



Demonstrating the Efficacy of Dual Energy Computer Tomography with Gemstone Spectral Imaging Software to Determine Mixed and Single Composition ex vivo Urolithiasis

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Objective: To assess the capability of determining the mixed chemical composition of urinary stones using spectral imaging properties of Dual Energy Computed Tomography (DECT) Gemstone Spectral Imaging (GSI) software.

Material and Methods: Twenty-six single and 24 mixed composition ex vivo urinary stones with known chemical composition determined by Fourier-transform infrared spectroscopy (FTIR) prior to this project were scanned with DECT imaging and GSI in vitro. The major components of the stones included Uric Acid (UA), Calcium Oxalate (CaOx), Calcium Phosphate (CaP), Magnesium Ammonium Phosphate (MAP), and Cystine (Cys). A histogram to display the distribution of the effective atomic number (Z-eff) of each pixel of the tested area, spectral curve (40–140 keV, with 10 keV interval) and Hounsfield Units (HU) of each stone scanned was provided with analysis of monochromatic images at 140 keV in the axial plane.

Results: The overall pooled sensitivity, specificity, and accuracy of DECT for identifying major stone composition were 0.802, 0.831, and 0.807, respectively, with a 95% confidence interval. Accuracy was 100% for identifying UA and Cys stones.

Conclusion: DECT is a superior imaging modality when compared to low dose computed tomography kidney ureter bladder scans. It allows for improved characterization of major components of urinary stones, in an accurate, non-invasive approach to pre-treatment. This can translate to urologists having greater confidence in determining patient suitability for medical or surgical management of their renal stones, in clinical practice.

Keywords: endourology, basic research, dual energy computer tomography, DECT, GSI, gemstone spectral imaging

Introduction

Urolithiasis is a common pathology treated by urologists. The prevalence ranges from 1% to 13% worldwide, with an incidence of 0.13% per year in Australia.¹⁻³ Treatment options for urolithiasis are determined by a number of variables, such as location, stone size, composition and morphology.^{4,5} Stone composition in particular helps determine the need for surgical or medical intervention. The most common stone compositions include calcium oxalate (70%), calcium phosphate (20%), uric acid (8%), and cystine (2%), with others being quite rare.^{6,7} Uric acid stones are suitable for medical management in the form of oral chemolysis via alkalization of the urine with sodium bicarbonate, titrating to a pH of 7.0–7.2, with a success rate as high as 70–80%.^{4,8} In addition to this, calcium phosphate, calcium oxalate and cystine stones are of particularly high density which makes their management resistant to shockwave lithotripsy and more suitable for more invasive options.^{4,9} This makes distinguishing stone composition an area of interest as it provides insight and guidance into treatment options.

Low-dose non-enhanced computed tomography Kidney, Ureter and Bladder (CT KUB) is the current gold standard for diagnosing urolithiasis, with sensitivity of 94–100% and specificity of 97%.^{5,10} However, due to its single energy it is limited in evaluation of stone compositions due to the overlap between attenuation values of different stone types.¹¹ Dual-energy CT (DECT) is a recent development which utilises a combination of high-energy and low-energy scanning (80 and 140 keV) during a single acquisition to measure the attenuation of different tissues, which allows for identification of the composition of a tissue/material.^{5,9,11,12} This technique is being used to differentiate between compositions of urinary stones to assist in treatment.¹³ In combination with DECT, Gemstone Spectral Imaging (GSI) Software[®] (GE Medical Systems, LLC. Waukesha, WI, U.S.A) can be used to provide the image processing and analysis by comparing stones to a reference based on Zeff and Hounsfield spectral curves. Studies thus far have reported DECT as having near 100% sensitivity and specificity for characterizing the chemical composition of renal stones greater than 3mm, into UA vs NUA.^{14–17} Further, a prospective study in 2016 showed how DECT can change planned management in 5% of patients due to characterisation of the urinary calculi.¹⁸ Majority of these studies have been completed on pure or nearly pure stones. Most stones, however, are composed of a mixture of different compositions, with pure single stones only accounting for a small proportion.⁵

Objective

Our study aims to determine how well DECT can distinguish mixed stone compositions, in addition to determining single stone compositions instead of classifying them as UA or NUA, utilising CT Gemstone Spectral Imaging Software[®] (GE Medical Systems, LLC. Waukesha, WI, U.S.A). This will provide more evidence to support the use of DECT as the standard protocol when imaging urinary calculi.

Method

Preparation of Urinary Stones

Fifty urinary stones with known mixed and single chemical composition were collected from a local biochemical laboratory. The chemical composition of each stone was determined by Fourier-transform infrared spectroscopy (FTIR) prior to this project commencing. This was done by sampling a fragment of a larger stone while retaining the residual fragments. Stones were deemed to have a major component if the composition was greater than 25% and minor if it was less than 25%. The largest of the remaining fragments were used for our test. These were placed on an agar plate for stability while undergoing the imaging.

Scanning of Urinary Stones

The urinary stones on each agar plate were scanned with a GE Revolution CT[®] scanner (GE Medical Systems, LLC. Waukesha, WI, U.S.A) together with the CT Gemstone Spectral Imaging (GSI)[®] software (GE Medical Systems, LLC. Waukesha, WI, U.S.A). The scanning was done in a blinded manner by the radiographer. The data is then transferred to a separate CT workstation with GSI enabled (Advantage Windows, version 4.5; GE Healthcare).

Image Processing

A region of interest (ROI) is selected in GSI software over the maximal axial dimensions of the calculi. The software is then able to produce four Graphs/Images for each stone (Histogram/Spectral HU Curve/Monochromatic image with ROI and HU/Scout Image) an example of this is shown in [Figure 1](#).

GSI Results

[Figures 1](#) and [2](#) provide an example of the data obtained for each individual stone scanned. [Figure 1](#) is a histogram of the Z-eff score. The software analyses the voxels within the region of interest of the stone to create the individual bars of the graph. The bars of the graph correlate to a predicted Z-eff score and the overall approximate percentage composition at that score.

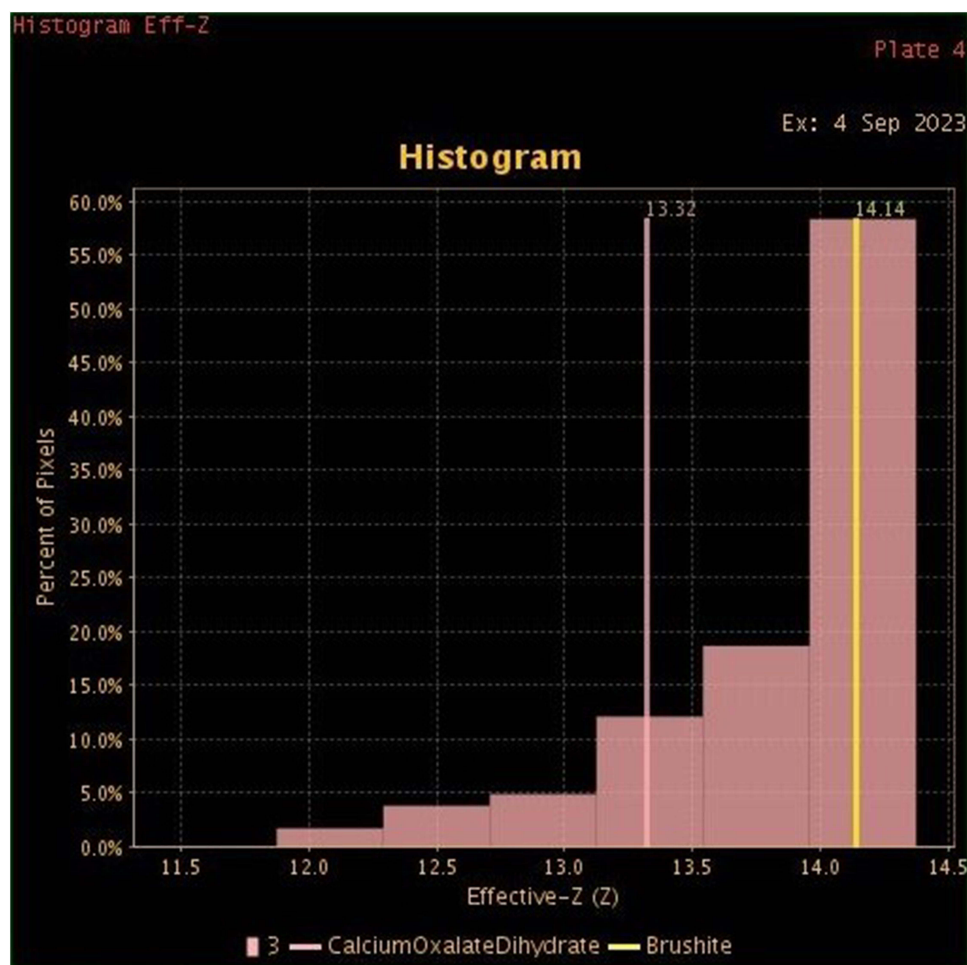


Figure 1 Example of effective Z histogram for the region of interest of the specific stone analysed.

Further, a spectral HU curve as shown in Figure 2 is created by plotting the recorded HU levels of the ROI at the various energy levels (40–180 keV, with 10 keV interval). There is a standard deviation of HU for each energy level.

Figure 3 highlights a monochromatic image of the target stone and ROI selected being scanned with the mean HU assessed at 140keV.

Analysis of GSI Results

A trained radiographer analysed each stone scan using the spectral histogram and spectral HU curves developed for each stone ROI with the GSI software. This was done in a blinded manner.

Reference Z-eff scores of certain stone types can be added to the histogram to assist in composition identification. These can be either uric acid (6.95), MAP (9.74), cystine (11.02), calcium oxalate dihydrate (13.32), and brushite (14.14). Reference HU curves added to the ROI spectral HU curve these can be either uric acid, MAP, cystine, calcium oxalate dihydrate and brushite an example shown in Figure 2.

Using the references from the software with the histogram and spectral curves, a result of composition is established that best fits the software reference.

The results were recorded and then correlated to the known chemical composition previously determined of the stone fragment using FTIR. Statistical analysis of the results was conducted using IBM® SPSS® V.28 (IBM Corporation, New Orchard Road, Armonk, NY, U.S.A.).

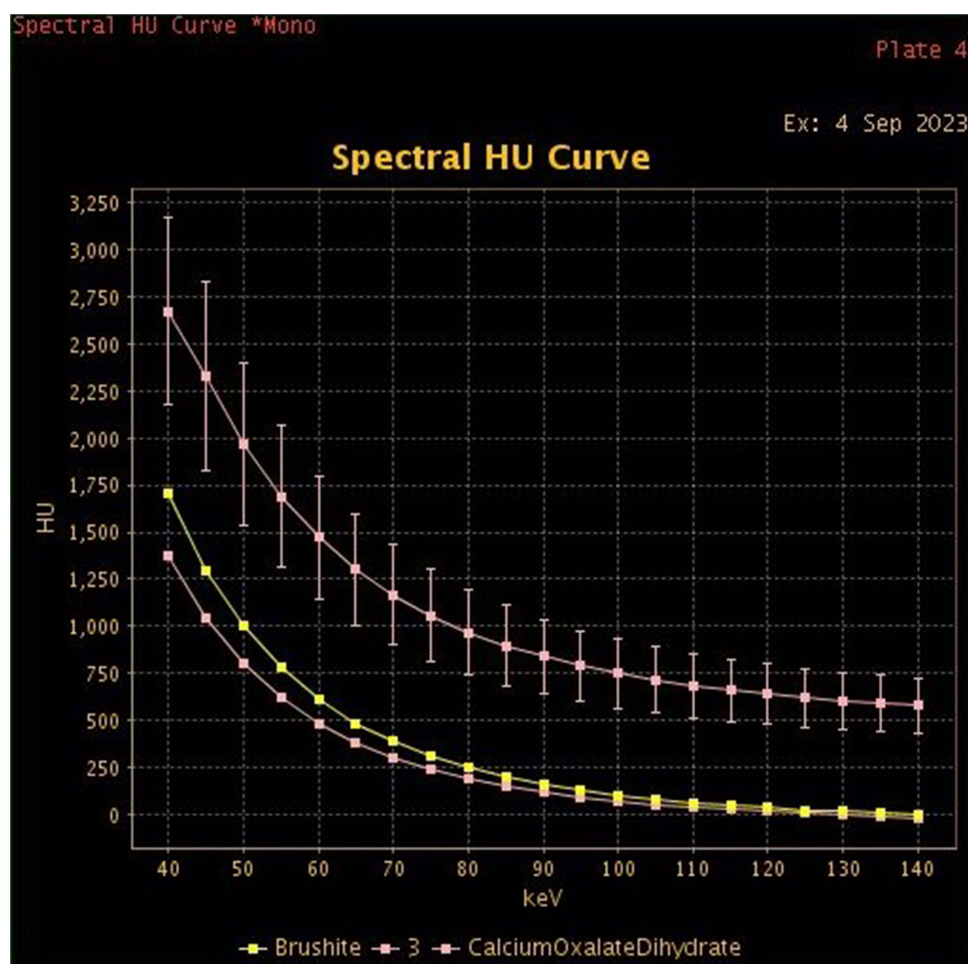


Figure 2 Example of a spectral Hounsfield Unit curve obtained for the region of interest of the specific stone analysed.

Abbreviations: HU, Hounsfield Units, KeV; Kiloelectron volt.

Results

The laboratory stone compositions, stone size and GSI results at 140 keV are listed in [Table 1](#).

There were a total of 26 pure stones and 24 mixed composition stones. Of the pure stones, 7 were uric acid (UA), 8 calcium oxalate (CaOx), 2 calcium phosphate (CaP), 3 Magnesium Ammonium Phosphate (MAP), and 6 Cystine (Cys) stones. With the mixed stones, there were 11 MAP/CaP, 10 CaOx/CaP, 2 UA/CaP, and 1 UA/CaOx stones.

The accuracy in determining each stone type is shown in [Figure 4](#). DECT correctly identified the major component of 44 of 50 stones, 22 pure and 22 mixed composition stones. When differentiating between UA vs NUA alone, DECT identified all 8 of 8 UA stones correctly.

The sensitivity, sensitivity, and accuracy of DECT in determining the different stone compositions are reported in [Table 2](#). Overall pooled sensitivity, specificity, and accuracy of DECT in identifying major stone composition were 0.802 (95% CI: 0.696, 0.908), 0.831 (95% CI: 0.784, 0.878), and 0.807 (95% CI: 0.760, 0.854), respectively.

Discussion

Sensitivity and Specificity

The use of CT KUB for the identification of urolithiasis has been widely established as the gold standard. However, when it comes to further characterization of the urinary stone, there is growing evidence demonstrating that DECT has better sensitivity and specificity compared to CT KUB.¹⁹

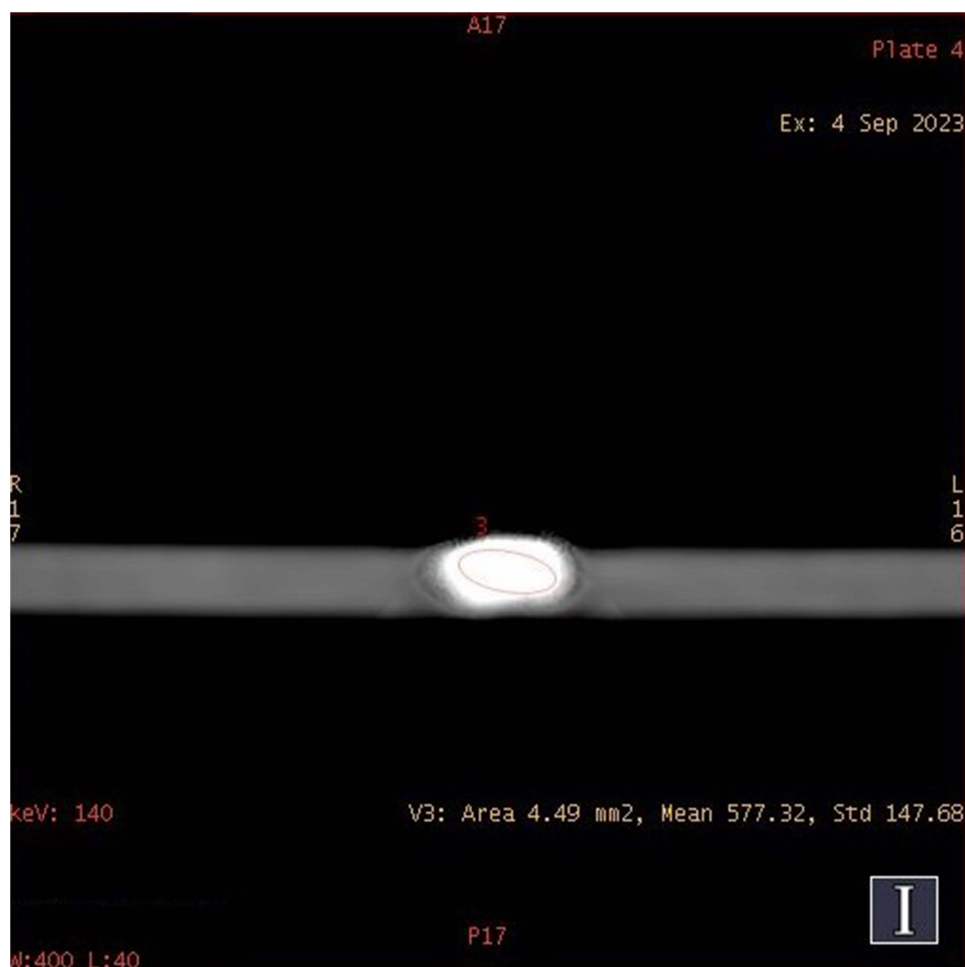


Figure 3 Example of ex vivo urinary calculi with highlighted region Interest used for analysis with associated mean Hounsfield Units.

Abbreviations: KeV; Kiloelectron volt.

DECT utilizes two different X-ray energy levels, allowing for improved tissue characterization based on differences in material composition. Traditional low-dose CT KUB may struggle to differentiate between certain types of stones with similar densities, leading to false negatives.²⁰ In contrast, DECT's ability to distinguish materials based on their atomic number and development of a HU spectral curve increases the sensitivity, making it more adept at identifying a broader range of stone types. A previous study in 2001 has shown that, by using HU, it may help evaluate nephrolithiasis.²⁰ This

Table I Individual Gemstone Spectral Imaging Analysis Results Compared to Fourier-Transform Infrared Spectroscopy

STONE	STONE DIAMETER (mm)	SINGLE OR MIXED COMPOSITION	MAJOR COMPONENT 1	MAJOR COMPONENT 2	MINOR COMPONENT	GSI RESULT
1	2.7	SINGLE	UA			UA
2	0.8	SINGLE	Cys			Cys
3	1.2	SINGLE	CaOx			CaOx
4	2.7	MIXED	MAP	CaP		CaP
5	1.6	MIXED	MAP		CaP	MAP / CaPu
6	2.3	MIXED	MAP	CaP		CaOx / CaP

(Continued)

Table 1 (Continued).

STONE	STONE DIAMETER (mm)	SINGLE OR MIXED COMPOSITION	MAJOR COMPONENT 1	MAJOR COMPONENT 2	MINOR COMPONENT	GS1 RESULT
7	3.0	MIXED	MAP	CaP		MAP / CaP
8	3.1	MIXED	CaP		UA	CaOx
9	3.4	MIXED	MAP	CaP	Ammonium Urate	CaP
10	2.5	SINGLE	UA			UA
11	4.7	MIXED	UA		CaOx	UA / CaP
12	5.1	SINGLE	Cys			Cys
13	2.8	SINGLE	Cys			Cys
14	2.8	SINGLE	Cys			Cys
15	3.8	SINGLE	UA			UA
16	2.9	SINGLE	CaOx			MAP
17	1.5	SINGLE	CaOx			CaOx
18	2.4	MIXED	CaOx		CaP	CaOx / CaP
19	2.0	MIXED	CaOx		CaP	CaOx / CaP
20	2.5	MIXED	CaOx		CaP	CaOx / CaP
21	1.8	SINGLE	CaOx			CaP
22	2.4	SINGLE	CaOx			CaP
23	1.1	SINGLE	CaOx			CaOx / CaP
24	1.0	SINGLE	CaOx			CaOx / CaP
25	1.8	SINGLE	CaOx			CaOx
26	1.8	SINGLE	UA			UA
27	2.0	SINGLE	UA			UA / CaP
28	2.7	SINGLE	UA			UA
29	2.6	SINGLE	Cys			Cys
30	2.4	SINGLE	Cys			Cys
31	3.6	SINGLE	CaP			CaOx / CaP
32	1.9	SINGLE	CaP			CaOx / CaP
33	1.9	SINGLE	MAP			MAP
34	2.4	SINGLE	MAP			CaP
35	2.9	MIXED	CaOx	CaP		CaOx / CaP
36	5.0	MIXED	CaOx	CaP		CaP
37	3.0	MIXED	MAP	CaP		MAP / CaP
38	2.3	MIXED	MAP	CaP		MAP / CaP
39	1.4	MIXED	MAP	CaP		MAP

(Continued)

Table 1 (Continued).

STONE	STONE DIAMETER (mm)	SINGLE OR MIXED COMPOSITION	MAJOR COMPONENT 1	MAJOR COMPONENT 2	MINOR COMPONENT	GSI RESULT
40	3.2	MIXED	MAP	CaP	Ammonium Urate	CaOx / CaP
41	2.0	MIXED	CaOx	CaP		CaOx / CaP
42	2.1	MIXED	CaOx	CaP		CaOx / CaP
43	2.0	MIXED	MAP	CaP		CaOx / CaP
44	2.0	SINGLE	MAP			MAP
45	3.5	MIXED	CaP		UA	CaOx
46	2.0	MIXED	MAP		CaP	CaOx / CaP
47	3.7	SINGLE	UA			UA
48	2.1	MIXED	CaOx	CaP		CaOx / CaP
49	1.6	MIXED	CaOx	CaP		CaOx / CaP
50	3.4	MIXED	CaP		CaOx	CaOx / CaP

Abbreviations: GSI, Gemstone Spectral Imaging; MAP, magnesium ammonium phosphate; CaOx, Calcium Oxalate; CaP, Calcium Phosphate, Cystine; Cys, UA; Uric Acid, mm; Millimetres.

process has been the mainstay of calculi evaluation, however in comparison, our study has demonstrated that it can identify major stone composition reliably with a sensitivity of 0.802 (95% CI: 0.696, 0.908). This is particularly valuable when determining treatment strategies, as different stone types may require distinct interventions. Two previous studies have shown that low-dose CT KUB, while effective in visualizing stones, lacks the specificity needed for precise composition identification, and one study recorded a specificity of 40% for stone composition^{7,20}. This is compared to our study which had a specificity of 0.831 (95% CI: 0.784, 0.878) for major stone composition identification. Despite our stones being mostly 3mm or smaller, our pooled sensitivity and specificity were comparable to other studies.^{6,8,14} The increased accuracy provided by DECT with the identification of renal stone composition allows urologists to have greater confidence in patient suitability for medical or surgical management.

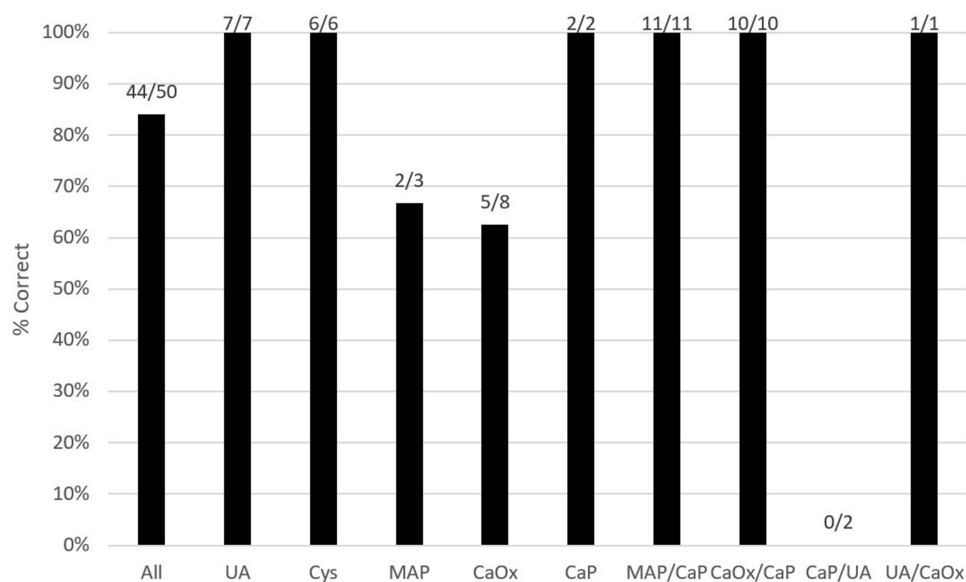


Figure 4 Comparison of accuracy of dual energy computer tomography for identifying all major stone components and each individual stone major composition.

Abbreviations: MAP, magnesium ammonium phosphate; CaOx, calcium oxalate; CaP, calcium phosphate; Cys, cystine; UA, uric acid.

Table 2 Individual Major Component Identification Using Dual Energy Computer Tomography

	Sensitivity	Specificity	Accuracy
Calcium Oxalate	0.7647	0.7273	0.74
Uric Acid	1	1	1
Cystine	1	1	1
Calcium Phosphate	0.85	0.6	0.7
MAP	0.5	0.9722	0.84

Abbreviations; MAP, magnesium ammonium phosphate.

Uric Acid and Cystine Calculi

DECT has demonstrated notable advancements in accurately identifying uric acid calculi, marking a significant stride in urinary stone analysis since being developed and used in the early 2000s.²⁰ The distinctive capability of DECT to leverage dual-energy settings enhances its ability to discern the unique attenuation patterns of different materials. Previous research findings indicate up to 100% accuracy in identifying uric acid.^{14,21,22} With our work, we have also demonstrated 100% accuracy for uric acid calculi identification and expanded on this and shown a 100% accuracy with cystine stone identification. In contrast, conventional imaging methods like low-dose CT KUB may encounter challenges in distinguishing certain stone types, and DECT's precision is particularly evident in its reliability for these specific compositions and allows confidence in diagnosis without the need for biochemical analysis. This will allow for these specific renal stones to have early appropriate medical management without the need for invasive procedures.

Radiation Exposure Low Dose CT KUB Vs DECT

A consideration with any radiation-based imaging modality is the potential impact of increased dose delivered to the patient at the time of imaging. This fortunately has been previously shown to not have a significant difference in radiation dose and in fact had an overall reduction 36% using DECT while providing increased accuracy of stone composition at 93% compared to low dose CT KUB.²³ The study was comparable to ours in that the maximum energy used was 140keV.

Limitations

The urinary stones sampled in this study were the remaining fragments from the FTIR process completed to determine the overall stone composition. This does introduce an inherent sampling error risk secondary to the FTIR process which needs to be accepted.

Accurately identifying the precise composition of urinary stones, particularly those comprised of CaP, MAP, and CaOx, poses a notable challenge due to their relatively close atomic numbers; 14.14, 9.74, and 13.32, respectively. The proximity of these atomic numbers can result in overlapping attenuation characteristics and similar spectral curves, which made it difficult for DECT to unequivocally differentiate between these stone types. The intricate nature of stone composition becomes evident when faced with these subtle distinctions, raising concerns about potential misclassifications. This can be seen in the difficulty in identifying the two mixed stones with CaP as a major component and UA as a minor component. Chemical composition between CaP and CaOx has a degree of similarity which may contribute to the difficulties in differentiation which other studies have also found.^{6,16} It is also possible that the UA minor component caused the results to be subtly more reflective of CaOx. However, had these compositions both been major components, it may have provided more evidence that it was a mixed stone during analysis. Of note, this is from a sample size of only two stones. Despite these challenges, our experiment demonstrated adequacy in sensitivity, specificity and overall accuracy. By amalgamating data and leveraging the comprehensive capabilities of DECT, the technique can overcome the individual limitations associated with these closely related atomic numbers and provide increased accuracy when compared to low dose CT alone.^{5,10,24} This underscores the importance of not solely relying on isolated measurements of

either the HU or mean effective Z-score and histogram but rather considering the combination of results for a more reliable assessment of stone composition.

Another limitation is that the study is an in vitro phantom study. Multiple stones were placed into agar plates and scanned which does not emulate stone location or true medium in which stones are in patient cases. However, similar studies have been conducted which show agreement between phantom studies and clinical studies.^{25,26} Despite this, there is a need for the current study to be correlated with clinical studies.

Conclusion

In conclusion, our study investigated the efficacy of DECT in determining the composition of urinary stones, focusing on both single and mixed compositions. DECT demonstrated high sensitivity and specificity in identifying major components, with a pooled sensitivity of approximately 80.2%, specificity of 83.1%, and an overall accuracy of 80.7%. The technique excelled in accurately identifying uric acid and cystine stones, achieving 100% accuracy for both. However, challenges were encountered in distinguishing between Calcium Phosphate, Magnesium Ammonium Phosphate (MAP), and Calcium Oxalate due to their close atomic numbers and similar spectral curve appearance. Despite these difficulties, the study highlighted that DECT can overcome limitations associated with traditional low-dose CT KUB imaging. It provides a more precise characterization of stone composition for early management of renal stones. The importance of this becomes significant for patients who are planning non-invasive management of urinary calculi in the form of extracorporeal shockwave lithotripsy (ESWL) as stones that are radiolucent, very hard and resistant to ESWL, such as brushite, cystine, uric acid and calcium oxalate monohydrate. With DECT, most of these stones can be determined pre-operatively and accurately. The findings underscore the significance of considering DECT as an alternate tool in guiding treatment decisions for urolithiasis, especially in cases involving mixed stone compositions. Further clinical research and advancements in DECT technology may contribute to refining its capabilities and addressing current limitations in stone composition differentiation.

Informed Consent

Not needed as the research did not involve human participants nor animals.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

None of the authors has any potential conflict of interest to disclose.

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