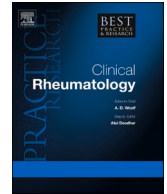


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Imaging of crystal-induced arthropathies in 2025

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ABSTRACT

In recent years, imaging has become an essential tool in the assessment of crystal-induced arthropathies (CIAs), including gout, calcium pyrophosphate deposition disease, and basic calcium phosphate crystal deposition. Advances in imaging have improved diagnosis and disease monitoring, leading to its integration into classification criteria and clinical guidelines.

Ultrasound (US), conventional radiography (CR), and dual-energy computed tomography (DECT) each offer unique advantages. US is a widely accessible, cost-effective, and dynamic tool, while DECT provides crystal-specific images, aiding particularly in gout diagnosis. CR, though less sensitive to early crystal deposition, remains valuable for evaluating structural damage and chronic changes.

Despite these advances, challenges remain. The specificity and sensitivity of imaging findings need further validation, and the clinical relevance of certain imaging features is debated. This review summarizes recent developments, highlights key strengths, and discusses unresolved issues, emphasizing areas where future research is needed to optimize imaging use in CIAs.

1. Introduction

Crystal-induced arthropathies (CIAs), including gout, calcium pyrophosphate deposition (CPPD) disease, and basic calcium phosphate (BCP) deposition disease, have garnered increasing research interest in recent years [1–3]. Significant progress has been made in defining diagnostic pathways and improving disease monitoring. This growing interest is partly driven by the high prevalence of these conditions, which are frequently encountered in daily clinical practice, as well as by the need to refine diagnostic approaches, which should not rely solely on clinical features but also incorporate direct evidence of crystal deposition in joints or tissues [4,5].

At the same time, technological advances in imaging have led to higher spatial resolution and improved tissue representation, enabling clearer visualization of crystal deposits. Consequently, the integration of imaging techniques into the diagnostic and monitoring processes for CIAs has evolved naturally from these developments.

In recent years, several scientific societies have evaluated the utility and finally endorsed the use of imaging for the assessment of CIAs, recognizing the substantial added value offered by various modalities for both diagnosis and disease monitoring (Table 1) [4–6].

In this review, we provide an overview of the current evidence on the use of imaging in CIAs, with a focus on dual-energy computed tomography (DECT), ultrasound (US), and conventional radiography (CR). Magnetic Resonance Imaging (MRI) will not be covered in

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Table 1

Recommendations by Scientific Societies regarding imaging in the diagnosis and monitoring of CIAs. MTP: metacarpophalangeal; US: ultrasound; DECT: dual-energy computed tomography; SFA: synovial fluid analysis; CR: conventional radiography; MSU: monosodium urate; OA: osteoarthritis; CPPD: calcium pyrophosphate deposition; BCPD: basic calcium phosphate deposition.

Guidelines	Key Features - Gout
2023 EULAR Recommendations on Imaging in Crystal-Induced Arthropathies	- Imaging should be performed in both symptomatic joints and disease-specific target sites (e.g., 1st MTP joint). - Recommended imaging modalities: US and DECT. - If typical imaging features of gout are present, SFA may not be required for diagnosis. - Monitoring: US and DECT can monitor crystal deposition, US can assess inflammation, and CR can evaluate structural damage. - Prediction of flares: Assessing the amount of MSU crystal deposition by US or DECT may help predict future flares.
2022 American College of Radiology Imaging Appropriateness Criteria	- Initial imaging modality in suspected cases of gout: CR. - Following imaging: US or CT.
2018 EULAR Evidence-Based Recommendations for the Diagnosis of Gout	- Imaging is recommended when clinical diagnosis is uncertain, especially if SFA is not possible. - CR: Useful for detecting MSU crystal deposition but has limited value for diagnosing gout flares. - US: More helpful for diagnosis by detecting tophi and the DC sign, which is highly specific for urate deposits.
2015 ACR/EULAR Classification Criteria	- High diagnostic value for imaging evidence of urate deposition in symptomatic joints or bursae. - US: Presence of the DC sign. - DECT: Direct visualization of urate crystal deposits. - CR: At least one typical erosion in the hands and/or feet.
Guidelines	Key features - CPPD
2023 EULAR Recommendations on Imaging in Crystal-Induced Arthropathies	- Imaging should be performed in both symptomatic joints and disease-specific target sites (e.g., knees and wrists). - Recommended imaging modalities: CR and US for peripheral joints, CT for axial involvement. - Monitoring: Serial imaging is not recommended.
2023 ACR/EULAR Classification Criteria	- Imaging of at least one symptomatic joint by CR, US, CT, or DECT is required if SFA is not possible. - Crowned dens syndrome on imaging is a sufficient criterion. - CR: Presence of hand/wrist OA in atypical joints. - Presence of CPPD on CR, US, CT, or DECT. - Absence of CPPD on US, CT, or DECT have a negative impact. - More peripheral joints with evidence of CPPD on imaging increase classification probability.
2022 American College of Radiology Imaging Appropriateness Criteria	- Initial imaging modality in suspected cases of CPPD: CR. - Following imaging: US or CT.
2011 EULAR Recommendations for CPPD deposition	- CR: Radiographic chondrocalcinosis supports the diagnosis of CPPD, but its absence does not exclude it. - US: Can detect CPPD in peripheral joints with possibly better sensitivity and specificity than CR.
Guidelines	Key features - BCPD
2023 EULAR Recommendations on Imaging in Crystal-Induced Arthropathies	- Imaging should be performed in both symptomatic joints and disease-specific target sites (e.g., shoulders). - Recommended imaging modalities: CR and US - Monitoring: Serial imaging is not recommended

this review, as current guidelines and recommendations consistently agree that, due to its intrinsic limitations, MRI does not currently offer additional advantages over the aforementioned techniques. Furthermore, inflammation and structural damage that can also be assessed by imaging in CIAs fall beyond the aim of this chapter, which will focus on the role of imaging in tracking crystal deposition.

2. GOUT

Gout is a common crystal arthropathy with an estimated prevalence of 4 % among American adults [3]. Although synovial fluid analysis remains the diagnostic gold standard, it is not always feasible in clinical practice [7]. Consequently, the 2015 ACR/EULAR classification criteria emphasize the value of US and DECT for detecting monosodium urate (MSU) crystal deposition [4]. Their role has been confirmed in the 2018 updated EULAR evidence-based recommendations for the diagnosis of gout [7]. More recently, the 2023 EULAR recommendations on imaging in CIAs further reinforce the critical role of imaging not only for diagnosis but also for monitoring disease progression and crystal burden [6].

2.1. Diagnosis

The use of US in gout and other CIAs relies on the distinct physical properties of crystal deposits, which exhibit high acoustic impedance, allowing them to be distinguished from surrounding tissues and generating characteristic US images. However, US is inherently operator-dependent, as both image acquisition and interpretation are often performed in real-time by the same examiner. This underscores the critical importance of adequate training to ensure accurate assessment. In fact, pitfalls and technical errors are common [8,9], and examiners must be well-trained to recognize and minimize these challenges.

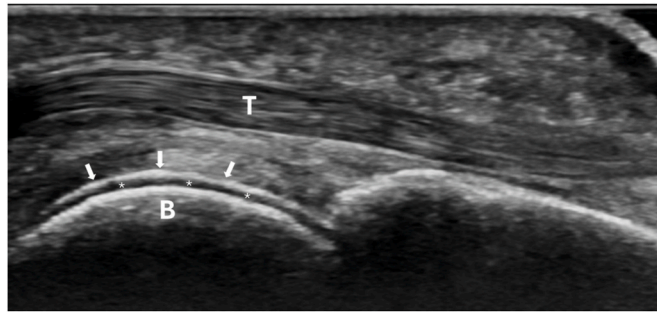


Fig. 1. Ultrasound image: Plantar long axis view of 2nd MTP joint. A double contour sign (arrows) is visible over the metatarsal head (B), consisting of hyperechoic cortex, an overlying anechoic hyaline cartilage (asterisks), and a superficial layer of hyperechoic crystalline material (arrows). T: flexor tendon.

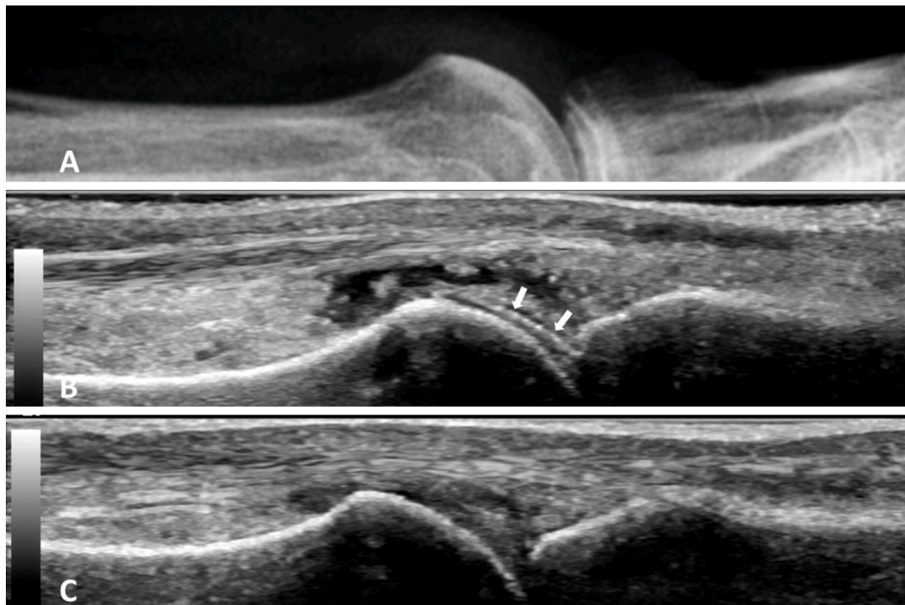


Fig. 2. (A): Conventional radiograph (CR) of 1st MTP joint. (B, C): Long-axis dorsal ultrasound images of the same joint in the same patient. A sonographic double contour sign is seen at baseline (arrows - panel B) and disappears at the 4-month follow-up scan after urate-lowering therapy (panel C). Notably, the baseline CR did not detect crystal deposition on the hyaline cartilage of the metatarsal head (panel A).

The diagnostic value of US in gout has been well established through a large international multicenter study, which reported a sensitivity of 76.9 % and a specificity of 84.3 % [10]. In addition, US has demonstrated moderate to excellent reliability across multiple studies [11,12].

The Outcome Measures in Rheumatology (OMERACT) US Working Group - Gout Subgroup has developed definitions for elementary US lesions in gout: double contour (DC) sign, tophi, aggregates, and bone erosions [11,13].

The DC sign is defined as an abnormal hyperechoic band over the superficial margin of the articular hyaline cartilage, independent of the angle of insonation, which may be either irregular or regular, continuous or intermittent, and can be distinguished from the cartilage interface sign [11,13]. The DC sign is considered a hallmark feature of gout, with strong diagnostic value. It has a high specificity for gout diagnosis (89 %) but only moderate sensitivity (65 %) [14]. Due to its diagnostic accuracy and reliability, the DC sign has been incorporated into the 2015 ACR/EULAR gout classification criteria as a recognized imaging feature of gout [4](Fig. 1). The deposition of the MSU crystal on the top of the hyaline cartilage, which contributes to the typical sonographic DC sign, is not typically visible on CR and DECT [15,16] (Figs. 2 and 3).

Tophi are complex structures composed of aggregates of MSU crystals embedded in a vascularized fibrous matrix, surrounded by an inflammatory cellular “corona” rich in macrophages and other cells [17] (Fig. 4). Sonographically, they are defined by OMERACT as circumscribed, inhomogeneous, hyperechoic and/or hypoechoic aggregations, which may or may not generate acoustic shadowing, and can be surrounded by a thin anechoic rim [11,13]. They may be located intraarticularly or within tendons. The ability of tophi to produce acoustic shadowing is directly related to the concentration of MSU crystals, as well as the size and chronicity of the deposits.

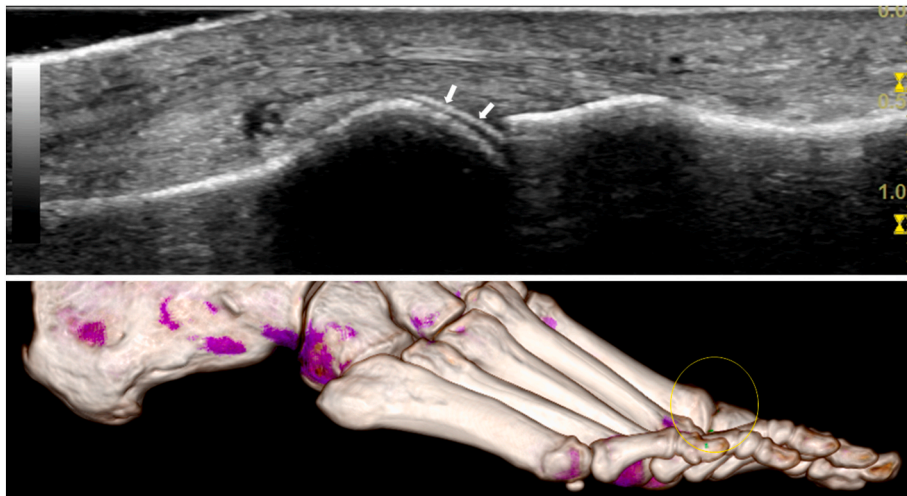


Fig. 3. (Top): Ultrasound image of 1st MTP joint showing a double contour sign (arrows). (Bottom): Dual-energy CT scan of the same joint, taken on the same day, revealing no detectable deposition on the 1st metatarsal head (circle).

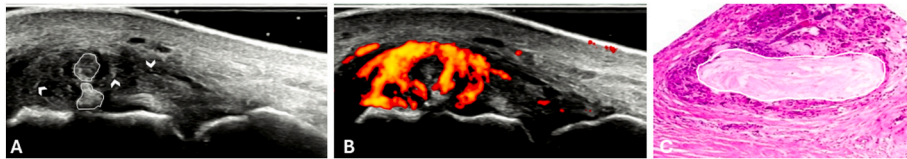


Fig. 4. (A, B): Ultrasound (US) images of the long-axis view of the 1st MTP joint in a patient with gout. Tophi (outlined by a thin white line) appear as inhomogeneous formations (ranging from hypoechoic to hyperechoic) surrounded by an anechoic rim. Hypoechoic synovitis with aggregates (arrowheads) is also present. Power Doppler examination allows a better assessment of the degree of inflammation (panel B), that is particularly severe around the tophi and within the synovitis. C: histological image of monosodium urate crystalline material (outlined by a thin white line), surrounded by a cellular layer and embedded in fibrous and vascularized tissue. Importantly, US can also monitor inflammation: power Doppler signal around tophi or in joints tends to reduce as flares and synovitis are controlled, offering a window into the inflammatory component of gout that serum urate alone doesn't provide.

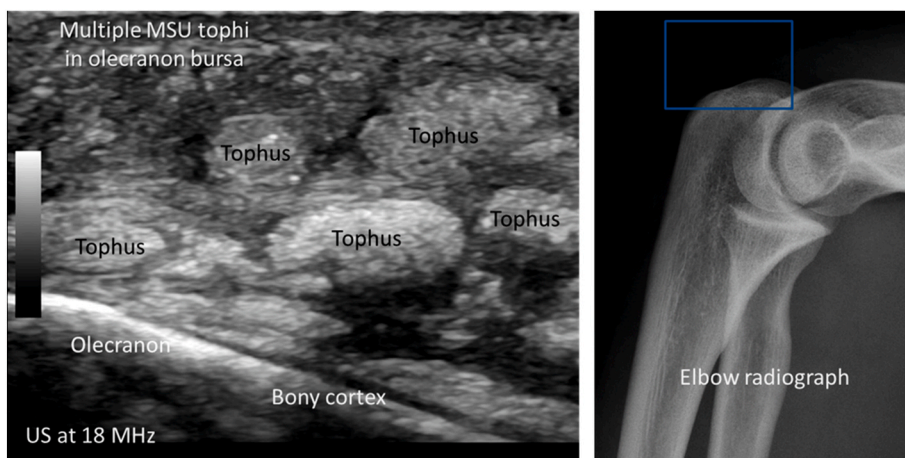


Fig. 5. Ultrasound (US) image (left panel) and conventional radiograph (CR - right panel) of the olecranon area, taken on the same day. US reveals multiple hyperechoic tophi in the olecranon bursa, which are not visible on CR.

An *in vitro* study demonstrated that US wave attenuation increases with higher MSU crystal concentrations, allowing differentiation between gout-related deposits and CPP crystal deposits, the latter of which do not generate acoustic shadowing, even at high concentrations [18]. Although tophi are highly specific for gout (93.3 %), their sensitivity for diagnosing gout is relatively low (53.4 %)

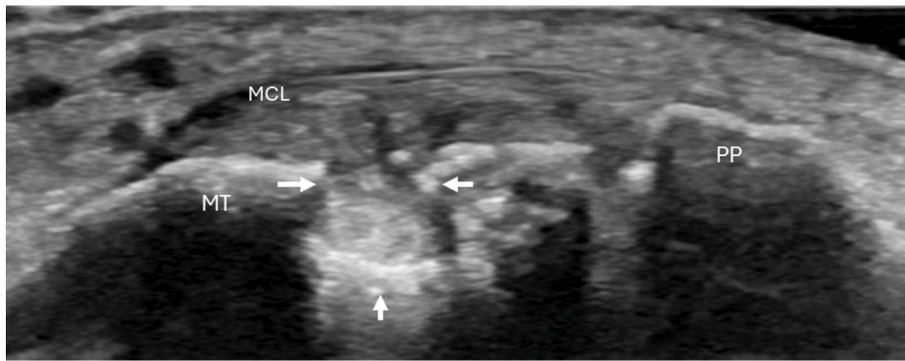


Fig. 6. Long-axis ultrasound image of the medial side of the metatarsophalangeal joint. Hyperechoic crystalline material is seen eroding the bone. Arrows: cortical erosion. MCL: medial collateral ligament. MT: metatarsal head. PP: proximal phalanx.

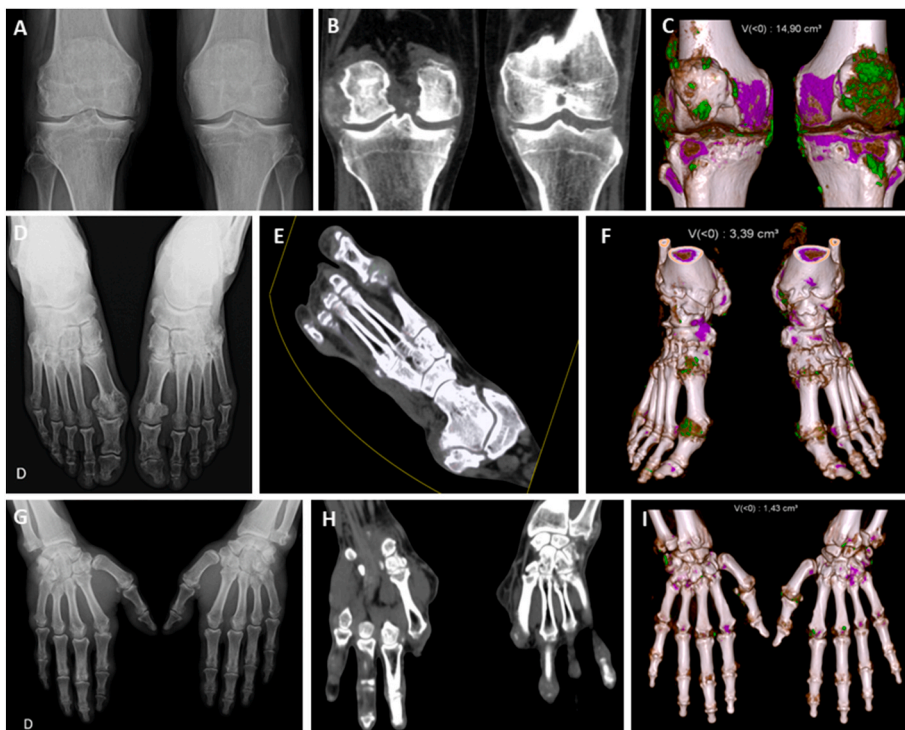


Fig. 7. Imaging appearances of the knees (A, B, C), feet (D, E, F), and hands (G, H, I) in a 51-year-old man with a history of gout since age 20, who had never received urate-lowering therapy. Shown are conventional radiography (CR, panels A, D, G), conventional computed tomography (CT, panels B, E, H), and dual-energy CT (DECT, panels C, F, I). DECT images appear as 3D reconstructions processed in 'gout' mode using Siemens Syngovia®.

[14]. As a result, tophi are not included in the current classification criteria. Tophi are well visualized on US, but they are not typically detected on CR (Fig. 5).

Aggregates are defined by US as bright hyperechoic, isolated spots too small to fulfil the tophus definition and characterized by maintaining their high degree of reflectivity when the insonation angle is changed, which may be either intraarticular or intra-tendinous [11,13]. They may represent the earliest sign of MSU crystal deposition, however due to their low specificity (32 %), they should only be scored if other elementary lesions suggestive of gout are present [19].

US can also detect cortical erosions, intra- and/or extra-articular discontinuity of the bone surface, visible in two perpendicular planes, a consequence of chronic tophus deposition [13]. These erosions often present with thin marginal overhangs, are typically multifocal and predominantly located on the medial side of the metatarsal head of the 1st MTP joint [20] (Fig. 6). Unlike rheumatoid arthritis, erosions in gout are not caused by synovial pannus tissue invading subchondral bone. At the tophus-bone interface osteoblasts are decreased, and numerous osteoclast-like cells are found. MSU crystals alter the ratio of RANKL to OPG in stromal cells, favoring

osteoclastogenesis [21,22]. Cortical erosions are specific for gout diagnosis (93.3 %), though their sensitivity is relatively low (51.6 %) [14]. Compared to CR, US is significantly more sensitive for detecting erosions. In a study comparing 29 gout patients with 22 controls, US identified erosions in 67 % of patients, whereas radiography detected erosions in only 28 % [23]. Furthermore, both the presence of a DC sign and tophi are independent risk factors for subsequent bone erosion development, emphasizing the prognostic value of US findings in gout [24].

The use of DECT in gout, and more generally in CIAs, is based on the principle that attenuation of tissues, reflected by their CT attenuation, depends on their mass volumetric (electron) density, their atomic number (Z), and the energy of the photon beam produced by the machine. DECT scans produce two energy beams (typically 80 and 140/150 kV), whose attenuations (in Hounsfield units (HU)) are combined by post-processing algorithms providing a specific biochemical signature of each voxel, which will be coded as containing MSU or not (sufficiently to be detected) [25,26]. The voxels considered by the post-processing software as containing MSU are added up and presented in 3D reconstructions to provide a total volume of MSU deposits and their distribution (Fig. 7) [27]. This method of detection is not fully specific for MSU, as some structures may exhibit similar dual-energy attenuations and be miscoded as MSU, such as nails or intra-articular structures (e.g. menisci) [28]. DECT identifies extra-articular MSU crystal deposition only (except in rare cases of large intra-articular tophi) [29], as long as they are of sufficient size (above the spatial resolution, usually of 500 µm for peripheral joints, which, because of partial volume effects, allows the detection of >1 mm deposits) [30]. Studies involving patients at different disease stages and with various disease durations showed that up to 50 % of patients with symptoms lasting less than 2 years did not have detectable MSU deposits of sufficient size to be considered non-artefactual in DECT [31,32]. In default post-processing settings, 1 mm lesions are usually considered artefactual and should be removed manually, as are other known artifacts (e.g. nail beds) [7].

In clinical practice, evidence of MSU crystal deposits in US (DC sign) or DECT accounted for half the required points to classify as having gout in the 2015 ACR/EULAR classification criteria [4]. Moreover, the 2023 EULAR recommendations reaffirmed that identifying MSU crystal deposition on US or DECT in patients with a typical clinical picture of gout is sufficient for diagnosis, without the need for synovial fluid analysis [6]. A distinct advantage of US over other imaging modalities (besides its wide availability, low cost, bedside approach, and no radiation) is the availability of standardized definitions and the ability to detect even very small MSU crystal aggregates. This high-resolution detection capability allows for earlier identification of crystal deposition. In clinical practice, DECT is particularly valuable in challenging diagnostic scenarios, especially in patients with symptom duration longer than two years, where crystal burden is more likely to be detectable. It is also suggested that DECT could detect axial MSU deposits, however its utility remains highly debated due to the high rate of artifacts, and needs to be further explored [33]. Spinal tophi, though rare, can be detected using conventional CT and DECT, typically in patients with tophaceous disease. Clinical examination plays a crucial role in identifying cutaneous tophi, which may raise suspicion of axial tophi as a potential cause of neurological symptoms. In such cases, CT or DECT should be performed for accurate assessment. CR, due to its inability to detect early crystal deposition, can be useful in gout only for assessment and follow-up of late joint damage [6].

2.2. Monitoring

Monitoring disease progression and crystal deposition is crucial in gout, as effective therapies can achieve complete symptom remission and crystal dissolution [3,34].

The OMERACT US scoring system allows for longitudinal monitoring of gout patients over time [11]. The score ranges from 0 to 3: grade 0 equals “absence” of MSU deposits, grade 1 to “possible” presence of MSU deposition, grade 2 to “definite but minimal” MSU deposition, and grade 3 to “definite and severe” MSU deposition.

US-detected gout lesions have been shown to improve with effective urate-lowering therapy (ULT) [35]. After starting ULT, both the DC sign and tophi can diminish or resolve when serum urate levels are sustained at therapeutic target levels (Fig. 2). A longitudinal study reported that they both decrease significantly within months of ULT, with some changes seen as early as 3–6 months [36]. Notably, a greater decrease in tophus size and a higher rate of DC sign resolution were observed in patients who achieved a more stringent therapeutic target (serum urate <5 mg/dL) compared to those with levels between 5 and 6 mg/dL [37]. The DC sign tends to disappear earlier than tophi, especially when tophi are large and compact. As a result, DC sign is the earliest indicator of crystal dissolution and thus of ULT efficacy [38]. A 2023 prospective study confirmed these findings, in patients who achieved target serum urate levels, showed dramatic reductions in US lesion scores over 12 months: tophi shrank in dimensions and the semiquantitative score for DC sign fell rapidly (often significantly by 3 months). By contrast, patients whose urate remained above target had little to no reduction in tophus size and only minor changes in US scores [39]. This indicates that US is sensitive to change – it can track improvements in crystal load when treatment is effective, and it reflects treatment failure by showing persistent or growing deposits [40].

As suggested by the 2023 EULAR recommendations, reviewing “before and after” images – such as a tophus shrinking or crystal line disappearing – can also motivate adherence, as it makes the invisible progress of urate lowering visible to patients [6] (Fig. 2).

DECT is being increasingly considered for disease monitoring, as proposed by the 2023 EULAR recommendations on imaging of CIAs [6]. MSU crystal volume observed in DECT correlates with clinical outcomes, particularly the risk of upcoming flares and onset of comorbidities and even mortality [41,42]. This ability is both useful at baseline when initiating ULT, and throughout follow-up. DECT is the only imaging technique capable of quantifying the volume of MSU crystal dissolution during ULT. When ULT is well conducted, massive crystal debulking is observed with DECT during the first year of treatment, and DECT are usually negative for MSU deposits at 2 years [43,44]. Using DECT to monitor MSU crystal dissolution at baseline only makes sense if baseline deposits are substantial. When patients with small volumes of MSU deposits at baseline are considered, dissolution under well conducted ULT is disappointing, with only very partial crystal depletion at 18 and 24 months and over 50 % persistence of baseline deposits remaining, as a significant share

of artifacts are inherently considered [45,46]. In another study involving groups of patients with more significant deposits at baseline, the change in MSU crystal volume measured with DECT was more substantial, and reached around 80 % of depletion [47]. The kinetics of MSU crystal depletion assessed with DECT seem highly related to serum urate levels. A study compared the kinetics of dissolution of MSU deposit, and showed that a significantly greater crystal dissolution of deposits was obtained at 12 months (−85 % vs −40 %) in patients achieving an SU level <5.0 mg/dl than in those achieving <6.0 mg/dL [43]. A pooled analysis from three studies involving DECT measurements of MSU deposits, showed that a significant decrease of MSU volume was observed in people having serum urate levels below 5.0 mg/dL, and a significant increase in those with levels >8.0 mg/dL, with non-significant changes for serum urate levels in between [48]. In the future, this data suggests that DECT may be used to adjust and personalize serum urate levels targets to obtain optimal crystal dissolution.

Importantly, MSU volume and its dissolution measured with DECT correlates with the absence of new flare recurrence and overall achievement of gout remission [43,49]. The first study using DECT to predict the risk of flares showed on 78 patients that for each 1 cm³ increase in DECT MSU volume in foot deposits, the risk of flare increased 2.03-fold during the first 6 months after initial assessment (OR 2.03 (1.15–4.38)) [41]. In the NOR-GOUT study, baseline DECT semi-quantitative measurement of MSU crystal burden was predictive of the flare risk in months 9–12 and in year 2 after treatment initiation [50]. Conversely, having a negative DECT for MSU seems protective of flares, as shown in the 211 ULT-naïve patients included in the CRYSTALILE cohort and initiating T2T ULT, a total of 9/39 (23.1 %), 3/26 (11.5 %) and 1/18 (5.6 %) patients with a DECT volume of MSU crystals <0.1 cm³ (considered artefactual) had flares at 6, 12 and 24 months, respectively, compared with 18/45 (40.0 %), 9/36 (25.0 %) and 2/18 (11.1 %) patients with a volume ≥0.1 cm³ ($p > 0.05$). This data suggest that DECT can help identify patients at a higher risk of flaring at ULT initiation, could help the physician to personalize care by discontinuing flare prophylaxis at an appropriate time to avoid flare-ups after treatment is discontinued [51]. EULAR recognized that monitoring MSU deposits with DECT provides additional information to usual care, and that the decision on when to repeat DECT scans depends on clinical circumstances [6].

In conclusion, both US and DECT are effective tools for monitoring crystal deposition burden, which in turn correlates with the risk of flares. A key clinical application of this monitoring is the potential to establish imaging-based thresholds (for both US and DECT) to guide prophylaxis initiation and discontinuation, as well as to personalize serum urate targets for optimal crystal dissolution [52]. As highlighted in the 2023 EULAR recommendations, the frequency of imaging assessments for gout monitoring should be tailored to clinical circumstances [6]. Patients with a high crystal burden may benefit from more frequent and prolonged evaluations, while those with low or no detectable deposition may require less intensive monitoring.

3. CPPD

CPPD is one of the most common forms of inflammatory arthritis, with an estimated prevalence ranging from 7 % to 13.7 % at around 60 years of age, increasing with age to approximately 50 % in individuals over 80 [1]. The use of imaging in CPPD dates back to 1960, even before the condition was formally recognized, when Zitnan and Sitaj identified “chondrocalcinosis articularis” on CR [53].

Imaging techniques have become essential for detecting CPP crystal deposition, providing a valuable alternative to synovial fluid analysis [54]. This is particularly important given the limitations of synovial fluid analysis in terms of accuracy and feasibility, especially in non-inflammatory presentation of CPPD and in cases of axial involvement. The value of imaging is further reinforced by a growing body of supportive evidence in literature, especially its inclusion in the 2023 ACR/EULAR classification criteria, and the EULAR recommendations on imaging in crystal-induced arthropathies [5,6,55].

3.1. Diagnosis

Regarding the classification of CPPD disease, the 2023 ACR/EULAR classification criteria emphasize the importance of imaging in CPPD identification. In case an individual does not have a positive synovial fluid analysis, imaging confirmation is required for classification. Notably, imaging evidence of CPPD in symptomatic joints, along with the presence of CPP crystals in at least four joints, contributes 41 out of the 57 points necessary for classification [5].

According to the 2023 EULAR recommendations, in the diagnostic assessment of CPPD, CR and US are the preferred imaging modalities for peripheral joint assessment, while CT is recommended for evaluating axial involvement. The recommendations also emphasize the importance of always evaluating disease-specific target sites, in the case of suspected CPPD, this includes the knees and wrists, as they are the most commonly affected joints [6].

CR remains the most used first-line imaging technique for CPPD diagnosis, due to its wide availability, low cost, and ability to capture a comprehensive view of the entire joint. Historically, radiographic cartilage calcification, known as chondrocalcinosis, was considered non-specific for CPPD, as other calcium crystals were thought to produce a similar radiographic appearance [54]. However, in 2022, an international panel of experts introduced specific radiographic definitions aimed at distinguishing CPP deposits from other calcium crystals deposits [56]. According to these updated definitions, CPP deposits on radiography appear as linear or punctate opacities in the region of fibrocartilage, hyaline cartilage, synovial membrane, joint capsule, or within tendons or entheses. In contrast, BCP crystal deposits tend to appear denser, with a nummular, radio-opaque appearance, and are typically found in periarticular regions. These definitions were validated for reliability and diagnostic accuracy at knee level, using histology as the reference standard [57]. They demonstrated high reliability, with kappa values between 0.70 and 1 across different knee structures, and confirmed very high specificity (ranging from 93 % to 100 %). However, sensitivity remained low (between 32 % and 48 %), in line with previous studies. As a result, these new radiographic definitions for CPPD are highly specific and allow for a confident diagnosis of CPPD when findings are present. However, it is important to note that the absence of radiographic evidence does not rule out CPPD [57]. Another

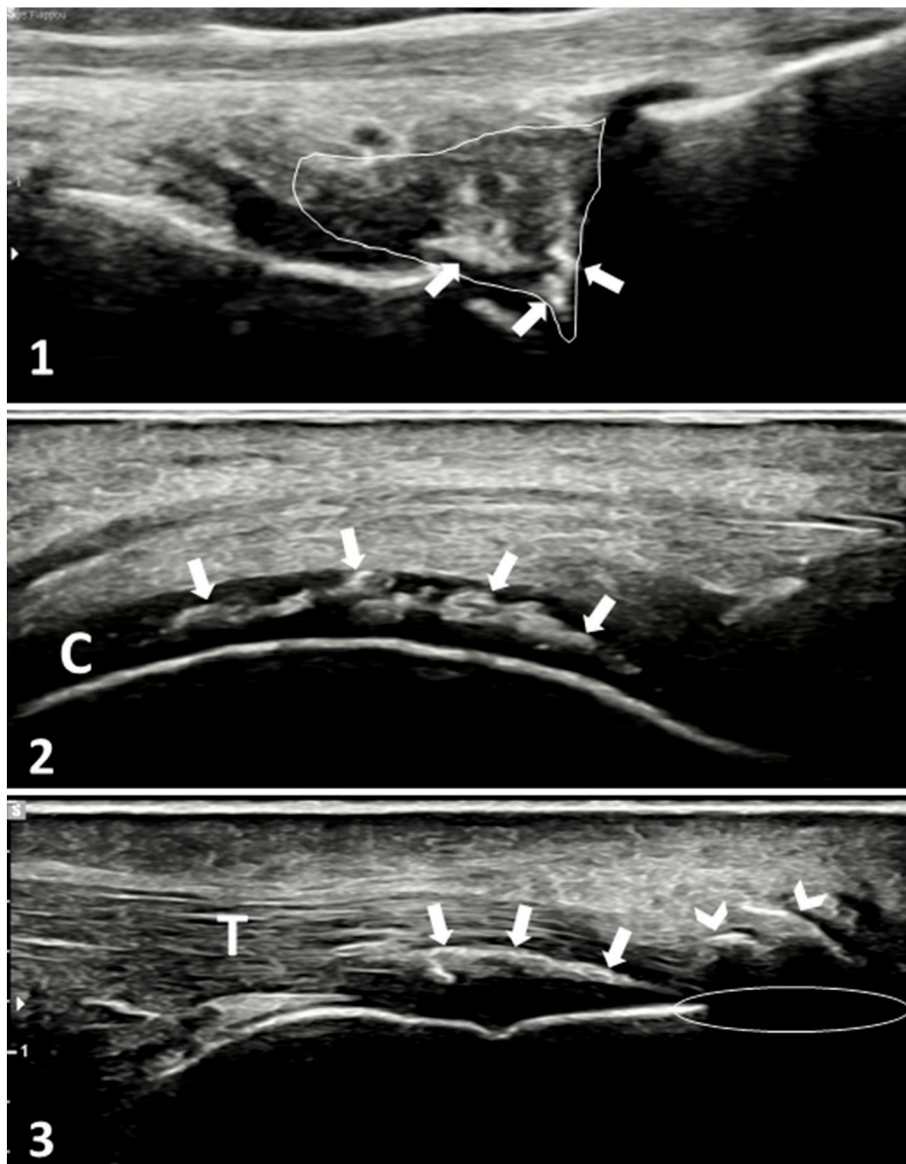


Fig. 8. Typical ultrasound (US) appearance of calcium pyrophosphate deposition (CPPD). In panel 1, arrows indicate CPPD in the meniscus (outlined by a white line). In panel 2 arrows indicate CPPD within the anechoic cartilage layer (C). In panel 3, arrows indicate CPPD in the Achilles tendon, while arrowheads mark an enthesophyte in the same tendon. Notably, the enthesophyte creates posterior shadowing, obscuring the normal bone profile (oval-shaped line), whereas CPPD (arrows) does not cause posterior attenuation of the US beam, allowing clear visualization of the bone profile.

radiographic feature highlighted in the 2023 ACR/EULAR classification criteria, which helps classify a patient as having CPPD, is the presence of osteoarthritis in atypical joints, particularly osteoarthritis of the scaphotrapezotrapezoid joint in the absence of first carpometacarpal joint involvement, as well as osteoarthritis affecting the 2nd and 3rd metacarpophalangeal joints [5].

Over the past decade, US has significantly advanced the diagnosis of CPPD. Its wide availability, safety, and ability to enable direct, real-time joint assessment during clinical visits make it one of the most valued imaging tools among rheumatologists. As emphasized in the EULAR recommendations, a key advantage of US is its capacity to evaluate not only CPP deposits but also associated inflammation and early joint damage, offering a more comprehensive assessment of the patient's condition [6].

In 2017, the OMERACT US Working Group – CPPD Subgroup developed consensus-based US definitions for CPPD, focusing on key features such as localization, shape, echogenicity, and behavior of CPP deposits during dynamic assessment [58,59]. According to these definitions CPP deposits were described as hyperechoic structures (similar to bone cortex) that do not create acoustic shadowing, with variable size and shape, localized within fibrocartilage, hyaline cartilage or tendons (parallel to the tendons fibers and not continuous with the bone profile), that typically remain fixed and move synchronously with the cartilage or tendon during dynamic

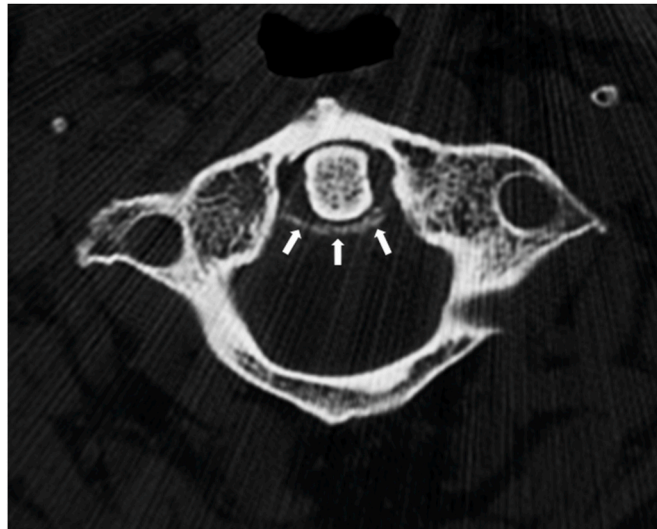


Fig. 9. Calcium pyrophosphate deposition of the transverse retro-odontoid ligament (arrows) in a 75-year old woman presenting with crowned dens syndrome, in axial view of conventional computed tomography. CPPD appearance at CT has been defined as “calcific deposits, typically linear and less dense than cortical bone, in the transverse retro-odontoid ligament (transverse ligament of the atlas, often with an appearance of two parallel lines in axial views” [56].

scanning [58,59] (Fig. 8). These definitions have been validated, demonstrating good reliability, especially at the knee (menisci and hyaline cartilage) and wrist (triangular fibrocartilage complex), which are the most commonly affected structures [58,59]. In addition, they proved high accuracy for CPPD detection at the knee compared to histology (overall accuracy of 75 %), with sensitivity ranging from 71 % to 87 % and specificity ranging from 68 % to 88 % across different joint structures [60]. EULAR recommends always assessing the knees and wrists in cases of suspected CPPD, as these are the most frequently involved joints [6]. However, to further enhance the diagnostic accuracy of US beyond the recommended assessment of the knees and wrists (as advised by EULAR), the evaluation of the hips should also be included, as this has been shown to achieve sensitivity and specificity greater than 90 % [61].

Furthermore, US has proven some ability in distinguishing CPPD from other CIAs based on the deposits' distinct sonographic characteristics. In a recent proof of concept study Filippou et al., showed that CPP crystals, even at high concentrations, can be differentiated from urate and hydroxyapatite crystals because they do not exhibit acoustic shadowing on US, in contrast to other crystals, which tend to attenuate the beam at increasing concentrations [18].

DECT post-processing algorithms, which were designed to distinguish urate from calcium in gout patients, are not applicable to discriminate calcium-containing crystal deposits. While in gout DECT exploits the fact that MSU crystals increase the electronic density (Rho) of the tissue they are deposited which translates in CT in increased Compton scattering of the X-ray beams, the characterization and discrimination of calcium crystals with DECT depends on the quantity of the photoelectric effect (quantified in Z_{eff} and dual-energy index (DEI) values) produced by the tissue [62]. No automatized identification of CPP crystal deposits is yet available in post-processing software as it is in gout, and so far obtaining DECT values of deposits requires manual delineation of regions of interest [27]. A proof-of-concept study including 21 patients with chondrocalcinosis and 19 controls, demonstrating that menisci with CPP crystal deposits exhibited specific DECT parameters different from calcification-free menisci, but also from the hydroxyapatite contained in subchondral and trabecular bone [62]. To determine if DECT could discriminate between CPPD and BCP deposition, another study compared the DECT parameters of calcifications from 13 patients with BCP deposition disease and 11 CPPD patients, using Raman spectroscopy as the gold standard to ascertain each crystal type [63]. The results showed that BCP deposits exhibited higher Z_{eff} ($p < 0.05$) and DEI values ($p < 0.01$) than CPP crystals once adjusted on calcification density, and proved the concept that DECT can discriminate between “pure” BCP deposits and CPP-containing chondrocalcinosis. In clinical practice however, DECT is not needed to distinguish BCP from CPP deposits given that in general shape of deposits and localization make it easy to identify both crystals, except maybe in certain cases in the cervical spine. In other words, DECT could be more specific than conventional CT for CPPD. The most common and specific spinal manifestation of CPPD is the calcification of the transverse retro-odontoid ligament, best observed in conventional CT, giving the odontoid process (dens) of C2 vertebrae the appearance of wearing a crown (crowned dens) (Fig. 9). CPPD at the atlanto-axial joint, alar ligament, and within the pannus adjacent to the dens tip are also characteristic [56]. When accompanied by acute inflammatory upper neck pain, the presence of this characteristic calcification defines the crowned dens syndrome, which is pathognomonic for CPPD disease [5]. Calcification of the transverse retro-odontoid ligament is not rare in patients with chronic symptoms of CPPD disease, particularly when peripheral CPPD is extensive [64]. Other less frequent manifestation of spinal CPPD can be observed in CT around facet joints and within intervertebral discs, often associated with structural damage including erosions.

The second question is the sensitivity of DECT for CPPD. Using in-house post-processing settings based on DEI values, a pilot study including 10 CPPD patients showed 90 % sensitivity versus 40 % for plain X-rays, a performance close to what is generally expected for conventional CT [65]. A study including 132 patients with ($n = 82$) or without ($n = 50$) chondrocalcinosis was designed to determine

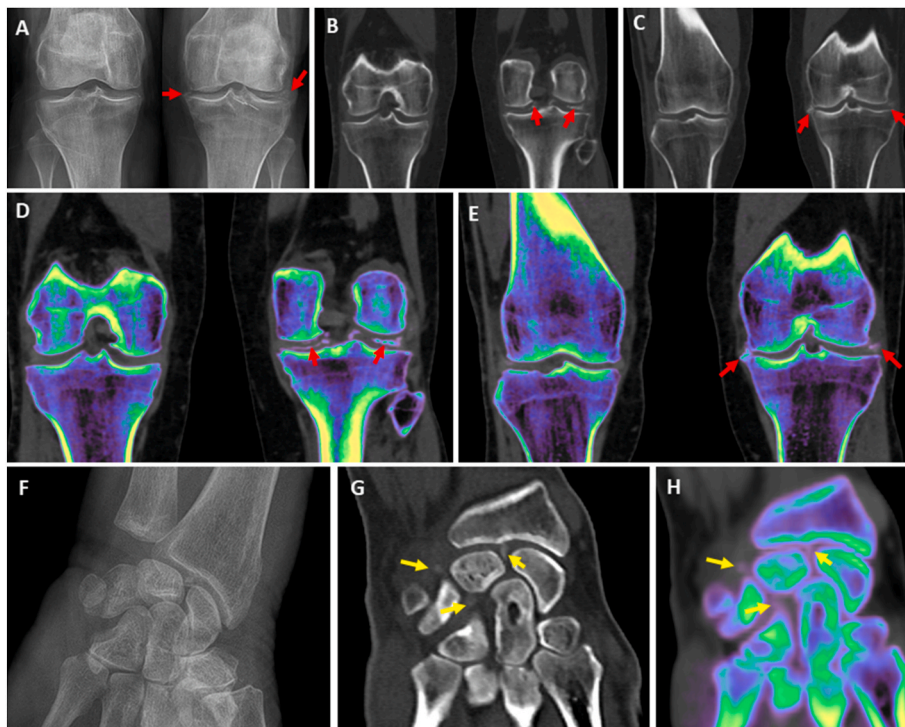


Fig. 10. Imaging evidence of calcium pyrophosphate deposition (CPPD) in a 75-year-old woman with persistent CPP crystal inflammatory polyarthritis. Knee imaging in CR (A), CT (B and C) and DECT (D and E) demonstrating evidence of CPPD in the hyaline and fibrocartilage (menisci) of the left knee (red arrows). Left wrist imaging includes CR (F), CT (G) and DECT (H), showing radiocarpal, intra-carpal, and carpal triangular ligament CPPD (yellow arrows) barely seen in CR. DECT images (D, E, H) were post-processed in 'Rho/Z' mode (Siemens Syngovia®) and colored according to their effective atomic number (Zeff).

the ability of DECT to detect modifications of DECT parameters of menisci from patients with CPPD on pre-specified slices where chondrocalcinosis was not visible on conventional CT [66]. Despite a numerical trend towards increased DEI values for menisci in the CPPD group, the difference did not reach statistical significance ($p = 0.09$), suggesting that in clinical practice, DECT does not provide improved sensitivity for CPPD than conventional CT (Fig. 10).

With diagnostic performances close to US and observing the same deposits, but with less availability and some degree of irradiation, conventional CT and DECT were not considered first-line imaging techniques for the diagnosis of CPPD, except when axial involvement is suspected.

The potential of advanced imaging techniques, including US, CT and DECT, to provide evidence of CPPD was acknowledged in the 2023 ACR/EULAR classification criteria for CPPD disease, and most importantly, was recognized their key role in excluding the diagnosis when negative [5].

3.2. Monitoring

The 7th recommendation from the EULAR taskforce is clear: "In CPPD and BCP disease, serial imaging is not recommended, unless there is an unexpected change in clinical characteristics". This recommendation reflects the fact that the rate of CPP crystal deposition is unknown and, above all, there are currently no available treatments capable of dissolving CPP crystals [1,55]. However, the taskforce also acknowledged that in certain cases, such as rapid symptom progression, imaging may be helpful to assess whether this correlates with disease severity or to identify potential alternative diagnoses. Furthermore, imaging studies aimed at monitoring patients with calcium crystal deposition diseases would be fundamental for gaining a better understanding of the natural history of these conditions. On this front, US is currently the only imaging technique capable of providing a semiquantitative assessment of CPP crystal burden, enabling the monitoring of crystal deposits through the OMERACT scoring system [67]. This system grades the presence of CPP crystals in the knees (menisci and hyaline cartilage) and wrists (triangular fibrocartilage complex) on a 4-point scale, ranging from 0 to 3: grade 0: no findings consistent with CPPD; grade 1: ≤ 3 single spots or 1 small deposit; grade 2: > 3 single spots, or > 1 small deposit, or at least 1 larger deposit occupying ≤ 50 % of the structure examined in the reference image; grade 3: deposits occupying more than 50 % of the structure examined in the reference image [67].

In conclusion, the OMERACT US scoring system could provide valuable insights into the evolution of CPP crystal deposition over time, for example, after acute flares. It could also shed light on the complex relationship between CPPD, osteoarthritis, and joint damage, and serve as a valuable tool for monitoring the efficacy of potential treatments. Moreover, OMERACT is also developing an

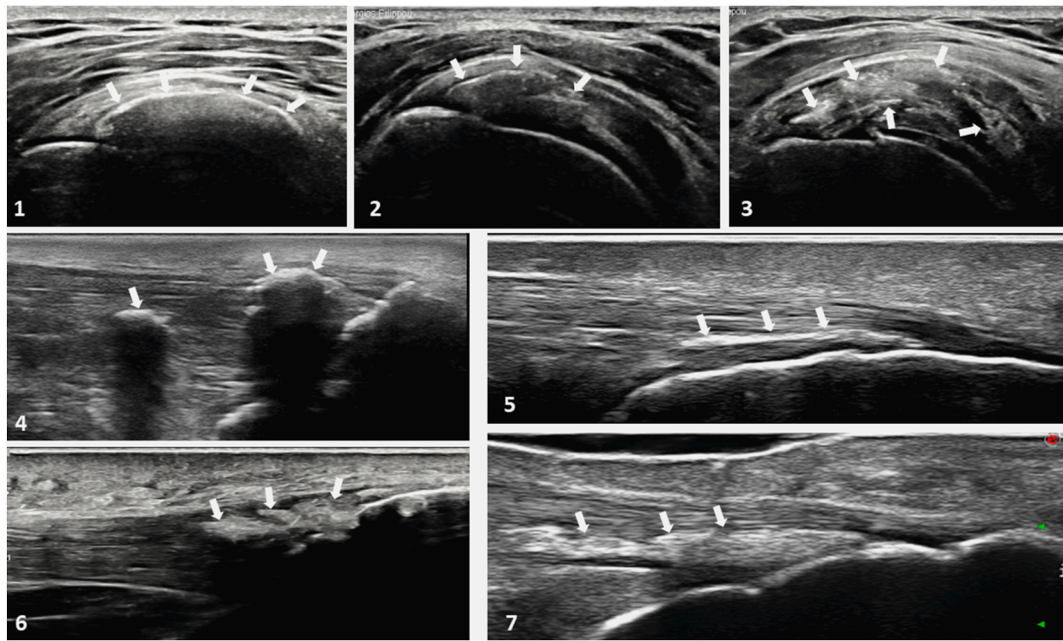


Fig. 11. Aspect of different crystal depositions in tendons at ultrasound (US). (1): Large basic calcium phosphate (BCP) crystal deposition in the supraspinatus tendon. Arrows indicate the hyperechoic arc-shaped deposit causing acoustic shadowing (bone profile not visible). (2): BCP deposition in the resorption phase. Arrows indicate a hyperechoic arc-shaped calcification, appearing less dense, allowing partial visualization of its internal structure and the underlying bone profile. (3): Calcium pyrophosphate crystal deposition (CPPD) in the supraspinatus tendon. Diffuse, inhomogeneous, and amorphous deposits (arrows indicate both linear and irregular shaped deposits), without acoustic shadowing. (4): BCP deposition in the Achilles tendon (arrows), showing arc-shaped hyperechoic deposits with significant US beam attenuation. (5): CPPD in the Achilles tendon. A linear hyperechoic line, following the tendon fibers' long axis without creating acoustic shadowing (arrows). (6): Tophi in the patellar tendon (arrows), appearing as irregular hyperechoic deposits with acoustic shadowing. (7): A distinct pattern of CPPD in the Achilles tendon. The deposit (arrows) is larger than in panel 5 and appears more irregular, resembling MSU deposition (as seen in panel 6). However, despite its size, it does not cause acoustic shadowing, only mild US beam attenuation.

artificial intelligence tool for the identification and scoring of CPPD using US to facilitate the detection of CPPD. In contrast, for conventional CT and DECT, no automatic volume measurement has yet been developed for CPPD, imposing manual delimitation of deposits, which would be both time-consuming and insufficiently reproducible. More research is needed on cohorts with pre-established sequential scans to gather more knowledge on CPPD.

4. BCP

BCP crystals typically deposit in both articular and periarticular tissues but can also be found in other tissues like vessels or skin [68]. Based on the localization of the deposition, the main clinical manifestations of BCP-related arthropathies can be a calcific periarthritis or a rapidly progressive destructive arthropathy which finds its prototype in the so-called Milwaukee shoulder even if this type of arthropathy can involve other large joints [69]. Further, BCP crystals are considered to be fundamental in the pathogenesis of osteoarthritis, but the exact mechanisms are not well understood, and the analysis of this aspect is beyond the scope of this review. The epidemiology of BCP arthropathies is not known.

According to the 2023 EULAR recommendations for the use of imaging in CIAs in clinical practice, imaging is necessary for the diagnosis of BCP crystal arthropathies and the recommended modalities are US and CR. Even if this statement may seem obvious, the level of evidence is low (2b) and this is due to the lack of studies demonstrating directly the association between imaging findings and crystal nature of the calcifications [31].

BCP periarticular calcifications are mainly found at the insertion site of tendons, typically in regions where relative hypoxia occurs such as the supraspinatus tendon insertion [70]. Their aspect on imaging may differ according to the phase (resting phase or resorptive phase) [71], but in any case, US and CR remain the main imaging exams for the diagnosis [6].

At US, BCP crystals generally create posterior attenuation of the US beam even at lower concentrations while on the contrary, CPP crystals generally do not create acoustic shadowing even in higher concentrations [18]. Another hint that could further aid US differentiation of calcium crystals is the aspect. BCP calcifications (at the resting phase) appear as arc-shaped formations [71] while CPP calcifications most of the times appear as hyperechogenic lines that follow the long axis of the tendon fibers (personal experience). At the resorptive phase, the deposits generally become "soft" (only partial attenuation of the US beam) and with an irregular shape even if they may assume variable shape [71] (Fig. 11).

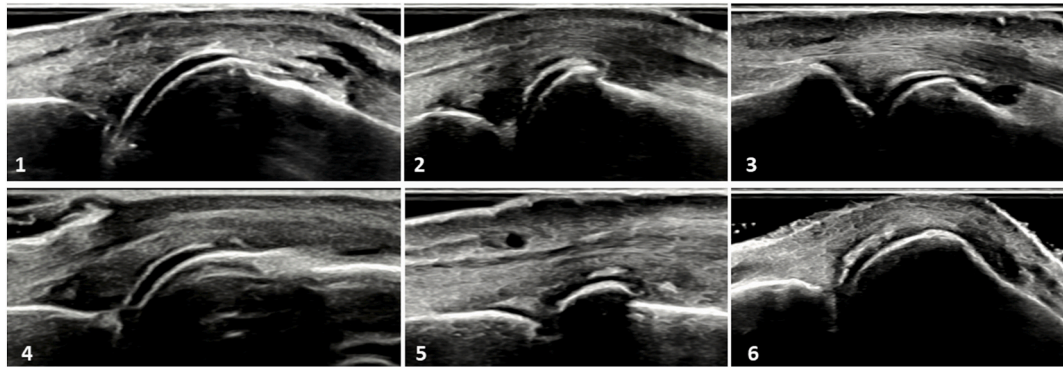


Fig. 12. Ultrasonographic double contour (DC) signs. (1): The typical DC sign in a patient with gout, appearing as a clear, continuous hyperechoic line atop the hyaline cartilage (HC), ending precisely where the HC terminates. (2-6): Different patterns of pseudo-DC sign in CPPD. Pattern (4) closely mimics the classical DC sign of gout. In the other cases, the irregular thickness of the DC (2, 5 and even more evident in 6), the extension beyond the HC (3), and in some cases the “distance” from the HC (5) help differentiate gout-DC from CPPD-DC in static images. Arrows and symbols were intentionally omitted to allow an unobstructed evaluation of small details.

On CR, BCP calcifications appear as amorphous, dense round or oval shaped deposits with well-defined borders during the resting phase while they become less dense and cloudy with a not well-defined profile during the resorptive phase [70].

Highly destructive arthropathy of the shoulder (Milwaukee shoulder) may be suspected in patients with large joint effusion and functional loss. Joint crepitus is frequently present. US demonstrates a large effusion in the joint and peri-articular structures (such as bursae) that could be completely anechoic but most of the times hyperechoic spots are present that could represent crystal aggregates, debris or even blood clots. Rupture of the rotator cuff is another US finding that raises suspicion as well as irregularities of the bone profile. At CR, a cranial subluxation of the humeral head can be present, indirect sign of the rotator cuff lesion, and osteoarthritis of the glenohumeral joint [69].

As for CPPD, serial imaging for monitoring deposition is not recommended in BCP unless there is a change in clinical scenario [6].

5. Challenging scenarios and controversies on the assessment of CIAs with imaging

5.1. The double contour sign

The DC sign, as previously described, is widely recognized as a hallmark of MSU crystal deposition, with strong diagnostic value, as demonstrated by its inclusion in the 2015 ACR/EULAR gout classification criteria [4]. However, evidence suggests that this sign is not entirely specific for gout, as it has also been observed in CPPD, with reported prevalence rates ranging from 7 % to 20 % in previous studies and a sensitivity of 78.9 % for CPPD diagnosis [10,72,73]. In CPPD, the deposition of CPP crystals over the hyaline cartilage produces what is referred to as the pseudo-DC sign [74]. Although the precise mechanism underlying the pseudo-DC sign has not been fully elucidated, a cadaveric study has provided an anatomopathological explanation: in gout, MSU crystals adhere directly to the surface of the hyaline cartilage, forming the classic DC sign. In contrast, in CPPD, CPP crystals form within the joint capsule or ligaments just above the cartilage surface, producing a sonographic appearance that mimics the DC sign [74]. Typically, the gout-related DC sign appears as a sharply defined, regular hyperechoic line closely following the contours of the underlying bony cortex, terminating exactly where the hyaline cartilage ends. Conversely, the pseudo-DC sign in CPPD tends to be thicker, more irregular, and can extend beyond the cartilage margins, following the overlying capsule [75] (Fig. 12). A key distinguishing feature between these two signs lies in their behavior during dynamic US scanning. The DC sign in gout moves synchronously with the hyaline cartilage, since the MSU crystals are directly adhered to the cartilage surface. In contrast, the pseudo-DC sign moves asynchronously; the capsule or ligament remains relatively stationary while the underlying cartilage moves in the opposite direction [74,76] (Video). However, this dynamic difference depends on the biomechanics of each joint and may not always be pronounced. For example, in joints where the bone and capsule move in strong opposition (e.g., the proximal radio-ulnar joint), the dynamic difference is striking, in contrast, in joints where the bone and the capsule move more synchronously (e.g., the shoulder), this difference is less evident.

Additionally, it is also noteworthy that in previous ex vivo studies deposition of CPP crystals has been also identified on the surfaces of menisci, creating a DC sign on the meniscus [77]. More recent studies have shown that in 2.4 % of CPPD cases, the double contour sign was indistinguishable from the classic gout DC sign, both in static and dynamic assessments [76].

In summary, while the DC sign in gout primarily results from a single mechanism—MSU crystal deposition on joint surfaces—the DC sign in CPPD may arise from multiple mechanisms. One possibility is the formation of CPP crystals within the joint capsule, including ligaments, above the hyaline cartilage surface. In such cases, dynamic scanning is crucial for accurately identifying the location of CPPD. Another potential mechanism involves CPP crystal deposition directly on the surface of the hyaline cartilage or other joint structures, such as the menisci. These deposits may develop through two processes: (1) crystals released from their original site of formation into the joint space, where they subsequently settle on cartilage surfaces, with or without an acute attack, or (2) the migration of pre-existing CPP deposits toward the cartilage surface. Additionally, superficial deposits could emerge either through

direct crystallization in the outermost cartilage layers or as a result of hyaline cartilage thinning, which exposes deeper crystal deposits.

Notably, recent studies have described a radiological DC sign, termed "cartilage icing" [78]. This sign has been described both in gout and CPPD, and the mechanism underlying its formation may be similar to those responsible for the US DC sign.

Furthermore, there is evidence that the pseudo-DC sign can also occur in the first MTP joint in patients with acute arthritis resembling classic podagra [79]. Therefore, due to the distinct anatomical locations of crystal deposition, specific static imaging characteristics, and differences in dynamic scanning behavior, US can play a valuable role in differentiating between the gout-related double contour sign and the pseudo-double contour sign of CPPD. In cases where sonographic features are inconclusive, scanning additional specific sites for CPPD and gout (for example, wrists and knees) may aid in diagnosis.

In conclusion, while the US DC sign can be observed in both gout and CPPD, the underlying pathogenetic mechanisms differ. Sonographers should be aware of these distinctions and receive proper training to differentiate between the two conditions using both static and dynamic scanning techniques [8]. Another important consideration is the terminology used to describe these signs. Traditionally, the term "DC" has been associated with MSU crystal deposition and applying the same name to a similar but distinct lesion in CPPD may cause confusion. Given the ongoing reassessment of CPPD terminology [80], pseudo-terms—such as "pseudo-DC sign"—should be avoided. Instead, standardized terminology specific to CPPD should be established to enhance clarity and precision in clinical and research settings [81].

5.2. The aggregates in ultrasound

Aggregates are recognized as one of the elementary US lesions in patients with gout. They were first defined by OMERACT in 2015 as: "Heterogeneous hyperechoic foci that maintain their high degree of reflectivity, even when the gain setting is minimized or the insonation angle is changed, and which occasionally may generate posterior acoustic shadowing" [82]. However, during the initial web-based and subsequent patient-based exercises, aggregates failed to achieve acceptable reliability values, with an inter-reader kappa of 0.209 in the patient-based exercise [13,82]. This raised concerns regarding their reliability and utility in research settings.

In 2021, the OMERACT revisited the definition of aggregates. Following three rounds of a Delphi survey, aggregates were redefined as: "Bright hyperechoic, isolated spots too small to fulfill the tophus definition and characterized by maintaining their high degree of reflectivity when the insonation angle is changed", irrespective of anatomical location. Importantly, an overarching principle was introduced, specifying that "aggregates can only be scored in a patient if other ultrasound features suggestive of gout, such as DC sign and/or tophus, are present or have previously been present at the patient level, and if the aggregates are not located inside a tophus" [11]. This revised definition was tested on static images and demonstrated significantly improved reliability, with a kappa of 0.71 for intra-reader agreement and 0.61 for inter-reader agreement [9]. In addition, a scoring system for aggregates was developed, yielding similar intra- and inter-reader kappa values (0.74 and 0.61, respectively) [83].

Despite these improvements, several conceptual issues remain unresolved. The primary limitation is the lack of a validated method to definitively demonstrate that an aggregate—even in patients with gout—represents actual accumulation of MSU crystals. As previously discussed, the resolution of DECT is insufficient to detect deposits of this size, and no other imaging modality can currently verify that a hyperechoic spot on US corresponds to MSU crystal aggregates. A recent attempt by Liu et al. compared US findings with polarized light microscopy in suspensions containing decreasing concentrations of MSU crystals derived from tophi, joints with acute gout attacks, and artificially created crystals. Their findings indicated that while aggregates were observed in suspensions from tophi and joints, no aggregates appeared in suspensions with artificial crystals. This suggests that the US appearance of aggregates may not be due to the crystals themselves but rather to other substances (e.g., cells, proteins) that promote crystal clumping [84]. This could explain the low specificity of this US lesion, as similar aggregates capable of reflecting the US beam may form in response to other stimuli, not just MSU crystals. Moreover, hyperechoic spots within joints and periarticular tissues are observed in other conditions, such as CPPD, rheumatoid arthritis, and even Baker's cysts containing air bubbles [85], indicating that these findings are not specific to gout. The new OMERACT overarching principle partially addresses this issue by requiring the presence of additional US features indicative of gout.

Another conceptual challenge arises in longitudinal studies. In theory, aggregates should initially increase as larger tophi and DC deposits dissolve following ULT, due to the fragmentation and redistribution of smaller MSU aggregates. However, in a longitudinal study by Berner Hammer et al., aggregates decreased in parallel with tophi and DC sign at all time points (baseline, 3, 6, and 12 months), raising further doubts about the nature and pathophysiological relevance of these hyperechoic spots [38].

In conclusion, aggregates remain a nonspecific US finding and should only be assessed in joints where other sonographic features of urate deposition are present. While they likely reflect the presence of MSU crystal deposition, direct confirmation is still lacking. Their relevance in clinical practice and their value as a monitoring tool in gout management remain to be fully established.

5.3. The importance of the discriminatory ability of imaging for calcium crystals

As previously discussed, a key challenge in the role of imaging for calcium crystal-induced arthropathies is its ability to distinguish between different types of calcium crystals. Thanks to newly developed definitions and precise descriptions of elementary lesions, US and CR appear to be quite specific for CPPD. However, a similar standardization process is needed for BCP-related arthropathies in order to enhance the accuracy of imaging for this condition as well.

Regarding DECT, some proof of concept studies suggest that DECT may have a limited ability to differentiate between CPP and BCP [62,63]. The overlap between DECT values (particularly Zeff and DEI) of the different calcium-containing deposits make DECT hardly

Practical points

- In gout, US and DECT are highly specific for detecting MSU crystals and are the recommended imaging modalities for gout diagnosis. If characteristic imaging findings are present, synovial fluid analysis is not necessary for diagnosis.
- In gout, US and DECT can monitor crystal deposition, assess treatment response, and help predict future flares. CR remains valuable for evaluating structural damage.
- US has a higher spatial resolution than DECT for detecting MSU crystal deposits.
- The US DC sign can be observed in both gout and CPPD, but results from different mechanisms. US can distinguish (most of the time) gout-DC from CPPD-DC using static and dynamic assessment thanks to peculiar characteristics.
- In CPPD and BCP, CR and US are the recommended modalities for diagnosis; CT and DECT may be useful in cases of axial CPPD involvement.
- The presence of CPPD in multiple peripheral joints on imaging increases the likelihood of diagnosis. Wrists and knees should be prioritized in imaging evaluation.
- Validated standardized imaging definitions exist for US in gout, and CR and US in CPPD, ensuring specificity. No validated imaging definitions are available for BCP.
- Imaging findings should always be interpreted in the context of clinical symptoms and laboratory evaluation.

Research agenda

- In gout, further research is needed to define the role of imaging in disease management, particularly in guiding flare prophylaxis and ULT.
- In CPPD, imaging may help monitor changes in crystal burden and the association with OA. Longitudinal studies could help to better understand the natural history of CPPD.
- In BCP deposition disease standardized imaging definitions need to be developed and tested for reliability and accuracy in diagnosis.
- Comparative studies aimed to assess and improve the discriminatory ability of different imaging techniques especially regarding calcium crystals, could provide a great potential for a better understanding of calcification processes, not only in joints but also in other tissues (for example blood vessels), and the association between calcium crystals and joint damage.
- Evaluating the diagnostic performance of emerging advanced imaging techniques in CIAs, such as SPCCT.

applicable in clinical practice so far. New generation of multi-energy spectral photon-counting CT (SPCCT), based on the same principles of DECT but offering higher spatial resolution and multiple levels of energy to combine, will improve both the level of detection (sensitivity) and discrimination potential (specificity) in the coming years [86]. These advancements will also be beneficial for the management of gout, as it should increase the sensitivity for smaller MSU deposits that are below the spatial resolution threshold of DECT.

The correct and precise identification of calcium crystals could open new highways for better understanding of not only CPPD and BCP-related arthropathies but also osteoarthritis. The role of calcium crystals in osteoarthritis is considered to be essential both for the development and progression of joint damage, yet the exact pathogenetic mechanisms remain unclear [1,69]. The availability of imaging techniques capable of discriminating the type and possibly quantifying the amount of calcium crystals in joints would represent a significant step toward elucidating the relationship between calcium crystals and osteoarthritis [87].

6. Summary

The field of CIAs is likely where imaging has undergone the most significant technological and scientific advancements in the past decade. Imaging has become a fundamental component in the assessment of CIAs and, unlike other rheumatologic diseases where its adoption still faces resistance, it has been incorporated into various classification criteria and recommendations with considerable weight. However, further progress is needed, and novel approaches could enhance and refine imaging techniques, optimizing their application in both routine clinical practice and research to benefit patients with CIAs.

CRediT authorship contribution statement

Silvia Sirotti: Writing – review & editing, Writing – original draft, Visualization, Validation, Data curation, Conceptualization.

Tristan Pascart: Writing – review & editing, Writing – original draft, Visualization, Validation, Data curation, Conceptualization. **Ralf Thiele:** Writing – review & editing, Writing – original draft, Visualization, Validation, Data curation, Conceptualization. **Georgios Filippou:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Data curation, Conceptualization.

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none.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.berh.2025.102063>.

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