



Musculoskeletal Ultrasound in Rheumatology – New Horizons

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Abstract

Musculoskeletal ultrasound is a non-ionizing, cheap, reproducible, reliable imaging method, well accepted by the patients, that plays an important role in daily rheumatology practice. It can be used to assess joint and periarticular involvement, including tendon, bursae, enthesitis, skin thickness, nails, lung and large vessels. Musculoskeletal ultrasound is more sensitive than physical examination, improves the diagnostic process, monitoring of treatment response, the accuracy of joint and soft tissue injections. It has proved its role as an important imaging modality in a number of rheumatic diseases – inflammatory joint diseases, systemic connective tissue diseases, large-vessel vasculitides, and degenerative and metabolic bone diseases.

Keywords

enthesitis, musculoskeletal ultrasound, rheumatology, synovitis

INTRODUCTION

Musculoskeletal ultrasound (MSUS) has played a major role in rheumatology in the last decade. It has been proven to be a valuable method in diagnosing, treatment monitoring and ultrasound-guided procedures. In 2001, Backhaus et al. published guidelines for the performance of ultrasound examination for each of the joint regions.¹ In 2005, Wakefield et al. published definitions for ultrasonographic pathology.² MSUS has been demonstrated to have good reproducibility and interobserver reliability.³ The advantages MSUS offers can be of technical nature such as no ionizing radiation in using the method, it is a low-cost method, easy to perform, reproducible and well tolerated by patients, and of clinical nature such as provision of real-time imaging, of better sensitivity than physical examination, enables assessment of many structures over a relatively short time, allows dynamic examination during movement of the joints

and tendons, and explores the region of interest from many planes, detects subclinical synovitis, enthesitis, early erosions and improves efficacy of articular and periarticular procedures.⁴ These advantages of using MSUS in rheumatic diseases will be reviewed successively in this paper.

MSUS in inflammatory joint diseases

Rheumatoid arthritis (RA).

MSUS as an imaging modality is included in the European League Against Rheumatism (EULAR) recommendations as a method with proven role in patients with RA.⁵

MSUS in establishing diagnosis of RA.

MSUS is more sensitive than a physical examination for the assessment of synovitis (**Fig. 1**).⁶ Adding MSUS to the new 2010 ACR/EULAR classification criteria for RA increases their sensitivity.⁷

MSUS as a predictor of progression from undifferentiated arthritis to clinical RA.

Horton et al. (2017) performed Gray Scale (GS) and Power Doppler (PD) assessment of synovitis of 26 joints of patients with undifferentiated arthritis in an observational prospective study and found that GS synovitis was predictive of disease progression to RA.⁸

MSUS for detection of structural damage

MSUS is more sensitive in detecting destructive bone changes in RA patients than conventional radiography, without losing its specificity.⁹

MSUS for RA prognosis: as a predictor for disease outcome.

Persistent synovitis with positive PD signal has been proven to be a predictor of future development of erosions. Dougados et al. (2013) found that synovitis on MSUS is a predictor for radiographic damage irrespective of the modality used (GSUS, PDUS).¹⁰

MSUS for monitoring the effect of treatment.

Evidence in literature shows that MSUS is more sensitive than clinical examination in assessing synovitis.⁶ MSUS can be used for therapy monitoring.^{11,56} Different grading systems for GSUS and PDUS synovitis have been developed. In clinical practice semi-quantitative scale 0-3 grade is most common. There is evidence that the scoring systems, which include a reduced number of joints, correlate to a great extent with the scoring systems, which assess big number of joints (examples - 12 joints (Hammer et al., Naredo et al.), 6 joints (Perricone et al.), 12, 28, and 44 joints (Hammer et al.).¹²⁻¹⁴ The German ultrasound score of 7 joints (US7) is the first to combine soft tissue pathology (synovitis, tenosynovitis) and destructive bone changes (erosions) in a single scoring system. US7 score gives a rapid assessment of disease activity and is feasible for use in daily clinical practice.¹⁵

MSUS for assessment of remission⁵⁷

Some patients in remission, according to the clinical criteria, experience progression of structural damage and deterioration of functional capacity over time. This can be explained by the persistence of subclinical inflammation, found only by imaging modalities (Magnetic Resonance Imaging (MRI), MSUS).¹⁶ There is evidence that the presence of a PD signal is a strong predictor of subsequent radiographic progression and a recent relapse in RA patients in remission.^{17,18}

In 2016, the International Task Group of experts in MSUS published a paper with 6 practical algorithms for the use of ultrasound in patients with RA in daily rheumatology practice. These algorithms were used to establish diagnosis (algorithms 1 and 2), to monitor the effect of treatment (algorithms 3, 4 and 5) and to assess low disease activity or remission (algorithm 6).¹⁹

Seronegative Spondyloarthritis (SpA)

Psoriatic Arthritis (PsA)

MSUS aids in making a diagnosis of PsA by detecting subclinical involvement (for example enthesal pathology in patients with skin psoriasis without symptoms of arthritis), assessing disease activity, therapy monitoring through demonstration of structural and inflammatory lesions (of joints, tendons, skin, and nails).

Five major targets of disease process exist in PsA – skin, joints, nails, tendons and entheses; MSUS can be used to assess each of them. PDUS has been proven to detect increased perfusion in psoriatic plaques and to demonstrate nail involvement (onychopathy), together with GSUS, it can also be used to detect presence of synovitis, paratenonitis, tenosynovitis in PsA patients.²⁰ Sandobal et al. (2014) found a significant difference in the mean distance between ventral plate-bone margin of distal phalanx in patients with PsA and in patients with skin psoriasis in comparison with healthy controls.²¹ Enthesis of extensor tendon to distal interphalangeal joint (DIP) has been proven to be in close relationship with the nail. In 2016, during meeting of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA), a sonographic index for assessment of nail entheses to determine morphology and presence of PD signal from the nails was proposed, which can aid dermatologists and rheumatologists in making prognosis for the presence and severity of PsA (Fig. 2).²²

In patients with psoriasis without PsA

Evidence exists that patients with psoriasis have subclinical enthesitis, which can be assessed by MSUS.^{23,24} The most commonly affected sites by subclinical enthesitis are the Achilles tendon (33.3%), distal patellar tendon (22.2%), proximal patellar tendon (16.7%), the quadriceps tendon (16.7%), and plantar fascia (11.1%).²⁴

MSUS in monitoring treatment response

MSUS can be used to monitor disease activity in patients with PsA. There is discordance between clinical indices for disease activity of PsA and sonographic findings. Michelsen et al. (2016) found that Disease Activity in Psoriatic Arthritis (DAPSA) and Disease Activity Score for 28 joints (DAS28) reflect to a greater extent sonographic activity than Composite Psoriatic Disease Activity Index (CPDAI) and Psoriatic Arthritis Disease Activity Score (PASDAS).²⁵ Sonographic PD score – 5TPD - Five Targets PD for Psoriatic Disease – has been developed for monitoring treatment effect through monitoring change in 5 components, assessed by MSUS – joints, tendons, entheses, skin and nails.²⁶

MSUS for differential diagnosis

Skin psoriasis or psoriatic arthritis

MSUS may aid clinicians in differentiating between psoriasis and PsA: as mentioned earlier, sonographic examination can detect presence of subclinical synovitis and enthesitis and distinguish nail changes between patients with skin psoriasis and PsA.^{24,27}

RA or PsA

In 2006, Fourniè et al. demonstrated the presence of erosive synovitis and tenosynovitis in patients with RA and PsA, while extrasynovial pathology – enthesitis, enthesopathy of flexor tendon attachment to the distal phalanx, juxta-articular periosteal reaction and subcutaneous thickening of finger pad or of the whole finger – only in PsA patients. The authors concluded that inflammation of the fibrous skeleton of the fingers, detected by PDUS, can be used to distinguish RA from PsA.²⁸

Gutierrez et al. (2011) introduced sonographic patterns as potential biomarkers for PsA. 'PTI' pattern (peritenon extensor tendon inflammation) was found in MCP joints in a large percentage of PsA patients and in none of RA patients. The authors concluded that this finding could have a potential role in making a differential diagnosis between RA and PsA at the level of MCP joints.²⁹

Zayat et al. (2015) proved that the number and size of ultrasound-detected erosions of wrists, MCP, proximal interphalangeal (PIP) and MTP joints can aid in differentiating PsA from RA and osteoarthritis (OA). Patients with RA have a greater number of and larger erosions as compared to patients with PsA; and the number and size of erosions in PsA is also larger than those in OA. Presence of large erosions of specific joints like second and fifth MCP, fifth MTP and the distal ulna is highly specific and predictive of RA.³⁰

Other Spondyloarthritides (SpA)**MSUS can be used in diagnosing peripheral SpA^{23,58}**

There is a precise consensus-based definition for enthesitis detected by MSUS.³¹ Physical examination is not reliable enough to detect enthesitis due to lack of obvious signs of inflammation in enthesal involvement. MSUS has been proven to have good sensitivity and specificity in detecting enthesitis. Different sonographic indices exist for assessment of enthesal inflammation. Madrid Sonographic Enthesitis Index (MASEI index) is so far the most complete and the only index using the OMERACT definition of enthesopathy. It has a sensitivity of 83.3% and specificity of 82.8% in diagnosing SpA in patients that present a score ≥ 18 . MASEI combines GSUS and PDUS assessment of enthesitis, bursae and bone cortex for upper and lower limbs.³² A novel method - sonoelastography - is a promising instrument, which can detect early inflammatory changes in tendons and enthesitis (Fig. 3).³³

MSUS for monitoring treatment response

The role of MSUS in monitoring the effect of Tumor-necrosis Factor blockers (TNF-blockers) on enthesitis has been established. Naredo et al. (2010) examined 14 peripheral enthesitis at baseline and at month 6 after initiation of treatment with TNF-blockers. They assessed both inflammatory lesions (thickening, hypoechogenicity, PD signal) and structural lesions (enthesophytes, erosions). They found that inflammatory lesions and bursitis, adjacent to

the enthesitis, demonstrate significant improvement at 6 months after initiation of biologic therapy, while chronic lesions worsen.³⁴

MSUS in degenerative and metabolic arthropathies**Osteoarthritis (OA)**

MSUS is mentioned in the new EULAR recommendations from 2017 for the use of different imaging modalities in OA patients. It can be used as a method for detection of soft tissue lesions and for performing procedures under US-guidance in specific situations for example – in difficult-to-assess joints like the hip joint, in joints with considerable deformity and in patients with obesity.³⁵ MSUS is used for making an early diagnosis of OA, for determining the type and extent of bone and cartilage damage and for detection of synovitis. MSUS reveals the role of soft tissues as a source of pain, a contributing factor for disease progression and may facilitate treatment monitoring.^{36,59} MSUS is a predictor for progression of knee joint OA and can be used as an imaging biomarker.³⁷

Crystal arthropathies**Gout**

MSUS is included in the new 2015 ACR/EULAR classification criteria for the diagnosis of gout – presence of double-contour sign of the hyaline cartilage, defined as hyperechoic irregular signal enhancement over the surface of hyaline cartilage, which is not dependent on the angle of penetration of the ultrasound beam (Fig. 4).³⁸ Other typical sonographic lesions in patients with gout are tophus and aggregates.^{39,60,61}

Chondrocalcinosis (Calcium Pyrophosphate Deposition Disease –CPPD)

The presence of hyperechoic focuses inside the hyaline cartilage or in the fibrocartilage (for example triangular fibrocartilage of the wrist, meniscus in knee joint) detected by MSUS, can be used in addition to conventional radiography and microscopic detection of calcium pyrophosphate dihydrate crystals for making the diagnosis of CPPD.⁴⁰

MSUS in systemic connective tissue diseases and systemic vasculitides**Progressive systemic sclerosis (SSc)****Measurement of skin thickness**

Skin in SSc patients can be examined by ultrasound machines, that are equipped with a high-frequency probe (18MHz). MSUS can be used to measure thickness of the skin and subcutaneous tissues, which improves assessment of the extent of skin involvement and can differentiate between limited and diffuse form of SSc. Determination of

dermal thickness and its echogenicity can help in classifying patients with SSc in oedematous, fibrotic or atrophic phase of the disease.⁴¹ Elastography is an imaging modality, which visualizes the elastic properties of the skin by presenting colour map superimposed over GS image. It can improve reliability of sonographic measurement of dermal thickness at finger level, by assisting the differentiation of derma-hypoderma interface (Fig. 5).⁴² There is evidence in the literature that high-frequency ultrasound can be used to measure skin ulcers and can possibly be used as an outcome measure in clinical trials.⁴³

Lung involvement

Interstitial lung disease (ILD) can be found in patients with very early SSc. Presence of B-lines on lung ultrasound (LUS) correlates with the extent of ILD, assessed by High-Resolution Computed Tomography (HRCT). LUS is a very sensitive method for detecting ILD even in patients with very early SSc.⁶² Using LUS as a screening method for ILD may be feasible to guide further investigation with HRCT.⁴⁴ Ultrasound Lung Comets (ULCs) are often found in patients with SSc, more often in diffuse than in limited SSc, and correlate with assessment of lung fibrosis by HRCT.⁴⁵

Joint and soft tissue lesions

The presence of synovitis and tenosynovitis in patients with SSc is more often found by MSUS than by physical examination.⁶³ With comparison to RA, the following sonographic findings are specific for SSc – the presence of sclerosing tenosynovitis and soft tissue calcifications.⁴⁶

Systemic lupus erythematosus (SLE)

MSUS can be used to detect joint and tendon involvement in patients with SLE. Sonographic findings depend on the type of arthropathy and disease activity. MSUS is a valid and reliable instrument for monitoring involvement of musculoskeletal system and treatment response in patients with SLE.⁴⁷

Dermatomyositis/Polymyositis (DM/PM)

Sonographic examination of the muscles in inflammatory myopathies can detect increased muscular echogenicity, which can be graded by comparing the muscle with the adjacent bone structures. Early in the disease course the muscle may have increased PD signal due to increased muscle vascularisation. Inclusion body myositis is characterised by increased echogenicity of the commonly affected muscles (finger flexors, quadriceps) and these muscles have more pronounced atrophy in comparison to the other inflammatory myopathies. Unique sonographic finding in juvenile dermatomyositis is the presence of intramuscular calcifications.⁴⁸ The acute phase of poly- and dermatomyositis is characterised by normal or increased size, low echogenicity and increased perfusion of the affected muscles. In chronic phase size and perfusion of the affected muscles are decreased and echogenicity is increased.⁴⁹

Sjögren syndrome.

Sonographic examination of major salivary glands has been proven to be a highly specific instrument for early di-

agnosis of primary Sjögren syndrome.⁵⁰ Cornec et al. found that if salivary gland ultrasonography score is added to the American-European Consensus Criteria for Sjögren's Syndrome (AECG) criteria this would increase their sensitivity from 77.9% to 87.0%.⁵¹

Large-vessel vasculitides

Giant-cell arteritis (GCA)

The halo sign, especially when bilateral, is a strong predictor for GCA with level of accuracy high enough (sensitivity 91.60% and specificity 95.83%) to recommend introducing sonographic examination of vessels in routine clinical practice, as well as its inclusion in the development of future classification criteria (Figs 6A, 6B).⁵²

Takayasu's Arteritis (TA)

MSUS of carotid and subclavian arteries aids the early diagnosis of TA. In young women with unclear symptoms and laboratory findings of generalised inflammatory process, the primary extracranial branches of the aortic arch should be examined by ultrasound to diagnose early TA.⁵³ Moreover, sonographic examination of the morphological changes of the wall of carotid arteries can be used to monitor disease progression.⁵⁴

Ultrasound-guided articular and periarticular procedures

MSUS can be used to guide fluid aspiration, articular/periarticular steroid injections, tendon procedures – calcific tendinosis lavage and aspiration (barbotage), tendon fenestration (tenotomy or dry needling), cyst aspiration, drainage of an abscess or hematoma, foreign body removal, percutaneous biopsies of joints, bursae, tendon sheaths, major salivary glands, muscles and perform nerve blocks. It can also guide needle placement for fluoroscopy-guided procedures, such as arthrography, tenography, bursography, or MR arthrography.⁶⁵⁻⁶⁷

Two methods exist: 1. Indirect method – ultrasound is used to mark the puncture site. 2. Direct method – ultrasound visualizes the penetration of the needle during the procedure.⁵⁵

Image-guided musculoskeletal interventions can be divided into several groups: device-guided technique (real-time visualization); freehand technique; indirect technique (prerecorded visualization); direct technique (real-time visualization); fusion imaging-guided, sequential imaging-guided, multiple imaging intervention (e.g., US + CT, US → MR, US → CT, fluoroscopy → CT), intraoperative image-guided intervention (e.g., arthroscopy, intraoperative US).⁶⁵

Ultrasound offers several advantages over conventional or other image-guided procedures: 1. Allows diagnosis of articular and periarticular fluid collections and aids early intervention; 2. Reveals minimal fluid collections and allows the aspiration of so called dry joints; 3. Facilitates planned intervention based on the location, size, or shape of lesion; 4. Helps avoid unsuccessful attempts at aspiration

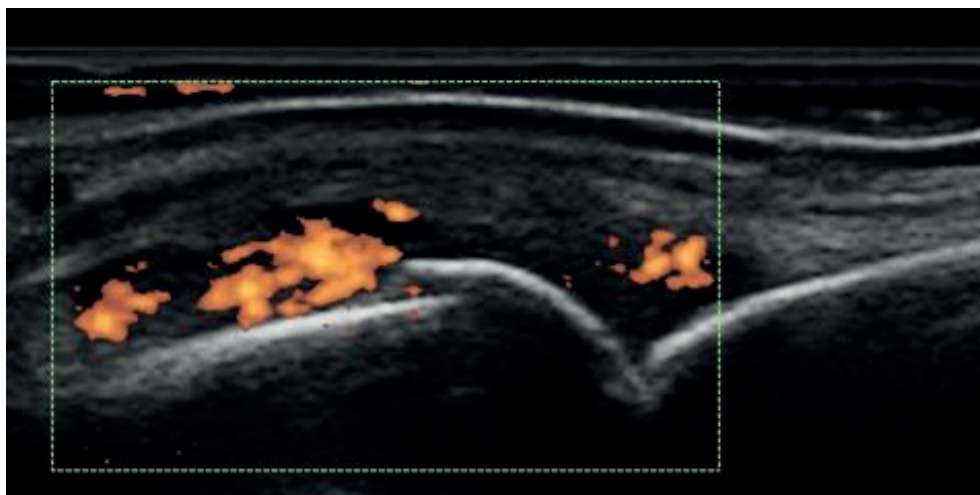


Figure 1. Dorsal longitudinal scan of the second metacarpophalangeal joint (MCP) in a patient with RA. Synovitis of MCP 2 – PDUS – Grade 2.

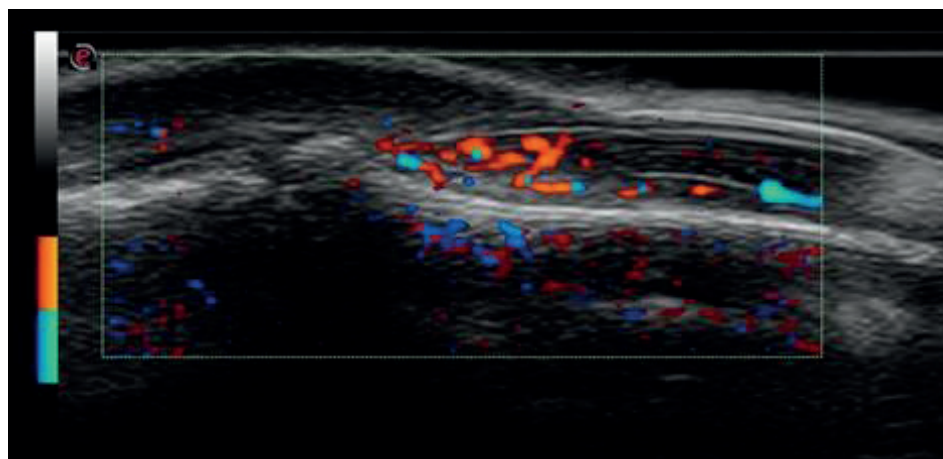


Figure 2. Dorsal longitudinal scan of the distal interphalangeal joint and the nail of a patient with PsA. There is an increased PD signal of the nail bed.

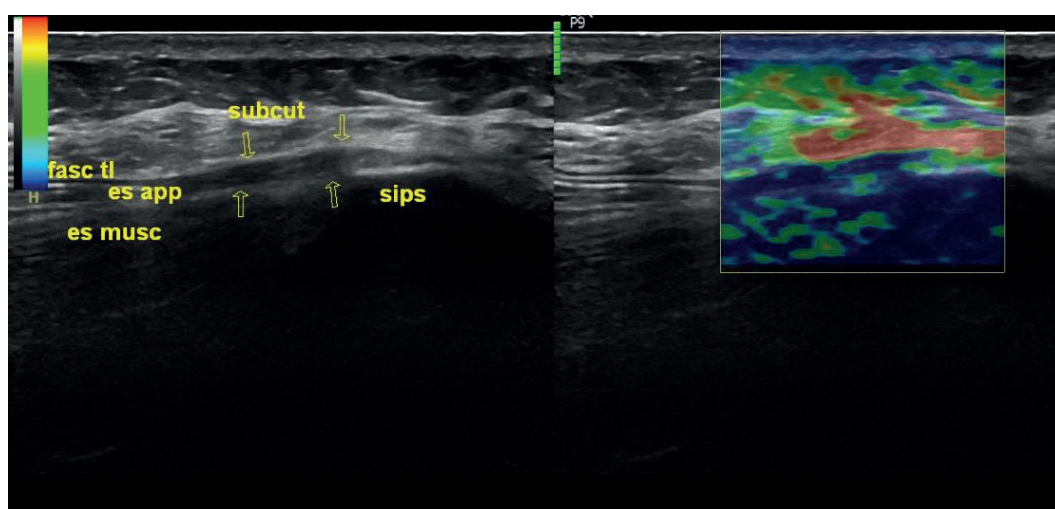


Figure 3. Sonoelastography of erector spinae enthesis, showing signs of enthesopathy – red colour indicates softening due to oedema. sips: spina iliaca posterior superior, es musc: erector spinae muscle, es app: erector spinae apponeurosis, fasc tl: thoracolumbar fascia, subcut: subcutaneous tissue; arrows – enthesis of erector spinae muscle.

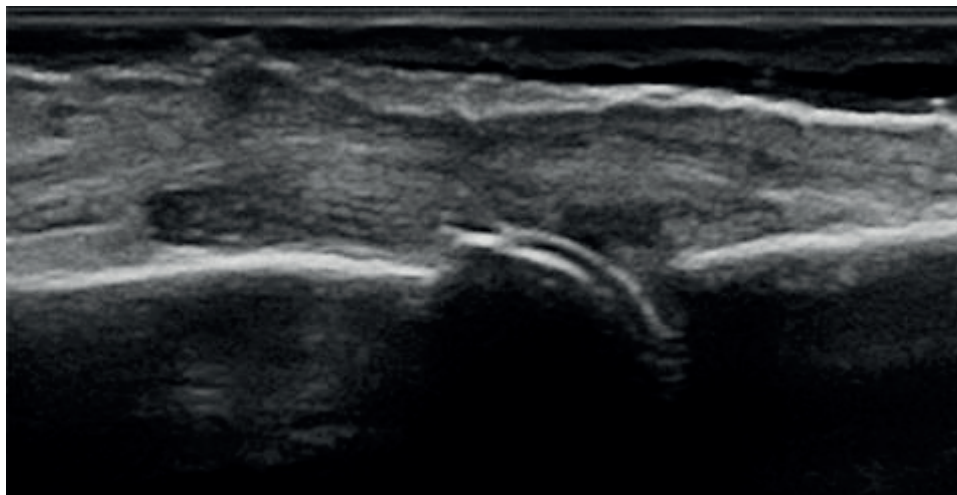


Figure 4. Dorsal longitudinal scan of the second MCP joint in a patient with gout. Synovitis grade 2 on GSUS and presence of 'Double contour sign' of the hyaline cartilage.

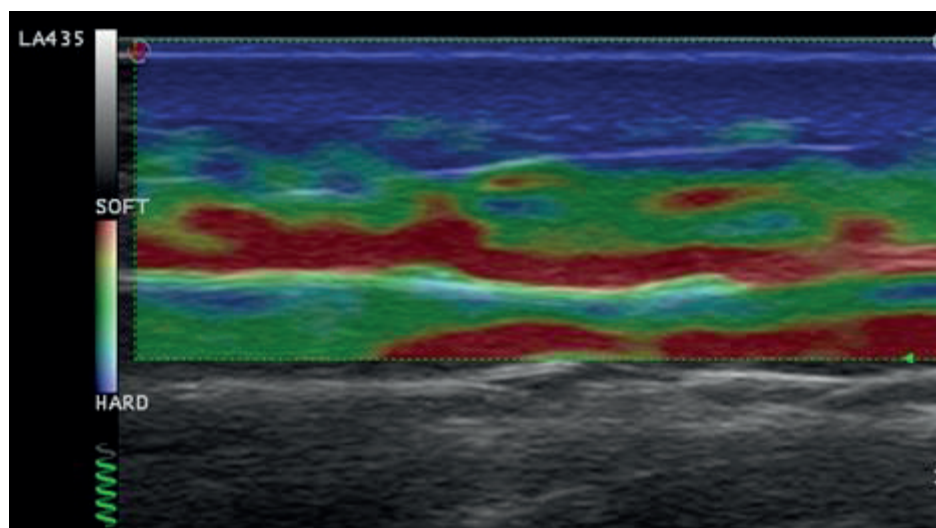


Figure 5. Elastography of the skin of a patient with Systemic sclerosis. Blue colour indicates increased thickness.

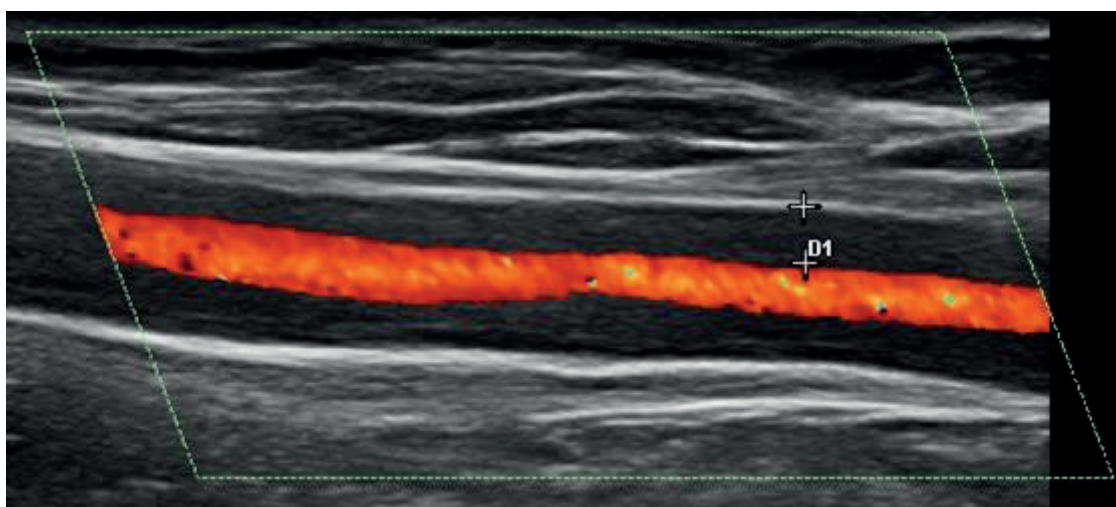


Figure 6 A.

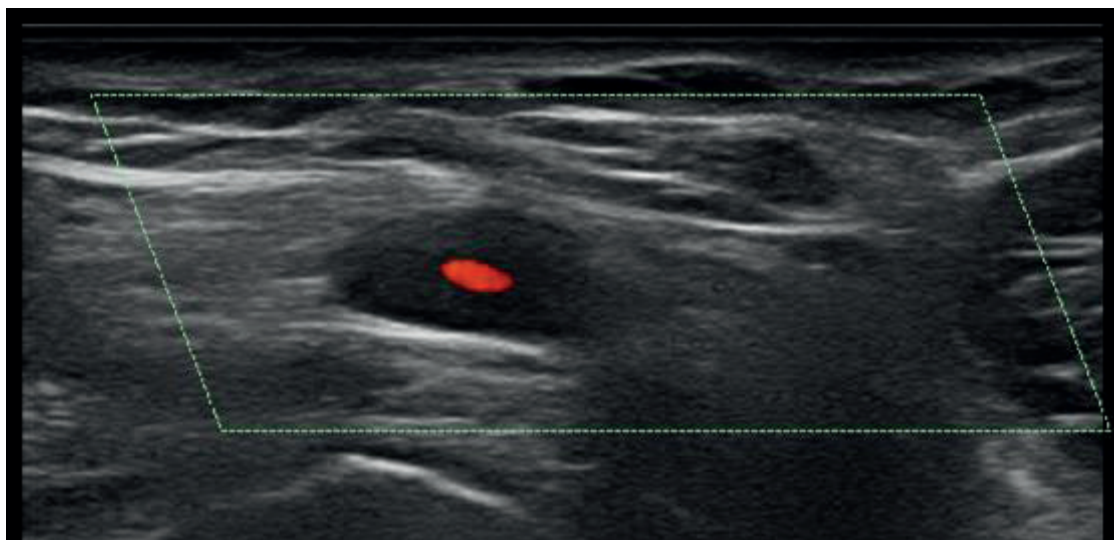


Figure 6 B.

Figure 6. “Halo sign” - hypoechoic wall thickening of the right axillar artery in a patient with Giant-cell arteritis on Colour Doppler Ultrasound **A.** Longitudinal scan **B.** Transverse scan

from truly dry joints or tendon sheaths; 5. Better diagnostic yield (for culture or crystal identification) of arthrocentesis due to accurate needle placement; 6. Prevents and reduces injury of adjacent periarticular or intra-articular structures; 7. Avoids the use of ionizing radiation; 8. Bedside approach needs no general anesthesia; 9. Better intraprocedural compliance by children.⁶⁵

CONCLUSION

MSUS is a powerful instrument for detecting joint and soft tissues pathology and can be used as an imaging biomarker in many rheumatic diseases. It can be used to determine the anatomical extent of inflammation and structural damage in early arthritis, to monitor disease course and determine treatment efficacy. It also facilitates accurate joint and soft tissue aspirations and injections.⁶⁴

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УЗИ костно-мышечной системы в ревматологии - новые горизонты

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Абстракт

УЗИ костно-мышечной системы - это неионизирующая, недорогая, воспроизводимая и надёжная техника визуализации, которая хорошо воспринимается пациентами и играет важную роль в повседневной практике ревматологии. Его можно использовать для оценки поражения суставов и околоуставных суставов, а также сухожилий, боров, энтез, толщины кожи, ногтей, лёгких и крупных сосудов. УЗИ костно-мышечной системы более чувствительно, чем физическое обследование, улучшает диагностический процесс, контролирует реакцию на лечение, точность инъекций ротовой полости и мягких тканей. Он доказал свою роль важного устройства визуализации при ряде ревматологических заболеваний - воспалительных заболеваниях суставов, системных заболеваниях соединительной ткани, васкулите крупных сосудов, а также при дегенеративных и метаболических заболеваниях костей.

Ключевые слова

УЗИ костно-мышечной системы, синовит, энтезит, ревматология
