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# Can stone composition be predicted by plain X-ray and/or non-contrast CT? A study validated by X-ray diffraction analysis

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## Abstract

**Background:** The stone composition has a great influence on the outcome of its treatment. There are several tests to predict the composition of stones preoperatively and stone analysis postoperatively. Herein, we want to evaluate if the stone composition could be predicted from plain X-ray KUB (PKUB) and/or non-contrast CT (NCCT) validated by in vitro X-ray powder diffraction analysis (XRD).

**Methods:** Between April 2014 and March 2016, 100 cases with urinary tract stones were included in the study. The radio-opacity of the stones in PKUB, stone density by NCCT, and after stone extraction, XRD were performed. Statistical analysis for the results was performed using Chi-square and Fisher exact tests for categorical variables and Mann-Whitney *U* and Kruskal-Wallis *H* for the nonparametric variables. The receiver operating characteristic curve was constructed to determine the best cutoff value.

**Results:** This study included 74 males and 26 females with a median age of 32 years (range 2–70). Regarding the radio-opacity by PKUB, there were 30 stones dense opaque, 44 opaque, 21 faint opaque, and 5 radiolucent. XRD revealed 97 mixed and 3 pure stones. The calcium oxalate monohydrate (COM) stone composition could be predicted in dense opaque stone by PKUB in 75.9% and urate composition in the radiolucent stone by 40%. The cutoff value of HU density by NCCT to the dense opaque stones in the PKUB was > 1020 and for radiolucent stones was < 590.

**Conclusion:** Stone radio-opacity by PKUB and its attenuation value by NCCT could successfully predict its calcium oxalate monohydrate, struvite, and urate composition. However, the chemical stone analysis is still required as most stones are mixed.

**Keywords:** Urinary stones, Plain KUB, Non-contrast CT, X-ray powder diffraction analysis

## 1 Background

The lifetime prevalence of urinary stones is about 10–14% [1]. Stone composition significantly affects both treatment outcomes and preventive measures [2]. Nearly no currently available stone analysis methods can facilitate preoperative assessment. The attenuation value in some radiological modalities can predict the stone

composition. There are two ways to measure the attenuation value, density by non-contrast CT (NCCT), and radio-opacity by plain X-ray KUB (PKUB) [3].

The Hounsfield unit (HU) determined by the NCCT was suggested as a useful predictor of the urinary stone compositions [4]. HU is a normalized index of X-ray attenuation, named after Sir Godfrey Newbold Hounsfield, based on a scale of – 1000 (air) to +1000 (bone), with water being zero [5]. A previous study classified the stone's radio-opacity in PKUB in comparison with the opacity of the last rib into 4 categories: dense opaque, opaque, faint opaque, and radiolucent [6].

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There are many techniques for stone analysis; chemical analysis, thermogravimetric analysis, polarizing light microscopy, scanning electron microscopy, infrared spectroscopy, X-ray powder diffraction analysis (XRD), and energy-dispersive X-ray analysis [7].

Our study aims to see if urinary stone composition could be predicted by PKUB and/or NCCT characteristics validated by in vitro XRD analysis.

## 2 Methods

This is a prospective hospital-based cross-sectional study. The study included 100 cases with urinary tract stones attending our department between April 2014 and March 2016. The sample size was calculated using Epi-Info™ 7.1 for Statistical Calculation using the following parameters: power of the study 80%, population size 20,000, and expected frequency 50%, the margin of error 9%, and confidence level of 97%. This yielded a sample size of 99. The sample size in our study is 100 stone samples. The study was submitted to and approved by our institutional ethics committee.

Stone radio-opacity in PKUB was determined in comparison with last rib opacity into; more opaque than the last rib (dense opaque), nearly equal to last rib opacity (opaque), less opaque than the last rib (faint opaque) or radiolucent determined by two investigators (M.G., A.E.). The patients scanned with the use of a second-generation dual-energy multi-detector CT scanner, using our clinical urinary stone protocol: 80 and 120 kV with tin filter, 240 quality reference mAs, and 1 mm collimation, 0.5 s rotation time, 64 slides, and stone density (HU) reported.

### 2.1 The technique of XRD analysis

Stones are retrieved either after lithotripsy, extracorporeal shockwave lithotripsy (ESWL), or open surgery. XRD is a tool used for identifying the atomic and molecular structure of a crystal, in which the crystalline atoms cause a beam of incident X-rays to diffract in many specific directions. The distance between similar atomic planes in a mineral, the inter-atomic spacing, called the *d*-spacings, is measured in angstroms. Sixty-Nine Files of *d*-spacings for hundreds of thousands of inorganic compounds are available from the International Centre for Diffraction Data (ICDD). Many other sites contain *d*-spacings of minerals such as the American Mineralogist Crystal Structure Database (AMCSD) [8].

The urinary stone sample was pulverized and analyzed by XRD using Philips PW 1710 X-Ray Diffractometer (Japan) with Beta filtering using a graphite monochromator. The crystalline components were identified using the ICDD database and the semiquantitative composition

determined using the relative intensity of the different bands.

A few grams of the stone powdered and mounted uniformly on a glass slide assuring a flat upper surface, and then rotated in the collimated X-ray beam of the XRD unit. The diffraction pattern is recorded using a cylindrical camera. Once all *d*-spacings of a certain substance have been determined, manual or automated search-match routines compare the *d*-spacings of the unknown to those of known materials derived from the ICDD cards.

### 2.2 Statistical analysis

We encoded all data in the Microsoft Excel spreadsheet and performed statistical analysis using IBM SPSS program version 20. The data are tested for normality using the Anderson–Darling test and for homogeneity variances before further statistical analysis. Categorical variables are described by number and percent, while continuous variables are described by mean, standard deviation, and median. Chi-square and Fisher exact tests were used to compare categorical variables. Comparison between continuous data was performed using *t* test and ANOVA (for normal distribution variables). Mann–Whitney *U* and Kruskal–Wallis *H* were used for the nonparametric variables. The receiver operating characteristic (ROC) curve was constructed to determine the best cutoff value.

## 3 Results

The study included 100 stones from 100 patients (74 males and 26 females). The median age was 32 years (range 2–70). The mean BMI was 27.3 kg/m<sup>2</sup>. The following interventions were performed, PCNL for 46 patients, open renal surgery for 23, ureteroscopy for 21, and 10 cases were post-ESWL. The mean stone size was 2.9 ± 1.3 cm.

XRD revealed only 3 (3%) stones were of pure component (two calcium oxalate monohydrate COM stones and one cystine stone). The remaining 97 (97%) stones were of the mixed component. There were no brushite or calcium carbonate stones. Table 1 shows the distribution of the major components of the mixed stones.

In PKUB, the degree radio-opacity was as follows; 30 stones were dense opaque, 44 opaque, 21 faint opaque, and 5 radiolucent. There was no significant correlation between the BMI and the stone opacity by PKUB ( $P=0.59$ ). Most of the calcium oxalate monohydrate (COM) stones (60%) were dense opaque, all urate stones were radiolucent, and most of the struvite stones (75%) were faint opaque.

**Table 1 Distribution of mixed stones**

Stone type	No
Calcium oxalate monohydrate (COM)	37
Basic calcium phosphate (CaPo4)	34
Calcium oxalate dihydrate (COD)	12
Struvite	4
Urate	2
CaPo4 and COM	2
CaPo4 and COD	1
CaPo4 and struvite	1
COM and COD	1
COD and struvite	2
CaPo4 and COM and COD	1
Total	97

In NCCT, the mean (SD) HU was 1195.3 (146.8) for COM stones, 443.8 (99.3) for urate stones, and 527.8 (138.5) for struvite stones. Calcium oxalate dihydrate (COD) and calcium phosphate (CaPo<sub>4</sub>) stones are misidentified by PKUB and NCCT (no significant relation).

Table 2 shows that there was a significant relation between COM, struvite, and urate stones and their densities in HU by NCCT. The more the HU density of the stone, the more liability to have COM as a major component, while the less HU density of the stone, the more liability to have urate and/or struvite as the major components.

Also, there was a significant relation between COM, struvite, and urate stones with their degrees of opacity in the PKUB. Most of the COM stones were dense opaque, while all the urate stones were radiolucent in the PKUB. Most of the struvite stones were faint opaque in the PKUB. However, about 25% of struvite stones included

**Table 3 Relation between type of the stone and its KUB findings**

	Dense opaque Median	Opaque Median	Faint opaque Median	Radiolucent Median	P value
Ca (Po4)	30.95	37.25	33.3	30.8	0.079
COM	40.3	28.2	20	20	0.003**
COD	26.8	16.7	20	20	0.122
Struvite	0	6.35	16.7	7.7	0.004**
Urate	0	0	6.7	10.5	0.001**
Cystine	0	0	0	0	0.291

\*\*Statistically significant difference (P level < 0.01)

in this study were radiolucent and overlapped with urate stones as shown in Table 3.

To determine the NCCT sonogram HU attenuation level with both the highest specificity and sensitivity, the study applied the receiver operating characteristic (ROC) curve to set the best cutoff value of HU. The cut-off value of HU density by NCCT to the dense opaque stones in the PKUB was more than 1020 (Fig. 1).

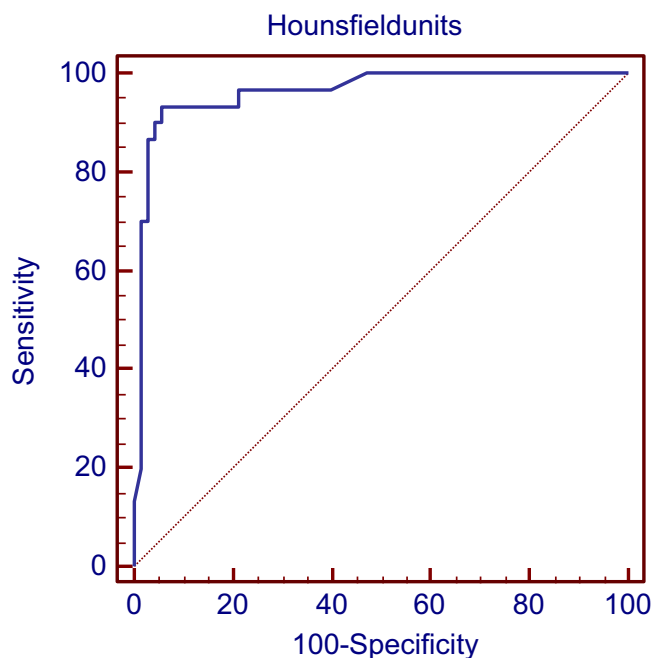
Stones of HU density more than 590 were mostly radiopaque stones and those of HU density less than 590 were mostly radiolucent stones (Fig. 2). Figure 3 shows that most of the stones of HU density between 590 and 680 were faint opaque stones in PKUB. Figure 4 shows that most of the stones of HU density between ≤ 590 were radiolucent stones in PKUB.

Table 4 represents multiple linear regression analysis performed to assess the most significant predictors of the stone composition. It revealed a significant correlation between COM, struvite, and urate stones with their degrees of radio-opacity by PKUB, and their HU

**Table 2 Relation between density of the stone in HU, size of the stone, and its PKUB findings**

	PKUB findings				P value
	Dense opaque	Opaque	Faint opaque	Lucent	
HU					
Mean ± SD	1195.3 ± 146.8	868.1 ± 149.4	527.8 ± 138.5	443.8 ± 99.3	0.001**
Median	1195	885	500	400	
Size					
Mean ± SD	2.9 ± 1.3	2.8 ± 1.2	3.2 ± 1.4	2.6 ± 1.1	0.711
Median	2.5	2.6	3	3	

\*\*Statistically significant difference (P level < 0.01)



Cut off value, sensitivity and specificity of stone density in Hounsfield units regarding dense opacity in KUB:

	dense opaque					
	AUC	Cutoff	Sensitivity	Specificity	PPV	NPV
<b>Hounsfield units</b>	0.963	>1020	93.3	94.3	87.5	97.1

AUC; area under the curve- PPV; positive predictive value- NPV; negative predictive value

**Fig. 1** ROC curve of dense opacity in PKUB about density in Hounsfield units

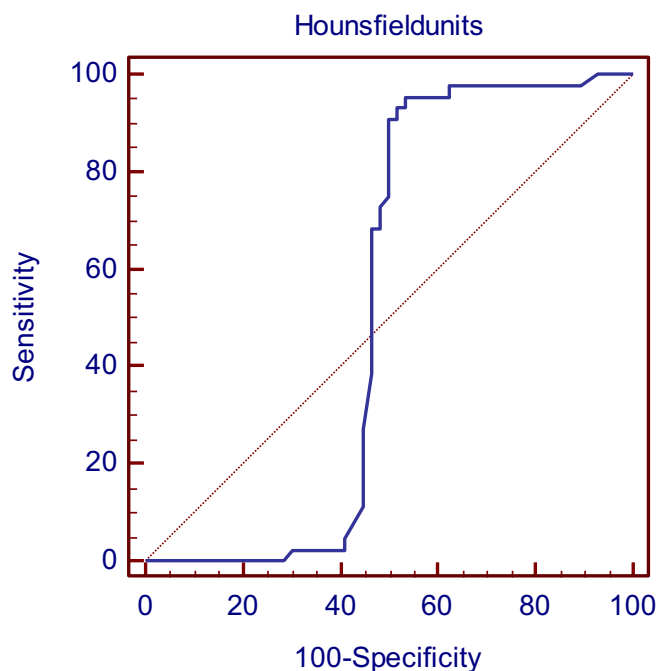
densities by NCCT were found as shown in Table 4. In other words, the presence of radiolucent stones on PKUB could predict a urate composition in 40% of cases. Besides, the presence of dense opaque stone on PKUB could predict a COM stone composition in 75.9%. The presence of faint opaque stone on PKUB can predict a struvite stone composition in 15%.

**4 Discussion**

Preoperative prediction of the stone density and composition is of utmost importance affecting both the treatment option and the prevention measures [9]. Correlation of the CT stone attenuation level with the stone composition is studied extensively in the recent literature; however, no data are available in the literature about the correlation with PKUB findings [10].

An in vivo study evaluated NCCT in predicting stone composition and found a significant difference between the HU measurements of uric acid and calcium oxalate stones [11]. Another study suggested that ‘attenuation/stone size ratio’ was an important predictor in differentiating uric acid and calcium oxalate stones (3). Others stated that for calcium stones, the ability of NCCT (density in HU) to predict stone composition was limited, likely due to the mixed stone composition [12]. An ex vivo study stated that the dual-source CT simultaneously operated in the dual-energy mode allows for the accurate differentiation between uric acid (UA)-containing and non-UA-containing urinary calculi using XRD as the gold standard [13].

In our study, the stone size was not a significant factor in the prediction of the stone composition by the NCCT



Cut off value, sensitivity and specificity of stone density in Hounsfield units regarding the opaque stone in KUB:

	Opaque					
	AUC	Cutoff	Sensitivity	Specificity	PPV	NPV
<b>Hounsfield units</b>	0.523	≤1010	95.45	46.43	58.3	92.9

**Fig. 2** ROC curve of opaque stone in PKUB regarding its density in Hounsfield units

or PKUB, but there was a significant relation between stone type (COM, struvite, and urate stones) and their densities in HU by NCCT.

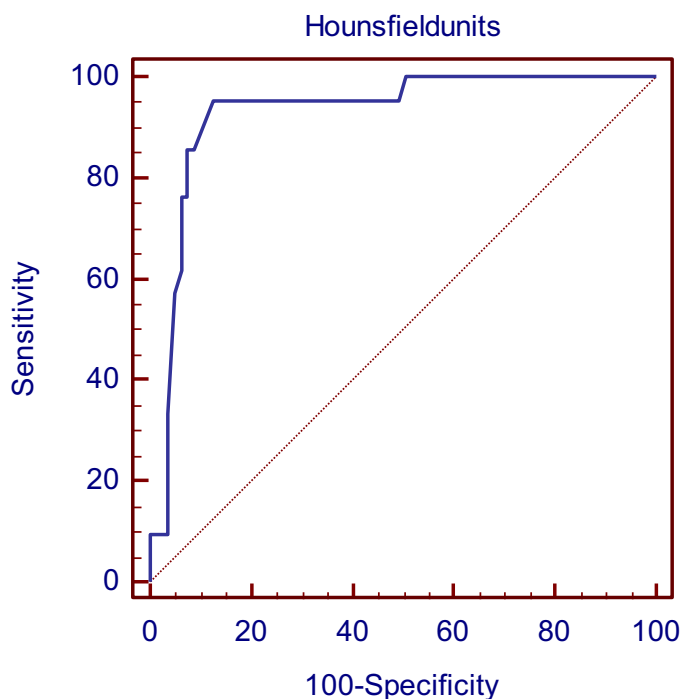
The correlation between the stone compositions by infrared spectrometry and stone morphology, location, and size by plain PKUB studied and identified five different patterns of radiographic appearances of the stones. They concluded that the prediction of stone composition from stone morphology on plain PKUB may not be accurate enough [14].

We found that the cutoff point of HU density by NCCT as regarding radio-opacity in PKUB is 590 HU. Stones of HU attenuation values more than this level are radio-opaque and vice versa. Some authors stated

that redoing the XRD phase analysis after heat treatment considerably enhances the capabilities of the method [15].

As we get some stones after lithotripsy, parts of the stone for analysis will be missing, and stone analysis may not reflect the complete picture; this is a limitation of our study. Another limitation that needs further investigation is the relationship between bone density, BML, and skin-to-stone distance and the categorization of stone opacity in PKUB.

A recent study revealed that PKUB has reasonable accuracy for urolithiasis > 5 mm composed of pure calcium salts, particularly those of the upper renal tract [16]. Another study stated that the use of HU stone



Cut off value, sensitivity and specificity of stone density in Hounsfield units regarding faint opacity in KUB:

	faint opaque					
	AUC	Cutoff	Sensitivity	Specificity	PPV	NPV
<b>Hounsfield units</b>	0.927	≤680	95.24	87.34	66.7	98.6

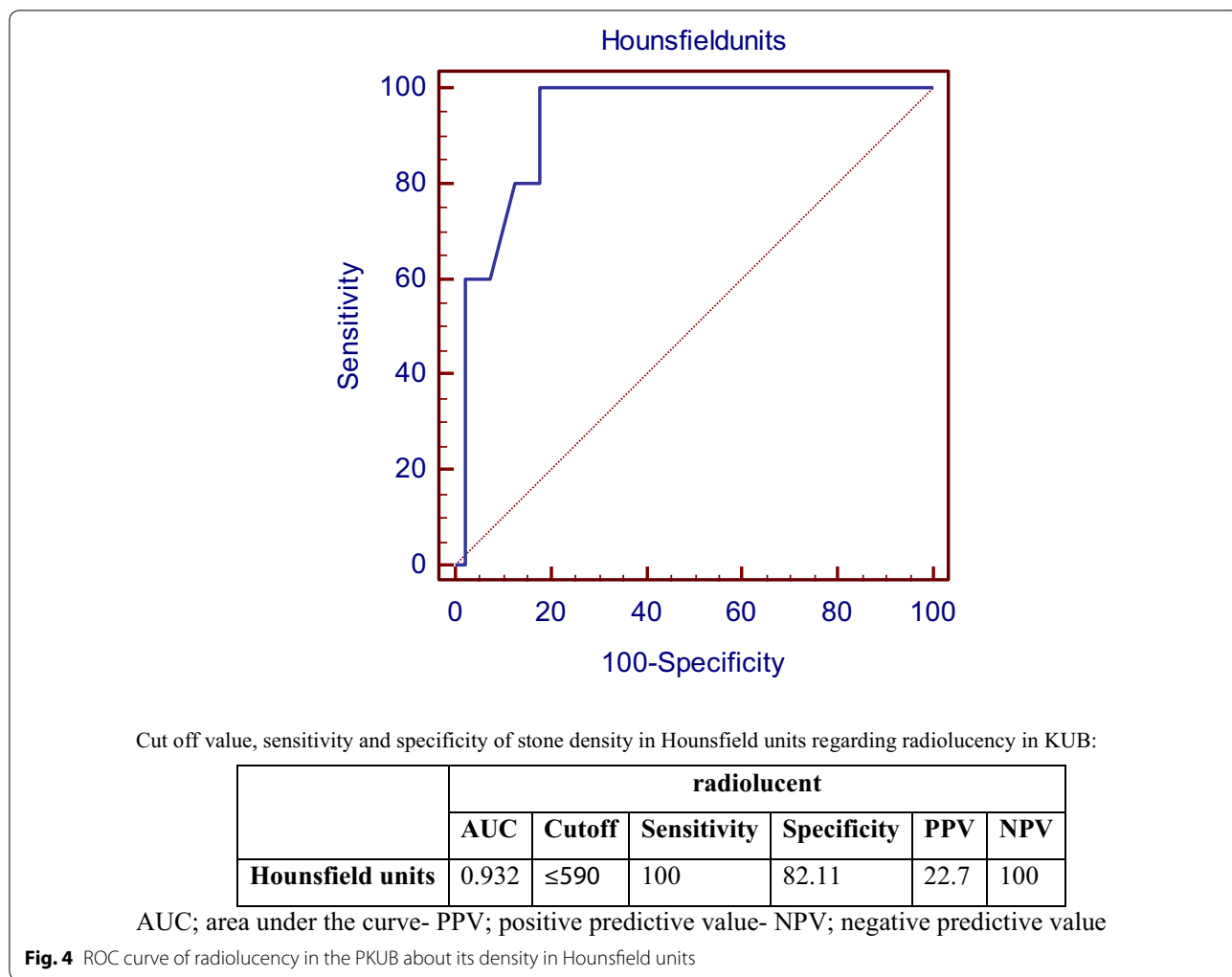
AUC; area under the curve- PPV; positive predictive value- NPV; negative predictive value

**Fig. 3** ROC curve of faint opacity in plain PKUB about the density of the stones in Hounsfield units

density by NCCT revealed statistically significant differences among all pure and most of the mixed urinary stones; however, differentiation of pure COM and mixed COM was possible only in the tissue window [17].

**5 Conclusion**

Stone radio-opacity by PKUB and its attenuation value by NCCT could successfully predict its calcium oxalate monohydrate, struvite, and urate composition and hence its treatment option. However, the chemical stone analysis is still required as most stones are mixed.



**Table 4 Multiple linear regression analysis to assess the most significant predictors of stone composition**

	<b>CaPO4 P value</b>	<b>COM P value</b>	<b>COD P value</b>	<b>Struvite P value</b>	<b>Urate P value</b>
HU	0.143	0.000**	0.095	0.001**	0.000**
Dense opaque	0.091	0.001**	0.17	0.25	0.414
Opaque	0.35	0.416	0.225	0.935	0.696
Faint opaque	0.321	0.12	0.514	0.029*	0.578
Lucent	0.651	0.264	0.366	0.069	0.011*

\*Statistically significant difference (P level < 0.05)

\*\*Statistically significant difference (P level < 0.01)

HU Hounsfield unit, CaPO<sub>4</sub> basic calcium phosphate, COM calcium oxalate monohydrate, COD calcium oxalate dihydrate

**Abbreviations**

PKUB: Plain X-ray KUB; NCCT: Non-contrast computed tomography; XRD: X-ray powder diffraction analysis; COM: Calcium oxalate monohydrate; HU: Hounsfield unit; ESWL: Extracorporeal shockwave lithotripsy; ICDD: International Centre for Diffraction Data; AMCSD: American Mineralogist Crystal Structure Database; ROC: Receiver operating characteristic; BMI: Body mass index; PCNL: Percutaneous nephrolithotripsy; SD: Standard deviation; COD: Calcium oxalate dihydrate; UA: Uric acid.

**Acknowledgments**

None.

**Authors' contributions**

MG developed the concept of the manuscript and contributed to drafting and submission. AMM contributed to design, writing, and revision. AhE contributed to design, data interpretation, and revision. MSA contributed to design and revision. AyE contributed to data collection and statistical analysis. HAA developed the concept of the manuscript and critical revision. EO developed the concept of the manuscript and revision. All authors agreed to be personally accountable for their own contributions and ensure that questions related to the accuracy or integrity of any part of the work, even ones in which they were not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature. All authors read and approved the final manuscript and revisions for submission.

**Funding**

None.

**Availability of data and material**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Ethics approval and consent to participate**

The study was submitted to and approved by our ethics committee of the Faculty of Medicine, Assiut University. The ethics committee's reference number was not available. Formal written consent was taken from all participants.

**Consent for publication**

Consent for publication was taken from all participants.

**Competing interests**

The authors declare that they have no competing interests.

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Received: 17 December 2019 Accepted: 25 September 2020

Published online: 19 November 2020

**References**

- Curhan GC (2007) Epidemiology of stone disease. *Urol Clin N Am* 34(3):287–293
- Kim SC, Coe FL, Tinmouth WW, Kuo RL, Paterson RF, Parks JH, Munch LC, Evan AP, Lingeman JE (2005) Stone formation is proportional to papillary surface coverage by Randall's plaque. *J Urol* 173(1):117–119 **discussion 119**
- Motley G, Dalrymple N, Keesling C, Fischer J, Harmon W (2001) Hounsfield unit density in the determination of urinary stone composition. *Urology* 58(2):170–173
- Tiscione D, Ruggeri L, Beltrami P, Cerruto MA, Cielo A, Gigli F, Zattoni F (2009) Using computed tomography to predict in vivo stone chemical composition. *Urologia* 76(2):107–111
- Brooks RA (1977) A quantitative theory of the Hounsfield unit and its application to dual-energy scanning. *J Comput Assist Tomogr* 1(4):487–493
- Lim KH, Jung JH, Kwon JH, Lee YS, Bae J, Cho MC, Lee KS, Lee HW (2015) Can stone density on plain radiography predict the outcome of extracorporeal shockwave lithotripsy for ureteral stones? *Korean J Urol* 56(1):56–62
- Fazil Marickar YM, Lakshmi PR, Varma L, Koshy P (2009) Elemental distribution analysis of urinary crystals. *Urol Res* 37(5):277–282
- Brady JB, Newton RM, Boardman SJ (1995) New uses for powder XRD experiments. *J Geol Educ* 43:466–470
- Patel SR, Haleblan G, Zabbo A, Pareek G (2009) Hounsfield units on computed tomography predict calcium stone subtype composition. *Urol Int* 83(2):175–180
- Huang CC, Chuang CK, Wong YC, Wang LJ, Wu CH (2009) Useful prediction of ureteral calculi visibility on abdominal radiographs based on calculi characteristics on unenhanced helical CT and CT scout radiographs. *Int J Clin Pract* 63(2):292–298
- Nakada SY, Hoff DG, Attia S, Heisey D, Blankenbaker D, Pozniak M (2000) Determination of the stone composition by non-contrast spiral computed tomography in the clinical setting. *Urology* 55(6):816–819
- Stewart G, Johnson L, Ganesh H, Davenport D, Smelser W, Crispen P, Venkatesh R (2015) Stone size limits the use of Hounsfield units for prediction of calcium oxalate stone composition. *Urology* 85:292–295
- Stolzmann P, Schevel H, Rentsch K, Schertler T, Frauenfelder T, Leschka S, Sulser T, Marincek B, Alkadhi H (2008) Dual-energy computed tomography for the differentiation of uric acid stones: ex vivo performance evaluation. *Urol Res* 36:133–138
- Wang SC, Hsu YS, Chen KK, Chang LS (2004) Correlation between urinary tract pure stone composition and stone morphology on plain abdominal film. *J Chin Med Assoc* 67(5):235–238
- Nalbandyan VB (2008) X-ray diffraction analysis of urinary calculi: the need for heat treatment. *Urol Res* 36:247–249
- O'Kane D, Papa N, Manning T, Quinn J, Hawes A, Smith N, McClintock S, Lawrentschuk N, Bolton DM (2016) Contemporary accuracy of digital abdominal X-ray for follow-up of pure calcium urolithiasis: is there still a role? *J Endourol* 30(8):844–849
- Their KZ, Mansour O, Madbouly K, Elsobky E, Abdel-Khalek M (2005) Determination of the chemical composition of urinary calculi by non-contrast spiral computerized tomography. *Urol Res* 33:99–104

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