Magnetic Resonance Imaging of Sacroiliitis in Patients with Spondyloarthritis: Correlation with Anatomy and Histology

Magnetresonanztomografie der Sakroiliitis bei Patienten mit Spondyloarthritis: Korrelation mit Anatomie und Histologie

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Zusammenfassung

Die Magnetresonanztomografie (MRT) der Sakroiliakalgelenke hat sich als probates Mittel zur Frühdiagnostik der Sakroiliitis bei inkonklusivem Röntgenbild etabliert. Ein positiver MRT-Befund hat dabei eine ähnlich hohe Bedeutung wie der Nachweis von HLA-B27. Der Nachweis der Sakroiliitis in der Bildgebung ist einer der Schlüsselbefunde in der Klassifikation der axialen Spondyloarthritis entsprechend der Kriterien der Assessments in Ankylosing Spondylitis (ASAS) Gruppe. Frühe Zeichen der Sakroiliitis sind die Enthesitis des artikulären Faserknorpels, Kapsulitiden und Osteitiden. In späteren Stadien kommen strukturelle (chronische) Veränderungen hinzu, dazu gehören Fettdepositionen, Erosionen, subchondrale Sklerosierungen und transartikulären Knochenbrücken bis hin zur Ankylose. Diese MRT-Befunde werden histologischen Darstellungen von Gelenkbiopsaten gegenüber gestellt. Bei aktiver Sakroiliitis dominiert histologisch ein proliferatives, pannusartiges Bindegewebe, welches neben Fibroblasten und Fibrozyten aus T-Zellen und Makrophagen. Später dominieren von neu gebildetem Knochen umgebene Knorpelinseln sowie Reste zellulärer Infiltrate. Kenntnisse der Morphologie der Sakroiliakalgelenke und der pathologischen Mikro- und Makroanatomie der Sakroiliitis sind hilfreich für das Verständnis der magnetresonanztomografischen Befunde.

Sacroiliitis and Spondyloarthritis

Sacroiliitis is an important clinical and diagnostic feature of ankylosing spondylitis (AS) [1] and

Abstract

Magnetic resonance imaging (MRI) of the sacroiliac joints (SIJs) has become established as a valuable modality for the early diagnosis of sacroiliitis in patients with inconclusive radiographic findings. Positive MRI findings have the same significance as a positive test for HLA-B27. Sacroiliitis is one of the key features of axial spondyloarthritis (SpA) in the classification proposed by the Assessments in Ankylosing Spondylitis (ASAS) group. Early signs of sacroiliitis include enthesitis of articular fibrocartilage, capsulitis, and osteitis. In more advanced disease, structural (chronic) lesions will be visible, including periarticular fatty deposition, erosions, subchondral sclerosis, and transarticular bone buds and bridges. In this article we describe magnetic resonance (MR) findings and provide histologic biopsy specimens of the respective disease stages. The predominant histologic feature of early and active sacroiliitis is the destruction of cartilage and bone by proliferations consisting of fibroblasts and fibrocytes, T-cells, and macrophages. Advanced sacroiliitis is characterized by new bone formation with enclosed cartilaginous islands and residual cellular infiltrations, which may ultimately lead to complete ankylosis. Knowledge of the morphologic appearance of the sacroiliac joints and their abnormal microscopic and gross anatomy is helpful in correctly interpreting MR findings.

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other forms of spondyloarthritis (SpA) [2]. While sacroiliitis can be diagnosed by conventional radiography in established disease, a more sensitive diagnostic tool such as magnetic resonance

Fig. 1 Normal anterior anatomy of the sacroiliac joints (SIJ). **a** Schematic representation of the ear-shaped joint surface and of the oblique coronal slice. **b** Oblique coronal section of gross anatomic specimen showing the right SIJ (indicated by black arrows) as a continuous structure. **c** Microanatomic detail of the anterior joint space (H&E staining, original magnification $\times 10$). The articular cartilage on the iliac side (black arrowheads), consisting of a mixture of hyaline and fibrous cartilage, is altogether thinner than the pure hyaline cartilage on the sacral side (black double arrowhead). The anterior sacroiliac ligament (black arrows) gradually blends with the periosteum of the ilium and is therefore considered an enthesis (discontinuity due to cutting artifact). **d** Demonstration of iliac fibrocartilage (left) containing collagen fibers and sparse chondrocytes and sacral hyaline cartilage (right) rich in chondrocytes (H&E staining, original magnification $\times 500$). **e** T1-weighted fat-suppressed 3D gradient echo (GRE) image with high signal intensity of the articular cartilage.

Abb. 1 Normale anteriore Anatomie der Sakroiliakalgelenke (SIG). **a** Schematische Darstellung der ohrförmigen Gelenkfläche und der schräg koronaren Schnittrführung. **b** Schräg koronare anatomische Präparation des rechten SIG (schwarze Pfeile) mit glatter, durchgängiger Gelenkfläche. **c** Mikroanatomisches Detail des anterioren Gelenkanteils und der Gelenkkapsel (HE-Färbung, 10fache Vergrößerung). Der iliakale Gelenkknorpel (schwarze Pfeilspitzen), bestehend aus einer Mischung von hyalinem und Faserknorpel, ist dünner als der rein hyaline Gelenkknorpel der sakralen Gelenkfläche (schwarze Doppelpfeilspitze). Das anteriore sakroiliakale Band (schwarze Pfeile) geht kontinuierlich in das Periost des Os ilium über und entspricht einer Enthese (Unterbrechung aufgrund von Schneideartefakten). **d** Darstellung des iliakalen Faserknorpels (links) mit Kollagenfasern und spärlichen Chondrozyten und dem sakralen hyalinen Knorpel (rechts) reich an Chondrozyten (HE Färbung, 500fache Vergrößerung). **e** T1-gewichtete fettsupprimierte wasserverstärkte 3D Gradientenecho (GRE)-Sequenz mit hoher Signalintensität des Gelenkknorpels.

imaging (MRI) is necessary for evaluating patients with early disease. Demonstration of sacroiliitis is one of the key criteria for axial SpA in the classification of the Assessments in Ankylosing Spondylitis (ASAS) group [3].

SpA patients suffer from pain and stiffening of the axial skeleton and also to some degree the peripheral joints, predominantly the lower extremity. There is a high association with the HLA-B27 antigens and extraskeletal manifestations such as psoriasis, anterior uveitis or inflammatory bowel disease may occur.

The clinical key symptom of SpA is inflammatory back pain characterized by onset before age 40, insidious onset, relief with movement, no improvement with rest, and pain at night (with improvement after getting up) [4]. Despite this clear definition,

the symptoms are often mistaken for chronic low back pain, and an average of 8.5 years elapse after the onset of clinical symptoms before the diagnosis of AS – the prototype of SpA – is made in HLA-B27-positive patients [5]. The delay is even longer, 11.4 years on average, in HLA-B27-negative patients or in women [5]. To improve on this situation, decision-making trees have been proposed to simplify and speed up the diagnosis of SpA [6]. This has been widely acknowledged and as a consequence MRI has been approved to contribute to the classification of SpA in terms of the newly developed ASAS classification criteria [3]. Sensitivities and specificities of over 90% [7–10] and a high positive likelihood ratio of approx. 9.0 [6] clearly indicate that MRI should be used early so that patients may benefit from early initiation of a

Fig. 2 Normal posterior anatomy. **a** Schematic representation of the angulated oblique coronal section depicting the cartilaginous portion of the sacroiliac joint superiorly and inferiorly and portions of the fibrous compartment (retroarticular space) in between, which is due to the ear-shaped joint surface. **b** Oblique coronal section of gross anatomic specimen. There is smoothly margined articular cartilage in the cartilaginous compartment (indicated by arrows), while the interosseous ligaments are embedded in fatty tissue in the retroarticular space (black arrowheads). **c** Microanatomic overview through the plane indicated in **a** (H&E staining, original magnification $\times 10$). **d** T1-weighted TSE image of the right SIJ with its anterior cartilaginous part (white arrows) and its posterior retroarticular space containing interosseous ligaments (white arrowheads) and fatty connective tissue.

Abb. 2 Normale posteriore Anatomie. **a** Schematische Darstellung der schräg koronaren Schnitthführung mit Darstellung des knorpeligen Gelenkkompartiments superior und inferior sowie Teilen des fibrösen Gelenkkompartiments (Spatium retroarticulare) dazwischen, da die knorpelige Gelenkfläche ohrförmig konfiguriert ist. **b** Schräg koronare anatomische Präparation. Der Gelenkknorpel ist glatt begrenzt (Pfeile), während die interossären Ligamente in das Fettgewebe des Spatium retroarticulare eingebettet sind (schwarze Pfeilspitzen). **c** Mikroanatomischer Überblick entsprechend der in **a** angegebenen Schnitthlinie (HE Färbung, 10fache Vergrößerung). **d** T1-gewichtete TSE Sequenz des rechten SIG mit dem anterioren knorpeligen Gelenkkompartiment (weiße Pfeile) und dem posterior gelegenen Spatium retroarticulare und den dort befindlichen interossären Ligamenten (weiße Pfeilspitzen) und fetthaltigem Bindegewebe.

rigorous therapeutic regimen [11]. The positive likelihood ratio of MRI of the sacroiliac joints (SIJs) is as high as that of the HLA-B27 blood test [6]. However, one has to be aware that a reliable MRI diagnosis of sacroiliitis crucially depends on a thorough clinical history. It has been shown that analysis of MRI alone has a sensitivity of 64% and a specificity of 80%, which increase to 95% and 98%, respectively, when images are interpreted in conjunction with clinical data [12].

Anatomy, Histology and Biochemistry as a Basis for Imaging

Histological examinations of biopsy specimens from the SIJs [13–16] and autopsy preparations [17] have improved our understanding of the pathogenesis of SpA. These specimens, in part also presented in this review article, were acquired in the setting of a research project with approval of the local ethics committee during the course of CT-guided steroid injections in painful patients [16]. In general, joint biopsies are not needed

for routine follow-up of SpA patients. As a result of these investigations, the demonstration of tumor necrosis factor alpha (TNF-alpha) messenger ribonucleic acid (mRNA) in cellular infiltrates in these biopsy specimens [15] opened up a new era of therapy with TNF-alpha inhibitors [18–21]. MRI of the axial skeleton has an important role in monitoring patients on TNF-alpha therapy [18, 22–24].

The complex anatomy of the sacroiliac joints has been described in detail [25, 26]. MRI of the SIJs is performed in the oblique coronal plane with acquisition of a T1-weighted turbo spin echo (TSE) sequence, a T1-weighted fat-suppressed 3D gradient echo (GRE) sequence for the depiction of cartilage, and a fat-saturated T1-weighted GRE sequence after contrast administration. The slice thickness should be 1.5–2.0 mm and dynamic, time-resolved MRI sequences are not generally needed for the diagnosis of sacroiliitis but may be potentially useful in monitoring disease activity [8, 27]. Alternatively, if contrast medium administration is not possible, a short tau inversion recovery (STIR) sequence may be used. As a recommendation of the ASAS group, a T1-weighted TSE sequence and a STIR sequence are sufficient for

Fig. 3 48-year-old HLA-B27-positive man with early SpA and a three-month history of inflammatory back pain. **a** Biopsy specimen (Goldner staining, 250x magnification) showing highly vascularized fibrous proliferation (P) adjacent to cartilage (C). **b** 500-fold magnification showing the proliferative tissue adjacent to metaplastic cartilage (M). APAAP (alkaline phosphatase anti-alkaline phosphatase) technique with monoclonal antibodies to CD3-positive T-lymphocytes (arrows). **c** T1-weighted TSE image showing contour irregularities (arrow) and diffuse para-articular signal decrease of the iliac bone. **d** T1-weighted oblique coronal fat-saturated image immediately after contrast injection showing linear enhancement of articular fibrocartilage of the right SIJ with clear delineation of single erosion of iliac bone (arrow). Slightly increased signal intensity of the para-articular bone marrow regions suggesting osteitis. Please note normal left SIJ. **e** T1-weighted true coronal fat-saturated image acquired 4 min after contrast injection demonstrates improved depiction of enthesitis with osteitis predominantly on the iliac side. Arrow indicates same bony erosion as in **d** (**c–e**: Original MR images were replaced by equivalent state-of-the-art MR images.)

Abb. 3 48-jähriger HLA-B27 positiver Patient mit früher SpA und entzündlichem Rückenschmerz seit drei Monaten. **a** Gelenkbiopsat (Goldner-Färbung, 250fache Vergrößerung) mit stark vaskularisierter fibröser Proliferation (P) in Nachbarschaft des Knorpels (C). **b** 500fache Vergrößerung zeigt Proliferationsgewebe metaplastischem Knorpel (M) benachbart. APAAP (alkaline phosphatase anti-alkaline phosphatase) Technik mit monoklonalen Antikörpern gegen CD3-positive T-Lymphozyten (Pfeile). **c** T1-gewichtete TSE Sequenz zeigt Konturunregelmäßigkeiten (Pfeil) und einen diffusen paraartikulären Signalabfall des Os ilium. **d** T1-gewichtete schräg koronare fettgesättigte Sequenz unmittelbar nach Kontrastmittelinjektion mit linearem Enhancement des Faserknorpels des rechten SIG und Darstellung einer singulären Erosion im Os ilium (Pfeil). Etwas erhöhte Signalintensität des paraartikulären Knochenmarks hinweisend für Osteitis. Normaler Befund am linken SIG. **e** T1-gewichtete, streng koronare fettgesättigte Sequenz 4 Min. nach Kontrastmittelinjektion mit verbesserter Darstellung der Enthesitis und Osteitis insbesondere im Os ilium. Der Pfeil markiert die gleiche Erosion wie in **d** (**c–e**: Die originalen MRT-Aufnahmen wurden durch äquivalentes State-of-the-art Bildmaterial ersetzt.)

MRI of the sacroiliac joints [28]. However, these recommendations are intended to be applicable worldwide and therefore may be regarded as the “minimal standard”.

The SIJ consists of a cartilaginous part and a fibrous (or ligamentous) compartment with very strong anterior and posterior sacroiliac ligaments [29]. This makes the SIJ an amphiarthrosis with movement restricted to slight rotation and translation [29]. The articular surface being ear-shaped (► Fig. 1a), different articular portions will be depicted, depending on the slice position. Anterior oblique coronal images (► Fig. 1b, e) only show the cartilaginous joint portion, while more posterior sections (► Fig. 2a, d) show both cartilaginous and ligamentous portions. Another specific feature of the SIJs is that two different types of cartilage cover the two articular surfaces. While the sacral cartilage is purely hyaline, the iliac side is covered by a mixture of hyaline and fibrous cartilage (► Fig. 1d) [29, 30]. Due to its fibrocartilaginous components, the sacroiliac joint is a so-called articular enthesitis [31].

The extracellular matrix of fibrocartilage is rich in proteoglycans and glycosaminoglycans, which are strongly hydrophilic mol-

ecules and attract water, thereby ensuring the stable elasticity of cartilage [32]. Damage to a joint by inflammatory or degenerative processes leads to a loss of these negatively charged macromolecules. As a result, there is greater affinity of gadolinium complexes from paramagnetic contrast agents, which also possess a negative charge, to the extracellular matrix of fibrocartilage [33]. This is the mechanism underlying late enhancement in damaged joints [34, 35].

Sacroiliitis and MRI

Unlike conventional radiography and computed tomography, which only demonstrate structural or chronic changes, MRI depicts both active (acute) and structural signs of sacroiliitis. Active changes are subsumed under the label of enthesitis and include fibrocartilaginous enhancement, predominantly at the iliac joint surface, capsulitis, and juxta-articular osteitis (► Fig. 4). Florid, or active, stages of sacroiliitis are characterized by proliferative inflammatory tissue destroying cartilage and bone (► Fig. 4, 5).

Fig. 4 24-year-old HLA-B27-positive man with early axial SpA and florid sacroiliitis with erosions and a 12-month history of inflammatory back pain. **a** H&E staining (original magnification x400) of biopsy specimen of right SIJ. Fibrous proliferation (P) rich in fibroblasts destroying the cartilage (C) with formation of so-called lacunae (arrowheads) and reactive chondroblast activation (arrows) **b** Immunohistological section of the interface between cartilage (C) and fibrous proliferations (P) with cellular infiltrations (original magnification 250x, APAAP technique, monoclonal antibodies to CD68-positive macrophages). **c** T1-weighted TSE image showing a wavy and blurred cortical layer of the iliac joint surface due to erosions (arrowheads) and patchy iliac subchondral sclerosis on the right SIJ (S) and slight, linear subchondral sclerosis on the left SIJ. Note that the sacral joint surfaces are well preserved due to the thicker hyaline cartilage layer. Fat deposition is evident on both sides of the left SIJ. **d** Fat-saturated T1-weighted GRE image in oblique coronal plane after contrast administration showing enhancement of the articular fibrocartilage and of the erosions (arrows) as well as of the para-articular bone marrow (asterisks). Note that the erosions in the left SIJ, which are surrounded by a thin zone of sclerosis, display markedly weaker contrast enhancement. (**c, d**: Original MR images were replaced by equivalent state-of-the-art MR images.)

Abb. 4 24-jähriger HLA-B27 positiver Patient mit früherer axialer SpA und florider Sakroiliitis mit Erosionen. Seit 12 Monaten bestehender entzündlicher Rückenschmerz. **a** HE-Färbung (400fache Vergrößerung) eines Gelenkbiopsats des rechten SIG. Fibröse Proliferationen (P) mit zahlreichen Fibroblasten, die den Knorpel (C) zerstören und sogenannte Lakunen (Pfeile) bilden sowie reaktive Aktivierung von Chondroblasten (Pfeile) **b** Immunohistologische Darstellung des Übergangs zwischen Knorpel (C) und fibrösen Proliferationen (P) mit zellulären Infiltraten (250fache Vergrößerung, APAAP Technik, monoklonale Antikörper gegen CD68-positive Makrophagen). **c** T1-gewichtete TSE Sequenz mit welliger und unscharfer iliakaler Gelenkkontur aufgrund von Erosionen (arrowheads) und fleckiger iliakaler subchondraler Sklerose (S) des rechten SIG und geringer, linearer subchondraler Sklerose des linken SIG. Die sakralen Gelenkflächen sind gut erhalten aufgrund der dickeren hyalinen Knorpelschicht. Darstellung von Fettdepositionen iliakal und sakral am linken SIG. **d** Fettgesättigte, schräg koronare T1-gewichtete GRE Sequenz nach Kontrastmittelapplikation mit Enhancement des faserknorpeligen Gelenkknorpels und von Erosionen (Pfeile) sowie paraartikulärer Osteitis (Sterne). Die Erosionen des linken SIG, welche von einer dünnen Sklerosezone umgeben sind, zeigen ein deutlich schwächeres Kontrastmittelenhancement. (**c, d**: Die originalen MRT-Aufnahmen wurden durch äquivalentes State-of-the-art Bildmaterial ersetzt.)

This tissue consists of fibroblasts and fibrocytes, T-cells, and macrophages [16]. Ingrowth of vessels is one of the reasons why there is a signal increase on contrast-enhanced images (• Fig. 5). There is controversy about the term “synovitis” because only sparse amounts of synovial, villus-like tissue are histologically demonstrated between the iliac and sacral cartilage near the anterior and posterior joint capsules with obliteration in the further course of the disease [17].

Enthesitis is depicted as contrast medium enhancement of the joint capsule and within the articular fibrocartilage and may extend continuously from the joint to the pericapsular tendon and ligament attachments (• Fig. 3, 4). Pericapsular soft tissue (fat and muscle) typically shows no enhancement in spondyloarthritis – which is the case only in septic sacroiliitis (so-called lava cleft phenomenon) [36].

Fig. 5 39-year-old HLA-B27-positive man with AS (10-year history). There is chronic sacroiliitis with low inflammatory activity. **a** H&E staining (original magnification x250). The biopsy specimen of the right SIJ shows extensive destruction of cartilage (C) with only residual cartilage fragments and cellular infiltrates and a predominance of trabeculae (B), suggesting formation of new bone. **b** T1-weighted TSE image showing para-articular sclerosis of both joints, more pronounced on the iliac sides. The joint spaces appear blurred as in early ankylosis. **c** Fat-saturated, oblique coronal T1-weighted GRE image after contrast administration showing only very sparse enhancement within localized erosions. Corresponding iliac and sacral erosions are visible in both joints. Erosive damage has led to pseudodilation (arrowhead) of the joints. In addition there are bone buds (arrow) as signs of early ankylosis. (**b, c**: Original MR images were replaced by equivalent state-of-the-art MR images.)

Abb. 5 39-jähriger HLA-B27 positiver Patient mit AS (10 Jahre Erkrankungsdauer). Chronische Sakroiliitis mit geringer entzündlicher Aktivität. **a** HE-Färbung (250fache Vergrößerung). Gelenkbiopsat des rechten SIG zeigt ausgedehnte Zerstörungen des Gelenkknorpels (C) mit residuellen Knorpelfragmenten und zellulären Infiltraten aber prädominanten Trabekeln (B), hinweisend für Knochenneubildung. **b** T1-gewichtete TSE Sequenz mit paraartikulärer Sklerose beider SIG, betont auf der iliakalen Seite. Die Gelenkspalten erscheinen unscharf wie bei beginnender Ankylose. **c** Fett-gesättigte, schräg koronare T1-gewichtete GRE Sequenz nach Kontrastmittelapplikation und nur sehr spärlichem Enhancement innerhalb von einzelnen Erosionen. Korrespondierende iliakale und sakrale Erosionen beider SIG. Die erosive Zerstörung hat zur Pseudoerweiterung (Pfeilspitzen) der Gelenke geführt. Zusätzlich Darstellung von Knochenknospen (Pfeile) als Zeichen einer beginnenden Ankylose. (**b, c**: Die originalen MRT-Aufnahmen wurden durch äquivalentes State-of-the-art Bildmaterial ersetzt.)

Early periarticular osteitis denotes inflammation of bone marrow areas adjacent to the sacroiliac joints predominantly on the iliac side (► Fig. 3). It represents an extension of inflammation of articular fibrocartilage of the SIJs. The size of the bone marrow area affected by osteitis is a measure of the inflammatory activity of sacroiliitis and is graded by using semiquantitative techniques

[25]. Osteitis is also currently the only parameter that defines a positive MRI finding in the classification of the ASAS group, especially when it is present in two or more slices [28]. The signal intensity of osteitis varies with the interval between image acquisition and contrast medium injection (► Fig. 3).

Fig. 6 33-year-old HLA-B27-positive patient with a long history of AS. T1-weighted TSE image showing complete ankylosis of both sacroiliac joints. "Phantom joints" suggest the former joints (arrows).

Abb. 6 33-jähriger HLA-B27 positiver Patient mit langjährig bekannter AS. T1-gewichtete TSE Sequenz mit kompletter Ankylose beider SIG. "Phantomgelenke" deuten die ehemaligen SIG an (Pfeile).

At later stages areas of osteitis are transformed into periarticular deposits of fatty tissue [25, 37]. Chronic sacroiliitis is further characterized by erosions, subchondral sclerosis, transarticular bone bridges, and bone buds (● Fig. 5, 6). These processes may ultimately lead to complete ankylosis of the sacroiliac joints, which is seen on MRI as a so-called phantom joint.

Erosions are depicted on MR images as discontinuities of the cortical bone. Erosions are contiguous with the joint space. Erosions in sacroiliac arthritis initially tend to occur on the iliac side of the joint [38], due to its fibrocartilaginous components, and may later progress to corresponding erosions also on the sacral side (● Fig. 5). Strong contrast enhancement indicates active erosion, while so-called smooth erosions display much weaker enhancement and are characterized by the presence of marginal sclerosis (● Fig. 4). Several confluent erosions have the appearance of a string of beads and lead to so-called pseudodilation of the sacroiliac joint as they progress further (● Fig. 5).

Subchondral sclerosis is seen as areas of low or no signal on all sequences. They often predominate on the iliac side (● Fig. 4) and only later affect the periarticular area on the sacral side as well (● Fig. 5). Sclerosis shows no enhancement after contrast medium administration.

Bone buds (● Fig. 5) and transarticular bone bridges are the first sign of ankylosing processes of the SIJ. They are more clearly identified by computed tomography since bony structures are depicted only indirectly on MR images. The presence of bone bridges leads to increasing blurring of the joint cleft until complete ankylosis occurs. Transarticular bone bridges are characterized by low signal intensity on all sequences. When there is complete ankylosis, the SIJ is seen as a low-intensity line surrounded by deposits of fatty tissue, which is hyperintense on T1-weighted images. This condition is referred to as a phantom joint (● Fig. 6).

Summary

In summary, MRI of the sacroiliac joints sensitively detects both active and structural changes, making it an ideal imaging modality for early diagnosis and follow-up of sacroiliitis in axial spondyloarthritis. Some of the changes are subtle and can only be detected after administration of a paramagnetic contrast agent, especially in early disease.

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