Hong Kong J Radiol. 2017;20:98-102 | DOI: 10.12809/hkjr1716838

REVIEW ARTICLE

CME

Diagnosing Gout with Dual-energy Computed Tomography: Principles, Diagnostic Performance, and Clinical Application

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ABSTRACT

Gout is an inflammatory response to deposition of monosodium urate (MSU) crystals in soft tissues and joints, and is the most common form of inflammatory arthritis in adults. Dual-energy computed tomography (CT) is a non-invasive tool for diagnosis, volume quantification of MSU crystals, and monitoring of treatment response. Dual-energy CT is included in the 2015 American College of Rheumatology / European League Against Rheumatism gout classification criteria. Although dual-energy CT has lower sensitivity when restricted to individual crystal-proven gouty joints in non-tophaceous disease, its diagnostic performance is good to excellent for tophaceous gout.

Key Words: *Arthritis, gouty; Dual-energy computed tomography; Gout; Uric acid*

中文摘要

雙能電腦斷層掃描診斷痛風：原理、診斷性能和臨床應用

曾佩琪、袁銘強

痛風是對軟組織和關節沉積尿酸鈉（MSU）的炎症反應，是成人中最常見的炎性關節炎形式。雙能電腦斷層掃描（CT）是非侵入性診斷工具並用於測量MSU結晶體積定量和監測治療反應。它被列入2015年美國風濕病學院／歐洲防風濕病聯盟痛風分類標準。雖然雙能CT在偵測個別結晶痛風關節的非痛風石疾病的靈敏度較低，但對痛風石有良好診斷性能。

INTRODUCTION

Gout is an inflammatory response to deposition of monosodium urate (MSU) crystals in soft tissues and joints, and is the most common form of inflammatory arthritis in adults. The incidence of gout has increased in many parts of the world over the past 50 years.[1] The three stages of the natural history of gout are acute gouty arthritis, intercritical period, and chronic articular and tophaceous gout. Initial presentation involves painful episodes of peripheral joint synovitis, followed by joint damage and deformity, chronic usage-related pain, and subcutaneous tophus deposition. Presentation varies widely; some patients present with chronic gouty arthritis as the first manifestation.

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Submitted: 30 Dec 2016; Accepted: 20 Mar 2017.

Disclosure of Conflicts of Interest: All authors have disclosed no conflicts of interest.

DIAGNOSIS

The gold standard of diagnosing gout is the presence of MSU crystals in fluid aspirated from a joint, bursa, or tophus on polarised light microscopy. MSU crystals are typically larger within tophi (up to 40 μm in length) and are densely packed into bundles.[2] The yield is highest during an acute gout attack, whereas no MSU crystals may be detected during an intercritical period. Synovial fluid aspiration and polarising microscopy may not be sensitive enough for diagnosis and are not commonly used in primary or acute care settings.[3]

According to the 2015 American College of Rheumatology / European League Against Rheumatism (ACR / EULAR) gout classification criteria, the diagnosis of gout can be made without a concurrent acute symptomatic episode. Dual-energy computed tomography (CT) is newly added as a diagnostic tool. The entry criterion for gout is the presence of at least one episode of swelling, pain, or tenderness in a peripheral joint or bursa. The sufficient criterion for gout is the presence of MSU crystals in a symptomatic joint, bursa, or tophus. In the ACR / EULAR gout classification criteria, there are four clinical criteria, two laboratory criteria, and two imaging criteria, with a maximum score of 23. A score of ≥8 indicates a diagnosis of gout. The clinical criteria include the pattern / site of joint and bursa involvement during a symptomatic episode (range, 0 to +2), clinical characteristic of symptomatic episode (range, 0 to +3), time course of episode (range, 0 to +2), and clinical evidence of tophus (range, 0 or +4). The laboratory criteria include serum urate concentration (range, -4 to +4), and synovial fluid analysis of a symptomatic joint or bursa (negative, -2; not done, 0). The imaging criteria include MSU deposition in a symptomatic joint and bursa on dual-energy CT or B-mode ultrasonography (double-contour sign on articular cartilage) [negative, 0; positive, +4], and the presence of at least one gout-related joint erosion of the feet or hands on radiography characterised by cortical osteolysis with sclerotic margin and overhanging edge (negative, 0; positive, +4). The presence of both imaging criteria constitutes a score of 8 and meets a gout diagnosis.[4]

DUAL-ENERGY COMPUTED TOMOGRAPHY

In dual-energy CT, dual X-ray tubes or a single X-ray tube with different peak kilovoltages are used to simultaneously acquire two sets of images. The ability of dual-energy CT to discriminate between two materials depends on the difference between each material's characteristic CT number ratio (CT number of low-energy image to CT number of high-energy image). The difference between the CT number ratios of any two materials is determined by the separation between the low- and high-energy spectra and the effective atomic numbers of the evaluated materials. The larger the spectral separation, the better the two materials can be discriminated.[5,6] Dual-energy CT can be used to differentiate uric acid (gouty urate crystals) from calcium (bone or dystrophic calcification) in musculoskeletal tissue (Figure 1).[5] Two- and three-dimensional colour maps can be co-registered and fused with corresponding CT images for a simultaneous display of anatomy and localisation of urate deposits (Figure 2).

In a case-control study of 20 patients with tophaceous gout and 10 controls with other arthritic conditions, dual-energy CT achieved 100% sensitivity and specificity.[6] In a study of 31 patients with suspected gout who underwent joint aspiration and dual-energy CT, dual-energy CT achieved 100% sensitivity and 79% to 89% specificity.[7] In a study of 40 patients with crystal-proven gout (17 tophaceous and 23 non-tophaceous) and 40 controls with other arthritic conditions, dual-energy CT achieved 78% sensitivity and 93% specificity.[8] Diagnosing gout is more challenging in patients with non-tophaceous gout. In a study of 11 patients with crystal-proven non-tophaceous gout and 10 with tophaceous gout, dual-energy CT detected MSU deposits in one or more joint area in seven (64%) patients with non-tophaceous gout but only in three (25%) of 12 joints confirmed by aspiration, whereas MSU deposits were detected in all 10 patients with tophaceous gout.[9]

In addition, dual-energy CT can be used to quantify MSU deposition within tophi, with intra-reader and inter-reader intraclass correlation coefficients of 1.0 (for volume measurement) and bias estimates of 0.01 cm^3; reliability of dual-energy CT did not vary with different sites or sizes of tophi.[8] False-negative results can be due to less-dense tophi with lower crystal concentrations, small size of tophi / crystals (<2 mm), or technical parameters.[10-12] Although in one study dual-energy CT demonstrated the presence of intra-osseous gout,[13] a false-negative result may occur when diagnosing intra-osseous gout with pathological fracture.[14] This is postulated to be related to the abundant background calcium in the trabecular bone, and the drop of CT

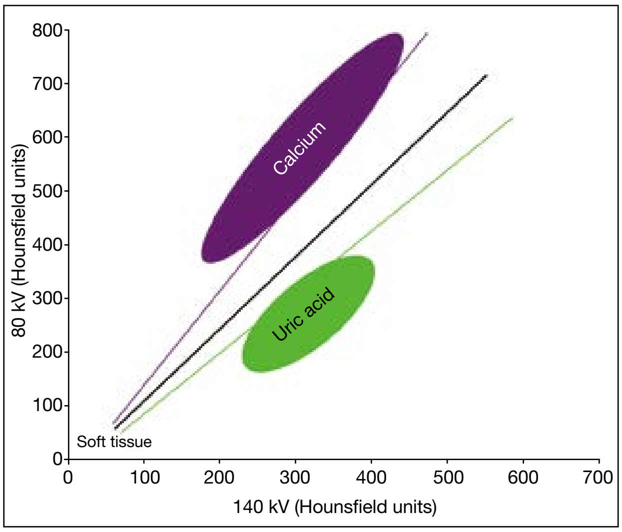

Figure 1. This algorithm separates the chemical composition of compounds based on their differential attenuation of the 80 kV and 140 kV X-ray beams. Uric acid (with a low atomic weight number), calcium (with a high atomic weight number), and soft tissue can be accurately differentiated from one another based on their differential absorption levels of the X-ray beams.

value of uric acid is cancelled out by the rise in CT value of calcium within the same voxel.[14] In such clinical context, a further postulation is made about the overall effect of fracture healing on the intra-osseous gout and the software performance of gout algorithm in dual-energy CT.[15] False-positive results may appear in tissues with a similar index value to MSU deposits (such as keratin found around nail beds [Figure 3] and in the skin), in joints with severe osteoarthritis, in regions of beam hardening and metal artefacts, or in the shape of single pixels scattered around the image, probably related to image noise.[7,16]

The most common presentation of gouty arthritis is acute painful monoarthropathy of the distal appendicular skeleton in middle-aged men and post-menopausal women. Gout with atypical presentation may be mistaken for malignancy or infection. Magnetic resonance imaging signal pattern of gouty tophus is non-specific; dual-energy CT can more readily identify MSU crystals (Figure 4). Dual-energy CT can also more readily identify spinal MSU crystal deposition. Spinal gout is rare and has various presentations from back pain to nerve or spinal compression and can develop in a short time or over many years. Most such patients have a history of gout or hyperuricaemia, but spinal gout can also be the first manifestation. Most imaging tools are non-specific, cannot exclude other causes

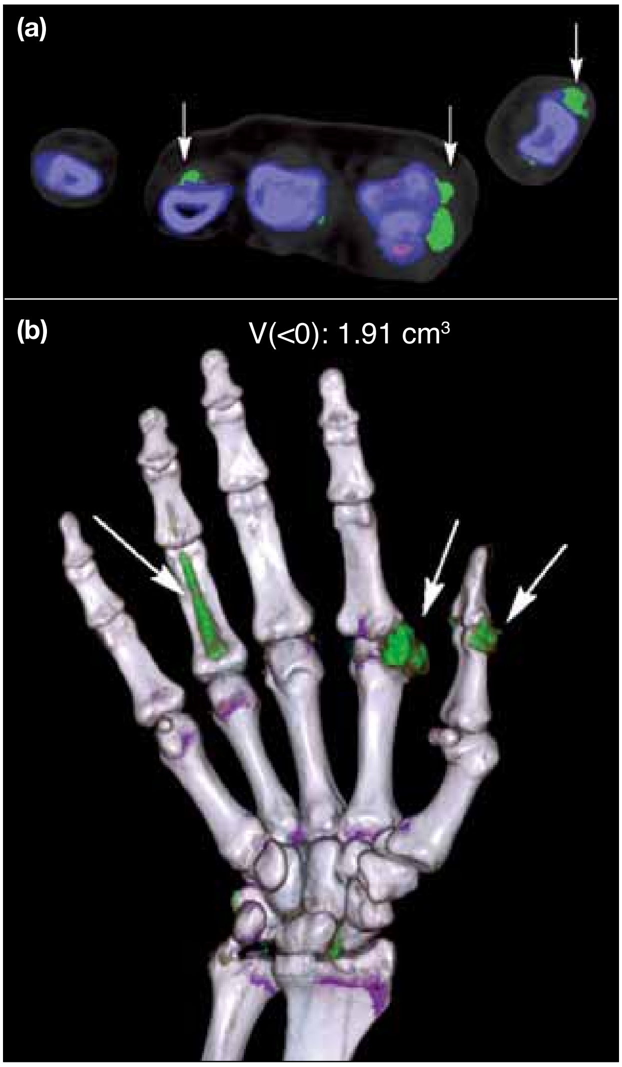

Figure 2. (a) Two-dimensional axial and (b) three-dimensional fusion dual-energy computed tomography of the hand showing periarticular monosodium urate deposits at the interphalangeal joint of the right thumb, the metacarpophalangeal joint of the right index finger, and the flexor tendons of the right ring finger (arrows). All monosodium urate deposits amount to a volume of 1.91 cm^3.

Figure 3. Dual-energy computed tomography of the foot showing an artefact at the nail bed (arrow).

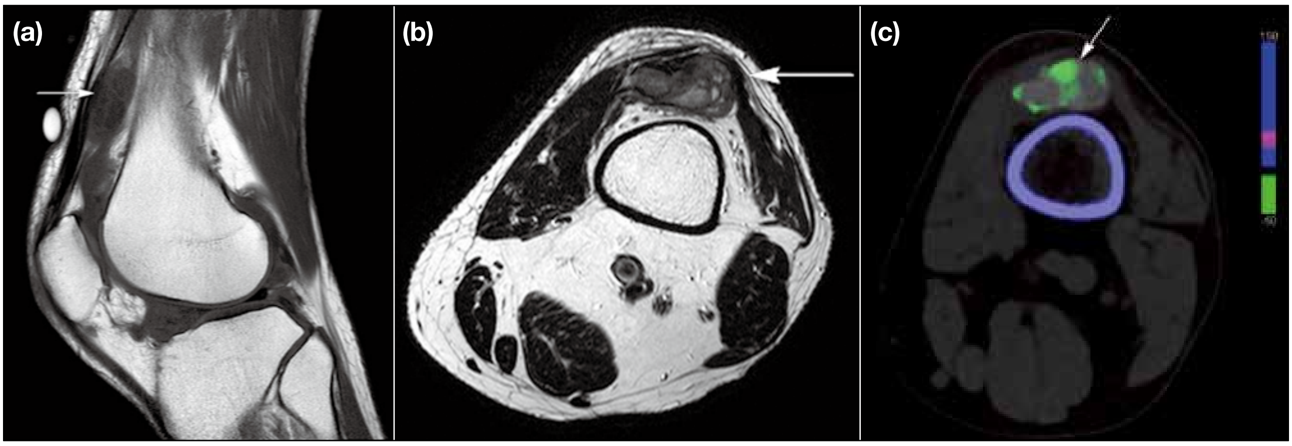

Figure 4. (a) Sagittal T1-weighted and (b) axial T2-weighted magnetic resonance images of the knee joint showing a lobulated homogeneously T1-hypointense and heterogeneously T2-hyperintense mass involving the quadriceps tendon (arrows). (c) Axial dual-energy computed tomography showing the mass containing monosodium urate deposits (arrow).

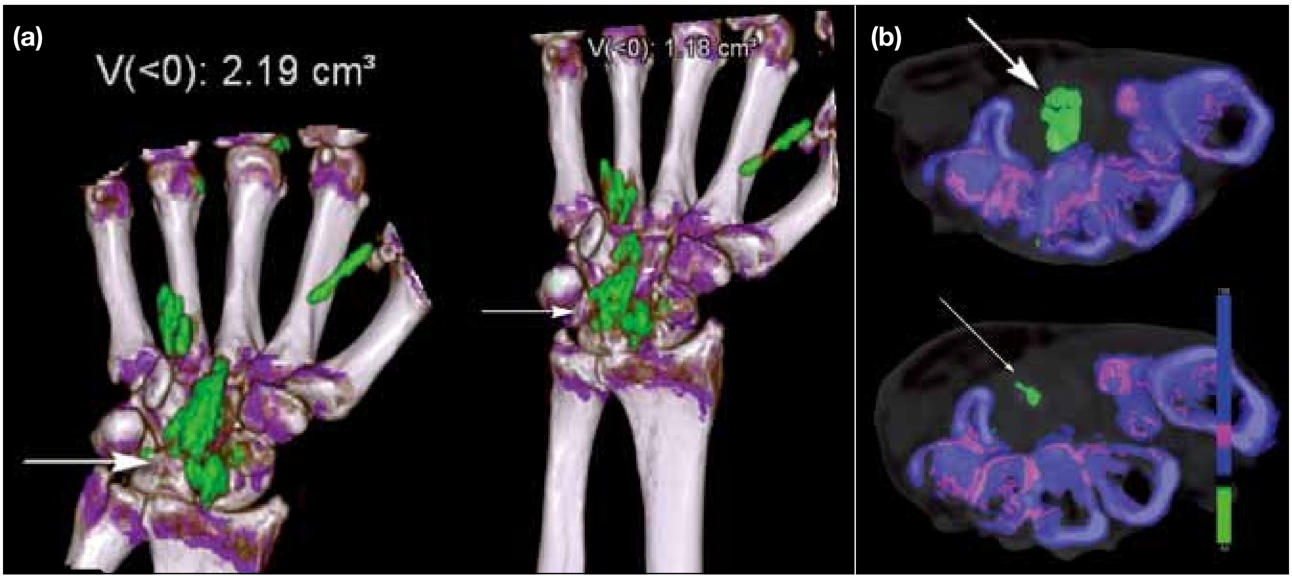

Figure 5. (a) Three-dimensional fusion and (b) two-dimensional axial dual-energy computed tomography of the hand showing a decrease in the volume of monosodium urate deposits at the carpal tunnel (arrows) from 2.19 cm^3 to 1.18 cm^3 after 5 months of urate-lowering therapy.

of spinal mass, and usually lead to a more invasive measure such as open surgery or needle biopsy.[17] Dual-energy CT can be used to assess subcutaneous and deep-tissue MSU deposits. The use of a computerised volume assessment software enables calculation of MSU deposit volume and MSU crystal-specific volume (as opposed to total tophus volume that includes inflammatory tissue response). Dual-energy CT may facilitate better management and improve sensitivity to change in subsequent treatment response (Figure 5). The number and maximal volume of tophi measured by dual-energy CT decrease significantly after urate-lowering therapy.[18]

CONCLUSION

Dual-energy CT enables volume quantification of MSU deposits for monitoring the treatment response. Although dual-energy CT has lower sensitivity when restricted to individual crystal-proven gouty joints in non-tophaceous disease, its diagnostic performance is good to excellent for tophaceous gout.

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