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Unmet Needs in Spondyloarthritis: Imaging in Axial Spondyloarthritis

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ABSTRACT. Imaging biomarkers in axial spondyloarthritis (axSpA) are currently the most specific biomarkers for the diagnosis of this condition. Despite advances in imaging, from plain radiographs—which detect only damage—to magnetic resonance imaging (MRI)—which identifies disease activity and structural change—there are still many challenges that remain. Imaging in sacroiliitis is characterized by active and structural changes. Current classification criteria stress the importance of bone marrow edema (BME); however, BME can occur in various diseases, mechanical conditions, and healthy individuals. Thus, the identification of structural lesions such as erosion, subchondral fat, backfill, and ankylosis is important to distinguish from mimics on differential diagnosis. Various imaging modalities are available to examine structural lesions, but computed tomography (CT) is considered the current reference standard. Nonetheless, recent advances in MRI allow for direct bone imaging and the reconstruction of CT-like images that can provide similar information. Therefore, the ability of MRI to detect and measure structural lesions is strengthened. Here, we present an overview of the spectrum of current and cutting-edge techniques for SpA imaging in clinical practice; namely, we discuss the advantages, disadvantages, and usefulness of imaging in SpA through radiography, low-dose and dual-energy CT, and MRI. Cutting-edge MRI sequences including volumetric interpolated breath-hold examination, ultrashort echo time, zero echo time, and deep learning–based synthetic CT that creates CT-like images without ionizing radiation, are discussed. Imaging techniques allow for quantification of inflammatory and structural lesions, which is important in the assessment of treatment response and disease progression. Radiographic damage is poorly sensitive to change. Artificial intelligence has already revolutionized radiology practice, including protocolization, image quality, and image interpretation.

Key Indexing Terms: artificial intelligence, axial spondyloarthritis, magnetic resonance imaging

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Introduction

Axial spondyloarthritis (axSpA) is a chronic inflammatory condition primarily affecting the spine and sacroiliac joints (SIJ). In the imaging assessment of SpA, radiography is the modality of choice for screening purposes, whereas computed tomography (CT) is not routinely obtained for evaluation of SpA as it comes with a large radiation burden. Major strengths of magnetic resonance imaging (MRI) are its lack of radiation exposure, selective tissue contrast weighting, and high-contrast resolution that allows for excellent visualization of bone marrow changes. On the other hand, direct bone imaging on MRI remains challenging due to the low proton content. Recently, several novel techniques have emerged to create CT-like images of pelvic bones, such as susceptibility weighted imaging (SWI), ultrashort echo time (UTE), and synthetic CT MRI sequences, including automated segmentation of pelvic bones. Structural damage is caused by inflammation and the subsequent repair mechanisms. Whereas structural damage in the SIJ is mostly relevant for the diagnosis of the disease, structural damage in the spine is one of the major determinants of functional status and spinal mobility in axSpA.[1] The aim of this review is to present what is known about currently clinically available and new innovative techniques in SpA imaging in clinical practice and research, including for diagnosis and progression, and the unmet needs that should be addressed. This review explores new directions and technologies that hold promise for enhancing our understanding of the disease process and the role of antiinflammatory therapy in axSpA.

The current state of imaging in axSpA

Radiographs have been the mainstay of imaging in axSpA since the identification of axSpA as a diagnostic entity. Radiographs can measure damage and progression, but have poor sensitivity and are imprecise, particularly in terms of assessing the SIJ. They cannot identify inflammation. The advent of MRI revolutionized our ability to detect inflammation, particularly osteitis via bone marrow edema (BME), capsulitis, and enthesitis. MRI is more sensitive to detecting structural damage of the SIJ, measuring not just erosions but also backfill, ankylosis, and subchondral fatty marrow replacement. Current modalities measure different components of the disease (Table).[2] Damage is measured by radiographs and CT scans, whereas inflammation is best imaged by MRI. MRI can also measure certain structural components of disease and can be transformed into CT-like images (synthetic CT). Various modalities are discussed below in detail (see Box for different applications).

CT. CT has an excellent soft tissue–bone contrast and high spatial resolution. Therefore, it is the reference imaging modality for evaluating structural changes of the calcified bone structure in the SIJ. CT is widely available and has a short examination time. Unfortunately, CT is associated with radiation exposure. Regardless its superiority at detecting erosions, sclerosis, and ankylosis in the SIJ, standard CT and low-dose CT fail to adequately visualize BME.[3]

There are several new hardware developments to improve the image quality and reduce the radiation exposure of CT scans. For example, tin filtration of the x-ray beam reduces the amount of harmful radiation by filtering low-energy photons that are usually absorbed by the patient's body and never reach the CT detector. Although this can reduce the image contrast, it will also markedly reduce the radiation exposure and ensure sufficient image quality. On the other hand, new detector technologies, namely photon-counting CT, promise an increase in sensitivity to radiographs and better spatial resolution, allowing further dose reduction and improvement of image quality.[4]

Dual-energy CT (DECT) acquires 2 datasets of images simultaneously at different energy levels (eg, 80 kV and 140 kV), and allows for differentiation between calcium and hydrogen/fat. Virtual noncalcium images can be rendered by subtracting calcium from cancellous bone, allowing visualization of BME, which is often displayed in color-coded maps. Using DECT, inflammatory BME can be detected in the sacrum and ilium in patients with sacroiliitis. Other applications include detection of urate crystal depositions in the SIJ of patients with gout. Counterintuitively, the radiation dose of DECT is comparable with conventional CT because it is divided between both energy levels.[5]

With the rapid evolution of artificial intelligence (AI) as a novel technique, synthetic CT (or bone MRI) has been developed (Figure). This method uses a convolutional neural network (CNN), with CT scans as the ground truth.[6] As such, radiodensity contrast of osseous structures can be mapped from MRI to CT, creating radiograph-like and CT-like images without ionizing radiation. This technique has the advantage of providing quantitative Hounsfield unit maps like conventional CT and a fully automatic postprocessing process that does not require user input. This technology was clinically validated in the SIJ, spine, and pelvis.[6-8] In the study by Jans et al, these synthetic CT images in patients with sacroiliitis depicted structural lesions with higher diagnostic accuracy and reliability than T1-weighted MRI, and with reliability comparable to CT.[6]

Table. Imaging modalities in axial spondyloarthritis.

	Modality	Findings	Limitations
Sacroiliac joint	Radiographs	Identifies radiographic sacroiliitis, including subchondral sclerosis, erosions, joint space changes, and ankylosis	Has low sensitivity, specificity, and reliability
	Low-dose CT	Provides higher sensitivity, specificity, and reliability for sacroiliac structural changes compared to radiographs, and lower radiation exposure, making it a safer option	May be more challenging to obtain in some regions and centers
	MRI	Effective in capturing structural alterations such as subchondral sclerosis, erosions, backfill, joint space changes, ankylosis, and fat lesions	Requires an erosion-sensitive sequence for better detection of erosions (eg, T1-weighted fat-saturated gradient echo sequence such as VIBE)
Spine	Radiographs	Detects new bone formation (syndesmophytes) and minor changes such as erosion, sclerosis, and vertebral squaring	Has low sensitivity to change and takes only a small amount of damage into account
	Low-dose CT	Offers higher sensitivity in detecting new bone formation and other structural changes in the spine compared to radiographs[2]	Not offered by all imaging centers
	MRI	Captures various structural changes, including fatty lesions, erosions, sclerosis, and potentially syndesmophytes	Recognition of new bone formation still cannot be performed routinely

CT: computed tomography; MRI: magnetic resonance imaging; VIBE: volumetric interpolated breath-hold examination.

Box. Practice points.

- Low-dose CT is a more sensitive and specific imaging tool compared to radiography, and can detect erosions with an equivalent radiation exposure.
- DECT combines the detection of structural lesions and BME, and could be an alternative for patients contraindicated to MRI.
- VIBE, SWI, UTE, ZTE, and synthetic CT MRI sequences depict the cortical outline of the bones better compared to conventional MRI. MRI-based synthetic CT can create HU maps.
- MRI with synthetic CT can become a 1-stop modality in the evaluation of BME and structural bone changes in sacroiliitis.

BME: bone marrow edema; CT: computed tomography; DECT: dual-energy CT; HU: Hounsfield unit; MRI: magnetic resonance imaging; SWI: susceptibility-weighted imaging; UTE: ultrashort echo time; VIBE: volumetric interpolated breath-hold examination; ZTE: zero echo time.

MRI. The introduction of MRI and the subsequent shift from identifying structural lesions, as detected by radiography, toward active inflammation has been an important step toward an earlier diagnosis. This became necessary with the advent of modern biologic or targeted synthetic disease-modifying antirheumatic drugs, which allow for effective suppression of inflammation.[9] These therapies can help to preserve the physical functionality of patients with axSpA before structural changes, especially ankylosis, appear.

MRI is the imaging modality of choice in evaluating BME fat-suppressed fluid-sensitive images such as fat-suppressed T2-weighted images, short tau inversion recovery, chemical shift Dixon method, or spectral attenuated inversion recovery.[9] Contrast media is usually unnecessary for assessing the SIJ. However, BME seen in MRI is a very sensitive but less specific imaging sign of axSpA. It is present in several groups, including healthy individuals, patients with mechanical load, and postpartum women.[10] For this reason, the last update of the Assessment of Spondylarthritis international Society (ASAS) criteria shifts the focus from the mere presence of active inflammation to include the overall opinion accounting for structural changes. New MRI sequences that allow for better depiction of erosions can be applied. These sequences can be easily obtained on MRI machines and include volumetric interpolated breath-hold examination (VIBE) gradient echo, UTE, SWI, and zero echo time (ZTE) sequences.[11]

Structural damage assessment

SIJ scoring systems. In addition to the radiographic scoring system of the modified New York criteria[12] and MRI-specific assessment of SIJ damage, scoring systems like the Spondyloarthritis Research Consortium of Canada (SPARCC) MRI SIJ structural score[13] and the Berlin MRI scoring system (including later modifications) have been developed.[14]

Spine scoring systems. The modified Stoke Ankylosing Spondylitis Spine Score (mSASSS)[15] is commonly used and is included in the ASAS–Outcomes Measures in Rheumatology (OMERACT) core outcome set,[16] but has limited sensitivity. CT syndesmophyte score is a newer measure that may offer better quantification of syndesmophyte growth.[17] Overall, low-dose CT seems to be the most promising imaging method to assess structural damage of the spine in axSpA in the future. It is expected that, with CT, the duration of study seeking the therapeutic effect on structural damage progression could be reduced at least by half, from the current minimum of 2 years to 1 year.

Recent advances and potential future developments. Recent innovations include ultralow-dose CT with AI-supported reconstruction of images, SWI producing CT-like images from MRI,[18] and synthetic CT derived from MRI data (Figure).[5] All these advances have an aim of improving detection of structural damage while simultaneously lowering or avoiding ionizing radiation. Additionally, AI is showing promise in enhancing the standardized recognition of structural damage in SIJ on imaging, which might be helpful for both clinical and research applications.[19-21]

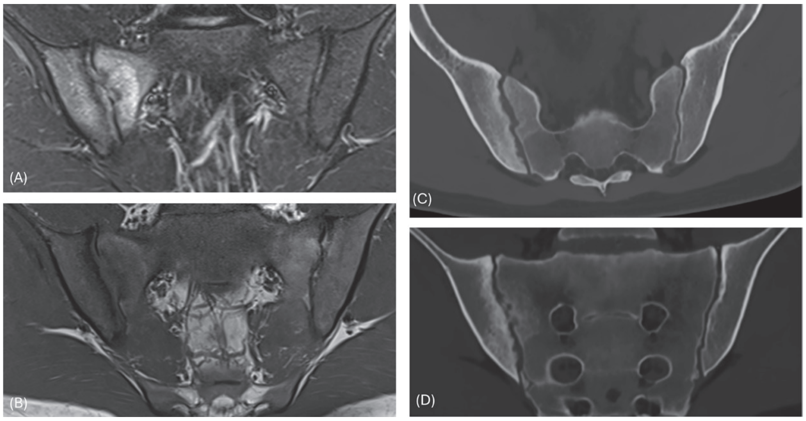

Figure. Synthetic CT images look like CT images, although they are derived from MRI studies. MR images show active and structural lesions of the sacroiliac joint. (A) Active bone marrow edema is seen on the STIR image. (B) T1 image shows erosion. (C,D) Bone MR images make the presence of erosions and sclerosis more evident. CT: computed tomography; MR: magnetic resonance; MRI: magnetic resonance imaging; STIR: short tau inversion recovery; T1: T1-weighted MRI.

New directions. The sequence of inflammation, repair, and new bone formation is a hallmark of axSpA, connecting inflammation with subsequent structural damage.[22] Emerging technologies like synthetic CT derived from MRI[16] and molecular imaging, including 18F-fluorodeoxyglucose (FDG) and fibroblast activation protein inhibitor positron emission tomography (PET),[23] hold promise for improving structural damage assessment and prediction in axSpA. AI is increasingly being explored for the standardized evaluation of radiographic progression in axSpA,[24] which could lead to more accurate and efficient monitoring, especially in clinical studies.

AI in axSpA imaging

AI has emerged as a transformative technology with unprecedented potential in various fields, including medical imaging. Recent advances in AI indicate early signs of a technological revolution that may potentially transform all aspects of radiology including acquisition, interpretation, report generation, and, ultimately, disease prediction.

Image reconstruction. AI has the potential to enhance spine image reconstruction with improvements in image quality and acquisition time as well as a reduced radiation dose. AI algorithms can be used to reduce noise in MRI and CT images by learning the patterns of noise in the data using a variety of deep learning (DL) techniques. For instance, a previous study showed that a DL-based noise reduction algorithm could improve the signal-to-noise ratio (SNR) of lumbar spine MRI scans by up to 30%.[25] Similar studies of lumbar spine CT have shown that DL-enhanced images have significantly lower noise compared to the original scan.[26]

DL reconstruction algorithms can also be used to enhance the resolution of MRI by learning relationships between different coordinates in the image. State-of-the-art AI algorithms have demonstrated significant improvements in image quality of lumbar spine MRI.[27,28] Reconstruction algorithms and noise reduction techniques can also be used to reduce acquisition times of lumbar spine MRI.

An important direction in image reconstruction is the reduction of radiation dose in lumbar spine CT scans by reconstructing high-quality images from fewer datapoints. A recent study shows that an AI-based DL algorithm could reconstruct high-quality images from CT scans of the lumbar spine that were acquired, at a dose up to 72% lower than the standard-of-care (SOC) dose.[29]

AI for synthetic modalities is very promising. Synthetic CT can be used to reduce radiation dose while still maintaining diagnostic accuracy.[29] Synthetic MRI has the potential to improve image quality by reducing noise and artifacts and can enhance the diagnosis of spinal disorders. Last, AI-powered synthetic imaging can be used to personalize imaging by considering patient-specific factors such as age, gender, and body habitus, thereby improving the accuracy of diagnosis and subsequent management.

Fast MRI acquisitions modify conventional imaging protocol variables to decrease scan times while maintaining resolution at the cost of increased image noise (ie, reduced SNR). Common strategies to shorten acquisition times exploit *k*-space data redundancy or spatial correlation (ie, partial Fourier parallel imaging and compressed sensing). Modifications include reducing excitations, raising bandwidth, and increasing parallel imaging factors. These acceleration approaches inherently suffer from reduced SNR or blurring, resulting in insufficient imaging quality. DL image enhancement can increase SNR.[30] DL-based image denoising methods applied to compromised fast scan data can restore SNR and maintain image sharpness and SOC image quality.

DL-based methods employing a deep CNN directly applied to raw *k*-space data have developed rapidly for various MRI areas, including undersampled data reconstruction, segmentation, superresolution, and denoising. Using a DL reconstruction method developed to improve SNR and reduce ringing artifacts on lumbar spine MRIs (commercially available AIR Recon DL, GE HealthCare), Han et al demonstrated that DL reconstruction combined with fast acquisitions has potential to provide diagnostic image quality noninferior to SOC lumbar spine MRI. The lumbar spine MRI protocol was 52% faster and was able to provide scores noninferior to the standard protocol for apparent SNR, visualization of anatomical structures, and diagnostic confidence, as blindly evaluated by 1 junior and 2 senior subspecialty radiologists.[31]

Synthesizing new images from available images is an active area of research in MRI. DL image reconstruction can create synthetic images from existing datasets. AI for synthetic modalities, known as virtually generated MRI, is promising, as the physical acquisition of particular sequences would no longer be necessary. Generative adversarial networks (GANs) based on a DL architecture can be used to generate synthetic images from different MRI contrasts as input. A GAN consists of a generator network and a discriminator network. The generator network learns to synthesize realistic images, whereas the discriminator network learns to distinguish real from fake (synthesized) images. During the learning process, these networks compete against each other, resulting in the generator network progressively learning to synthesize images with increasingly realistic appearance.[32]

CT and MRI are complimentary modalities routinely obtained for the radiologic evaluation and surgical planning of patients with spine pathology. Roberts et al developed a DL algorithm producing 3-D lumbar spine CT images from MRI data using a supervised 3-D cycle-GAN model, which has the potential to reduce patient radiation.[32]

Using UTE or ZTE MRI coupled with DL-based noise reduction, Hahn et al demonstrated that CT-like images that depict bone erosions in axSpA can be generated. Two radiologists compared CT and these synthetic bone images and established that the correlation between the CT and synthetic images ranged from 0.66 to 0.85 and was radiologist dependent.[33]

AI tools have enabled automated and robust segmentation of spinal structures such as vertebrae, intervertebral discs, and the spinal canal. In particular, DL algorithms have previously shown good performance in segmenting complex structures even in the presence of noise, artifacts, and anatomical variations. Models trained on larger datasets can identify complex features from spine images, enhancing the diagnosis and classification of various pathologies such as fractures, spinal tumors, or degenerative conditions. Specialized algorithms such as GANs and variational autoencoders show potential for reconstructing images from undersampled or noisy data, resulting in faster acquisition times while preserving diagnostic accuracy. SpineNet,[34] a multitask architecture, developed automated classification of several spinal conditions, including central canal stenosis on sagittal and axial T2-weighted images.[35]

In a well-designed multicenter study across different MRI vendors, Bressem et al demonstrated the ability for trained AI models to classify active inflammatory and structural changes in the SIJs, with accuracies ranging from 75% to 79%.[21]

AI has the potential to assist image analysis, benefiting patient management and workflow efficiency. The majority of studies are preliminary, retrospective, or single-center, with small sample sizes. Manual radiologist labeling of images, believed to be the most accurate method for training models, is labor intensive and can limit the number of studies that can be used for training. Many models require postprocessing using semiautomated software that typically depends on active human input (ie, placing regions of interest to segment and discriminate between anatomic structures). This step limits its real-world implementation in clinical practice.

The AI models are limited in their generalizability; further work is therefore needed to ensure their reliability and reproducibility before they can be translated successfully into clinical use. Randomized controlled trials and large multicenter studies will be required to validate these applications and facilitate their integration into routine clinical practice. DL methods need further validation with larger scale studies in external centers with prospective evaluation of a greater number and variety of patients.

Future work will focus on testing and documenting, pooling data from multiple collaborating institutions to increase heterogeneous test sets for research and evaluation of machine learning (ML) tools by multidisciplinary teams. Individual researchers are encouraged to use publicly available datasets and to test algorithms online and provide feedback, reporting cases of success or failure and comparing results with published work.

3-D CNNs can offer better performance but are computationally expensive; moreover, medical imaging data must often be downsampled to accommodate currently available hardware limitations. Further advances in computer hardware and innovative data processing solutions are likely required to develop more robust ML models with human-level performance.

Cultural challenges are also potentially significant barriers to resolving the technological challenges outlined above. Robust ML diagnostic tools require large, annotated datasets (tens of thousands of training images from multiple institutions) and run into systemic barriers from data privacy concerns, increasing the challenge of integrating computer-aided diagnostics into a traditional clinical workflow. Despite standard data anonymization, medical imaging data are subject to strict regulations regarding storage, transmission, and usage, creating challenges in assembling a large dataset.

Another significant cultural challenge is the concept of AI as a "black box." The inability for us to see how DL systems make their decisions is problematic. Although we can see the input and output, the system's code or the logic that produced the output is not inherently transparent. Explainable AI is a branch of this technique that tries to make the used methodology transparent to all users.

Given this black box nature, accountability for medical decisions would also be a challenge to establish. If an AI model makes a wrong diagnosis, would the responsibility fall on the clinician using the ML system or the manufacturer of the device? This obscure nature also has great implications regarding the marketing approval of novel AI tools, which require deeper testing and verification compared to other technologies, and thus a longer time to market and at greater cost.

Conclusion

Imaging in axSpA has exponentially advanced our understanding of this disease. Modalities like MRI have enabled earlier detection of disease with inflammatory lesions before damage ensues, and newer erosion-specific sequences have added to specificity in disease diagnosis and assessment. Advancements in structural damage assessment in axSpA, particularly in the SIJ and spine, are reshaping our understanding of disease progression and influencing the clinical assessment in daily clinical practice and research. Innovations in imaging modalities, scoring systems, and AI integration hold the promise of more accurate detection and better monitoring for patients with axSpA.

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