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# Dual-energy computed tomography for characterizing urinary calcified calculi and uric acid calculi: A meta-analysis

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ABSTRACT

*Objective:* A meta-analysis was conducted to determine the accuracy of dual-energy computed tomography (DECT) for differentiating urinary uric acid and calcified calculi.

*Methods:* The databases PubMed, EMBASE, Web of Science, and the Cochrane Library were searched up to May 2016 for relevant original studies. Data were extracted to calculate the pooled sensitivity, specificity, diagnostic odds ratio (OR), positive and negative likelihood ratios (PLR and NLR), and areas under summary receiver operating characteristic (AUROC) curves for analysis.

*Results:* Nine studies (609 stones in 415 patients) were included. For differentiating uric acid (UA) and non-UA calculi with DECT, the analysis indicated: pooled weighted sensitivity, 0.955 (95% CI, 0.888–0.987); specificity, 0.985 (95% CI, 0.970–0.993); PLR, 0.084 (95% CI, 0.041–0.170); NLR 33.327 (95% CI, 18.516–59.985); and diagnostic OR 538.18 (95% CI, 195.50–1478.5). The AUROC value was 0.9901. For calcified stones, the analysis indicated: pooled weighted sensitivity, 0.994 (95% CI, 0.969–1); specificity, 0.973 (95% CI, 0.906–0.997); PLR, 11.200 (95% CI, 4.922–25.486); NLR 0.027 (95% CI, 0.010–0.072); and diagnostic OR 654.89 (95% CI, 151.31–2834.4). The AUROC value was 0.9915.

*Conclusion:* This meta-analysis found that DECT is a highly accurate noninvasive method for characterizing urinary uric acid and calcified calculi.



## 1. Introduction

Urolithiasis, or the formation of stones in the urinary tract, is a common cause of colicky pain and urinary tract obstruction. The prevalence of urolithiasis has been estimated at 10%–14% [1]. The composition of urinary stones can be diverse, but significantly influences the treatment plan. Stones formed of uric acid crystals can be managed by urine alkalinization. The non-surgical treatment of other stones, such as those containing calcium, is more problematic and these are also highly resistant to extracorporeal shockwave lithotripsy. Surgical removal is needed when non-invasive approaches fail [2,3].

Computed tomography (CT) of the abdomen and pelvis is currently the standard means of evaluating urinary stones [4]. CT accurately illustrates the size and location of urinary stones [5–7], and CT attenuation values provide clues to stone composition [8,9]. However, there is a substantial overlap in density between uric acid, mixed calculi, struvite, and cystine; therefore, density per se is inadequate for the differentiation of different stone types [9].

Dual-energy computed tomography (DECT) may be an alternative for differentiating urinary stone types [10]. By means of simultaneous low- and high-energy acquisition, DECT is capable of depicting the composition of materials with similar electron densities, but different photon absorption [11–13]. Since stones containing uric acid, cystine, or calcium differ by molecular weights, DECT may be able to identify them.

Among the retrospective and prospective studies that have evaluated the utility of DECT for identifying stone composition, some of them have shown that DECT had high diagnostic sensitivity and specificity for both uric acid and non-uric acid stones [14–19]. However, data regarding the diagnosis of non-uric acid stones is scarce [10,14,17,19–24]. This study is a meta-analysis focusing on the accuracy of DECT for characterizing uric acid calculi and calcified calculi.

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## 2. Material and methods

### 2.1. Search method

A search of the PubMed, EMBASE, Web of Science, and Cochrane Library was performed to identify relevant articles published between January 1979 and May 2016. The following search phrases were used: "dual-energy computed tomography OR dual-energy CT OR DECT" and "urinary stone OR renal stone OR kidney stone OR urinary calculi OR urinary calculus OR urinary calculosis OR urolithiasis OR nephrolithiasis". This search strategy involved the use of free-text words and Medical Subject Headings (MeSH) terms to increase the sensitivity of the search, without language restriction. Two investigators (Xingju Zheng and Yuanyuan Liu) extracted the data, and any problems were solved by discussion.

### 2.2. Inclusion and exclusion criteria

The inclusion criteria of this meta-analysis were: (1) using DECT to evaluate the nature of the urinary stones; (2) an *in vivo* study; (3) available data for completing a 2 × 2 contingency table; (4) data on a per-stone basis; and (5) using infrared spectroscopy or crystallography as the reference standard.

The exclusion criteria were: (1) multiple articles published of the same study population (in this case, the publication with the most abundant data was chosen); (2) *in vitro* studies only, animal experiments, reviews, case reports, letters, or comments; and (3) existence of more than 4 "No" or "Unclear" in QUADAS 2 assessment.

### 2.3. Quality assessment and data extraction

The methodological quality of the included studies was assessed with the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) [25]. Characteristics of each study were extracted, including the authors, publication year, country of origin, gender distribution, number of urinary stones, study design, energy application of the DECT, and the dose of DECT. For each study, we recorded the true and false positive and true and false negative values, and constructed 2 × 2 contingency tables.

### 2.4. Statistical analysis

All analyses were performed using Stata (version 12.0) and the Meta-DiSc software (version 1.4). The threshold effect was assessed by Spearman's correlation coefficient between the logarithm-transformed sensitivity values and the logarithm-transformed values of 1–specificity, as calculated by Meta-Disc 1.4 [26].

If a probability ($P$) value < 0.05 or a strong positive correlation was found, we considered this as confirmation of a threshold effect [26,27]. We then chose to use sensitivity, specificity, and positive and negative likelihood ratios (PLR and NLR, respectively) to estimate diagnostic accuracy. If there was no threshold effect present, we pooled the sensitivity, specificity, PLR, and NLR, and constructed summary receiver operating characteristic (ROC) curves to analyze the diagnostic performance of DECT for the detection of urinary stones. $P < 0.1$ or $I^2 > 50\%$ indicated significant heterogeneity (using the Q statistic of the chi-squared test) [28]. The random effects model or fixed effects model was used to analyze jointly the final data [29].

If there is notable heterogeneity without a threshold effect, this may indicate heterogeneity. We therefore performed subgroup, sensitivity, and meta-regression analyses to discover the origin of the heterogeneity. Publication bias was assessed using Deeks' funnel plot, as well as an asymmetry test [30]. $P < 0.05$ was considered a statistically significant difference.

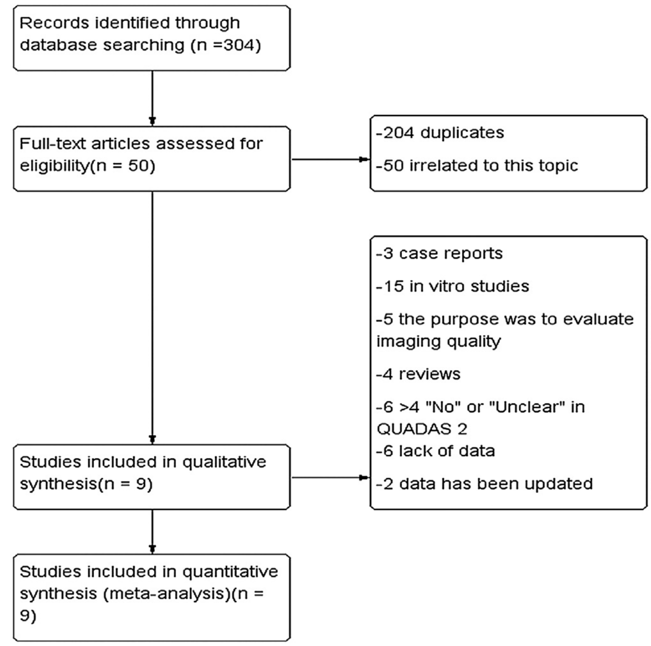


**Fig. 1.** Flowchart of the study selection process.

## 3. Results

### 3.1. Characteristics of studies

The search process is summarized systematically in Fig. 1. After searching the online databases, 304 potentially relevant articles were initially retrieved. The following items were excluded: 204 duplicate articles, and 50 for irrelevance. After reading the full text, 35 did not meet the inclusion criteria, and another 6 were excluded for insufficient data to construct the contingency table. Finally, 9 articles were included in our analysis. The baseline characteristics of the included studies are summarized in Tables 1 and 2. The quality of the included studies was good (Fig. 2).

### 3.2. Quantitative synthesis

The threshold effect was estimated by Spearman's rank correlation. The correlation coefficients for uric acid and calcium-containing calculi were 0.034 ($P = 0.931$) and −0.371 ($P = 0.468$) respectively, which indicated an absence of threshold effect in the accuracy estimates for detecting these stones.

In the pooled analyses, heterogeneity was also absent for stones containing uric acid ($I^2 = 0\%$, $P = 0.962$) and calcium ($I^2 = 0\%$, $P = 0.865$). Therefore, we pooled the sensitivity, specificity, PLR, and NLR results by using fixed-effects coefficient binary regression models.

For differentiating uric acid (UA) and non-UA stones with DECT, the analysis indicated the following: pooled weighted sensitivity 0.955 (95% confidence interval [CI], 0.888–0.987); specificity 0.985 (95% CI, 0.970–0.993); PLR 33.327 (95% CI, 18.516–59.985); NLR 0.084 (95% CI, 0.041–0.170); and diagnostic odds ratio (OR) 538.18 (95% CI, 195.50–1478.5). The forest plots of pooled sensitivity, specificity, NLR and PLR for UA stones are shown in Fig. 3. The AUROC value was 0.9901.

For calcified stones, analysis of the 6 included articles indicated: pooled sensitivity 0.994 (95% CI, 0.969–1); specificity 0.973 (95% CI,