Quantification of Urinary Stone Volume: Attenuation Threshold–based CT Method—A Technical Note[1]

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Purpose: To compare two threshold-based computed tomographic (CT) methods for the quantification of urinary stone volume; to assess their accuracy and precision at varying tube voltages, tube currents, and section thicknesses in a phantom; and to determine interobserver agreement with each of these methods in a pilot clinical study.

Materials and Methods: After institutional review board approval, written informed consent was waived. The study was HIPAA compliant. Thirty-six calcium oxalate stones were scanned in an anthropomorphic phantom. For the fixed threshold method, stones were segmented with 0.6-mm-thick sections by using attenuation thresholds of 130 and 575 HU (equal to half of mean attenuation of all stones). For the variable threshold method, stones were segmented at an attenuation threshold equal to half of the attenuation of each stone and at variable section thicknesses (0.6, 1, and 3 mm), tube currents (150, 100, and 50 mAs [reference]), and tube voltages (100 and 80 kVp). Normalized Bland-Altman analysis was used to assess the bias and precision of the two CT methods compared with that of the fluid displacement method (reference standard). Two independent readers retrospectively measured stone volumes in 17 patients (male-to-female ratio, 1.4; mean age, 55 years), and interobserver agreement was assessed by using Bland-Altman limits of agreement.

Results: The variable threshold method was more accurate and precise than the fixed threshold method with an attenuation threshold of 130 HU ($P < .0001$). Thinner sections (0.6 and 1 mm) resulted in more accurate ($P < .05$) and precise ($P < .0001$) stone volume measurements than 3-mm-thick sections. With the variable threshold method, no significant difference was seen in the accuracy and precision of stone volume measurements at various tube currents and tube potentials. Interobserver agreement was high with the fixed and variable threshold methods ($r > 0.97$).

Conclusion: An attenuation threshold–based CT method can be used to quantify urinary stone volume even at low radiation doses. The most accurate and precise method utilizes variable attenuation derived from the attenuation of each stone and thin sections.

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Urolithiasis is a chronic and largely recurrent disease with a relapse rate of 50% in 5–10 years (1). Refractory pain, loss of work time, renal failure, and even death may result from recurrent urinary stone disease (2). Although there has been progress in the minimally invasive surgical and interventional management of stone disease (3), medical treatments play a pivotal role in preventing stones and inhibiting their growth in patients with metabolically active disease (4,5).

Unenhanced computed tomography (CT) is the initial imaging modality of choice for patients with acute flank pain, because it can be used to detect obstructing urinary tract stones and plan their management (6,7). Despite these advances, recurrent episodes of flank pain due to obstructing urinary stones continue to result in frequent visits to the emergency room (8). In patients with recurrent stone disease, CT is used also to depict the size, number, and location of urinary stones to assess metabolic activity—defined as stone growth or new stone formation in 1 year (9–11). Stone size has been typically described by using maximal axial diameter. However, this measurement is a poor indicator of stone volume and therefore not reflective of total stone burden, particularly because stones are often multiple and each stone typically has a complex three-dimensional shape (12,13).

Prior studies (13–21) have attempted to quantify urinary stone volumes by using CT. Yoshida et al (14) assessed

whether stone volume could be used to assess stone fragility before extracorporeal shock wave lithotripsy. Stone volume was calculated by summing all voxels with attenuation more than 100 HU. In another study (15), CT-based stone volume measurements were used to predict a stone-free state after extracorporeal shock wave lithotripsy. However, to the best of our knowledge, prior studies have not assessed the accuracy of a similar method to quantify urinary stone volumes.

Attenuation threshold–based CT methods have been developed to quantify the volume of calcium in the coronary arteries to assess vascular calcifications due to atherosclerosis (22–24). We believe that such methods could be applied both for diagnosis of urinary stones and at follow-up in patients with urinary stones to predict the success of urologic intervention, to determine if medical therapy is necessary, and to tailor medical treatments. The purpose of this study was to compare two threshold-based CT methods for the quantification of urinary stone volume; to assess their accuracy and precision at varying tube voltages, tube currents, and section thicknesses in a phantom; and to determine interobserver agreement with each of these methods in a pilot clinical study.

Materials and Methods

Reference Standard for Stone Volume

Our institutional review board approved the Health Insurance Portability and Accountability Act–compliant pilot clinical study prior to the retrospective review of patient CT images; written informed consent was waived. Thirty-six

calcium oxalate stones were obtained as deidentified samples from a human stone bank. The reference standard for stone volumes was determined by using a fluid displacement technique (25). Stone volumes were determined by measuring the stone mass (M_S) with a milligram balance (ALC-320.3; Acculab, Bohemia, NY) and by comparing measurements of the mass of the water-filled flask with stones with that without stones. Specifically, double-distilled water was introduced into a 1000-mm^3 volumetric flask and was measured to obtain water-filled flask mass (M_{FW}), water mass (M_W), and water density (D_W). Subsequently, each stone was placed within the flask, and the mass of the stone-containing flask filled with double-distilled water up to 1000 mm^3 was measured (M_{FS}). With this method, the stone volume measurement is based on the concept that the difference between the masses of the water-filled flask with the stone and without the stone is equal to the difference between the stone mass and the mass of the displaced water with similar volume to the stone. The mass of the displaced water equals the product of water density (D_W) and stone volume (V_S); therefore, the equation can be summarized as $M_{FS} - M_{FW} = M_S - (D_W \cdot V_S)$ or as $V_S = (M_S + M_{FW} - M_{FS})/D_W$. With repeated measurements of mass of a flask filled with double-distilled water, the standard error of this method was 6 mm^3.

Advances in Knowledge

- A CT attenuation threshold–based method can be used to quantify urinary stone volumes accurately and reproducibly; urinary stone volume quantification is most accurate with a variable attenuation method (bias = 2%, precision = 20%) and thin sections (0.6 and 1 mm).
- Urinary stone volumes can be quantified accurately with CT by using low tube currents (50, 100, and 150 reference mAs) and tube potentials (80 and 100 kVp).

Implication for Patient Care

- Accurate volumetric quantification of urinary stones may prove helpful in monitoring metabolic activity and tailoring medical treatments, as well as predicting the success of urologic interventions in patients with urinary calculi.

Phantom Experiment

Thirty-six calcium oxalate stones (size range, 1.1–11.8 mm by using a digital caliper) were embedded in ground meat with an attenuation (30 HU) comparable to the attenuation of unenhanced renal parenchyma. Subsequently, the embedded stones were placed within the slots (dosimetric holes) of a commercially available abdominal anthropomorphic phantom (Alderson Rando; Radiology Support Devices, Long Beach, Calif). The phantom was stabilized on the CT table by using adhesive tape and padding to avoid movement during table feed. The phantom was positioned at the gantry isocenter and was scanned with a 64–detector-row CT scanner (Sensation 64; Siemens Medical Solutions, Forchheim, Germany) with parameters used in our clinical practice for evaluation of patients with acute flank pain (120 kVp, 0.5-second gantry rotation time, 64 × 0.6-mm detector configuration, 1.2 beam pitch, and 200 mAs [reference]). The reference tube current (CARE Dose 4D; Siemens Medical Solutions) is a user-specified effective tube current (tube current divided by pitch) for obtaining desired diagnostic quality with the use of a combined modulation type of automatic exposure control at CT. The reference tube current value represents effective tube current for scanning a reference adult subject weighing 70–80 kg. The scanner estimates subject size from a localizer radiograph and increases the applied tube current relative to the reference tube current for individuals smaller than the reference adult subject and decreases applied tube current for larger individuals. In our department, all kidney stone CT examinations are performed by using this combined modulation technique for radiation dose optimization. Images were reconstructed at 0.6-, 1-, and 3-mm-thick sections with no overlap. The phantom was rescanned by using reference tube currents of 150 (applied effective tube current of 101 mAs), 100 (applied effective tube current of 67 mAs) and 50 (applied effective tube current of 33 mAs) mAs with other parameters held constant; it was then rescanned at tube potentials of 80 and 100 kVp while maintaining a constant CT dose index.

Of 36 stones, two were excluded because of gas in the adjacent ground meat. CT data were segmented (by using 0.6-mm-thick sections), and volumes for the remaining 34 stones were calculated by using commercially available software (OsiriX, Mac OS X, version 3.3.2; OsiriX Foundation, Geneva, Switzerland) and both fixed and variable threshold methods (26) (Fig 1). For the fixed threshold method, stones were segmented by using two fixed attenuation thresholds: 130 HU (the threshold used to determine coronary calcium volume) and an attenuation (575 HU) equal to half of the mean attenuation of all stones in the study (1150 HU ± 290 [standard deviation]). For the variable threshold method, stones were segmented by using individual attenuation thresholds equal to half of the measured mean attenuation of each stone. Attenuations were measured by positioning a region of interest within each stone by using a soft-tissue window setting (window width = 340 HU, window level = 40 HU) at the section containing the largest portion of the stone. The region of interest was selected as the largest circular or elliptical region contained entirely within the stone and not including the margins. To assess the effect of variable section widths by using the variable threshold method, stone volumes were also measured by using 1- and 3-mm-thick sections.

All measurements were performed by one observer (S.D., with 4 years of experience interpreting abdominal CT images) who was unaware of the reference standard stone volumes. All stone volumes were remeasured by using the reference standard after the phantom experiments to confirm the stability of the stones throughout the study.

Clinical Study

We retrospectively identified from a review of electronic medical records clinically indicated CT images obtained in 17 consecutive patients (10 men [mean age, 63 years; age range, 49–82 years] and seven women [mean age, 43 years; age range, 19–65 years]) with urinary stones between March 1 and March 30, 2009 by using our department's CT scanning stone protocol, as described above. Stone volumes were measured by using 0.6-mm-thick sections. There were 24 stones in 17 patients, six of whom had more than one stone; three patients had two stones, one patient had three stones, and one patient four stones.

Interobserver Agreement

Two independent observers (S.D.; M.L.S., with 7 years of experience interpreting abdominal CT images), who had not read the images clinically, measured the maximum axial diameter of urinary stones and determined stone volumes by using both the fixed and variable threshold methods to assess interobserver agreement. For the fixed threshold method, the stones were segmented by using an attenuation threshold equal to half of the average of the attenuation of all stones as determined by each observer separately. Both observers were trained initially by performing measurements in consensus for a set of 10 ureteral stones that were not included in the study. Both observers were aware of the number and locations of stones in each patient. All measurements were performed by using magnified (×10) transverse CT images and a soft-tissue window setting (window width = 340 HU, window level = 40 HU). Time required to perform volume measurements was recorded.

Statistical Analysis

To assess the accuracy and precision of volumes derived from the fixed and variable threshold methods compared with the reference volumes, a normalized Bland-Altman analysis was performed to evaluate the mean difference (ie, bias) and standard deviation of difference (ie, precision) between each CT method and the reference standard. For this purpose, values were normalized as measured value divided by reference standard × 100.

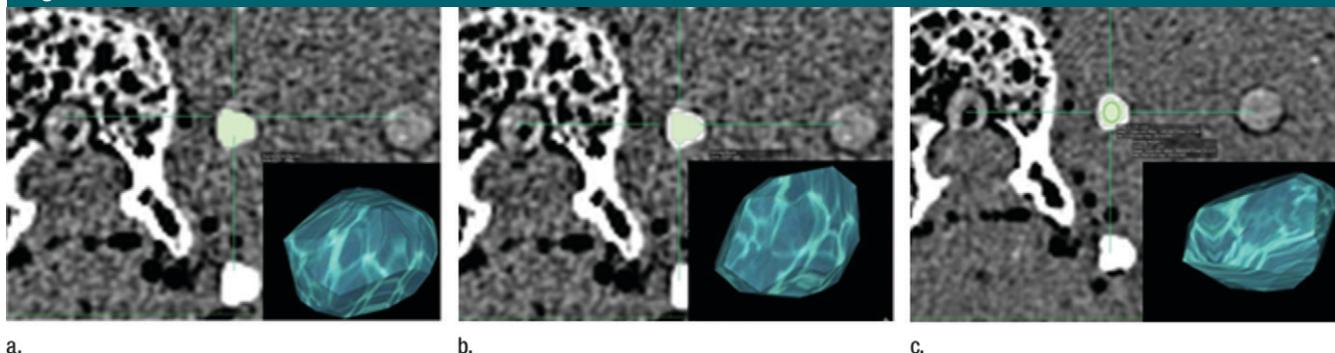To examine the effect of CT scanning parameters (section thickness, tube

Figure 1

a.   b.   c.

Figure 1: **(a–c)** Magnified ($\times$10) CT and reconstructed three-dimensional (lower right) images of urinary stone in a phantom with soft-tissue window setting (width = 340 HU, level = 40 HU). With the fixed threshold method, the stone volume measured 221 mm^3 and 135 mm^3 with segmentation threshold set at **(a)** 130 HU and at **(b)** 575 HU (half of the mean attenuation of all stones), respectively. **(c)** With the variable threshold method, the measured stone volume (115 mm^3) with segmentation threshold set at 700 HU (half of the stone attenuation of 1400 HU) was closer than with the fixed threshold method to reference standard stone volume (120 mm^3).

current, tube potential) on the accuracy and precision of the stone volume measurements, a one-way analysis of variance, followed by pair-wise comparisons with a Tukey test, was conducted for each parameter. Differences in bias were assessed by applying analysis of variance to differences, while differences in precision were assessed by applying analysis of variance to the squared differences. All comparisons were made to the volume measurements obtained with a CT scanning protocol used in our clinical practice with 0.6-mm section thickness.

To estimate interobserver agreement, Bland-Altman limits of agreement were calculated for the paired measurements between observers for each method. The mean of the two observers' measurements was used as an estimate of reference volume; for each method, the value used in the analysis was the difference (in percentages) between observer measurements divided by the mean of the two measurements for each stone. Pearson correlation between the two CT-based volume measurements was calculated to assess linear association between the two observers' measurements.

Statistical analysis of the data was performed with a software program (MedCalc, Mariakerke, Belgium). The means ± standard deviations of stone attenuations and volumes were determined for each protocol separately (Table 1).

Table 1

Stone Volume Measurements for Variable Threshold Method and Stone Attenuations at Scanning Parameters

Parameter	Stone Attenuation (HU)	Stone Volume (mm^3)	Bias (%)	Precision (%)
Section thickness (mm) (200 mAs [reference], 120 kVp)				
0.6	1150 ± 290	55.1 ± 51.2	2	20
1	1140 ± 280	54.3 ± 49.3	5	28
3	860 ± 330*	49.7 ± 49.2	26[†]	87[‡]
Reference tube current (mAs) (120 kVp, 0.6-mm section thickness)				
150	1130 ± 290	54.6 ± 50.6	2	22
100	1150 ± 300	52.8 ± 50	−1	22
50	1125 ± 275	52.2 ± 50	−2	22
Tube voltage (kVp) (with constant CTDI, 0.6-mm section thickness)				
100	1280 ± 380*	52.1 ± 49.4	−4	18
80	1440 ± 420*	52.7 ± 51.8	−4	21

Note.—Unless otherwise indicated, data are means ± standard deviations. Normalized Bland-Altman analysis was performed to assess the bias (ie, mean percentage differences between each CT method and reference standard) and precision (ie, standard deviation of percentage differences) of CT-based volume measurements. All were compared with the volume measurement obtained with CT protocol used in our clinical practice, with 0.6-mm section thickness. CTDI = CT dose index.

* = $P < .001$.

[†] = $P < .05$.

[‡] = $P < .0001$.

Results

Phantom Study

Fixed and variable threshold methods.— By using the fluid displacement technique as a reference standard, the mean stone volume was 55.2 mm^3 ± 51.9 (range, 4.1–213.5 mm^3). By using the fixed threshold method, accuracy and precision of mean CT stone volume (54.4 mm^3 ± 56) for an attenuation threshold of 575 HU (a value equal to half of the mean attenuation of all stones, 1150 HU) (bias = −10% [$P = .04$], precision = 30%) were superior to those of mean CT stone volume (112.9 mm^3 ± 91.8) for a threshold of 130 HU (bias = 147%, precision = 79%; $P < .0001$). With the variable threshold method using half of the
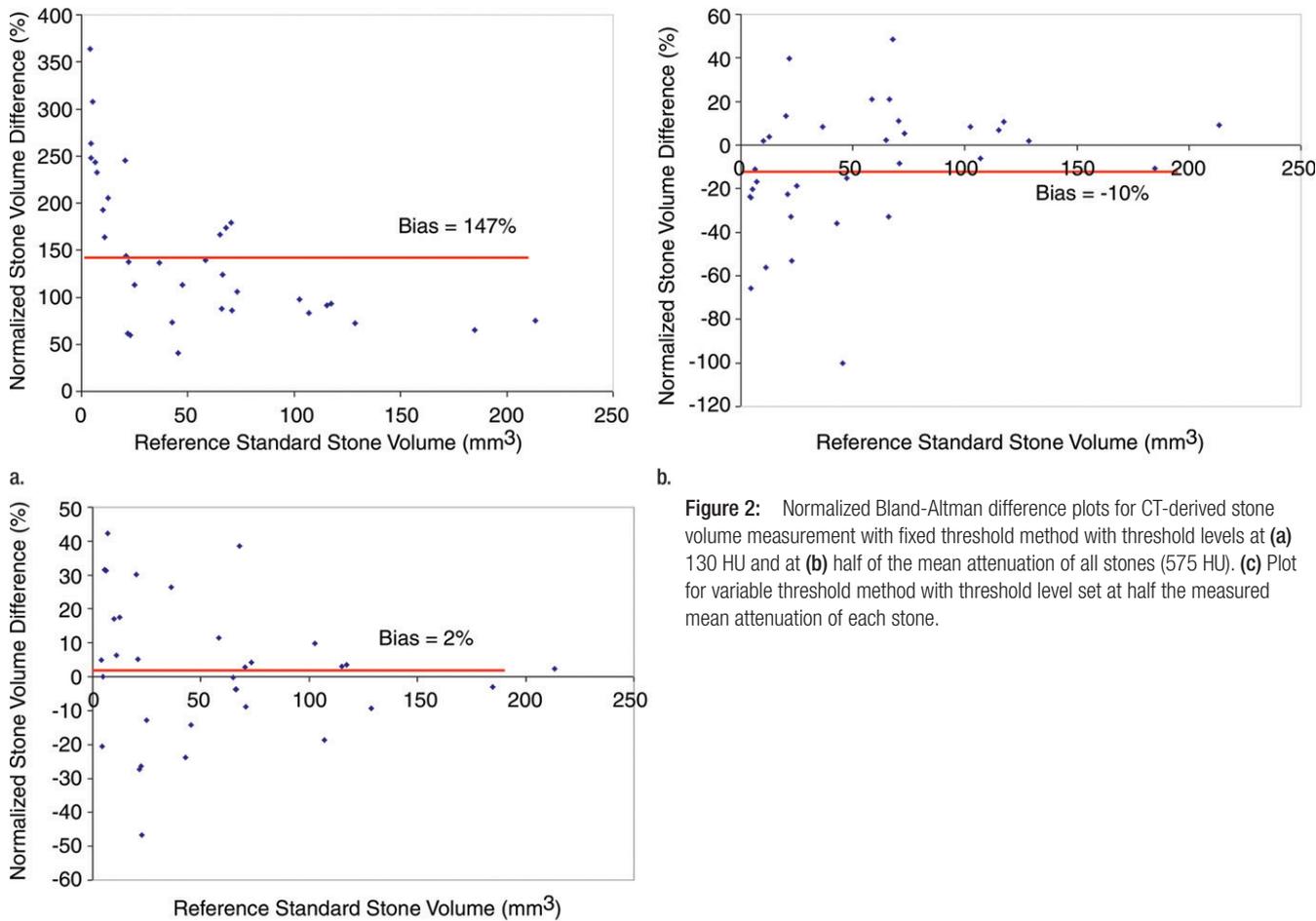
Figure 2

a.

b.

c.

Figure 2: Normalized Bland-Altman difference plots for CT-derived stone volume measurement with fixed threshold method with threshold levels at **(a)** 130 HU and at **(b)** half of the mean attenuation of all stones (575 HU). **(c)** Plot for variable threshold method with threshold level set at half the measured mean attenuation of each stone.

attenuation of each stone, the accuracy and precision (bias = 2%, precision = 20%) of mean CT stone volume (55.1 mm³ ± 51.2) were improved further compared with those of the fixed threshold method (Fig 2). For the variable threshold method, the volume of larger (>3 mm, n=24) stones (bias=1%, precision=19%) was more accurate and precise than that for smaller (≤3 mm, n = 10) stones (bias = 5%, precision = 23%).

Variable section thicknesses, tube currents, and tube potentials.—By using the variable threshold method, stone volume measurements with 0.6-mm-thick (55.1 mm³ ± 51.2; bias = 2%; precision = 20%) and 1-mm-thick sections (54.3 mm³ ± 49.3; bias = 5%; precision = 28%) were superior to stone volumes with 3-mm-thick sections (49.7 mm³ ± 49.2; bias =

26% [P=.02]; precision=87% [P<.0001]). All stones were detectable at lower tube currents and tube potentials. Bias and precision of volume measurements by using the variable threshold method at

variable tube currents (200, 150, 100, and 50 mAs [reference]) and tube voltages (120, 100, and 80 kVp; while maintaining a constant CT dose index) were not significantly different (Table 1).

Table 2

Interobserver Comparisons of Stone Maximum Axial Diameter and Volume Measurements by Using Fixed and Variable Threshold Methods in 17 Patients

Measurement	Mean Percentage Difference between Observers*	95% Limits of Agreement (%)	Correlation Coefficient*
Volume with fixed threshold method	8.7 (0.7, 16.7)	−25, 42.4	>0.99 (0.997, 0.999)
Volume with variable threshold method	5.3 (−3.3, 13.8)	−32.4, 45	0.974 (0.949, 0.99)
Maximum axial diameter	12.4 (7.9, 16.9)	−9, 34.4	0.98 (0.953, 0.991)

* Numbers in parentheses are 95% confidence intervals.

Clinical Study

The mean attenuations for urinary stones were 868 HU ± 410 for observer 1 and 834 HU ± 370 for observer 2. The observers independently used half of the mean attenuation of stones (434 and 417 HU, respectively) as attenuation thresholds for the measurement of stone volumes with the fixed threshold method. Interobserver agreement (Table 2) revealed that the Bland-Altman limits of agreement were narrowest for maximum axial diameter measurements in comparison with volume measurements with the variable and fixed threshold methods. Correlation coefficients derived from comparisons between each pair of observations indicated high correlation for each measurement ($r >$ 0.97). It took observers approximately 30 seconds to perform each volume measurement.

Discussion

We demonstrated that attenuation threshold–based CT methods can be used to quantify urinary stone volume accurately and with high precision; the variable threshold method was the most accurate (bias = 2%, precision = 20%). Threshold-based volumetric quantification methods have been applied in the assessment of coronary artery calcification (20–23) and pulmonary nodules (27). An attenuation threshold of 130 HU has been used to segment calcified vascular plaques (28). Therefore, we first chose an attenuation threshold of 130 HU to segment calcium oxalate stones by using the fixed threshold method; however, the stones with different attenuation were not accurately or precisely segmented (bias = 147%, precision = 79%). Volume measurements improved when a mean attenuation of all stones (575 HU) was used instead (bias = −10%, precision = 30%). However, the variable threshold method resulted in more accurate and precise stone volume measurement than the fixed threshold method. Fixed threshold methods do not consider partial volume effects (23). Marginal voxels, which are partially occupied by stone and partially by surrounding media, are difficult to segment accurately with a fixed attenuation threshold; the subsequent volume measurement typically either is under- or overestimated, because of too high or too low threshold levels, respectively.

Although previous studies have shown that 3-mm-thick transverse CT sections were sufficient for depicting small obstructing ureteral stones (29), we found that thinner CT sections (1 and 0.6 mm) yielded more accurate measurements of urinary stone volumes. Indeed, thinner sections have been found also to improve quantification of vascular calcification volumes (24). Although this has a zero radiation burden, given current CT protocol for acute flank pain, thin-section reconstruction and archival would be impractical for all patients suspected of having stones. However, for selected patients with known urolithiasis who may undergo serial imaging or urologic interventions, this method yields a more precise and accurate measurement of stone volume and burden. The 30-second postprocessing time is considered negligible in comparison with the additional reconstructions and image archival.

Stone volume measurements with the variable threshold method were just as accurate and precise with tube currents as low as 50 mAs [reference] with applied effective tube current of 33 mAs. Patients who have metabolically active disease may require many CT scans during their lifetime; these scans could result in substantial cumulative radiation exposure (30). Therefore, low-dose CT scans would be advantageous to implement in clinical practice because stone detectability has been shown not to be compromised with a tube current of 50 mAs or lower for multi–detector row CT scans (31). The same CT scanning protocols could be used to quantify stone volumes. For the variable threshold method, urinary stone volume measurements were not affected by lower tube voltages. As expected, the attenuation threshold level increased because it was derived from higher attenuations of individual stones at lower tube voltages.

In addition to accuracy and precision, a CT-based method of quantifying urinary stone volumes should be reproducible so that it can be used to track changes in stone volume over time. Interobserver variability is an important quality to assess because often different radiologists interpret serial CT images. Our findings were similar to the results of a study (32) of colorectal polyps in which interobserver agreement for linear and volumetric measurements of polyps were compared. Although limits of interobserver agreement were wider for stone volume measurements than for maximum axial diameters, this increased interobserver variability may be acceptable because volume is a more reliable indicator of stone burden. An interval increase in stone diameter is accompanied by a greater percentage increase in volume. Therefore, volume measurements can reveal the same change in stone size with a wider limit of interobserver agreement than required by diameter measurements.

Volume measurements may also be useful in caring for patients with acute flank pain and after urologic interventions. Bandi et al (15) have shown that stone volume is a good predictor of stone-free status after extracorporeal shock wave lithotripsy. Volumetric information may replace axial stone diameter in predicting spontaneous passage of obstructing ureteral stones and determining whether to recommend ureteroscopy, extracorporeal shock wave lithotripsy, percutaneous nephrolithotomy, or conservative management (14–21).

Our study had several limitations. First, our phantom study was limited to calcium oxalate stones, the most common stone encountered in clinical practice, but the data may not apply to other stone types. Because an optimal attenuation threshold for determining stone volume is dependent on stone composition, an attenuation threshold–based CT method for measuring the volume of other stone subtypes may yield different results. Measurements of stones imbedded in an anthropomorphic phantom were not subject to respiratory motion or adjacent radio-opaque surrounding structures (eg, nephrostomy), both of which could make stone segmentation

more difficult. In the phantom study, the observer was blinded to the reference standard volume measurements but not to the parameters of CT protocol when measuring the stone because it was obvious to the observer which images were thin section and which protocols utilized a low dose because of the presence of more noise. The accuracy and precision of volumetric quantification of urinary stones were not reassessed in the clinical study. We have shown that the variable threshold method for volumetric quantification of stones larger than 3 mm is more accurate and precise for than stones 3 mm or smaller. However, this method of assessing for change in stone size might not be applicable to small stones. Finally, we used the fluid displacement technique as the reference standard for the urinary stone volumes. This method also has measurement error, particularly in small stones. For example, stones 1 mm in diameter have volume smaller than our reference standard error range. However, this error did not affect our ability to compare the two CT-based methods.

In conclusion, we described a CT-based method of quantifying urinary stone volume. A method that uses a variable stone attenuation (equal to half of the measured mean attenuation of each stone) yielded more accurate and precise volume measurements than a method that uses a fixed attenuation threshold. The pilot clinical data showed that this method can be used to reproducibly quantify stone volume in patients with urolithiasis. The variable attenuation method can be used as a research tool in future studies to correlate interval changes in CT-derived stone volume with traditional indexes of metabolic activity, such as urine biochemical composition in stone formers, and to predict the success of urologic interventions.

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