

The Ultrasound Imaging Module: A Report from the GRAPPA 2010 Annual Meeting

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ABSTRACT. In a plenary session at the 2010 meeting of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA), the use of sonography for evaluating articular disease and enthesitis in psoriasis and psoriatic arthritis (PsA) was reviewed. Ultrasound can readily demonstrate signs of synovitis, erosions, and osteoproliferation. There is a need to develop ultrasound joint indices to evaluate and follow PsA longitudinally. Sonography is able to depict ultrastructural features of enthesitis, as well as increased vascularity. Sonographic signs of subclinical enthesitis in patients with psoriasis have been reported by 2 groups, 1 of which has reported limited longitudinal data that suggest baseline composite enthesitis scores may predict future risk of PsA. Although recent studies have studied mostly lower extremity entheses, further work is needed to clarify if other areas need to be included, especially within the framework of the synovial enthesal complex. The study design of the PREPARE (Prevalence of Psoriatic Arthritis in Adults with Psoriasis) trial was also presented. (J Rheumatol 2012;39:404–7; doi:10.3899/jrheum.111234)

Key Indexing Terms:

PSORIATIC ARTHRITIS

DOPPLER SONOGRAPHY

ENTHESITIS

At the annual meeting of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) in December 2010, an imaging plenary session, chaired by Mikkel Østergaard and Gurjit S. Kaeley, included modules on ultrasound (US) and magnetic resonance imaging (MRI). These 2 advanced imaging techniques are increasingly utilized for diagnostic purposes to assess the presence of synovitis, enthesitis, and other aspects of inflammation. Further, they may identify joint damage earlier than plain radiography. A comprehensive review of US in PsA by Dr. Kaeley and a presentation of the PREPARE (Prevalence of Psoriatic Arthritis in Adults with Psoriasis) trial by Dr. Bakewell are summarized below.

Systematic Review of US Use in Psoriatic Arthritis

A systematic literature review was undertaken to examine the current use of US to image the peripheral manifestations in psoriatic arthritis (PsA), using the following terms in various combinations: PsA, psoriatic enthesitis, US, sonography (or ultrasonography), and Doppler. A total of 138 articles were identified (137 by PubMed search; one by hand search). Of these, 107 articles were excluded (26 were non-English, 22 were review articles, and 59 were not relevant to this discus-

sion). The remaining 31 publications are cited here and include those focused on articular disease (n = 12) and those that deal with enthesitis (n = 19).

Sonography in the Evaluation of Articular Disease in PsA

Of the 12 articles with an articular focus, 4 reported studies of the joints of the hand and wrist^{1,2,3,4}. Weiner, *et al* reported better sensitivity of US and plain radiography in detecting erosions and osteoproliferations than MRI. However, MRI had better sensitivity in detection of synovitis³. In a small study comparing healthy controls with patients with rheumatoid arthritis (RA) and PsA (5 each), Wiell, *et al* reported greater sensitivity for detecting pathologic change compared with plain radiographs and clinical evaluation⁴. US detected osteoproliferation more frequently at the distal interphalangeal joints. The authors also showed that US had fair reliability and high concordance with MRI for erosive changes, but moderate concordance for inflammatory changes⁴. Of note, both the aforementioned studies used a transducer with a frequency below 15 MHz. It is possible that sensitivity may improve with use of contemporary high-frequency transducers.

Three studies have examined patients with PsA longitudinally in response to therapy^{1,5,6}. Iagnocco, *et al*⁶ and Fiocco, *et al*⁵ reported good reliability in assessing knee joint synovitis with sonography. Reduction in B-mode synovial hypertrophy as an exploratory endpoint was reported in a study of methotrexate-refractory patients with PsA who were given methotrexate plus cyclosporine or placebo¹.

In comparison with sonographic studies in RA patients, US indices of joint examination have not been developed or validated in patients with PsA, where peripheral arthritis has heterogeneous presentations. Future indices may need to include representative joints of the hands and feet as well as large joints.

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Sonography in the Evaluation of Enthesitis in Psoriasis and PsA

Nineteen articles examined enthesitis in cohorts that were solely or partly composed of psoriasis and PsA patients. Some investigators concentrated their efforts on an anatomical area^{7,8,9,10}. Of note, Falsetti, *et al* studied the lateral deltoid origin and proposed that sonographic signs of enthesitis at this site may have a high diagnostic specificity⁷. In an MRI study of shoulders of patients with ankylosing spondylitis, Lambert, *et al* also reported on the specificity of enthesitis of the deltoid origin¹¹. Although traditional lower extremity entheses have been examined by several investigators, only one study in patients with PsA has examined the medial and lateral ankle compartments: Galluzzo, *et al* found that up to one-third of a largely asymptomatic cohort of patients with PsA had posterior tibial tendon tenosynovitis¹². There has been some debate whether the study of entheses should be expanded to the synovial enthesal complex and to areas such as the posterior tibial tendon (e.g., the bone pulley entheses)¹³. A similar argument has been made in proposing dactylitis as a functional entheses. Earlier reports suggested that dactylitis was caused predominantly by flexor tendon tenosynovitis^{14,15}. However, recent studies have demonstrated diffuse edema within the digit^{16,17,18}. Sonography may demonstrate diffuse dorsal edema, as well as edema in the extensor tendon and increased Doppler signal.

With regard to occult musculoskeletal inflammation in patients with psoriasis, several authors have reported sonographic examination of these patients^{9,19,20,21,22,23,24}. Although all these studies have relied upon examination of entheses, not all reported duration of psoriasis or the PASI (Psoriasis Area and Severity Index) or NAPS (Nail Psoriasis Severity Index) scores; nor did they control for the use of retinoids. The most recent studies by Gisondi, *et al* and Gutierrez, *et al* reported that patients with psoriasis had an increased composite lower extremity enthesal GUESS (Glasgow US Enthesitis Scoring System) score compared to controls^{23,24}. Gutierrez, *et al* also reported finding Doppler US signal more often in patients with psoriasis²⁴; Gisondi, *et al* did not utilize Doppler. Another difference between the 2 studies was that Gutierrez, *et al* found calcaneal erosions in a minority of patients while Gisondi, *et al* reported none. Gisondi, *et al* also proposed modifying the GUESS score by not scoring radiologically detected enthesophytes; the authors believed that large osteophytes may not be specific for spondyloarthritis. However, this approach has not been validated, and others believe the opposite — that large osteophytes may be more specific for spondyloarthritis²⁵.

The aforementioned studies used the GUESS composite score to evaluate enthesitis. A search of the literature identified other composite scoring systems for evaluating enthesitis (Table 1), all of which record various ultrastructural changes at the entheses^{26,27,28,29,30,31,32}. However, as noted above, there are different approaches to treating some of the elemen-

tal lesions (Table 2)^{26,27,28,29,30,31,32}. In addition, power Doppler is not universally used by all the groups. Most of these indices were developed in a heterogeneous group of patients with spondyloarthritis, predominantly patients with ankylosing spondylitis. It is not clear if the indices will be helpful in patients with psoriasis or PsA. It will be important to maintain a balance between feasibility and comprehensiveness in the number and selection of entheses studied, as well as to examine aspects of B-mode ultrastructural change and vascularity by Doppler in a longitudinal manner.

Prevalence of PsA in Adults with Psoriasis (PREPARE) Trial: An Estimate from Dermatology Practice

GRAPPA was eager to hear about the PREPARE trial with regard to the utility of US and MRI imaging modalities, as well as the value of PsA screening questionnaires and careful rheumatologic examination in the evaluation of patients with psoriasis. Although results are not yet available, the study design was presented to the group by Dr. Bakewell.

The primary objective of this clinical trial (sponsored by Pfizer) is to determine the prevalence of PsA in patients with psoriasis presenting to dermatologist offices. Designed as a phase 4, multicenter, randomized, nontherapeutic interventional trial, the goal is to enroll 1000 subjects with psoriasis at 50 different international sites. Once enrolled, subjects attend 2 or 3 sequenced visits.

Visit 1, dermatology evaluation. In addition to history and physical examination, all enrolled subjects will complete 1 of 3 randomly selected questionnaires: the Toronto PsA Screening questionnaire (ToPAS), Psoriasis Epidemiology Screening Tool (PEST), or the Psoriasis and Arthritis Screening Questionnaire (PASQi). Six different health outcome measures will also be used to examine quality of life, productivity, and healthcare resource utilization.

Visit 2, rheumatology evaluation. In addition to history, physical examination, and laboratory studies, the rheumatologist will diagnose the presence or absence of PsA, which will address the primary objective of the study. Health outcomes measures will also be performed.

Visit 3, imaging. This optional visit will occur at selected centers, during which the patient will undergo imaging, including US, MRI, and plain radiographs.

The study is also designed to ascertain the prevalence of previously undiagnosed PsA, with the hope that earlier diagnosis and intervention will ultimately lead to improved outcomes.

Discussion and Future Collaborative Efforts within GRAPPA

The group discussed the use of sonography to examine nail changes in psoriasis. Although ultrastructural nail changes as well as vascular changes have been described, no studies to date have examined this in a systematic fashion. The group

Table 1. Summary of selected enthesal scoring systems.

Entheses Examined	GUESS	MASEI	SEI	Spanish School	“Sono” MASES	D’Agostino
Knee (quadriceps and patellar)	+	+	+	+		+
Achilles tendon	+	+	+	+	+	+
Plantar fascia	+	+	+	+		+
Triceps		+				
Elbow—medial and lateral epicondyle				+		+
1st and 7th costosternal joints					+	
Anterior and posterior iliac spines, iliac crests					+	
5th lumbar spinous process					+	
Greater trochanter						+
Pubis						+
Tibialis anterior tendon						+
Doppler		+		+	+	+

GUESS: Glasgow Ultrasound Enthesitis Scoring System²⁷; MASEI: Madrid Sonographic Enthesitis Index²⁸; SEI: Sonographic Enthesitis Index²⁶; Spanish School³¹; “Sono” MASES: Maastricht Ankylosing Spondylitis Entheses Score^{29, 30}; D’Agostino, *et al*³².

Table 2. Ultrastructural elements utilized in selected enthesal scoring systems.

Enthesal Morphology	GUESS	MASEI	SEI	Spanish School	“Sono” MASES	D’Agostino
Peritendinous fluid			+			
Tendon structure		+	+	+	+	+
Tendon thickness	+	+	+	+		+
Adjacent bursitis	+	+	+	+	+	+
Adjacent periosteal changes, including bone erosions	+	+	+	+	+	+
Enthesis calcification	+	+	+	+	+	+
Tendon tear/loss of tendon thickness			+			
Enthesis Doppler		+	+	+	+	+

GUESS: Glasgow Ultrasound Enthesitis Scoring System²⁷; MASEI: Madrid Sonographic Enthesitis Index²⁸; SEI: Sonographic Enthesitis Index²⁶; Spanish School³¹; “Sono” MASES: Maastricht Ankylosing Spondylitis Entheses Score^{29, 30}; D’Agostino, *et al*³².

also discussed controlling for the use of retinoids, which may cause calcification at entheses; only one study (Gisoni, *et al*) has controlled for this²³. Although subclinical enthesitis has been reported by 2 groups studying patients with psoriasis without articular symptoms, the significance of these findings is unclear. Preliminary retrospective analysis of the original cohort reported by Gisoni, *et al* suggested that the small number of patients who progressed to PsA had a high baseline GUESS score; however, these patients also had high PASI and NAPSI scores²².

The group expressed interest in future collaboration in the use of US in patients with PsA, including developing sonographic indices for evaluation and followup of articular manifestations. Since PsA is heterogeneous, the index would need to evaluate representative joints as well as features unique to PsA such as periostitis. Consensus will also be necessary regarding which entheses to examine sonographically, which ultrastructural components to include, whether to consider the

synovial enthesal complex, and the need for longitudinal followup of subclinical or asymptomatic enthesitis in patients with psoriasis.

In summary, sonography offers an excellent opportunity to study joint and enthesal disease in psoriasis and PsA. It may detect subclinical disease, provide insight to the heterogeneous pathophysiology of musculoskeletal inflammation, and assist in correlating the patient’s symptoms. However, more work must be done to reach a consensus on the methods used to examine and follow patients with psoriasis or PsA.

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