Dual-energy computed tomography compared with ultrasound in the diagnosis of gout

Michael Gruber¹, Gerd Bodner¹, Eva Rath², Gabriela Supp², Michael Weber¹ and Claudia Schueller-Weidekamm¹

Abstract

Objectives. The aim of our study was to compare dual-energy CT (DECT) with US for the diagnosis of gouty arthritis and to correlate the imaging findings with results from synovial fluid aspiration whenever possible.

Methods. We recruited 21 patients (17 male and 4 female) who presented with a clinical suspicion of acute or chronic gout in 37 joints. DECT scans of the hands, wrists, feet, ankles, knees and elbows were performed. For post-processing, a colour-coding gout software protocol was used. US examinations of the same joints were performed. In addition, joint fluid aspiration was performed in a total of 14 joints.

Results. DECT images were positive for urate crystal deposits in 25 of 37 joints. US findings were positive in 24 of 37 examined joints. In 12 of 14 joints the synovial fluid aspiration was positive. CT and US findings correlated in 32 of 37 joints (86.5%; $\kappa = 0.698$, $P < 0.001$). CT and synovial fluid results correlated in 12 of 14 joints (85.7%; $\kappa = 0.417$, $P = 0.119$). US and cytology findings correlated in 14 of 14 joints (100%; $\kappa = 1$, $P < 0.001$).

Conclusion. DECT and US have comparable sensitivity for the detection of gouty arthritis in a clinical setting. However, DECT results should be interpreted carefully, as there could be some false-negative findings.

Key words: gout, gouty arthritis, dual-energy CT, ultrasound, synovial fluid.

Introduction

In the past 20 years the prevalence of gout has increased in industrialized nations [1]. Gout affects about 8.3 million Americans, or ~3.9% of the US population, according to the National Health and Nutrition Examination Survey of the Centers for Disease Control and Prevention [2]. Women are less likely to have gout than men, but in the post-menopausal years the gender difference in disease incidence decreases [3]. Patients who develop gout are more likely to be >50 years of age [4].

Gout is characterized as a metabolic disorder in which there is either an increase in the production of uric acid or a decrease in the excretion of uric acid, resulting in hyperuricaemia [5]. Long-lasting hyperuricaemia causes deposition of MSU crystals in the joints and soft tissues, triggering gouty arthritis and, if not properly treated, the formation of gouty tophi [6].

An acute attack of gouty arthritis is one of the most painful experiences reported throughout medical history [7]. Therefore it is important to diagnose gout as quickly and accurately as possible to provide an accurate therapy. Although serum uric acid levels are the most important risk factor for gout, these levels do not confirm or exclude gout, as many patients with hyperuricaemia do not develop gout, and, during acute attacks, serum levels may even be normal [8]. For typical presentations of gout (such as recurrent podagra with hyperuricaemia), a clinical diagnosis alone is reasonably accurate, but not definitive without crystal confirmation. Demonstration of urate crystals in synovial fluid or tophus aspirates permits a definitive diagnosis of gout and is considered the gold standard in the diagnosis of gout [8].

In some cases the differentiation between gout, septic arthritis and immune-induced inflammatory diseases of
the joints can be difficult, and, even in established gout, infection cannot be excluded on clinical presentation alone. Thus non-invasive techniques to accurately diagnose uric acid crystals within joints and periarticular soft tissue would be helpful to identify gout in patients with atypical inflammatory arthropathies and rule out gout as a diagnostic possibility in others.

US is an imaging technique that has attracted considerable interest in the field of rheumatology in recent years [9]. US has the potential to detect pathognomonic findings such as the double contour sign, which is caused by urate crystal deposits on cartilage surfaces, or the starry sky, which is characterized by urate crystals within the joint fluid [10]. In addition, tophaceous material in periarticular regions, adjacent synovialitis and joint effusion can be easily obtained with US [11–17]. US increases the rate of successful joint fluid aspirations (JFAs) by visualization of the intra-articular needle position. A new imaging technique, dual-energy CT (DECT), allows direct visualization of uric acid crystal deposits and bone structures at the same time, using different display colours. The attenuation of uric acid crystals differs significantly from that of bone, depending on the kilovolt setting of the X-ray tube, and therefore can be differentiated by DECT. DECT is a sensitive, non-invasive and reproducible method for identifying uric acid deposits in joints and in periarticular soft tissues in patients suspected of having gout [18]. The utility of DECT in the assessment of gout in the extremities and in the axial skeleton in patients suspected of having gout or in those suspected of having gout has been well described in the literature [18–25]. However, none of these studies compared DECT with US and evaluated the reliability of each method in diagnosing gout. The aim of our study was to compare DECT with US for the diagnosis of gouty arthritis and to correlate the imaging findings with results from synovial fluid aspiration whenever possible.

Methods

Patients

Between March 2010 and April 2012 we consecutively recruited 21 patients (17 male and 4 female) with an average age of 55 years (age range 32–79 years) with a clinical suspicion of acute or chronic gout in 37 joints in different anatomical regions, such as the hand and wrist [11], elbow [1], knee [3], or ankle and foot [22] (Table 1). In 13 patients, both hands and wrists or knees or ankles and feet were evaluated because of pain in the joints and a strong suspicion of chronic gouty arthritis bilaterally. In one patient, hands and wrists, and ankles and feet were assessed during one examination. Written informed consent for inclusion in this study was obtained from all patients. The study was approved by the Ethical Committee of the Medical University of Vienna and the General Hospital of Vienna.

DECT examination

A 128-row dual-source CT scanner (Somatom Definition Flash; Siemens Healthcare, Forchheim, Germany)

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L: left; R: right. Results of CT, US, JFA and duration of symptoms; a: acute; c: chronic, which means symptoms for a duration of ≥3 months; 1: positive; 0: negative; x: not performed.
equipped with two X-ray tubes and two corresponding detectors was used. In DE mode, these tubes scan at two different kilovolt levels, with simultaneous acquisition of two datasets, allowing for material-specific differences in the attenuation of the scanned tissue. The scan parameters were as follows: detector collimation $2 \times 64 \times 0.625 \text{mm}$ and rotation time $300 \text{ms}$. The kilovolt level of tube A was set to $140 \text{kV}$ and the level of tube B was set to $80 \text{kV}$. Tube current parameters were different, according to the scanned anatomical region: tube A reference (ref.) milliampere second (mAs) = 55, tube B ref. mAs = 255, for hands and wrists, elbows, ankles and feet; and tube A ref. mAs = 70, tube B ref. mAs = 300 for the knee.

Transverse sections were reconstructed from the DE datasets, with a composition of 0.3 in the soft tissue kernel (D30) and bone kernel (D45). Sagittal and coronal reformations in bone window settings were performed. The transverse soft tissue kernel datasets of both tubes were loaded onto a Syngo Multi-Modality Workplace (Siemens Healthcare, Forchheim, Germany) and reconstructed with a commercially available software program (DE Gout; Siemens Healthcare, Forchheim, Germany). This software uses automatic colour-coding visualization to detect uric acid crystals. The colour-coding datasets were reconstructed and reviewed in the transverse, sagittal and coronal image planes, with a slice thickness of $0.6 \text{mm}$ and an increment of $0.6 \text{mm}$. All scans were obtained without intravenous contrast agent.

**US examination**

US examinations of the same joints were performed on a 21 patients and a total of 37 joints by a 15- or 18-MHz probe (dependent on the anatomical region) with a Logic E9 US machine (General Electric Healthcare, Buckinghamshire, UK). US examinations were performed within 7 days of the CT scans by a US examiner with 10 years of experience in musculoskeletal US or by a US examiner with 8 years of experience in musculoskeletal US. The examinations were performed by one sonographer in each patient. Both US examiners were blind to the DECT examination results. They classified the examination findings as positive for the presence of gouty arthritis when they found the presence of MSU crystal deposits and/or the starry sky sign and/or the double contour sign.

MSU crystal deposits are normally located intra- or periarticularly, and they can be depicted as circumscribed hyperechogenic structures at US. The starry sky sign is defined as tiny hyperechogenic structures within the synovial fluid that represent small urate crystals floating in the synovial fluid. The double contour sign occurs in joints in which urate crystals are located at the surface of the hyaline cartilage. On US examination a so-called double contour can be seen at the cartilage surface of these joints. In three cases it was difficult to decide whether the findings were concordant with gout. In these doubtful cases a consensus interpretation of the images of the two examiners was reached.

**JFA**

JFA was conducted by one US examiner on 10 patients and a total of 14 joints (in 4 patients aspiration was performed in 2 joints). All aspirations were obtained in combination with the US examination and the joints were punctured under US guidance (Fig. 1). There was no complication in any of the procedures. The aspirated synovial fluid was viewed under a polarizing microscope within minutes after aspiration by a rheumatologist with 5 years of experience in microscope examinations. When synovial fluid contained MSU crystals, bright yellow, needle-like, negatively birefringent crystals were seen.

**Image evaluation**

DECT images were evaluated by two musculoskeletal radiologists (which were not the same physicians who performed the US examinations) with 10 and 5 years of experience in musculoskeletal radiology. The readers were blinded to the patients’ clinical data and they were also blinded to the results of the US examinations.

**Fig. 1** US-guided aspiration of joint fluid of the left fourth metatarsophalangeal joint of a 79-year-old male.
They read the images independently of each other. The images were read on standard colour, thin-film transistor monitors (Barco View, Kortrijk, Belgium) and the ambient light was subdued and constant for all reading sessions. The images were presented using a commercially available picture archiving and communication system (PACS) (IMPAX; Agfa-Gevaert, Mortsel, Belgium). The readers were asked to classify the examination findings as positive or negative for the presence of MSU crystals. They reviewed colour-coded transverse section images, as well as images reconstructed in the sagittal and coronal planes. There was no disagreement between the two readers regarding the presence of crystal deposits, because of the objective comprehensible criteria. In a second step they evaluated the possible presence of artefacts, which were defined as infinitesimal scattered pixilation on the colour-coded images.

Statistical analysis
All statistical analyses were performed by a statistician using SPSS 19.0 (SPSS Inc., Chicago, IL, USA). Agreement between the different methods was measured by Cohen’s $\kappa$ coefficient, as well as the relative frequency of the corresponding diagnosis. In addition, 95% CIs for relative agreement were calculated.

Results
DECT
In 16 of 21 patients, DECT examinations were positive. In a total of 37 joints evaluated with DECT, urate deposits were seen in 25 joints.

US
US findings were positive for gouty arthritis in 15 of 21 patients. In 24 of 37 joints the US examiners found the presence of MSU crystal deposits and/or the starry sky sign and/or the double contour sign. In three joints the examiners detected a double contour sign and in eight joints they saw a starry sky sign. The most frequently detected sign of gouty arthritis was the deposition of MSU crystals, which was seen in 19 joints.

JFA
The presence of gout was evaluated by synovial fluid aspiration in 10 patients, of which 1 was negative. In 12 of 14 joints the aspirated fluid contained MSU crystals (Fig. 2).

Correlations
DECT and US findings correlated in 32 of 37 joints (86.5%; $\kappa = 0.698, P < 0.001$) (Fig. 3). In three joints the DECT findings were positive while US examination was negative and in two joints the US results were positive while DECT did not show any urate crystal deposits. DECT and synovial fluid results correlated in 12 of 14 joints (85.7%; $\kappa = 0.417, P = 0.119$). There was one patient who had a positive result at the JFA but a false-negative result on DECT, and there was one patient with a positive finding on DECT and a negative result at synovial fluid aspiration. US and cytology findings correlated in 14 of 14 joints (100%; $\kappa = 1, P < 0.001$).
Discussion

This prospective study demonstrates that DECT, as well as US, are practical tools for diagnosing gouty arthritis in a non-invasive manner in patients suspected of having gout. It is known that uric acid crystals are often localized in periarticular tissues and tendons. DECT has an advantage in diagnosing gout, especially in those locations where US examinations provide only limited validity (Fig. 4). Another benefit of DECT is its potential to reliably differentiate between calcium pyrophosphate deposition disease, also termed pseudogout, and gout [18]. The calcium pyrophosphate deposits are typically intrachondrally localized and can be differentiated from urate crystals on the cartilage surface in most of the patients by US as well [26].

US examinations are more cost effective compared with DECT, and besides economic issues, the lack of radiation exposure becomes increasingly important. There has been a rapid increase in the population dose from medical radiation over the past 20 years, particularly due to the increased use of CT [27]. However, patients who suffer from gout are, in the majority of cases, older patients with decreased radiation-associated cancer risks. In addition, the cancer risk from CT examinations of the extremities is very low. The mean effective dose of the CT examinations in our study was <1 mSv.

Several studies have shown that US is a good tool to diagnose gout in cases with the characteristic appearance of gout in the joints [11-16]. It has been reported that up to 25% of synovial fluid aspirations may not reveal uric acid crystals in patients who have acute disease [5, 28]. The reason for these high false-negative results may be due in part to non-image-guided aspirations. In our study the synovial fluid aspiration was performed under US guidance. However, there was one patient with positive findings on the DECT examination and a negative result from the synovial fluid, which might have been caused by problems during the aspiration procedure or which was a false-positive result in the DECT. Unfortunately, the patient refused another aspiration, so a false-negative cytology result cannot completely be excluded.

US examinations were performed by two examiners with long-standing experience in musculoskeletal US. In three cases it was difficult to decide whether the findings were concordant with gout. In these doubtful cases a consensus interpretation of the images by the two examiners was used. The diagnosis of gout by DECT, on the other hand, was easier to establish and there was no disagreement between the two readers of the CT images.

On the other hand, in one patient with a positive cytology from JFA, a false-negative result on DECT was found. Glazebrook et al. [31] also presented the case of a patient who had a positive cytology from JFA and positive synovial biopsy for MSU crystals in the third metacarpophalangeal joint, but false-negative results on DECT. This case shows that negative DECT findings should be interpreted carefully and cannot absolutely exclude gouty arthritis. Therefore, in our opinion, concomitant diagnostic modalities such as US and JFA would be desirable to diagnose or exclude gouty arthritis.

Fig. 4 Transverse sections of DECT of the left knee of a 50-year-old male after utilization of the material decomposition algorithm.

Tophaceous deposits in atypical locations, such as the tendon of the popliteus muscle, the medial collateral ligament (A) and the tibial insertion portion of the posterior cruciate ligament (B). US of the knee was negative and only a minor joint effusion was detected.
Our study had some limitations, beginning with a selection bias on the side of the referring rheumatologists with regard to the type of patients who were included in our study and who underwent DECT. In our study we included patients that were assigned from the rheumatology department to confirm the presumptive diagnosis of gout. All patients were seen by an experienced rheumatologist, who established this presumptive diagnosis. That is why we had many patients with positive findings. This subset may not be representative of all at-risk patients, so generalizability may be limited.

Furthermore, the statistical power was limited because of the small sample size of only 21 patients. In addition, only 10 of 21 patients (14 of 37 joints) underwent JFA, and there was also a bias for patients in whom aspirations were performed. We included more male patients than females (17 to 4) with suspected gouty arthritis, and this might be considered another limitation. However, the incidence of gouty arthritis in males is five to six times higher compared with females, which is also reflected by our numbers. Another limitation might be that each patient was examined by only one sonographer. Nevertheless, the two examiners who performed the US examinations had long-standing experience in musculoskeletal US.

For typical presentations of gout (such as recurrent podagra with hyperuricaemia), a clinical diagnosis alone is reasonably accurate, but not definitive without crystal confirmation [7]. In uncertain cases the confirmation of urate crystal deposits is required, and the way to confirm the presence of MSU crystals depends on the clinical presentation and on the patient. Tophi can be localized in unexpected locations, even as the first sign of gout, and vigilance is required when unusual symptoms or signs occur in a patient with gout [28]. DECT is a method with high sensitivity and specificity for the detection of crystal deposits [22] in periarticular regions, as well as in tendons, skin, bones, and ligaments, but the availability is low and the costs are high. In our opinion, DECT is a good tool for early diagnosis of gout, but it should not be used for follow-up examinations because of the radiation exposure. Our study shows that US provides comparable or even better results than JFA and DECT in the diagnosis of gouty arthritis (US and JFA correlated in 14 of 14 joints, but in only 12 of 14 joints in DECT examinations), but it also indicates that atypical crystal deposit locations can be easily missed (Fig. 4). US performed by experienced examiners is an excellent tool, especially for follow-up examinations in patients with gouty arthritis, due to the lack of radiation exposure, good availability, and cost-effectiveness. Dalbeth et al. [32] compared a variety of studies for various methods of tophus assessment in gouty arthritis. They concluded that physical measurement techniques and US measurement of tophus size appear to meet most aspects of the OMERACT filter. However, in particular cases DECT, as well as US, could be negative and patients may have to undergo JFA for a definitive diagnosis. In conclusion, DECT is a helpful examination in the assessment of patients with gout, while US has comparable or even better results and should be performed especially in patients with a typical clinical presentation of gout to confirm the diagnosis.

### Rheumatology key messages

- Dual-energy CT is a promising method for the detection of crystal deposits in gouty arthritis.
- US should be performed in patients with a typical clinical presentation of gout to confirm the diagnosis.
- Dual-energy CT and US have comparable results in the detection of gouty arthritis.

### Disclosure statement: The authors have declared no conflicts of interest.

### References


