# Ultrasound in crystal-related arthritis

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**ABSTRACT**

*In the last decade, an increasing number of rheumatologists have been using ultrasound (US) for assessing patients with gout and calcium pyrophosphate deposition (CPPD) disease. The high reflectivity of the crystalline aggregates and the ability of US to detect even minimal crystal deposits explain the high sensitivity of this imaging technique. Furthermore, the peculiar distribution within the target tissues results in the generation of typical US patterns and explains the excellent specificity of some US findings. The large spectrum of US findings and their wide combination generate different scenarios in different patients and also in the same subject. Such a high variety impaired the standardisation of the definitions of each US finding.*

*This review presents the main US findings indicative of crystal deposits, discusses the available evidence supporting the use of US in patients with gout and CPPD disease, and provides a research agenda to guide further investigations.*

*The combined US examination of the target tissues and the clinically involved sites represents the key issue to obtain the best compromise between accuracy and feasibility, in the daily US assessment of patients with crystal-related arthropathies. Moreover, the US guided aspiration of synovial fluid may enhance the possibility to reach a crystal-proven diagnosis, making US a complementary tool, not in contrast, with microscopy, which rests the current gold standard.*

*Finally, even if at moment other US findings are not included among the typical ones for crystal-related arthropathies, it is possible that in the future, thanks to continuous technological advances, we will be able to identify other specific patterns of pathology.*

## Introduction

In the last years, an increasing number of rheumatologists have been using ultrasound (US) in patients with gout and calcium pyrophosphate deposition (CPPD) disease (1-10). Growing evidence is in favour of the high accuracy of the grey-scale US in the detection of both monosodium urate (MSU) and calcium pyrophosphate (CPP) crystals (1-30). Thus, US may represent a useful imaging technique in daily rheumatology practice to confirm the suspicion of crystalline arthropathy. However, it must be kept in mind that the high sensitivity and specificity values were obtained by experts in musculoskeletal US, using high-end US systems.

The high reflectivity of the crystalline aggregates and the ability of US, especially with high frequency probes, to detect even minimal deposits explain the high sensitivity of this imaging technique in revealing MSU and CPP crystals (11-12). Furthermore, the peculiar distribution within the target tissues results in the generation of typical sonographic patterns and explains the excellent specificity of some US findings (11-12).

The diagnostic value of US was tested investigating patients with definite clinical diagnosis of gout or CPPD disease and disease control patients (1, 2, 6, 14-17). Moreover, in patients with gout, the construct validity of US is supported by data obtained in studies showing the encouraging correspondence in the identification of tophi when comparing US findings with those of other imaging techniques (*i.e.* MRI and TC) (13-14). Fewer data are available for CPPD, being only few the studies that investigated the concurrent and the construct validity of US in a limited number of anatomic sites, especially in the lower limbs (17-21).

In 2010 in the publication of the recommendations about the terminology and diagnosis of CPPD, the European League Against Rheumatism (EULAR) CPPD Task Force recognises the important role of US, defining its sensitivity and specificity as "excellent and possibly better than those of conventional x-rays", which are universally considered

the standard reference among the imaging modalities (7). Similarly, in the 2012 American College of Rheumatology Guidelines for Management of Gout, US is mentioned among the new imaging approaches for detecting anatomic changes of early disease not visualised by plain radio-graphy and it is recommended for the identification of tophi, together with CT, or dual-energy CT (8). This review presents the main US findings indicative of crystal deposits, discusses the available evidence supporting the use of US in patients with gout and CPPD disease, and provides a research agenda to guide further investigations.

## US findings

Either the MSU or the CCP crystal deposits share, as common feature, the high reflectivity of the US beam, which does not depend on the angle of insonation. Nevertheless, their sonographic appearance is quite heterogeneous, in terms of size (ranging from submillimetre spots to aggregates larger than 1 cm), superficial outline (which can be well or poorly defined), internal echostructure (according to a homogeneous or inhomogeneous aggregation of the crystal deposits) and topographic distribution (which changes depending on the affected tissue and the involved aspect of the anatomic district). Of note, apparently in contrast with the high reflectivity, crystal aggregates can show the unexpected absence of the acoustic shadow ("soft tophi"), which can be considered another characteristic feature, even if not constant, but distinctive from the appearance of other hyper-reflecting structures, such as bone. The generation of the acoustic shadowing depends mainly on the density of the crystal aggregates and is independent of their size (2, 11, 12).

This large spectrum of US findings and their wide combination generate different scenarios in different patients and also in the same subject. Such a high variety has also made difficult to standardise the definition of each single US finding and resulted in different terms used (Table I). The value to assign to each US finding (*i.e.* hyperechoic spot) depends mainly on its topographic distribution in the different tissues. The elective predilection of MSU crystals to deposit on the hyaline cartilage surface generates the "double contour sign", which may be detected also in joints with no signs of inflammation (Figs. 1-3). CPP crystals can also be depicted at the hyaline cartilage level, but their location is inside the cartilage (usually, in the middle layer) (Fig. 4). This different distribution of the crystal deposits can be used to distinguish MSU from CPP crystals, as confirmed in several studies focused on gouty patients.

According to the very few investigations that have described the US features of the crystal deposits at tendon level, both MSU and CPP crystal aggregates appear as subtle hyperechoic bands usually not generating acoustic shadowing (Fig. 5) (4, 11, 13, 18, 22, 24, 29, 30).

The limited use of power and colour Doppler, unlike most of the other US applications in rheumatology, makes this area of research peculiar and particularly attractive.

**Table I.** US findings indicative of MSU (**A**) and CPP (**B**) crystal aggregates and the corresponding most common definitions used to describe them.

| **A.** US finding | US definition |
|---|---|
| Double contour sign | A focal or diffuse enhancement of the superficial margin of the articular cartilage whose reflectivity is independent of the angle of insonation (1,4,5,11,12,17).<br>A distinct and slightly irregular layer of hyperechoic material overlying the anechoic hyaline cartilage (2). |
| Hyperechoic spots | Spots, 1 mm in size with the same echogenicity of the bony cortex (1).<br>Hyperechoic microparticles (2) |
| Soft tophus-like lesion | A deposit showing an inhomogeneously echoic "echotexture" (1).<br>Hypoechoic to hyperechoic, inhomogenous appearance of "wet sugar clumps" (2).<br>Hypoechogenic nodule surrounded by a hyperechogenic rim (13). |
| Hard tophus-like lesion | A deposit appearing as a hyperechoic band generating a posterior acoustic shadow (1). |
| Mixed tophus like lesion | A deposit showing ultrasound features of both soft and hard tophus (1). |
| Bright stippled foci and hyperechoic areas | monosodium urate deposits within the thickened hypoechoic synovia and the joint space (16). |
| "Snowstorm" appearance of the synovial fluid | Hyperechoic spots in the synovial fluid floating within the joint cavity in acute inflammation (11). |
| **B.** | |
| Hyaline cartilage calcification | Hyperechoic spots within the cartilage layer not generating a posterior acoustic shadow (4,11,17,21,29).<br>Hyperechoic, crystalline material layered in the centre of the anechoic hyaline cartilage (2).<br>Thin hyperechoic band, parallel to the surface of the hyaline cartilage (19,20). |
| Meniscal calcification | Several thin hyperechoic spots within the fibrocartilage (19,21). |
| Tendon calcification | Linear hyperechogenic deposit positioned at the major axis of the tendon that does not create posterior shadowing (11, 29).<br>Hyperechoic thin deposits not in continuity with the bone profile observed within the fibrillar tendon structure (18). |
| "Punctate" pattern | Hyperechoic rounded or amorphous-shaped areas in fibrocartilage or tendons (11,19). |

## Validity issues

*Scanning protocol*

In the initial publications, the application

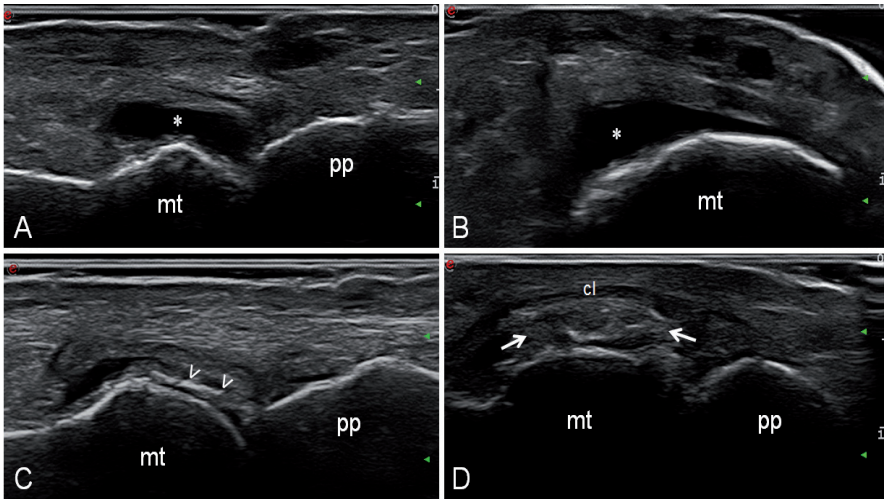


**Fig. 1.** Acute attack of gout. First metatarsophalangeal joint. Dorsal longitudinal (**A**) and transverse (**B**) views showing anechoic joint cavity widening indicative of exudative synovitis. **C**. The dorsal longitudinal view with the joint in flexed position allows the detection of the double contour sign (**arrowhead**). **D**. The medial longitudinal view reveals the presence of inhomogeneous material with subtle hyperechoic bands not generating acoustic shadowing (**arrows**) in-between the metatarsal head and the collateral ligament. **mt**: metatarsal head; **pp**: proximal phalanx; **cl**: medial collateral ligament, *: synovial fluid.

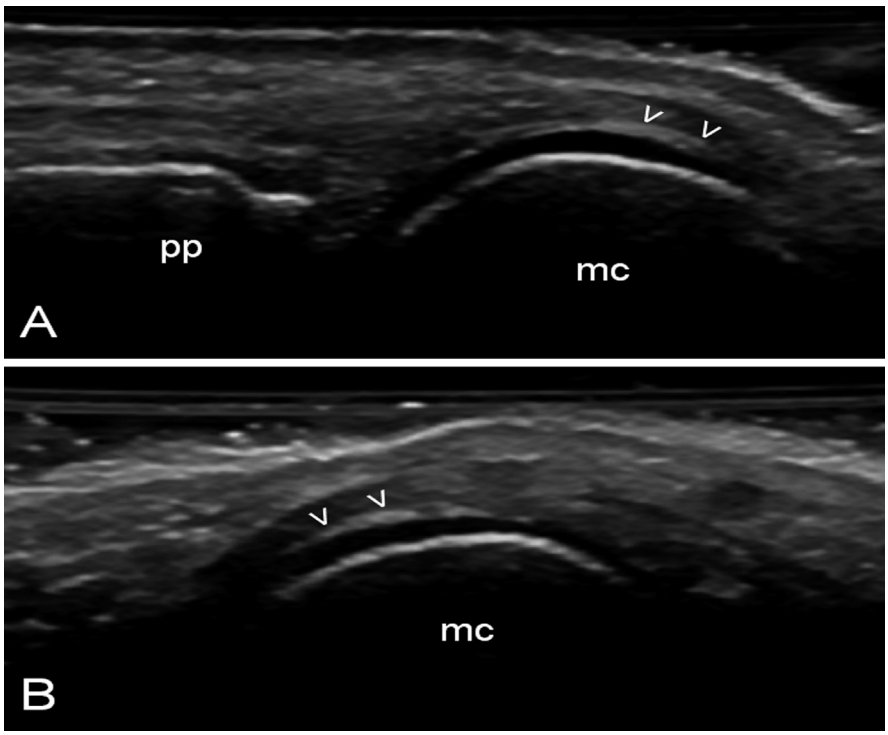


**Fig. 2.** Tophaceous gout. Metacarpophalangeal joint. Dorsal longitudinal (**A**) and transverse (**B**) views showing a representative example of double contour sign due to the inhomogeneous MSU crystal deposition on the cartilage surface resulting in an enhancement of the chondro-synovial interface (**arrowheads**). **mc**: metacarpal head; **pp**: proximal phalanx.

of US was tested at the typical anatomic sites affected by the gout and CPPD disease, with a predilection for the first metatarsophalangeal (MTP) joint and the knee. Even if US allows for a quick, safe and cheap multi-site and multi-tissue assessment, in the daily clinical routine, a practical rule is to start the sonographic examination guided by the clinical suspicion based on the patient's history and the physical findings. Nevertheless, US can reveal the presence of crystal aggregates also in asymptomatic sites with no previous clinical involvement. Thus, the first MTP joint, the elbow, the patellar and the Achilles tendons, in gouty patients, and the hyaline cartilage and the fibrocartilage in the knee, the triangular ligament of the wrist, the Achilles tendon and the plantar fascia, in those with CPPD disease, should be considered sites to scan even if not clinically involved. The position of the anatomic site under examination is fundamental to ensure the best exposure of the cartilage surface to the US beam. For instance, the maximal flexion of the metacarpophalangeal joint is essential to ensure the perpendicular insonation of the metacarpal head hyaline cartilage using the dorsal views.

Unlike microscopic examination, US assessment does not require the presence of synovial fluid or tophaceous material for detecting crystal aggregates. Thus, it can be performed also during the gout or pseudogout intercritical periods. Moreover, US can be used to detect and to guide the aspiration of even minimal amount of synovial fluid which results sufficient to obtain a microscopic crystal identification.

*Gout*

The double contour sign is the US finding indicative of crystal deposit most frequently investigated and the one considered almost pathognomonic of hyperuricemia or gout, with a substantial agreement in the literature (10-22). The reported sensitivity of this sign is high in different anatomic sites, including small joints such as the first MTP joint, and large ones such as the knee. However, its sensitivity depends on the width of the cartilage surface reachable by the US beam. The relatively lower sensitivity found in some studies can be explained by their study design: only one anatomic site investigated even if not clinically involved. Thus, a clinically guided multi-site US examination should be recommended to increase the sensitivity of the double contour sign.

Nevertheless, in spite of the largely accepted diagnostic utility of the double contour sign, it is interesting to note that several validity issues still require dedicated studies to be addressed. To date, there is evidence supporting the reproducibility of this sign (discrimi-

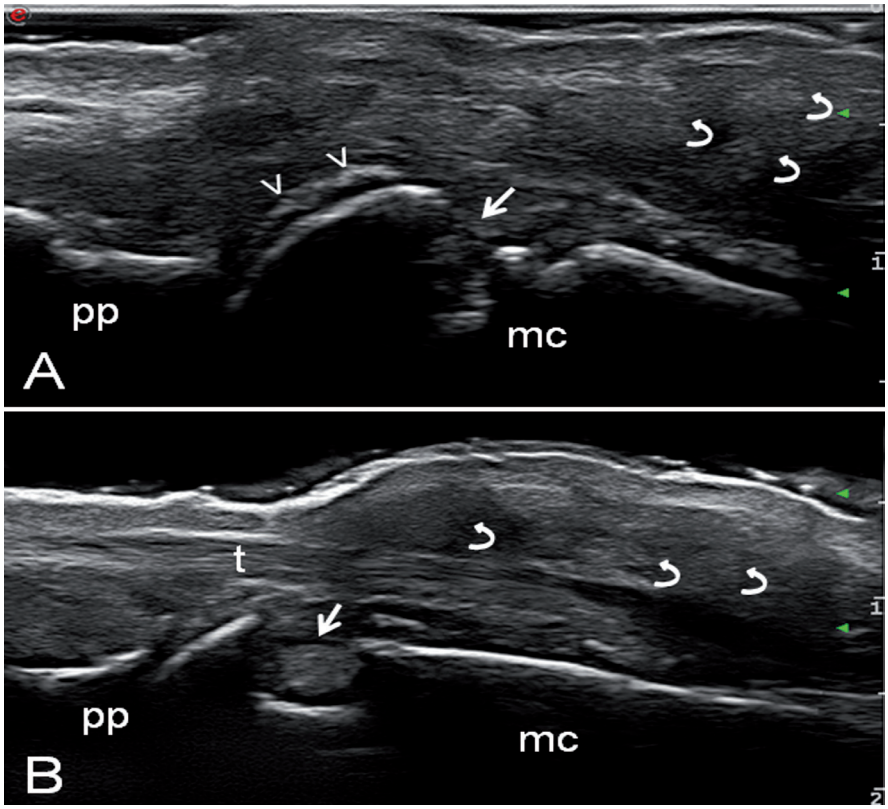


**Fig. 3.** Tophaceous gout. Metacarpophalangeal joint. Dorsal longitudinal view showing subcutaneous tophaceous deposits appearing as cloudy areas (**curved arrows**), double contour sign (**arrowheads**), and bone erosion at the bare area with inhomogeneous material within the erosive crater. **mc**: metacarpal bone; **pp**: proximal phalanx; **t**: finger extensor tendon.

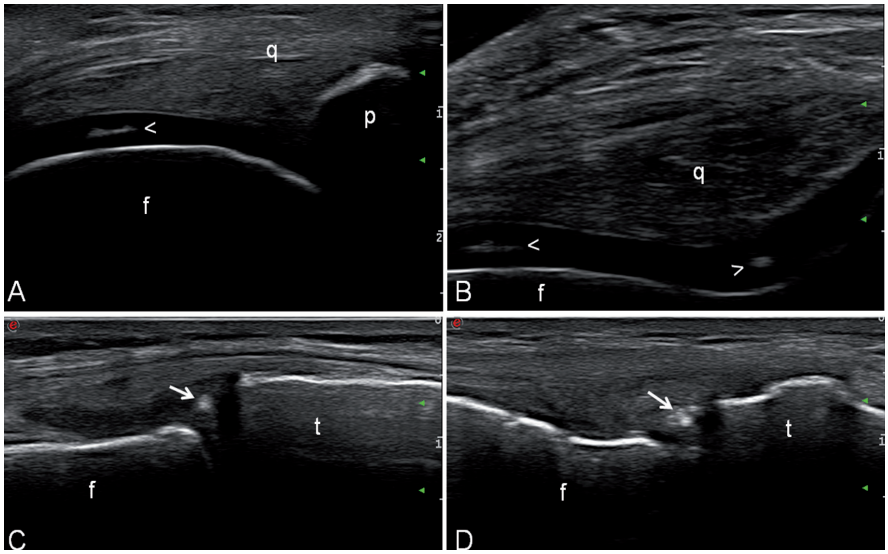


**Fig. 4.** CPPD disease. Knee. Anterior suprapatellar longitudinal (**A**) and transverse (**B**) views showing hyperechoic spots within the femoral hyaline cartilage not generating acoustic shadowing (**arrowheads**). Medial (**C**) and lateral (**D**) longitudinal views revealing meniscal calcifications which appear as hyperechoic spots in-between femur and tibia within the external meniscal material (**arrows**). **f**: femur; **q**: quadriceps tendon; **p**: upper pole of the patella.

nant validity) and a preliminary study reporting its disappearance in a small cohort of patients receiving urate-lowering therapy (25).

The results obtained for the other US findings indicative of MSU deposits, are more conflicting and require further investigations. This can be related to several reasons. First, the lack of a detailed description defining the US findings indicative of the MSU crystal deposits at tissues other than hyaline cartilage. This is mainly due to the wide spectrum of US features and it makes difficult to find an all-embracing description. In fact, several terms were used to indicate the MSU deposits and this represents a strong limitation to compare the results of different studies. Second, the US findings indicative of MSU deposits require further validation, especially those used to detect intra-tendinous crystals.

To overcome limitations, such as the relatively low sensitivity of specific US signs or the confounding appearance of US findings with higher sensitivity, recent studies have proposed approaches mainly based on the multi-tissue and multi-site US evaluation.

From the assessment of 17 joints and 8 tendons in 29 patients with crystal-proven gout, Peiteado *et al*. have extracted a 6-minute four-joint (bilateral knees and first MTP joints) US assessment based on two US abnormalities, *i.e*. double contour sign and hyperechoic cloudy areas. Such an approach was found feasible and these findings were detected in 97% of the patients (23).

More recently, Naredo *et al*. proposed a more novel approach, using the combination of a comprehensive US evaluation, including different US findings (intra-articular and intrabursal, and tendon and ligament tophi, double contour sign), at different tissues (synovial recesses of joint and bursae, tendons, ligaments, articular cartilages) in several anatomic sites of upper and lower limbs. The results of these study seem to suggest that merging the information provided by the presence of different US abnormalities and their topography may improve the accuracy in gout diagnosis, without losing feasibility. The proposed 12-structure assessment (bilateral radio-carpal joint, first metatarsal head cartilage, talar cartilage, second metacarpal head or knee femoral condyle cartilage, patellar and triceps tendons) yields high sensitivity and specificity (85% and 83%, respectively), with a high positive and good nega-

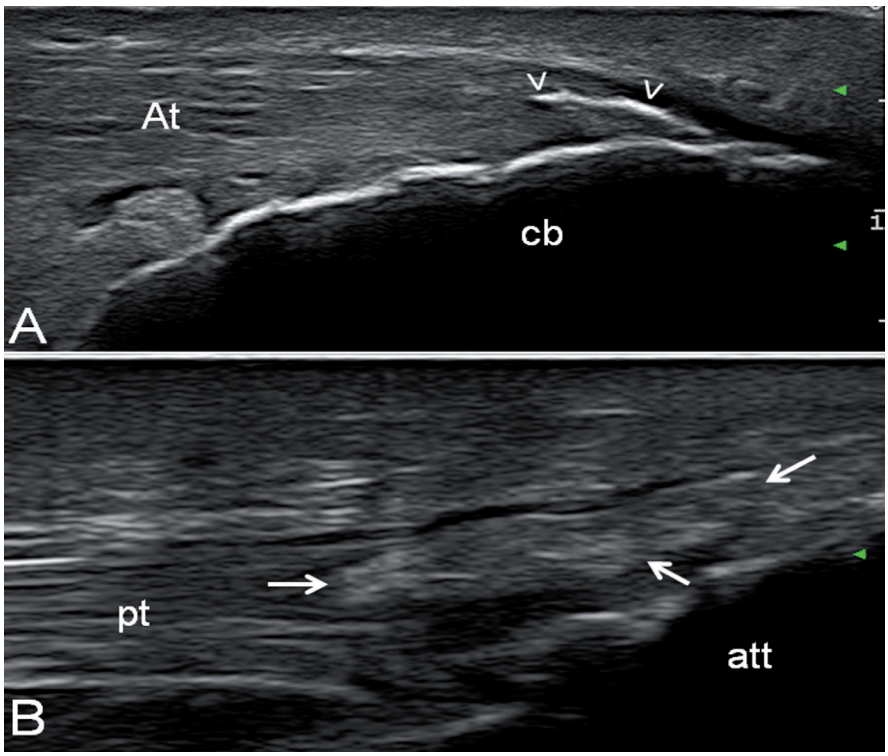


**Fig. 5.** Gout. Representative examples of chronic enthesopathy. **A**. Longitudinal view of the Achilles tendon showing an intra-tendinous thin hyperechoic band not generating acoustic shadowing at the insertion into the calcaneal posterior tuberosity. **B**. Longitudinal view of the patellar tendon showing an echotextural derangement due to the presence of inhomogeneous tophaceous material. **cb**: calcaneal bone; **At**: Achilles tendon; **att**: anterior tibial tuberosity; **pt**: patellar tendon.

tive predictive values (92% and 71%, respectively) for diagnosing gout (9).

Even if these studies provide results which can be of help in the daily practice to improve the feasibility, the extremely high variety of the US scenarios in gouty patients makes difficult to accept a fixed pre-defined scanning protocol which does not include the clinical information.

In a recent study, our group has shown that the acquisition of the skills required to identify and interpret the main US findings in gout, can be obtained with a 7-day dedicated training-programme (24). A correct identification of the US features indicative of MSU crystal deposits entails avoiding not only missing the US findings, but also their false positive detection. Thus, a deep knowledge of the tips and tricks in the US of crystalline arthropathies is crucial for avoiding misinterpretations (11, 12).

*CPPD disease*

The specificity for the presence of the CPP crystals in the hyaline cartilage is not well known. Only few studies have investigated this US pattern of crystal distribution. Our group have found a specificity of 97.6% in a blind evaluation of 264 knees in 132 patients comparing 48 CPPD subjects with 32 gouty patients and other 52 disease controls (rheumatoid arthritis, psoriatic arthritis and osteoarthritis) (17). In the same study, the presence of hyperechoic spots within the hyaline cartilage layer of the femoral knee showed a relatively low sensitivity 68.7%. In all patients the diagnosis was made according to McCarty criteria, supporting the construct validity (26).

The other characteristic target tissue for the deposition of CPP crystals is the fibrocartilage, which was object of recent studies comparing the US findings obtained *in vivo* and those acquired in the menisci samples after knee replacement surgery, in a total of 6 patients and 11 menisci (27, 28). Higher sensitivity and specificity values were obtained with the *ex vivo* US assessments rather than with the *in vivo* ones (67 and 100% *vs*. 44 and 50%, respectively). The microscopic analysis was used as gold standard for the diagnosis. Possible explanations of these results could related to technical limitations due to obese patients and/or late stage of knee osteoarthritis, or to the presence of a small vessel generating false positive findings (27).

These results, even if in a very small population, are important because underlying the need for further investigations to clarify the accuracy of the US identified CPP crystal deposits at fibrocartilage level.

The third tissue target for CPP crystal deposition using US is the tendon. These crystal aggregates present a characteristic distribution in the tendon, appearing as hyperechoic linear deposits parallel to the fibrils, generally without acoustic shadowing and not in continuity with the bone (11, 12, 18).

US detected frequently and with a high specificity (98–100%) calcaneal intratendinous calcifications, even in asymptomatic subjects with chondrocalcinosis. Furthermore, the US findings showed high agreement with radiographic results (18).

As for gout, the multi-site and multi-tissue US assessment has been performed in patient with CPPD disease. In 42 patients, the hyaline cartilage and the fibrocartilage were assessed at knee, wrist and metacarpophalangeal joint level, and the tendons were scanned at the heels level (*i.e*. Achilles tendon and plantar fascia), and CPP crystals were found in at least two anatomic sites with a mean of four anatomic sites (29).

Recently, a multicentre study has investigated the prevalence of CPP deposits at shoulder level, which is generally not included among the most typical target sites for CPPD. Rotator cuff tendons and the acromion-clavicular fibrocartilage were the most frequently affected tissues (30).

## Conclusion

In conclusion, US may be considered a powerful tool in the hands of the rheumatologist in the suspicion of a crystalline arthropathy. Some highly specific US findings, if carefully handled, may be critical for shortening the time required for the diagnosis. The identification of the double contour sign or the intratendinous tophi can lead to a diagnosis of gout or of a hyperuricemic

condition. The presence of hyperechoic spots or aggregates within the hyaline cartilage layer or in the fibrocartilage are strongly indicative of CPPD disease. Other US findings, more common but less specific, such as hyperechoic spots in synovial tissue or tendons, can contribute to generate or increase the suspicion of a crystalline arthropathy but may be frequently found also in other conditions.

The combined US examination of the target tissues and the clinically involved sites represents the key issue to obtain the best compromise between accuracy and feasibility, in the daily US assessment of patients with crystal-related arthropathies.

Moreover, the US guided aspiration of synovial fluid may enhance the possibility to reach a crystal-proven diagnosis, making US a complementary tool, not in contrast, with microscopy, which remains the current gold standard.

Finally, even if, at present, other US findings are not included among the typical ones for crystal-related arthropathies, it is possible that in the future, thanks to continuous technological advances, we will be able to identify other specific patterns of pathology.

**Key messages**

1. US is a sensitive technique for detecting both MSU and CCP crystal deposits.
2. MSU and CCP crystal deposits share, as a common feature, the high reflectivity of the US beam, which does not depend on the angle of insonnation.
3. The cartilage is the most frequently investigated tissue and the double contour sign is highly specific for gout.
4. Intratendinous hyperechoic linear bands parallel to the fibrils, generally without acoustic shadowing can be considered evocative for crystal deposits.
5. A clinically-driven multi-tissue US assessment of selected anatomic sites is the best approach to scan patients with crystal-related arthropathies in the daily clinical practice.
6. US can be used to detect and to guide the aspiration of even a minimal amount of synovial fluid, which is essential to reach the microscopic identification of MSU or CPP crystals.

## References


1. WRIGHT SA, FILIPPUCCI E, MCVEIGH C *et al*.: High-resolution ultrasonography of the first metatarsal phalangeal joint in gout: a controlled study. *Ann Rheum Dis* 2007; 66: 859-64.
2. THIELE RG, SCHLESINGER N: Diagnosis of gout by ultrasound. *Rheumatology* 2007; 46: 1116-21.
3. DELLE SEDIE A, RIENTE L, IAGNOCCO A *et al*.: Ultrasound imaging for the rheumatologist X. Ultrasound imaging in crystal-related arthropathies. *Clin Exp Rheumatol* 2007; 25: 513-7.
4. FILIPPUCCI E, SCIRÈ CA, DELLE SEDIE A *et al*.: Ultrasound imaging for the rheumatologist. XXV. Sonographic assessment of the knee in patients with gout and calciumpyrophosphate deposition disease. *Clin Exp Rheumatol* 2010; 28: 2-5.
5. FILIPPUCCI E, MEENAGH G, DELLE SEDIE A *et al*.: Ultrasound imaging for the rheumatologist XXXVI. Sonographic assessment of the foot in gout patients. *Clin Exp Rheumatol* 2011; 29: 901-5.
6. OTTAVIANI S, RICHETTE P, ALLARD A, ORA J, BARDIN T: Ultrasonography in gout: a case-control study. *Clin Exp Rheumatol* 2012; 30: 499-504.
7. ZHANG W, DOHERTY M, BARDIN T *et al*. European League Against Rheumatism recommendations for calcium pyrophosphate deposition. Part I: terminology and diagnosis. *Ann Rheum Dis* 2011; 70: 563-70.
8. KHANNA D, FITZGERALD JD, KHANNA PP *et al*.: American College of Rheumatology. 2012 American College of Rheumatology guidelines for management of gout. Part 1: systematic nonpharmacologic and pharmacologic therapeutic approaches to hyperuricemia. *Arthritis Care Res* 2012; 64: 1431-46.
9. NAREDO E, USON J, JIMÉNEZ-PALOP M *et al*.: Ultrasound-detected musculoskeletal urate crystal deposition: which joints and what findings should be assessed for diagnosing gout? *Ann Rheum Dis* 2013 May 24. [Epub ahead of print].
10. MATHIEU S, PEREIRA B, COUDERC M *et al*.: Usefulness of ultrasonography in the diagnosis of gout: a meta-analysis. *Ann Rheum Dis* 2013; 72: e23.
11. GRASSI W, MEENAGH G, PASCUAL E, FILIPPUCCI E: "Crystal clear"-sonographic assessment of gout and calcium pyrophosphate deposition disease. *Semin Arthritis Rheum* 2006; 36: 197-202.
12. FILIPPUCCI E, DI GESO L, GRASSI W: Tips and tricks to recognize microcrystalline arthritis. *Rheumatology* 2012; 51: 18-21.
13. GERSTER JC, LANDRY M, DUFRESNE L, MEUWLY JY: Imaging of tophaceous gout: computed tomography provides specific images compared with magnetic resonance imaging and ultrasonography. *Ann Rheum Dis* 2002; 61: 52-4.
14. PEREZ-RUIZ F, MARTIN I, CANTELI B: Ultrasonographic measurement of tophi as an outcome measure for chronic gout. *J Rheumatol* 2007; 34: 1888-93.
15. HOWARD RG, PILLINGER MH, GYFTOPOULOS S *et al*.: Reproducibility of musculoskeletal ultrasound for determining monosodium urate deposition: concordance between readers. *Arthritis Care Res* 2011; 63: 1456-62.
16. RETTENBACHER T, ENNEMOSER S, WEIRICH H *et al*.: Diagnostic imaging of gout: comparison of high-resolution US versus conventional X-ray. *Eur Radiol* 2008; 18: 621-30.
17. FILIPPUCCI E, RIVEROS MG, GEORGESCU D *et al*.: Hyaline cartilage involvement in patients with gout and calcium pyrophosphate deposition disease. An ultrasound study. *Osteoarthritis Cartilage* 2009; 17: 178-81.
18. FALSETTI P, FREDIANI B, ACCIAI C *et al*.: Ultrasonographic study of Achilles tendon and plantar fascia in chondrocalcinosis. *J Rheumatol* 2004; 31: 2242-50.
19. FREDIANI B, FILIPPOU G, FALSETTI P *et al*.: Diagnosis of calcium pyrophosphate dihydrate crystal deposition disease: ultrasonographic criteria proposed. *Ann Rheum Dis* 2005; 64: 638-40.
20. FILIPPOU G, FREDIANI B, GALLO A *et al*.: A "new" technique for the diagnosis of chondrocalcinosis of the knee: sensitivity and specificity of high-frequency ultrasonography. *Ann Rheum Dis* 2007; 66: 1126-8.
21. CIAPETTI A, FILIPPUCCI E, GUTIERREZ M, GRASSI W: Calcium pyrophosphate dihydrate crystal deposition disease: sonographic findings. *Clin Rheumatol* 2009; 28: 271-6.
22. PINEDA C, AMEZCUA-GUERRA LM, SOLANO C *et al*.: Joint and tendon subclinical involvement suggestive of gouty arthritis in asymptomatic hyperuricemia: an ultrasound controlled study. *Arthritis Res Ther* 2011; 13: R4.
23. PEITEADO D, DE MIGUEL E, VILLALBA A *et al*.: Value of a short four-joint ultrasound test for gout diagnosis: a pilot study. *Clin Exp Rheumatol* 2012; 30: 830-7.
24. GUTIÉRREZ M, DI GESO L, ROVISCO J *et al*.: Ultrasound learning curve in gout: a disease-oriented training program. *Arthritis Care Res* 2013; 65: 1265-74.
25. THIELE RG, SCHLESINGER N: Ultrasonography shows disappearance of monosodium urate crystal deposition on hyaline cartilage after sustained normouricemia is achieved. *Rheumatol Int* 2010; 30: 495-503.
26. MCCARTY DJ: Calcium pyrophosphate dihydrate crystal deposition disease. *In*: SCHUMACHER HR JR (Ed.) *Primer on the Rheumatic Diseases*. 10th ed. Atlanta: Arthritis Foundation; 1993: 219e22.
27. FILIPPOU G, BOZIOS P, GAMBERA D *et al*.: Ultrasound detection of calcium pyrophosphate dihydrate crystal deposits in menisci: a pilot in vivo and ex vivo study. *Ann Rheum Dis* 2012; 71: 1426-7.
28. FILIPPOU G, ADINOLFI A, BOZIOS P *et al*.: Do not hallow until you are out of the wood! ultrasonographic detection of CPP crystal deposits in menisci: facts and pitfalls. *Scientific World Journal* 2013 (in press).
29. FILIPPOU G, FILIPPUCCI E, TARDELLA M *et al*.: Extent and distribution of CPP deposits in patients affected by calcium pyrophosphate dihydrate deposition disease: an ultrasonographic study. *Ann Rheum Dis* 2013; 72: 1836-9.
30. FILIPPUCCI E, DELLE SEDIE A, RIENTE L *et al*.: Ultrasound imaging for the rheumatologist. XLVII. Ultrasound of the shoulder in patients with gout and calcium pyrophosphate deposition disease. *Clin Exp Rheumatol* 2013; 31: 659-64.