Imaging Techniques: Options for the Diagnosis and Monitoring of Treatment of Enthesitis in Psoriatic Arthritis

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Key Indexing Terms: Psoriatic arthritis; Magnetic resonance imaging; Ultrasonography; Outcome assessment; Diagnostic imaging

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Funding: This review article was sponsored by Novartis Pharmaceuticals Corporation.

Conflict of interest disclosure:

C. Bakewell has received consultancy fees from and/or served on speakers bureaus for AbbVie, Novartis Pharmaceuticals Corporation, Pfizer, and Sanofi Genzyme/Regeneron.

S. Z. Aydin has received honoraria from Abbvie, Novartis, Pfizer, UCB, Janssen, Lilly, and Celgene.

V. K. Ranganath has served on the Data and Safety Monitoring Board for Amgen, has received consultancy fees from Bristol-Myers Squibb; and has received grants for investigator-initiated studies from Genentech, Mallinckrodt, and Pfizer.

L. Eder has received research or educational grants and/or consultancy fees from Amgen, Abbvie, Janssen, Pfizer, Novartis, UCB, Celgene, and Eli Lily.

G. S. Kaeley has received consultancy fees from Novartis Pharmaceuticals Corporation.

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Short running head (max 4 words): Imaging in Enthesitis

Word count (3000 words maximum): 2999

Figures/tables (4 total): 1 table; 3 figures

References (50 maximum): 50

Abstract (145 words of 150 limit)

Psoriatic arthritis (PsA) affects up to 30% of patients with psoriasis and may include musculoskeletal manifestations such as enthesitis. Enthesitis is associated with joint damage, and early detection and treatment are essential to management of the disease. Traditionally assessed by clinical examination and conventional radiography, entheseal inflammation can now be more accurately assessed earlier in the disease using techniques such as ultrasound, magnetic resonance imaging, computed tomography, and molecular imaging. However, there is little consensus on the optimum definition for diagnosing enthesitis in PsA or on the ideal scoring system for measuring response to treatment. This review aims to summarize the benefits and limitations of different imaging modalities in the assessment of enthesitis. It also proposes that adoption of standardized definitions and validation of scoring systems and imaging techniques in clinical trials will allow the efficacy of new treatment options to be assessed more accurately.

Introduction

Psoriatic arthritis (PsA) is a chronic inflammatory disease that affects up to 30% of patients with psoriasis (1, 2). Musculoskeletal manifestations of PsA may include peripheral arthritis, spondylitis in the spine, and enthesitis and/or dactylitis. PsA can affect multiple types of soft tissue and has a variable presentation of synovitis, which is commonly asymmetrical (3).

Approximately 60% to 80% of patients with PsA will develop enthesitis (1), defined as inflammation of the entheses, the areas where tendons, ligaments, or joint capsules insert into the bone (2). Enthesitis is one of the first signs of disease and has been proposed to be the primary lesion in PsA (4), a finding that has led to its inclusion in the Classification Criteria for Psoriatic Arthritis (CASPAR) (5) and the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) core disease domains for PsA (6). Enthesitis is also associated with joint damage and is an indicator of disease severity (1). The importance of enthesitis is further highlighted by its inclusion in the Outcome Measures in Rheumatology (OMERACT) PsA core domain set, warranting evaluation in clinical trials and observational studies of PsA (7).

Early diagnosis and treatment of PsA are critical given that delays in rheumatologic assessment by ≥ 6 months are associated with long-term radiographic progression and detrimental functional outcomes (8). Therefore, identifying enthesitis, a marker of early disease, can lead to early treatment initiation before irreversible structural damage occurs (2). However, identifying enthesitis in the clinic can be challenging, and incorporating imaging modalities in the assessment of enthesitis may be useful.

This narrative review describes imaging modalities used to detect enthesitis and discusses ways in which standardized definitions and validated scoring systems and imaging techniques will allow a more accurate assessment of treatment options. We include relevant information identified from a targeted literature search (see Appendix) focused on PsA, enthesitis, and the imaging techniques used in the assessment of enthesitis.

Clinical assessment and imaging techniques used to assess enthesitis

Clinical assessment

Palpation is used to detect the presence of local tenderness and soft tissue swelling in the clinical examination of enthesitis (9) (Figure 1A). Physicians apply pressure to each site with the dominant thumb, until the nail bed blanches, asking patients to provide subjective reports of tenderness (10). Several indices have been developed to help standardize the clinical diagnosis of enthesitis (2, 11, 12) (Table 1A), although only the Leeds Enthesitis Index (LEI) has been specifically developed for PsA (11).

Assessing enthesitis by clinical examination is noninvasive, inexpensive, and relatively fast and can be conducted as needed without onward referral or access to specialized equipment or facilities. However, clinical identification of enthesitis can be challenging. Assessments are dependent on subjective reports by the patient and physician and do not provide complete information on the extent of entheseal involvement or the presence of subclinical enthesitis (9). Moreover, tenderness over an entheseal area can also be present in conditions that mimic enthesitis, such as tendinitis or mechanical injury, making a clinical diagnosis subject to false-positive results (2).

Conventional radiography

Clinical examination can be combined with conventional radiography (9). Typical radiographic features visible in entheses of patients with PsA include enthesophyte formation, new bone formation, and bony irregularities (13) (Figure 1B). Radiography is also particularly useful for monitoring syndesmophytes in spinal entheses (14).

The cost of taking conventional radiographs is low, as is the need for specialized facilities. However, x-rays do not reveal inflammation in soft tissue structures; hence, only damage associated with chronic enthesitis, and not early disease, is visible (2, 13, 15). Therefore, the usefulness of radiography for diagnosing enthesitis in early PsA is limited (2, 13, 15). Similarly, the benefits of using radiography to monitor enthesitis in peripheral sites are limited. These limitations have highlighted the need for more-sensitive imaging techniques in the assessment of enthesitis.

Ultrasound

Ultrasound is widely used because it is inexpensive and accessible, is nonionizing and noninvasive, and produces real-time images, allowing documentation of clinical information at the point of care with minimal risk of harm to the patient (2, 16). Most published ultrasound studies in PsA have focused on the entheses of the lower extremities; however, more recent scoring systems have incorporated upper-extremity entheses, recognizing the confounding factors of body weight and biomechanics on the lower-extremity entheses (17). Gray-scale ultrasound (Figures 1C, 1D, 2A, and 2B) can detect both acute (eg, increasing thickness, hypoechogenicity) and chronic inflammation or changes (eg, erosions, enthesophytes) (18). These components, including chronic changes, have recently been reported to be part of the definition of enthesitis (19, 20) and may be important for differentiating patients with PsA from those without disease (20). A sonographic Doppler signal (Figure 1D) can be used to detect active inflammation, evidenced by abnormal vascularization (20) (Figure 2C and 2D). It has also proven useful in identifying subclinical involvement of entheses prior to development of symptoms (20-22). A consensus definition of enthesitis by ultrasound assessment was recently proposed by the OMERACT Ultrasound Working Group (UWG) and states that enthesitis is a hypoechoic and/or thickened insertion of the tendon within 2 mm of the bony cortex, which exhibits a Doppler signal if active, with possible erosions and enthesophytes/calcifications as signs of structural damage (19, 22). However, defining enthesitis as being within 2 mm of the bony cortex remains an area of active debate, with the GRAPPA UWG maintaining that the enthesis boundary could also extend beyond this cutoff or to within the adjacent bursa (20). This is consistent with the concept of the “enthesis organ” or the “synovio-entheseal complex” that comprises more than the joint insertion site alone and includes the nearby synovium (23); thus, the OMERACT UWG’s current definition may not fully capture all the inflammatory changes due to enthesitis.

Several scoring systems have been devised for enthesitis assessment by ultrasound (2, 19-21, 24-28) (Table 1B). The OMERACT UWG Enthesitis Score was developed in conjunction with the consensus definition of enthesitis. This scoring system emphasizes defining lesions at the enthesis as being within 2 mm of the cortical bone and those outside the enthesis as being in the tendon or bursa, as well as the benefit of scoring each component as present or absent (19) (Table 1B). The GRAPPA UWG is also working on a scoring system designed specifically to assess enthesitis in PsA for

diagnostic purposes (20). The GRAPPA UWG identified 5 lesions and 6 entheseal sites (Table 1B) as being critical for identifying patients with PsA and is currently working on validating and finalizing the scoring method (20).

Other ultrasound scoring methods have been used to assess enthesitis for diagnosis and entheseal response to treatment (Table 1B). Although most scoring systems have a reasonable level of reliability and sensitivity, they were developed and evaluated in spondyloarthritis (SpA) rather than PsA specifically (7). Additionally, most of these approaches also have a strong focus on entheses in the lower extremities of the body, which may be confounded by mechanical changes caused by aging, physical activity, and obesity (7, 29).

Some limitations associated with ultrasound in the assessment of enthesitis include its inability to identify any intraosseous abnormalities associated with active enthesitis (30) and the lack of guidelines regarding Doppler settings for enthesitis imaging. Further difficulties involve standardization of settings on different machines (9) and weak signals and artefacts due to the small number of blood vessels in entheses and proximity to bone (21); however, visualizing avascular fibrocartilage at entheseal sites with ultrasound is possible (31).

Magnetic resonance imaging (MRI)

MRI is a powerful nonionizing imaging technique that can be used to evaluate axial or peripheral entheses (2, 15). MRI sequences for enthesitis evaluation typically are T1 weighted; T2 weighted with fat suppression or short tau inversion recovery; or T1 weighted with fat suppression after contrast administration (30). Due to its ability to detect small differences in water content between adjacent tissue types, MRI can detect early signs of enthesitis that are not visible using radiography (15) and can provide high-resolution evidence of soft tissue abnormalities such as thickening of tendons and ligaments, joint effusions and inflammation, bone erosions, enthesophytes, and intraosseous bone marrow edema (30) (Figure 3A and 3C).

The Psoriatic Arthritis Magnetic Resonance Imaging Score (PsAMRIS) is the most studied scoring system for measuring destructive and inflammatory changes in the hands and feet in PsA; however, it

is not specific for assessing enthesitis (32, 33). PsAMRIS was devised by the OMERACT MRI Working Group and has been shown to have good intra-reader and inter-reader reliability (29, 33). PsAMRIS includes measures of synovitis, tenosynovitis, periarticular inflammation, bone marrow edema, bone erosion, and bone proliferation (32). Further application of PsAMRIS in randomized controlled trials of PsA is warranted (29).

Given the lack of MRI scoring systems for evaluating enthesitis, the OMERACT MRI in Arthritis Working Group recently developed the heel enthesitis scoring system (HEMRIS) for use in patients with SpA or PsA (34). Both inflammatory and structural MRI findings were included, with HEMRIS showing good inter-reader agreement for status scores and for changes in inflammatory parameters over time. Notably, the heel enthesitis score was especially reliable when the mean score of 2 readers was used, an approach that is typically used in clinical trials. Overall, HEMRIS is a promising tool, and validation in clinical trials will be important.

Whole-body (WB) MRI is a novel approach that allows visualization of the entire body in 1 examination but has lower image resolution than conventional MRI (33) (Figure 3D). A proof-of-concept study showed that enthesitis was the most common pathology detected by WB-MRI and that significantly more locations of enthesitis were identified with WB-MRI than with clinical examination (35). GOLMePsA, an ongoing trial of golimumab and methotrexate in early PsA, is expected to provide data on the role of WB-MRI as an outcome measure by assessing the effect of treatment on inflammation as visualized using WB-MRI and ultrasound (36). However, WB-MRI carries some limitations. For instance, subtle enthesitis can sometimes only be visualized following administration of contrast media (35). Additionally, agreement between WB-MRI and clinical examination is often < 50%, and readability and reproducibility of WB-MRI for distal peripheral joints are low due to poor resolution. Thus, further clarity surrounding the generalizability of this technique for detecting enthesitis is required (37, 38).

The OMERACT MRI Working Group has taken the first steps toward standardizing the process of WB-MRI, including image acquisition and definitions of key pathologies and has developed a preliminary OMERACT scoring system for the assessment of inflammatory arthritis using WB-MRI

(39). The GRAPPA MRI Working Group has also been investigating outcome measures for trials in PsA and is proposing to conduct a longitudinal, multicenter, and preferably randomized treatment study in patients with active PsA that will assess WB-MRI of peripheral and axial joints and entheses according to the OMERACT recommendations (24). The study will also incorporate assessment of feet and hands using PsAMRIS, as well as knees and hips using Knee and Hip Inflammation MRI Scoring Systems (24).

Newer MRI techniques have also been developed. Diffusion-weighted imaging MRI is a technique based on the Brownian motion of water, which is reduced in inflammation (15). Diffusion-weighted imaging MRI provided good differentiation between active and inactive ankylosing spondylitis; however, enthesitis and synovitis were not evaluated, and further studies are needed to assess the usefulness of this technique (40). Ultrashort echo time MRI (UTE MRI) has also been investigated as it allows changes at the entheses to be viewed at higher resolution and earlier than conventional MRI (41). A recent study has shown that UTE MRI can be used for morphological and quantitative evaluation of entheses in patients with PsA (41).

Despite the benefits described above, MRI has many limitations. It is expensive and time consuming and often requires referral to specialist facilities. MRI examinations are not suitable for patients with claustrophobia, pacemakers, or metal implants (15). Furthermore, MRI may result in adverse effects from the administration of contrast media (eg, nephrogenic systemic fibrosis in patients with renal insufficiency, allergic reaction). MRI cannot always exclude enthesitis; due to limited water accumulation, MRI signals are often low in structures that make up the entheses (42). Therefore, MRI alone may not be sufficient to consistently detect clinically meaningful changes in enthesitis (43). For instance, in the HEEL study of etanercept versus placebo in patients with SpA and heel enthesitis, significant improvement was observed with etanercept by clinical assessment using patient's global assessment but not by MRI (43). However, the trial size was small and only calcaneal bone marrow edema was considered (43). The development and use of composite scoring systems like HEMRIS may improve the utility of MRI in PsA.

Computed tomography (CT) and scintigraphy

CT has high spatial resolution and can detect structural changes, such as erosions. However, standard-resolution CT imaging is limited in its ability to detect synovial inflammation due to poor iodine contrast resolution and longitudinal data regarding its usefulness in diagnosing and monitoring enthesitis are lacking (44). Dual-energy CT iodine mapping, which improves iodine contrast resolution, has a higher spatial resolution than MRI and has shown promise in detecting inflammatory lesions, especially lesions in small joints (eg, distal interphalangeal [DIP] joints) (45, 46). Additional studies are needed to determine the role of this technique in the diagnosis of early-stage PsA and assessment of therapeutic effects. Positron emission tomography (PET)/CT using ^{18}F-fluorodeoxyglucose (FDG) may also be of value given that a retrospective study found high accumulation of FDG in the entheses of patients with SpA (47). In this study, PET/CT-FDG had a higher sensitivity for evaluating enthesitis than MRI; however, this was a small-scale, retrospective study, and further studies are needed.

Scintigraphy can also be used in PsA; radioisotopes that selectively bind to specific tissue types are taken internally, and the radiation they emit is captured by external detectors. However, due to lack of specificity, scintigraphy has been largely replaced by ultrasound and MRI (35, 44). Immunoscintigraphy aims to improve on the current technique by using a radiolabeled tumor necrosis factor (TNF) inhibitor (certolizumab pegol [CZP]) to detect TNF-α–driven inflammation in vivo (48). A recent study found that peripheral and axial inflammation could be detected in patients who received intravenous injections of radiolabeled CZP, with a strong correlation with therapy response: joints with no uptake of the tracer were more likely to remain tender despite treatment with CZP. These newer imaging modalities are promising but carry the limitation of exposing patients to radiation. Further evaluation of these modalities is necessary.

Using imaging to monitor treatment response in clinical trials

Multiple clinical trials have assessed the efficacy of biologic and small-molecule drugs in the treatment of enthesitis in PsA (2). However, the number of patients within these trials who have enthesitis at baseline varies widely (24% to 83%) (2). That is because patients with PsA are generally enrolled into clinical trials of biologic agents based on the CASPAR criteria, which do not mandate the presence of enthesitis (5); to date, very few trials have listed enthesitis as an inclusion criterion.

Overall, there is a need for studies that assess the effect of treatment on enthesitis and use imaging as an objective measure. Based on a search of ClinicalTrials.gov for studies that required ≥ 1 entheseal site at baseline and used imaging to assess response to treatment, only 2 studies have been designed to date and are currently ongoing.

The ACHILLES trial (NCT02771210) (49) is an ongoing phase 3, randomized, quadruple-blind study investigating the efficacy of secukinumab in the resolution of Achilles tendon enthesitis, including effects on inflammation as assessed by MRI, in PsA and axial SpA. The primary outcome measure is the proportion of patients with resolution of Achilles tendon enthesitis at week 24 as assessed by the LEI; secondary outcome measures include the percentage of patients with improvement of bone marrow edema as assessed by PsAMRIS. Key inclusion criteria are active PsA or axial SpA and MRI-positive heel enthesitis at baseline.

The ULTIMATE trial (NCT02662985) (50) is an ongoing phase 3, randomized, triple-blind study investigating the sensitivity of ultrasound to describe the time course of response to secukinumab in joint synovitis and enthesitis in PsA. The primary outcome measure is the difference between secukinumab and placebo in terms of joint synovitis at week 12 as assessed by the PDUS Global OMERACT-EULAR Synovitis Score; secondary outcome measures include improvement in enthesitis at week 12 as assessed by the Spondyloarthritis Research Consortium of Canada Enthesitis Index. Key inclusion criteria include active PsA and ≥ 1 clinically involved enthesitis site at baseline.

Results of these trials are anticipated to provide much-needed data on the validation of new imaging techniques and scoring scales in the monitoring of enthesitis during clinical trials.

Summary

Early diagnosis and treatment of PsA may prevent disease progression and structural damage (8). Given that enthesitis is a marker of PsA and an indicator of disease severity, early identification and treatment of enthesitis in patients with PsA is of great importance. Historically, enthesitis has been assessed using a combination of clinical examination and conventional radiography. However, the

usefulness of these techniques in the early identification of enthesitis is limited. Newer imaging techniques have since been developed (21, 30) that allow for direct visualization of the enthesis and related structures and offer the potential to systematically assess enthesitis earlier in the disease course, possibly leading to improved patient outcomes.

Despite this progress, there is currently no gold standard technique to detect enthesitis (9). Additionally, more research into the utility of ultrasound and MRI for the diagnosis and monitoring of enthesitis in PsA is required. Standardized definitions, imaging techniques, and operator protocols are needed, as are validated scoring systems. Clinical trials that focus on the treatment of enthesitis and use imaging to assess treatment response will allow the efficacy of new therapeutic agents to be assessed and compared more accurately. As technical improvements in imaging are realized, different imaging tools and scoring systems may be preferred for entheses in the lower limbs compared with those in non–weight-bearing, smaller structures. Overall, available data highlight the importance of incorporating imaging modalities in the clinical assessment and management of patients with PsA.

Acknowledgment

Medical writing support was provided by Victoria Kinsley, PhD (SciMentum) and Karen Chinchilla, PhD (ArticulateScience LLC), funded by Novartis Pharmaceuticals Corporation, East Hanover, New Jersey, in accordance with Good Publication Practice (GPP3) guidelines (http://www.ismpp.org/gpp3).

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Figure legends

Figure 1.

(**A**) Nail changes, dactylitis, and distal interphalangeal joint (DIP) subluxation, as seen during clinical examination. (**B**) Conventional radiographs (x-rays) of the same patient, exhibiting of "wispy periostitis," and DIP subluxation (indicated by the arrow). (**C**) Ultrasound providing a longitudinal view of the DIP extensor tendon (indicated by the triple asterisk), showing enthesitis in the hand (extensive cortical irregularity indicated by the downward arrow; DIP joint indicated by the upward arrow). Synovial effusion at the DIP joint can be seen (indicated by the double asterisk) as can synovial hypertrophy (single asterisk). (**D**) Power Doppler ultrasound (PDUS) showing the same area of damage as panel C, with Doppler signal indicating active inflammation around the cortical irregularity.

Figure 2.

(**A**) A large enthesophyte (as indicated by the arrow) as well as significant retrocalcaneal bursitis and bursal synovitis (as indicated by the double asterisk). Retrocalcaneal bursal effusion can also be seen, as indicated by the single asterisk). (**B**) Achilles enthesitis which includes large erosions (as indicated by the arrow) and cortical irregularities. (**C**) Significant bone proliferation of the calcaneus (indicated by the arrows), as well as tendon hypoechogenicity, thickening, and loss of fibrillar echotexture. (**D**) Active inflammation as indicated by Doppler signal, located at the distal portion of the Achilles tendon.

Figure 3.

(**A**) Short T1 inversion recovery (STIR) magnetic resonance imaging (MRI) showing high signal intensity at the Achilles tendon insertion (enthesitis, indicated by the yellow arrow) and bone marrow edema (short thin arrow). Long thin arrow shows high signal intensity in the synovium of the ankle joint (synovitis). Image reproduced with permission from McQueen F, et al. *Arthritis Res Ther*. 2006;8:207. © BioMed Central Ltd 2006. (B) T1-weighted, contrast-enhanced MRI showing inflammation at enthesis (indicated by the yellow arrow) and bone erosion at the tendon insertion

(short thin arrows). Image reproduced with permission from McQueen F, et al. *Arthritis Res Ther*. 2006;8:207. © BioMed Central Ltd 2006. (C) Dynamic contrast-enhanced MRI technology superimposed on an axial T1-weighted dynamic MRI of the wrist showing tenosynovitis. The wrist synovial membrane is outlined in blue (joint synovial membrane compartment indicated by SYN) and regions around the tendon sheaths are yellow (first to third extensor compartment indicated by EI-III, first and second flexor compartment indicated by FI-II). Reprinted with permission from The Journal of Rheumatology, Cimmino MA, et al. *J Rheumatol*. 2012;39(Suppl 89):44-48. All Rights reserved. (D) Whole-body MRI enables visualization of multiple potential sites of enthesitis in 1 scan but at a lower resolution than conventional MRI. Østergaard M, et al. *Best Pract Res Clin Rheumatol*. 2016;30:624-637. Copyright 2008, with permission from Elsevier.

Table 1. Clinical indices **(A)** and ultrasound scoring scales **(B)** used in the assessment of enthesitis

A. Clinical indices used for the assessment of enthesitis

Index Name/Scoring System	Originally Devised for	No. of Sites Examined	Sites Examined	Features	Imaging Modality
Leeds Enthesitis Index (LEI)* (2, 11)	PsA	6	Bilateral lateral epicondyles, medial femoral condyles, and Achilles tendon insertions	Only index specifically developed for PsA; has been used in several PsA trials—Developed by clinical identification of the most frequent enthesitis sites Physical examination measuring tenderness as either present (1) or absent (0) at each site, resulting in an overall score of 0-6 Higher count indicates greater enthesitis burden Most reliable index for PsA; correlates most closely with disease activity compared with MASES and SPARCC	None
Spondyloarthritis Research Consortium of	SpA	16	Bilateral Achilles tendons, plantar fascia insertion at the	Assessment sites based on power Doppler US in SpA and MRI studies in AS. Most common sites for enthesitis were identified	None

Canada (SPARCC) index* (2, 11)			calcaneus, patellar tendon insertion at the base of the patella, quadriceps insertion into the superior border of the patella, supraspinatus insertion into the greater tuberosity of the humerus, and medial and lateral epicondyles	Physical examination measuring tenderness as either present (1) or absent (0) at each site, resulting in an overall score of 0-16 Higher count indicates greater enthesitis burden Modified versions measuring 6-8 more commonly involved sites have shown greater responsiveness Not validated for use in PsA, although has been tested in this patient population	
The Maastricht Ankylosing Spondylitis Enthesis Score (MASES)* (2, 11, 12)	AS	13	First costochondral joints, seventh costochondral joints, posterior and anterior superior iliac spines, iliac crests, proximal insertion of Achilles tendons, fifth lumbar spinous process (does not assess many of	Developed from the Mander/Newcastle Enthesitis Index (most comprehensive index for AS, with 66 clinically accessible enthesis sites) Most specific and sensitive sites were selected to reduce assessment time Physical examination measuring tenderness as either present (1) or absent (0) at each site, resulting in an overall score of 0-13 Higher count indicates greater enthesitis burden	None

			the peripheral sites characteristic of PsA)	Not validated for use in PsA, although a PsA-modified version has been developed	

AS, ankylosing spondylitis; MRI, magnetic resonance imaging; PsA, psoriatic arthritis; SpA, spondyloarthritis; US, ultrasound.

*LEI, MASES, and SPARCC have all been used in recent trials of PsA (2).

B. Ultrasound scoring scales used in the assessment of enthesitis

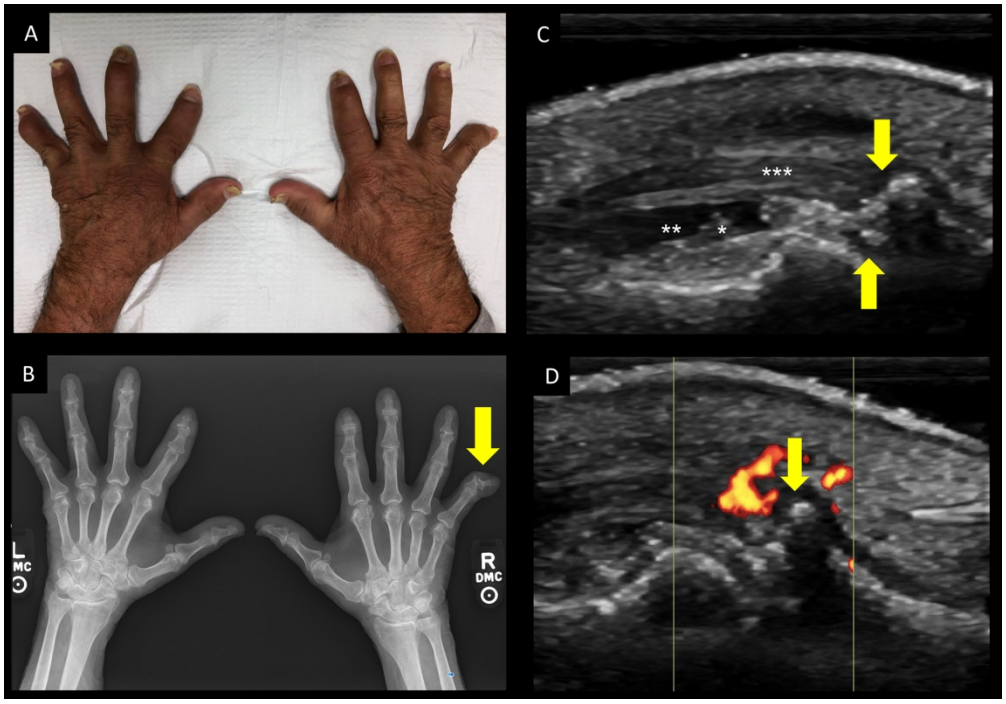
Index Name/ Scoring System	Originally Devised for	No. of Sites Examined	Sites Examined	Features	Imaging Modality
OMERACT Ultrasound Working Group (19)	SpA and PsA	4 (3 lower limbs, 1 upper body)	Superior and inferior poles of the patella, calcaneal insertion of Achilles tendon; lateral condyle of the elbow	Developed to monitor changes in inflammatory lesions following treatment	Gray scale and PD
				Evaluates global enthesis involvement in an individual patient	
				Each enthesis evaluated (yes/no basis) for seven elementary components (hypoechogenicity, increased thickness, enthesophyte, calcification, bone erosion, bone irregularity and PD)	
				Next steps will be to weigh the different inflammatory components and test their sensitivity to change	

The GRAPPA Ultrasound Working Group (20, 24)	PsA	6 (4 lower limbs, 2 upper body)	Patellar ligament insertions into distal patella and tibial tuberosity, Achilles tendon, plantar fascia; supraspinatus, lateral epicondyle	Developed to allow for early diagnosis of PsA	Gray scale and PD
				Evaluates global enthesis involvement in an individual patient	
				Assesses 5 elementary lesions (hypoechogenicity, thickening, enthesophyte, erosions and Doppler signal) of six entheseal sites	
				Identified 6 entheseal sites important for distinguishing patients with PsA from those without the disease: patellar ligament insertions into the distal patella and tibial tuberosity, Achilles tendon and plantar fascia insertions into the calcaneus, common extensor tendon insertion into the lateral epicondyle, and supraspinatus insertion into the superior facet of the humerus	
				Aims to distinguish patients with PsA from age and sex-matched healthy controls, and monitor response to treatment	
Glasgow	SpA	5 (lower limb	Quadriceps tendon,	Developed for diagnosis of SpA	Gray scale

Ultrasound Enthesis Scoring System (2, 21, 25)		only)	patellar ligament (proximal and distal), Achilles tendon, plantar aponeurosis	Assesses 18 features of 5 entheses—grading individual enthesis involvement First scoring system to be published (2002)	
Sonographic Enthesitis Index (26)	AS	5 (lower limb only)	Quadriceps tendon, patellar tendon (proximal and distal), Achilles tendon, plantar aponeurosis	Developed for monitoring disease activity and entheseal response to treatment Evaluates global enthesis involvement in an individual patient Differentiates between inflammatory and structural damage Does not differentiate between involvement of enthesis, body of tendon, and bursa	Gray scale
Madrid Sonographic Enthesitis Index (21, 27)	SpA	6 (5 lower limbs, 1 upper body)	Quadriceps tendon, patellar tendon (distal and proximal), Achilles tendon, proximal plantar fascia; distal triceps tendon	Developed for the diagnosis of SpA Evaluates global enthesis involvement in an individual patient Scores calcifications, bursae, erosions, PD signal, and thickness and structure	Gray scale and PD
D'Agostino et al.	SpA	9 (lower	Great tronchanter, pubis,	Developed for diagnosis of SpA	Gray scale and

(28)		body entheses)	quadriceps tendon, patellar tendon, tibialis anterior tendon, Achilles tendon, plantaris fascia, lateral epicondyle, medial epicondyle	5 stages to grade individual enthesis involvement	PD
				Differentiates between early enthesitis, morphological alterations, and inactive lesions	

AS, ankylosing spondylitis; GRAPPA, Group for Research and Assessment of Psoriasis and Psoriatic Arthritis; MRI, magnetic resonance imaging; OMERACT, Outcome Measures in Rheumatology; PD, power Doppler; PsA, psoriatic arthritis; SpA, spondyloarthritis; US, ultrasound.



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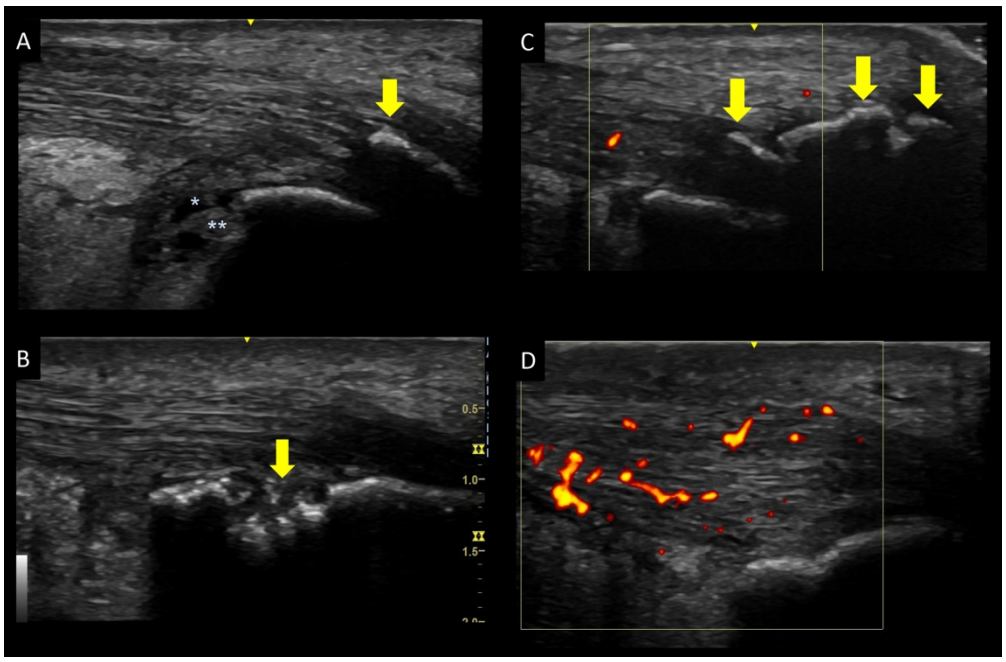

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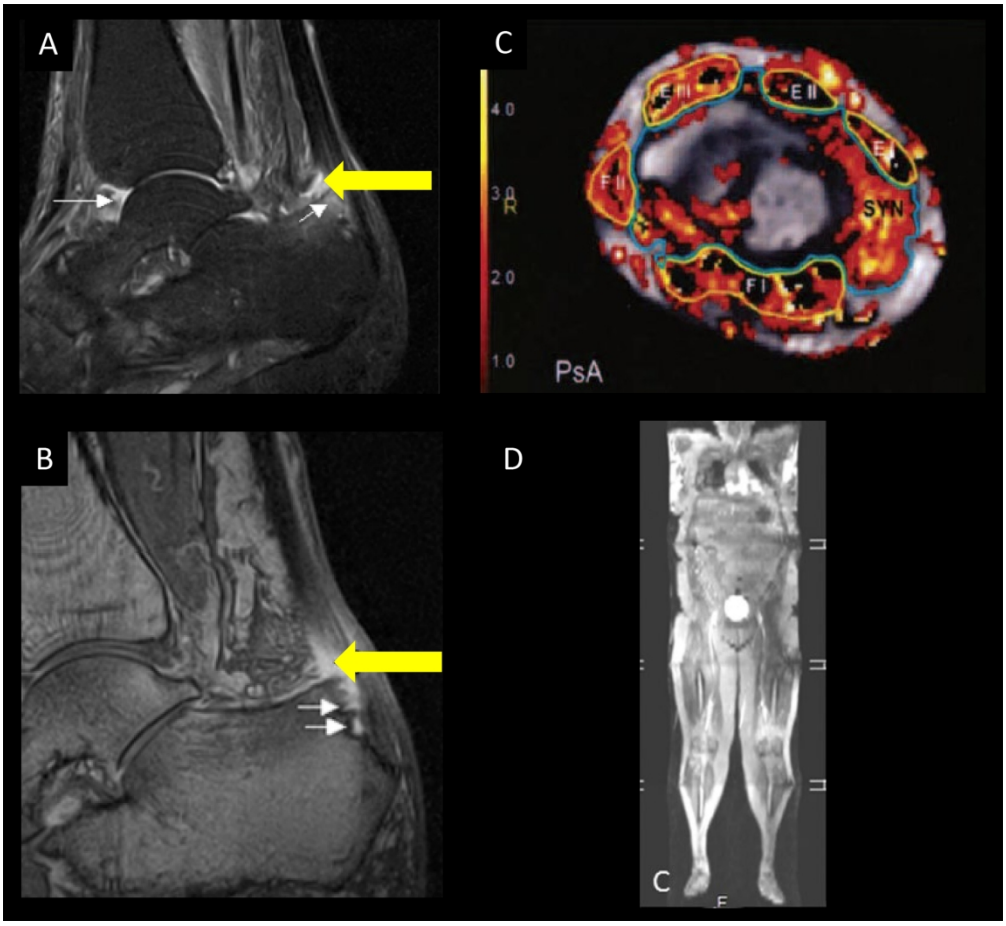

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Appendix and data supplements

Literature review search strategy

Relevant literature was identified by conducting a targeted search of the medical literature available in PubMed. Broad searches were initially performed using “enthesitis” alone and in combination with several different terms, including “psoriatic arthritis,” “imaging,” “conventional radiography,” “ultrasound,” “magnetic resonance imaging,” “computed tomography,” “spectral computed tomography,” “scintigraphy,” “GRAPPA,” and “OMERACT.” Only English-language articles indexed in PubMed through December 2018 were included. Titles, abstracts, and full reports of the identified articles were screened for relevance. Additional articles were identified using terms such as “Leeds Enthesitis Index,” “Spondyloarthritis Consortium of Canada,” “Psoriatic Arthritis Magnetic Resonance Imaging Score,” “Glasgow Ultrasound Enthesis Scoring System,” “Spanish Enthesitis Index,” and “Madrid Sonographic Enthesitis Index” from the references cited in articles of interest and based on the authors’ knowledge of the published literature. Articles were considered relevant if they presented data on enthesitis in psoriatic arthritis or on imaging techniques used in its assessment.