Musculoskeletal ultrasound—a state of the art review in rheumatology. Part 2: Clinical indications for musculoskeletal ultrasound in rheumatology

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Rheumatologists remain divided on whether they should introduce musculoskeletal ultrasound (MSUS) into their clinical practice. A central issue in the application of MSUS in clinical rheumatology is the need for proof of clinical relevance and improved patient care. There is now accumulating evidence that MSUS improves clinical diagnosis and intervention skills. High-resolution ultrasound is superior to clinical examination in the diagnosis and localization of joint and bursal effusion and synovitis. MSUS is the imaging modality of choice for the diagnosis of tendon pathology. MSUS is seven times more sensitive than plain radiography in the detection of rheumatoid erosions, allowing earlier diagnosis of progressive rheumatoid arthritis. Ligament, muscle, peripheral nerve and cartilage pathology can also be readily demonstrated by MSUS. There is exciting evidence that MSUS may potentially be used by rheumatologists to non-invasively diagnose and monitor not just joint and muscle disease but also nerve compression syndromes, scleroderma, vasculitis and Sjögren's syndrome. Joint aspiration and injection accuracy can be improved by MSUS, with initial evidence confirming improved efficacy. As the number of rheumatologists performing MSUS increases and the technical capabilities of MSUS improve, there is likely to be a growing number of proven clinical indications for the application of MSUS in rheumatology practice. This paper reviews the evidence for the application of MSUS in rheumatology.

KEY WORDS: Musculoskeletal ultrasound, Synovitis, Erosion, Enthesitis.

MSUS is now routinely used by a growing number of rheumatologists throughout Europe for proven clinical indications in diagnosis, monitoring and intervention. The past two decades have seen revolutionary advances in the imaging resolution, capabilities and cost of MSUS imaging equipment. There has also been the establishment of training courses, aids and guidelines, the training of an increasing number of rheumatologists to trainer level and the publication of a wide range of literature validating the application of MSUS in clinical rheumatology. Thus there now exists a critical mass for the widespread development of MSUS as part of rheumatology training. There is no rheumatological disease that MSUS cannot potentially be applied to and this paper reviews the clinical applications of MSUS in rheumatology.

Joint and bursal effusion and synovitis (Fig. 1)

MSUS has an extremely useful application in daily rheumatological practice in differentiating fluid from soft tissue. In fact, the first clinical application of MSUS was in differentiating fluid-filled Baker's cysts from the calf swelling associated with deep vein thrombosis [1]. The detection of a fluid collection in joints, bursae, tendon sheaths and soft tissues is a useful sign of inflammation, though it is also helpful in diagnosing soft tissue injuries, soft tissue cysts and musculoskeletal infections. The presence of a fluid collection allows aspiration for diagnosis and local injection for relief of symptoms [2]. MSUS enhances the clinical detection of fluid collections and MSUS increases the success of subsequent intervention.

Minimum volume detected

The resolution of MSUS now allows for the detection of minute amounts of fluid in asymptomatic joints of healthy subjects [3, 4]. Studies of the ankle and hip in cadavers confirm that ultrasound (US) can detect effusions as small as 1–2 ml in volume [4–6]. The minimum effusion detectable in small joints of the hands and feet is not known and interobserver agreement for US detection of effusion in these joints is reported to be only 79% compared with that of bone erosion (91%), synovitis (86%) and power Doppler signal assessment (87%) [7]. But using MSUS to detect and localize small joint effusions is effective in clinical practice. In patients with inflamed metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints, MSUS improved accurate needle placement from 59% by palpation guidance to 96% by MSUS guidance [8].
Localization of joint effusion

US allows localization of fluid collections in different parts of joints with the potential to improve the success of aspiration. US and magnetic resonance imaging (MRI) confirm that the posterior olecranon recess contains a large proportion of the fluid in elbow effusions [9, 10] and this approach may improve the success of aspiration. The posterior approach may be better for aspirating fluid from the shoulder [11] as the fluid is frequently located in this part of the joint. In the authors’ experience, fluid in small joints (PIP, MTP) is more frequently located proximal to the radiological joint line, probably due to the effect of the force the overrunning tendon [12]. US is especially useful in localizing fluid collections in deeper joints such as the hip joint and around joint prostheses [13]. A pilot study showed that using US to localize effusions and guide aspiration produced a 3-fold increase in the rate of successful aspiration when compared with conventional aspiration of the peripheral joints [12].

Correlation of clinical and US detection of joint fluid

MSUS has been confirmed to be superior to clinical examination in the detection of effusion, even in a large and relatively easily palpable joint such as the knee joint [14, 15]. Further studies need to be done to confirm if MSUS is more sensitive than clinical examination in the detection of effusions in all peripheral joints. If the presence of joint fluid is taken as the hallmark of inflammation, then the classification criteria of rheumatoid arthritis (RA) and the clinical diagnosis of mono-, oligo- and polyarthritis will probably need to be re-evaluated in the future due to more widespread clinical use of US which may be a more accurate means of determining the number of inflamed joints.

Can MSUS differentiate the nature of the effusion?

It is important to understand the limitations of MSUS in the evaluation of joint effusions. MSUS cannot yet accurately differentiate whether a fluid collection is inflammatory, infectious or haematogenous in most cases and aspiration of fluid—which is more successful with MSUS guidance—remains the gold standard. MSUS can give a basic estimate of fluid viscosity, aiding selection of the appropriate gauge size needle for aspirating a fluid collection. Finally it is important to appreciate that some types of effusion, such as high-pressure echogenic effusion, can be mistaken for synovitis as the fluid will appear hyperechoic and is not easily displaceable by the probe.

Synovitis

The presence of joint, bursal or tendon sheath effusion is used as an excellent, indirect correlate of synovial inflammation and improves MSUS visualization of synovial thickening, proliferation and villous formation. In the absence of an effusion, synovitis is diagnosed by the presence of an abnormally thickened hypoechoic region, usually measured in a standard plane with reference to an established normal range or to the contralateral normal joint. Already MSUS is detecting significant degrees of synovitis not determined by clinical examination [16, 17] and can reliably discriminate inflammatory and non-inflammatory joint disease. The detection of subclinical synovitis may lead to a re-evaluation of the clinical classification of arthritis as oligoarticular or polyarticular. In the absence of an effusion and when there is minimal synovial thickening, synovitis can be difficult to visualize. Improvements in imaging resolution and the introduction of power Doppler now allow imaging of smaller degrees of synovitis with a reported accuracy equal to that of dynamic MRI [18].

Bone

Bone is often regarded as a barrier to the use of US in settings such as cartilage evaluation and echocardiography. But MSUS has a number of applications in the evaluation of disease of the bony cortex and periosteum.
The rheumatoid erosion (Fig. 2)

One of the most exciting applications of MSUS in rheumatology is in the evaluation of bone erosion in RA. The detection of joint erosion on plain radiography is a key diagnostic criterion and outcome measure in RA. However, MSUS is capable of detecting up to seven times more erosions than plain radiography in early RA [19]. Thus it has been proposed that MSUS detection of erosion should be included in the diagnostic criteria of early RA [20] and there is ongoing work to assess the role of MSUS as an outcome measure in RA. MSUS can also be used to guide bone biopsy of rheumatoid erosions for research purposes [21].

Bone cortex and periosteal pathology

MSUS has also been used in the evaluation of fractures, osteomyelitis and bone neoplasia where bone cortex abnormalities and periosteal reaction are prominent features of the disease process.

Tendon, ligament

In the last decade, MSUS has become the gold standard for examination of tendons [22, 23]. Tenosynovitis (Fig. 3), paratendonitis and tendon tear are routinely detected by MSUS. MSUS is superior to MRI in the detection of longitudinal split tendon tear, subluxed tendon and snapping tendon and has the advantage of allowing dynamic tendon examination. MSUS may also demonstrate focal or diffuse tendonitis, calcified tendonitis and tendinosis and tendon xanthomas, though subtle changes may be missed or misinterpreted due to anisotropy. Power Doppler sonography is a promising method for grading tenosynovitis and also for detecting tendonitis, but does not distinguish tendonitis from tendinosis. Similar pathological changes in ligaments can also be detected by MSUS.

Enthesitis, dactylitis

Lower limb midline enthesitis and common extensor muscle enthesitis of the elbow are readily detected by US. US is more...
sensitive in detection of enthesitis than clinical examination [24, 25]. Thickened enthesis, erosion, enthesophyte and adjacent bursitis are common findings on US. After case reports, increased power Doppler sign is also proposed as an important sign of enthesitis in a large cohort study [26]. In dactylitis, tenosynovitis, synovitis, tendonitis and accompanying subcutaneous oedema are the most common findings on US [27, 28]. MSUS has also been used to perform guided biopsy of the enthesis for research purposes [29].

Skin

The development of higher-frequency probes (13–20 MHz) has allowed skin thickness and oedema to be visualized and there are a number of potential applications in rheumatology.

Scleroderma

Clinical evaluation of skin thickness in scleroderma is currently used to assess the severity of skin disease and response to treatment but has poor interobserver variability [30]. US assessment of skin thickness in scleroderma showed that skin thickness was increased over the proximal phalanx of the right second finger and forearm compared with controls [31]. Skin thickness of the forearm was inversely correlated with disease duration. The interobserver variability was remarkably small, being 1% for the phalanx and 0.0016% for the forearm. US criteria of scleroderma have been successfully used to differentiate scleroderma from other skin plaques with a diagnostic sensitivity of 92% and a specificity of 100% [32]. Thus MSUS may be developed as a diagnostic and quantitative tool in scleroderma.

Soft tissue infection

Other pathologies such as subcutaneous oedema, cellulitis, necrotizing fasciitis, subcutaneous abscess and cystic and solid dermal masses can be depicted by MSUS. MSUS-guided aspiration aids rapid microbiological diagnosis and institution of treatment in soft tissue infections [33, 34].

Hyaline cartilage (Fig. 4)

On ultrasonography normal hyaline cartilage appears anechoic or hypoechoic with well-marked margins. A disadvantage of MSUS is that most articular cartilages—femoral head and condyle, talus, humeral head, capitulum humeri, head of MCP—can only be examined partially by ultrasound due to the limited acoustic window of bony joints. MRI allows imaging of the
entire cartilage but studies are required to establish if findings in the areas of cartilage visualized by MSUS are equally applicable to the entire joint cartilage as assessed by MRI. Intra-articular sonography may have a role in evaluating the entire hyaline cartilage and intra-articular fibrocartilages and ligaments in the future [35, 36].

Osteoarthritis
MSUS features of osteoarthritis (OA) include focal or diffuse thinning of the cartilage layer, presence of osteophytes, less well demarcated synovial space–cartilage interspace, loss of clarity of the cartilaginous band and increased intensity of the posterior bone–cartilage interface and there is ongoing work in developing a diagnostic and quantitative role for MSUS in OA [37–43].

Other diagnostic applications
Other diagnostic applications include MSUS detection of chondocalcinosis [44, 45] and costochondritis [46].

Peripheral nerves
In recent years MSUS has proved to be a useful tool in assessing peripheral nerve morphology, particularly in the case of focal lesions such as nerve compression. Unlike computed tomography (CT) and MRI where scanning is performed in standardized planes at set intervals, MSUS can be rapidly aligned along the axis of the nerve to be studied and provides superior measurement and imaging definition capability.

Carpal tunnel syndrome
The most common nerve entrapment syndrome is the carpal tunnel syndrome (CTS). MSUS easily identifies the median nerve from tendons as it is hyperechoic and speckled in transverse section but does not demonstrate anisotropy and has a hyperechoic fascicular pattern in longitudinal section. The area of compression and post-compressive swelling are readily identified. Additional information on the cause of nerve compression in the carpal tunnel may also be obtained by MSUS through imaging of tenosynovitis or tendon effusion, amyloid deposition, hypertrophied accessory muscle, increased fatty tissue, ganglion cyst or variant median artery.

MSUS criteria of carpal tunnel syndrome
Many investigators have attempted to define US criteria for the diagnosis of CTS [47–58]. These include (i) volar bulging of flexor retinaculum, (ii) thickened flexor retinaculum, (iii) maximal depth of carpal tunnel, (iv) focal or diffuse swelling or flattening of the nerve, (v) increased mean cross-sectional area of the nerve at different levels, (vi) increased cross-sectional diameters of the nerve and (vii) increased flattening ratio. A median nerve cross-sectional diameter of >0.098 cm² at the
tunnel inlet has been reported to have a sensitivity of 89% and a specificity of 83% [59]. Though MSUS has not replaced nerve conduction studies it is certainly more acceptable to patients. These studies suggest that it may become the initial investigation for carpal tunnel syndrome.

Other nerve entrapments
MSUS can detect other nerve entrapments in fibrous tunnels but sonographic criteria have not yet been agreed. These include the ulnar nerve as it passes through the cubital and Guyon’s tunnels, the common peroneal nerve at the fibular neck and the posterior tibial nerve at the tarsal tunnel [60].

Nerve tumours
MSUS may also be used to identify peripheral nerve tumours such as neurofibromas and schwannomas [61, 62] and the fibrotic pseudotumour known as Morton’s neuroma [63].

Muscle
MSUS demonstrates skeletal muscle fibres in fine detail and has an established role in the localization and assessment of partial and complete muscle rupture. The presence of a fluid collection and/or fibre discontinuity are the most reliable signs of muscle rupture. MSUS is useful for follow-up examination to monitor healing and to detect possible complications such as scars, calcifications, myositis ossificans, serous cyst or hernia [64]. MSUS may also be used to image polymyositis, muscle infarction, rhabdomyolysis, muscular dystrophies and benign and malignant tumours [33, 34, 64, 65]. MSUS and MRI have a similar capacity to demonstrate the features of inflammatory muscle disease, though MRI is currently more sensitive for the detection of oedema while MSUS has the advantage of allowing guided biopsy and aspiration of muscle pathology.

Vasculitis and Raynaud’s disease
Arterial involvement in Takayasu’s and giant cell arteritis can be detected by US when there is an acoustic window for the vessel section involved. US may have particular usefulness in guiding biopsy of involved vessels, particularly in temporal arteritis which is characterized by ‘skip lesions’. Characteristic features of large vessel vasculitis include a hypoechoic swollen artery wall with surrounding oedema (‘halo sign’) and an irregular narrowed lumen [66].

Temporal arteritis
In temporal arteritis, US has been correlated with clinical and histological findings in many studies, with a reported diagnostic sensitivity of US of 33–100% and a specificity of 68–100%. Though there is currently no agreement on the role of US in the diagnosis of giant cell arteritis, it is suggested that the application of colour Doppler with duplex gives increased sensitivity of 95–100% [67, 68]. Further standardization of scanning techniques and diagnostic criteria is required before US can be used to diagnose giant cell arteritis without performing a temporal artery biopsy.

Takayasu’s arteritis
In Takayasu’s arteritis, US and angiography have complementary imaging roles, with US demonstrating inflammatory thickening of the arterial wall (the ‘Makkaroni phenomenon’) while angiography provides information on the vascular lumen. US has a similar diagnostic utility to angiography, but only in a limited number of vessels that are accessible to US imaging [66]. Thus angiography or MR angiography allows a more complete evaluation of the arterial system but US can be effectively used to non-invasively localize arteritis and to follow the response to treatment. Further study is required to compare US and MR angiography in the diagnosis and monitoring of large vessel vasculitis.

Raynaud’s phenomenon
Initial studies suggest that US quantitation of arterial flow can differentiate patients with Raynaud’s phenomenon from normal subjects and that US evaluation of intimal wall thickness and elasticity can potentially differentiate primary and secondary Raynaud’s disease [69, 70].

Sjögren’s/salivary glands
US features of salivary gland size and parenchyma can differentiate patients with Sjögren’s syndrome from normal subjects, and US features of salivary glands correlate with labial gland histology but require further validation [71, 72].

Interventional musculoskeletal ultrasonography
Aspiration of synovial fluid, therapeutic intra-articular and intralesional injection therapy, nerve blocks and soft tissue biopsy are usually performed using palpation of bony landmarks for guidance. However, it has been reported that 50% of conventional joint injections are inaccurately placed [73]. MSUS may be used to assist needle positioning within the selected target area and to facilitate all of the invasive rheumatological procedures such as aspiration of fluid, decompression of cysts, drainage of abscess or haematoma, biopsy and local injection of drugs [21, 74, 75]. For complete accuracy, MSUS should precede and guide local injection therapy whenever practically possible, especially when fluid collections are deep or when the inflammatory process is adjacent to anatomical structures that could be seriously damaged by the injection [76, 77].

Intralesional injections under sonographic guidance are not always performed according to traditional routes. The best approach to the target area may be decided case by case on the basis of the sonographic features of the lesion. The progression of the needle can be accurately controlled step by step on the monitor until the tip of the needle is properly placed on the selected target. When necessary, visualization of the needle tip can be enhanced by the injection of a small amount of hyperechoic steroid suspension [78], hyperechoic saline or highly echogenic sterile air (<0.5 ml) or the use of power Doppler to detect motion [2]. MSUS may be useful in the pre-operative assessment of patients undergoing synovectomy or other surgical procedures and in the post-operative follow-up to assess tissue healing or inflammation.

The clinical benefit of MSUS guidance of injections in routine practice remains to be fully determined. The use of MSUS to localize joint and soft tissue fluid collection greatly improves the rate of diagnostic synovial fluid aspiration, particularly in small joints [8, 12]. MSUS-guided injection improves accuracy and reduces the risk of injecting into tendon, adipose tissue, muscle, nerve or skin resulting in inefficacy and tissue damage. Moreover, attempted aspiration of a dry joint can be avoided and the use of very high-frequency transducers (>10 MHz) allows accurate identification of the safest site of injection even in patients with limited joint cavity, tendon sheath widening or
Clinical indications for MSUS in rheumatology

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Table 1. Current, developing and potential indications for MSUS in rheumatology

dry joints [79]. However, no study has directly compared MSUS-guided and clinical-guided injection of synovial joints. One study shows that MSUS-guided injection of plantar fasciitis seems to be no more effective than blind injection of the region [74] but this was insufficiently powered. The use of MSUS has been shown to improve the speed and accuracy of nerve blocks [80] of the supraclavicular nerve [81] and ulnar nerve [82].

Inflammation and power Doppler (Fig. 5)
Power Doppler US is an imaging technique particularly apt for assessing low-velocity flow in small vessels (e.g. synovium) that has evolved rapidly over the last few years [83]. There has been substantial growth in its application in the diagnosis and quantitation of synovitis because of its high sensitivity for the identification of increased blood perfusion in the synovium [84]. The combination of high-resolution probes and the latest generation of power Doppler workstations allows a clear depiction of an even minimal increase of perfusion in several inflammatory conditions such as tenosynovitis and enthesitis [26]. These exciting technological developments are likely to allow visualization of blood flow in healthy joints in the future.

Synovitis and enthesis
Power Doppler has been demonstrated to be reliable for assessing inflammatory activity in the MCP joints of patients...
with RA, using dynamic MRI as the standard [18] and an abnormal power Doppler signal at the cortical bone of entheses should be regarded as a highly specific feature of the spondyloarthropathies [26]. Power Doppler images of active synovitis are quite impressive, if we consider that no signal is detected in the normal synovial membrane (Fig. 1). A significant correlation between the power Doppler signal and the degree of vascularity of the synovial tissue, as demonstrated by haematoxylin and eosin stain and immunohistochemistry, has been recently reported [85].

Even if there is still no convincing evidence about the application of power Doppler in therapy monitoring, it appears to be a promising tool and it is reasonable to predict an exciting use in the future for this technique in one of the most critical and controversial areas of experimental and clinical rheumatology. Dramatic short-term changes of power Doppler signals occur after an intra-articular injection of steroids. The loss of signal is linked to clinical improvement. Therapy-induced power Doppler changes have also been described after treatment with methotrexate, etanercept, infliximab and leflunomide [86].

Conclusion
Rheumatologists can already apply MSUS in a number of established and proven clinical indications in diagnosis, monitoring and intervention (Table 1). Even if rheumatologists were to use MSUS solely to improve two fundamental clinical skills—the clinical diagnosis of inflammation and the accuracy of corticosteroid injection—the evidence published to date suggests that this may lead to significant improvements in patient care. It is important that rheumatologists further establish this evidence base to support the development of MSUS in rheumatology. There are already a growing number of potential diagnostic and monitoring applications of MSUS that require careful evaluation. Newer technologies are likely to make MSUS more accessible to a greater number of rheumatologists and allow imaging of articular structures and pathological processes to a previously unimaginied degree.

Acknowledgements
Dr Balint’s work was supported by the Hungarian Medical Research Council (grant number XI.281).

The other authors have declared no conflicts of interest.

References
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