



# Combining non-contrast and dual-energy CT improves diagnosis of early gout

Seul Ki Lee<sup>1,2</sup> · Joon-Yong Jung<sup>1</sup> · Won-Hee Jee<sup>1</sup> · Jennifer Joohee Lee<sup>3</sup> · Sung-Hwan Park<sup>3</sup>

Received: 6 May 2018 / Revised: 17 July 2018 / Accepted: 14 August 2018 / Published online: 17 September 2018  
© European Society of Radiology 2018

## Abstract

**Objectives** To determine the incremental value of non-contrast CT (NCCT) on dual-energy CT (DECT) in symptomatic first metatarsophalangeal (MTP) joints in early gout.

**Methods** One hundred and fifteen painful joints were consecutively enrolled and gout was diagnosed based on the 2015 EULAR/ACR criteria and/or arthrocentesis. Two readers independently evaluated DECT alone and combined NCCT and DECT (NCCT+DECT) based on four semiquantitative scales. Sensitivities and specificities were compared using McNemar's test. AUC was compared.

**Results** Of the 115 joints, 72 were defined as an early gout group and 43 as a gout-negative group after exclusion. The sensitivity and specificity for the early gout group on DECT alone were as followed: reader 1 – 52.8% and 100.0% and reader 2 – 51.4% and 100.0%. NCCT+DECT results were as follows: reader 1 – 79.2% and 93.0% and reader 2 – 79.2% and 95.3%. AUC was significantly higher in NCCT+DECT compared to that in DECT alone for the early gout group (0.888 vs. 0.774 for reader 1,  $p = 0.0004$ ; 0.896 vs. 0.816 for reader 2,  $p = 0.0142$ ). The false-negative cases on DECT occurred more frequently with the first-onset gout, and tended to be affected by a longer duration of symptoms in the *post-hoc* analysis.

**Conclusion** The combined analysis of NCCT and DECT improves diagnostic capabilities in symptomatic early gout involving the first MTP joint.

## Key Points

- MSU crystal depositions in early gout may be seen on non-contrast CT, while still being undetectable by DECT.
- Combining non-contrast CT and DECT improves detection of early gout.
- False negatives of DECT are more common than previously reported in cases of first-onset gout.

**Keywords** Gout · Metatarsophalangeal joint · Tomography, x-ray computed · Dual-energy CT · Uric acid

## Abbreviations

ACR	American College of Rheumatology
AUC	Area under receiver operating characteristic curve
CPPD	Calcium pyrophosphate deposition disease

DECT	Dual-energy computed tomography
EULAR	European League Against Rheumatism classification
MSU	Monosodium urate
MTP	Metatarsophalangeal
NCCT	Non-contrast computed tomography
ROC	Receiver operating characteristic

✉ Joon-Yong Jung  
jjdragon112@gmail.com

- <sup>1</sup> Department of Radiology, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul 06591, Republic of Korea
- <sup>2</sup> Present address: Department of Radiology, Dongguk University Ilsan Hospital, Gyeonggi-do 10326, Republic of Korea
- <sup>3</sup> Division of Rheumatology, Department of Internal Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul 06591, Republic of Korea

## Introduction

Gout is an inflammatory arthritis in which monosodium urate (MSU) crystals are deposited in joints, cartilage and soft tissues [1]. The course of gout includes recurrent attacks in intercritical periods since the initial attack and chronic tophaceous gout [2]. The classic presentation of acute gout is 'podagra' or pain

affecting the first metatarsophalangeal (MTP) joint, which is seen in approximately half of the cases [3]. Prompt diagnosis and timely initiation of therapy in its early stage are critical in preventing progressive joint destruction [4, 5].

The diagnosis of gout is based on microscopically detecting negatively birefringent needle-shaped MSU crystals found in synovial fluid. However, aspiration of the joint can be challenging, especially in patients with small amounts of joint fluid. Dual-energy computed tomography (DECT) is an alternative modality for diagnosing gout, showing MSU crystals [6–8]. Due to its high sensitivity and specificity for gout, it has been recently included into the 2015 European League Against Rheumatism classification (EULAR)/American College of Rheumatology (ACR) criteria for gout [9]. However, many studies included chronic tophaceous gout, the diagnosis of which is clinically obvious without DECT [6–8]. More recent studies have excluded chronic tophaceous gout and DECT demonstrated low sensitivities [10–13]. Therefore, the diagnostic value of DECT in early gout requires further assessment.

DECT provides virtually both grey-scale reformation similar to non-contrast images and colour-coded material-specific images. Our hypothesis is that virtual grey-scale reformatted non-contrast CT can complement colour-coded images of DECT in detecting crystal deposition in the early stages of gout. Therefore, this study was designed to investigate the diagnostic benefit of non-contrast CT to complement colour-coded DECT in symptomatic first MTP joints in early gout.

## Material and methods

### Study patients

This study was approved by the institutional review board of our hospital, which allowed us to waive the requirement of patient informed consent for the retrospective design.

Inclusion criteria were as follows: (i) history or presence of clinical manifestation of podagra and (ii) DECT screening of both feet with our DECT protocol for gout between April 2015 and August 2017. For each patient, index joints were limited to the first MTP joints (according to the definition of ‘podagra’). Both affected joints in single patient were classified as individual samples. 208 symptomatic joints were consecutively sampled from 180 patients. Exclusion criteria were established for the purpose of isolating early gout from treated and chronic tophaceous gout as follows: (i) presence of palpable tophi ( $n = 24$ ), (ii) presence of characteristic erosions on radiographs ( $n = 4$ ), and (iii) known gout under urate-lowering therapy ( $n = 65$ ). Therefore, 93 joints were excluded. Final diagnosis of an individual case was based on the 2015 EULAR/ACR criteria by two rheumatologists (S.H.P. and J.H.L. with 25 and 8 years of experience in rheumatology, respectively) and/or synovial fluid aspiration (Fig. 1) [9].

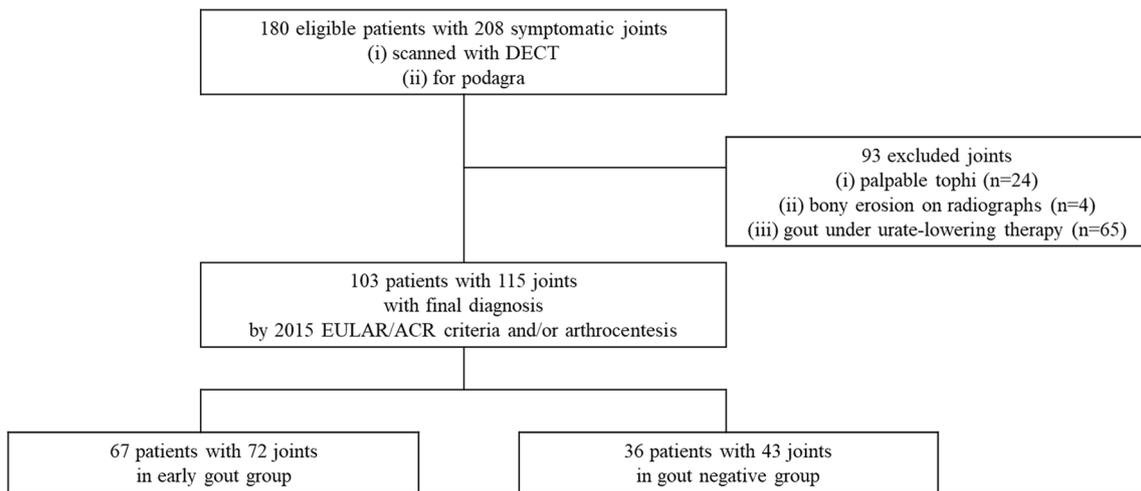
Clinical characteristics related to gout were obtained from the medical records including gender, age, duration of symptoms, serum uric acid level, and the presence of a previous medication history for remission of acute flare such as non-steroidal anti-inflammatory drugs (NSAIDs) and/or colchicine [14].

### DECT examination and image reconstruction

All scans were performed using a first-generation DECT system (Somatom Definition64; Siemens Healthineers) equipped with two x-ray tubes using tube A, 140 kV and 55mA; tube B, 80 kV and 243 mA; pitch, 0.7; gantry rotation time, 1.0 s. Automated attenuation-based tube current modulation was used in all DECT scans with average radiation doses of 10.3 mGy (0.03 mSv) for the foot and ankle. All scans were obtained without an intravenous contrast agent. Both feet were scanned simultaneously in a supine position. Axial images were reconstructed with both dual-energy soft tissue kernel (D30s) and standard soft tissue kernel (B30s) with a slice thickness of 0.75 mm. In addition, we used regular grey-scale reformations from 140 kVp tube energy using kernel B30s for routine diagnostic interpretation on a picture archiving and communication system. We also synthesised grey-scale CT images with weighted energies (40% of 80 kV images mixed with 60% of 140 kV images). These CT images were virtual non-contrast CT images (namely, NCCT), which served as an alternative to conventional polychromatic 120 kV single-energy CT images for detection of bony erosions, hyperdense deposits, and other pathologies [15]. The reconstructed axial images of both tubes with kernel D30s were loaded onto a multi-modality workspace (Gout, Syngo Dual Energy, Siemens Healthineers, Erlangen, Germany). The software employs a material decomposition algorithm to identify uric acid and calcium voxels according to their material-specific dual energy properties. A colour-coded display was used for easy distinction of uric acid shown as green, cortical bone as blue, and medullary bone as pink. The colour-coded materials were overlaid on both multi-planar reformatted cross-sectional and 3D volume rendering images (namely, DECT). Post-processing for generation of material-specific images takes approximately 2 min.

### Image analysis

Two musculoskeletal radiologists (J.Y.J. and S.K.L. with 8 and 2 years of experience in musculoskeletal radiology, respectively) who were blinded to the patient’s clinical data independently reviewed the images by two separate reading sessions: DECT alone, and then NCCT and DECT combination (NCCT+DECT). In the first session, the presence of green colour-coded voxels was analysed with four-scale semiquantitative scores for MSU crystals in the index joint as follows: grade 1, absence of green colour-coded voxels; grade 2,



**Fig. 1** Flowchart summarising the inclusion of patients and joints in the study with the reference of standard from the 2015 EULAR/ACR guideline and/or arthrocentesis

presence of green colour-coded voxels regarded as artifacts (including skin artifacts, metallic artifacts, beam hardening from dense cortical bone, or motion artifacts); grade 3, small sized green colour-coded voxels less than or equal to two consecutive slices; grade 4, definite green colour-coded voxels more than two consecutive slices (Table 1). Cases with blue colour-coded voxels in the index joint were regarded as negative; however, they were recorded separately. Cases with a grade of more than 2 were considered positive. At the second session, NCCT was analysed with four-scale semiquantitative scores for the hyperdense deposits in the painful joint as follows: grade 1, absent hyperdense deposits; grade 2, equivocal density between soft tissue and hyperdensity; grade 3, probable hyperdense deposits; grade 4, definite hyperdense deposits (Table 1 and Fig. 2). DECT was analysed in the same manner as the first session. Cases with a grade of more than 2 were considered positive on both DECT and NCCT. For the combined interpretation of DECT and NCCT, the case was regarded as positive for gout when individual interpretation

of DECT or NCCT were positive unless positive NCCT showed blue colour-coded voxels on DECT.

**Statistical analysis**

The sensitivity, specificity and accuracy of two reading sessions for the early gout group were compared using McNemar’s test. The area under the receiver operating characteristic curve (AUC) based on the four-semiquantitative scale was also compared. Inter-observer reliability was assessed using Cohen’s kappa ( $\kappa$ ). Data were analysed using MedCalc statistical software version 11.5.1.0 (MedCalc Software bvba). *P*-values of less than 0.05 were considered statistically significant for the above analyses.

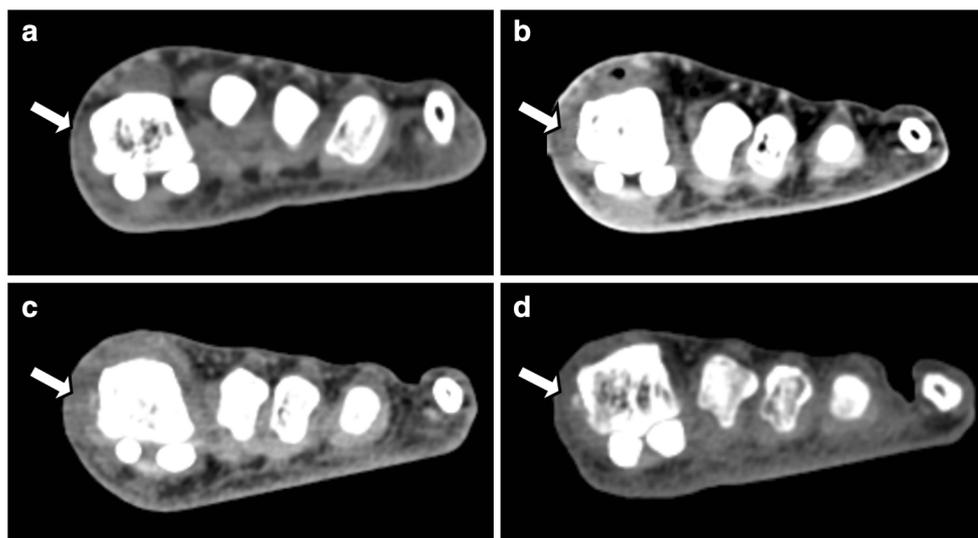
**Retrospective re-review and post hoc analysis**

False-positive and -negative cases were re-reviewed in consensus by the two readers to reveal possible reasons for false

**Table 1** Four-scale semiquantitative scores on dual-energy CT (DECT) and non-contrast CT (NCCT)

4-Scale semiquantitative scores for MSU crystals in index joint on DECT				
	Score 1	Score 2	Score 3	Score 4
Green colour-coded voxels	Absent	Present	Present	Present
If present, size or location		Artefact by skin, metal, dense cortical bone, motion, etc.	Focal, less than or equal to 2 consecutive slices	Definite, more than 2 consecutive slices
4-Scale semiquantitative scores for hyperdense deposits in index joint on NCCT				
	Score 1	Score 2	Score 3	Score 4
Hyperdense deposits	Absent	Present	Present	Present
If present, density		Density more than or equal to soft tissue	Probable hyperdensity more than soft tissue	Definite hyperdensity similar to calcification

**Fig. 2** Analysis of non-contrast CT. **a** ‘Grade 1’ is defined as absence of hyperdense deposits (arrow) in a painful left first metatarsophalangeal (MTP) joint. **b** ‘Grade 2’ is defined as equivocal showing density between soft tissue and hyperdensity (arrow) in a painful left first MTP joint. **c** ‘Grade 3’ is defined as probable hyperdense deposits (arrow) in a painful left first MTP joint. **d** ‘Grade 4’ is defined as definite hyperdense deposits (arrow) in a painful left first MTP joint



interpretations. Separately, all cases immediately after arthrocentesis were retrospectively reviewed to estimate the influence of arthrocentesis on the imaging analyses. Additionally, clinical and laboratory parameters including first-onset gout, symptom duration, serum uric acid level and the number of positive MSU crystals on arthrocentesis were retrospectively compared between the true-positive and false-negative cases within the early gout group. This was conducted to explore the possible association of clinical features and ability to detect the deposition of MSU crystals on DECT. First-onset gout was defined when the patients who had experienced the acute gout attack for the first time visited our clinic prior to receiving any medication.

## Results

### Patient characteristics

A total of 115 joints from 103 patients (mean age,  $50.9 \pm 13.6$  years; female,  $n = 6$ ) were finally enrolled in the study. Fifty-two patients fulfilled the 2015 EULAR/ACR criteria for gout. Forty patients underwent joint aspiration. Among them, MSU crystals were detected in 17 patients, and none were found in five patients, while aspiration failed in 18 patients. Seventy-two joints in 67 patients were categorised as gout positive, the early gout group, while 43 joints in 36 patients were categorised as gout negative. Among the early gout group, 49 joints out of 45 patients were first-onset (49/72, 68.1%). The gout-negative group consisted of patients with osteoarthritis ( $n = 13$ ), calcium pyrophosphate deposition disease (CPPD,  $n = 4$ ), cellulitis ( $n = 4$ ), inflammatory arthritis ( $n = 3$ ), and medication-induced arthralgia ( $n = 2$ ). Seventeen symptomatic first MTP joints with borderline hyperuricemia were classified as the gout-negative group based on the 2015

EULAR/ACR criteria [9]. Among the borderline hyperuricemia patients, two patients underwent joint aspiration with inconclusive results. Other patients showed ambiguous foot pain, so arthrocentesis could not be performed. All of these patients no longer visited the outpatient clinic. There were significant differences between gender, symptom duration and serum uric acid levels between the early gout group and the gout-negative group, except for age (Table 2).

### Sensitivity, specificity and accuracy for early gout

The sensitivity and accuracy of NCCT+DECT were significantly higher than those of DECT alone for the early gout group for both readers. However, there was no significant difference in the specificity between DECT alone and NCCT+DECT for the early gout group for both readers (Table 3).

### ROC analysis

There was a significantly higher AUC in NCCT+DECT compared to DECT alone to diagnose early gout group (0.888 vs. 0.774 for reader 1,  $p = 0.0004$ ; 0.896 vs. 0.816 for reader 2,  $p = 0.0142$ ).

### Interobserver agreement

Interobserver agreement between the two readers was substantial in two image sets as follows: 0.950 in DECT alone and 0.922 in NCCT+DECT, respectively.

### Retrospective re-review and post hoc analysis

There were 34 and 35 false-negative cases on DECT alone for readers 1 and 2, respectively (Fig. 3). However, there were no

**Table 2** Patient demographics

	Early gout group (n = 72)	Gout-negative group (n = 43)	p-value
Male, n (%)	71 (98.6)	37 (86.0)	0.006*
Age, mean (SD), y	49.8 (13.2)	52.7 (14.2)	0.279
Symptom duration, median (range), week	2.9 (1–4.3)	8.6 (1.7–25.7)	0.019*
Serum urate, mean (SD), mg/dl	7.5 (1.4)	5.9 (1.9)	< 0.0001*
Synovial aspiration, n (positive MSU crystal, n)	35 (18)	8 (0)	

MSU monosodium urate

\*Indicates significance

false-positive cases on DECT alone for either reader. In contrast, there were 15 false-negative cases for both readers as well as three and two false-positive cases on NCCT+DECT for readers 1 and 2, respectively. Among the false-positive cases on NCCT+DECT, two cases were confirmed as CPPD and one case had osteoarthritis at the joint.

Of the 21 cases who had DECT within a week after arthrocentesis, one case was classified as ‘grade 1’ on NCCT+DECT and ‘grade 0’ on DECT alone by both readers, which was classified into the gout-negative group. The case was also negative arthrocentesis. Four cases and three cases were classified as ‘grade 2’ on NCCT+DECT and ‘grade 1’ on DECT alone by reader 1 and reader 2, respectively, and finally only one case was gout negative (borderline hyperuricemia). Joint aspirations failed in all of them. Sixty cases and 17 cases were classified as ‘grade 3 or 4’ on NCCT+DECT by reader 1 and reader 2, respectively, which were all classified into the early gout group. Among them, ten cases were coded as green on DECT in index joint. MSU crystals were found in ten cases, and aspirations failed in the other cases.

Clinical characteristics between the true-positive and false-negative cases for the early gout group are summarised in Table 4. The p-value in *post hoc* analysis was not adjusted for multiple comparison, and  $p < 0.05$  was considered statistically significant for the aforementioned analyses. False-negative cases on DECT alone occurred more frequently in first-onset gout ( $p <$

0.001 for both readers, Fig. 4). However, false-negative cases on NCCT+DECT were not associated with first-onset gout ( $p = 0.027$  for reader 1 and 0.121 for reader 2). A longer duration of symptoms tended to be associated with false-negative cases on DECT alone ( $p = 0.050$  for reader 1, Fig. 4). The number of positive synovial fluid aspirations among arthrocentesis cases and the serum uric acid level showed no significant differences between the true-positive and false-negative cases on both DECT alone and NCCT+DECT.

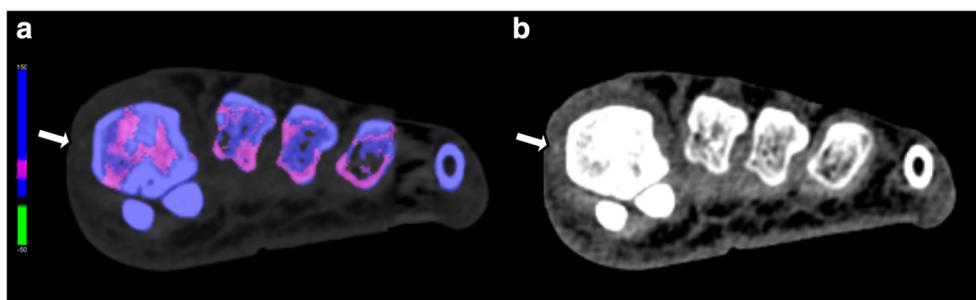
### Discussion

This study showed that the sensitivity of DECT alone among the early gout group was lower than those of previous studies [9, 16]. Presumably, the amount or concentration of MSU crystals in the patient population of our study was below the detection limits of DECT. This is based on previous studies showing that DECT could only detect MSU crystals with a minimum diameter of 2 mm [17] and a volume concentration of more than 15–20% [18, 19]. MSU crystal deposition in the early stage of gout was influenced by the relatively vigorous active chemotaxis and phagocytosis of leukocytes [17, 18]. These chemical compositions might lead to detrimental effects on detecting MSU crystals by DECT. Jia et al [13] found different sensitivities at different disease durations of

**Table 3** Diagnostic performance of dual-energy CT (DECT) alone and non-contrast CT (NCCT)+DECT per joint for diagnosis of early gout

	Reader 1		Reader 2	
	DECT alone	NCCT+DECT	DECT alone	NCCT+DECT
Sensitivity, %	52.8 (38/72)	79.2 (57/72)	51.4 (37/72)	79.2 (57/72)
p-value		< 0.0001*		< 0.0001*
Specificity, %	100.0 (43/43)	93.0 (40/43)	100.0 (43/43)	95.3 (41/43)
p-value		0.2500		0.5000
Accuracy, %	70.4 (81/115)	84.3 (97/115)	69.6 (80/115)	85.2 (98/115)
p-value		0.0009*		0.0001*

\*Indicates significance



**Fig. 3** False-negative case of dual-energy CT (DECT) alone on the left first metatarsophalangeal (MTP) joint. A 62-year-old man presented recurrent pain at the left first MTP joint for 6 months. This patient visited outpatient clinics for the first time due to metatarsalgia. Synovial fluid aspiration identified MSU crystal. Serum uric acid level was 7.3 mg/dL. **a**

DECT shows no areas of green pixelation in the left first MTP joint (arrow). **b** Non-contrast CT (NCCT) shows hyperdense deposits with soft tissue density in the left first MTP joint (arrow). Both readers graded as ‘grade 1’ for DECT alone and ‘grade 3’ for NCCT+DECT. This correlates well with the results of joint aspiration

35.71%, 61.54% and 92.86% in the first onset, less than 24 months and more than 24 months groups, respectively. Their results suggest that the diagnostic value of DECT is limited during the early stages of gout. Our study also showed similar results in the early gout group when we analysed DECT alone.

Ultrasound is a first-line imaging modality for gouty arthritis despite the limited sensitivity of crystal deposition in the extra-articular spaces [1, 20]. Advanced techniques such as shear wave elastography can compensate for the weakness of the ultrasound, as shown in a recent paper [21]. The presence of MSU crystals along the articular cartilage, the so-called ‘double contour sign’, is also a useful sign for early detection of gout [22, 23], and has been included in the 2015 EULAR/ACR Gout Classification Criteria [9]. We speculated that hyperdense deposition on NCCT can be used as an early sign of acute gout flare similar to the ‘double contour sign’ in ultrasound. NCCT may be able to visualise the hyperdense MSU deposits, which are below the detection threshold of DECT. Hyperdense deposits on NCCT might be useful prior to MSU crystals being detected by DECT in

the context that the role of imaging is to detect the disease at its preclinical stage to prevent joint damage and associated risks in gout. However, it has been noted that the sole use of NCCT has limited specificity for gout because hyperdense deposits can be found in other crystal arthropathies like CPPD [24]. In some of these cases, blue colour coding in DECT can be a complementary feature to differentiate CPPD from MSU crystal deposition if the colours appear. Therefore, combined analyses of DECT and NCCT were carried out to maintain the ability of DECT to differentiate MSU crystals from CPPD in our study. Despite the fact that the hyperdense deposits are not always colour-coded on DECT, the combined evaluation of NCCT and DECT achieved improved sensitivity without a significant decrease in the specificity in our study.

It is important to note that the 21 cases in which DECT was performed within a week after the arthrocentesis were not excluded. Due to this, there was concern of post-procedural haemorrhage, which may complicate the NCCT interpretation. In the clinical context, DECT is frequently used as an adjunct to microscopic fluid analysis particularly where

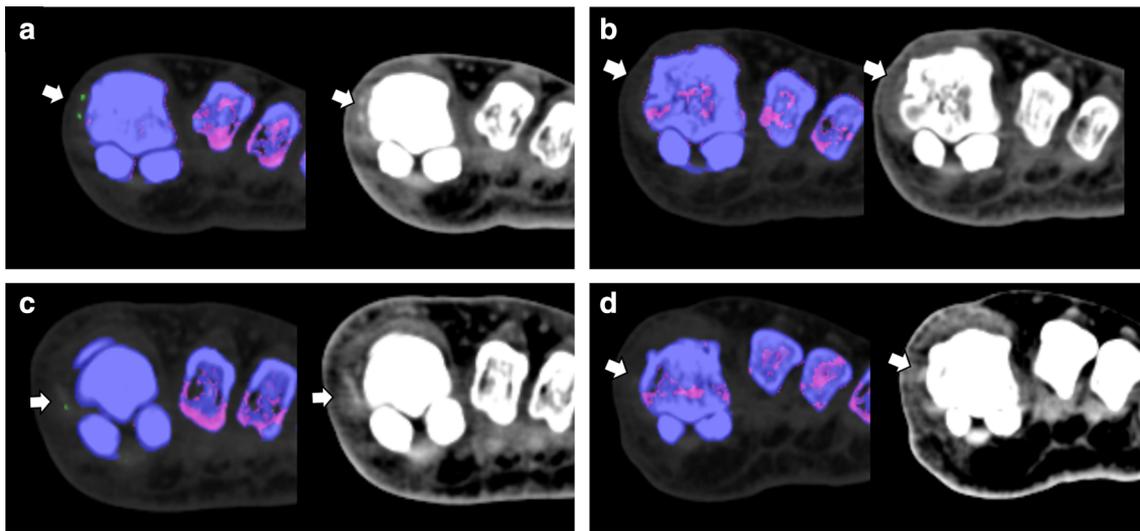
**Table 4** Difference in clinical characteristics between true-positive (TP) and false-negative (FN) cases for early gout

Reader 1	DECT alone		<i>p</i> -value	NCCT+DECT		<i>p</i> -value
	TP (n = 38)	FN (n = 34)		TP (n = 57)	FN (n = 15)	
Gout						
First-onset gout, n (%)	18 (47.4)	31 (91.2)	< 0.001 <sup>#</sup>	35 (61.4)	14 (93.3)	0.027
Symptom duration, median (range), week	2 (1–4.3)	4.3 (2–12.9)	0.050	2.9 (1–8.6)	3 (1–8.6)	0.880
Serum urate, mean (SD), mg/dl	7.6 (1.5)	7.5 (1.3)	0.818	7.6 (1.3)	7.4 (1.6)	0.577
Positive MSU on arthrocentesis, n	7/35	12/35	0.262	15/35	4/35	0.882
Reader 2	DECT alone		<i>p</i> -value	NCCT+DECT		<i>p</i> -value
	TP (n = 37)	FN (n = 35)		TP (n = 57)	FN (n = 15)	
Gout						
First-onset gout, n (%)	18 (48.6)	31 (88.6)	< 0.001*	36 (63.2)	13 (86.7)	0.121
Symptom duration, median (range), week	2 (1–4.3)	4.3 (2–12.9)	0.069	2.1 (1–8.6)	3 (1–8.6)	0.847
Serum urate, mean (SD), mg/dl	7.6 (1.5)	7.5 (1.3)	0.762	7.6 (1.3)	7.3 (1.6)	0.508
Positive MSU on arthrocentesis, n	6/35	13/35	0.129	16/35	3/35	0.490

Comparison was done using the Mann-Whitney U-test and Pearson’s chi-square test. *P*-value from Fisher’s exact test

DECT dual energy CT, NCCT non-contrast CT, MSU monosodium urate

\*Indicates statistical significance



**Fig. 4** Difference in clinical characteristics between true positive (TP) and false negative (FN) cases for early gout. **a** A 40-year-old man presented with metatarsalgia for 14 days (urate: 7.0 mg/dl, arthrocentesis: not performed [N/P]). This patient had taken intermittent medication to control the acute flare and this case was true positive (TP) for dual-energy CT (DECT) (arrows). **b** A 59-year-old man presented with metatarsalgia for 14 days (urate: 8.3 mg/dl, MSU [+]). This patient was first-onset gout and

this case was false-negative (FN) for DECT (arrows). **c** A 40-year-old man presented with metatarsalgia for the first time (urate: 4.6 mg/dl, MSU [+]). The symptom onset was 7 days ago and this case was TP for DECT (arrows). **d** A 39-year-old man presented with metatarsalgia for the first time (urate: 7.9 mg/dl, arthrocentesis: N/P). The symptom onset was 30 days ago and this case was FN for DECT (arrows)

arthrocentesis failed. The retrospective analysis on the arthrocentesis cases demonstrated that there were no false-positive cases in patients who received arthrocentesis recently. Contrary to our concern that recent arthrocentesis would increase the number of false positives, only false-negative cases for the early gout group on NCCT occurred in three patients. Therefore, it is not necessary for DECT to be postponed in patients who recently received arthrocentesis.

The false-negative cases on DECT alone were associated with first-onset gout and tended to be affected by a longer duration of symptoms in the *post hoc* analysis. A previous study suggested that the quantity of MSU crystal deposition related to the duration of the disease [25], corresponding to our result that first-onset gout increased the occurrence of false-negative cases. In contrast, the duration of symptoms tended to be shorter among the true-positive cases than the false-negative cases using DECT alone. This is counterintuitive as the longer duration of disease might lead to a denser deposition of MSU crystals. However, there are earlier studies reporting that the MSU crystals would be resolved with time by the combined action of macrophages and local tissue pH change [26, 27]. Therefore, it is assumed that the shorter term of attack with the DECT exam may be associated with maintaining undissolved MSU crystals.

There were several limitations to our study. There was selection bias because of the retrospective nature of the study where the clinicians did not refer all patients with first metatarsalgia for DECT consecutively. Second, the number of cases confirmed by arthrocentesis is relatively small. Alternatively, we utilised the 2015 EURAL/ACR criteria for diagnosing gout in our study [9,

28]. The data were not analysed on a per-patient basis and thus 12 patients included both feet. However, the analysis of one foot did not significantly influence the other foot as each was independently interpreted for gout. Third, there was no use of the second-generation of DECT and the protocol using a Tin filtered 140 kVp tube in the second-generation DECT may show a different diagnostic performance. Fourth, we used virtual NCCT synthesised with the composition ratio of 0.4. Some studies have shown that a mixed image is similar to conventional CT images [15, 29, 30], while others revealed that a monochromatic 80 keV image has the highest contrast-to-noise ratio for lesion detection [31, 32]. The optimised protocol of the virtual NCCT needs to be further studied in comparison to the conventional CT images. Lastly, this study was carried out within a single institution. The diagnostic and therapeutic algorithm may vary at other institutions. However, the management of patients with suspected gout in our institution was performed using the current guidelines [33, 34].

Previous studies regarding the diagnostic performance of DECT for gout explored patients with gout who had a long-standing and/or tophaceous stage of the disease [6–8]. The diagnostic performance of DECT in patients with long-standing tophaceous gout cannot be generalised to the entire disease spectrum including early and non-tophaceous gout [11]. Owing to the relatively low sensitivity of DECT during the early stages or non-tophaceous gout, a supplementary exam should be considered. Based on the results of our study, it is strongly suggested that the addition of NCCT to DECT could improve the diagnostic accuracy in symptomatic patients with early gout. In addition, the hyperdense deposits on NCCT without colour-coding on

DECT might be regarded as MSU deposits in patients with suspected gout.

In conclusion, the combination of NCCT and DECT improved sensitivity in symptomatic patients with early gout.

**Funding** The authors state that this work has not received any funding.

### Compliance with ethical standards

**Guarantor** The scientific guarantor of this publication is Joon-Yong Jung.

**Conflict of interest** The authors of this manuscript declare no relationships with any companies whose products or services may be related to the subject matter of the article.

**Statistics and biometry** No complex statistical methods were necessary for this paper.

**Informed consent** Written informed consent was waived by the Institutional Review Board.

**Ethical approval** Institutional Review Board approval was obtained.

### Methodology

- Retrospective
- Diagnostic or prognostic study
- Performed at one institution

### References

1. Girish G, Melville DM, Kaeley GS et al (2013) Imaging appearances in gout. *Arthritis*. <https://doi.org/10.1155/2013/673401>
2. Dalbeth N, Pool B, Gamble GD et al (2010) Cellular characterization of the gouty tophus: a quantitative analysis. *Arthritis Rheum* 62:1549–1556
3. Monu JU, Pope TL Jr (2004) Gout: a clinical and radiologic review. *Radiol Clin North Am* 42:169–184
4. Terkeltaub R (2010) Update on gout: new therapeutic strategies and options. *Nat Rev Rheumatol* 6:30–38
5. Schlesinger N, Dalbeth N, Perez-Ruiz F (2009) Gout—what are the treatment options? *Expert Opin Pharmacother* 10:1319–1328
6. Choi HK, Al-Arfaj AM, Eftekhari A et al (2009) Dual energy computed tomography in tophaceous gout. *Ann Rheum Dis* 68:1609–1612
7. Glazebrook KN, Guimarães LS, Murthy NS et al (2011) Identification of intraarticular and periarticular uric acid crystals with dual-energy CT: initial evaluation. *Radiology* 261:516–524
8. Choi HK, Burns LC, Shojania K et al (2012) Dual energy CT in gout: a prospective validation study. *Ann Rheum Dis* 71:1466–1471
9. Neogi T, Jansen TL, Dalbeth N et al (2015) 2015 Gout Classification Criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis Rheumatol* 67:2557–2568
10. Baer AN, Kurano T, Thakur UJ et al (2016) Dual-energy computed tomography has limited sensitivity for non-tophaceous gout: a comparison study with tophaceous gout. *BMC Musculoskelet Disord*. <https://doi.org/10.1186/s12891-016-0943-9>
11. Bongartz T, Glazebrook KN, Kavros SJ et al (2015) Dual-energy CT for the diagnosis of gout: an accuracy and diagnostic yield study. *Ann Rheum Dis* 74:1072–1077
12. Dalbeth N, House ME, Aati O et al (2015) Urate crystal deposition in asymptomatic hyperuricaemia and symptomatic gout: a dual energy CT study. *Ann Rheum Dis* 74:908–911
13. Jia E, Zhu J, Huang W, Chen X, Li J (2017) Dual-energy computed tomography has limited diagnostic sensitivity for short-term gout. *Clin Rheumatol*. <https://doi.org/10.1007/s10067-017-3753-z>
14. Finkenstaedt T, Manoliou A, Toniolo M et al (2016) Gouty arthritis: the diagnostic and therapeutic impact of dual-energy CT. *Eur Radiol* 26:3989–3999
15. Werncke T, Meyer BC, Wacker FK, von Falck C (2014) Virtual single-source computed tomography using dual-source acquisition: a new technique for the dose-neutral intraindividual comparison of different scan protocols. *Invest Radiol* 49:742–748
16. Taylor WJ, Fransen J, Jansen TL et al (2015) Study for updated gout classification criteria: identification of features to classify gout. *Arthritis Care Res (Hoboken)* 67:1304–1315
17. Glazebrook KN, Kakar S, Ida CM, Laurini JA, Moder KG, Leng S (2012) False-negative dual-energy computed tomography in a patient with acute gout. *J Clin Rheumatol* 18:138–141
18. Melzer R, Pauli C, Treumann T, Krauss B (2014) Gout tophus detection—a comparison of dual-energy CT (DECT) and histology. *Semin Arthritis Rheum* 43:662–665
19. Diekhoff T, Kiefer T, Stroux A et al (2015) Detection and characterization of crystal suspensions using single-source dual-energy computed tomography: a phantom model of crystal arthropathies. *Invest Radiol* 50:255–260
20. Naredo E, Uson J, Jiménez-Palop M et al (2014) Ultrasound-detected musculoskeletal urate crystal deposition: which joints and what findings should be assessed for diagnosing gout? *Ann Rheum Dis* 73:1522–1528
21. Wang Q, Guo LH, Li XL et al (2018) Differentiating the acute phase of gout from the intercritical phase with ultrasound and quantitative shear wave elastography. *Eur Radiol*. <https://doi.org/10.1007/s00330-018-5529-5>
22. Zhu L, Zheng S, Wang W, Zhou Q, Wu H (2017) Combining hyperechoic aggregates and the double-contour sign increases the sensitivity of sonography for detection of monosodium urate deposits in gout. *J Ultrasound Med* 36:935–940
23. Klauser AS, Halpern EJ, Strobl S et al (2018) Gout of hand and wrist: the value of US as compared with DECT. *Eur Radiol*. <https://doi.org/10.1007/s00330-018-5363-9>
24. Rosenthal AK, Ryan LM (2016) Calcium pyrophosphate deposition disease. *N Engl J Med* 374:2575–2584
25. Wu H, Xue J, Ye L, Zhou Q, Shi D, Xu R (2014) The application of dual-energy computed tomography in the diagnosis of acute gouty arthritis. *Clin Rheumatol* 33:975–979
26. Sun Y, Ma L, Zhou Y et al (2015) Features of urate deposition in patients with gouty arthritis of the foot using dual-energy computed tomography. *Int J Rheum Dis* 18:560–567
27. Hu HJ, Liao MY, Xu LY (2015) Clinical utility of dual-energy CT for gout diagnosis. *Clin Imaging* 39:880–885
28. Wallace SL, Robinson H, Masi AT, Decker JL, McCarty DJ, Yü TF (1977) Preliminary criteria for the classification of the acute arthritis of primary gout. *Arthritis Rheum* 20:895–900
29. Yu L, Christner JA, Leng S, Wang J, Fletcher JG, McCollough CH (2011) Virtual monochromatic imaging in dual-source dual-energy CT: radiation dose and image quality. *Med Phys* 38:6371–6379
30. Yu L, Primak AN, Liu X, McCollough CH (2009) Image quality optimization and evaluation of linearly mixed images in dual-source, dual-energy CT. *Med Phys* 36:1019–1024
31. Mileto A, Nelson RC, Samei E et al (2014) Dual-energy MDCT in hypervascular liver tumors: effect of body size on selection of the

- optimal monochromatic energy level. *AJR Am J Roentgenol* 203:1257–1264
32. Grant KL, Flohr TG, Krauss B, Sedlmair M, Thomas C, Schmidt B (2014) Assessment of an advanced image-based technique to calculate virtual monoenergetic computed tomographic images from a dual-energy examination to improve contrast-to-noise ratio in examinations using iodinated contrast media. *Invest Radiol* 49:586–592
  33. Khanna D, Fitzgerald JD, Khanna PP et al (2012) 2012 American College of Rheumatology guidelines for management of gout. Part 1: systematic nonpharmacologic and pharmacologic therapeutic approaches to hyperuricemia. *Arthritis Care Res (Hoboken)* 64:1431–1446
  34. Khanna D, Khanna PP, Fitzgerald JD et al (2012) 2012 American College of Rheumatology guidelines for management of gout. Part 2: therapy and antiinflammatory prophylaxis of acute gouty arthritis. *Arthritis Care Res (Hoboken)* 64:1447–1461