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# Turning the page in osteoarthritis assessment with the use of ultrasound

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## Abstract

**Purpose:** This narrative review summarizes the last 5 years of published, peer-reviewed research on the use of musculoskeletal ultrasound (US) in osteoarthritis (OA).

**Recent findings:** Multiple features relevant to OA can be visualized on US, including synovitis, erosion, enthesitis, osteophytes, cartilage damage, meniscal extrusion and popliteal cysts. US can be used to confirm a diagnosis of OA or make an alternate diagnosis in the clinical setting. When a standardized protocol is used, US is a reliable modality for assessment of the features of OA. Findings on US can predict progression and response to therapy in OA of the hand and knee and can allow characterization of risk factors in a cost-effective, non-invasive, repeatable manner.

**Summary:** US is becoming more widely used in OA imaging and has clear value in addition to radiography and clinical assessment. US will likely prove useful in defining phenotypes and providing treatment guidance in OA.

### Keywords

ultrasound; osteoarthritis; imaging; osteophytes; cartilage; synovitis

## Introduction

Osteoarthritis (OA) is the most common form of arthritis and is a frequent contributor to disability [1] that will affect 25–50% of U.S. adults by age 85 [2–4]. Imaging, most commonly radiography, is frequently used in OA, whether to exclude alternate diagnoses, confirm the OA diagnosis in atypical presentations, or evaluate for concomitant pathologies or severity. However, radiography is insensitive to early changes of OA and to change over time, and this modality is not able to assess soft tissues or inflammation. Both magnetic resonance imaging (MRI) and ultrasound (US) allow imaging of a variety of features relevant to OA, including osteophytes, effusions, synovitis, enthesitis, bursitis, and cartilage pathology. To date, particularly in the United States, MRI has been more widely utilized in

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Human and animal rights

All reported studies/experiments with human or animal subjects performed by the authors have been previously published and complied with all applicable ethical standards (including the Helsinki declaration and its amendments, institutional/national research committee standards, and international/national/institutional guidelines).

clinical and research settings for OA, although MRI is much more expensive and time-consuming compared with US. In addition, MRI is not feasible in many common clinical settings, including for individuals with claustrophobia, larger body habitus, or metal implants. In contrast, US allows point-of-care assessment without radiation or need for contrast, can incorporate dynamic maneuvers as well as multiple joint assessments in a single visit, and is more cost-effective than MRI.

A recent systematic review summarized studies assessing the validity of US against radiography, MRI, histology or arthroscopy of the knee, hand, and hip [5]. At the knee, between US and radiography, there were strong correlations for osteophytes, moderate for effusion and meniscal extrusion, but weak correlations for cartilage thickness. US and MRI at the knee generally demonstrated strong correlations. Fewer studies have considered validity of hand US, finding weak to moderate correlations with other imaging modalities. This narrative review will summarize the last 5 years of published literature on musculoskeletal US for osteoarthritis.

## Recommendations for use of US in OA

The American College of Rheumatology in 2012 put forth a set of general “reasonable use” criteria for US in rheumatology, focused primarily on inflammatory features relevant to arthritis, but not specifically to OA [6]. The European League Against Rheumatism (EULAR) provided more specific guidance regarding clinical imaging of OA in peripheral joints in 2017 [7]. The EULAR recommendations noted that imaging is not needed to make a diagnosis in a typical presentation of OA but could be used in atypical presentations to help confirm OA or make an alternative diagnosis. Imaging was also not recommended for routine follow-up in OA. When imaging is indicated, conventional radiography was recommended before other modalities, although US or MRI were recommended for soft tissue features, and computed tomography (CT) or MRI for bony features when needed. It was also noted that imaging might improve injection accuracy, but this increased accuracy had an unclear impact on clinical outcomes in most cases [7].

Additionally, the EULAR group proposed a research agenda which emphasized the need for methodologically robust studies to explore: the added value of imaging for diagnosis and its cost-effectiveness; whether imaging can, in a clinically beneficial way, identify phenotypes, target therapy, or quantify response to therapy; features that could predict response to therapy; and benefits of imaging guidance for therapeutic purposes [7]. While many of these questions remain pertinent to the field of US in general and as it relates to OA, some studies adding to the literature in these areas since these recommendations were published are discussed below.

## Key features of OA visible on US

The Outcome Measures in Rheumatology (OMERACT) group recently released updated definitions of US-detected pathologies in rheumatic disorders [8]; those most relevant to OA include synovitis, erosion, and enthesitis:

- *Synovitis:* "presence of a hypoechoic synovial hypertrophy regardless of the presence of effusion or any grade of Doppler signal (Figure 1A)."
- *Erosion:* "Intra- and/or extra-articular discontinuity of bone surface (visible in two perpendicular planes)." Erosive OA in the hand is discussed in greater detail below.
- *Enthesitis:* "Hypoechoic and/or thickened insertion of the tendon close to the bone (within 2mm from the bony cortex) which exhibits Doppler signal if active and that may show erosions, enthesophytes/calcifications as a sign of structural damage."

Although enthesophytes can be seen in OA [9, 10], they are more characteristic of psoriatic arthritis and other seronegative spondyloarthropathies, which are often in the differential particularly for distal interphalangeal joint-predominant OA. One study assessed bilateral weight-bearing entheses (quadriceps insertion, patellar tendon origin and insertion, Achilles tendon insertion, and plantar fascia) in participants with psoriatic arthritis (n=19), nodal hand OA (n=25), and healthy control (n=28) individuals, finding that both psoriatic and OA patients had higher US enthesitis scores than did healthy controls, but enthesopathy was common in both arthritis types and this feature did not differentiate between the two [11]. The authors also raised the concern that since the age groups are similar, US in patients with skin psoriasis and joint pain may not be able to differentiate early psoriatic arthritis from OA in this patient population [11].

Definitions for various "elementary lesions" were also provided in the OMERACT paper; those most relevant to OA were osteophytes, defined as a "step-up bony prominence at the bony margin that is visible in two perpendicular planes (Figure 1B)," and cartilage damage, defined as "loss of anechoic structure and/or thinning of cartilage layer, and irregularities and/or sharpness of at least one cartilage margin [8] (Figure 1C)." Some additional features particularly relevant to knee OA were reviewed by Okano et al in 2019 [12], such as meniscal extrusion (Figure 1B) and popliteal cysts (Figure 1D), both readily identified using US.

Additionally, as calcium pyrophosphate deposition often co-exists with OA, these deposits were described by the OMERACT group as "hyperechoic deposits of variable shape," localized within fibrocartilage, hyaline cartilage, tendon, and/or synovial fluid, without posterior shadowing, generally moving with the structure in which they are located (with the exception of synovial fluid) during dynamic assessment [8]. In one study of patients with clinical knee OA, 69% had evidence of crystal deposition (most commonly in cartilage) while only 3 patients had chondrocalcinosis by radiography; the presence of crystals was not associated with Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores, but was associated with higher odds of bursitis and synovitis [13].

## Reliability

There is a general opinion in the OA field (and other subdisciplines in rheumatology) that US is heavily operator dependent (for both capturing images and interpretation), and lacks the necessary reliability for use in both patient care and research. However, it is essential to

recognize that all imaging assessments have similar challenges, and this is not an issue limited to US alone. A large study about a decade ago considered the reliability of semi-quantitative radiographic joint space narrowing assessment in knee OA, reporting kappa values for agreement ranging from 0.56-0.72 [14]. Similarly, a systematic review of semi-quantitative grades on MRI found inter-reader correlation coefficients (ICCs) that ranged from 0.77 (meniscus) to 0.94 (cartilage quality); the kappa for synovitis was lower, at 0.52 [15]. The above noted recent review and meta-analysis of reliability of US in OA [5] reported pooled estimates of inter-rater reliability at the knee ranging from good to excellent; higher for popliteal cysts and osteophytes and lower for effusion/synovitis. An OMERACT study demonstrated good reliability for assessment of synovitis, cartilage damage, medial meniscal extrusion, and osteophytes in knee OA (kappa statistics: 0.67, 0.55, 0.75, 0.73, respectively) [16]. For hand OA, reliability of assessments of osteophytes, synovitis and synovial hypertrophy has been reported as substantial to excellent [5]. In 2016, OMERACT published a reliability study for cartilage and osteophytes in finger joints [17], finding better agreement for osteophytes than for cartilage, the latter of which was not recommended given problematic assessment. Thus, when properly performed using standardized protocols (as should always be the case for imaging in research), US is as reliable as other imaging modalities.

## Ultrasound for hand osteoarthritis

### Hand OA: Overall

As just mentioned, the OMERACT group found osteophyte scoring in the finger joints to be reliable (kappa ~0.7) while cartilage damage assessments were less so (kappa 0.3-0.4) [17]. Another group compared various ultrasound-based hand joint scores with conventional radiography in 62 patients with equivocal exam findings who did not initially meet ACR clinical criteria for hand OA [18]. Two 10-joint scores (both included the 2$^{nd}$ and 3$^{rd}$ proximal interphalangeal joints [PIP] and carpometacarpal [CMC] joint, but differed on inclusion of either the 2$^{nd}$ and 3$^{rd}$ metacarpal joint or the 2$^{nd}$ and 3$^{rd}$ distal interphalangeal joint [DIP]) were found to be more sensitive for osteophyte detection compared with conventional radiography. Additionally, joint tenderness was more strongly correlated with osteophytes on US than with osteophytes on radiography [18]. A small study assessing change 6 times over a year in the interphalangeal joints found weak correlations between clinical features and Australian Canadian Osteoarthritis Hand Index scores and sonographic assessments in the PIPs, with none in the DIPs [19].

Two studies compared patients with either OA or RA involving the hands. The first compared patients with established RA (n=224) and OA (n=73) affecting the hands, but with equivocal clinical examinations leading to referral for US, with a 22-joint US protocol (wrist, MCP, PIP bilaterally). Nearly 10% of OA patients had any power Doppler signal compared with 46% of RA patients; synovial hypertrophy was seen in both groups but was more severe in the RA patients, demonstrating that active inflammation can be seen in both conditions [20]. Another study focused on metacarpal head cartilage damage in RA (n=52) and OA (n=34) patients [21]. Here, both RA (36%) and OA (44%) joints demonstrated frequent cartilage damage by US, although the distributions were different. In the RA

patients, the 2nd and 3rd MCP were most affected, while in OA the damage was distributed across all joints, and slightly more frequently seen in the dominant hand [21].

### Erosive and inflammatory hand OA

There has been ongoing debate regarding inflammatory and/or erosive OA, including its definition(s) and whether this condition is a separate disorder or simply represents the more severe spectrum of hand OA. US is an ideal modality for assessing inflammatory features in hand OA given its accessibility, cost-effectiveness, and ease of performing routine follow-up examinations, so several studies have been performed in this area. Marshall et al., discuss this literature in an excellent 2018 review in *Nature Reviews Rheumatology*, noting that inflammatory changes including synovitis, tenosynovitis, and effusions are frequent in patients with either erosive OA or nodal hand OA [22].

Haugen et al, assessed synovitis in both erosive and non-erosive hand OA, finding that power Doppler signal was more commonly present in erosive than in non-erosive OA, and patients with erosive OA tended to have more severe synovitis and were more likely to progress [23]. However, when compared across similar radiographic severity, the differences were not as marked, consistent with the idea that erosive OA is a severe form of hand OA, but on the same disease spectrum [23]. Several studies have demonstrated an association between active synovitis, particularly as indicated by positive power Doppler signal, and structural OA progression, including development of erosions in hand OA [24–27]. This association indicates that US could identify those patients or those joints at greatest risk for progression, although associations with pain are less clear.

### Thumb base OA

In addition to erosive hand OA, thumb base OA is often considered a separate phenotype of hand OA with specific characteristics. It has long been recognized that thumb base OA, compared with OA of the finger joints, can be particularly functionally limiting [28]. A recent clinical trial (COMBO: Effect of combined conservative therapies on clinical outcomes in patients with thumb-base osteoarthritis) for symptomatic thumb-base OA included US and found an association between power Doppler signal and VAS pain, although Doppler signal was present in only 14% of the 93 patients [29]. Other US features were not associated with pain, although there were correlations between US and radiographic features [29]. Kroon et al. investigated imaging correlates of pain in thumb base OA, finding that in contrast to studies in interphalangeal OA, osteophytes were more strongly associated with pain than inflammatory features, and that there was an additive effect between osteophytes and MRI-detected synovitis. In this study, although US abnormalities were common, significant associations were not seen with pain (although the subset with US [n=87] was smaller than that with MRI [n=202]) [30].

## Ultrasound for knee osteoarthritis

### Associations between US features, intra-operative findings, and radiography in knee OA

One study specifically compared US findings to intra-operative findings in late-stage knee OA (n=57), finding that US had a very high sensitivity (>90%) for medial femoral condylar

cartilage damage, osteophytes, effusion/synovitis, and medial meniscal damage, although specificity was generally much lower [31]. Another study also found a correlation between US and medial (but not lateral) cartilage damage by arthroscopy [32]. US is more often compared to more readily accessible clinical examination or other imaging modalities. Several studies have reported significant correlations between OA features on US and radiography, particularly for osteophytes (medial more so than lateral) where US is more sensitive than radiography [32–35].

## Associations between US features and patient reported outcomes in knee OA

There is a known discordance between radiographic features and symptoms [36], and many researchers have sought to utilize advanced imaging to address this issue. US has been of particular interest given its many advantages as noted above, and some recent studies have explored the potential association between knee OA and symptoms. In a study of 52 patients with bilateral knee OA, knee pain was correlated with osteophytes and cartilage thickness, but not with meniscal protrusion or effusion [37]. Similarly, in a study of 80 patients with knee OA, US features of cartilage damage, osteophytes, and synovial effusion were associated with poorer WOMAC scores [38]. In a study of 194 knees with and without pain, cartilage damage on US was associated with worse VAS, WOMAC and Lequesne index scores [39]. A group from the Philippines compared US features to VAS pain ratings, finding that lateral/medial cartilage clarity, medial cartilage thickness, medial meniscal protrusion, and medial osteophytes at the femoral margin distinguished between groups with minimal versus substantial pain [40]. Sarmanova et al, employed a case-control design to compare three groups with early knee pain, established knee pain, and no knee pain, respectively. They found that baseline effusion and synovial hypertrophy were associated with both early and established knee OA, power Doppler signal was uncommon, and the association with pain was not independent of radiographic knee OA [41]. A large meta-analysis of synovial change in knee OA and knee pain included 24 studies in OA/pain populations and 5 in general or control populations, finding a high prevalence of effusion (52%), synovial hypertrophy (42%), and power Doppler (33%) in people with knee OA or knee pain compared to 20%, 15%, and 16%, respectively in non-OA controls. Those with OA had greater pathology by US than those with knee pain alone, and power Doppler signal presence was associated with pain in 2 studies of symptomatic knee OA [42].

## Features specific to knee OA: meniscus and popliteal cyst

Some US features relevant to OA are specific to the knee, such as meniscal extrusion and popliteal cysts, both of which can be easily assessed using this non-invasive modality but are not seen on radiography. As nicely stated by Podlipska et al, “knee US could be employed as a complementary imaging technique to radiography, especially when MRI is not justified, to possibly clarify tissue-specific structural OA degeneration not depicted by radiographs [34].” Among 270 patients with medial radiographic knee OA, medial meniscal extrusion was associated with increased osteophyte area, decreased medial joint space width, and greater odds of rapid joint space narrowing (≥ 25% loss from baseline) over 3 years [43]. Medial radial displacement of the medial meniscus (corrected for body size) was associated with radiographic OA progression in another study of individuals with medial knee pain (n=55), and was noted to be a potential predictor of progression [44]. Popliteal cyst,

although not specific to OA as it can be seen in various types of knee arthritis, is readily evaluated using US. A study of 125 patients with knee OA found that the presence of a popliteal cyst at baseline was significantly associated (OR~3) with both radiographic and clinical progression of knee OA over 2 years [45]. Synovial hypertrophy had a suggestive association with progression (OR~2) but was not a statistically significant predictor in that sample [45].

### US features and therapeutic injection

In general, and as noted by the EULAR guidelines, while US guidance does appear to improve accuracy of joint injections, the associated improvement in clinical outcomes is not always clear. In addition to guiding injection, US may have a role in patient selection and prediction of response to injection. Calvet et al, followed a prospective cohort of 132 symptomatic knee OA patients with effusion confirmed by US for a year following initial intra-articular aspiration and corticosteroid injection [46]. Predictors of improved pain at one year (an outcome observed in 2/3 of patients) included baseline pain, as well as pain and US effusion assessed at one month [46]. An observational study found that among 33 patients meeting ACR clinical criteria for knee OA, of whom 19 got intra-articular corticosteroid and 14 did not, the synovial thickness and power Doppler signal at one week decreased more in the injection group and were associated with reduced pain; those who did not receive injection generally had increased (rather than decreased) synovial thickness [47].

### Other applications of US in OA

In addition to these more traditional applications, a few groups have applied US to novel questions relevant to OA and its risk factors. Gelhorn et al, assessed muscle thickness via US compared with strength testing in 23 patients with symptomatic knee OA using a protocol developed for this study. They found that higher muscle bulk was associated with less pain, and that quadriceps bulk assessed by US was more strongly correlated with pain and function than was isometric strength assessed using a dynamometer (although this was not observed for other muscle groups) [48].

Femoroacetabular impingement (FAI) is a known risk factor for hip OA [49], and early identification of FAI could be key to prevention efforts. A study of 44 patients with radiographic findings suggestive of FAI and hip pain, but without radiographic hip OA, found that about 2/3 had a labral abnormality on US, while 41% had cartilage abnormalities, 39% had bone contour changes, and 30% had osteophytes [50]. Among 12 healthy control participants of similar sex and age, only one male volunteer had labral calcifications while the other 11 had no findings on US, suggesting that US may be able to identify early pathologic change prior to the development of hip OA in the setting of FAI [50].

## Conclusions

This narrative review summarizes the last approximately 5 years of published research on the application of musculoskeletal ultrasound in osteoarthritis, which is primarily focused on hand and knee OA. While the majority of studies are still rather limited in size, population (often only in patients with OA, or from a single clinical setting), and design (primarily

cross-sectional), there is growing support for utility of US in OA assessment. US is more sensitive than conventional radiography, particularly for osteophytes, which are often used to define early OA, and thus may allow earlier identification of OA changes in a joint. Additionally, US provides detailed imaging of soft tissues (including cartilage, meniscus, ligament/tendon, synovium, fluid collections, and crystal deposits) in a more accessible and cost-effective manner compared with MRI, with additional advantages including ability to image multiple joints and dynamic imaging. US can be as reliable as other imaging modalities when standardized protocols and scoring systems are employed. US has the added benefit of being a valuable interventional tool, useful for guidance of procedures such as intra-articular injections and in the growing area of US-guided synovial biopsy [51].

Future studies should address some of the above noted shortcomings in the literature to date, by including more diverse populations, assessing changes in healthy controls as well as those with pain or radiographic change, employing standardized imaging protocols and scoring assessments, and including a longitudinal component to assess responsiveness to change over time. The relatively recent trend to include US in clinical trials may improve our understanding of how this powerful tool can best be used as both a predictor and an outcome (using baseline and longitudinal change in features, respectively). Ultrasound holds significant promise as an imaging tool in osteoarthritis, and in the future could be used at the bedside to provide diagnostic and prognostic information as well as guide both systemic and local treatment decisions and applications.

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Conflicts of interest

Dr. Nelson reports grants from NIH/NIAMS and the Rheumatology Research Foundation, during the conduct of the study; personal fees from Flexion Therapeutics, Inc, GlaxoSmithKline, MedScape, and Health Press, Ltd., outside the submitted work; and is the current Chair of the Examination Subcommittee for the American College of Rheumatology Musculoskeletal Ultrasound Certification (RhMSUS) Oversight Committee.

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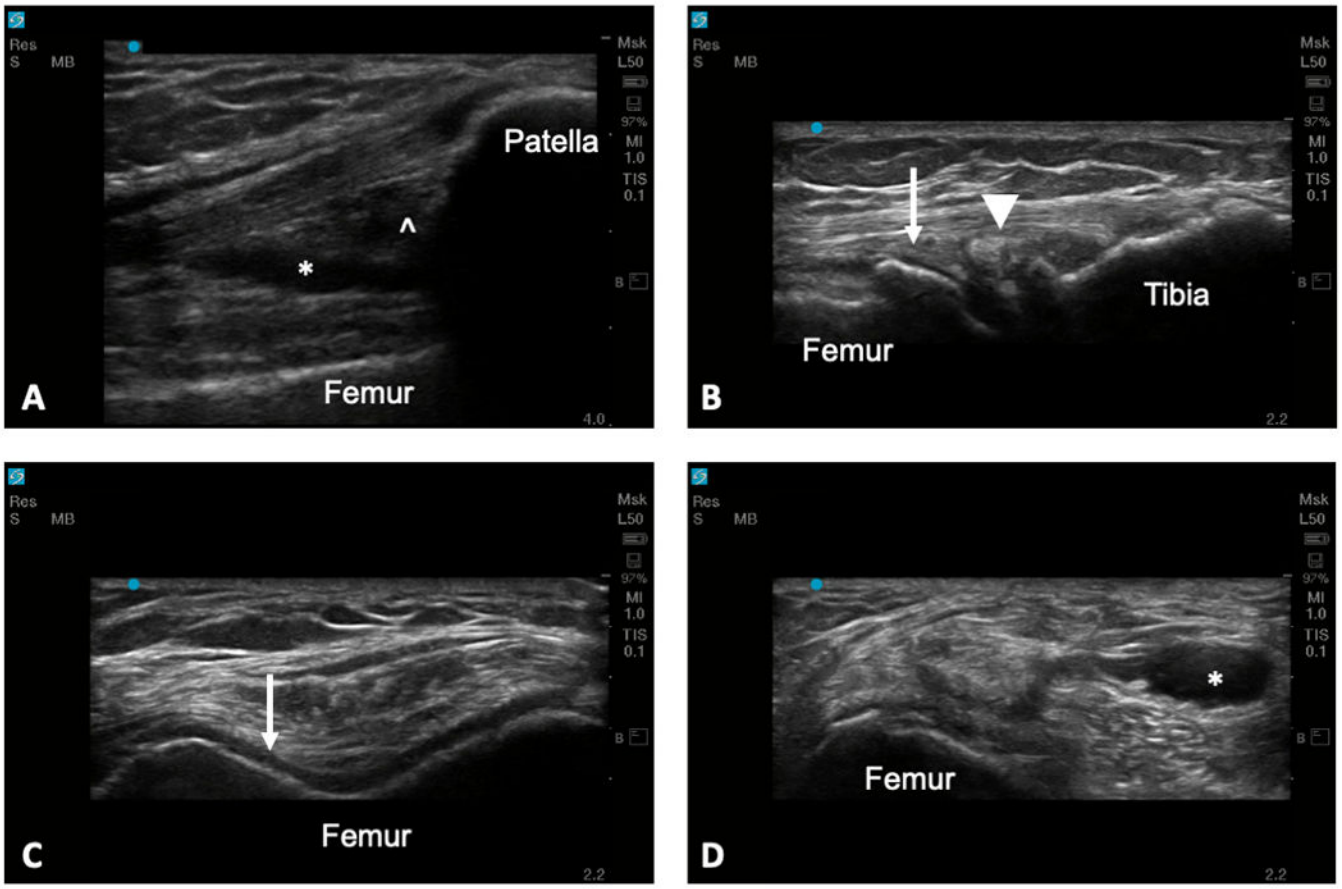


**Figure 1:**

Representative US images from the right knee of a 74-year-old woman. By convention, the left side of the image is proximal/medial.

A: Suprapatellar Longitudinal image showing a small effusion (*) and surrounding synovitis (^)

B: Lateral Longitudinal image showing moderate osteophytes (arrow) and mild meniscal extrusion (arrowhead)

C: Suprapatellar Transverse image in flexion showing mild loss of cartilage thickness and increased echogenicity (arrow)

D: Posterior Transverse image showing a small popliteal cyst (*).