Review Article

Cutting Edge Technologies in the Imaging of Spondyloarthritis

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Abstract

The classification, monitoring, and early detection of axial spondyloarthritis poses significant challenges for health-care professionals owing to the etiology of the disorder. As no unique gold standard is set to confirm diagnosis, current practice relies on imaging the sacroiliac joint, focusing on features of inflammatory changes, and structural changes. New innovations and developments have resulted in significant improvements in the imaging of spondyloarthritis and have provided further development in the understanding of the disease. These recent imaging advances and their relevant pitfalls are discussed in this review.

Key Words: *Bone marrow edema, computed tomography, erosions, lesions, magnetic resonance imaging, sacroiliac joints, sacroiliitis*

Introduction

Axial spondyloarthritis (axSpA), is a chronic, multisystem inflammatory disorder involving primarily the sacroiliac joints (SIJs) and the axial skeleton.[1] Radiographic changes of sacroiliitis have conventionally been the key imaging feature in the diagnosis of SpA. Other features include sclerosis, erosion, joint space narrowing, and ankyloses, which form the hallmark of the Modified New York Criteria for radiographic grading of sacroiliitis [Table 1].[2]

Currently, plain film radiography is still used to assess early radiographic signs, gradual progression and as an aid for the classification of structural lesions. However, in recent years, the use of advanced medical imaging such as fat-suppressed magnetic resonance imaging (MRI) sequences and short-TI inversion recovery (STIR) sequence have been a growing trend. Features such as backfill, fat metaplasia, and ankylosis constitute some of the structural changes visible on MRI.[2] However, the hallmark of spondyloarthropathy is bone marrow edema (BMO) and active inflammatory lesions such as active erosions.[2]

Although the use of MRI has been of great diagnostic utility, the last decade has resulted in the emergence of enhanced technological modalities focusing on improved imaging and evaluation of SpA, which have shown superiority in the detection of both BMO and structural lesions.

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Advancements in the Imaging of Erosions and Lesions

Plain film radiography still serves as the reference for total SIJ disease burden and the grading of structural lesions, of which, erosion is a defining characteristic in SpA. However, limitations of plain radiography restrict the assessment of erosions resulting in diminished reliability and sensitivity. The complex anatomy of the SIJ do not allow a complete view of the joint on a standard antero-posterior view.[3] Although radiographs have been established as the standard in screening and grading modality of sacroiliitis, it has been found to have low reliability.[4] As such, the Ferguson view (a modified AP pelvis X-ray view) has been suggested, but it has yet to prove any added advantage.[3] Performance and reliability scores were similar for both views.[4] In addition, plain films provide limited assessment capabilities as SIJ changes may be obscured by overlapping structures such as bowel gas, which could imitate erosions.[5] These are compounded by the associated radiation exposure burden to patients.

Consequently, new advances in the imaging of erosions have been an area of important research.[6] Both computed tomography (CT) and MRI T1 spin-echo (T1SE) sequences are utilized in the examination of erosions, with CT

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considered the gold standard.[7] CT shows higher sensitivity and specificity; however, due to its high radiation dose, it is not routinely used in clinical practice. In comparison, MRI T1SE has a sensitivity of 61%–79% and a specificity of 88%–95%, in erosion recognition, numbers equivalent to BMO detection on STIR.[7,8]

Other studies have shown that T1-weighted fat-saturated or T2-weighted gradient echo sequences, may be beneficial in recognition of erosive features.[9] Their reliability, however, remains under scrutiny as compelling evidence and comparison to T1SE images is nonexistent.[9]

Nonetheless, the addition of these newer techniques into routine MRI scanning protocols requires in-depth analysis. MRI has its restrictions in aiding the identification of erosions with indistinct features when comparing the boundaries of subcortical bone marrow and erosion.[7] In addition, the distinction between joint space and cortical space remains an area of difficulty due to limited contrast differentiation, and this inherent decreased contrast resolution reduces the sensitivity of the technique in the detection of erosions.[7]

Three-Dimensional Magnetic Resonance Imaging Sequences

Three-dimensional (3D) MRI sequences provide images in all three planes, as well as datasets that can be reformatted in freely selectable orientations, which is advantageous in the assessment of the SIJs. With its lack of radiation exposure and its rich soft-tissue contrast, additional analysis to identify its role in the detection of erosions is crucial. The investigated sequences are gradient-echo (GRE) sequences and expected to provide high contrast between cartilage, joint cavities, and cortical bone.[10] One of the drawbacks of these sequences is that fat-suppressed images do not gauge fat metaplastic structural lesions in the SIJs.[10]

3D volume interpolated breath-hold examination (VIBE) sequences are at the forefront of this recent analysis [Figure 1].[8,11] It is a fat-saturated 3D GRE sequence with nearly isotropic resolution, completed with short acquisition times and preserved image quality.[12] The data sets collected within a single breath-hold allow for the generation of T1-weighted image images.[12]

Bennett *et al*. found that 3D VIBE sequences allowed for the identification of 16% more patients with erosions; moreover, it exhibited a higher sensitivity (95%) than MR-T1W (79%).[13] The specificity for erosion detection was shown to be 93% by Diekhoff *et al*. when compared to 3.0 T MRI in 110 SpA patients and 18 controls.[11] These findings of higher sensitivity and comparable specificity were also seen in reports by Baraliakos *et al*. who assessed 3D VIBE images versus 1.5 T MRI images in 109 SpA patients.[8] Furthermore, readers agreement on findings of erosion was shown to be higher on 3D VIBE

Table 1: New York sacroiliitis radiological grading criteria

Grade	Findings
0	No abnormalities
	Sacroiliac joints normal
I	Suspicious for abnormalities
	Blurring of the joint margins
II	Minimal sclerosis with some erosion
	Solitary erosions
	Juxta-articular sclerosis in small sacral or iliac areas
III	Advanced abnormalities
	Definite sclerosis on both sides of joint
	Numerous erosions with widening of joint space with or without ankylosis
	Possible partial ankylosis
IV	Complete ankylosis

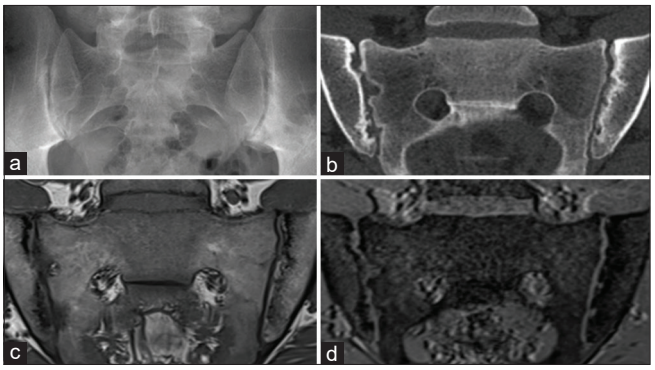

Figure 1: Images of a 27-year-old male with erosions in both sacroiliac joints. With reference to computed tomography (b), erosions are better depicted on three-dimensional volume-interpolated breath-hold examination images (d) than on T1-weighted magnetic resonance images (c) and on the radiograph (a)

than MR-T1 and CT.[8,11,13] However, this may be the result of an increased rate of false positives on 3D VIBE due to more artifacts.[8,14] Application of this imaging modality is reliant on the patient's ability to hold their breath, which subsequently effects motion artifacts and can restrict both image quality and thus reduce readers' ability to assess erosion.[14]

Other 3D sequences have also been investigated for the discovery of erosions in patients with SpA, among them 3D water suppressed balanced steady-state free precession sequence (b-WS-SSFP).[7] When compared to T1WI and plain radiography, Hu *et al*. found that b-WS-SSFP had superior specificity and sensitivity in the detection of erosion. The added benefits are of short scanning time and zero radiation burden.[7]

3D fast low angle shot and 3D double excitation in the steady-state sequence use in the SpA were studied by Algin *et al*.[15] The studies reported a substantial increase in the detection score of cartilage and bone cortex erosions compared to MR-T1.[13] In addition, the use of spoiled 3D GRE variants which generate in-phase and out-of-phase

images with water and fat only specific sequences can be used to study cartilage and lesions such as tissue backfill in SpA [Figure 2].

Although relevant studies are scarce and require additional supportive data, 3D MRI sequences have been shown to be advantageous in the detection of erosions in the SIJs and therefore warrant further studies to validate their diagnostic value.

Bone Magnetic Resonance Imaging

Accelerated by breakthroughs in artificial intelligence, bone MRI techniques continue to progress and appear to hold the key for the future diagnosis of SpA. Free from ionizing radiation, it can be used to construct images that resemble radiographic and CT images. This technique builds on a 3D T1-weighted multiple gradient echo (T1w-MGE) MRI, producing high-quality multiplanar images following a single acquisition, and thus eliminating multiple sequences with identical tissue contrast in different planes.[16]

This has been shown to be effective in the assessment of osseous structures and has been utilized in the evaluation of SIJs [Figure 3]. Twenty-five patients were studied to assess osseous structural lesions (fat lesions and erosions) in SpA, using varied contrast densities facilitated through the use of T1w-MGE.[17] Bone MRI has been found to reveal comprehensive detail of structural osseous lesions.[17]

Advancements in the Imaging of Bone Marrow Edema

Dual-energy computed tomography

Conventional CT utilizes a single polychromatic X-ray beam emitted from a single source and received by a single detector, while dual-energy CT (DECT) offers the ability to analyze and characterize material composition through image acquisition at two different energy levels, typically at 80 and 140 kV. The data generated depends on differences in photon attenuation of the various materials found in the human body. Materials have unique attenuations at different energy levels, those with low atomic numbers such as water, display small differences in attenuation while materials with high atomic numbers like iodine, display large differences in attenuation at different photon energies. Consequently, DECT can be employed to assess tissues at both low and high high-energy levels,

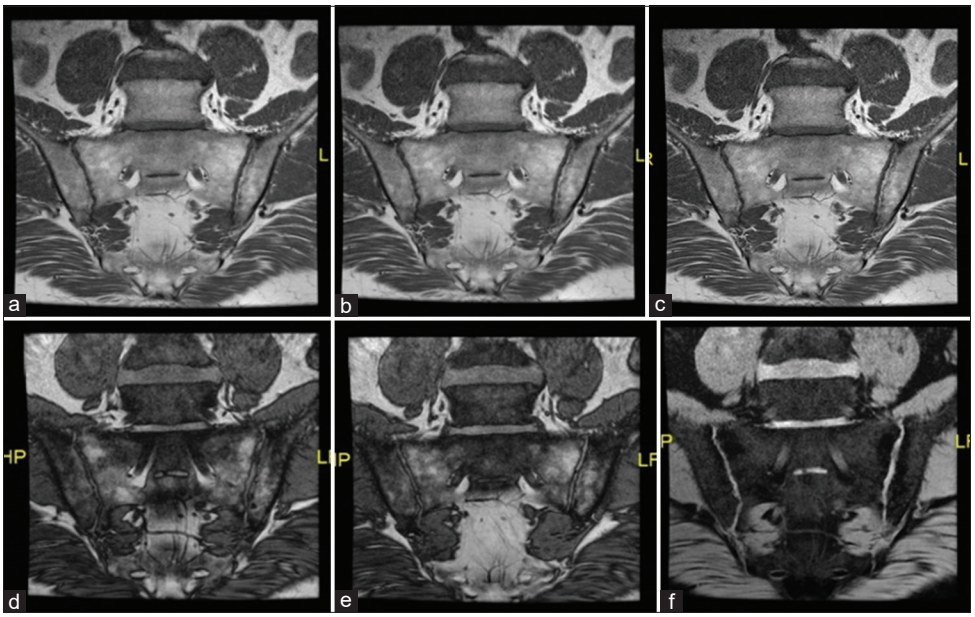

Figure 2: Coronal oblique images (a-c) of the sacroiliac joint demonstrate tissue backfill, on the T1 in-phase fat images, in the inferior aspect of the left sacroiliac joint. This is better assessed in (d and e) on the out-phase LAVA. Image (f) shows sclerosis is better appreciated on the Water phase with definition of "backfill" as cartilage signal

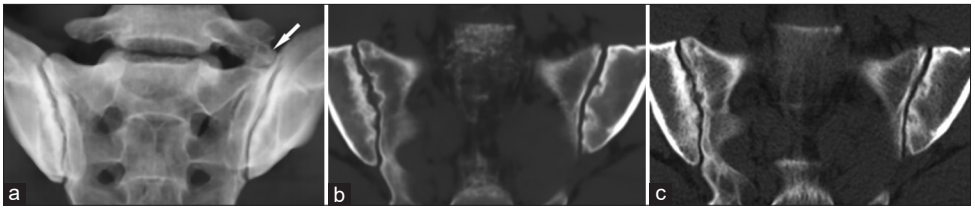

Figure 3: Images of a 30-year-old male with sacroiliitis. (a) The tilted "radiograph-like" image synthesized using bone magnetic resonance imaging provides an overview of the sacroiliac joints. Partial sacralization of L5 is clearly demonstrated (arrow). Osseous aspects of the sacroiliac joints and erosions are well depicted on the "CT-like" bone magnetic resonance imaging image (b). Comparing with the computed tomography image (c)

using polychromatic X-ray beams to differentiate between different elements. DECT volume datasets are used to generate algorithms which are then used to construct virtual noncalcium (VNCa) images.[18] The algorithms are based on the X-ray absorption of bone minerals and bone marrow, thus allowing for the detection of BMO.

VNCa images can be displayed as gray-scaled or as color-coded maps [Figure 4], which range from a blue color representing fat/yellow bone marrow to a green color representing water/BMO to a yellow-reddish color representing red marrow/blood content.[18] This provides both a visual and quantitative evaluation of the comparative water content assumed as BMO. VNCa DECT image also provides the option of overlay, allowing for the concurrent evaluation of both bone marrow and bone density. In addition to a radiation dose that is relatively equal to a standard CT, Wu *et al*. demonstrated the DECT has a sensitivity ranging from 87% to 93%, and a specificity ranging from 91% to 94% in detecting inflammatory BMO in a 47-SpA patient study.[18]

However, recognition of BMO using DECT has its limitations, as red bone marrow and sclerotic areas show a distribution mimicking BMO and thus lead to misjudgment and subsequently misdiagnosis.[6] In addition, subcortical BMO (within 2–3 mm from the cortical bone) is inadequately evaluated.[18] DECT's use of VNCa, material composition techniques, and virtual monoenergetic images, has shown success in the assessment of sacroiliac BMO. In order for DECT to be reliably and comprehensively exploited in the detection of BMO as a primary modality, additional validation is required.

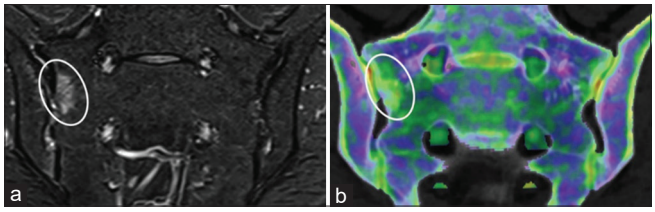

Figure 4: Magnetic resonance imaging and dual energy computed tomography of a 29-year-old female with sacroiliitis. (a) Magnetic resonance short-TI inversion recovery image demonstrates subchondral high signal in the right sacroiliac joint (circle), representing bone marrow edema. (b) Bone marrow edema (circle) is displayed as bright green areas with yellow and red spots on the dual-energy computed tomography image

Diffusion-weighted imaging

Diffusion-weighted imaging (DWI) is a method of signal contrast generation based on measuring the random Brownian motion of water molecules.[19] Thus, allowing the mapping of the diffusion process of molecules and evaluation of molecular function, through which tissue architecture patterns can then be analyzed. This technique has been utilized to quantitatively assess BMO, as interstitial bone edema in patients with SpA leads to widening of the extracellular space, which demonstrates diffusion restriction and thus leads to an increase of extracellular water resulting in high-yield signal on DWI.

In addition, apparent diffusion coefficient (ADC) values [Figure 5] can be calculated using magnitude of diffusion within tissue in DWI, to assess changes associated with tissue integrity and bone marrow changes.[20] Raised ADC values have been found to not only be an early indicator of SpA,[21] but also provide a correlation to disease activity, response to treatment and have been related to improved precision in detecting sacroiliitis.[22]

Nonetheless, DWI does not provide any significant addition to the information provided in fat-suppressed T2-weighted sequence images.[23] DWI alone lacks specificity and may be misleading, as demonstrated by Kucybała *et al*.[24] using STIR images as a reference, noted that the assessment of SpA on DWI yielded a low specificity (54%) for BMO identification.[24] In addition, reader evaluation of the ADC value is a source of inconsistencies compounded by the long duration of post-processing time. As a result, DWI has a limited role in the evaluation of SpA, further reach and data will play a vital role in its future progression.

Advancements in the Imaging of Sacroiliitis

Radionuclide technology

Although, in the past, radionuclide imaging had been thought to be of limited diagnostic value. It is now a promising area of development in imaging of sacroiliitis, as a result of new findings of increased uptake of radionuclides on bone scintigraphy. Improvements in technology in bone scintigraphy, single-photon emission CT (SPECT), combined SPECT/CT, fluoride positron-emission tomography (PET)/CT and immunoscintigraphy, have all began to play

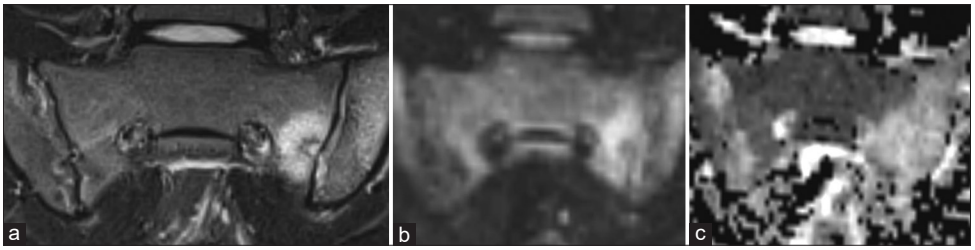

Figure 5: Magnetic resonance imaging of a 17-year-old male with sacroiliitis. (a) MR short tau inversion recovery image demonstrates bone marrow edema in both sacroiliac joints, in particular the left sacroiliac joint. (b) Diffusion-weighted magnetic resonance image (b = 500 s/mm^2) demonstrates high signal of the bone marrow edema. (c) Apparent diffusion coefficient map demonstrates elevated apparent diffusion coefficient values of bone marrow edema

a role in the detection of SpA.[25] Song *et al*. found that bone scintigraphy with technetium-99 m-labeled methylene diphosphate had a sensitivity of 50% in the diagnosis of sacroiliitis.[26] Although low, it was compared to MRI as the gold standard tool in assessing sacroiliitis, which was only found to have sensitivity of 70%.[26]

On the other hand, single-photon emission CT SPECT had a sensitivity and specificity of 80% and 97%, respectively, in the assessment of 46 patients with sacroiliitis.[27] This can be owed to its superior slice-by-slice 3D radionuclide uptake.

Combined SPECT/CT imaging has also been used to evaluate sacroiliitis, as it allows for enhanced anatomical characterization and lesion assessment. In a 20-patient study of SIJs involvement, it was found to have a sensitivity of 80%, and specificity of 84%.[28] PET/CT alone has not been found to be of value in the imaging of sacroiliitis. However, when combined with fluoride (bone tracer of osteoblastic activity), it showed an accuracy of 79%, in the detection of sacroiliitis.[29]

Immunoscintigraphy with radio-labeled monoclonal tumor necrosis factor α (TNF-α) antibodies and human immunoglobulin as imaging tracers has also been an area of growing interest [Figure 6]. A recent study of patients with both axSpA and peripheral SpA, on treatment with TNF-α, demonstrated therapy response on scintigraphy which corresponded well with the findings on MRI and matched clinical response.[30] The future of radionuclide technology in the imaging of SpA shows potential as a sensitive and specific tool for the diagnosis of sacroiliitis. With growing interest in this field increased scientific studies examining and comparing it use are anticipated and required.

Conclusion

Early detection, classification, and monitoring of SpA patients grow in its reliance on radiological imaging. With this growth, advancements in imaging technologies become a necessity to enrich patient care and develop disease recognition. In particular, DECT images have shown potential in the assessment of SpA focusing on features of sacroiliac BMO. 3D MRI sequences provide valuable information relating to both erosions and bone lesions, while bone MRI techniques illustrate abnormal findings of structural osseous lesions. Although worthwhile in diagnosing sacroiliitis, radionuclide imaging has insufficient date to support it legitimacy. These emerging imaging techniques [summarized in Table 2] in SpA are promising

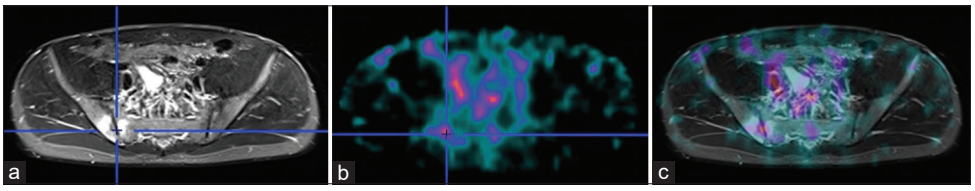

Figure 6: Distribution of Tc^{99m}-radiolabeled certolizumab pegol (a tumor necrosis factor-α antibody) in sacroiliac joints 4–5 h postinjection in a patient with axial spondyloarthritis. Distinct bone marrow edema on magnetic resonance imaging (a) is shown in the right sacroiliac joint, with an increased tracer uptake on single-photon emission computed tomography (b). (c) is a fusion of magnetic resonance imaging and single-photon emission computed tomography

Table 2: Summary of cutting edge imaging technologies in axial spondyloarthritis

Imaging biomarker	Technique	Benefits	Limitations
BMO	DWI with ADC maps	Quantitative evaluation of disease activity	Time consuming for quantitative analysis
		May improve specificity for spondyloarthritis	Uncertain reliability
BMO	Dual-energy CT	Quantitative evaluation	Ionizing radiation
		Provides an alternative for BMO detection, especially for patients not accessible to MRI	Limited in detecting BMO close to cortical bone
			Low accuracy in sclerotic areas
Erosions	Three-dimensional MRI sequences	High contrast between cartilage and cortical bone	More subject to artifacts
		Improved spatial resolution	Reliability need further validation
		Multiplanar reconstruction	
Erosions	BoneMRI	Get "Radiograph-like" and "CT-like" images from MR scans	Not yet commercially available
		Excellent depiction of osseous structures	
Inflammation cytokine: TNF-α	Immunoscintigraphy with TNF-α antibody	Visualize inflammation on a biomolecular level *in vivo*	Further validation needed
		provide objective evidence for therapy response prediction	

ADC: Apparent diffusion coefficient, BMO: Bone marrow edema, DWI: Diffusion-weighted imaging, TNF: Tumor necrosis factor, VIBE: Volume-interpolated breath-hold examination, MRI: Magnetic resonance imaging

in enhancing the diagnostic accuracy and confidence in SpA and worth further application in future. The addition of these tools in future evaluation of SpA is advisable and warrants further analyses.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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