bloomfeld RS, DiSantis DJ et al (2013) MR enterography in the management of patients with Crohn disease. Radiographics 29:1827–1846
52. Kleer CG, Appelman HD (2001) Surgical pathology of Crohn's disease. Surg Clin N Am 81(1):13–30
53. Horsthuis K, Bipat S, Bennink RJ, Stoker J (2008) Inflammatory bowel disease diagnosed with US, MR, scintigraphy, and CT: meta-analysis of prospective studies. Radiology 247(1):64–79
54. Punwani S, Rodriguez-Justo M, Bainbridge A et al (2009) Mural inflammation in Crohn disease: location-matched histologic validation of MR imaging features. Radiology 252(3):712–720
55. Rimola J, Ordás I, Rodriguez S, García-Bosch O, Aceituno M, Llach J, Ayuso C, Ricart E, Panés J (2011) Magnetic resonance imaging for evaluation of Crohn's disease: validation of parameters of severity and quantitative index of activity. Inflamm Bowel Dis 17(8):1759–1768. doi:10.1002/ibd.21551 **(Epub 2010 Nov 8)**
56. Zappa M, Stefanescu C, Cazals-Hatem D et al (2011) Which magnetic resonance imaging findings accurately evaluate inflammation in small bowel Crohn's disease? A retrospective comparison with surgical pathologic analysis. Inflamm Bowel Dis 17(4):984–993. doi:10.1002/ibd.21414
57. Harisinghani MG, Wittenberg J, Lee W et al (2003) Bowel wall fat halo sign in patients without intestinal disease. AJR Am J Roentgenol 181(3):781–784
58. Dignass A, Van Assche G, Lindsay JO et al (2010) The second European evidence-based consensus on the diagnosis and management of Crohn's disease: current management. J Crohns Colitis 4(1):28–62
59. Van Assche G, Dignass A, Panes J et al (2010) The second European evidence-based consensus on the diagnosis and management of Crohn's disease: definitions and diagnosis. J Crohns Colitis 4(1):7–27
60. Lee SS, Kim AY, Yang SK et al (2009) Crohn disease of the small bowel: comparison of CT enterography, MR enterography, and small-bowel follow-through as diagnostic techniques. Radiology 251(3):751–761
61. Maccioni F, Bruni A, Viscido A et al (2006) MR imaging in patients with Crohn disease: value of T2- versus T1-weighted gadolinium-enhanced MR sequences with use of an oral superparamagnetic contrast agent. Radiology 238(2):517–530
62. Martinez MJ, Ripolles T, Paredes JM, Blanc E, Marti-Bonmati L (2009) Assessment of the extension and the inflammatory activity in Crohn's disease: comparison of ultrasound and MRI. Abdom Imaging 34(2):141–148
63. Pilleul F, Godefroy C, Yzebe-Beziat D et al (2005) Magnetic resonance imaging in Crohn's disease. Gastroenterol Clin Biol 29(8–9):803–808
64. Satsangi J, Silverberg MS, Vermeire S, Colombel JF (2006) The Montreal classification of inflammatory bowel disease: controversies, consensus, and implications Gut 55(6):749–753 **(PubMed PMID 16698746; PubMed Central PMCID PMC1856208)**
65. Sahni VA, Ahmad R, Burling D (2007) Which method is best for imaging of perianal fistula? Abdom Imaging 33:26–30
66. Schäfer A-O, Langer M (2010) MRI of rectal cancer, vol 5. Springer, Berlin. doi:10.1007/978-3-540-72833-7_2
67. O'Malley RB, Al-Hawary MM, Kaza RK, Wasnik AP, Liu PS, Hussain HK (2012) Rectal imaging: part 2. Perianal fistula valuation on pelvic MRI—what the radiologist needs to know. AJR Am J Roentgenol 199(1):W43–W53. doi:10.2214/AJR.11.8361 **(Review PubMed PMID 22733931)**
68. Dagia C, Ditchfield M, Kean M et al (2010) Feasibility of 3-T MRI for the evaluation of Crohn disease in children. Pediatr Radiol 40:1615–1624
69. Chang KJ, Kamel IR, Macura KJ et al (2008) 3.0-T MR imaging of the abdomen: comparison with 1.5 T1. Radiographics 28:1983–1998
70. Hori M, Oto A, Orrin S, Suzuki K, Baron RL (2009) Diffusion-weighted MRI: a new tool for the diagnosis of fistula in ano. J Magn Reson Imaging 30(5):1021–1026. doi:10.1002/jmri.21934
71. Proscia N, Jaffe TA, Neville AM et al (2010) MRI of the pelvis in women: 3D versus 2D T2-weighted technique. AJR Am J Roentgenol 195:254–259
72. Ording Müller LS, Avenarius D, Olsen OE (2011) High signal in bone marrow at diffusion-weighted imaging with body background suppression (DWIBS) in healthy children. Pediatr Radiol 41(2):221–226. doi:10.1007/s00247-010-1774-8 **(Epub 2010 Jul 23)**

73. Park JJ, Kim CK, Park SY, Park BK (2015) Parametrial invasion in cervical cancer: fused T2-weighted imaging and high-*b*-value diffusion-weighted imaging with background body signal suppression at 3 T. Radiology 274(3):734–741. doi:10.1148/radiol.14140920 **(Epub 2014 Oct 7)**
74. Hussain SM, Outwater EK, Joekes EC et al (2000) Clinical and MR imaging features of cryptoglandular and Crohn's fistulas and abscesses. Abdom Imaging 25:67–74
75. Schwartz DA, Loftus EV, Tremaine WJ et al (2002) The natural history of fistulizing Crohn's disease in Olmsted County, Minnesota. Gastroenterology 122:875–880
76. Gupta N, Bostrom AG, Kirschner BS, Cohen SA, Abramson O et al (2008) 2008. Am J Gastroenterol 103(8):2092–2098
77. Aloi M, Lionetti P, Barabino A, Guariso G, Costa S, Fontana M, Romano C, Lombardi G, Miele E, Alvisi P, Diaferia P, Baldi M, Romagnoli V, Gasparetto M, Di Paola M, Muraca M, Pellegrino S, Cucchiara S, Martelossi S (2014) SIGENP IBD Group. Phenotype and disease course of early-onset pediatric inflammatory bowel disease. Inflamm Bowel Dis 20(4):597–605. doi:10.1097/01.MIB.0000442921.77945.09
78. Parks AG (1961) Pathogenesis and treatment of fistula-in-ano. Br Med J 5224:463–469
79. Parks AG, Gordon PH, Hardcastle JD (1976) A classification of fistula-in-ano. Br J Surg 63:1–12
80. Compton Gregory L, Bartlett Murray (2014) Perianal disease in pediatric Crohn disease: a review of MRI findings. Pediatr Radiol 44:1198–1208
81. de Miguel CJ, del Salto LG, Rivas PF et al (2012) MR imaging evaluation of perianal fistulas: spectrum of imaging features. Radiographics 32:175–194
82. Bartram C, Buchanan G (2003) Imaging anal fistula. Radiol Clin N Am 41:443–457
83. Tougeron D, Savoye G, Savoye-Collet C, Koning E, Michot F, Lerebours E (2009) Predicting factors of fistula healing and clinical remission after infliximab-based combined therapy for perianal fistulizing Crohn's disease. Dig Dis Sci 54(8):1746–1752. doi:10.1007/s10620-008-0545-y **(Epub 2008 Nov 12)**
84. Shenoy-Bhangle A, Nimkin K, Goldner D et al (2013) MRI predictors of treatment response for perianal fistulizing Crohn disease in children and young adults. Pediatr Radiol 44:23–29
85. Barker PG, Lunniss PJ, Armstrong P et al (1994) Magnetic resonance imaging of fistula-in-ano: technique, interpretation and accuracy. Clin Radiol 49:7–13
86. Szurowska EE, Wypych JJ, Izycka-Swieszewska EE (2007) Perianal fistulas in Crohn's disease: MRI diagnosis and surgical planning: MRI in fistulazing perianal Crohn's disease. Abdom Imaging 32:705–718
87. Beets-Tan RGR, Beets GLG, van der Hoop AGA et al (2000) Preoperative MR imaging of anal fistulas: does it really help the surgeon? Radiology 218:75–84
88. Katsanos K, Papathanasopoulos A, Christodoulou D, Tsianos E (2009) Perianal fistulizing Crohn's disease: imaging modalities and therapeutic challenges. Ann Gastroenterol N Am. http://www.annalsgastro.gr/index.php/annalsgastro/article/view/768. Accessed 12 November 2015
89. Jordán J, Roig JV, García-Armengol J, García-Granero E, Solana A, Lledó S (2010) Risk factors for recurrence and incontinence after anal fistula surgery. Colorectal Dis 12:254–260