Emerging Imaging Techniques in Spondyloarthritis

Dual-Energy Computed Tomography and New MRI Sequences

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KEYWORDS

• Spondyloarthritis • Dual-energy computed tomography • MRI • Sacroiliac joints

KEY POINTS

- Imaging of the sacroiliac joint is important for axial spondyloarthritis. Bone marrow edema and erosions are key imaging features of sacroiliitis.
- Dual-energy computed tomography (CT) can detect inflammatory bone marrow edema in the sacroiliac joints and provides an alternative choice for patients in whom MRI is contraindicated.
- Three-dimensional MRI sequences improve the visualization of erosions on MRI.
- BoneMRI is a new MRI sequence that allows radiographlike and CT-like images to be generated based on magnetic resonance (MR) images using a deep-learning method, bringing MR the potential to be a 1-stop imaging modality for spondyloarthritis.

INTRODUCTION

Axial spondyloarthritis (SpA) is a group of chronic inflammatory diseases predominantly affecting the axial skeleton.[1] The inflammation typically affects the sacroiliac joints (SIJs) and spine, with sacroiliitis playing a key role in the classification of the disease. As objective evidence for SpA, imaging of the SIJs is an important focus in rheumatology and radiology journals.[2] Imaging features of sacroiliitis can be classified into active inflammatory lesions, of which bone marrow edema (BME) is the hallmark of disease activity,[3] and structural changes, including erosions, sclerosis, ankylosis, backfill, and fat metaplasia, characterizing structural aspects of progressive disease.[3] In clinical practice, the state-of-the-art imaging modality for detection of BME is

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fat-suppressed MRI sequences such as the short tau inversion recovery (STIR) sequence, and, although structural MRI scores exist, radiography still serves as the reference for grading structural lesions.[4]

In the last decade, numerous studies have focused on new techniques for improving lesion visualization and evaluation in SIJs, including both BME and structural lesions (Fig. 1). This article presents an overview of the emerging imaging techniques and provides an insight into the future application of these methods.

EMERGING IMAGING TECHNIQUES FOR BONE MARROW EDEMA

New MRI Techniques

Fluid-sensitive MRI sequences (STIR, T2-weighted sequence with fat suppression [T2-FS]) have been widely used for the detection of BME in SpA for many years and are an important component of the Assessment of Spondyloarthritis International Society (ASAS) classification criteria.[2] Recently, Greese and colleagues[5] proposed that T2-FS may have a better image quality as well as better detection of BME compared with STIR sequences. On T2-FS images, more patients were classified as positive MRI using ASAS criteria than on STIR images.[5] Magnetic resonance (MR) sequences using other fat saturation techniques have also been explored in SIJs, including spectral attenuated inversion recovery (SPAIR) T2-weighted sequence (hybrid fat saturation technique, which combines an inversion recovery pulse with an adiabatic radiofrequency pulse)[6] and T2-weighted multipoint Dixon sequence (fat suppression based on chemical shift).[7] These sequences have shorter scan time or better image quality than STIR/T2-FS, and provide alternatives for BME detection in patients with axial SpA.

A novel MRI technique for BME detection is diffusion-weighted imaging (DWI). DWI is based on the signal attenuation caused by the incoherent thermal motion of water molecules.[8,9] Edema in bone marrow may lead to an increase of extracellular water and yield high signal on DWI.[9–11] Furthermore, bone marrow changes can be quantitatively evaluated using apparent diffusion coefficient (ADC) values calculated from DWI images (Fig. 2). Patients with axial SpA may have increased ADC values despite the appearances on routine MRI sequences still being normal.[10] ADC values have been shown to be related to disease activity,[12] are sensitive to therapeutic response,[13] and may improve the specificity in detecting sacroiliitis.[14] However, an important

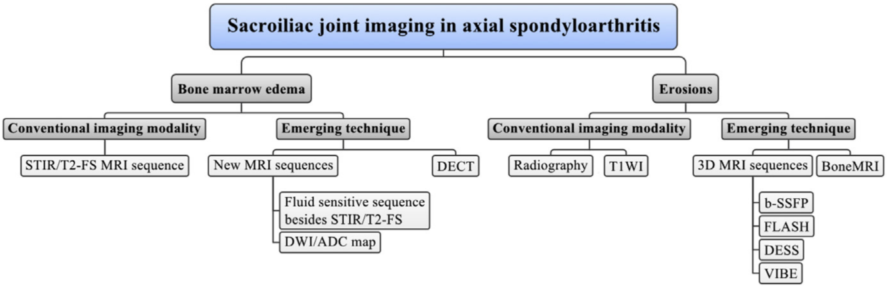

Fig. 1. Imaging modalities for SIJ in axial spondyloarthritis. 3D, three-dimensional; ADC, apparent diffusion coefficient; b-SSFP, balanced steady-state free precession sequence; DECT, dual-energy computed tomography; DESS, double excitation in the steady-state sequence; DWI, diffusion-weighted imaging; FLASH, fast low-angle shot; GRE, gradient echo; T1WI, T1-weighted imaging; T2-FS, T2-weighted fat suppression; VIBE, volume-interpolated breath-hold examination.

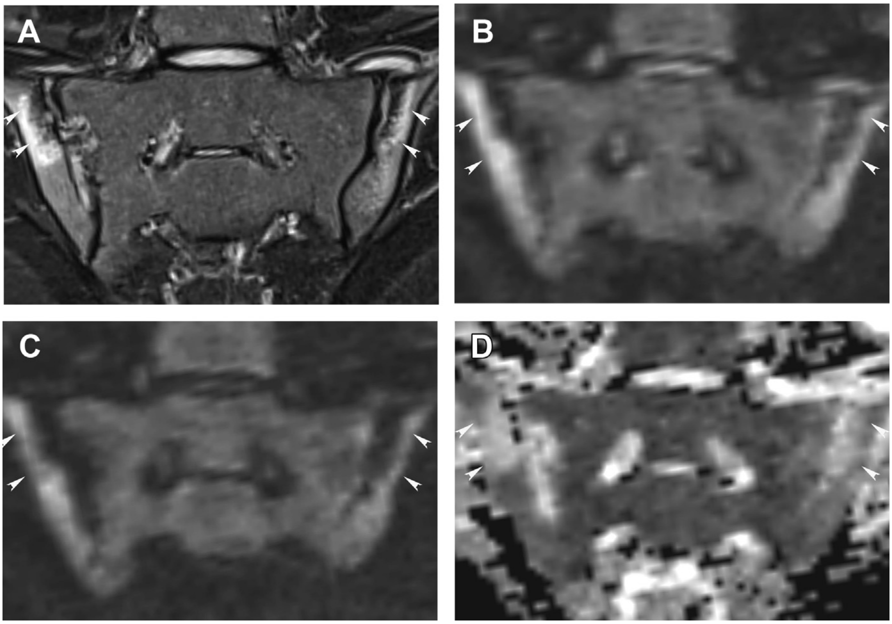

Fig. 2. MRI of a 17-year-old girl with sacroiliitis. (*A*) MR STIR image shows BME in both SIJs (*arrowheads*). (*B*) Diffusion-weighted MR image (b = 500 s/mm^2) and (*C*) diffusion-weighted MR image (b = 1000 s/mm^2) show high signal of the bone marrow edema (*arrowheads*). (*D*) ADC map shows increased ADC values of bone marrow edema (*arrowheads*).

caveat is that the spatial resolution of DWI images is not optimal. Visual analysis on DWI does not provide additional value to T2-FS images in inflammatory BME detection in SIJs.[11] Recently, Kucybala and colleagues[15] showed that visual analysis on DWI and ADC maps alone yielded a low specificity (54.0%) for BME detection using STIR images as a reference in 49 patients suspected for SpA. In addition, the postprocessing time and the variability of ADC value measurements among different readers and MR units remain a challenge preventing widespread technique application. For these reasons, debate continues as to the value of DWI in SpA.[16]

Dual-Energy Computed Tomography

Although it is widely used for BME detection, the cost of MRI is high and the acquisition time is long. Furthermore, MRI has been the only technique for BME visualization in vivo for a considerable period. In a proportion of patients, MRI is contraindicated. The emerging technique of dual-energy computed tomography (DECT) provides an innovative alternative for BME detection in SpA.

The main difference between DECT and conventional computed tomography (CT) is that DECT involves the acquisition of images at 2 different energy levels (typically at 80 and 140 kV). DECT can therefore differentiate between elements with a high atomic number, such as iodine, xenon, and calcium, and most of human body tissues with low atomic numbers, including carbon, oxygen, hydrogen, and nitrogen.[17] CT images equivalent to conventional 120-kV CT can be derived from the original datasets. Meanwhile, the radiation dose of DECT is equal to standard CT because it is divided between the 2 energy levels.[18] For rheumatic diseases, DECT has been applied in gout (urate detection[19]), rheumatic arthritis (BME detection[20] and iodine mapping[21]), psoriatic arthritis (iodine mapping[22]), and for other crystal arthropathies such as calcium pyrophosphate deposition disease.[23]

BME can be detected by DECT through a virtual noncalcium (VNCa) technique.[24] Using an algorithm based on the x-ray absorption features of bone mineral, yellow bone marrow, and red bone marrow, calcium can be subtracted. Bone marrow can be visualized and displayed on a color-coded map (**Fig. 3**). Color coding ranged from blue (fat/yellow bone marrow), green (water/BME), to yellow/red (increasing red marrow/blood content). An increase of water content in bone marrow can be evaluated both visually and quantitatively through the measurements of CT numbers.[24–27] In addition, the overlay of VNCa images on CT images allows the simultaneous assessment of bone marrow and bone. The feasibility of DECT for detecting inflammatory BME in the SIJs has been shown by Wu and colleagues[27] in a group of 47 patients with SpA. Compared with MRI, DECT showed good sensitivity and specificity for inflammatory BME in SIJs by different readers, with a range of 87% to 93% and 91% to 94%, respectively.[27]

Several limitations should be noted for the application of DECT for BME detection in SpA. BME of the subcortical area (within 2–3 mm from the cortical bone) cannot be accurately detected,[24,25,27] although this limitation has the potential to be overcome with further improvement of the technique. Moreover, red bone marrow and sclerotic areas may mimic BME lesions on VNCa images, and inexperienced readers may misinterpret these findings.[24]

In summary, although further validation is needed, DECT is useful for sacroiliac BME evaluation, especially in patients with SpA with contraindications to MRI.

EMERGING IMAGING TECHNIQUES FOR STRUCTURAL LESIONS IN SPONDYLOARTHRITIS

As another focus of research, erosion plays the most important role of all structural lesions in SpA.[28] As the traditional imaging method of choice, the role of radiography (**Fig. 4**A) has been challenged.[29] CT of the SIJs can provide the best representation of osseous lesions (**Fig. 4**B, E); however, it is not routinely used in clinical practice because of high radiation dose.[30] On MRI, the T1-weighted spin-echo (T1SE) sequence (**Fig. 4**C, F) is the most commonly used for detecting erosions in SpA, and is more reliable and accurate than radiography.[31–33] The interreader reliability of erosion detection on T1SE is comparable with BME detection on STIR (κ value 0.72 vs 0.61).[34] Using CT as a gold standard, the reported sensitivity and specificity of T1SE in erosion detection are 61% to 79% and 88% to 95%, respectively.[32,33,35]

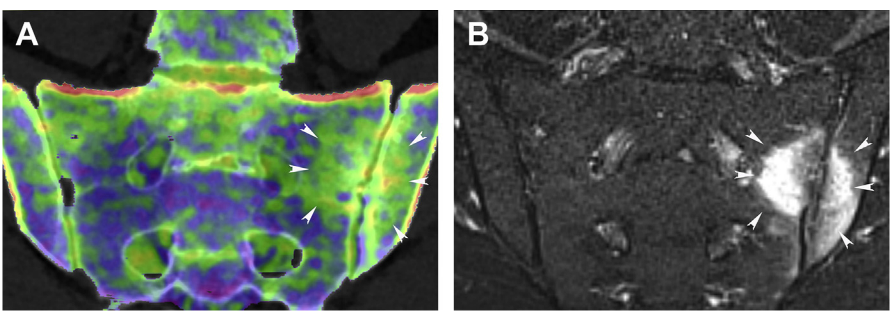

Fig. 3. Dual-energy CT and MRI of a 28-year-old man with sacroiliitis. BME (*arrowheads*) of the left SIJ is displayed as bright green areas with yellow and red spots on the dual-energy CT image (*A*), corresponding with the high signal on the MR STIR image (*B*).

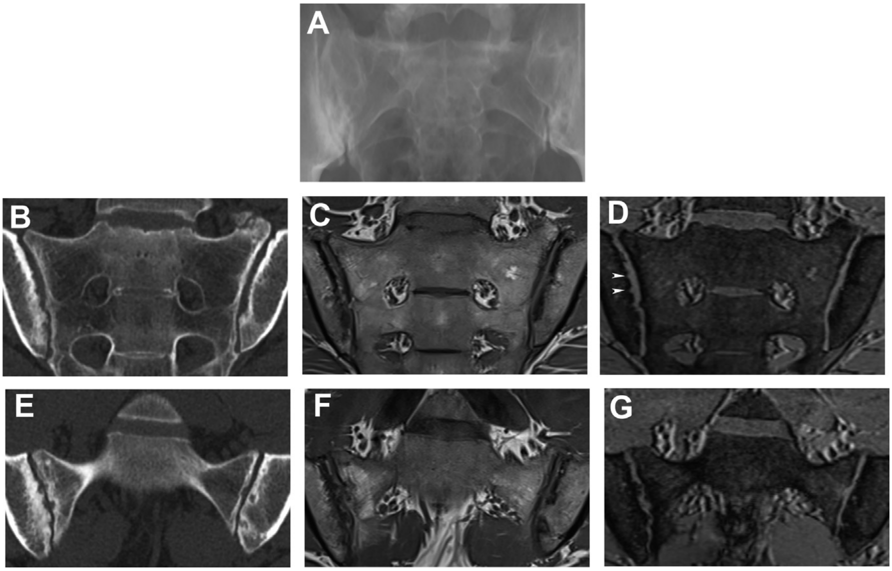

Fig. 4. Radiograph (*A*), CT (*B*, *E*), T1-weighted MRI (*C*, *F*), and VIBE MR images (*D*, *G*) of a 30-year old man with erosions in both SIJs. With reference to CT, erosions are better depicted on VIBE images than on T1-weighted MR images and on radiograph, especially the small erosions in the upper iliac side of the right SIJ (*arrowheads*).

There are still limitations of routine T1-weighted imaging (T1WI) sequences. The partial volume effect, limited contrast between cortical bone and joint space, as well as the unclear boundaries between erosions and subcortical bone marrow[32] decrease the accuracy of erosion detection. Thus, new MRI sequences and techniques have been studied to improve the visualization of erosions on MRI.

Three-Dimensional Magnetic Resonance Sequences (High-Resolution Sequences)

Three-dimensional (3D) MRI sequences or high-resolution sequences have the advantage of higher spatial resolution, lower partial volume effects, and multiplanar reconstruction.[36] In the last decade, several 3D sequences have been studied for the detection of erosions in axial SpA. These techniques include 3D fast low-angle shot (FLASH),[37] 3D double excitation in the steady-state sequence (DESS),[37] 3D water-suppressed balanced steady-state free precession sequence (b-WS-SSFP),[32] and 3D volume-interpolated breath-hold examination (VIBE)[35,38] sequences. Besides the high spatial resolution, the applied sequences are gradient echo (GRE) sequences intrinsically, thus can potentially better depict erosions of SIJs by virtue of their high contrast between joint cavity, cartilage and cortical bone.[39]

Among the 3D MRI sequences, the 3D VIBE sequence has been of most interest in recent years (Fig. 4D, E). The VIBE sequence affords short acquisition times without reducing image quality and allows generation of T1-weighted images with fat suppression.[40] The 3D VIBE sequence has shown a higher sensitivity and interreader reliability for detecting erosions than T1WI, with reference to CT. Diekhoff and colleagues[38] found a patient-level sensitivity of 95% and specificity of 93% for erosion detection using 3D VIBE sequences on 3.0-T MRI in 110 patients suspected for SpA and 18 healthy controls. The sensitivity and specificity of T1WI for erosion detection in the same cohort were 79% and 93% respectively. Higher sensitivity and similar specificity of VIBE compared with T1WI were also found by Baraliakos and colleagues[35] in another cohort of 109 patients with SpA, on a 1.5-T MR scanner. In addition, VIBE images tend to display more erosions than CT,[35,38] which might indicate that a higher sensitivity benefits from the better visualization of cartilage. Because VIBE sequences may be subject to more artifacts than routine spin-echo T1WI, including intravoxel dephasing and susceptibility to paramagnetic effects, the higher sensitivity of VIBE than CT could also be attributed to a higher rate of false-positive findings caused by paramagnetic artifacts.[35] Further studies are needed to validate the diagnostic value of 3D VIBE sequences in SpA classification.

Despite the limited number of studies, 3D MRI sequences showed promising results in the detection of erosions in SIJ. It is worth noting that all the examined 3D sequences are fat suppressed and cannot be used for evaluating fat deposition in SIJs, which is another lesion of interest in SpA.[41] The 3D MRI sequences cannot yet substitute for routine T1WI.

BoneMRI

Apart from 3D GRE sequences, a novel MR technique, BoneMRI images, has been developed thanks to the rapid advancement of artificial intelligence techniques. BoneMRI involves radiodensity contrast mapping optimized from MRI to CT based on 3D T1-weighted multiple gradient echo (T1w-MGE) MRI, using a deep learning–based approach.[42] With the BoneMRI technique, radiographlike and CT-like images can be acquired without ionizing radiation. Radiodensity contrast of osseous structures can thus be visualized on MR images. The BoneMRI technique has been successfully applied in the SIJs (**Fig. 5**). These images were acquired through a deep-learning training process using CT and T1w-MGE of the SIJs in 25 patients suspected for SpA. Studies on the image quality and diagnostic accuracy for osseous structural lesions of BoneMRI are ongoing.

The BoneMRI technique is a new horizon for evaluation of osseous structural lesions in SpA. More details of osseous structures in SIJs can be visualized on BoneMRI images, facilitating MRI to become a 1-stop modality for imaging of axial SpA. For future research, the value of BoneMRI should be tested in larger cohorts of patients with or

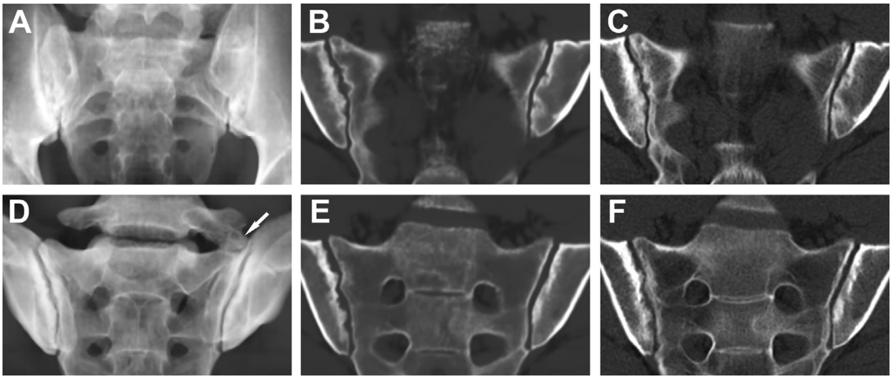

Fig. 5. Radiographlike images (*A*, *D*), CT-like images (*B*, *E*) acquired using BoneMRI technique, and CT images (*C*, *F*) of the same patient as in **Fig. 4**. The CT-like BoneMRI images have a high similarity to CT images. The osseous SIJs and erosions are well depicted on CT-like BoneMRI images. On the tilted view of the radiographlike image (*D*), the partial sacralization of L5 is more clearly shown (*arrow*).

Table 1
Summary of emerging imaging techniques in axial spondyloarthritis

Lesions of SIJ	Modality	Imaging Technique	Benefits	Limitations
BME	MRI	Fat-suppressed sequences: T2-SPAIR and T2-weighted multipoint Dixon sequence	Better image quality compared with STIR Shorter scan time	Reliability needs further validation
	MRI	DWI with ADC maps	Quantitative evaluation of disease activity May improve specificity for spondyloarthritis	Time consuming for quantitative analysis Questionable reliability
	CT	Dual-energy CT	Quantitative evaluation Provides an alternative for BME detection, especially for patients not accessible to MRI	Ionizing radiation Limited in detecting BME close to cortical bone Low accuracy in sclerotic areas
Erosions	MRI	3D GRE MRI (FLASH, DESS, b-WS-SSFP, VIBE)	High contrast between cartilage and cortical bone High spatial resolution and lower partial volume effects Applicable for multiplanar reconstruction	More subject to artifacts Reliability need further validation
	MRI	BoneMRI	Get radiographlike and CT-like images from MR scans Excellent depiction of osseous structures	Not yet commercially available

suspected for SpA. The diagnostic accuracy of BoneMRI images should also be compared with existing MR sequences for evaluation of structural lesions, including routine T1WI and 3D MRI sequences, as mentioned earlier.

SUMMARY

Imaging of the SIJs is one of the cornerstones in the diagnosis and monitoring of SpA. Evaluation of BME and structural lesions are both important for understanding the disease procedure. DECT provides an extra choice for imaging of BME in SIJs, whereas 3D MRI and BoneMRI techniques can better depict osseous structural lesions than routine MRI sequences. These emerging imaging techniques (summarized in Table 1) provide novel techniques that will enhance the characterizations of lesions in patients with axial spondyloarthropathy.

DISCLOSURE

The authors have nothing to disclose.

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