Editorial

The Sound of Enthesis



The enthesis, a 1-millimeter universe, is an area of great interest for the spondyloarthritis (SpA) research community. Our understanding of this critical anatomical area has dramatically improved over the past few years, but much remains to be learned. Ultrasonography (US) provides an innovative approach to the investigation of this still mysterious point of union between bone and other anatomical structures (tendon, ligament, aponeurosis, capsule)[1,2,3,4,5,6,7,8].

Entheses appear to be perfect targets for US because most of them are superficial and can be explored with very high frequency probes[9,10,11,12]. The availability of high-resolution equipment has opened up new and fascinating possibilities in the assessment of minimal details of tendons, fibrocartilage, and bone surface. The level of spatial resolution of widely available 18 MHz probes has broken the 0.1-mm barrier, allowing access to an impressive amount of otherwise unobtainable images of the various phases of early and late inflammatory and degenerative changes involving the enthesis. This plethora of images can be problematic. US researchers are facing the challenge of how best to interpret, organize, and classify an incredibly wide range of new findings. These challenges are similar to those faced by astronomers after the tsunami of images generated by the Hubble space telescope.

The most impressive aspect of US in the assessment of enthesopathy is the wide range of both grayscale and power Doppler (PD) patterns even in patients with early or subclinical disease[13,14].

The main entheseal abnormalities that can be detected by US include tendon edema, loss of fibrillar echotexture, tendon thickening, tendon tear, calcific deposits, bone erosion, enthesophytes, adjacent bursitis, and increased blood perfusion (intraentheseal and/or perientheseal). Combinations of these findings generate complex mosaics that will require new methodologies in interpretation and standardization.

A first step is the preliminary US definition of enthesopathy by the Outcome Measures in Rheumatology group (OMERACT)[15]. It is defined as an "abnormally hypoechoic (loss of normal fibrillar architecture) and/or thickened tendon or ligament at its bony attachment (may occasionally contain hyperechoic foci consistent with calcification), seen in 2 perpendicular planes that may exhibit Doppler signal, and/or bony changes including enthesophytes, erosion, or irregularity"[15]. Other attempts at standardization of enthesopathy include the Glasgow Ultrasound Enthesitis Scoring System (GUESS) and the Madrid Sonographic Enthesis Index (MASEI)[16,17].

In this issue of *The Journal*, Naredo and coworkers, in a large study involving 35 centers using the same US equipment, have demonstrated that US including PD assessment can be used as a valuable tool to assess response to therapy in SpA[18]. It is noteworthy that Spain has a uniform training program supported by the Spanish Society of Rheumatology and the highest percentage of rheumatologists trained in musculoskeletal US. If sonographic equipment is regarded as a musical instrument then the Spanish Ultrasound Orchestra is performing high quality concerts.

In spite of this, their study did not attempt complete standardization of scanning protocols among study participants. Had they done so, it might have improved the quality of the results, especially for PD assessment, which is influenced by both the scanning technique and patient position. Changes in the position of the knee or foot can dramatically alter the typical PD findings indicating an active enthesitis of the lower limbs (quadriceps, patellar, and Achilles tendon)[19].

The article by Naredo and coworkers is the first that has separately evaluated response to therapy of different US abnormalities at multiple entheseal sites. This approach opens up new possibilities in the field of therapy monitoring of SpA. The study demonstrated a highly significant improvement of both morphologic abnormalities (hypoechogenicity and/or thickening) and PD signal. A significant improvement of adjacent bursitis has also been observed. Conversely, entheseal cortical abnormalities

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(bone erosion and/or enthesophytes) and entheseal calcifications did not improve throughout the followup period, in spite of therapy.

These results confirm that US is a powerful and sensitive tool to explore both activity and severity of the inflammatory process involving the enthesis. It is possible, in a single image, to demonstrate even minimal inflammatory features (edema, thickening, adjacent bursitis and local perfusion) alongside features indicating inflammatory-related anatomical damage (bone erosion and/or enthesophytes). The authors also demonstrated that entheseal abnormalities are sensitive to change for monitoring response to therapy in patients with SpA.

The potential of US can be regarded as even more promising, considering that the study was carried out with a relatively low Doppler frequency (not higher than 7 MHz) in contrast with the higher frequencies now routinely available.

On the basis of their experience, the authors stress that "US imaging *could be* incorporated as a complementary tool into the overall assessment of SpA involvement and disease activity, as well as being incorporated into the monitoring of response to therapy." We don't agree with this soft position. As extremists of US imaging, we believe that it is time to accept that US *must be* incorporated as a basic tool into the overall assessment of SpA involvement and disease activity, as well as being incorporated into the monitoring of response to therapy.

The research agenda includes several critical issues that must be addressed:

- Which is the best approach to quantification of US findings?
- How many entheseal sites should be routinely examined in daily clinical practice?
- What are the gold standard technical requirements for a comprehensive assessment of the enthesis in patients with SpA?
- Which US findings should be systematically assessed in daily rheumatological practice in order to get the best compromise between scanning time and clinically relevant information?

New technological solutions for unresolved problems are on the horizon. 3D and 4D US offer new avenues in standardization and quantification of findings. Elastosonography is a useful adjunct to conventional US in the evaluation and characterization of tendon involvement[20]. An even more exciting perspective is offered by fusion imaging (a process of combining information from 2 or more imaging modalities into a single image). The combination of high resolution/high sensitivity grayscale and PD US with magnetic resonance imaging (MRI) enables detailed assessment of both the extent and topographic relationship between bone edema (and other morphofunctional MRI findings) and grayscale and PD data. The near future promises exciting challenges.

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