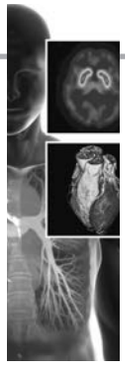


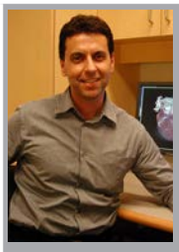
Imaging gout: brought back to the forefront with dual-energy computed tomography

"The capability afforded by DECT to provide 3D-rendered imaging will also allow for improved communication not only between clinicians, but also with patients, which may motivate them to be more aggressive and adherent to the treatment of gout."

The incidence and prevalence of gout has been rising rapidly in the USA, with the prevalence increasing by nearly 150% within a decade [1]. Gout is the most common form of inflammatory arthritis and affects more than 3–5 million adults in the USA [1,2]. These recent shifts have been attributed to lifestyle, dietary and socioeconomic factors [3]. Gout is perhaps one of the oldest described arthritidies and literature accounts have described it as the 'disease of kings' owing to its association with rich foods and alcohol intake. What was once believed to be a disease that was well managed and well understood has now found its way back into the medical forefront owing to changes in dietary habits and also to the complacency of the medical community of its quasi-simple management that has resulted in patients presenting with more severe and debilitating forms of this disease. Several studies have suggested that the overall compliance with published recommendations in routine clinical practice is low [4]. This previous lack of interest is further demonstrated by poor disease monitoring and patient compliance [4]. A recent study found that only 27.5% of patients had their uric levels measured on at least an annual basis [4]. Research in this field is expanding owing to the ability to 'see' gout via dual-energy computed tomography (DECT), which one was not previously capable of visualizing, and to confirm the presence of monosodium urate deposition noninvasively. DECT has now opened the opportunity to image gout more accurately, and treat and monitor this complex disease process.

Dual-energy CT is a concept that has been around in the radiology field for decades, but has gained popularity given the recent advances in technology, which have enabled one to routinely use it in daily practice. It is exciting from an imaging perspective to be able to scan tissues at different energy levels, which allows for the prospect of being able to more accurately determine the chemical composition of tissues. DECT was initially designed for the detection of uric acid renal calculi and was serendipitously expanded so this technique could be used to detect monosodium urate deposits in other body parts [5]. The concept behind DECT is based on the principle that compounds with different atomic weights will absorb the x-ray beam by different degrees. The two different data sets are subsequently analyzed by specialized software that allows for accurate separation of materials from one another, in other words, monosodium urate from adjacent soft tissues and calcium.

Currently, DECT is the only imaging method that can confirm the diagnosis of gout with high accuracy and specificity [6]. There have been several studies published to date that describe several potential areas of integrating DECT into the diagnostic workup for patients with gout [6,7]. Benefits include the use of diagnosing gout in hard to examine anatomy regions, such as the disc spaces, vertebral bodies and ligaments of the spine. Furthermore, it can be useful in determining intra-articular tophus within the knee joint and along tendons and ligaments, such as the posterior cruciate ligament and anterior cruciate ligament. Early detection and identification of disease is crucial in guiding early intervention to maintain the integrity of these structures as they would be more prone to rupture. DECT's clinical utility is also realized in technically challenging aspiration cases in acutely inflamed joints or where aspirate material is not readily obtained or indeterminate aspiration results. Although the gold standard of diagnosing gout is aspiration and documenting the presence of negatively birefringent needle-shaped monosodium urate crystals in an aspirate, arthrocentesis is only performed on 11% of patients [8]. This procedure is typically reserved for diagnostic dilemmas or in the acute setting. Instead, the diagnosis is commonly dependent on clinical assessment and the response to medications.



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The clinical utility and longevity of a test is measured by its patient risk–benefit ratio. DECT must be measured against the gold standard of aspiration, which is an invasive procedure, and thus carries the complications of bleeding, infection and damage to adjacent structures. In addition, DECT must be measured against a clinical assessment that runs the risk of an incorrect diagnosis and the institution of medications that carry severe life-threatening side effects. The risk of aspiration and improperly diagnosing and managing a patient are compared with a DECT scan where the primary risk is radiation, which is minimal given the scanning of radioinsensitive organs (i.e., the extremities). This will be judged in the future by randomized studies that may demonstrate DECT to be the primary gold standard in the diagnosis of gout.

> "*What was once believed to be a disease that was well managed and well understood has now found its way back into the medical forefront owing to changes in dietary habits and … the complacency of the medical community…*"

As alluded to earlier, there have been numerous newly described risk factors and associations with gout that have been attributed to this rising epidemic. The high calorie, low fiber western diet, as well as the advent of newer diets, such as Atkins and the Miami Beach diet, can be presumed to play a role in the development of gout. The consumption of two or more sugar-sweetened soft drinks per day in males has been correlated with an increased relative risk of gout by 1.85 [9]. Furthermore, increasing alcohol consumption has also been correlated with an increased relative risk of gout [3]. Adiposity, weight gain and hypertension have all been found to be independent risk factors of gout, which is a huge concern given the increasing rate of obesity in the USA [3]. There is a substantial increase in the prevalence of insulin resistance and metabolic syndrome with rising uric acid levels [10,11]. Prospective studies have also found that gout is a marker for an increased risk of myocardial infarction, cardiovascular mortality and stroke [12,13]. DECT's ability to detect disease at preclinical stages allows for early treatment not only aimed at preventing articular, bony, ligamentous and tendon damage, but also for avoiding the numerous associated risks.

Dual-energy CT has also revealed monosodium urate deposition in what has not been classically described in imaging literature, such as the predilection for the superficial and deep hand flexor tendons, cruciate and collateral knee ligaments, knee extensor mechanism and within the midfoot tarsal articulations [6]. This ability to give insight into new patterns of disease is now bringing gout to the forefront by generating more interest in the development of new more effective drugs owing to its capability to be a useful tool in confirming the presence of disease, accurately depicting the distribution of disease and, as of recently, accurate reproducible quantification of the volume of disease. This capability will stimulate the impetus for drug companies to develop and improve their current gout medications by making them more effective with an improved side-effect profile. In fact, the US FDA recently approved the first new gout drug in over 40 years with several other medications currently in development. The uric acid-lowering medication allopurinol has been the primary medication for decades, yet its toxicity profile consists of potentially fatal reactions including toxic hepatitis, renal failure and cytopenias, and may even precipitate an acute gout attack. By using DECT, patients taking urate-lowering medications can be monitored for appropriate treatment responses and thus the effectiveness of the medications can be determined.

To conclude, gout is a disease that was once thought to be simple and forgotten but has now been brought to the forefront by diet and technological advancements via DECT, which has stimulated interdisciplinary collaboration between rheumatologists and radiologists to focus on a better understanding of the disease and will hopefully motivate drug companies to initiate better therapeutic choices. The capability afforded by DECT to provide 3D-rendered imaging will also allow for improved communication not only between clinicians, but also with patients, which may motivate them to be more aggressive and adherent to the treatment of gout. The ability to image and display gout may rewrite how the imaging and understanding of gout has been previously taught in radiological and rheumatological literature, and may be instrumental in answering the many questions that remain regarding gout.

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