Imaging of gout: findings and pitfalls. A pictorial review.

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ABSTRACT

Gout is the most common crystal arthropathy, accounting for up to 5% of all arthritis. The hallmark of the disease is hyperuricemia with the subsequent deposition of monosodium urate (MSU) crystals in the intra- and extra-articular soft tissues and bones, leading to inflammation of these tissues. Recurrent intermittent flares can result in chronic gouty arthritis leading to cartilage and bone destruction. The most sensitive and specific imaging methods for diagnosing acute gout are ultrasound and dual energy computed tomography (DECT). In the chronic or tophaceous gout, imaging may depict tophi and their local destructive effect on surrounding tissues with characteristic findings on radiographs. In this pictorial review the imaging features of acute and chronic gout on radiographs, ultrasound, and DECT are presented, as well as imaging pitfalls that one needs to be aware.

Keywords: Gout; Gouty arthritis; Tophi; Ultrasound; DECT; Radiography

INTRODUCTION

Gout is the most common crystal arthropathy. The hallmark of the disease is hyperuricemia with subsequent deposition of monosodium urate (MSU) crystals in the kidneys, as well as in the synovial membrane, synovial fluid, cartilage and bone, initiating the inflammatory response seen in gouty arthritis. Crystals can also precipitate into the periarticular soft tissues, leading to the typical gouty tophus, which is hallmark feature of the chronic gout.

Both the prevalence and incidence of gout are increasing in many developed countries due to a combination of genetic and environmental factors[1].

Most patients present between the ages of 30-60 years. The incidence is 2 to 6-fold higher in men than in women[1]. A typical patient is a 50-year-old man, with excessive purines in his diet, and with metabolic syndrome[2-3].

Four clinical stages of the disease have been recognized: asymptomatic hyperuricemia, acute gouty arthritis, inter-critical gout, and chronic tophaceus gout.

CLINICAL PRESENTATION OF THE ACUTE GOUT

90% of first gout attacks are monoarticular. Involvement of the first metatarsophalangeal joint (MTP), termed "podagra ", is classical but only accounts for 50% of cases[4-5]. Difficulties in initial diagnosis may result in delays in subsequent treatment and management, and may be due to different factors[6-7]. Any peripheral joint may be affected, as may the axial skeleton. Apart from the first MTP, there is a predilection for the first interphalangeal joint (great toe), other MTP, knee, ankle and midfoot, elbows, wrists and hands joints. Less common sites of disease include the shoulder, hip, sacroiliac joints and the spine. Pain and inflammation at the affected joint may mimic septic arthritis. Ultimately aspiration may be needed to provide a definite diagnosis. Radiographs in early gout have a low sensitivity and specificity and a negative result from polarized light microscopy of synovial fluid due to low concentrations of crystals in the early stage of disease may also lead in misdiagnosis. In addition, gout may have an atypical presentation in elderly patients with polyarticular involvement of the small joints of the hands and feet, female predilection and early development of tophi.

CLINICAL PRESENTATION OF CHRONIC GOUT

Chronic gout is now less uncommon due to early diagnosis and treatment. In chronic disease, there is progressive cartilage and bone damage due to osteo-

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clast activation. This stage of the disease is characterized by deposition of MSU crystals, known as tophi. Tophi represent a mixture of monosodium monohydrate crystals in a matrix of amorphous debris comprised of urate, proteinaceous deposits and lipids with a surrounding foreign body reaction[5,6]. They are present in around 40% of patients, and occur later in the course of the disease, usually after 10 years. They are characteristically found in a periarticular distribution (e.g. medial to first MTP), bursal (e.g. olecranon and prepatellar), and intratendinous (e.g. quadriceps and patellar tendons). Rarely tophi occur in acute disease, which may mimic tumor infiltration. If left untreated, this stage of disease can be debilitating and cause severe morbidity.

IMAGING FEATURES OF THE ACUTE GOUT

The most sensitive and specific imaging methods for diagnosing acute gout are ultrasound (US) and dual energy computed tomography (DECT). Radiographic findings are non-specific [5].

FEATURES OF EARLY GOUT ON RADIOGRAPHS:

- asymmetric soft tissue swelling around the affected joint
- normal peri-articular bone mineralization, unlike rheumatoid arthritis (RA)
- periostitis, as a result of periarticular inflammation
- rarely peri-articular erosions or skin fistula related to gouty tophus, typically in the elderly.

FEATURES OF EARLY GOUT ON ULTRASOUND

- effusion in the affected joint which is anechoic in early disease. Subsequently, hyperechoic foci may appear, representing MSU crystals measuring less than 1 mm (the "starry sky" sign) (Figure 1A). Larger MSU aggregates, referred to as micro-tophi, may result in a "snowstorm" (Figure 1B) appearance. These may have variable echogenicity (Figure 2)[5-6,8].
- synovial hypertrophy and bursitis, which are often seen but are non-specific. The presence of MSU embedded in synovium may increase the specificity [5-6].
- the "double contour" sign, which results from deposition of gout crystals on the surface of the articular cartilage.[9] The crystals eventually create a continuous hyperechoic line overlying the articular cartilage, paralleling the subchondral bone. This is most commonly seen at the dorsal aspect of the first MTP joint. The "double contour" sign should be differentiated from hyperechoic foci within the substance of the cartilage, which is seen with calcium pyrophosphate dyhydrate deposition (CPPD). [9] The "double contour" sign can disappear with successful urate-lowering therapy [9].

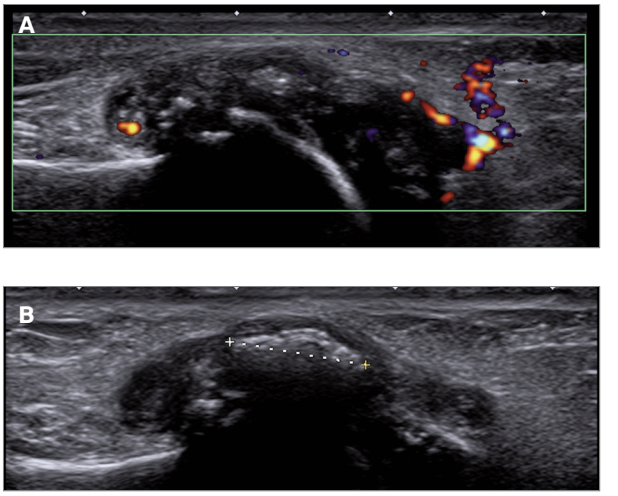


FIGURE 1. Ultrasound features of an early gout: a) a "starry sky" sign; b) micro-tophi (between crosses)

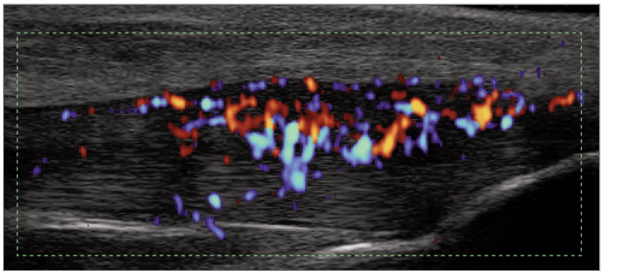


FIGURE 2. Distal patellar tendon infiltration by a hypoechoic and highly vascularized tophus

Imaging pitfalls may result from the "cartilage interface sign", in which the surface of the hyaline cartilage is more reflective when associated with overlying fluid. The cartilage interface sign should disappear as the angle of isonation is altered. The "double contour" sign may sometimes also be seen with CPPD deposition.

FEATURES OF EARLY GOUT ON DECT:

DECT evaluates and identifies material-specific differences in attenuation and allows for classification of the chemical composition of the scanned tissues, enabling specific characterization and separation of gout deposits from the surrounding tissue[5,10]. Depending on the software available the tissues can be color-coded and fused onto grey-scale two-dimensional (2D) and three-dimensional (3D) computed tomography images

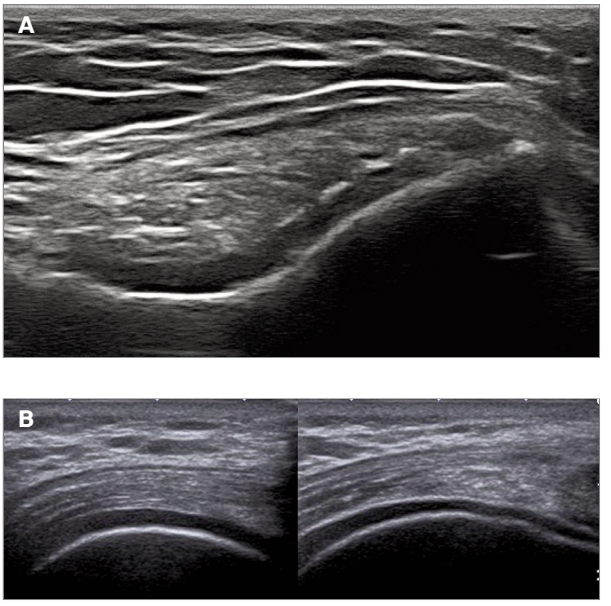


FIGURE 3. A "double-contour" sign seen in the knee joint: a) early intermittent crystals on the lateral anterior condyle cartilage b) crystals creating a continues line on the loaded surface of the medial condyle, transverse (left image) and longitudinal scan (right)

to allow the depiction of gouty deposits. Alternatively, using spectral analysis, a region of interest can be placed over suspected tophi giving an estimate of the composition of the material according to an effective Z-value, which can be compared with known values for certain materials (Figure 4)[6].

Advantages of DECT in early gout include[5,6,9]:

- DECT allows for even small MSU deposits to be detected, and therefore enables an earlier diagnosis than other imaging modalities;
- DECT may show gout deposits even in patients with asymptomatic hyperuricemia;
- DECT has a comparable sensitivity for detecting crystals to US, having an advantage in certain locations where US access may be poor (for instance, in the posterior compartment of the knee);
- DECT has the ability to reliably distinguish between CPPD disease and gout crystals, unlike US;
- DECT quantification of urate deposition using automated volumetric applications has been shown to be highly reproducible. Thus, DECT can be used for initial assessment of the disease burden and for serial assessment of patients with gout to assess response to therapy.

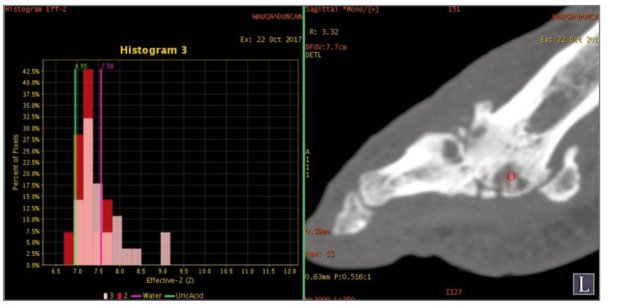


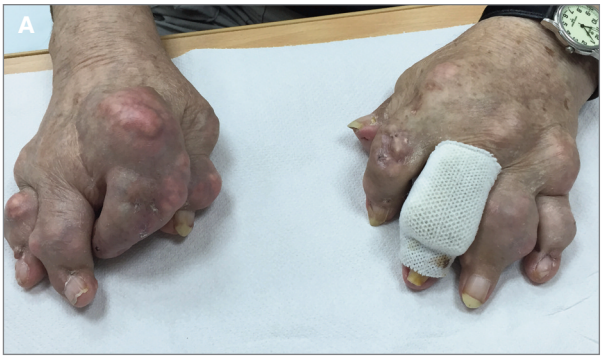
FIGURE 4. DECT of the first MTP joint with spectral analysis. Established erosive arthropathy of 1st MTP joint. The red region of interest cursor is positioned over an erosion of the metatarsal head with the effective Z value shown on the bar graph. The average effective Z value of urate is depicted by the green line, showing that the erosion contains a significant amount of urate crystals.

IMAGING FEATURES OF CHRONIC GOUT

In chronic gout, imaging may depict tophi and their local destructive effect on surrounding tissues.

FEATURES OF CHRONIC GOUT ON RADIOGRAPHS[5,6,11] (FIGURE 5):

- tophi: are typically radiodense and ovoid, and may be calcified. They most commonly occur at the Achilles tendon and the retroachilles bursa, olecranon bursa and extensor mechanism. They may not be radiographically visible until they reach 5-10mm in size and may mimic rheumatoid nodules, or osteophytes if located at interphalangeal joints.
- erosions: result from intra-osseous extension of tophi. Initially occur in a periarticular distribution, and later there may be extension into the joint with sclerotic margins and an overhanging edge. In contradistinction to RA, gout typically results in non-symmetric, larger erosions, and in a distribution not typical for RA.
- pseudotumor of gout: these are lytic, expansile cystic lesions resulting from intra-osseous deposition of MSU crystals, with predilection for the superolateral aspect of the patella. When large this may be mistaken for malignant tumour, infarct or enchondroma. Also, for a long time the joints space is preserved and there is no bone loss which additionally differ gout grom RA.
- pathological fractures, with a "cupping" appearance resulting from collapse of the subchondral bone, "mushrooming" from enlargement of the ends of bone due to new bone formation, or pencil-in-cup appearance due to tapering of the shaft from osteoly-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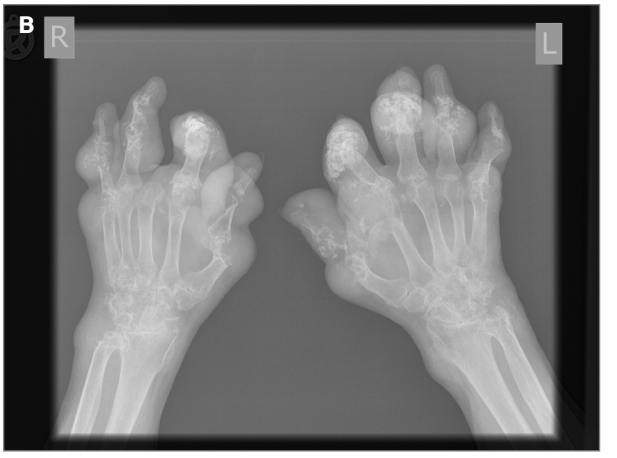
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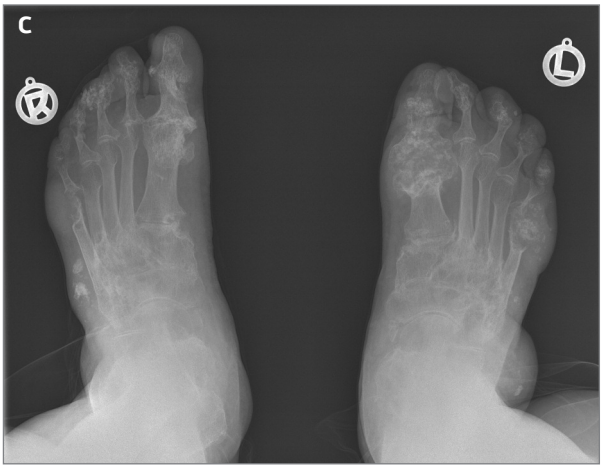
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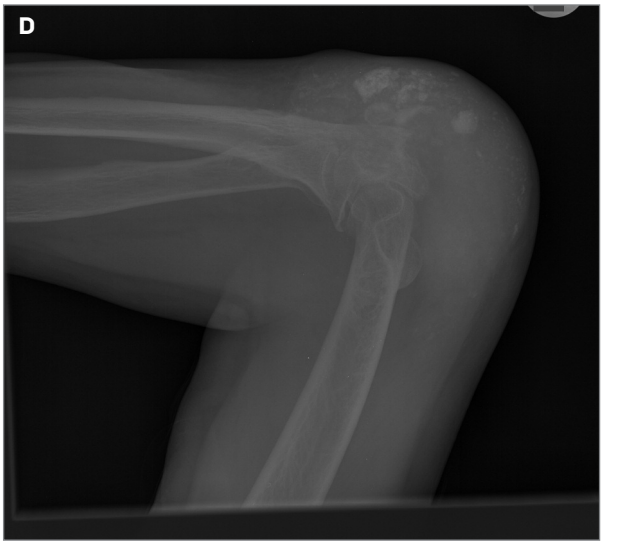
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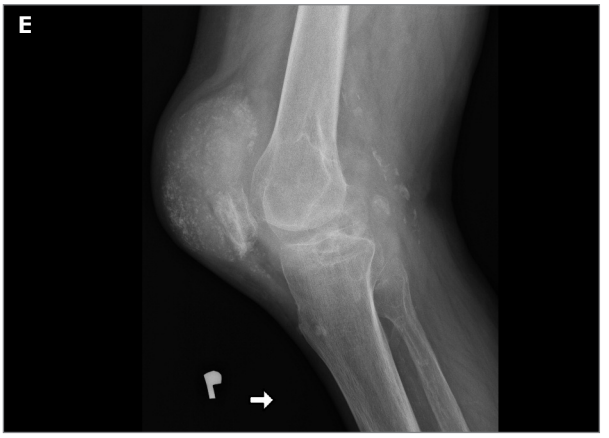
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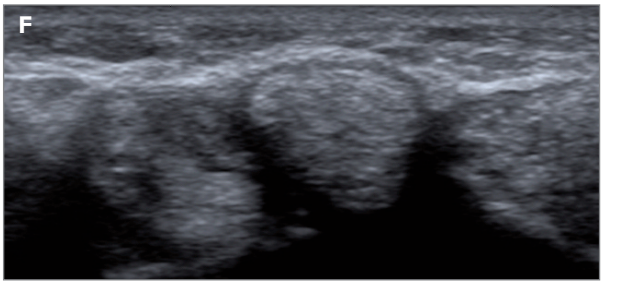
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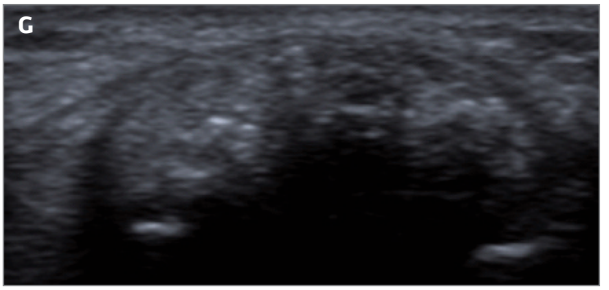
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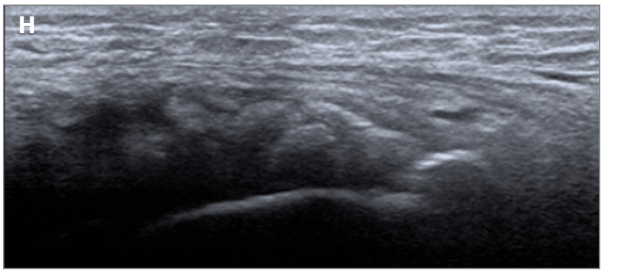
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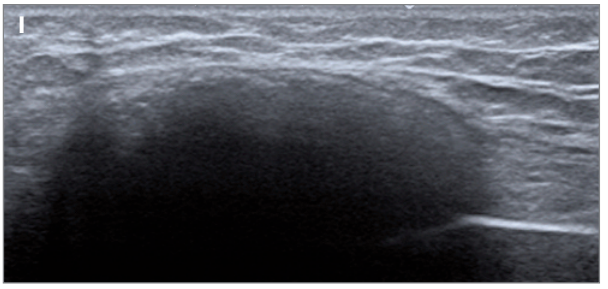

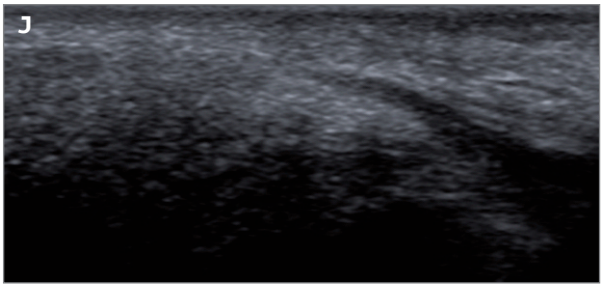

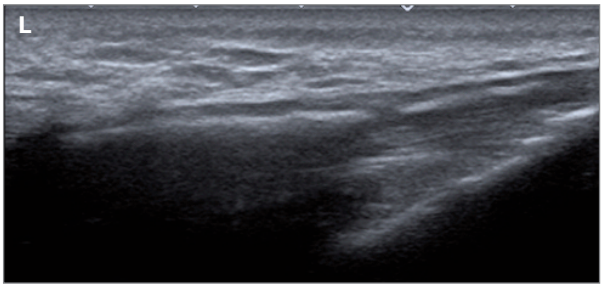

FIGURE 5. A 70-year old man, with chronic gout, mutilans form. a) Clinical photographs of the hands; b) hands radiograph, PA view: soft tissue nodular thickening with increased density (tophi), with calcifications. Mutilans form of hands deformations with large destructive osteolytic lesions in carpal and interphalangeal joints, with erosions resulting from intraosseous extension of tophi showing characteristic sclerotic edges. Bone loss; c) feet radiograph, AP view: soft tissue nodular thickening with increased density (tophi) with calcifications. Mutilans form of disease, with large destructive osteolytic lesions in MTP1 and IP joints of first toes (L>R) and MTP5 left, to less extent MTP 2-5 of the right foot. Moderate erosive lesions in Lisfranc joint of the right foot. Secondary osteoarthritis in tarsus. Bone loss; d) left elbow, lateral radiograph: topus/tophi with calcifications and bone loss. Notice the osteolytic lesions of the left olecranon and distal humerus; secondary osteoarthritis with join space narrowing; e) right knee, lateral radiograph: increased radiodensity of periarticular soft tissues with calcifications, single calcifications seen at the level of metaphyses of the crura, popliteal fossae. Bone loss. Well defined erosions and cysts, mainly tibia, that results in secondary osteoarthritis; f-l) Different presentation of tophi at ultrasound: f) hyperechoic tophi in the wrist joint; g) hyperechoic tophus containing tiny calcifications; h) hyperechoic tophus containing MSU aggregates; i) a topus in the olecranon bursa with calcified surface, j) tiny calcifications in the suprapatellar recess; l) MSU aggregates within the patellar tendon.

sis (like in advanced psoriatic arthritis; PsA or RA).
- normal bone mineralization, unlike RA, except the mutilans form which presents with osteolysis of bones.
- secondary osteoarthritis.

FEATURES OF CHRONIC GOUT ON US[5-6,9,12]: (FIGURE 5)

- tophi: appear as well circumscribed, hyperechoic or hypoechoic nodules, which are initially uniform. With chronicity, they become non-homogenous ("wet clumps of sugar" sign), with characteristic tiny internal hyperechoic echoes or aggregates. There may be a surrounding halo as a result of peri-tophus inflammation, or a posterior acoustic shadow
- tendinopathy: tendon delamination, tears and enthesopathic lesions, often with hyperechoic echoes representing MSU crystals or micro-tophi.
- erosions: an intra- and/or extra- articular discontinuity of the bone surface, seen in at least two planes.

FEATURES OF CHRONIC GOUT ON DECT[5-6,9]:

In addition to the ability to sensitively and specifically detect MSU crystals, DECT is an objective method of quantification of urate deposition for serial assessment of patients with gout to assess response to therapy (Figure 6).

PITFALLS ENCOUNTERED WITH DECT[5-6,9,13-15]:

- microscopic tophi may be missed due to a limit of detection crystals of around 2 mm in diameter;
- less dense tophi may be missed due to small MSU deposits as well as non-tophaceous gout, because like joint aspiration DECT relies on the presence of MSU deposits in sufficient number and concentration;
- gout in patients on urate lowering therapy, when the urate burden is below the detectable range, may not be seen;
- detection and quantification of MSU deposits using US and MRI may not be directly comparable, as these modalities will also show the non-urate components of regions of inflammation;
- false positive colour-coding may occur in patients

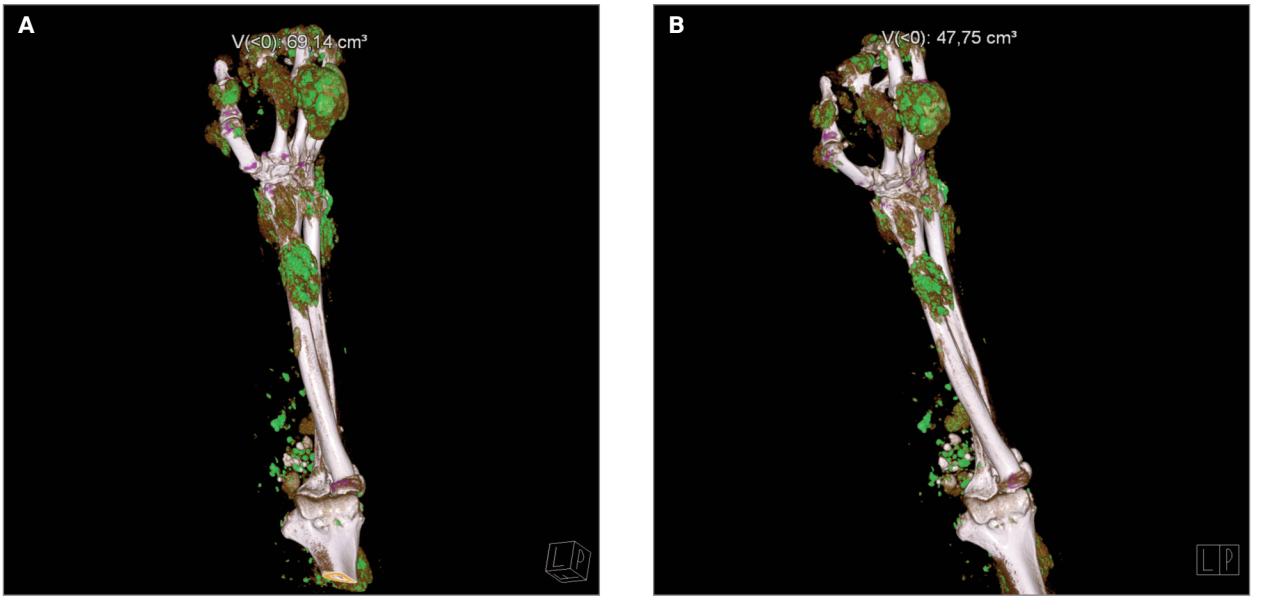

FIGURE 6. DECT of the right forearm with volume of crystals measurement: a) initial study; b) DECT quantification of urate deposition shows good response to treatment at 6 months follow - up.

with osteoarthritis, around joint replacements, in the skin and nail beds. Physiologic MSU deposition may also occur in the costal cartilages and intervertebral discs in middle-aged and older men.

CONCLUSION

Gout has a number of specific imaging features on US which are useful in making the diagnosis. DECT has the ability to confirm the diagnosis, and delineate and quantify gout. Radiographic, Magnetic Resonance (MRI) and Computed Tomography (CT) findings may be helpful in making the correct diagnosis, but lack of specificity.

The high diagnostic value of imaging has translated to clinical practice. The most recent ACR and EULAR classification criteria of 2015 now include US and DECT imaging features for the identification and delineation of gout[15].

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