Magnetic resonance imaging in ankylosing spondylitis

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Although x-rays are still the standard for the assessment of structural sacroiliac joint changes and the diagnosis of ankylosing spondylitis (AS), magnetic resonance imaging (MRI) sequences are necessary for assessment of active sacroiliitis. Conventional radiographs of the spine are the basis for the detection of AS-related structural spinal changes, such as syndesmophytes and ankylosis. MRI of the spine is useful for the assessment of inflammatory changes, and potentially for the diagnosis of early and active stages of the disease. MRI sequences useful for the assessment of active disease are the short tau inversion recovery, the T2-fat saturated and the T1 post-gadolinium MRI sequences. For assessment of structural changes, the T1-weighted MRI sequence is used. Both sacroiliac joint and spinal changes can be quantified by evaluated scoring systems. These systems are mostly used in clinical trials to quantify the impact of therapy, such as anti-tumor necrosis factor-α agents, on spinal inflammation.

Ankylosing spondylitis (AS) is the major subtype of the heterogeneous group of the spondyloarthritides (SpA), which comprises reactive SpA, psoriatic SpA, SpA associated with inflammatory bowel diseases and undifferentiated SpA (uSpA). Imaging plays an important role in diagnosis, classification and monitoring of patients with AS. The standard imaging approach is conventional plain radiography of sacroiliac joints and spine. However, magnetic resonance imaging (MRI) and ultrasound are of increasing importance in clinical practice and clinical trials.

Many different anatomical structures may be involved in AS. The most characteristic features are inflammation of the sacroiliac joints (SIJ) and of spinal structures, as well as new bone formation leading to syndesmophytes and ankylosis. Various spinal sites may be affected, in part dependent on the stage of the disease [1]. In later stages of the disease, inflammatory lesions affect the spine in approximately 60–80% of the cases. There are different patterns of axial involvement. The vertebral bodies may be affected by spondylitis or, together with the intervertebral disks, by spondylodiskitis. Furthermore, the surrounding soft tissues may be affected by spinal enthesitis and zygoapophyseal, costovertebral and costosternal joints by spondylarthritis [2]. Peripheral manifestations of the musculoskeletal system are mainly seen in the peripheral joints and entheses. Imaging is an important part of classification criteria for AS. The modified New York criteria combine clinical features with definite radiological criteria [3]. This is relevant for the diagnosis in clinical practice and classification of AS and for the differentiation of AS from uSpA [4].

MRI has clear advantages in the detection of active inflammatory lesions in the axial skeleton as well as in the peripheral joints and entheses, while for diagnosis and classification of AS, and also for the detection of chronic structural changes, conventional radiographs of the SIJ and the spine are still the gold standard [5].

In general, the musculoskeletal system in patients with AS may show two types of abnormalities on imaging: active inflammatory changes and chronic structural changes. The structural changes can be further differentiated in erosive changes and changes with bone proliferation. The different imaging techniques have different capacities to assess AS-related changes (**Table 1**). While, in general, conventional radiographs and computed tomography (CT) have advantages in the detection of structural changes [5], MRI is superior in detecting active changes. The indications for the use of the techniques differ, and therefore they are often used complementarily.

Imaging of the sacroiliac joint in AS

Imaging of the SIJ plays an important role in AS, since almost all patients with AS do have involvement of the SIJ. Furthermore, imaging of structural changes in the SIJ is the major item in the modified New York criteria for the classification and diagnosis of AS [3].

MRI of the sacroiliac joints in AS

MRI of the SIJ is useful for visualization of the complicated anatomy of the SIJ, including abnormalities of the periarticular tissues, such as joint capsule, subchondral bone, entheses and ligaments,

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future medicine

Table 1. Imaging techniques and sensitivity of assessment of acute and chronic changes in ankylosing spondylitis.

	Acute/inflammatory changes	Chronic/bony changes
Conventional radiographs	+	+
Computed tomography	+	++
Scintigraphy	+	-
MRI	++	+
MRI–T1-weighted sequence	+	+
MRI–post-T1-weighted, STIR and T2–FS sequence	++	-

FS: Fat saturated; MRI: Magnetic resonance imaging; STIR: Short tau inversion recovery.

which are difficult to detect by other methods. MRI is especially valid for the detection of inflammation in the axial skeleton in AS patients. The MRI results correlate well with conventional histology and immunohistological findings [6].

By contrast with other imaging techniques, MRI is not associated with radiation exposure. This makes the technique favorable, especially in young women, children or patients who are likely to have repeated, frequent examinations. However, routine access to MRI, optimal technical equipment and skilled staff is not widely available, and costs of MRI are still rather high [7]. Furthermore, patients with a pacemaker or with older types of metal implants cannot be examined by MRI. In addition, the rather long duration of the procedure (~20–30 min) renders the technique poorly applicable for some patients because of intolerable pain and stiffness in the supine position [8].

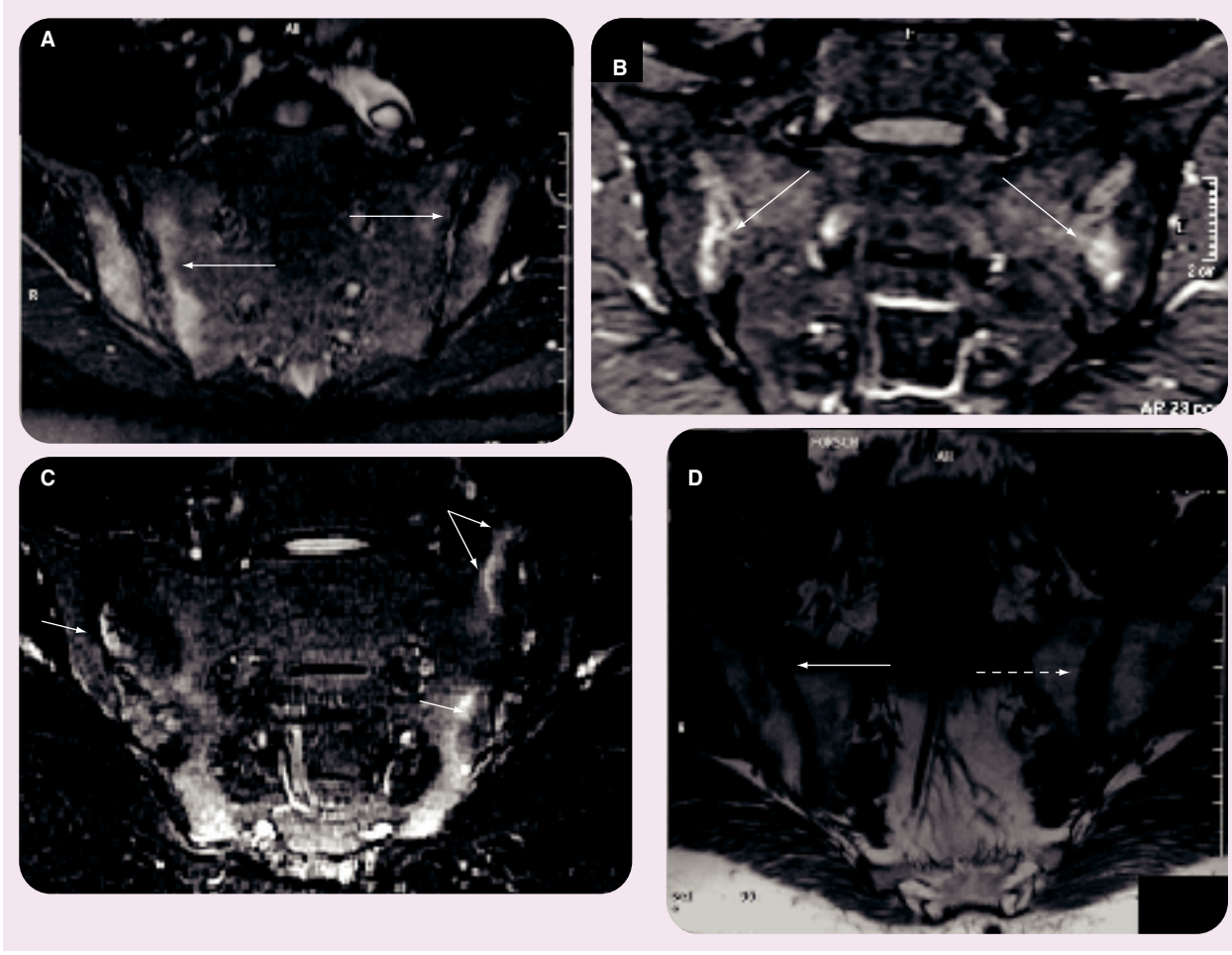
In MRI examination of the SIJ, oblique transaxial sections should be used (**Figure 1**) [6]. Paraxial slices may provide additional information on the SIJ in a few patients [9].

For the assessment of inflammatory SIJ lesions, the appropriate MRI sequences are the short tau inversion recovery (STIR) technique (**Figure 1A**), the T1-weighted turbo spin–echo sequence after application of a contrast agent (gadolinium diethylenetriamine-penta-acetic acid [T1/Gd-DTPA]) (**Figure 1B**) and the T2-weighted gradient–echo sequence after fat suppression (FS) (**Figure 1C**) [10,11]. The T1/Gd-DTPA turbo spin–echo sequence depicts inflammation in the SIJ by detection of enhancement of contrast agents, especially in areas with hypervascularization. The STIR and T2–FS techniques are able to assess inflammation by depiction of bone-marrow edema, thus, without the use of contrast agent. Although the T2–FS sequence has been used more frequently in the past, the new STIR technique is now often preferred because of its superior fat/water contrast obtained by total suppression of the fat signal [8]. In contrast to MRI of the spine [12], the question whether application of contrast agents provides additional information in the examination of the SIJ has not been resolved. Preliminary results suggest that STIR imaging is 90% compatible with techniques using post-gadolinium T1-weighted MRI [8]. The use of dynamic MRI of the SIJ on the basis of an early scoring proposal should not be widely used anymore because of its problematic performance in routine care with too many positive but nonspecific results [10].

The importance of MRI examinations of the SIJ for the diagnosis of early disease stages of SpA in patients with inflammatory back pain (IBP) was evaluated recently, among other diagnostic tools [13]. According to this evaluation, the highest likehood ratios for accurate diagnosis were obtained when MRI examinations together with the occurrence of HLA-B27 were taken into account. It was concluded that this approach may be used in clinical practice with a high degree of confidence in order to diagnose axial SpA at an early stage in patients who lack radiographic sacroiliitis but complain of IBP symptoms.

MRI can also be useful for the assessment of chronic SIJ changes, since the grading of SIJ changes is essential for the classification of AS [14–16]. However, the performance of MRI for assessment of structural SIJ changes has not been standardized to date. There is recent evidence that plain radiography performs better in detecting chronic changes than MRI [5]. Currently, the most frequently used MRI sequences for quantification and assessment of structural SIJ lesions are the T1-weighted turbo spin–echo sequence (usually performed before application of contrast material) (**Figure 1d**) and gradient echo techniques [8]. The whole topic has been extensively evaluated by the Assessment in Ankylosing Spondylitis (ASAS)/Outcome Measured

Figure 1. Magnetic resonance imaging examinations of the sacroiliac joints in patients with ankylosing spondylitis.



(A) Short tau inversion recovery magnetic resonance imaging (MRI). **(B)** T1-weighted MRI of the sacroiliac joints (SIJ) after application of contrast agent with typical increased signal intensity due to contrast agent enhancement in inflammatory regions, **(C)** T2-weighted MRI of the SIJ after fat suppression. **(D)** T1-weighted MRI of the SIJ of the same patient as in **(B)**, before application of contrast agent. Enhancement of contrast agent due to inflammation (hypervascularization) demonstrates the typical decreased signal intensity compared with post-gadolinium images.

in Rheumatology Clinical Trials (OMERACT) MRI in AS working group. All available scoring systems for the use of MRI of the SIJ in AS have been validated recently, setting the conditions for further evaluation in this important field [17]. Several recent studies with biologicals, such as infliximab and etanercept [18,19], have shown definite clinical efficacy on disease activity and improvement of inflammation of the SI joints and the spine [18,20–22].

MRI of the pubic symphysis in AS

Involvement of the pubic symphysis in AS occurs in up to 25% of patients. In most occasions this is only detected in late stages of the disease when advanced abnormalities in the SIJ have already been detected [23]. Involvement of the pubic symphysis detected by conventional radiography ranges from minimal changes to erosions, parasymphyseal osteosclerosis, apparent destruction and ankylosis [23]. Symphysitis in earlier stages of disease may be detected by scintigraphy or by MRI using T1/Gd-DTPA, T2–FS or STIR techniques where it appears as subcortical, anteriorly located bone-marrow edema, indicating either enthesitis or pelvic instability with a correspondingly decreased signal on T1-weighted images.

Involvement of the symphysis may be of clinical relevance, but is not generally critical for the diagnosis of AS or SpA.

Imaging of the spine in AS

The classification of AS is based on the modified 1984 New York criteria [3], which mainly rely on the detection and the degree of structural changes in the SIJ obtained by conventional x-rays. However, conventional radiographs are known to have a rather low sensitivity to detect sacroiliitis and spondylitis in early stages of disease [24]. This may cause diagnostic problems, since the mean time between the first symptoms and the diagnosis of AS ranged between 5 and 9 years in one study [25]. The other problem with the New York criteria is that approximately 3–5% of patients with AS do not have unequivocal structural changes in the SIJ [26], but only spinal changes (classical syndesmophytes). Similarly to the SIJ, conventional radiographs are still the gold standard for the assessment and quantification of structural spinal lesions. Recently, T1-weighted MRI has also been successfully used to assess structural changes [27]. Overall, spinal MRI performs best in the identification and quantification of active spinal lesions, where it has proved superior when compared with other imaging techniques [12,20,21,28–30].

MRI of the spine in AS

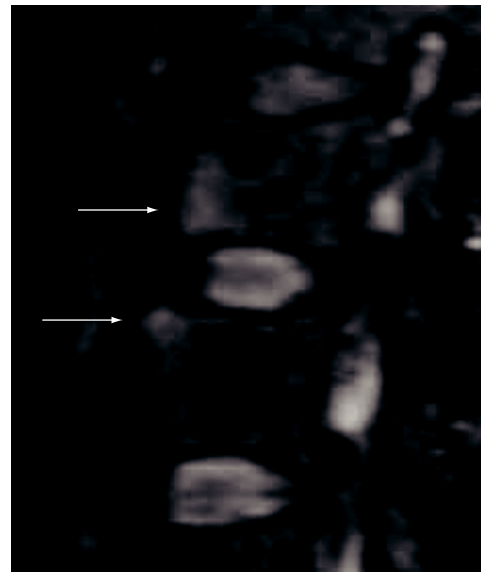
MRI is currently considered the most sensitive method for imaging of spinal inflammation [1,12,28,29,31]. Positron emission tomography techniques have not been evaluated for this purpose to a sufficient degree. MRI is being increasingly tested to classify and diagnose patients with early AS [13]. In patients with AS, spinal MRI has been used to assess spinal inflammation as an indicator of disease activity and a possible predictor of response to therapy. The evaluation of MRI as a tool to define allocation to different therapeutic strategies, such as treatment with biologicals, is currently ongoing [20,21,28,30].

Spondylitis

Inflammation of the vertebral body and adjacent structures (sSpondylitis anterior, Romanus lesion, shiny corner sign and vertebral osteitis) has been considered as a rather early sign of spinal involvement in patients with AS. First described by Romanus in 1952 [28,32], it represents a rather typical radiographic sign of spinal involvement in AS, which was most frequently seen in the thoraco–lumbar region at T10–T12 (**Figure 2**) [31]. When using MRI, spondylitis anterior is typically observed as a decreased signal in T1-weighted MRI and an increased signal in T1-weighted MRI after gadolinium contrast. Similar findings are obtained using the T2-weighted MRI or the STIR sequence. The typical appearance of spondylitis is not always limited to the vertebral edges, but may also spread to the entire vertebral body as a sign of generalized inflammation [33–35]. The signal intensity within the disk may remain normal during vertebral inflammation. High signal intensity on T1- and T2-weighted images with no enhancement following intravenous contrast is known to indicate fat accumulation [33]. Furthermore, diskovertebral junctions may display low signal intensity on T1- and T2-weighted images when a marginal sclerosis occurs after a spondylitis [33].

Spondylitis anterior is an active osteitis and enthesitis at the junction of the anulus fibrosus and the longitudinal ligaments with the anterior longitudinal ligament, the vertebral body and the intervertebral disk. Although the assumption that syndesmophytes occur as a consequence of the inflammation and repair reaction, it is still not proven whether, in later stages, active inflammation may result in erosive and later in sclerotic changes and reactive new bone formation, including syndesmophytes at the corner of the affected vertebral bodies. Less frequently, these

Figure 2. Romanus lesions in the anterior edge of the vertebral body, as depicted by STIR MRI in the lumbar spine of an AS patient.



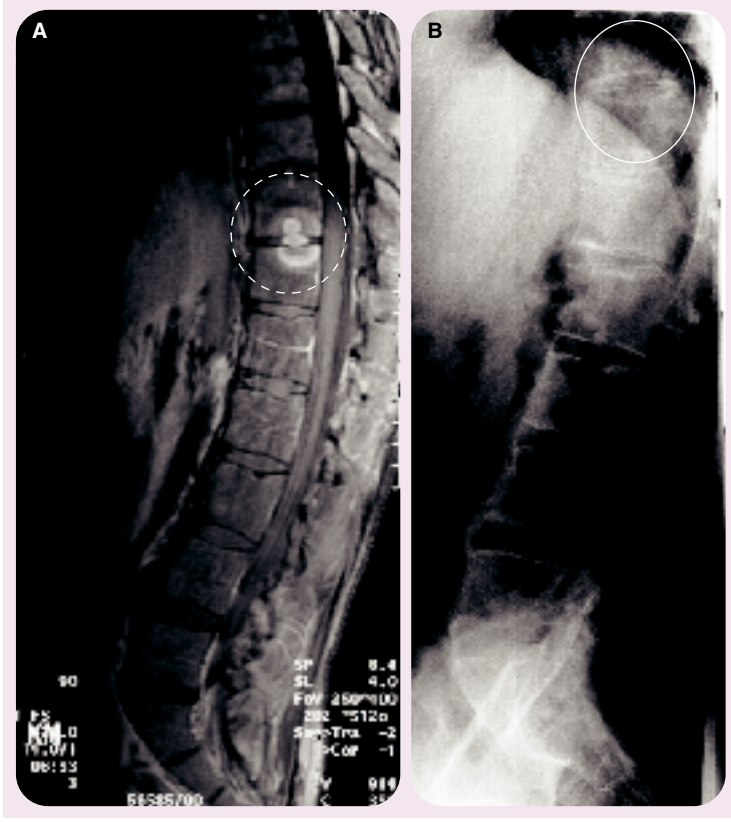
AS: Ankylosing spondylitis; MRI: Magnetic resonance imaging; STIR: Short tau inversion recovery.

changes are also seen at the posterior vertebral edges [31,33]. Spondylitis is rare in SpA patients without an established diagnosis of AS [34].

Spondylodiskitis & diskitis

Inflammation of the intervertebral space (diskitis) and the disk together with the vertebral body (spondylodiskitis, Andersson lesion, **Figure 3A**) are also rather typical signs of spinal inflammatiAon in patients with AS. In contrast to conventional radiographs, where only the consequences of spondylodiskitis are visible in later disease stages, MRI is able to detect such changes already in early phases [36,37]. Accordingly, negative radiographic findings are sometimes accompanied by positive MRI findings indicative of spondylodiskitis (**Figure 3B**) [36,37]. Asymptomatic spondylodiskitis may occur in multiple spinal segments in approximately 8% of the patients in early disease [38]. The incidence of spondylodiskitis, which may occur without major clinical symptoms, has been estimated at 15% in patients with AS [24,38]. The first radiographic descriptions of spondylodiskitis were published by Andersson in 1937 [39] and later by Dihlmann in 1978 [40], who proposed to distinguish inflammatory and noninflammatory spondylodiskitis. Using MRI, spondylosdiskitis is characterized by a circumscript hemispherical erosive lesion, which is often surrounded by an area of low signal intensity in one of two neighbored vertebral bodies (**Figure 3A**). By the course of the disease, spondylodiskitis may develop into transdiskal proliferation processes without marginal syndesmophytes. By contrast, the noninflammatory spondylodiskal lesion is a transdiskal fracture for different reasons, such as advanced disk degeneration and inflammation or osteoporotic processes. It should be noted that the described early lesions, inflammatory or noninflammatory, are very similar to Modic I lesions which have been described to lead to erosive osteochondrosis [41], while late spondylodiskitis bear similarity to Modic II lesions in MRI. Therefore, they cannot be used for diagnostic purposes *per se* without clinical evidence of AS related symptoms [24].

Figure 3. Anderson lesion as detected in magnetic resonance imaging and conventional radiography in patients with ankylosing spondylitis.



(A) Andersson lesion, as detected by contrast agent (Gd-DTPA)-enhanced magnetic resonance imaging (MRI) with the typical circumscribed hemispherical erosive lesion (dotted circle), which is often surrounded by an area of low signal intensity in one of two neighbored vertebral bodies. **(B)** In contrast to the MRI, the corresponding x-ray image does not show any pathological sign (continuous circle).

Costovertebral joints

Inflammatory lesions in the costovertebral joints are also characterized by low-density signals in T1-weighted MRI and high-density signals in MRI sequences sensitive to depict inflammation. Affection of costovertebral joints in AS leads to a reduced chest expansion – a frequent finding in AS [3]. This symptom may be explained by both active and structural spinal changes.

Scoring of spinal MRI in AS

MRI is now increasingly used for the evaluation of the influence of anti-inflammatory drugs (such as antitumor necrosis factor [TNF]-α agents) on spinal inflammation in randomized clinical trials (RCT) [28,30]. In order to quantify active spondylitic changes in patients with AS, MRI scoring methods have been developed: the best evaluated scoring system is the AS spinal MRI scoring system (ASspiMRI) [8,12,22,27,28,30,42,43]. This scoring system distinguishes disease activity (ASspiMRI-a) and chronicity (ASspiMRI-c). Scoring for both activity and chronicity is performed on a graded scale from 0 to 6. Inflammatory activity, as assessed by the ASspiMRI-a, quantifies either the enhancement after T1/Gd-DTPA, or the bone marrow edema detected by

the STIR or the T2–FS technique. The ASspiMRI-a values erosions as both inflammatory and chronic changes. Chronicity is assessed by the ASspiMRI-c by grading structural lesions in T1-weighted MRI sequences (before application of contrast agents). For the quantification of active and structural spinal lesions, the ASspiMRI evaluates vertebral units, which are defined as the region between two virtual lines drawn through the middle of each vertebral body.

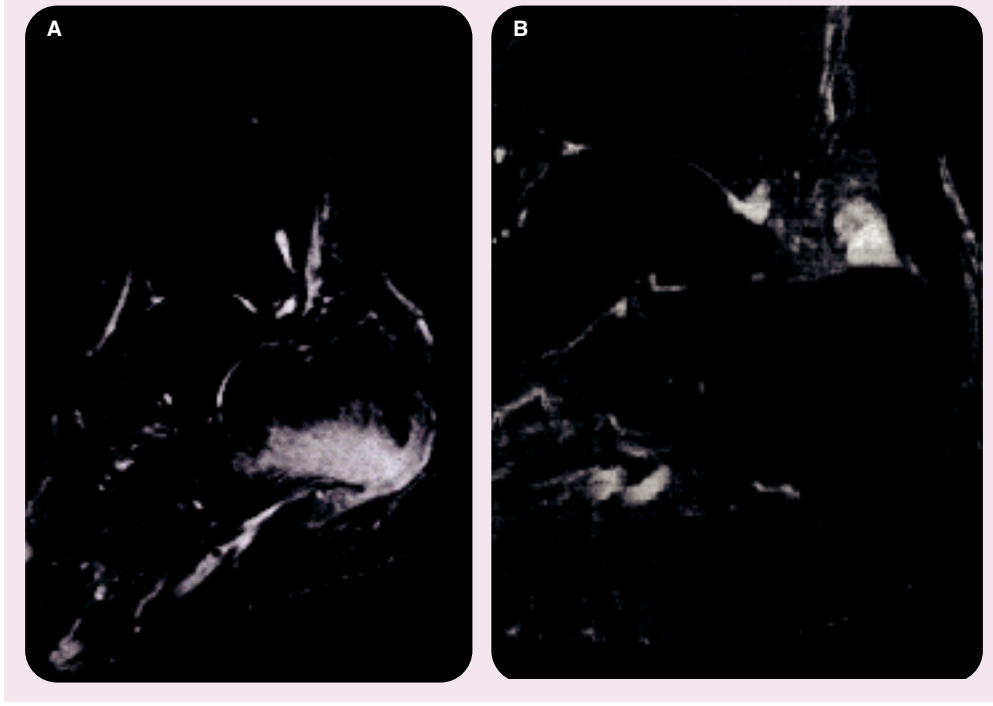
Almost the entire spine, from C2 to S1, is captured by the ASspiMRI, which comprises 23 vertebral units (VUs; the bony region above and below an intervertebral disk, including the disk region). Thus, the range of the scoring system is 0–138 for both the activity and the chronicity index respectively. A modification of the ASspiMRI-a is described by investigators from Berlin, and omits erosions as a sign of inflammation [44].

Another scoring system available for scoring of spinal lesions in AS is the system developed by the Spondyloarthritis Research Consortium of Canada (SPARCC) [45]. This scoring system evaluates only six diskovertebral units (DVU) (the definition of DVU is similar to that of the VU in the ASspiMRI), selected on the basis of presence of inflammation (global judgement). It assigns additional scores to intensity and depth of inflammation. The ASAS/OMERACT MRI in AS Working Group is currently evaluating all available scoring methods and modifications, in order to find out whether it is possible to prioritize a scoring system for as the assessment of inflammation in clinical trials with AS patients. This is an important issue, since several recent studies with biologicals, such as infliximab and etanercept [18,45,46], have demonstrated definite clinical efficacy on disease activity, and improvement of inflammation in the spine [18,20–22].

Extravertebral manifestations of AS

Peripheral extravertebral manifestations, such as enthesitis and bursitis, occur frequently in patients with spondyloarthritides. In active inflammatory lesions, MRI shows a decreased signal in T1-weighted sequences and increased signal in T2-weighted sequences or STIR sequences. Frequently affected sites of enthesitis in SpA are the Achilles tendon and the retrocalcanear bursa at the calcaneus (**Figure 4**), the

Figure 4. Affection of the calcaneus in the STIR MRI sequence (A) and involvement of the retrocalcanear bursa in the gadolinium-enhanced MRI sequence (B) as an extraspinal manifestation in two patients with ankylosing spondylitits.



MRI: Magnetic resonance imaging; STIR: Short tau inversion recovery.
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trochanter major and the pes anserinus. Enthesitis is depicted as hyperintensity in the STIR or the T2-weighted sequence, with strong enhancement after contrast [24]. Peripheral enthesitis may clinically appear as arthritis, and differentiation can be achieved by MRI using inflammation-sensitive sequences [47]. Human leukocyte antigen (HLA)-B27-positive SpA patients are predicted to develop higher peripheral pathology with respect to extravertebral-disease-related manifestations, such as plantar fasciitis, as compared with HLA-B27 negative patients [48].

Conclusion

In summary, x-rays are still the standard for the assessment of structural SIJ changes and the diagnosis of AS. For assessment of active sacroiliitis, MRI sequences are necessary.

Conventional radiographs of the spine are the basis for the detection of AS-related structural spinal changes, such as syndesmophytes and ankylosis. MRI of the spine is useful for the assessment of inflammatory changes, and potentially for the diagnosis of early and active stages of the disease.

MRI sequences useful for the assessment of active disease are the STIR, the T2-fat saturated and the T1 post-gadolinium MRI sequences. For assessment of structural changes, the T1-weighted MRI sequence is used.

Both SIJ and spinal changes can be quantified by evaluated scoring systems. These systems are mostly used in clinical trials to quantify the impact of therapy, such as anti-TNF-α agents, on spinal inflammation.

Future perspective

MRI will be extensively used for the diagnosis and monitoring of treatment in ankylosing spondylitis. Inflammatory spinal lesions and sacroiliitis will become pathognomonic for the diagnosis of the disease and will contribute, together with other clinical and laboratory tools, for setting the diagnosis of AS in early stages.

Executive summary

Imaging of the sacroiliac joint in ankylosing spondylitis

- Magnetic resonance imaging (MRI) of the sacroiliac joints (SIJ) is accurate for detection of acute and chronic SIJ lesions in ankylosing spondylitis (AS) patients.
- MRI results correlate well with conventional histology and immunohistological findings.
- MRI examinations together with the presence of human leukocyte antigen-B27 have the highest likelihood ratio for the accurate diagnosis of AS already in early stages.

Imaging of the spine in AS

- MRI is currently considered the most sensitive method for imaging of spinal inflammation.
- Short tau inversion recovery (STIR) and Gd-DTPA sequences are both able to detect spinal inflammation in AS patients.
- T1-weighted MRI can be used for assessment of chronic spinal lesions, but conventional x-rays still represent the gold standard for depiction of such changes.

Extravertebral manifestations of AS

- Enthesitis is depicted as hyperintensity in the STIR or the T2-weighted sequence, with strong enhancement after application of contrast agent.

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