Recommendations of the ESSR Arthritis Subcommittee on Ultrasonography in Inflammatory Joint Disease

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Abstract

This article presents the recommendations of the European Society of Musculoskeletal Radiology Arthritis Subcommittee on the use of ultrasonography (US) in rheumatic disease, focused on the examination of joints in the adult population. The recommended examination technique and protocols used in a radiologic work-up are discussed. The main US features that can lead to a final diagnosis in the most common rheumatic diseases are addressed. The differential diagnosis that should be considered at image interpretation is presented. The role of US in interventional procedures and clinically important recent developments is also discussed.

Keywords
- ultrasound
- inflammatory joint disease
- arthritis
- ESSR

Indications for Ultrasound in Inflammatory Joint Disease

High-resolution ultrasonography (US) has become a powerful diagnostic tool in inflammatory joint disease and has multiple roles: early diagnosis, disease activity assessment, follow-up/therapy monitoring, and intervention, both for diagnosis and treatment.

Fundamentally, US can help establish which components are affected, particularly with regard to synovium, enthesis, or cartilage. Synovitis is the predominant feature of early rheumatoid arthritis (RA), enthesis is a hallmark feature of spondyloarthritides (SpA), and changes in cartilage are important with US, be suggested, even when the disease is at an early stage.

Rheumatic disease that is clinically occult can be identified with US, which with the use of color or power Doppler is more sensitive in detecting disease activity. Also, classification of the disease as oligo- or polyarticular can be more precisely achieved with the aid of US.

Examination Technique and Protocols

Accurate rheumatologic US requires a high-end US machine with appropriate transducers. High-resolution linear transducers with 10- to 15-MHz frequencies are used for larger joints (shoulder, knee, elbows, and hip). The frequency should be adjusted to lower levels if higher penetration is required (in cases of deep joints such as the hips or in obese patients). Linear transducers of higher frequency or hockey-stick transducers with 12- to 18-MHz frequencies are used to examine smaller and more superficial joints, such as the joints of the hands and feet.

Optimal US imaging requires small movements of the US probe along with generous quantities of coupling jelly. It is important to apply minimal probe pressure and scan the whole area of the joint capsule in two perpendicular planes because pathology can be confined to one part of the joint only. Graded compression with the transducer, so-called sonopalpation, is useful to differentiate fluid (effusion) from solid tissue (synovial hypertrophy). Comparison with the contralateral/normal side can be obtained in cases of doubt, although it is important to recognize that many of the arthritides have a bilateral and symmetrical distribution.

Power or color Doppler should be applied to reveal hyper-vascularity due to neoangiogenesis. In the large joints, such as the knee and hip, it is important to examine the joint in more than one position because fluid or loose bodies may be displaced into the sonographic window.

On follow-up scans, the operator must ensure that scan parameters, positioning of the probe, and probe pressure are similar to previous examinations. Furthermore, there are many different techniques to quantify disease activity, ranging from measuring synovial volumes to assessing the amount of Doppler signal.

US imaging protocols differ according to the rheumatic disease under investigation. The joints to be evaluated generally are determined by the probability of involvement in a particular disease. Many protocols were devised for research trials, but in daily clinical practice the aim of US imaging is often simply to determine whether or not active synovitis is present in specific joints.

How to Examine the Joints

In RA the most commonly affected joints are the wrist, hand, knee, foot, and ankle. Consequently these joints are more commonly imaged and the most likely to suggest a diagnosis. The sacroiliac (SI) joints are deep lying and not reliably scanned. However, US may have a role for guiding SI joint injection.

The many approaches to assessing joints often depend on the clinical question, but for the inexperienced sonographer, Table 1 provides a guide to the most useful sites for detecting synovitis and effusion. Furthermore, bone surfaces should be carefully reviewed for erosion.

Tendons, bursae, and associated structures are also scanned in the context of inflammatory joint disease. The European Society of Musculoskeletal Radiology (ESSR) Arthritis Subcommittee recommends scanning according to the Musculoskeletal Ultrasound Technical Guidelines provided by the ESSR. Of note, it is important to scan the ulnar side of the wrist, the styloid process, and the extensor carpi ulnaris tendon in cases of possible RA. The examination of the tendons is tailored to the areas of suspected pathology.

Ultrasound Findings in Rheumatic Disease

Familiarity with the normal US features of joints, tendons, ligaments, and surrounding tissues is a prerequisite for performing an efficient US examination. The Outcome
Table 1 Joint scanning for detecting synovitis and effusion

<table>
<thead>
<tr>
<th>Joint</th>
<th>Sites for scanning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrist</td>
<td>Dorsal joint recesses of DRUJ, radio and ulnar carpal, intercarpal, and carpometacarpal joints</td>
</tr>
<tr>
<td>MCP, PIP, DIP joints</td>
<td>Dorsal and palmar aspects circumferentially</td>
</tr>
<tr>
<td>Ankle</td>
<td>Anterior tibiotar joint, dorsal joint recesses of mid-talar and tarsometatarsal joints</td>
</tr>
<tr>
<td>MTP, PIP, DIP joints</td>
<td>Dorsal and palmar aspects circumferentially</td>
</tr>
<tr>
<td>Glenohumeral joint</td>
<td>Anterior, posterior joint recesses, biceps tendon sheath</td>
</tr>
<tr>
<td>Elbow</td>
<td>Coronoid, olecranon fossa</td>
</tr>
<tr>
<td>Hip</td>
<td>Anterior joint recess</td>
</tr>
<tr>
<td>Knee</td>
<td>Suprapatellar, medial, and lateral parapatellar recesses, popliteal recess</td>
</tr>
</tbody>
</table>

Abbreviations: DIP, distal interphalangeal; DRUJ, distal radioulnar joint; MCP, metacarpophalangeal; MTP, metatarsophalangeal; PIP, proximal interphalangeal.

Measures in Rheumatology (OMERACT) group published a consensus of US definitions of pathologic findings seen in inflammatory arthropathies that are widely used.

Rheumatoid Arthritis
RA is a chronic inflammatory joint disease that, particularly if left untreated, can lead to joint destruction. Joint damage, including bone erosions, occur early, during the first 2 years of the disease in most patients, and up to 25% of patients develop radiographic erosions during the first 3 months of the disease. Early treatment of RA leads to control of the disease and prevention of permanent changes to the joints.

Conventional radiography (CR) has significant limitations compared with US in the diagnosis and follow-up of arthritis. Unlike CR, US can detect synovial hypertrophy and is also able to detect erosions earlier than CR. In addition to intra-articular changes, US can demonstrate extra-articular disease such as tenosynovitis, bursitis, and rheumatoid nodules. Recommendations on the use of imaging in RA were published by the European League Against Rheumatism (EULAR).

Table 2 Scoring system for classification of synovitis in grayscale and color/power Doppler

<table>
<thead>
<tr>
<th>Grade</th>
<th>Grayscale synovitis</th>
<th>Color/Power Doppler signal</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Absence of synovial thickening</td>
<td>Absence of flow signal</td>
</tr>
<tr>
<td>I</td>
<td>Mild synovial thickening</td>
<td>Single vessel signals</td>
</tr>
<tr>
<td>II</td>
<td>Moderate synovial thickening</td>
<td>Confluent vessel signals, extent &lt; 50% of synovium</td>
</tr>
<tr>
<td>III</td>
<td>Severe synovial thickening</td>
<td>Confluent vessel signals, extent &gt; 50% of synovium</td>
</tr>
</tbody>
</table>

*Mild synovial thickening: filling the angle between the periarticular bones, without bulging over the line linking tops; moderate synovial thickening: bulging over the line linking tops of the periarticular bones but without extension along the bone diaphysis; severe synovial thickening: bulging over the line linking tops of the periarticular bones and with extension to at least one of the bone diaphysis.

Synovitis
In RA the earliest detectable change is proliferation of the synovium seen in joints, tenosynovium, and within bursae. Active synovitis is characterized by neoangiogenesis that can be detected with power and color Doppler. Numerous studies have proven the correlation of the degree of disease activity with the extent of Doppler signal in thickened synovium (number of vessels). Various systems have been proposed in the literature for scoring synovitis. The ESSR Arthritis Subcommitte recommends a simple four-grade semiquantitative scoring system (Table 2), originally postulated by Szkułdarek et al, which has proven high reproducibility among rheumatologists and radiologists and high agreement when compared with magnetic resonance imaging (MRI).

Tenosynovitis is a frequent finding in RA and refers to the inflamed tendon sheath that is manifested as an effusion or synovial thickening around the tendon. Increased vascularity due to neoangiogenesis also reflects disease activity (Figs. 3 and 4). A scoring system for tenosynovitis in RA using a four-point grading system (0–3) was introduced by the EULAR/OMERACT group.

In cases of remission, synovial hypertrophy may persist and become more hyperechoic with a decrease in neoangiogenesis.

Erosions
Bone erosions are detected as cortical bone defects visualized in two perpendicular planes (Fig. 5). Erosions are sometimes filled with vessels in active erosive disease. The presence and progression of bone erosions in early disease are poor prognostic factors. US detects seven times more erosions than CR in early RA.

Peripheral Spondyloarthritis
SpA refers to a heterogeneous group of diseases including ankylosing spondylitis, reactive arthritis, psoriatic arthritis, inflammatory bowel disease–related arthritis, and undifferentiated SpA. This group of conditions has a strong association with the class 1 surface antigen HLA-B27. It exhibits a characteristic pattern of peripheral arthritis that is asymmetric, typically oligoarticular, and predominates in the lower extremities. Other characteristic features are sacroiliitis, spondylitis, enthesitis, dactylitis, and inflammatory eye disease. The role of US is confined to assessing peripheral SpA because sacroiliitis and spinal disease cannot be depicted reliably.
the use of imaging in SpA were published by EULAR and ESSR.\textsuperscript{21–23}

The hallmark of peripheral SpA is inflammation at the bone insertion of tendons, ligaments, and joint capsule called enthesitis. Benjamin et al used the enthesis organ concept to explain pathologic imaging findings including synovitis, bursitis, and extracapsular changes adjacent to ligaments and tendon entheses that are found in SpA.\textsuperscript{24,25} Numerous studies have shown that US is more sensitive in the detection of enthesitis than clinical examination.\textsuperscript{26,27} However, regarding the entheses of the lower limb, US findings may be related to inflammatory lesions or degenerative microtraumatic changes. Therefore it is important to avoid overdiagnosis of SpA based on US findings alone.\textsuperscript{28}

US features of enthesitis include tendon and ligament thickening at the enthesis and loss of the normal tendon/ligament echotexture with hyporeflectivity. Increased Doppler signal has also been proposed as an important sign.\textsuperscript{29,30}
The concomitant presence of new bone formation in the form of enthesophytes with erosive changes suggests the diagnosis of inflammatory enthesitis (► Fig. 6).

The typical US findings in peripheral SpA include digital tenosynovitis and dactylitis with involvement of the tendon pulleys and joints capsules. Inflammation of fatty tissue (i.e., the Kager fat pad) can also be encountered in peripheral SpA. Synovitis is frequently present, especially in the distal interphalangeal joints with asymmetric distribution.

Osteitis and bone marrow edema are important changes in peripheral SpA that may be detected with MRI but cannot be seen with US.

Crystal Arthropathies

Gout
Gout is an inflammatory condition caused by the precipitation of monosodium urate crystals within joints and in various soft tissues including tendons. Patients may present along a spectrum of disease activity ranging from hyperuricemia to hyperuricemia with asymptomatic joint deposition, through to acute or chronically symptomatic gout. The 2015 American College of Radiology/EULAR classification for gout has included imaging evidence of urate deposition in symptomatic joints or bursae in their classification criteria.31

In acute gout, patients present with a painful, swollen, and erythematous joint that in half of the cases is the first metatarsophalangeal (MTP) joint. Joints of the lower limb are commonly affected, and the main differential to be made is from inflammatory arthritis. In these cases, US may show a wide range of findings typical of acute inflammation including the following:

• Synovitis
• Fluid collections: There is a wide spectrum of findings in the synovial fluid of patients with gout ranging from homogeneous low echogenicity to dense highly echogenic material, with multiple hyperechoic spots of varying shape and size, with or without posterior acoustic shadowing (► Fig. 7)
Increased periarticular and intra-articular Doppler signal
Soft tissue edema
Bony erosions

The presence of microaggregates, presented as echogenic foci within the erosions, may help distinguish gout from other erosive conditions. Gouty erosions are typically seen in a juxta-articular distribution, with a predilection for the first MTP joint.

In chronic gout, the presence of tophi, tendon pathology, and bone erosions can be detected with US. Different US patterns are described in gout (Fig. 8–11).\(^{32,33}\)

An international group of experts presented consensus definitions for US lesions in gout that were subsequently validated.\(^ {34,35}\) Table 3 describes the consensus definitions on four US elementary lesions.

Dual-energy computed tomography (DECT) and MRI are the alternative imaging modalities for the depiction of radiographically occult changes in the early stages of the disease.\(^ {36}\)

**Calcium Pyrophosphate Dihydrate Crystal Deposition Disease**
Calcium pyrophosphate dihydrate deposition (CPPD) disease is characterized by crystal deposition in articular or periarticular tissues. It can be associated with cartilage calcification known as chondrocalcinosis and joint inflammation known as pseudogout.

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**Fig. 6** Longitudinal scan of the Achilles tendon insertion. (a) Thickening and heterogeneity of the Achilles tendon at the enthesis. (b) Increased color Doppler signal at the enthesis. Osteoproliferation (void arrow) and erosion (arrow).

**Fig. 7** Longitudinal scan of the first metatarsophalangeal joint in a patient with acute gout. Aggregates in the joint effusion (arrow).

**Fig. 8** Longitudinal scan of the second proximal interphalangeal joint in a patient with chronic gout. Synovial proliferation with echogenic foci and bone erosion (arrow).
On US, the appearance of CPPD aggregates range from tiny circumscribed hyperechoic spots to larger deposits with or without acoustic shadow. They may be visualized in various tissues including fibrocartilage, hyaline cartilage, tendons, and entheses.

A favored site for CPPD crystal deposition disease is the knee meniscus, where deposits appear as isolated or multiple hyperechoic spots usually without acoustic shadowing. Cloudy deposits in the triangular fibrocartilage complex are also highly specific for CPPD deposition (► Fig. 12).

The hyaline cartilage of the femoral condyles is an easily accessible site for the US detection of crystal deposits that may appear as isolated punctiform spots or clusters of varying size, typically located in the middle and superficial layers of the hyaline cartilage. The deposition of CPPD crystals in the middle layer of the cartilage may generate a sandwich-like appearance (crystal in between two layers of cartilage) that may be differentiated from gout.

CPPD crystal deposits can be detected in many asymptomatic joints including the elbow, hip, and metacarpophalangeal joints. In symptomatic joints, intra-articular crystal aggregates may be associated with effusions, synovial hypertrophy, and increased Doppler signal.

Differentiating between gout and CPPD is based on the characteristics of crystal aggregates and their preferential localization in different anatomical areas. The knee is the preferred site of CPPD crystals, and the big toe is often the site that of monosodium urate crystals. The double contour sign is highly specific for gout. Hyperechoic spots within the hyaline cartilage are specific for CPPD crystal deposition disease. The knee and wrist joints are frequently involved both in gout and in CPPD crystal deposition disease. It should be noted that both CPPD and monosodium urate crystals may be present in the same patient.

**Osteoarthritis**

OA is the most common joint disease and affects the weight-bearing joints, such as the hip, knee, and spine, and non-weight-bearing joints like the hands and thumbs.

CR still plays an important role in the diagnosis and follow-up of OA by demonstrating joint space narrowing, marginal osteophyte formation, subchondral sclerosis, and subchondral cyst formation. OA was previously a condition that was thought primarily to affect hyaline articular cartilage, but now it is considered a disease of the entire joint. The importance of assessing the entire joint means that imaging modalities like US, bone scintigraphy, CT, and MRI have assumed more important roles in the diagnosis, follow-up, and research of OA.

The role of US in the visualization of early cartilage damage is limited by the inaccessibility of substantial portions of the cartilaginous surface of the joints. The modality of choice at this stage of the disease is MRI because it can demonstrate cartilage changes and bone marrow edema.

The importance of US in OA imaging lies in its ability to visualize intra- and extra-articular soft tissue changes. The list of frequently encountered pathologies comprises joint effusion and synovitis, tendon and ligament abnormalities, bursitis, and Baker cysts.

The most clinically significant pathology detected by US is synovitis, associated with both symptoms and structural progression in OA (► Fig. 13). Keen et al showed that painful hand joints are more likely to have synovitis than asymptomatic joints, although the severity of findings did not correlate with the degree of symptoms.

Thus US could be significant both in the diagnosis and treatment follow-up because many of the current treatments have an anti-synovial effect. Further investigation is required, however, to clarify and establish the role of US in the diagnosis and treatment monitoring of OA.
Other Connective Tissue Disorders
Numerous connective tissue disorders can present with US findings with an appearance and distribution similar to RA. The list includes systemic lupus erythematosus (SLE), scleroderma, Sjögren syndrome, and mixed connective tissue disease.
US findings include synovitis with or without Doppler signal, tenosynovitis and tendinosis (especially in SLE where spontaneous tendon tears can occur), and erosions.

Differential Diagnosis
Synovitis
Synovial thickening is a nonspecific finding and does not always reflect an inflammatory arthritis. Synovial hypertrophy can be present in a variety of conditions such as hemophilic arthropathy and sarcoidosis. Synovial thickening may also be seen following trauma and in cases of infection including tuberculous arthropathy.

It should also be differentiated from synovial tumors such as a tenosynovial giant cell tumor that may be focal or diffuse. The intra-articular form of disease is also referred to as pigmented villonodular synovitis, and the localized form affecting the tendon sheath is referred to as giant cell tumor of tendon sheath. Less common synovial tumors such as lipoma arborescens, synovial hemangioma, synovial lipoma, synovial fibroma, synovial chondrosarcoma, and synovial tumor infiltration should also be considered.

Synovial tumors typically appear as hypoechoic nodules or masses with or without Doppler signal. In cases of diffuse tenosynovial giant cell tumor, joint effusion and bone erosions may also be present. In cases of lipoma arborescens, hyperechoic villous projections without Doppler signal are usually present in the joint cavity. Because the US appearances are not specific, MRI may be useful for further characterizing the lesions. Hemosiderin deposition, for example, may suggest a tenosynovial giant cell tumor. Ultimately, biopsy may be indicated to reach the correct diagnosis.

Effusion
Joint effusions are seen as a feature of many joint disorders. It is crucial to differentiate infectious from noninfectious joint effusion. Unfortunately, similar to other imaging modalities, US is unable to make this differentiation. Clinical and laboratory data may suggest the diagnosis, but fluid aspiration if necessary under US guidance is the gold standard for establishing the diagnosis.28

Enthesitis
US is excellent to depict and assess erosive and osteoproliferative changes at the entheses in patients with SpA.28 The differential diagnosis includes enthesopathy due to overuse and traumatic lesions.

Interventions
US is considered the preferred imaging modality for joint interventions due to its availability, lack of radiation exposure, and low cost. Real-time dynamic imaging allows safe access to technically challenging anatomical structures and joints. US is an important tool for guiding injections, both for diagnostic and therapeutic purposes.
US guidance significantly increases the rate of successful aspiration compared with conventional aspiration and allows accurate synovial biopsy. A randomized controlled trial established that sonographic needle guidance improves the performance, clinical outcomes, and cost effectiveness of intra-articular injections for inflammatory arthritis. Similarly, US-guided tendon sheath injections may avoid incorrect needle placement. US guidance is an essential component of tendon therapies including barbotage, dry needling, autologous blood and platelet-rich plasma injections, and high-volume injections.

Recent Developments

The following sections summarize new techniques that have yielded promising results with clinical importance.

Contrast-enhanced Ultrasound

Intravenous administration of microbubble US contrast agents used in US examinations aims at increasing the intensity of Doppler signals from small vessels. In a rheumatologic context, contrast-enhanced ultrasound (CEUS) can augment Doppler signal from vessels in the inflamed synovium. A multicenter trial investigated the capacity of CEUS to demonstrate vascularity in synovitis and compared it with that of grayscale and power Doppler US in patients with RA. The study concluded that CEUS yields substantially better differentiation between active and inactive synovitis.

Despite the increased sensitivity of CEUS, in most clinical circumstances, the use of high-quality equipment by a skilled sonographer is sufficient for an accurate diagnosis of synovitis, and at present the ESSR Arthritis Subcommittee does not recommend the routine use of CEUS.

Three-Dimensional Ultrasound

One of the difficulties encountered with US for follow-up studies is the lack of standardization of monitoring parameters. Three-dimensional US may play a role in improving standardization of both acquisition and interpretation.

Image Fusion

Fusion imaging can superimpose CT/MR data on US real-time imaging. This technique combines the advantages of the different imaging methods and may be useful in the multimodality follow-up of patients. US-guided procedures can be performed more accurately and safely when image fusion is applied, especially in anatomical areas that are better visualized with CT or MR imaging, such as the SI joints.

Elastography

The principle of sonoelastography is the presentation of the compressibility of tissues that is displayed in color or designated with absolute values. In a pictorial assay, inflammatory synovitis exhibited different elasticity values than infectious synovitis and synovial tumors. Further research is required because data are very limited in this field.

Limitations of Ultrasound

An important limitation of diagnostic US is the inability to penetrate bone cortex. This hinders assessment of bone marrow edema, a finding encountered in the early stages of most rheumatologic diseases. Bone marrow edema, the mainstay of the imaging arm in the Assessment of Spondyloarthritis International Society classification criteria, thus cannot be detected by US, and MRI is the investigation of choice. Furthermore, assessment of erosions and structural changes in deeper anatomical regions such as the spine, the SI joints, as well as parts of the peripheral joints, is not possible with US. Reproducibility, which may range depending on the examiner’s training level, and quantification are also important limitations.

Conclusion

Early diagnosis in inflammatory joint disease can be facilitated by imaging. US plays an important role in detecting changes in peripheral joints. A structured protocol in the examination of joints and related structures is a prerequisite for an efficient examination. Knowledge of the pathologic features of rheumatic diseases and their appearances on US is
mandatory. This consensus article of the ESSR Arthritis Subcommittee recommended examination protocols and discussed the main US features in different inflammatory joint diseases.

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