Title page

Can dual energy CT with fast kV-switching determine renal stone composition accurately?

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Abstract

Rationale and objectives

To determine whether a single source CT system utilizing fast kV switching and low dose settings can characterize (diameter and chemical composition) renal stones accurately when compared infrared spectroscopy

Materials and methods

The chemical composition of 15 renal stones was determined using Fourier transform infrared spectroscopy. The stones were inserted into a porcine kidney and placed within a water tank for CT scanning using both fast kV switching dual energy and standard protocols. Effective atomic number of each stone was measured using scanner software. Stone diameter measurements were repeated twice to determine intra-rater variation and compared to actual stone diameter as measured by micro CT.

Results

The chemical composition of three stones (1 calcium phosphate and 2 carbonite apatite) could not be determined using the scanner software. The composition of 10/12 remaining stones was correctly identified using DECT (83% absolute agreement; k=0.69). No statistical difference (p=0.051) was noted in the mean stone diameter as measured by clinical CT and micro CT.

Conclusion

DECT using fast kV switching may potentially be developed as a low dose clinical tool for identifying and classifying renal stones in vivo supporting clinical decision-making.

Keywords

Renal Stone; urolithiasis; dual energy computed tomography; micro CT

Introduction

Non-contrast computed tomography is the first-line imaging modality for patients with acute flank pain (1-3). However, the associated radiation risk remains a concern, particularly as the incidence of renal stones has increased over the recent years due to increasing levels of obesity and lifestyle changes both among children and adults (4-6). The chemical components of renal stones vary depending on the underlying causal agent. Calcium Oxalate (CaOx) stones are the most commonly occurring stone types accounting for 70% of cases while calcium phosphate, uric acid and cystine account for about 20%, 8% and 2% of cases respectively (7). Other stone types such as struvite occur more rarely; however, it is crucial that the chemical composition of the stone is accurately determined as this will guide the clinician in treatment planning (e.g. shock wave lithotripsy (SWL); endoscopic stone removal; lifestyle changes; pharmacological intervention) (7, 8). Spectral analysis of renal stones for analyzing chemical composition is advocated within clinical guidelines, (9) but can only be performed where the stone has been surgically removed or collected after spontaneous passage. Reliable in vivo stone analysis could have major importance for choice of treatment; i.e. if imaging clearly defines the stone as a cystine stone, this will direct the clinician to endoscopic methods for stone management, since cystine calculi are most often SWL resistant. Furthermore, such a finding would prone the clinician to perform an early metabolic evaluation, in order to start stone preventive therapy. Another example could be imaging clearly showing uric acid that often may be treated my oral litholysis, sparing patients for invasive treatments, and directing the clinician to look for metabolic syndrome (MS), since uric acid stone stone disease is often linked to MS that would need dietary advices for both stone prevention and other potential harmful effects of MS. In both these examples in vivo stone analysis potentially could change clinical management and lead to earlier prenventive measures, thereby personalizing stone management up-front.

For in vivo stone composition determination, the Hounsfield Units (HU) derived from standard 120kV single energy Computed Tomography (CT) have been proposed as an alternative approach with good ability to differentiate uric acid from calcium stones (10), although accuracy of classification is acknowledged to be influenced by stone size (11). The ability of single energy CT to differentiate between the less common cystine and struvite stones is recognized to be limited due to similarity and overlap in density and recorded HU values (12). In contrast, dual energy CT (DECT) using two x-ray tubes has been shown to be reasonably effective in differentiating between all stone types (13-21), but this technology is not routinely available within the general clinical setting and therefore its application to clinical practice is limited. Only a small number of studies have considered alternative approaches to achieving dual energy CT (e.g. sandwich detector; fast kV switching) (7, 12, 22-25). Importantly, studies evaluating sandwich detector technologies found low accuracy in chemical stone composition, especially at low dose (24, 25). In contrast while those studies considering fast kV switching reported inconsistent findings in the accuracy of chemical composition analysis, although it was noted that the CT technology used (40mm detector coverage) did not reflect scanner quality currently available (80-160mm detector coverage). No study using fast kV switching or sandwich detector technology as a method of dual energy CT imaging has specifically considered low dose (effective dose <3mSv (26)) scanning options in the detection and analysis of renal stones. Further, existing studies have focused their analysis on stones measuring >5mm. This experimental study was undertaken to determine whether a single source CT system (80-160mm detector coverage) utilizing fast kV switching, larger z-coverage and low dose settings may characterize renal stones accurately when compared to infrared (IR) spectroscopy as the laboratory reference standard.

Materials and methods

As this was an experimental study using a porcine kidney acquired from the meat industry, ethical approval was waived in accordance with Danish legislation and approval for data acquisition regarding stones was provided by the hospital manager (Journal no. 19/33519).

Micro-CT analysis

Fifteen renal stones were percutaneously removed from 15 patients (8 female, 6 male, 1 unknown; median age 53 years, age range 13 - 74 years) and chemical composition was determined using Fourier transform infrared (IR) spectroscopy. The largest diameter of the stones was determined using a Scanco µCT50 (5 stones) or Scanco VivaCT40 (10 stones) micro CT scanner (Scanco Medical, Brüttisellen, Switzerland) with a tube voltage of 70 kV, tube current of 114 µA, 0.5 mm Al physical filter and 1200 mgHA beam hardening correction. The voxel size was 5 and 10.5 µm in the two scanners, respectively. Each stone was positioned in the bottom of a Ø9mm tube and fixed with foam to avoid movement during scanning. The stones were manually contoured on 2D images and segmented using the scanner workstation and 3D renderings were generated and the maximum diameter was measured (Fig. 1). The dimension of each stone was measured in the x, y and z planes with the largest diameter considered representative of stone size.

Experimental setup

The experiment replicated the approach taken by Talso et al (2018) (27). The stones were individually inserted into a porcine kidney partly opened with a coronal cut (Fig. 2). The porcine kidney was immersed in a 36 x 39 x 17cm water tank filled with 12 liters of tap water to mimic the absorption of human tissue (Fig. 3) and scanned using a GE Revolution CT scanner (GE Healthcare, Waukesha, IL, USA). Scans were acquired using both fast kV switching dual energy

technique and standard helical protocol to permit comparison of radiation dose. Scan parameters are listed in table 1.

Image analysis

The images were analyzed by a senior radiographer (BM) with >20 years of experience using a GE Advantage Workstation Volumeshare 7 (GE Healthcare, Waukesha, IL, USA). A circular 1.82 mm^2 region of interest (ROI) was positioned in the center of each stone using the three orthogonal planes to guide ROI positioning. Effective atomic number (Z_{eff}) histograms were created for the ROIs and the histograms were compared with the Z_{eff} of preprogrammed scanner library of different materials (NIST curves, National Institute of Science and Technology) (Fig. 4). The observer was blinded to the chemical composition of the stones as determined by IR spectroscopy. Maximum stone diameter was measured using window-width of 300HU and window-level of 35HU and repeated after one week to determine intra-rater variation. Mean attenuation and noise was measured in water and kidney tissue using a 10 mm circular ROI. All image analyses were performed using 0.625 mm slice thickness.

Statistical analysis

Continuous variables were summarized by descriptive statistics. Absolute agreement between IR spectroscopy and DECT composition analysis was determined and Cohen's kappa calculated and interpreted according to the thresholds outlined by Landis and Koch (28). Stone diameter, as measured by clinical CT and micro CT, was tested for normality using the Shapiro-Wilk test and differences were tested using paired t-test. A Bland-Altman plot was generated for assessment of limits of agreement between repeated measurements. All analyses were performed using STATA/IC 16.0 (StataCorp. LP, College Station, TX, USA).

Results

While 15 stones were scanned and included in the analysis of stone diameter, 3 stones (1 calcium phosphate and 2 carbonite apatite) were excluded from the composition analysis due to the underlying composition data being absent from the CT scanner library of different materials.

Stone diameter and composition

No statistical difference (p=0.051) was noted in the mean stone diameter as measured by clinical CT (mean 4.0 mm; SD=1.18; range 2.2-5.1mm) and micro CT (mean 3.5mm; SD=1.6; range 0.88-6.22mm) or between first and second measurement in clinical CT (mean difference 0.04 mm, p=0.3). The Bland-Altman limits of agreement for the repeated measurements also illustrated narrow variation in measures (-0.25 to 0.33 mm) (Fig. 5).

The composition of 10/12 stones was correctly identified using DECT (83% absolute agreement; Cohen's kappa 0.69). All cystine, uric acid and struvite stones were correctly identified. The brushite stone was characterized as CaOx and one CaOx stone was characterized as cystine (Table 2).

Radiation dose

The mean Dose-Length Product (DLP) was 185.29 mGy*cm (SD 3.94) in DECT versus 68.95 mGy*cm (SD 3.41) in single energy mode. Using the conversion factor proposed by Dougeni et al (2012) (29) the measured DLP values translate into an estimated effective dose of 2.78 mSv and 1.03 mSv for dual and single energy mode respectively.

Discussion

In this experimental ex-vivo study using a porcine kidney, we found substantial agreement between infrared spectroscopy and DECT based characterization of renal stone type. The results are in line with previous studies performed using an older scanner model (12, 22). However, we have demonstrated that accurate stone classification can be achieved using a substantially lower radiation dose opening up the possibilities for wider clinical application for renal stone screening using CT technology. While the data from this study is not directly comparable to previous studies, our findings provide new insights into technological advances and opportunities for dose reduction. Importantly, previous authors have reported CTDIvol estimates of 19.11 mGy (23) and 10.73 mGy (22) in DECT, estimates at least 34% greater than that achieved in current study (Table 1). Our study also adds clinical legitimacy to stone diameter measurements undertaken by clinical CT as it included stones ranging in diameter from 0.88-6.22mm (mean diameter 3.5mm), whereas previous studies had a wider range including larger stone diameters (mean diameters >5mm).

While agreement in chemical composition between IR spectroscopy and DECT was not perfect, the results suggest that stone composition may be determined using fast kV switching DECT. The erroneous results for the brushite stone was probably related to rounding of the numeric result to nearest chemical element as the effective Z of brushite is 14.1 versus 13.8 for CaOx (i.e. a difference <0.5) making the difference problematic to detect (30). In contrast, the cystine stone characterized as CaOx was particularly small (diameter of 3.2 x 3.1 x 1.7 mm as measured by micro CT) and we speculate that the erroneous classification may be a result of partial volume effect as the smallest diameter measurement was less than three pixels. However, other stones of similar sizes were correctly characterized and so further work is required to confirm this.

Limitations

This study has a number of limitations. Firstly, the study included only a small sample of renal stones compared to previously published studies. However, these stones were generally small in diameter and better reflected current clinical investigative referrals, particularly where CT screening is in place. The composition of the stones in the sample was also not representative of a normal clinical sample, since a greater proportion of cystine stones was present. However, this does not invalidate the measurement data or the CT composition data presented above. The study did not differentiate between calcium monohydrate and calcium dihydrate which would be important from a clinical perspective, but at present it is not possible to distinguish between the two with the current technology. In an experimental study Duan et al (2013) (30) suggested analyzing the roughness of the stone surface using a shape index. The authors demonstrated reasonable accuracy, but apparently the method has not yet been tested clinically and it is not generally available. A further limitation was the use of a water tank of fixed size as this did not reflect the complexity of the abdomen or diversity of patient body habitus. Further studies investigating the clinical feasibility in vivo are needed and NIST curves for materials such as carbonite apatite must be incorporated into the scanner software and tested before implementation. In addition, it must be noted that while the dose in both single and dual energy CT was relatively low in this study, the DECT protocol, if adopted, would expose a patient to approximately 3 times the radiation dose (CTDIvol 7.15mGy) compared to standard single energy CT (CTDIvol 2.60mGy) and clinical assessment of its implementation should be undertaken. The dose difference in DECT is caused by a conservative protocol setup with restricted tube current modulation aiming to ensure data quality in the low kV dataset, and further investigation with regard to dose reduction is needed.

Conclusion

In conclusion, DECT with fast kV switching has very promising potentially as a clinical tool for identifying and classifying renal stones. Further research is needed before DECT with fast kV switching can be implemented as first line imaging tool in clinical practice.

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Figure and table legends

Fig. 1 Three-dimensional rendering (left) and a micro CT cross section of a Ø6.2 mm cystine stone (right)

Fig. 2 Renal stone (arrow) positioned in the pelvis of a porcine kidney.

Fig. 3 Porcine kidney immersed in a water tank with the kidney positioned in a smaller plastic container glued to the water tank to keep the kidney in place during the scan procedure.

Fig.4. ROI positioned in a cystine stone (left) and the corresponding histogram showing the effective atomic numbers in the ROI (right).

Fig. 5 Bland-Altman plot of repeated stone diameter measurements. The upper and lower horizontal lines indicate limits of agreement and the middle line indicate mean difference between the measurements. N=15.

All figures should be reproduced in color

Table 1 Scan parameters in standard helical and dual energy mode (*Adaptive Statistical Iterative Reconstruction)

Table 2 Agreement between IR spectroscopy and DECT composition analysis.

Table 3 Mean attenuation (HU) and standard deviation (SD) in water and kidney tissue measured in standard helical and dual energy CT

Figure 1

Click here to access/download;Figure;Fig 1 micro CT cystine stone.jpg

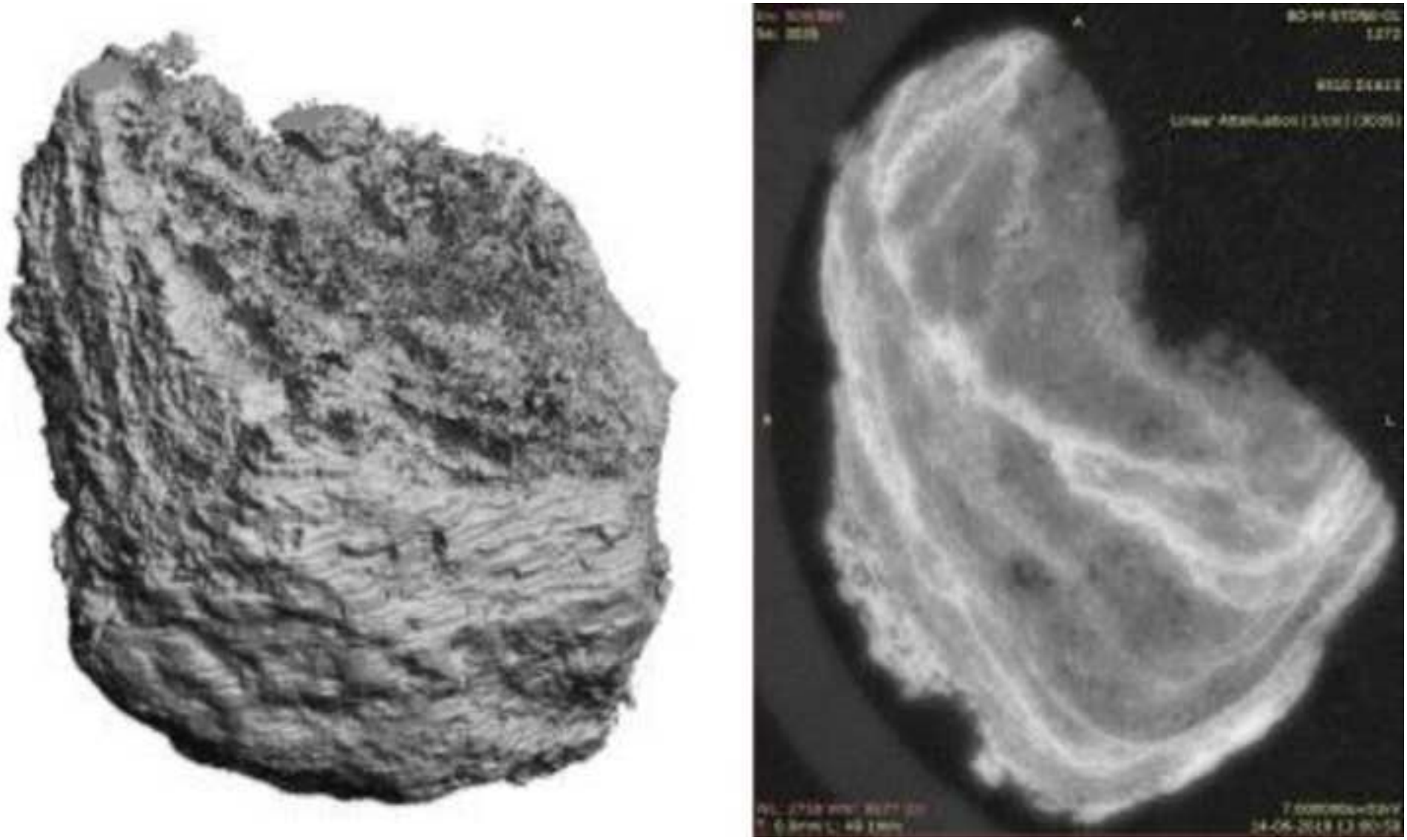

Figure 2

Click here to access/download;Figure;Fig 2 Stone in kidney.jpg

Figure 3

Click here to access/download;Figure;Fig 3 kidney water tank.jpg

Figure 4

Click here to access/download;Figure;Fig 4 ROI.jpg

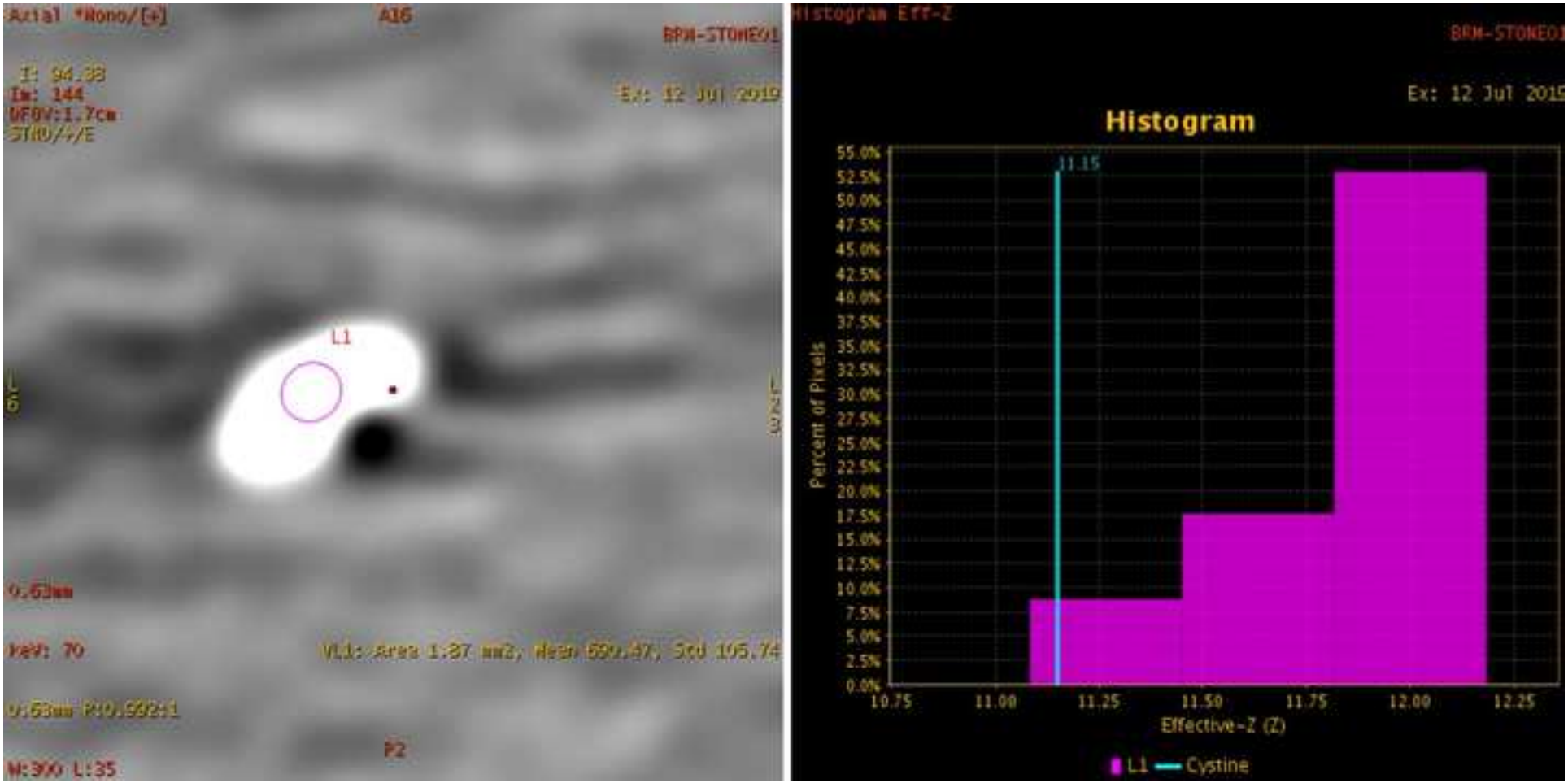

Figure 5

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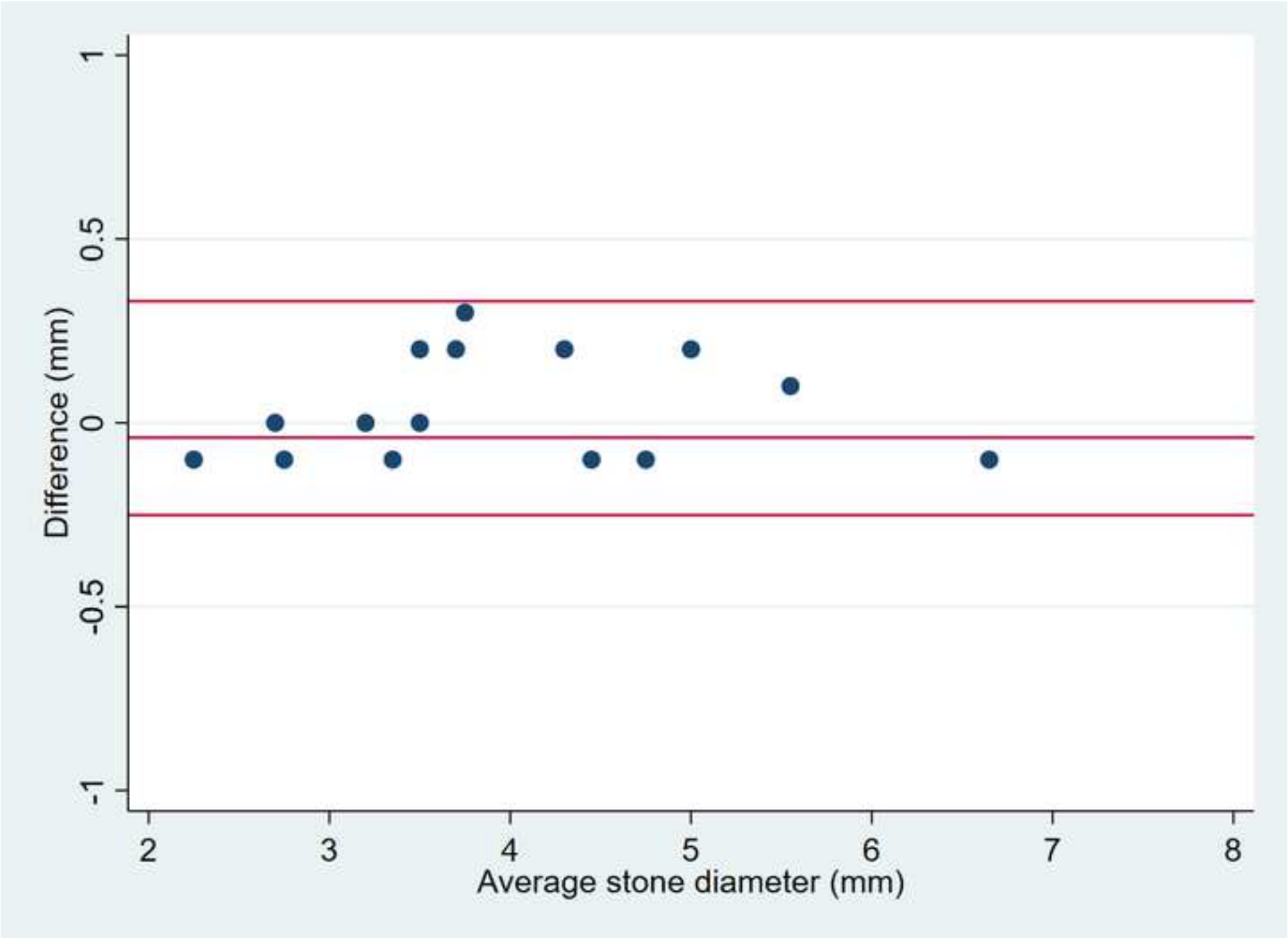

Table 1

	Standard helical	**Dual energy**
Tube voltage (kV)	120	80/140 fast kV switching
Image Quality Metric	Noise Index 27	Noise Index 27
Reconstruction	40 % ASiR V*	40% ASiR V*
Pitch	0.992	0.992
Rotation time	0.5	0.8
Bowtie filter	Body	Body
Detector configuration	128x0.625	128x0.625
Scan range	195 mm	195 mm
$CTDI_{vol}$	2.60 mGy	7.15 mGy

Table 2

Composition	**n**	**No. correctly identified**
Cystine	7	7
Calcium Oxalate	2	1
Uric acid	1	1
Struvite	1	1
Brushite	1	0
Total	12	10

Table 3

	HU_{Water}	HU_{Tissue}	SD_{Water}	SD_{Tissue}
Standard helical CT	0.9	49.8	25.8	22.0
Dual energy CT	1.6	47.9	23.6	21.0
Difference	0.7	-1.9	-2.2	-1
p-value	0.83	0.40	0.10	0.28

Abbreviations

CaOx	Calcium Oxalate
HU	Hounsfield Units
CT	Computed Tomography
DECT	Dual Energy Computed Tomgraphy
IR	Infrared (spectroscopy)
CTDIvol	Volumetric Computed Tomography Dose Index
MS	Metabolic Syndrome
NIST	National Institute of Science and Technology