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Characterization of Urinary Stone Composition by Use of Third-Generation Dual-Source Dual-Energy CT With Increased Spectral Separation

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Abstract

OBJECTIVE—The purpose of this phantom study was to determine the utility of a third-generation dual-source CT scanner with increased dual-energy spectral separation in differentiating urinary stone composition.

MATERIALS AND METHODS—Eighty-seven urinary stones from humans were scanned in 35-, 40-, 45-, and 50-cm wide anthropomorphic phantoms with a third-generation dual-source scanner (system A) with a high-energy beam of 150 kV plus 0.6-mm tin filtration (Sn). The low-energy data were acquired at 70, 80, 90, and 100 kV. A second-generation dual-source scanner (system B) was used to acquire data at 140 kV plus 0.4-mm Sn for the high-energy and 80 or 100 kV for the low-energy images. Volume CT dose index was matched for a given phantom size. CT number ratios were calculated and used to differentiate uric acid from non-uric acid stones and oxalate from apatite stones in an ROC analysis.

RESULTS—The area under the curve (AUC) of the ROC curve for uric acid versus non-uric acid stones increased for large phantoms. For example, for imaging of the 45-cm wide phantom with system A at the 100- and 150-kV Sn low- and high-energy combination, the AUC was 0.99, whereas for system B at the 100- and 140-kV Sn combination, the AUC was 0.86. At each phantom size and for all energy combinations, the AUC values for oxalate versus apatite stones were higher for system A than they were for any energy combination for system B.

CONCLUSION—Compared with use of second-generation dual-source CT, use of third-generation dual-source CT at the energy combination of 100 and 150 kV Sn improved classification of urinary stones across a wide range of phantom sizes and increased the ability to differentiate oxalate from apatite stones.

Keywords

CT; dual-energy CT; phantom; spectral separation; urinary stones

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Techniques to characterize urinary stone composition by use of dual-energy CT technologies have been under development since approximately 2006 [1–7]. Dual-energy differentiation of uric acid (UA) from non-UA stones can have nearly 100% sensitivity and specificity [5]. Unfortunately, this high accuracy is limited to patients with small body sizes and to small anthropomorphic phantoms (lateral width less than 40 cm) when 80-kV scans are acquired for the low-energy dataset [5]. Accuracy decreases in patients with a larger habitus (larger than 40 cm), even if 100-kV scans are used for the low-energy dataset [4]. These limitations are due to the high noise and artifact levels encountered with 80-kV settings for imaging of large patients and to the decreased spectral separation in the use of 100-kV settings for large patients. Furthermore, differentiation between non-UA stone types, that is, cystine, oxalate, and apatite is difficult [3]. Separation of these stone types in vivo may provide useful information for stone management, including interventional procedures, by providing, for example, an estimate of stone hardness, which is linked to stone type.

The discriminating power of dual-energy CT improves if the x-ray energy spectra used in a dual-energy CT system are better separated [3, 4]. In late 2013, a third-generation dual-source scanner with improved spectral separation was commercially introduced. The purposes of this study were to conduct a phantom evaluation of five common stone types to determine the utility of a third-generation dual-source CT scanner in differentiating urinary stone composition and to compare the results with those obtained with a second-generation system.

Materials and Methods

Stone Samples

Eighty-seven urinary stones were collected from the department of pathology and laboratory medicine at our institution, which operates a large referral service for stone composition analysis with infrared spectroscopy techniques. Institutional review board approval was not required for imaging of these deidentified stones, which were considered medical waste. Only one stone sample was collected from each patient, and there were no restrictions on stone size. All stones were composed of at least 90% of a common urinary stone material: UA ($n = 17$), cystine ($n = 5$), calcium oxalate ($n = 30$), brushite ($n = 5$), and apatite ($n = 30$). To avoid air bubbles on or within the stones, the stones were well hydrated by being placed in saline solution–filled plastic vials for 6 hours before being scanned in four torso-shaped water tanks with lateral dimensions of 35, 40, 45, and 50 cm, which were used to represent small, average, large, and obese adults (Fig. 1).

Dual-Energy CT Data Acquisition and Image Reconstruction

The stone-containing water tanks were scanned with two dual-source CT systems. System A (Somatom Force, Siemens Healthcare) had dual-energy tube potential pairs of 70 and 150 Sn, 80 and 150 Sn, 90 and 150 Sn, and 100 and 150 kV Sn, where Sn denotes the addition of a 0.6-mm flat tin (Sn) filter to the high-energy beam. System B (Somatom Definition Flash, Siemens Healthcare) had dual-energy tube potential pairs of 80 and 140 Sn and 100 and 140 kV Sn, where Sn denotes the addition of a 0.4-mm flat tin filter to the high-energy beam. The use of additional tin filtration on the high-energy tube and the wider difference in tube

potential increased spectral separation between the low- and high-energy spectra for system A relative to system B [4, 8] (Fig. 2).

The CT scan protocols followed those used in our routine clinical practice, which corresponded to a volume CT dose index of approximately 13.5 mGy for the 35-cm phantom. Automatic exposure control (CARE Dose 4D, Siemens Healthcare) was used. The quality reference effective tube current–time product values were determined and recorded for each energy combination to produce identical volume CT dose index values in the 35-cm phantom (Table 1). These settings were then used to scan the other phantom sizes, for which the system automatically adjusted the radiation output for the different sizes. Automatic tube potential selection (CARE kV, Siemens Healthcare) was not used because specific tube potential combinations were required as part of the dual-energy technique. Dual-energy images were reconstructed with a medium sharp soft-tissue dual-energy kernel (Qr40 for system A, D30f for system B) with a 300-mm FOV, 1.0-mm image thickness, and 0.8-mm image interval. The system A kernel included iterative reconstruction (Admire, Siemens Healthcare) with a strength setting of 3, which emulated the use in our clinical practice of iterative reconstruction on that system. The system B kernel did not include iterative reconstruction, which emulated the choice of our clinical practice not to use iterative reconstruction on that system.

Quantitative Image Analysis

Image quality was objectively evaluated by measurement of the mean CT number and noise (SD of CT numbers) on images from the middle of the scan range by use of a 2-cm-diameter uniform ROI in water near the center of the FOV. Images on which the mean CT number of water was less than –15 HU or greater than 15 HU were excluded from the analyses of stone composition. During data processing, all images were viewed by one of the investigators, and images showing substantial shading or ring artifacts were excluded (Fig. 3).

The CT number ratio, defined as the ratio between the low-energy image CT number and the high-energy CT number, was quantitatively assessed with a previously validated software tool based on Matlab software (version 2009a, Math-Works) [3]. After a cubic ROI was placed manually around the stone, 3D segmentation of the stones was performed automatically with a fixed-value CT number (150 HU). This procedure was performed on the 100-kV image from the 100- and 150-kV Sn scans for system A and the 100- and 140-kV Sn scans for system B to create a mask, which was subsequently projected to all the other images acquired with the other energy pairings. Stone sizes were measured with the mask. The CT number ratio was calculated for every pixel included in the stone segmentation mask. The mean CT number ratio for all pixels within the segmented stone was used to represent the CT ratio of that stone. Qu et al. [3] describe this approach in detail.

Statistical Analysis

ROC curves were generated by plotting sensitivity on the y-axis against 1 – specificity on the x-axis for varying values of the threshold used to separate stone types. They were used to illustrate the performance of a binary classification between UA and non-UA stones and, for non-UA calcium-containing stones, the classification between calcium oxalate and apatite

stones. The ROC AUC was used as an overall figure of merit for the classification task and was compared between the two dual-source CT systems. The optimal thresholds for the binary classification were determined by maximizing the sum of sensitivity and specificity, for which it was assumed that both sensitivity and specificity are of equal clinical importance. All statistical analysis was performed with JMP software (version 9, SAS Institute).

Results

The average stone size was 5.7 ± 3.1 mm (range, 2.9–12.0 mm). The 100- and 150-kV Sn combination on system A was the only combination on either system to produce acceptable image quality—as measured by the mean CT number of water and absence of artifacts—across all phantom sizes. The 70- and 150-kV Sn combination on system A avoided artifacts only for the 35-cm phantom. For system B, no energy combination avoided artifacts for the 50-cm phantom. The 80- and 140-kV Sn combination avoided artifacts only in phantoms 40-cm and smaller.

The measured image noise is shown in Table 2. The mean CT ratio values for each energy combination are shown in Table 3. For the small phantom size (35 cm), use of the 90- and 150-kV Sn and 100- and 150-kV Sn protocols provided CT number ratio separation (0.70 and 0.58) comparable to that of system B at 80- and 140-kV Sn (CT ratio, 0.69) but with less noise on the low-energy images (25.4 and 24.2 HU at 90-kV and 100-kV on system A versus 31.4 HU at 80 kV on system B).

The use of greater spectral separation increased the AUC for differentiation of UA and non-UA stones for larger phantom sizes. For the differentiation of UA from non-UA stones and the 100- and 150-kV Sn combination, system A had AUC values of 1.0, 0.99, 0.99, and 0.95 for the 35-, 40-, 45-, and 50-cm phantoms. For the differentiation of UA from non-UA stones and the 100- and 140-kV Sn combination, system B had AUC values of 1.0, 1.0, and 0.86 for the 35-, 40-, and 45-cm phantoms. The data at 50 cm had too high an artifact level to be used. A complete report of all AUC values for UA versus non-UA differentiation is shown in Figure 4A.

Similarly, for each phantom size and energy combination, the AUC for oxalate versus apatite stones was higher on system A than at any energy combination on system B (Fig. 4B). For the differentiation of oxalate from apatite stones and the 100- and 150-kV Sn combination, system A had AUC values of 0.83, 0.85, 0.80, and 0.78 for the 35-, 40-, 45-, and 50-cm phantoms. For the differentiation of oxalate from apatite stones and the 100- and 140-kV Sn combination, system B had AUC values of 0.75, 0.72, and 0.60 for the 35-, 40-, and 45-cm phantoms. The data at 50-cm had too high an artifact level to be used. A complete report of all AUC values for oxalate versus apatite differentiation is shown in Figure 4B.

Discussion

We evaluated the effect on image quality and stone classification of the improvement in spectral separation resulting from the use of 150-kV tube potential paired with 0.6-mm tin

filtration on the high-energy beam in a third-generation dual-source CT scanner. We found that this capability increased the CT number ratio values, which are an indirect measure of spectral separation, relative to those of a dual-source scanner with a maximum tube potential of 140 kV and minimal tube potential of 80 kV. Increased difference in CT number ratio between stone types is associated with better separation of stone types and allowed differentiation of UA and non-UA stones with high accuracy for patients measuring up to 50 cm in lateral dimension. It also improved separation between stone types with close effective atomic numbers, such as calcium oxalate and apatite stones. The largest spectral separation was achieved with system A at 70- and 150-kV Sn, but this combination showed photon starvation artifacts for all but the smallest (35 cm) phantom.

Although the currently available 80- and 140-kV Sn protocol has already been found to have good diagnostic accuracy for differentiating UA from non-UA stones both in vivo and ex vivo [1, 3, 4, 6], its application in patients of larger habitus is limited owing to the increase in image artifacts and noise [7]. The energy combinations achievable in system A had stronger x-ray penetration capabilities because of the use of 150 kV [8], and generally better image quality was achieved in large phantoms.

At approximately the same CT number ratio values, lower image noise was observed at the 90- and 150-kV Sn and 100- and 150-kV Sn combinations on system A than at the 80- and 140-kV Sn combination on system B. This finding implies that for the same dual-energy separability (i.e., the same CT number ratio values), the dose could be decreased on system A to match the higher noise of system B. These data suggest that a lower-dose 90- and 150-kV Sn or 100- and 150-kV Sn dual-energy scan on system A could be performed for patients of small habitus yet have image noise and diagnostic accuracy for characterizing UA stones similar to those of our current clinical technique on system B (80- and 140-kV Sn), although this requires clinical validation. Alternatively, the lower noise performance could be allowed to decrease errors in the stone characterization task.

The radiation output of the scanner, in terms of volume CT dose index, was between 13 and 14 mGy. This is comparable to the standard setting of 11 mGy for our routine single-energy stone protocols and 12–16 mGy for a routine abdominopelvic examination. Thus, for a modest increase in radiation output, information about stone composition can be obtained in a dual-energy CT examination. At our institution, all outpatient stone CT examinations are ordered by the referring nephrologist or urologist as dual-energy scans, and stone composition and volume are quantitatively reported. Use of system A may allow a decrease in dose to the point when the dual-energy stone examination approaches the dose of our routine low-dose stone protocol. We consider the small increase in dose of the dual-energy examination relative to our reduced-dose stone protocol to be an acceptable tradeoff in achieving lower image noise and hence more robust stone characterization.

The increased difference between the CT number ratios of materials may also facilitate differentiation of stone types with close effective atomic numbers, such as calcium oxalate and apatite stones. Calcium oxalate and apatite stones are the most common stone types in patients with nephrolithiasis, accounting for more than 80% of stones [9]. The physiopathologic factors underlying the formation of the two types of stones are different;

hence, in vivo differentiation between oxalate and apatite stones is of clinical significance [10]. Differentiation is hampered, however, by close effective atomic numbers (12.99–13.45 for oxalate, 15.74–15.86 for apatite) [3] and dual-energy CT scanners limited to 80- and 140-kV Sn examinations [11]. With 150-kV Sn combinations, the two stone types can be better differentiated from each other.

A minor limitation of this study was the exclusion of struvite stones. These stones were excluded because their mixed composition (apatite, oxalate, and calcium phosphate) made it difficult to obtain the highly accurate and pure composition needed to effectively assess the spectral separation differences [12]. Because of the small number of stones available, cystine stones were also excluded from our analyses. Another limitation was the lack of stones smaller than 2.9 mm. Previous work has shown that accuracy begins to decline in such small stones because of partial volume averaging over the small stones. In addition, we conducted the study only with phantoms. The strength of a phantom study is that stone type is known a priori, and hence the study design can be well controlled. Our results are motivation for additional studies with patients. Finally, we used CT number ratio as our metric for discriminating stone type, and this is only an indirect measure of spectral separation. However, because CT number ratio is used in commercial products for clinical stone characterization work, it is a clinically relevant metric.

Conclusion

Differentiation between UA and non-UA stones improved for the larger phantom sizes imaged in association with the increased spectral separation available with the third-generation dual-source CT scanner evaluated. Our findings suggest that this improved technology may be useful for imaging of patients of larger habitus and for decreasing image noise and dose in imaging of smaller patients. Patient studies are needed for confirmation. Furthermore, improved differentiation between calcium oxalate and apatite stones appears possible.

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Fig. 1. Photograph shows experimental setup. Human urinary stone samples were immersed in plastic vials filled with saline solution. Vials were scanned in torso-shaped water tanks 35, 40, 45, and 50 cm wide.

Fig. 2.

Simulated high- and low-energy spectra of two dual-source systems.

A, Graph shows energy spectra for third-generation dual-source system (system A) with 70- and 150-kV energy pair with 0.6-mm Sn (tin) filter installed on high-energy tube.

B, Graph shows energy spectra for second-generation dual-source system (system B) with 80- and 140-kV energy pair with 0.4-mm Sn (tin) filter installed on high-energy tube.

Fig. 3.

Sample axial CT images.

A, Acceptable image of 35-cm phantom acquired with system B at 80 and 140 kV Sn.

B, Unacceptable image of 50-cm phantom acquired with system A at 70 and 150 kV Sn.

A **B****Fig. 4.**

Area under the receiver operating curve (AUC) values for stone differentiation.

A and **B**, Graphs show AUC values for task of differentiating uric acid from non-uric acid stones (**A**) and calcium oxalate from apatite stones (**B**). **A** = system A, that is, CT system with increased spectral separation. **B** = system B, that is, dual-source dual-energy CT system with fewer tube potential combinations that have less separation between them. System A

maintains performance for renal stone material classification across all phantom sizes at 100- and 150-kV Sn combination.

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TABLE 1
Dual-Energy CT Scanning Protocols With Different Tube Energy Pairs on Two Dual-Source Scanner Systems for 35-cm Phantom

Parameter	System A ^a				System B ^b			
	70, 150 Sn	80, 150 Sn	90, 150 Sn	100, 150 Sn	80, 140 Sn	100, 140 Sn	100, 140 Sn	100, 140 Sn
Tube Potential Pair (kV)								
Quality reference effective tube current–time product (mAs)	1010	600	430	370	570	278		
Collimation (mm)	128 × 0.6	128 × 0.6	128 × 0.6	128 × 0.6	32 × 0.6	32 × 0.6		
Rotation time (s)	0.5	0.5	0.5	0.5	0.5	0.5		
Pitch	0.7	0.7	0.7	0.7	0.7	0.7		
Automatic exposure control	On	On	On	On	On	On		
Volume CT dose index (mGy)	13.28	13.48	13.64	13.54	13.30	13.41		

^a Sn indicates 0.6-mm tin filter.

^b Sn indicates 0.4-mm tin filter.

TABLE 2
Image Noise (in Hounsfield Units) Measured in a Water ROI on the Low- and High-Energy Images for Each Phantom Size

Phantom Size (cm)	Energy	System A				System B		
		70, 150 kV	80, 150 kV	90, 150 kV	100, 150 kV	80, 140 kV	100, 140 kV	100, 140 kV
35	Low	26.8	26.4	25.4	24.2	31.4	29.8	29.8
	High	29.0	26.9	27.8	33.4	30.8	30.5	30.5
40	Low	—	30.2	29.0	26.9	39.9	37.1	37.1
	High	—	31.6	32.9	36.9	34.8	34.3	34.3
45	Low	—	—	34.2	31.7	—	44.5	44.5
	High	—	—	36.4	43.2	—	41.8	41.8
50	Low	—	—	—	37.2	—	—	—
	High	—	—	—	46.9	—	—	—

Note—Dash [—] denotes datasets with unacceptable shading or ring artifacts due to photon starvation. Quantitatively, these data had a mean CT number in water less than −15 HU. A tin filter was used on all of the high-energy beams (see Table 1).

CT Number Ratios of Four Stone Types Scanned With Different Dual-Energy Protocols on Two Systems for the 35-cm Phantom

TABLE 3

Stone Type	System A				System B	
	70, 150 kV	80, 150 kV	90, 150 kV	100, 150 kV	80, 140 kV	100, 140 kV
UA	0.88 ± 0.07	0.90 ± 0.06	0.92 ± 0.07	0.96 ± 0.05	0.90 ± 0.05	0.97 ± 0.03
Cystine	1.55 ± 0.03	1.45 ± 0.06	1.37 ± 0.01	1.30 ± 0.04	1.33 ± 0.04	1.24 ± 0.01
Calcium oxalate and brushite	1.89 ± 0.07	1.71 ± 0.05	1.60 ± 0.04	1.52 ± 0.03	1.58 ± 0.05	1.38 ± 0.02
Apatite	2.00 ± 0.12	1.79 ± 0.09	1.68 ± 0.08	1.59 ± 0.06	1.63 ± 0.09	1.42 ± 0.05
All non-UA stones	1.91 ± 0.15	1.73 ± 0.11	1.62 ± 0.10	1.54 ± 0.09	1.59 ± 0.10	1.39 ± 0.06

Note—Data are mean ± SD. *t* tests for statistical significance were performed for uric acid (UA) versus all non-UA acid stones and for calcium oxalate plus brushite stones versus apatite stones. Differences were statistically significant in all comparisons ($p < 0.05$). A tin filter was used on all of the high-energy beams (see Table 1).