
Overview of musculoskeletal ultrasound for the clinical rheumatologist

S. Hassan

Rheumatology Division, Rush University
Medical Center, Chicago, USA.

Sobia Hassan, MD, MRCP, RhMSUS

Please address correspondence to:

Dr Sobia Hassan,

Rheumatology Division,

1611 W Harrison St., Suite 510,

Rush University Medical Center,

Chicago, IL 60612, USA.

E-mail: sobia_hassan@rush.edu

Received on August 29, 2018; accepted in
revised form on September 10, 2018.

Clin Exp Rheumatol 2018; 36 (Suppl. 114):
S3-S9.

© Copyright CLINICAL AND

EXPERIMENTAL RHEUMATOLOGY 2018.

Key words: musculoskeletal
ultrasound

ABSTRACT

Within the realm of rheumatology, the field of musculoskeletal ultrasound (MSUS) has grown exponentially over the last few decades. This review, aimed at the clinical rheumatologist, provides a basic overview of the principles of image generation and the commonly used clinical applications of MSUS, while also highlighting its advantages and limitations. In particular, the role of MSUS in the assessment of early and established rheumatoid arthritis, crystalline disease, the spondyloarthropathies and Sjögren's disease is discussed in more detail and by reviewing the pertinent literature.

Introduction

Since K.T. Dussik first published on the use of ultrasound (US) to image articular and periarticular tissues in 1958 and the first detailed US image of a human joint was published in 1972, the field of musculoskeletal US (MSUS) has grown exponentially (1). This growth has been driven by increased interest and utilisation by rheumatologists, as well as advances in technology that have led to the development of high resolution transducers that can image superficial structures such as joints, tendons and nerves in great detail and with a lateral and axial resolution of 0.1 mm. Many rheumatologists have come to regard MSUS as an extension of their clinical exam and an essential tool in their diagnostic armamentarium, with MSUS even being referred to as the rheumatologists' "third eye", "stethoscope", or "extended finger."

This article will provide a basic explanation of how MSUS produces images, its advantages and limitations, in addition to an overview of the ever expanding clinical applications of MSUS within the field of rheumatology.

A basic explanation of how MSUS produces images

Ultrasound refers to sound waves that have a frequency above the limits of human hearing (20–20,000 Hertz), with modern day machines generating sound waves in the order of 2–15 Mega Hertz. When connected to a power source, piezoelectric crystals in the transducer of the US machine vibrate to produce sound waves that then travel from the probe, through a coupling medium (gel) into the body. When the US waves encounter an acoustic interface (a change in density/stiffness between two adjacent tissues), some sound waves are reflected back to the probe while others travel down deeper into the body. Signals returning to the probe are converted into an electric signal and displayed as a black and white two dimensional image on the screen (Brightness "B" mode).

The greater the difference between two acoustic interfaces, the more sound waves that will be reflected back creating a "whiter" or "hyperechoic" image. An example of this would be at the interface between cartilage and bone, at which bone will appear as a hyperechoic (white) signal. If there is no difference in the density of two tissues, the sound waves will travel straight through with no reflection of waves and the image will appear black or anechoic (such as fluid within a cystic structure).

Whereas grey-scale US images provide morphological information on anatomical structures, the power Doppler (PD) capabilities of the US machine detect motion of moving blood vessels and display them as a colour signal. Within the realm of rheumatology, PD can be used to detect pathologic low flow states produced by small blood vessels in inflamed joints.

Competing interests: none declared.

Advantage of MSUS

US is a relatively cost effective and patient-friendly imaging modality as there is no associated ionising radiation or concern for claustrophobia. For many rheumatologists trained in MSUS, the availability of a machine at the point of care, provides the capacity to obtain immediate answers to clinical questions. US is also easily repeatable and can be used to assess several joints at one sitting (unlike MRI). In addition, dynamic studies can be performed which can be useful to demonstrate impingement syndrome of the shoulder, for example, or to “milk” small amounts of fluid into a joint for aspiration.

Limitations of MSUS

The disadvantages of US are its relatively small field of view compared to MRI and the fact that the US beam cannot penetrate beneath bone. In addition, US is highly operator dependent, with a steep learning curve. A number of artifacts (PD artifacts and anisotropy) may be seen that the sonographer should be aware of, so as not to mistakenly identify pathology where there is none. In addition, one must be careful not to over-interpret subtle US abnormalities that are detected by “sensitive” US machines and may not indicate disease.

Until recently, there has been variation in the definitions of US pathology (synovitis), a lack of standardised imaging protocols (wide range and number of joints used) and also variation of validity among scoring systems (2). However, there are increasing efforts to develop clearer definitions and standardised consensus-based scoring systems (3).

Clinical applications of MSUS for the rheumatologist

Panels of experts including those from the ACR (4), EULAR (5) and others (6) have established several scenarios where MSUS can be beneficial to the rheumatologist and within their scope of training as listed below:

1. To detect subclinical inflammatory arthritis and enthesitis.
2. To detect structural damage and ongoing disease activity in patients with established arthritis.
3. To identify signs of monosodium

Table I. US pathology findings and their OMERACT definitions.

US FINDING	OMERACT DEFINITION [7, 8]
Erosions (Fig 2)	An intra-articular discontinuity of the bone surface that is visible in two perpendicular planes.
Synovial effusion	Abnormal hypo or anechoic area that can be displaced or compressed but does not exhibit Doppler signal.
Synovial Hypertrophy/synovitis (Fig 1)	Abnormal hypoechoic intra-articular tissue that is non-displaceable and poorly compressible and which may exhibit a Doppler signal
Double Contour sign (Fig 2)	Abnormal hyper echoic band over the superficial margin of the articular hyaline cartilage, independent of the angle of insonation and which may be either irregular or regular, continuous or intermittent and can be distinguished from the cartilage interface sign.
Tophus (Fig 3)	Circumscribed, inhomogeneous, hyperechoic and/or hypoechoic aggregation (which may or may not generate posterior acoustic shadow), which may be surrounded by a small anechoic rim.
Tenosynovitis	Hypoechoic or anechoic thickened tissue with or without fluid within the tendon sheath, which is seen in 2 perpendicular planes and which may exhibit Doppler signal.
Enthesopathy	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, erosions, or irregularity.

urate (MSU) and calcium pyrophosphate dihydrate deposition (CPPD) in patients with crystalline arthritis.

4. To evaluate the cause of periarticular pain.
5. To assess nerve entrapments
6. To evaluate the parotid and submandibular glands in the evaluation of Sjögren’ disease.
7. To guide articular or periarticular aspirations and injections.

The shoulder, elbow, wrist, hand, knee, ankle and foot are the joints that are commonly imaged in MSUS. In more experienced hands, MSUS is also being used to guide biopsy of synovial tissue. US also has applications beyond imaging joint structures, including imaging vessels in the assessment of vasculitis and the lungs in the assessment of interstitial lung disease, as discussed in detail by others in this supplement.

MSUS use in the assessment of inflammatory arthritis

MSUS is useful to detect bone erosions, synovitis, tendon abnormalities,

rheumatoid nodules, tophi and other signs of crystal deposition (Table I, Figs. 1-4). In addition, the PD capabilities of US machines allow for the detection of pathological synovial blood flow. The presence of Doppler activity in a region of synovial hypertrophy is the most specific marker of “active” synovitis, but its absence does not necessarily indicate the absence of inflammation, due to the variable sensitivities and operator-dependent factors of various US machines.

The severity of grey-scale synovitis and PD activity can be graded according to semi-quantitative scoring systems (3).

Role of MSUS in the evaluation of rheumatoid arthritis (RA) and undifferentiated inflammatory arthritis (UIA)

Multiple studies have demonstrated that US has a higher sensitivity than clinical examination to detect synovitis, with the mean detection rate for synovitis at the hand and wrist being 2.18-fold higher using US (9).

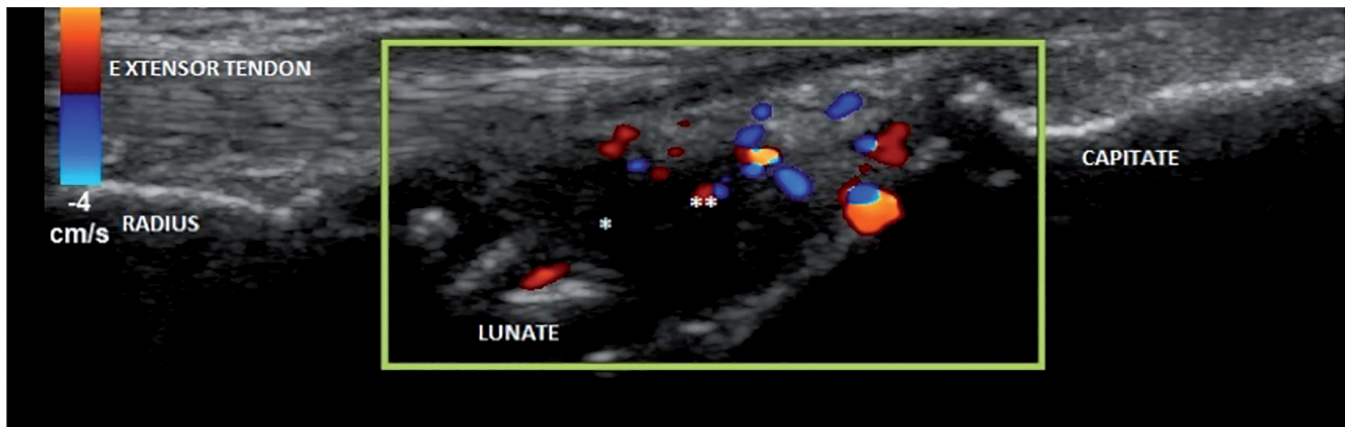


Fig. 1. US image showing the wrist of a patient with rheumatoid arthritis. *synovial hypertrophy and **positive power Doppler signal.

US also detects erosions at a higher rate than conventional radiography. In one study, Szkudlarek *et al.* used MRI, ultrasound, conventional x-ray, and clinical examination to evaluate 200 metatarsophalangeal (MTP) joints in 40 patients with RA and 100 MTP joints from 20 healthy controls. Erosive disease was identified in 65% of patients by US, compared with 50% of patients by MRI and 28% of patients by radiography. With MRI considered the reference method, the sensitivity of US for the detection of bone erosions (on a lesion, rather than patient, level) was 0.79, while the sensitivity for radiography was 0.32. The majority of erosions seen on US but not on MRI were seen at the 1st and 5th MTP joints, at which US has the capacity to image the lateral portions of these joints (10).

It therefore follows that US can have a vital role in the evaluation of early RA/UIA where exam findings can be subtle, and this has been corroborated by multiple studies (11-13).

Salaffi *et al.* examined 18 joints (bilateral wrists, 2-5th metacarpophalangeal (MCP) joints and proximal interphalangeal (PIP) joints) of 149 patients with UIA. 41% of this cohort developed RA at 1 year. The presence of synovitis on grey-scale and PD signal of one single joint significantly increased the probability of progression to RA with an odds ratio of 9.9, which was increased to 48 if more than three joints were involved (11).

Van der Ven examined 26 joints (bilateral wrists, 2-5th MCPs, PIPs and MTPs) in 159 patients with arthral-

gia. 16% of these patients developed inflammatory arthritis at one year and almost 60% of these patients had baseline US synovitis. The sensitivity and specificity of baseline US was 59% and 68% respectively. However, more statistically impressive was that a normal US at baseline had a negative predictive value of 89% (13).

US studies in the early RA group have also identified the importance of tendon involvement as an early marker of RA and a predictor of erosive damage. Patients with tenosynovitis of the extensor carpi ulnaris (ECU) tendons or the finger flexor tendons were 6 times as likely to be subsequently diagnosed with RA (14). In their study, Lilegraven *et al.*, found that baseline tenosynovitis on US appears to be predictive of erosive progression at 1 year (OR 7.18) and 3 years (OR 3.4) (15).

US studies have detected ongoing inflammation in RA patients even when clinical remission is present (9). In particular, PD signal has been identified as an important predictor of future relapse in such patients. In his cohort of early RA patients, Scire *et al.*, found that 95% of patients in DAS clinical remission had residual grey-scale synovitis and 41% of them had a positive PD signal. The presence of positive PD signal was associated with relapse within 6 months (86% sensitivity, 83% specificity, positive predictive value of 71% and a negative predictive value of 92%) (16). Baseline PD activity has also been shown to predict success of anti-TNF inhibitor treatment in RA patients (17). Based on all these findings, it might be

expected that incorporating MSUS in a treat to target (T2T) strategy would lead to superior clinical outcomes for patients with RA. However, 2 major studies (TaSER and ARCTIC) failed to show this (18, 19). In the TaSER trial, 111 patients with new RA or UIA were divided into a control group that comprised clinical and laboratory remission defined criteria (DAS 28/ESR remission group) or an intervention group that combined DAS 28/ESR and MSUS defined remission (total PD joint count ≤ 1). Step up treatment was standardised in both groups. The MSUS-driven T2T strategy led to more intensive treatment but there were no significant differences between ACR core set variables, except for DAS44 remission after 18 months (control 43%, intervention 66%; $p=0.03$). There was minimal radiographic progression (MRI/radiographic erosions) in both groups which were not statistically different (18).

Similar results were found in the ARCTIC study that monitored 238 patients with early RA for 2 years. 19% of those in the clinical tight control arm (DAS <1.6 and no swollen joints) versus 22% in US tight control arm (no PD) reached the primary endpoints (mean diff 3.3%, 95% CI -7.1% to 13.7%). Disease activity, physical function and joint damage were similar in both groups (19). Thus it appears that the incorporation of MSUS in all patients in a T2T strategy may lead to more intense treatment but with no significant additional benefit; however these studies did not mimic clinical practice, where MSUS would not be used in all

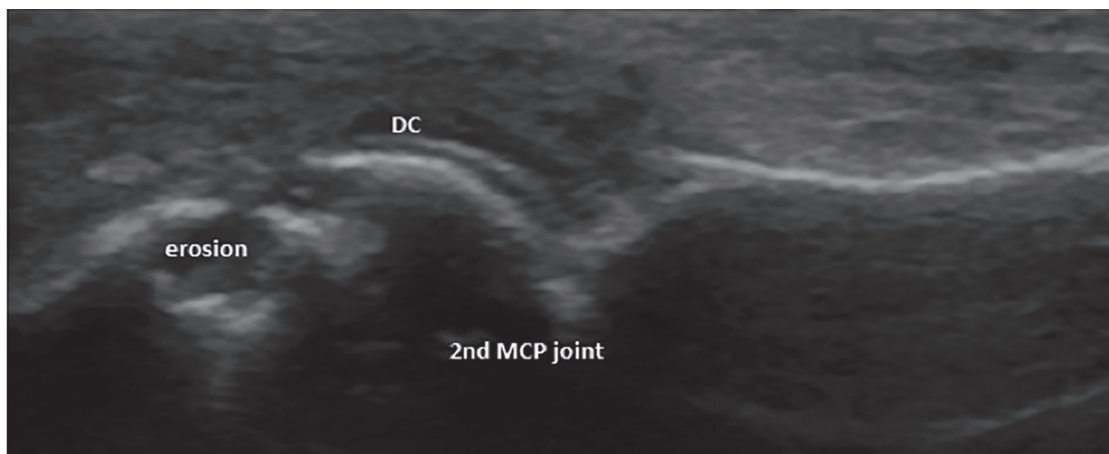


Fig. 2. US image of 2nd MCP showing a cortical defect consistent with erosion and a double contour (DC) sign in a patient with gout.

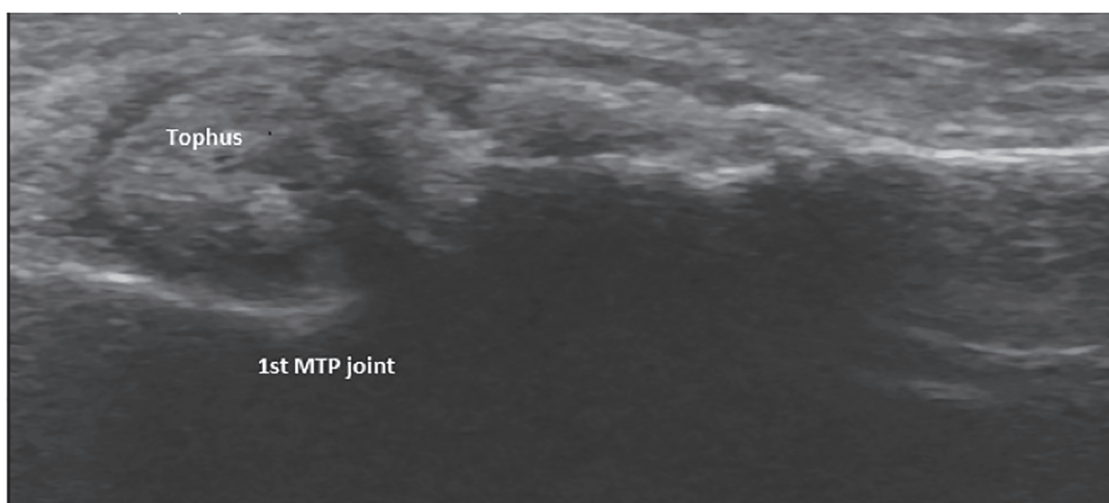


Fig. 3. US image of a 1st MTP joint showing a tophus in a patient with gout.

patients, but, like any test, would be used in cases of diagnostic uncertainty. The principal of randomising patients with clinical uncertainty about disease activity to MSUS, was not evaluated in TaSER and ARCTIC (20).

One caveat in the diagnosis of patients with suspicious arthralgia is that the presence of erosions and synovitis are not unique to inflammatory arthritis. In a study trying to identify US criteria for early arthritis, 100 healthy controls were matched to 100 patients with early arthritis. Bone erosions were identified in 11% of healthy controls, although 78% of these erosions were less than 2 mm. Grade 2 to 3 synovial hypertrophy was identified in 9% of healthy controls. Inclusion of two joints (rather than one) with synovial hypertrophy increased the specificity for detection of early arthritis from 90% to 98% (21). In addition to size, identification of erosions in the distal ulna, MCP2 or MTP5 can increase specificity for early RA (22).

Multiple studies of patients with osteoarthritis (OA) have also demonstrated the presence of synovitis, although it tends to be more localised and less marked when present (23-25). These findings also highlight how US can provide important insights into disease pathogenesis.

Role of MSUS in the evaluation of crystalline disease

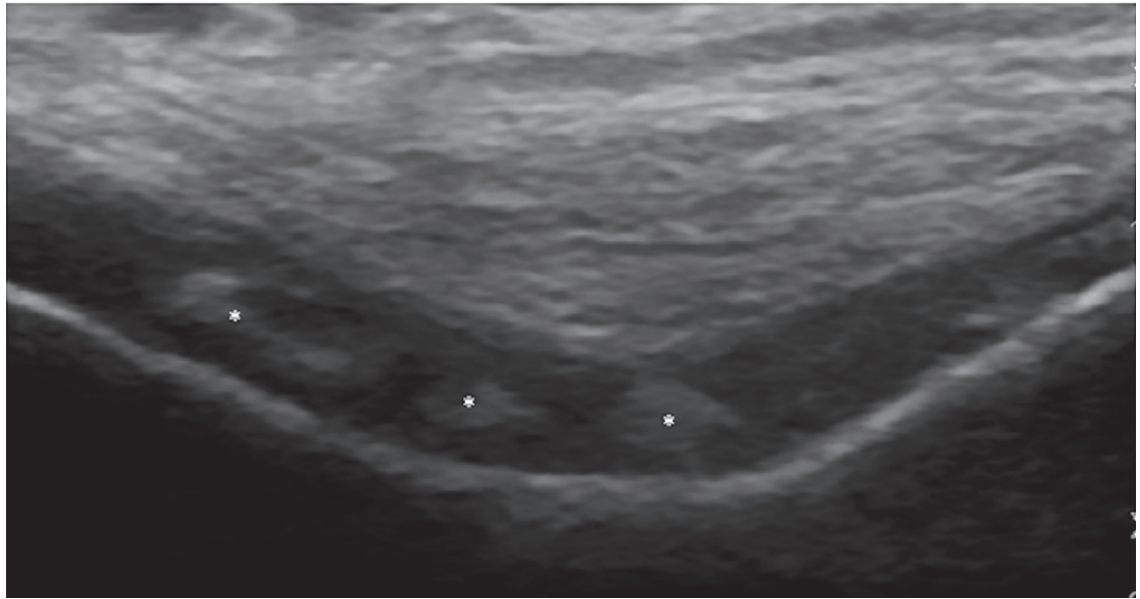
In patients with gout, MSUS can detect linear aggregates of monosodium urate (MSU) crystals layering over the cartilage (double contour sign (DCS), tophus and erosion (Figs. 2 and 3) (see article on gout in this supplement for greater detail). In addition, the synovium can demonstrate what is known as a snow-storm appearance due to hyper-echoic dots swirling in the synovium when the joint is agitated.

Erosive disease is detected more commonly by US than conventional x-ray, with one study reporting detection

of erosions in 28% of 1st MTP joints in patients with gout by x-ray *versus* 67% by US. Erosions were also seen in MTPs never clinically affected by gout (26). US can detect tophi in the synovium, soft tissue and tendons (patella, triceps, quadriceps and Achilles), many of which may not be visible on clinical examination.

A meta-analysis performed by Ogide *et al.* analysed data from 11 studies examining the usefulness of imaging modalities in the classification of gout when compared to MSU crystal confirmation as the gold standard and found that DCS and tophi had a pooled sensitivity of 83% and 65%, respectively, and a pooled specificity of 76% and 80%, respectively (27). US was found to contribute independently to identifying gout with an odds ratio of 7.2 (28). These findings, led to the incorporation of US criteria into the 2015 ACR/EULAR updated gout classification criteria, with their presence contribut-

Fig. 4. *Hyper-echoic deposits seen within the articular cartilage of the knee in a patient with chondrocalcinosis.



ing to 4 of the minimum of 8 required points for gout classification (29).

Ogdie *et al.* further analysed data collected from the Study for Updated Gout Classification Criteria (SUGAR), a large, multi-centre observational cross-sectional study of consecutive subjects with at least one swollen joint in whom gout would be included in the differential diagnosis.

US and arthrocentesis were performed in 824 patients, of whom 416 had positive MSU crystals identified by aspiration (cases). US was performed on the clinically affected joint(s) looking for DC sign, tophus and snowstorm appearance in these 416 patients and compared to 408 control patients in whom crystals were not seen. The sensitivity, specificity, PPV and NPV for the presence of any one of the US features were 76.9%, 84.3%, 83.3% and 78.1%, respectively.

Specificity was high, even in early disease, but sensitivity was modest and so the absence of one of these US features does not exclude gout. Sensitivity tended to be higher in those with a higher disease burden, such as those with long-standing disease (≥ 2 years of symptoms or tophi), although arguably these are the patients who can be more easily diagnosed without the use of MSUS (30).

Physicians should be aware that the DC sign can be identified in patients with asymptomatic hyperuricaemia, and a

clinical context is needed to diagnose gout. As structural and inflammatory changes such as tophi and enthesopathy can be identified in patients with asymptomatic hyperuricaemia, a better term might be “asymptomatic gout” (31).

Ultimately, MSUS may provide a non-invasive alternative method to diagnose gout and be particularly helpful when evaluating a patient outside the context of an acute attack, if aspiration yields no fluid or if the patient declines aspiration. Enhanced capacity to detect erosions or subclinical tophi by US may also influence treatment decisions and prompt the initiation of urate lowering therapy. In contrast to gout, in which MSU deposition occurs on the surface of articular cartilage, crystal deposition occurs within the articular cartilage in calcium pyrophosphate dihydrate deposition disease (CPPD) (Fig. 4). Deposits of calcification can also be identified in the fibrocartilage and within tendons by US in CPPD disease (32). Recently, new OMERACT US definitions for CPPD were found to be the most reliable (high kappa values both in intraobserver and interobserver evaluation) at the level of the hyaline cartilage and menisci of the knee, followed by the triangular fibrocartilage of the wrist. However, kappa values were low for other joint regions, tendons and synovial fluid (33, 34).

Role of MSUS in the evaluation of the spondyloarthropathies (SpA)

MSUS imaging in SpA can detect synovitis, erosion, bursitis, tenosynovitis and enthesitis. The imaging of tendon entheses in patients with SpA can show a variety of abnormalities including: thickening of the tendon, hypoechogenicity, local calcification, bony erosion and PD activity due to abnormal blood flow (35).

Many of the enthesal changes detected on US are subclinical. In one study, enthesitis was detected by US in 74% of psoriasis patients with SpA compared to 46% on clinical examination (36).

D’Agostino *et al.* evaluated the diagnostic accuracy of detecting enthesitis by PD US in patients with suspected SpA. 118 patients with suspected SpA based on suggestive symptoms were followed for 2 years after which a definite diagnosis was retained in 99 patients. PD detection of at least one vascularised entheses provided good predictive value for diagnosing SpA (sensitivity 76.5%; specificity 81.3%; positive likelihood ratio 4.1; OR 14.1; $p < 0.0001$) (37).

Ruysen *et al.* investigated the association between US entheses abnormalities and disease activity and MRI inflammatory lesions of the spine and sacroiliac joints in a cohort of patients suspected to have axial SpA. 55% of 402 patients in this cohort had US entheses structural abnormalities and

14% had PDUS abnormalities. US abnormalities were not correlated with disease activity in axial SpA but, the proportion of patients with syndesmo-phytes was higher in those with US enthesophytes (38).

MSUS in the evaluation of Sjögren's disease

In Sjögren's disease, the parotid and submandibular glands demonstrate inhomogeneity, which can vary in severity from isolated hypoechoic areas to large round or confluent hypoechoic areas with multiple cysts or calcifications (see also article with greater detail on Sjögren's syndrome in this supplement). Takagi *et al.* found that incorporating US Sjögren's criteria as an alternative to one of the three ACR classification items achieved 89–91% sensitivity, 87–96% specificity and 89% or 92% accuracy, which was comparable to that of the original ACR classification (39). Therefore, US could potentially replace a more invasive or painful test such as minor salivary gland biopsy, and US evaluation appears likely to be incorporated in future Sjögren's classification criteria.

Interventional MSUS

In addition to its diagnostic applications, MSUS may be used to guide articular injections or aspirations. This is particularly helpful with deep joints such as the hip, in the obese patient in whom procedures are technically challenging, or when trying to identify small pockets of fluid for aspiration. It can also safely guide periarticular injections such as tendon sheath injections where the correct placement of the needle is necessary to avoid complications and for maximal therapeutic benefit. A review of previously published articles on the use of MSUS guided injections found that there was generally greater accuracy and higher success rates when US was used for guidance, but it is unclear whether this translates into improved patient outcomes in the long run (40).

Interestingly, secondary analyses from the ARCTIC trial showed that US guided intra-articular glucocorticoid injections were not superior to palpation-

guided procedures. However, injections of swollen and non-swollen joints with moderate PD activity were found to be beneficial, whereas injections to joints with no PD activity were not efficacious (41). Therefore, US may be a valuable tool in selecting joints for intra-articular injection in RA.

Conclusions

The clinical applications of MSUS have expanded considerably over the last several decades owing to advances in technology, leading to growing interest and utilisation amongst rheumatologists across the globe. MSUS may play a vital role in the diagnosis of early inflammatory arthritis to detect subclinical synovitis or enthesitis. MSUS also may be useful in the monitoring of established disease, in which it can detect ongoing inflammation or structural damage. Additionally, features such as PD activity or tenosynovitis may help to predict which patients will respond to treatment, and which patients will relapse or develop future structural damage, although further investigation is needed to recognise whether incorporating MSUS into T2T strategies may lead to better clinical outcomes. Characteristic US features in patients with gout or Sjögren's disease may also provide non-invasive approaches to diagnosis. Ultimately, the rheumatology community will benefit from ongoing international efforts to further define the expanding role of MSUS in the assessment of rheumatic disease and to standardise and simplify scoring methods and imaging protocols.

References

1. KANE D, GRASSI W, STURROCK R, BALINT PV: A brief history of musculoskeletal ultrasound: 'From bats and ships to babies and hips'. *Rheumatology* (Oxford) 2004; 43: 931-3.
2. MANDL P, NAREDO E, WAKEFIELD RJ, CONAGHAN PG, D'AGOSTINO MA; OMERACT ULTRASOUND TASK FORCE: A systematic literature review analysis of ultrasound joint count and scoring systems to assess synovitis in rheumatoid arthritis according to the OMERACT filter. *J Rheumatol* 2011; 38: 2055-62.
3. TERSLEV L, NAREDO E, AEGERTER P *et al.*: Scoring ultrasound synovitis in rheumatoid arthritis: a EULAR-OMERACT ultrasound taskforce-Part 2: reliability and application to multiple joints of a standardised consen-

- sus-based scoring system. *RMD Open* 2017; 3: e000427.
4. MCALINDON T, KISSIN E, NAZARIAN L *et al.*: American College of Rheumatology report on reasonable use of musculoskeletal ultrasonography in rheumatology clinical practice. *Arthritis Care Res* 2012; 64: 1625-40.
5. MÖLLER I, JANTA I, BACKHAUS M *et al.*: The 2017 EULAR standardised procedures for ultrasound imaging in rheumatology. *Ann Rheum Dis* 2017; 76: 1974-79.
6. BACKHAUS M, BURMESTER GR, GERBER T *et al.*: Guidelines for musculoskeletal ultrasound in rheumatology. *Ann Rheum Dis* 2001; 60: 641-9.
7. WAKEFIELD RJ, BALINT PV, SZKUDLAREK M *et al.*: Musculoskeletal ultrasound including definitions for ultrasonographic pathology. *J Rheumatol* 2005; 32: 2485-7.
8. GUTIERREZ M, SCHMIDT WA, THIELE RG *et al.*: International Consensus for ultrasound lesions in gout: results of Delphi process and web-reliability exercise. *Rheumatology* (Oxford) 2015; 54: 1797-805.
9. COLEBATCH AN, EDWARDS CJ, ØSTERGAARD M *et al.*: EULAR recommendations for the use of imaging of the joints in the clinical management of rheumatoid arthritis. *Ann Rheum Dis* 2013; 72: 804-14.
10. SZKUDLAREK M, NARVESTAD E, KLARLUND M, COURT-PAYEN M, THOMSEN HS, ØSTERGAARD M: Ultrasonography of the metatarsophalangeal joints in rheumatoid arthritis: comparison with magnetic resonance imaging, conventional radiography, and clinical examination. *Arthritis Rheum* 2004; 50: 2103-12.
11. SALAFFI F, CIAPETTI A, GASPARINI S, CAROTTI M, FILIPPUCCI E, GRASSI W: A clinical prediction rule combining routine assessment and power Doppler ultrasonography for predicting progression to rheumatoid arthritis from early-onset undifferentiated arthritis. *Clin Exp Rheumatol* 2010; 28: 686-94.
12. HORTON SC, TAN AL, WAKEFIELD RJ, FREESTON JE, BUCH MH, EMERY P *et al.*: Ultrasound-detectable grey scale synovitis predicts future fulfilment of the 2010 ACR/EULAR RA classification criteria in patients with new-onset undifferentiated arthritis. *RMD Open* 2017; 3: e000394.
13. VAN DER VEN M, VAN DER VEER-MEERKERK M, TEN CATE DF *et al.*: Absence of ultrasound inflammation in patients presenting with arthralgia rules out the development of arthritis. *Arthritis Res Ther* 2017; 19: 202.
14. SAHBUDIN I, PICKUP L, CADER Z *et al.*: OP0015 Ultrasound-defined tenosynovitis is a strong predictor of early rheumatoid arthritis. *Ann Rheum Dis* 2015; 74 (Suppl. 2): 69-70.
15. LILLEGRAVEN S, BØYESEN P, HAMMER HB *et al.*: Tenosynovitis of the extensor carpi ulnaris tendon predicts erosive progression in early rheumatoid arthritis. *Ann Rheum Dis* 2011; 70: 2049-50.
16. SCIRE CA, MONTECUCCO C, CODULLO V, EPIS O, TODOERTI M, CAPORALI R: Ultrasonographic evaluation of joint involvement in early rheumatoid arthritis in clinical remission: power Doppler signal predicts short-term relapse. *Rheumatology* (Oxford) 2009; 48: 1092-7.

17. ELLEGAARD K, CHRISTENSEN R, TORP-PEDERSEN S *et al.*: Ultrasound Doppler measurements predict success of treatment with anti-TNF- α ; drug in patients with rheumatoid arthritis: a prospective cohort study. *Rheumatology (Oxford)* 2011; 50: 506-12.
18. DALE J, STIRLING A, ZHANG R *et al.*: Targeting ultrasound remission in early rheumatoid arthritis: the results of the TaSER study, a randomised clinical trial. *Ann Rheum Dis* 2016; 75: 1043-50.
19. HAAVARDSHOLM EA, AGA AB, OLSEN IC *et al.*: Ultrasound in management of rheumatoid arthritis: ARCTIC randomised controlled strategy trial. *BMJ* 2016; 354: i4205.
20. D'AGOSTINO MA, BOERS M, WAKEFIELD RJ, EMERY P, CONAGHAN PG: Is it time to revisit the role of ultrasound in rheumatoid arthritis management? *Ann Rheum Dis* 2017; 76: 7-8.
21. MILLOT F, CLAVEL G, ETCHEPARE F *et al.*: Musculoskeletal ultrasonography in healthy subjects and ultrasound criteria for early arthritis (the ESPOIR cohort). *J Rheumatol* 2011; 38: 613-20.
22. ZAYAT AS, ELLEGAARD K, CONAGHAN PG *et al.*: The specificity of ultrasound-detected bone erosions for rheumatoid arthritis. *Ann Rheum Dis* 2015; 74: 897-903.
23. D'AGOSTINO MA, CONAGHAN P, LE BARS M *et al.*: EULAR report on the use of ultrasonography in painful knee osteoarthritis. Part 1: prevalence of inflammation in osteoarthritis. *Ann Rheum Dis* 2005; 64: 1703-9.
24. VLYCHOU M, KOUTROUMPAS A, MALIZOS K, SAKKAS LI *et al.*: Ultrasonographic evidence of inflammation is frequent in hands of patients with erosive osteoarthritis. *Osteoarthritis Cartilage* 2009; 17: 1283-7.
25. KEEN HI, WAKEFIELD RJ, GRAINGER AJ, HENSOR EM, EMERY P, CONAGHAN PG: An ultrasonographic study of osteoarthritis of the hand: synovitis and its relationship to structural pathology and symptoms. *Arthritis Rheum* 2008; 59: 1756-63.
26. WRIGHT SA, FILIPPUCCI E, McVEIGH C *et al.*: High-resolution ultrasonography of the first metatarsal phalangeal joint in gout: a controlled study. *Ann Rheum Dis* 2007; 66: 859-64.
27. OGDIE A, TAYLOR WJ, WEATHERALL M *et al.*: Imaging modalities for the classification of gout: systematic literature review and meta-analysis. *Ann Rheum Dis* 2015; 74: 1868-74.
28. TAYLOR WJ, FRANSEN J, JANSEN TL *et al.*: Study for Updated Gout Classification Criteria: identification of features to classify gout. *Arthritis Care Res* 2015; 67: 1304-15.
29. NEOGI T, JANSEN TL, DALBETH N *et al.*: 2015 Gout classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Ann Rheum Dis* 2015; 74: 1789-98.
30. OGDIE A, TAYLOR WJ, NEOGI T *et al.*: Performance of ultrasound in the diagnosis of gout in a multicenter study: comparison with monosodium urate monohydrate crystal analysis as the gold standard. *Arthritis Rheumatol* 2017; 69: 429-38.
31. PINEDA C, AMEZCUA-GUERRA LM, SOLANO C *et al.*: Joint and tendon subclinical involvement suggestive of gouty arthritis in asymptomatic hyperuricemia: an ultrasound controlled study. *Arthritis Res Ther* 2011; 13: R4.
32. GRASSI W, MEENAGH G, PASCUAL E, FILIPPUCCI E *et al.*: "Crystal clear"-sonographic assessment of gout and calcium pyrophosphate deposition disease. *Semin Arthritis Rheum* 2006; 36: 197-202.
33. FILIPPOU G, SCIRÈ CA, ADINOLFI A *et al.*: Identification of calcium pyrophosphate deposition disease (CPPD) by ultrasound: reliability of the OMERACT definitions in an extended set of joints—an international multiobserver study by the OMERACT Calcium Pyrophosphate Deposition Disease Ultrasound Subtask Force. *Ann Rheum Dis* 2018; 77: 1194-9.
34. FILIPPOU G, CIRÈ CA, DAMJANOV N *et al.*: Definition and reliability assessment of elementary ultrasonographic findings in calcium pyrophosphate deposition disease: a study by the OMERACT Calcium Pyrophosphate Deposition Disease Ultrasound Subtask Force. *J Rheumatol* 2017; 44: 1744-9.
35. D'AGOSTINO MA: Ultrasound imaging in spondyloarthropathies. *Best Pract Res Clin Rheumatol* 2010; 24: 693-700.
36. HAMDY M, OMAR G, ELSHEREEF RR, ELLABAN AS, AMIN M: Early detection of spondyloarthropathy in patients with psoriasis by using the ultrasonography and magnetic resonance image. *Eur J Rheumatol* 2015; 2: 10-5.
37. D'AGOSTINO MA, AEGERTER P, BECHARA K *et al.*: How to diagnose spondyloarthritis early? Accuracy of peripheral enthesitis detection by power Doppler ultrasonography. *Ann Rheum Dis* 2011; 70: 1433-40.
38. RUYSSSEN-WITRAND A, JAMARD B, CANTAGREL A *et al.*: Relationships between ultrasound enthesitis, disease activity and axial radiographic structural changes in patients with early spondyloarthritis: data from DESIR cohort. *RMD Open* 2017; 3: e000482.
39. TAKAGI Y, SUMI MI, NAKAMURA H *et al.*: Ultrasonography as an additional item in the American College of Rheumatology classification of Sjögren's syndrome. *Rheumatology (Oxford)* 2014; 53: 1977-83.
40. CAZENAVE T, PINEDA C, REGINATO AM, GUTIERREZ M; PAN-AMERICAN LEAGUE AGAINST RHEUMATISMS (PANLAR) ULTRASOUND STUDY GROUP: Ultrasound-guided procedures in rheumatology. What is the evidence? *J Clin Rheumatol* 2015; 21: 201-10.
41. NORDBERG LB, LILLEGRAVEN S, AGA AB *et al.*: The impact of ultrasound on the use and efficacy of intraarticular glucocorticoid injections in early rheumatoid arthritis: secondary analyses from a randomized trial examining the benefit of ultrasound in a clinical tight control regimen. *Arthritis Rheumatol* 2018; 70: 1192-99.