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Utilizing ultrasound in the diagnosis and management of osteoarthritis

Annacarla Finucci[1], Vasilia Iorgoveanu[2], Iolanda Maria Rutigliano[1], Chiara Scirocco[1] & Annamaria Iagnocco*,[1]

[1]Rheumatology Unit, Dipartimento Medicina Interna e Specialità Mediche, Sapienza Università di Roma, Rome, Italy

[2]Rheumatology Unit, Sf. Maria Clinical Hospital, Bucharest, Romania

*Author for correspondence: annamaria.iagnocco1@gmail.com

Osteoarthritis (OA) is the most common rheumatic disease and the leading cause of disability and work impairment in elderly individuals. It is characterized by progressive degenerative changes in the diarthrodial joints at the level of hyaline cartilage, cortical bone, synovium and periarticular tissues (i.e., ligaments and bursae). Being a valuable tool in the assessment of joint abnormalities and due to its numerous advantages in comparison to other imaging techniques, in the last decades musculoskeletal ultrasound has been increasingly utilized in OA. Its characteristic of being a real-time technique, combined with its limited costs, feasibility and sensitivity to detect a wide range of pathological changes has led to increasing applications of this tool in the diagnosis and monitoring of OA.

Keywords: cartilage abnormalities • musculoskeletal ultrasound • osteoarthritis • osteophytes • synovitis

Osteoarthritis (OA) is a very common rheumatic disease and it represents a relevant public health issue [1]. It is characterized by articular cartilage degeneration, up to its break-down, and progressive changes in the other joint and periarticular structures. The pathogenesis of osteoarthritis has long been thought to be cartilage driven, but recent studies show an integrated role of subchondral bone and synovial membrane [2]. A loss of equilibrium between synthesis and degradation of cartilage components produces alterations of its structure and progressive cartilage thinning which are followed by a sequence of events that globally involve the joint and lead to impairment. Bony cortex undergoes subchondral bone sclerosis and production of osteophytes occurs as an attempt to balance biomechanical alterations caused by cartilage break-down. These bone changes can be shown during all the stages of the disease, even on the onset. It has been postulated that subchondral bone is the first site of damage and initiates cartilage degradation [2,3]. Synovitis is present in many cases, in early and late stages, usually having an episodic course and nonaggressive features. It is thought to be initiated by cartilage debris and catabolic mediators entering the synovial cavity and it contributes to the vicious cycle of damage of the joint, due to inflammatory mediators produced by synovial cells that lead to further cartilage damage [2]. At the level of periarticular tissues, typically OA involvement is represented by bursitis and tendons as well as ligaments irregularities [1,3–4].

Due to its ability to evaluate joint space narrowing and indirectly show cartilage thinning, for many years plain radiography has been considered the gold standard method for assessing joint changes in OA. It has the capability of demonstrating bony changes such as osteophytes and erosions, but it does not allow direct visualization of the cartilage layer and periarticular tissues involvement [5,6]. MRI has a great accuracy and sensitivity to highlight OA structural and inflammatory joint and periarticular changes. However, its widespread and routine use is limited by high costs and scarce availability of equipment [6,7]. Musculoskeletal ultrasound (MSUS) is emerging as a new

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valuable tool to assess joint abnormalities in patients affected by OA. It is a real time method that offers data for immediate correlations between image findings and clinical symptoms and signs of pathology. It allows direct visualization of hyaline cartilage and differentiation between early and late stage of its involvement. In early disease, cartilage borders become irregular, a progressively change in its homogeneity appears and thinning of the cartilage layer, up to its complete loss, progressively appears. In addition to cartilage assessment, MSUS is able to detect inflammatory changes such as synovial effusion, synovial hypertrophy and increased pathological vascularization within the synovial structures, which is reflective of active inflammation. Moreover, MSUS shows periarticular tissue abnormalities as well as bony cortex lesions [8–10]. Its multiplanarity and dynamic assessment offers a global evaluation of the joint while its noninvasiveness and absence of radiation burden correlates to a good patient's compliance. Recent technological advances of equipment, with the production of high end machines equipped with high-resolution probes and new softwares, improved the sensitivity of MSUS in the detection of a wide set of changes since early disease [10,11]. Furthermore, the implementation of new tools, such as 3D-US and fusion imaging techniques, are opening new interesting frontiers for a better visualization of OA-related abnormalities [12,13]. All those factors have positively influenced the widespread use of MSUS in the diagnosis and monitoring of OA.

At present, the main indications on the use of MSUS in OA are the detection of inflammatory and structural joint changes, such as synovitis, hyaline cartilage damage, osteophytes and erosions as well as the assessment of abnormalities within periarticular structures, such as ligaments and bursae. In addition, MSUS provides a useful guidance for local diagnostic and therapeutic procedures (i.e., fluid aspiration and intrarticular drug injections) and allows to monitor the progression of pathology and the response to local and systemic therapies over time [6,10,12,14–16].

Diagnosis

Joint findings in OA

MSUS detects both inflammatory and structural osteoarthritic joint abnormalities. It visualizes inflammatory features allowing the analysis of correlations with clinical and imaging findings, including prediction of disease progression, as recently demonstrated [17–19].

Inflammatory findings

Multiplanar and dynamic assessment of joints, according to standard scanning protocols for different sites, gives the possibility to effectively evaluate the different components of synovitis (i.e., synovial effusion and synovial hypertrophy). OMERACT definitions for components of synovitis in RA can be also applied to OA: synovial effusion is defined as an abnormal hypoechoic or anechoic intrarticular material that is displaceable and compressible but does not exhibit Doppler signal; synovial hypertrophy is an abnormal hypoechoic intrarticular tissue that is non-displaceable and poorly compressible and which may exhibit Doppler signal [20]. Synovitis is a frequent finding in OA patients. It usually has an episodic course and non aggressive trend. Power Doppler mode is useful to differentiate between active and inactive synovitis. Recent studies demonstrated that the presence of synovial hypertrophy and power Doppler signal correlates with radiographic progression [17,19]; this finding may have important implications on therapeutic strategies.

Structural findings

Articular cartilage

Early pathological changes in OA occurs at the level of the hyaline cartilage. Cartilage can be directly visualized in a large number of peripheral joints, using the appropriate acoustic windows. In the normal joint, it is imaged as an anechoic curvilinear band with regular margins (a thin chondrosynovial surface, and a thicker osteochondral surface). Thanks to technological advances, cartilage thickness can be accurately measured with new equipment and the cut-off values vary according to the size of the joint (0.5–1 mm for hand and foot joints, 3 mm at knee level). In different stages of disease MSUS is able to detect ultrastructural changes that reflect different pathological processes. In the early phases of OA, cartilage margins become irregular and lose their sharpness, reflecting tissue degeneration that leads to microcleft formation; successively a loss of homogeneity of the cartilage band is shown and alterations in the echotexture which becomes hypoechoic are present, due to the alterations of the local components; later on, a focal thinning appears which is followed by a global thickness reduction with joint space narrowing, along with progressive cartilage degradation (Figure 1). Although MSUS is able to visualize different cartilage changes, further studies and strategies are needed to individuate a reliable scoring system which is able to better describe the grade of cartilage involvement. In a recent study, a semiquantitative (0–3) score for cartilage damage showed poor reliability, particularly in terms of interobserver assessment, thus confirming the opportunity of applying a dichotomous score for cartilage assessment and the need for redefinitions of moderate cartilage abnormalities [2,10–12,21–23].

Bony cortex

In the normal joint, bony cortex appears as a continuous hyperechoic line. In OA, due to cartilage breakdown and redistribution of mechanical load, osteophytes are produced and are seen as bony protrusions at the margin of the joint (Figures 2–4) [10,14,23–25]. It has been demonstrated that MSUS is more sensitive than MRI in detecting osteophytes [26]. This statement finds an exception in the assessment of the internal osteophytes (i.e., osteophytes located in the deeper part of the joint that are not visible at the US scans). Internal osteophytes are more frequent in knee OA (mainly posterior tibia and internal femur). They can be visualized with MRI and can be differentiated from denudation areas of the subchondral bone, represented by complete loss of cartilage. Full thickness cartilage loss and intrachondral osteophytes protruding to the joint surface represent two distinct phenotypes of denudated bone areas that can be only measured by MRI [27]. Recently, OMERACT task force assessed the reliability of MSUS in scoring structural and inflammatory lesions in hand and knee OA. Particularly, on the basis of a consensus definition of osteophyte (a step-up of bony prominence at the end of the normal bone contour or at the margin of the joint seen in two perpendicular planes with or without acoustic shadow) they demonstrated that MSUS has a good to excellent intra- and inter-observer reliability in grading osteophytes at hand and knee level in patients with OA [23,25–29]. Another recent study focused on interobserver reliability and correlation between MSUS findings and WOMAC (Western Ontario McMaster University Osteoarthritis) index, in knee OA. They demonstrated an excellent interobserver agreement, not only for osteophytes but also for other analyzed items (cartilage thinning, synovial effusion, popliteal cyst, synovial thickening). Furthermore they observed a significant correlation between WOMAC index and MSUS findings [30].

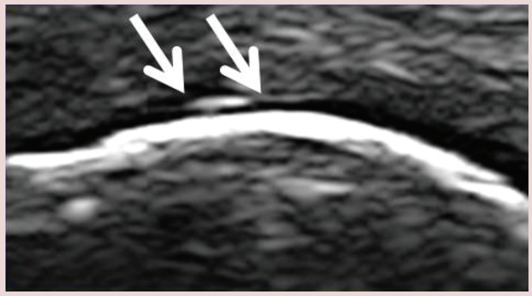

Figure 1. Ultrasound of the proximal interphalangeal joint in and osteoarthritis.
Evidence of cartilage thinning (arrows).

Hand OA may be erosive with evidence of a discontinuity of the bony surface, which is seen in two perpendicular planes by MSUS. Inflammatory features are associated with erosions development, thus it is possible to hypothesize a pathogenetic role for inflammation and its subsequent potential target for treatment [18,31]. Also for synovitis components, OMERACT definition of erosion originally applied to RA is applicable to OA too [20]. In OA joints, erosion detection can be hindered by the presence of osteophytes that limit the width of the acoustic window.

Additional US findings

Typical changes in periarticular tissues in OA are represented by involvement of bursae. Bursitis are identi-

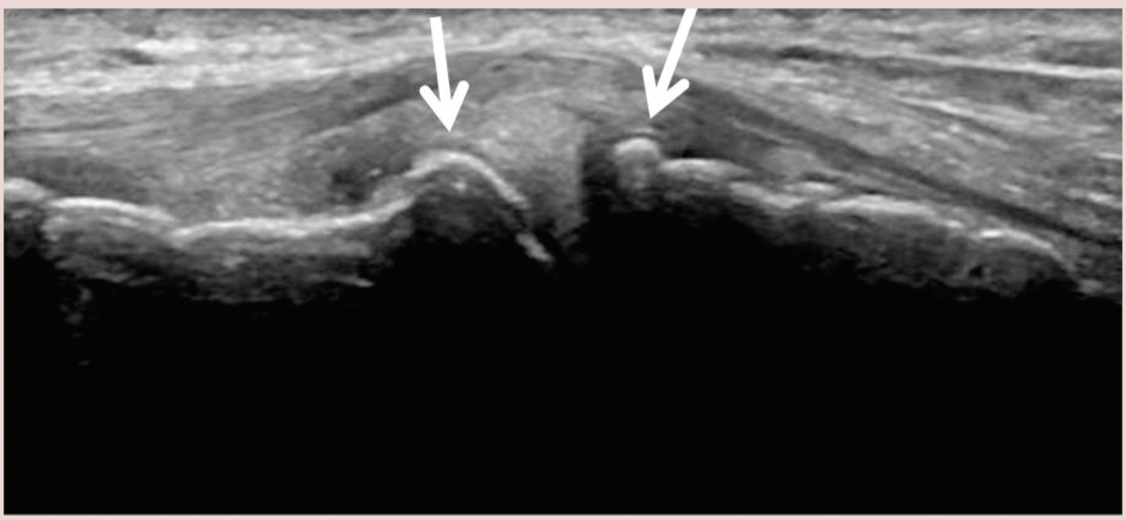

Figure 2. Musculoskeletal ultrasound of the knee in osteoarthritis. Medial longitudinal scan. Presence of osteophytes (arrows).

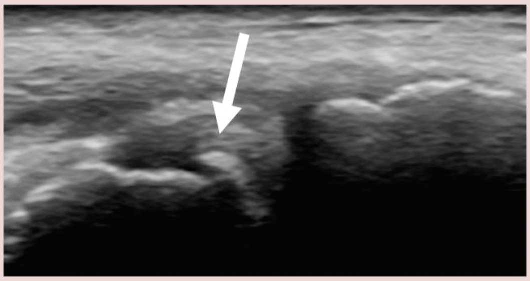

Figure 3. Ultrasound of the first carpo-metacarpal joint. Evidence of a medium size osteophyte (arrow).

fiable as the presence of hypoechoic or anechoic material within the bursa. In knee OA, Baker's cyst is a very common finding (Figure 5) and MSUS can be a useful tool not only for the identification, but also for fluid aspiration and local injections (Figure 6) [32,33]. Recently, sonographic evidence of Baker's cysts has been demonstrated to be a predictor of clinical and radiological progression of knee OA at 2-year follow-up [19]. Other bursitis that can be detected in patients with OA are anserine and infrapatellar bursitis, at the level of the knee, ileopsoas and throcanteric bursitis, in hip OA, bursitis of the first metatarsal joint in foot OA.

In knee OA, MSUS may identify protrusion or extrusion of the medial meniscus with concomitant displacement of the medial collateral ligaments. This sign seems to reflect a joint space narrowing and meniscus protrusion can be one of the first findings of knee OA. Menisci can only partially be visualized by ultrasonography, but MSUS is not able to give information on the deeper part of these periarticular structures [6,10,34–36].

In acromion-clavicular joint OA, a bulging of the intra-articular meniscus can be observed by MSUS. Those findings correlated with the severity of joint space narrowing and pain [6,10].

In hand OA, mucous cysts appear at sonographic assessment as hypoechoic areas delimited by sharp margins, located over the supero-lateral aspect of the distal interphalangeal joints [37,38].

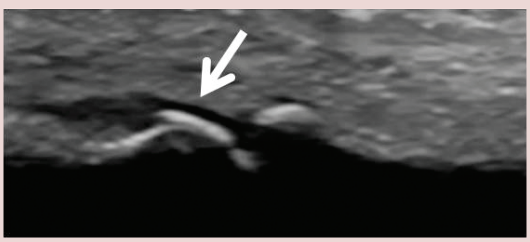

Figure 4. Ultrasound of the proximal interphalangeal joint in and osteoarthritis. Evidence of a small osteophyte (arrow).

Monitoring & treatment

MSUS is able to identify both inflammatory and structural changes in joints and periarticular tissues. For this reason it is a valuable tool to perform a follow-up of OA patient. The possibility to demonstrate synovitis allows to select patients with inflammatory abnormalities and who are prone to develop a progression of disease. Two recent studies demonstrated an association between synovial hypertrophy and radiological and clinical long term progression in hand and knee OA; in knee OA Baker's cysts too have been reported to be associated to disease progression [17,19]. Furthermore, by detecting synovitis and differentiating active from inactive disease by Doppler mode, MSUS has a relevant role in monitoring the disease and assessing the response to treatment at different joint sites. Recently, it has been shown that MSUS may demonstrate short-term reductions of joint abnormalities in the knee joint after corticosteroid therapy [32]. In addition, it has been reported that US-guided injections at the level of the first carpo-metacarpal joint with high molecular weight hyaluronic acid may be effective in decreasing local inflammation and pain [29,39–40].

Different studies demonstrated that MSUS is a feasible, safe and effective technique for intra-articular injections guidance and fluid aspiration procedures [15–16,32,39–40]. It allows to visualize the exact position of the needle which is of particular importance for deep joints procedures, reducing the risk of damage of the periarticular structures such as tendons, nerves and blood vessel as well as avoiding the use of invasive techniques [31,41].

Technique & equipment

MSUS examination should be performed according to a standard scanning protocol, following a multiplanar and dynamic joint assessment. A bilateral examination is recommended to compare anatomic structures from the two sides [24,42]. Guidelines for the application of MSUS in rheumatology are the reference standard to carry out a correct examination [43], along with a good knowledge of the scanning technique for different joints. A correct position of the examined joints has a relevant importance in order to increase the width of the acoustic windows and optimize the visualization of different anatomic structures [43]. For cartilage assessment the following patient positions are recommended: maximal flexion for hand joints and knee; extension for elbow, wrist, ankle and foot joints; intra- and extrarotation for hip and shoulder [44]. The correct visualization of the joint's component allows the appropriate interpretation of normal and pathological findings. For cartilage assessment, in addition to the use of the correct acoustic windows, which are different at various joint sites, a perpendicular insonation of the sonographic beam is fundamental, in order to avoid artifacts and improve the appropriate visualization of the cartilage margins.

The use of high-end equipment and multifrequency, high resolution probes allows to visualize the different joint structures. High frequency probes are appropriate for the assessment of superficial structures and small joints, while low frequency transducers are used for large joints and deep structures [10,13,43–44].

In terms of probe shape, hockey stick probes are used for assessing small joints, particularly in case of deformities and/or limited motion, and large footprint transducers are appropriate for evaluating large joints [43].

Both B-mode and power/colour Doppler modes are used for the assessment of osteoarthritic joints. The use of a correct machine setting, in terms of different parameters such as frequency, gain, image depth, focus positioning, Doppler pulse repetition frequency, is mandatory in the evaluation of different joint abnormalities [10,13,45]. Doppler techniques allow to study synovial hyperemia, differentiating between active and inactive pathology [45–47].

Limitations

The main limitation of MSUS is related to the limited visualization of some joint structures due to the inability of the US beam to penetrate through the bony cortex as well as to the small width of some acoustic windows. Operator dependence of MSUS, which is mostly related to the inexperience of the ultrasonographer, affects both phases of image acquisition and interpretation. This limitation can be attenuated by the use of a standardized scanning technique and the application of internationally approved definition of pathology. Another limitation is linked to the possibility that cartilage degeneration may influence US speed, altering the measurement of cartilage thickness [48]. The application of new tools (i.e., 3D-US and fusion imaging modalities) with an increased anatomical definition and standardization of image acquisition is expected to improve the reliability of MSUS in OA [12,13].

Use in the routine practice

The evidence that MSUS is a valid and reliable imaging technique in the assessment of a number of inflammatory and structural lesions in OA, has led to a progressive and widespread use of it in the routine clinical practice. Even though studies about its feasibility are still lacking, the fact that it is a quick-to-perform technique, its limited cost, patients' acceptance and the absence of radiation burden make it a feasible imaging tool to be used for a number of indications in OA.

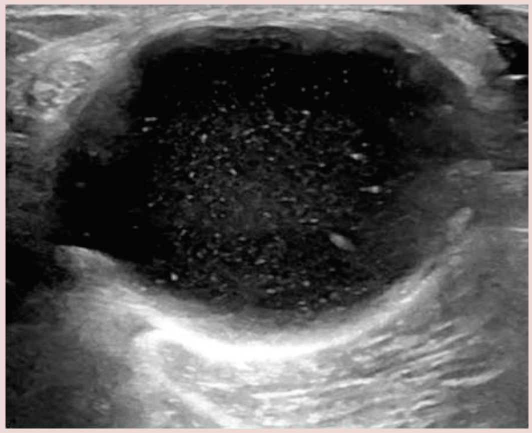

Figure 5. Musculoskeletal ultrasound of the popliteal area in knee osteoarthritis. Evidence of a Baker's cyst (arrow).

Conclusion

MSUS is a valuable tool in the evaluation of both structural and inflammatory alterations in joint and periarticular areas in OA. Those factors positively influence the use of MSUS in the diagnosis and monitoring the disease process at different stages as well as in the evaluation of the response to different treatments. In addition, MSUS is helpful in guiding diagnostic and therapeutic local procedures such as fluid aspirations, drug injections and biopsies.

Future perspective

The use of MSUS in OA assessment is relatively new so that some fields of research are still open, particularly concerning the application of new tools. Recently the OMERACT MSUS task force dem-

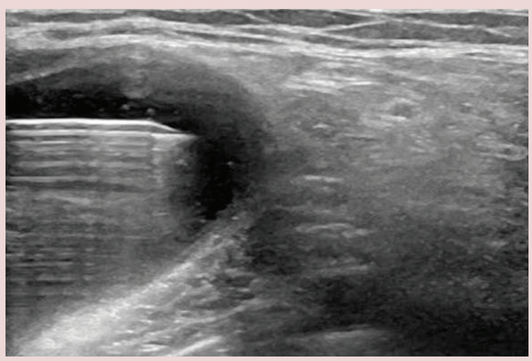

Figure 6. Ultrasound guided aspiration of fluid within the Baker's cysts in a patient with knee osteoarthritis (arrow).

onstrated good to excellent intra- and interobserver reliability in the assessment of structural and inflammatory changes in knee OA. From the evaluation of cartilage some difficulties were demonstrated, particularly in terms of scoring the severity of lesions [23,28]. Both in knee and hand OA, the reliability of MSUS in scoring cartilage abnormalities was lower than for other structural lesions (i.e., osteophytes) [23]. Further studies are needed to improve the standardization of the method in OA, especially for cartilage evaluation [29].

Promising research items seem to be related to new tools such as fusion imaging and 3D-US. Fusion imaging provides a multitechnique characterization (US and CT, US and MRI) of tissue abnormalities, offering anatomical detailed image of different joint structures [12]. 3D-US shows well defined images of joint details by automatic acquisitions of information with the volumetric probe; its use is expected to increase rapidly, particularly due to the reduced necessity of high experience of the operators in the acquisition phase [13,49].

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Executive summary

- Musculoskeletal ultrasound (MSUS) is a valuable tool to assess structural and inflammatory changes in articular and periarticular structures in osteoarthritis.
- MSUS is able to show different stages of disease and to monitor disease progression and response to pharmacological treatment.
- High level equipment and probes are necessary to provide detailed information about anatomical structures.
- MSUS is a safe, well-tolerated, limited-cost, feasible tool in the assessment of osteoarthritis.
- Further studies are needed for standardization and application of new sonographic tools.

References

Papers of special note have been highlighted as:
• of interest; •• of considerable interest

1 Loeser RF, Goldring SR, Scanzello CR, Goldring MB. Osteoarthritis: a disease of the joint as an organ. *Arthritis Rheum.* 64(6), 1697–1707 (2012).

2 Bijlsma JW, Berenbaum F, Lafeber FP. Osteoarthritis: an update with relevance for clinical practice. *Lancet* 377(9783), 2115–2126 (2011).

3 Benito MJ, Veale DJ, FitzGerald O, van den Berg WB, Bresnihan B. Synovial tissue inflammation in early and late osteoarthritis. *Ann. Rheum. Dis.* 64(9), 1263–1267 (2005).

4 Iagnocco A, Rizzo C, Gattamelata A *et al.* Osteoarthritis of the foot: a review of the current state of knowledge. *Med. Ultrason.* 15(1), 35–40 (2013).

5 Eckstein F, Le Graverand MH. Plain radiography or magnetic resonance imaging(MRI): which is better in assessing outcome in clinical trials of disease-modifying osteoarthritis drugs? Summary of a debate held at the World Congress of Osteoarthritis 2014. *Semin. Arthritis Rheum.* doi:10.1016/j.semarthrit.2015.06.001 (2015) (Epub ahead of print).

6 Iagnocco A, Naredo E. Osteoarthritis: research update and clinical applications. *Rheumatology (Oxford)* 51(Suppl. 7), vii2–5 (2012).

7 Tarhan S, Unlu Z. Magnetic resonance imaging and ultrasonographic evaluation of the patients with knee osteoarthritis: a comparative study. *Clin. Rheumatol.* 22(3), 181–188 (2003).

8 Grassi W, Filippucci E, Farina A. Ultrasonography in osteoarthritis. *Semin. Arthritis Rheum.* 34(6 Suppl. 2), 19–23 (2005).

9 Roemer FW, Eckstein F, Hayashi D, Guermazi A. The role of imaging in osteoarthritis. *Best Pract. Res. Clin. Rheumatol.* 28(1), 31–60 (2014).

10 Iagnocco A. Ultrasound in osteoarthritis. *Clin. Exp. Rheumatol.* 32(1 Suppl. 80), S48–52 (2014).

• **An extended complete survey of the use of US in the diagnosis and monitoring of osteoarthritis.**

11 Iagnocco A, Filippucci E, Ossandon A *et al.* High-resolution ultrasonography in detection of bone erosions in patients with hand osteoarthritis. *J. Rheumatol.* 32(12), 2381–2383 (2005).

12 Iagnocco A, Perella C, D'Agostino MA, Sabatini E, Valesini G, Conaghan PG. Magnetic resonance and ultrasonography real-time fusion imaging of the hand and wrist in osteoarthritis and rheumatoid arthritis. *Rheumatology (Oxford)* 50(8), 1409–1413 (2011).

13 Filippucci E, Meenagh G, Epis O *et al.* Ultrasound for the rheumatologist. XIII. New trends. Three-dimensional ultrasonography. *Clin. Exp. Rheumatol.* 26(1), 1–4 (2008).

14 Möller I, Bong D, Naredo E *et al.* Ultrasound in the study and monitoring of osteoarthritis. *Osteoarthritis Cartilage.* 16(Suppl. 3), S4–S7 (2008).

15 Robinson P, Keenan AM, Conaghan PG. Clinical effectiveness and dose response of image-guided intra-articular corticosteroid injection for hip osteoarthritis. *Rheumatology* 46(2), 285–291 (2007).

16 Qvistgaard E, Christensen R, Torp-Pedersen S, Bliddal, . Intra-articular treatment of hip osteoarthritis: a randomized trial of hyaluronic acid, corticosteroid, and isotonic saline. *Osteoarthritis Cartilage.* 14(2), 163–170 (2006).

17 Mathiessen A, Slatkowsky-Christensen B, Kvien TK, Hammer HB, Haugen IK. Ultrasound-detected inflammation predicts radiographic progression in hand osteoarthritis after 5 years. *Ann. Rheum. Dis.* doi:10.1136/annrheumdis-2015-207241 (2015) (Epub ahead of print).

•• **US GS and PD findings correlate to radiographic progression after 5 years in hand osteoarthritis.**

18 Hall M, Doherty S, Courtney P, Latief K, Zhang W, Doherty M. Synovial pathology detected on ultrasound correlates with the severity of radiographic knee osteoarthritis more than with symptoms. *Osteoarthritis Cartilage* 22(10), 1627–1633 (2014).

19 Bevers K, Vriezekolk JE, Bijlsma JW, van den Ende CH, den Broeder AA. Ultrasonographic predictors for clinical and radiological progression in knee osteoarthritis after 2 years of follow-up. *Rheumatology (Oxford).* 54(11), 2000–2003 (2015).

•• **Provides an association between synovial hypertrophy and Baker's cyst and clinical and radiological progression in knee osteoarthritis.**

20 Wakefield RJ, Balint PV, Szkudlarek M *et al.* OMERACT 7 Special Interest Group. Musculoskeletal ultrasound including definitions for ultrasonographic pathology. *J. Rheumatol.* 32(12), 2485–2487 (2005).

21 Nishitani K, Kobayashi M, Kuroki H *et al.* Ultrasound can detect macroscopically undetectable changes in osteoarthritis reflecting the superficial histological and biochemical degeneration: *ex vivo* study of rabbit and human cartilage. *PLoS ONE* 9(2), e89484 (2014).

22 Guermazi A, Hayashi D, Eckstein F, Hunter DJ, Duryea J, Roemer FW. Imaging of osteoarthritis. *Rheum. Dis. Clin. North Am.* 39(1), 67–105 (2013).

23 Hammer HB, Iagnocco A, Mathiessen A *et al.* Global ultrasound assessment of structural lesions in osteoarthritis: a reliability study by the OMERACT ultrasonography group on scoring cartilage and osteophytes in finger joints. *Ann. Rheum. Dis.* doi:10.1136/annrheumdis-2014-206289 (2014) (Epub ahead of print).

•• **A reliability exercise by OMERACT for the study of osteophytes and cartilage in hand osteoarthritis. The use of a semiquantitave US score for osteophytes reached a good reliability; on the contrary, further studies are needed to establish a reliable score for the study of the cartilage.**

24 Meenagh G, Filippucci E, Iagnocco A *et al.* Ultrasound imaging for the rheumatologist VIII. Ultrasound imaging in osteoarthritis. *Clin. Exp. Rheumatol.* 25(2), 172–175 (2007).

25 Iagnocco A, Perricone C, Scirocco C *et al.* The interobserver reliability of ultrasound in knee osteoarthritis. *Rheumatology (Oxford)* 51(11), 2013–2019 (2013).

26 Keen HI, Wakefield RJ, Grainger AJ, Hensor EM, Emery P, Conaghan PG. Can ultrasonography improve on radiographic assessment in osteoarthritis of the hands? A comparison between radiographic and ultrasonographic detected pathology. *Ann. Rheum. Dis.* 67(8), 1116–1120 (2008).

27 Frobell RB, Wirth W, Nevitt M *et al.* OA Initiative investigators. Presence, location, type and size of denuded areas of subchondral bone in the knee as a function of radiographic stage of OA – data from the OA initiative. *Osteoarthritis Cartilage* 18(5), 668–676 (2010).

28 Mathiessen A, Haugen IK, Slatkowsky-Christensen B, Bøyesen P, Kvien TK, Hammer HB. Ultrasonographic assessment of osteophytes in 127 patients with hand osteoarthritis: exploring reliability and associations with MRI, radiographs and clinical joint findings. *Ann. Rheum. Dis.* 72(1), 51–56 (2013).

29 Bruyn GA, Naredo E, Damjanov N *et al.* Ultrasound Task Force. An OMERACT reliability exercise of inflammatory and structural abnormalities in patients with knee osteoarthritis using ultrasound assessment. *Ann. Rheum. Dis.* doi:10.1136/annrheumdis-2014-206774 (2015) (Epub ahead of print).

•• **The majority of structural and inflammatory findings in knee osteoarthritis showed a good reliablity in US examination.**

30 Razek AA, El-Basyouni SR. Ultrasound of knee osteoarthritis: interobserver agreement and correlation with Western Ontario and McMaster Universities Osteoarthritis. *Clin. Rheumatol.* doi:10.1007/s10067-015-2990-2 (2015) (Epub ahead of print).

31 Kortekaas MC, Kwok WY, Reijnierse M, Stijnen T, Kloppenburg M. Inflammation is associated with erosive development in patients with hand osteoarthritis: a prospective ultrasonography study. *Arthritis Rheumatol.* doi: 10.1002/art.39438 (2015) (Epub ahead of print).

32 Keen HI, Hensor EM, Wakefield RJ, Mease PJ, Bingham CO 3rd, Conaghan PG. Ultrasound assessment of response to intra-articular therapy in osteoarthritis of the knee. *Rheumatology (Oxford)* 54(8), 1385–1391 (2015).

•• **US can provide 1-month follow-up of intrarticular corticosteroid injections in knee osteoarthritis; particularly, PD signal seems to be responsive and associated with pain.**

33 Iagnocco A, Naredo E. Ultrasound-guided corticosteroid injection in rheumatology: accuracy or efficacy? *Rheumatology (Oxford)* 49(8), 1427–1428 (2010).

34 Naredo E, Cabero F, Jimenez-Palop M, Collado P, Cruz A, Crespo M. Ultrasonographic findings in knee osteoarthritis: a comparative study with clinical and radiographic assessment. *Osteoarthritis Cartilage* 13(7), 568–574 (2005).

35 Kuroki H, Nakagawa Y, Mori K *et al.* Ultrasound properties of articular cartilage in the tibio-femoral joint in knee osteoarthritis: relation to clinical assessment (International Cartilage Repair Society grade). *Arthritis Res. Ther.* 10(4), R78 (2008).

36 De Miguel E, Cobo T, Uson J, Bonilla G, Martin-Mola E. Clinical and ultrasonographic findings related to knee pain in osteoarthritis. *Osteoarthritis Cartilage* 14(6), 540–544 (2006).

37 Usón J, Fernández-Espartero C, Villaverde V *et al.* Symptomatic and asymptomatic interphalageal

osteoarthritis: an ultrasonographic study. *Reumatol. Clin.* 10(5), 278–282 (2014).

38 Keen HI, Wakefield RJ, Grainger AJ, Hensor EM, Emery P, Conaghan PG. An ultrasonographic study of osteoarthritis of the hand: synovitis and its relationship to structural pathology and symptoms. *Arthritis Rheum.* 59(12), 1756–1763 (2008).

39 Bandinelli F, Fedi R, Generini S *et al.* Longitudinal ultrasound and clinical follow-up of Baker's cysts injection with steroids in knee osteoarthritis. *Clin. Rheumatol.* 31(4), 727–731 (2012).

40 Ingegnoli F, Soldi A, Meroni PL. Power Doppler sonography and clinical monitoring for hyaluronic acid treatment of rhizarthrosis: a pilot study. *J. Hand Microsurg.* 3(2), 51–54 (2011).

41 Micu MC, Bogdan GD, Fodor D. Steroid injection for hip osteoarthritis: efficacy under ultrasound guidance. *Rheumatology (Oxford)* 49(8), 1490–1494 (2010).

42 Iagnocco A, Filippucci E, Meenagh G *et al.* Ultrasound imaging for the rheumatologist. Ultrasonography of the shoulder. *Clin. Exp. Rheumatol.* 24(1), 6–11 (2006).

43 Backhaus M, Burmester GR, Gerber T *et al.* Guidelines for muscoloskeletal ultrasound in rheumatology. *Ann. Rheum. Dis.* 60(7), 641–649 (2001).

44 Filippucci E, Iagnocco A, Meenagh G *et al.* Ultrasound imaging for the rheumatologist. *Clin. Exp. Rheumatol.* 24(1), 1–5 (2006).

45 Iagnocco A. Imaging the joint in osteoarthritis: a place for ultrasound? *Best Pract. Res. Clin. Rheumatol.* 24(1), 27–38 (2010).

46 Iagnocco A, Epis O, Delle Sedie A *et al.* Ultrasound for the rheumatologist. XVII. Role of colour Doppler and power Doppler. *Clin. Exp. Rheumatol.* 26(5), 759–762 (2008).

47 Walther M, Harms H, Krenn V, Radke S, Kirschner S, Gohlke F. Synovial tissue of the hip at power Doppler US: correlation between vascularity and power Doppler US signal. *Radiology* 225(1), 225–231 (2002).

48 Ohashi S, Ohnishi I, Oka H *et al.* The effect of cartilage degeneration on ultrasound speed in human articular cartilage. *Mod. Rheumatol.* 22, 1–25 (2015).

49 Ju JH, Kang KY, Kim IJ, Yoon JU, Kim HY, Park SH. Three-dimensional ultrasonographic application for analyzing synovial hypertrophy of the knee in patients with osteoarthritis. *J. Ultrasound Med.* 27(5), 729–736 (2008).