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ACCURACY OF DUAL ENERGY CT SCAN IN PREDICTING STONE COMPOSITION AND ITS CORRELATION WITH STONE ANALYSIS - A PROSPECTIVE STUDY.

Urology

KEYWORDS: Dual energy CT, Stone composition, Stone analysis, Spectroscopy.

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ABSTRACT
Urinary tract stone disease or urolithiasis is a common problem worldwide. There are different modalities available for treatment of urinary tract stones disease which depends on stone composition, size, location, number and the patient factors. Knowledge of the composition of stones is a fundamental part of the preoperative patient evaluation, and this information influences treatment plans and prevention of recurrence. Currently stone composition can only be determined once it has been removed which is too late to impact treatment decisions. Recently, it has been shown that dual-energy CT (DECT) could be helpful in prediction of renal stone composition. The present study is being carried out to determine the accuracy of DECT in determining the composition of urinary tract calculi by correlating DECT prediction of stone composition with that of postoperative Fourier Transform Infrared Spectroscopy as the reference standard.

Introduction:

Urinary tract stone disease or urolithiasis is a common problem worldwide and is associated with considerable patient morbidity, mortality, affecting the quality of life as well as health care expenses. Urolithiasis has affected humans for centuries, affecting populations of almost every region, culture, and race. The lifetime prevalence of kidney stone disease is estimated at 1% to 15%, with the probability of having a stone varying according to age, gender, race, and geographic location (1, 2, 3).

There are different modalities available for treatment of urinary tract stone disease which depends on stone composition, size, location, number and the patient factors. Stone composition is an important factor crucial for the choice of ideal treatment modality, as well as planning preventive strategies, thereby avoiding recurrence and repeated interventions. Knowledge of the composition of urinary tract stones is a fundamental part of the preoperative patient evaluation, and this information influences treatment plans and recurrence prevention. Currently stone composition can only be determined once it has been removed which is too late to impact the treatment decisions. Thus, they offer no benefit during preoperative treatment planning.

Recently, it has been shown that dual-energy CT could be helpful in prediction of renal stone composition. Considerable investigation into the use of dual-energy CT for determining stone composition has led to mixed results. The present study is being carried out to determine the accuracy of dual-energy CT in determining the composition of urinary tract calculi by correlating dual-energy CT prediction of stone composition with that of postoperative Fourier Transform Infrared Spectroscopy (FTIR) analysis as the reference standard.

MATERIALS AND METHODS

All patients with renal stone attending the Department of Urology, Gauhati Medical College Hospital from February 2015 to October 2016, were included in this study.

All patients underwent CT-IVU with dual energy CT to know the size, location, number of stone, Hounsfield unit (HU) and to estimate stone composition. The stones retrieved were sent for Fourier Transform Infrared Spectroscopy (FTIR Analysis).

Dual energy CT:

The imaging protocol consisted of an unenhanced spiral scan with a single x-ray tube on the whole abdomen acquired along the craniocaudal direction with the patient in the supine position, followed by a dual-energy acquisition focused on the site of the stone previously detected. Technical parameters for the dual-energy scan were as follows: tube voltage 80 kVp and 140 kVp; reference tube current 96 mA and 400 mA with automatic exposure control; pitch factor 0.7:1; acquisition slice thickness 5 mm; reconstruction slice thickness 0.75 mm; reconstruction increment 0.5 mm; gantry rotation time 0.5 second; filter kernel B30f (mediumsmooth); field of view 26 cm; and detector con- figuration 20 × 0.6 mm. Images acquired with the dual-energy modality were postprocessed using a dedicated remote workstation (Leonardo, Siemens Healthcare) and dedicated software (Syngo Dual Energy Viewer, Siemens Healthcare) for the evaluation of the stone chemical composition. Referring to the manufacturer's standard settings, the software displayed calcium stones in blue and non-calcium stones in red colour (Figure 1)

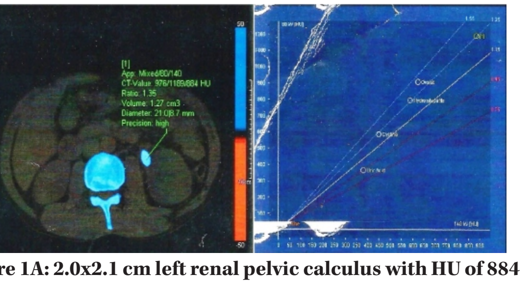

Figure 1A: 2.0x2.1 cm left renal pelvic calculus with HU of 884 to 1189 & low & high energy attenuation ratio of 1.35 suggestive of Hydroxylapatite stone.

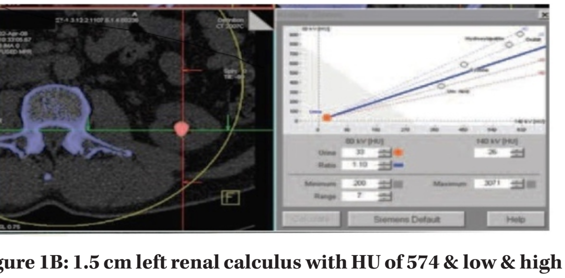

Figure 1B: 1.5 cm left renal calculus with HU of 574 & low & high energy attenuation ratio of 1.02 suggestive of Uric acid stone.

Fourier Transform Infrared Spectroscopy (FTIR Analysis):
It is a technique which is used to obtain an infrared spectrum of absorption or emission of a solid, liquid or gas. An FTIR spectrometer simultaneously collects high spectral resolution data over a wide spectral range.

The pulverized stone was mixed with an inert powdered support (dried potassium bromide) in a proportion of 0.5 to 2% in agate mortar. This mixture was transferred into an appropriate dye and pressed to form a transparent pellet 13 mm in diameter. The pellet assembled in a holder was placed in the IR beam of the spectrometer. The spectral region investigated was from 4000 to 400 cm−1; 32 scans were averaged with a 4 cm−1 resolution for each spectrum. A background spectrum was collected before every analysis, for the sample blank.

Spectra were then computer-matched with the Euclidean search application, a tool of SPECTRA NICODOM IR Library (obtained from Nicodom s.r.o., Hlavni 2727 CZ-14100 Praha 4, Czech Republic, EU) that compares the unknown spectrum with reference spectra contained in the library between 4000 and 400 cm−1. A report is then generated for the various stone components.

RESULTS AND OBSERVATIONS
This study was conducted in the Department of Urology, Gauhati Medical College & Hospital, Gauhati. The period of study was from 1st January 2015 to 1st November 2016.

A total of 52 patients with urolithiasis were included in this study. The age of the patients ranged from 13 yrs to 80 yrs (mean – 39.05 ± 14.47 yrs). Male: Female = 4.42: 1. 42 patients had single stone, 10 had multiple stones and 8 of the 10 patients multiple stones had bilateral stones for a total of 65 stones, the clinical characteristics of which are summarized in Table 1.

Stone Composition at Dual-Energy CT	Diameter (mm)			CT Density (HU)		Site		
	≤ 10	11–19	≥ 20	≤ 1000	> 1000	Kidney	Ureter	Bladder
Calcium oxalate	1	8	6	7	8	10	5	0
Cystine	2	6	4	3	9	8	4	0
Uric acid	4	4	0	5	3	7	1	0
Hydroxyapatite	9	9	6	23	1	10	11	3
Mixed stones	0	2	4	1	5	4	2	0
Total	16	29	20	39	26	39	23	3

Table 1: Characteristics of 65 Stones in 52 Patients Evaluated With Dual-Energy CT

The mean stone size was 16.58 mm (range, 7–46 mm), and the mean stone CT density was 1159.8 HU (range, 300–1915 HU). 39 stones (60%) were located in the kidneys, 23 (35.38%) were in the ureters and 3 (4.62 %) were in bladder.

Of the 65 stones analysed by Dual energy CT, 15 were calcium oxalate, 24 were hydroxylapetite, 8 were uric acid, 12 were cystine and 6 mixed (3 Hydoxylapatite+oxalate, 2 Calcium oxalate+cysteine and 1 Calcium oxalate+uric acid) stones.

In FTIR the all 15 predicted by Dual-energy CT to be calcium oxalate stones were found to be calcium oxalate (100%; exact confidence interval: 78% to 100%). Of the 24 hydroxylapetite only 1 stone was found to be hydroxylapetite and 23 were calcium oxalate (4.17%; exact confidence interval: 0% to 21%). Of the 8 uric acid stones FTIR found 7 to be uric acid and 1 calcium oxalate (87.5%; exact confidence interval: 47% to 99.68%). Of the 12 stones predicted to be cystine by Dual energy CT, FTIR found 8 to be cystine and 4 to be calcium oxalate (67%; exact confidence interval: 35% to 90%). Of the 3 Hydoxylapatite+oxalate mixed stones one was Hydoxylapatite+ oxalate, one Hydoxylapatite+uric acid and one Hydoxylapatite+ cysteine stone. Both stones predicted to be Hydoxylapatite+cysteine and Hydoxylapatite+uric acid came out to be Hydoxylapatite +oxalate.

According to dual-energy CT, stones were predicted to be composed of Non-uric acid (n=57) and uric acid (n = 8). Dual energy CT could not predict stone composition in one Non-uric acid stone, which it predicted to be uric acid stone. Agreement between dual-energy CT and stone analysis by FTIR was estimated in SPSS 21.0 using the Cohen kappa coefficient. Table 2 shows the agreement between dual-energy CT and stone analysis (FTIR) (Cohen κ = 0.925, perfect agreement) (p=0.0001).

Dual-Energy CT	Stone analysis		Total
	Non-uric acid	Uric acid	
Non-uric acid	57	0	57
Uric acid	1	7	8
Total	58	7	65

Table 2: Cross-table showing result of Dual energy CT & FTIR for Uric acid and Non-uric acid stones

Dual energy CT also predicted the composition of the different non-uric acid stones. Out of the Non-uric acid stones Dual CT predicted 23 to be calcium hydroxyapatite, 16 oxalate, 12 cystine and 6 of mixed composition.

Of the 57 non-uric acid stone Dual-energy CT could not identify the chemical composition of 27 stones correctly; 22 had a composition of Hydroxyapatite in dual-energy CT, which was found to be Calcium oxalate by FTIR, four had a prediction of Cystine in dual-energy CT, which was found to be Calcium oxalate by FTIR and one had a composition of Uric acid in dual-energy CT, which was determined to be Calcium oxalate.

Agreement between dual-energy CT and stone analysis by FTIR for different non-uric acid stone was estimated in SPSS 21.0 using the Cohen kappa coefficient. Table 3 shows the agreement between dual-energy CT and stone analysis (FTIR) (Cohen κ = 0.267, fair agreement) (p=0.0001).

Dual-Energy CT	Stone analysis				Total
	Calcium oxalate	Cystine	Hydroxyapatite	Mixed stone	
Calcium oxalate	15	0	0	0	15
Cystine	4	8	0	0	12
Hydroxyapatite	23	0	1	0	24
Mixed stone	0	0	0	6	6
Total	42	8	1	6	57

Table 3: Cross-table showing result of Dual energy CT & FTIR for different Non-uric acid stones

DISCUSSION
The different modalities of treatment for renal stone disease depends on stone composition, size, location, number and the patient factors. Stone composition is considered to be crucial for the choice of an ideal treatment modality. The knowledge of composition of urinary tract stones is a fundamental part of the preoperative patient evaluation, and this information influences treatment plans and recurrence prevention.

Conventional computed tomography (CT) has proven itself as an invaluable tool in kidney stone diagnosis. However, conventional CT has some limitations in analysis of stone composition, which is mostly based on Hounsfield unit (HU) values. Recently, several authors have reported efficacy of dual-energy CT in assessment of renal stone composition.

Li X. et. al. studied a total of 116 urinary stones with a known chemical composition determined by infrared spectroscopy which were further scanned using both gemstone spectral imaging and conventional polychromatic imaging (at 120 kVp) in vitro. The differences in the CT numbers at 120 kVp and 50 keV among the groups were statistically significant by binary comparison (P <.05), except for those at 120 kVp between uric acid and cystine (P = .121), whewellite and weddellite (P = .280), and brushite and carbapatite (P = .419). They were of the view that Gemstone spectral imaging dual-energy CT provides a novel method to better characterize pure urinary stones using the CT numbers at 50 keV (4).

In a study conducted by Hidas G et al, stones were pure in 22 (82%) of the 27 patients and mixed in four (15%), with the major component (60%–73%) of the mixed stones being carbapatite. One patient (4%) had a struvite stone. All six (100%; exact confidence interval: 54.07% to 100%) stones classified as uric acid at dual-energy CT were confirmed to be uric acid with x-ray diffraction. Fifteen (79%; exact confidence interval: 62% to 95%) of the 19 stones classified as calcium at dual-energy CT were confirmed to be calcium at chemical analysis. X-ray diffraction analysis results confirmed the cystine stone classification in one (100%) patient. The struvite stone was misdiagnosed, as anticipated from the in vitro findings (5).

Similarly, in our study stones were pure in 59 (90.77%) of the 65 stones and mixed in six (9.23%), with the major component (60% - 70%) of the mixed stone being hydroxylapatite. The 7 (87.5%; exact confidence interval: 47% to 99.68%) out of 8 stone classified as uric acid at dual energy CT were confirmed to be uric acid in FTIR. All fifteen (100%; exact confidence interval: 78% to 100%) stone classified as calcium oxalate at dual energy CT were confirmed to calcium oxalate in FTIR. The 8 (67%; exact confidence interval: 35% to 90%) of the 12 stone classified as cystine at dual energy CT were confirmed to be cystine in FTIR. But of the 24 stones classified as hydroxylapatite stones in dual energy CT, only one (4.17%; exact confidence interval: 0% to 21%) was confirmed to be hydroxylapatite in FTIR and 23 came out to be calcium oxalate.

Kulkarni N.M. et. al., in their study found that Single-source dual-energy computed tomography can accurately predict uric acid and non-uric acid stone composition in vitro and in vivo. Sub-stratification of non-uric acid stones of pure composition is possible both in vitro and in vivo. They further observed that in stones of mixed composition, the Zeff values reflect the dominant composition (6).

Giuseppina Manglaviti et. al., using dual-energy CT, found that stones were predicted to be composed of calcium oxalate (n = 33), cystine (n = 7), uric acid (n = 4), and mixed composition (n = 5). None of the stones in their study was predicted to be composed purely by hydroxyapatite. Of the five stones with mixed composition, one was predicted to be composed of uric acid and hydroxyapatite, and four were predicted to be hydroxyapatite and cysteine and they recorded substantial agreement between dual-energy CT and crystallography (Cohen κ = 0.684) (7).

Corbett J-H.et. al., in their study found that Single-source dual-energy CT with GSI accurately distinguishes uric acid and non-uric acid renal stones, but failed to subclassify calcium-based non-uric acid stones. Mixed uric acid and non-uric acid stones usually demonstrate characteristics of the dominant component (8).

George S. K. Fung et. al. studied a total of 48 calcium oxalate, calcium phosphate, and uric acid human kidney stone samples placed in individual containers inside a cylindric water phantom and imaged with a dual-energy CT scanner using the following three scanning protocols of different combinations of tube voltage, with and without a tin filter: 80 and 140 kVp without a tin filter, 100 and 140 kVp with a tin filter, and 80 and 140 kVp with a tin filter. For all three protocols, the uric acid stones were significantly different ($p < 0.001$) from the calciferous stones according to their dual-energy ratio values. For differentiating calcium oxalate and calcium phosphate stones, the difference between their dual-energy ratio values was statistically significant, with different degrees of significance (range, $p < 0.001$ to $p = 0.03$) for all three protocols. They found that the tin filter added to the high-energy tube and the use of a wider dual-energy difference are important for improving the stone differentiation capability of dual-energy CT imaging (9).

Mostafavi M.R. et. al. studied a total of 102 chemically pure stones in 6 separate groups. The determination of the chemical composition was performed using the absolute CT value measured at 120 kV. and the dual kilovolt CT values measured at 80 and 120 kV. The absolute CT value measured at 120 kV. was able to identify precisely the chemical composition of uric acid, struvite and calcium oxalate stones. It was imprecise in differentiating calcium oxalate from brushite stone and struvite from cystine stone. However, dual kilovolt CT value was able to differentiate these latter stones with statistical significance ($p < 0.03$). Uric acid stones were easily differentiated from all other stones using the absolute CT value (10).
In our study according to dual-energy CT, stones were predicted to be composed of Non-uric acid (n=57) and uric acid (n = 8). Dual energy CT failed to predict stone composition in one Non-uric acid stone, which was found to be uric acid stone. We found a perfect agreement between dual-energy CT and stone analysis (FTIR) in differentiating non-uric acid stone from uric acid stone (Cohen κ = 0.925, perfect agreement) (p=0.0001).

Our study further observed that Dual energy CT also predicted the composition of the different non-uric acid stones. Out of the Non-uric acid stones Dual CT predicted 23 to be calcium hydroxyapatite, 16 oxalate, 12 cystine and 6 of mixed composition.

Of the 57 non-uric acid stone Dual-energy CT could not identify the chemical composition of 27 stones correctly, 22 had a composition of Hydroxyapatite in dual-energy CT, which was found to be Calcium oxalate by FTIR, four had a composition of Cystine in dual-energy CT, which was found to be Calcium oxalate by FTIR and one had a composition of Uric acid in dual-energy CT, which was determined to be Calcium oxalate. We found a fair agreement between dual-energy CT and stone analysis (FTIR) in sub-classifying non-uric acid stones (Cohen κ = 0.267, fair agreement) (p=0.0001).

CONCLUSION
Dual Energy C.T. in our study revealed that it can near accurately predict the chemical composition of urinary tract stone pre-operatively which is clinically very relevant for treatment planning.

Dual-energy CT can accurately differentiate between uric acid and non-uric acid stones.

It can also predict the composition of different non-uric acid stones with fair amount of accuracy. However, Dual-energy CT fails to differentiate between calcium oxalate and calcium phosphate stones; which were grouped as "calcium stones" collectively.

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