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Urinary stone differentiation in patients with large body size using dual-energy dual-source computed tomography

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Abstract

Objective—To evaluate the ability of 100/Sn140 kV (Sn, tin filter) dual-energy CT to differentiate urinary stone types in a patient cohort with a wide range of body sizes.

Methods—80 human urinary stones were categorised into four groups (uric acid; cystine; struvite, oxalate and brushite together; and apatite) and imaged in 30–50-cm wide water tanks using clinical 100/Sn140 kV protocols. The CT number ratio (CTR) between the low- and high-energy images was calculated. Thresholds for differentiating between stone groups were determined using ROC analysis. Additionally, 86 stones from 66 patients were characterised using the size-adaptive CTR thresholds determined in the phantom study.

Results—In phantoms, the area under the ROC curve for differentiating between stone groups ranged from 0.71 to 1.00, depending on phantom size. In patients, body width ranged from 28.5 to 50.0 cm, and 79.1% of stones were correctly characterised. Sensitivity and specificity for correctly identifying the stone category were 100% and 100% (group 1), 100% and 95.3% (group 2), 85.7% and 60.9% (group 3), and 52.6% and 92.5% (group 4).

Conclusion—Dual-energy CT can provide in vivo urinary stone characterisation for patients over a wide range of body sizes.

Keywords

Dual-energy CT; dual-source CT; CT number ratio; urinary stones; body size

Introduction

Kidney stones have various elemental compositions that can influence the choice of medical or surgical treatments. For example, uric acid stones can be treated with medications that alkalise the urine, while other stone types, such as cystine or brushite, are highly resistant to extracorporeal shockwave lithotripsy, and surgical removal should be considered when

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spontaneous passage fails [1]. Non-invasive identification of stone composition therefore assists selection of a treatment strategy tailored to the patient's specific stone type.

Dual-energy CT (DECT) using a first-generation dual-source CT has been shown to reliably differentiate uric acid urinary stones from non-uric acid stones, both in phantoms [2-7] and in patient cohorts [6, 8]. Other DECT technologies, including dual-layer detectors [9] and fast-kilovoltage-switching [10] were successfully used to identify uric acid stones to a similar degree of accuracy. Different image post-processing techniques have been proposed to differentiate several kidney stone types, both ex vivo [5] and in vivo [11].

The second-generation dual-source CT includes an additional tin filter on the high-energy X-ray tube (Sn140 kV) to increase the X-ray spectral separation, which in turn increases the differences in the dual-energy CT number ratio (CTR) between stone types [12, 13]. Ex vivo phantom studies indicated that the use of the tin filter further improved the discrimination of uric acid and non-uric acid stones [14] and allowed discrimination among cystine, calcium oxalate, and calcium phosphate stones [7, 15].

Use of the standard 80/140 kV energies, with or without the tin filter, is not practical for patients with a large body size owing to the increased noise level and artefact in the 80-kV images. These patients could potentially benefit from using 100/Sn140 kV, as this will produce a much larger photon fluence for the low-energy spectrum [13]. Previous studies have shown that using filtration optimised for the 100/Sn140 kV imaging, higher DE contrast was achieved compared with 100/140 kV and 80/140 kV with factory-installed filtration [13]. Stone type differentiation using 100/Sn140 kV protocols was comparable to the 80/140 kV protocol [7, 13, 14].

When imaging a wider range of patient sizes, concerns arise regarding the effects of beam hardening and scattering. For example, the mean energy increases and mean CT number decreases with an increase in patient size. The rate of change is different for 100 and 140 kV. Therefore CTR corresponding to a specific material will change with body size. Thus use of size-adaptive thresholds may be necessary when performing stone characterisation in different patients.

In this study, we evaluated the ability of a 100/Sn140 kV dual-energy protocol on a second-generation dual-source CT system, using a previously validated image processing algorithm, to differentiate four pre-defined groups of stone types in a patient cohort with a wide range of body sizes, and determined the variation of CTR corresponding to different stone types as a function of size.

Materials and Methods

This two-phase study was approved by our institutional review board, biospecimen committee, and conflict of interest committee. All patient data were treated in a Health Insurance Portability and Accountability Act (HIPPA)-compliant manner.

Training phase: ex vivo phantom study

A phantom study was first performed to determine the dual-energy CTR thresholds for discriminating four groups of renal stone types. Eighty kidney stones were obtained from our referral laboratory, which performed compositional analysis via Fourier transform infrared spectroscopy. All stones were composed of 95% of a common urinary stone material including uric acid ($n=18$), cystine ($n=13$), struvite ($n=11$), calcium oxalate ($n=15$), brushite ($n=13$), or hydroxy/carbonate apatite ($n=10$). The average stone size was 6.1 mm (range 4.0–12.0 cm). All stones were hydrated in saline for 24 h and then embedded in

ground pork before they were placed in water phantoms with lateral widths of 30, 35, 40, 45, and 50 cm (Fig. 1).

The phantoms were imaged using a clinical 100/Sn140 kV protocol on a second generation dual-source CT system (Somatom Definition Flash, Siemens Healthcare, Forchheim, Germany). Imaging parameters for the 100/Sn140 kV acquisition matched our routine clinical dual-energy CT protocol: 64×0.6 mm collimation, 240 and 185 quality reference mAs for the 100 kV and 140 kV tubes, respectively, 0.5 s rotation time, and spiral mode with pitch = 0.6. Automatic exposure control was used. Dual-energy images were reconstructed using a medium smooth kernel (D30), with a 300-mm field of view, image thickness of 1.0 mm and 0.8 mm interval.

Dual-energy image processing was performed using previously validated, custom Matlab-based software (Matlab, version 2009a, Math-Works, Natick, MA, USA) [15]. In brief, a square region of interest (ROI) was defined manually by the user to indicate the location of the stone. The software then segmented the stone from surrounding tissues using a predefined CT number threshold (150 HU in this study) in the high-energy image and extracted a three-dimensional volume of interest containing the stone. The CTR was calculated as the CT number at 100 kV divided by the CT number at 140 kV for each voxel. The average CTR value of all voxels within the segmented stone was used for characterising the composition.

All 80 stones were categorised into one of four groups based on their calculated effective atomic numbers (Z_{eff}) [16]: group 1 ($n=18$) included uric acid stones ($\text{C}_5\text{H}_4\text{N}_4\text{O}_3$, $Z_{\text{eff}}=6.91$); group 2 ($n=13$) included cystine stones ($\text{C}_6\text{H}_{12}\text{N}_2\text{O}_4\text{S}_2$, $Z_{\text{eff}}=10.78$); group 3 ($n=39$) included struvite ($\text{Ca.MgNH}_4\text{PO}_4 \cdot 6\text{H}_2\text{O}$, $Z_{\text{eff}}=12.17$), calcium oxalate di- or mono-hydrate ($\text{CaC}_2\text{O}_4 \cdot 2\text{H}_2\text{O}$ or $\text{CaC}_2\text{O}_4 \cdot \text{H}_2\text{O}$, $Z_{\text{eff}}=12.99$ or 13.45) and brushite stones ($\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$, $Z_{\text{eff}}=13.82$); group 4 ($n=10$) included apatite stones ($\text{Ca}_{10}(\text{PO}_4)_6 \cdot (\text{CO}_3)$ or $\text{Ca}_{10}(\text{PO}_4)_6 \cdot (\text{OH})_2$, $Z_{\text{eff}}=15.74$ or 15.86).

Receiver operating characteristic (ROC) analysis was performed by plotting sensitivity versus 1 minus specificity at multiple thresholds. The point on the ROC curve closest to the upper left corner was used to identify the optimal threshold value for differentiating between two adjacent stone groups at each phantom size. A linear regression model was generated based on the thresholds observed for the five sizes of water tanks.

Testing phase: Retrospective patient study

Subjects were identified from a chart review of all patients referred for clinical DECT between June 2009 and June 2011. Inclusion criteria were:

1. The patient underwent DECT on a second-generation dual-source CT with our routine 100/Sn140 kV protocol;
2. The patient subsequently had a kidney stone removed;
3. Stone composition was analysed with Fourier transform infrared spectroscopy;
4. The stone had 80% of a single composition.

Image data were reconstructed with the same parameters used in the training phase. Reconstructed low- and high-energy images were exported to a dedicated offline workstation for composition analysis.

The same MatLab-based software was used for characterising stone composition. The lateral width of each patient was measured at the mid-kidney level and was used as the input

parameter to the previously determined regression model to determine size-adaptive thresholds. For visualisation purposes, stones were coloured according to stone type.

Volume CT dose index (CTDI_{vol}) was read from the DICOM dose report image stored with each patient's examination, and size-specific-dose-estimates (SSDE) were calculated [17]. Kidney stone size was measured automatically as the largest dimension across the stone. Image noise was measured in the mixed-kV images (50% linear combination of low and high images) as the standard deviation of CT numbers in a circular ROI placed over a homogeneous region (peritoneal fat) within the abdominal cavity at the mid-kidney level.

Results

Phantom Study

Volume CT dose index was 8.8, 13.1, 18.5, 22.7 and 26.2 mGy, and SSDE was 13.2, 16.4, 19.0, 18.8, 17.2 mGy, in the 30-, 35-, 40-, 45- and 50-cm phantoms, respectively. Measured image noise values were 22.0, 25.8, 30.9, 37.5 and 46.1 HU, respectively (Fig. 2).

The mean CTR values of each stone group at different phantom sizes decreased with increasing phantom size (Table 1). Subsequently, differences in CTR values between adjacent groups decreased with increasing phantom size (Table 1).

Receiver operating characteristic curves were plotted for each phantom size (Fig. 3). The area under the ROC curve (AUC) was 1.00 (95% CI, 1.00-1.00), 1.00 (95% CI, 0.95-1.00), 1.00 (95% CI, 0.90-1.00), 1.00 (95% CI, 0.93-1.00) and 1.00 (95% CI, 0.93-1.00) for differentiating the uric acid group from the cystine group at 30-, 35-, 40-, 45- and 50-cm phantoms, respectively. For differentiating the cystine group from the group containing struvite, oxalate and brushite stone types, the AUC was 0.90 (95% CI, 0.78-0.96), 0.85 (95% CI, 0.71-0.93), 0.90 (95% CI, 0.77-0.96), 0.87 (95% CI, 0.75-0.95), and 0.79 (95% CI, 0.65-0.89), respectively, as size increased. For differentiating the group containing struvite, oxalate and brushite stone types from the apatite group, AUC was 0.84 (95% CI, 0.65-0.94), 0.73 (95% CI, 0.52-0.88), 0.83 (95% CI, 0.66-0.94), 0.77 (95% CI, 0.55-0.92) and 0.71 (95% CI, 0.51-0.88), respectively. Thus, AUC decreased by as much as 0.13 as phantom width increased from 30 to 50 cm. The threshold values that optimally differentiated a stone group from its immediate neighbours were used in the analysis of the patient data (Table 2).

Patient Study

Average patient age was 57 ± 15 years (range 24 to 82 years) with an average lateral width of 36.4 ± 4.1 cm (range 28.5 to 50.0 cm). A total of 86 stones were collected from 66 patients (37 male, 29 female), with an average of 1.3 stones per patient. The stones included were Group 1, 3 uric acid; Group 2, 1 cystine; Group 3, 1 struvite, 61 calcium oxalate, 1 brushite; and Group 4, 19 apatite. The stones were collected from kidneys ($n=70$, 81.4%), ureters ($n=14$, 16.3%) and bladders ($n=2$, 2.3%) via percutaneous nephrolithotomy or ureteroscopy stone removal procedures. Average stone size was 7.2 ± 6.0 mm (range 0.8 to 25.7 mm).

Using the size-adaptive thresholds (Fig. 4), 68 of the 86 stones were correctly characterised for an overall accuracy of 79.1%. Sensitivity and specificity for identifying stone types were 100% and 100% (group 1), 100% and 95.3% (group 2), 85.7% and 60.9% (group 3), and 52.6% and 92.5% (group 4). Among 16 incorrectly characterised stones, 8 (50%) had a maximal diameter smaller than 4 mm (range 1.2 to 3.9). One of the 16 cases had a lateral abdominal size of 50 cm. Colour-coding was used for easy visualisation of stone type (Fig. 5).

Average CTDIvol was 14.6 ± 3.9 mGy (range 9.4 to 36.8). Average SSDE was 17.0 ± 2.8 mGy (range 13.6 to 30.5). Average image noise was 27.1 ± 5.4 HU (range 17.5 to 44.4 HU).

Discussion

This study demonstrated that the use of a 100/Sn140 kV DECT protocol with a custom post-processing method can differentiate among four groups of common stone types. In a patient cohort with a wide range of body habitus, use of size-adaptive thresholds for each patient provided an overall accuracy of 79.1% for stone type characterisation.

One of the limitations of DECT using 80/140 or 80/Sn140 protocols is that it is not recommended for larger patients. This is primarily due to insufficient tube current available when the tube is operated at 80 kV, resulting in excessive image noise for those images. In a study by Primak et al using an 80/140 kV protocol, accuracy and sensitivity for differentiating uric acid decreased from 100% and 100% in a medium-sized phantom to 93% and 88% in an extra-large phantom. Performance in the extra-large phantom further decreased for stones smaller than 3 mm in diameter (83% and 67%) [2]. Previous studies that demonstrated a high accuracy for distinguishing uric acid stones were conducted in small- to medium-sized anthropomorphic phantoms, ranging from 15 cm to 35 cm in diameter [3-8]. In a clinical study by Stolzmann et al, the average image noise was 12.5 ± 2.64 HU, which is relatively low compared with 27.1 ± 5.4 HU in our study, indicating a patient cohort with either small body size or higher dose levels [6].

In our institute, patients with lateral body size larger than 35 cm account for approximately 60% of the kidney stone disease patients. Therefore, in this study, we evaluated the feasibility of stone type differentiation using a 100/Sn140 kV protocol in a patient cohort with body sizes ranging from 28.5 to 50.0 cm in lateral width. Image noise increased as patient size increased, but was acceptable in all cases. An overall accuracy of 79.1% was achieved when differentiating four groups of stones, and 100% sensitivity and specificity for characterising uric acid stones, which is consistent with the results from a previous study using 80/140 kV (without a tin filter) [2]. This facilitates the use of this examination in larger patients, which account for roughly two thirds of our stone protocol CT population.

In the training phase of this study, a set of CTR thresholds were determined for each stone type and each of the five standard phantom sizes to create a linear regression model. Subsequently, thresholds specific to each patient could be determined based on that patient's abdominal size.

In vivo characterisation of stone types other than uric acid, such as cystine, struvite, oxalate, brushite and apatite, is a demanding clinical task. Several previous studies demonstrated a potential for using dual-energy CT to detect cystine and calcium-based stones. Cystine stones had a significantly different CTR [7, 15] or DE slope [5] from other stone types in several studies. Using 80/(Sn)140 kV protocols, a significant difference in CTR was found between struvite and apatite stones in two studies using first- [5] and second-generation DSCT [15]. Differentiation of brushite stones was attempted using an advanced dual-energy data processing technique [5]. However, no significant difference among these calcium-based stones was found in a different study that examined three combinations of low- and high-energy spectra [7].

In our study, six types of stones were categorised into four groups according to the calculated effective atomic numbers based on the chemical formula of each stone type [16]. Using a 100/Sn140 kV protocol, ROC analysis showed successful tests between these groups in all five phantom sizes (AUC range from 0.77 to 1.00). A lower AUC was found between group 3 (struvite, oxalate and brushite stones) and group 4 (apatite stones) and in

the larger phantom size. The testing phase of our study using patient data showed that differentiation among these four groups was feasible with high sensitivity of detecting group 1, 2 and 3 stones, and high specificity of detecting group 1, 2 and 4. Further differentiation among the stone types in group 3 was not evaluated in this study.

Our study had some limitations. Firstly, we included 80 stones in the ex vivo training phase, with 21% uric acid, 16% cystine, 14% struvite, 19% oxalate, 16% brushite and 14% apatite stones. These percentages do not match the typical prevalence in a general population, especially because the most common type is calcium oxalate and cystine is rare, with a prevalence less than 1% [18]. Thus, adjustment for sample selection bias is needed when prediction probability is to be assessed in a larger sample-size study. Sample numbers in the in vivo study reflect the typical prevalence of these stone types, where the most of the stones were oxalate stones, followed by apatite. The numbers of uric acid and cystine cases were limited to 3 and 1, respectively, which were correctly classified. In our institute, patients with uric acid stones are mainly treated with medications. Therefore only a few uric acid stone samples were collected from surgical procedures during the period of this retrospective study. The limited number of cystine stones is a reflection of low prevalence of such patients because of its rarity. This study was designed as a pilot study to demonstrate the feasibility of using 100/Sn140 kV protocol for patients with small to extra-large body sizes, and the sample size of this study was sufficient for this purpose.

Secondly, this study only considered kidney stones with pure composition, defined as having above 80% of a single component. In reality, most stones are of mixed composition [19]. When a stone has more than two compositions, the calculated dual-energy CTR is altered and may fall into any of two or three adjacent stone types. Stones with mixed compositions were included in several previous studies [4-6, 8, 20] and were classified according to the major component. This issue remains an area of further investigation.

In summary, the ability to successfully image patients using the 100/Sn140 kV protocol, without excessive noise for the low-energy (i.e. 100 kV) image, facilitates differentiation of urinary stones into one of the four pre-defined groups. This in vivo diagnostic test is achievable in patients with a wide range of body sizes.

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Abbreviations and acronyms

AUC	area under the curve
CT	computed tomography
CTDI_{vol}	Volume CT dose index
CTR	CT number ratio
DECT	dual-energy computed tomography
DSCT	dual-source computed tomography
HU	Hounsfield units
ROC	receiver operating characteristics

ROI	region of interest
SSDE	size-specific-dose-estimates
Z_{eff}	effective atomic numbers

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Key Points

- Dual-energy CT helps assessment of urinary stone composition in vivo.
- 100/Sn140 kV DECT differentiates among four stone types with 79.1% accuracy.
- In vivo diagnostic test achievable in patients with many body sizes.

Fig. 1.

Ex vivo phantom study. Renal stones were placed in the plastic vials filled with saline (A), embedded in ground pork (B) and placed in elliptical water phantoms with lateral widths of 30, 35, 40, 45, and 50 cm (C). Maximum intensity projection (MIP) images (D) were created to precisely locate the stones

Fig. 2. Sample images from each of the five phantom sizes. Image noise increased with phantom size even though the system output was adapted according to patient size. This reflects of our clinical practice of not requiring the same image noise in obese patients as in smaller patients

Fig. 3. Receiver operating characteristics curves for differentiating between (A) the cystine (CYS) stone group and struvite (STR), calcium oxalate and brushite (BRU) stone group; and (B) struvite, calcium oxalate and brushite stone group and apatite (APA) stone group, at five different water phantom sizes (30, 35, 40, 45 and 50 cm)

Fig. 4.

A linear model was generated based on the optimal thresholds at five standard sizes of water tanks in the training phase. The lateral abdominal size of each patient was fitted to the model to calculate size-adaptive thresholds for characterising stone types

Fig. 5.
Sample images of four cases with different stone types: uric acid (A, colour coded in *red*),
(B, *yellow*), calcium oxalate (C, green), and apatite (D, blue)

Dual-energy CT number ratio (CTR) of the four groups of urinary stones for phantom lateral widths from 30 to 50 cm. Group 1 included uric acid stones; group 2 included cystine stones; group 3 included struvite, calcium oxalate and brushite stones; group 4 included apatite stones. StDev: standard deviation

Table 1

Phantom size	30 cm	35 cm	40 cm	45 cm	50 cm
	Mean $\pm$ StDev	Mean $\pm$ StDev	Mean $\pm$ StDev	Mean $\pm$ StDev	Mean $\pm$ StDev
Group 1	0.99 $\pm$ 0.04	0.99 $\pm$ 0.04	1.01 $\pm$ 0.05	0.98 $\pm$ 0.05	0.98 $\pm$ 0.07
Group 2	1.24 $\pm$ 0.03	1.23 $\pm$ 0.06	1.19 $\pm$ 0.05	1.15 $\pm$ 0.06	1.17 $\pm$ 0.05
Group 3	1.37 $\pm$ 0.07	1.34 $\pm$ 0.08	1.31 $\pm$ 0.08	1.27 $\pm$ 0.08	1.26 $\pm$ 0.09
Group 4	1.45 $\pm$ 0.05	1.40 $\pm$ 0.05	1.39 $\pm$ 0.05	1.35 $\pm$ 0.06	1.32 $\pm$ 0.08

Dual-energy CT number ratio (CTR) thresholds for optimally differentiating between the two adjacent stone groups in different phantom sizes. Group 1 included uric acid stones; group 2 included cystine stones; group 3 included struvite, calcium oxalate and brushite stones; group 4 included apatite stones

Table 2

	30 cm	35 cm	40 cm	45 cm	50 cm
Group 1 vs. Group 2	1.19	1.17	1.08	1.05	1.08
Group 2 vs. Group 3	1.32	1.33	1.23	1.20	1.14
Group 3 vs. Group 4	1.46	1.43	1.41	1.38	1.39