Hounsfield Units for nephrolithiasis: predictive power for the clinical urologist

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COHEN A, ANDERSON B, GERBER G. Hounsfield Units for nephrolithiasis: predictive power for the clinical urologist. *Can J Urol* 2017;24(3):8832-8837.

Introduction: *We aim to determine the optimal method for measuring Hounsfield Units (HU) of calculi for the clinical urologist.*

Materials and methods: *We present a single institution prospective study from 2014-2015 for 125 consecutive patients. Demographics, baseline characteristics, imaging, and stone analysis were collected. CT scanners and settings were heterogeneous. Hounsfield units were measured by use of ellipsoid tool and free hand outline by two independent urology graders using Philips iSite PACs.*

Results: *Stone analysis demonstrated 26 pure calcium oxalate (CaOx) stones, 15 pure calcium phosphate (CaP) stones, and 7 uric acid stones, among other mixed types. Excellent agreement was notable amongst the two graders for ellipsoid and free hand grading, and values were consistent with those previously published with other methods. Mean grades for free-hand versus ellipse differed overall ($p = 0.006$) as ellipsoid HU measurement was consistently higher than free-hand measurement by an average of 107 units. Either method could differentiate between uric acid stones and any calcium containing stone ($p \leq 0.05$). The free-hand method demonstrated statistical difference between pure calcium oxalate and calcium phosphate stones ($p = 0.03$). Applying either method took less than 6 seconds.*

Conclusions: *For urologists lacking HU on their radiology reports, free hand or ellipsoid measurement may quickly provide an additional tool to guide management. Both methods differentiate between any calcium containing stone and uric acid stones.*

Key Words: stone composition, kidney calculi, nephrolithiasis, Hounsfield Units, tomography, computerized

Introduction

Hounsfield Units (HU) have become a pivotal tool in nephrolithiasis management. Some centers have demonstrated the ability to predict and differentiate stone composition by analysis of HU alone.[1] Likewise, Joseph et al, and other researchers have revealed the potential for HU to predict successful stone fragmentation during extracorporeal shock wave lithotripsy (ESWL).[2,3] In our practice, we find HU to be a key feature to counsel patients in selecting the best stone treatment but we often have difficulty replicating some of the more complex methodologies found in research studies.

HU were developed by Sir Godfrey Hounsfield, and are a standardized expression of CT output with a wide-range of clinical utility. These values are standardized with 0 to -1000 HU reflective of the radiodensity of water and air respectively at standard temperatures and pressures.[4] Dense materials, such as most kidney stones, appear white on CT scan and have corresponding HU values above ~350 HU. For over 30 years, it has been recognized HU may aid in stone type identification, particularly for differentiating between calcium and uric acid stone compositions.[5] Some centers propose the utility of renal papilla Hounsfield density in predicting nephrolithiasis in patients but this matter is unsettled.[6]

Despite the emerging literature demonstrating the possible clinical utility of HU in nephrolithiasis management, it is not necessarily regularly reported by radiologists. Indeed, in the series to be presented here, it was only present on 24% of reports. While strong communication between urologists and radiologists can mitigate this issue, with modern CT imaging programs, urologists can quickly and adequately measure the HU of stones while viewing an abdomino-

Accepted for publication January 2017

Acknowledgements
This work was supported by NIH P01 DK-56788. We appreciate the guidance of Elaine M. Worcester & Fredric L. Coe.

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pelvic CT scan. In this study, we aimed to determine an efficient method for measuring HU in renal and ureteral calculi for the clinical urologist.

Materials and methods

Our data comes from a single institution, prospectively collected database from 2014-2015 with 125 consecutive patients. Patients were consented in compliance with local Institutional Review Board (IRB). Patient demographics such as age, self-reported race, stone presentation history, and other comorbidities were collected. Preoperative creatinine, GFR, spot urine pH and preoperative urine culture were collected. Moreover, the imaging scan used to diagnose the stone was identified and accessed electronically, when possible. Given our status as a tertiary care center, often patients and their CT scans arrive from outside facilities and raw images are uploaded into our electronic medical record. Hence, CT scanner type, voltage, current, pitch or gantry cycle time were not available or recorded in all cases. For those scans taking place at our main campus, a One Philips iCT 256 slice scanner or One Philips Brilliance 64 slice scanner were utilized.

All patients entered into the database underwent ureteroscopic stone treatment performed by flexible digital ureteroscopy with an ACMI digital scope (Olympus America Inc., Southborough, MA, USA) or Flex-Xc flexible uretero-renoscope (Karl Storz Endoscopy-America, Inc., El Segundo, CA, USA) and holmium laser using Accumax 200 micron single-use holmium laser fiber by a single surgeon. A 2.4 Fr Zero Tip Nitinol stone retrieval basket was used as necessary until stones were removed to visual completion.

Stone material was collected at the time of surgery, and stone composition was determined by photomicroscopy and infrared spectroscopy (Beck labs, Indianapolis, IN, USA). Recurrent stone formers were defined by experiencing two or more distinct stone episodes occurring 6 months or more apart. Self-report of renal colic, stone passage, surgical intervention, or imaging was used as evidence for recurrence. Stone compositions were characterized both as continuous percentage of stone type for correlation analysis and as categorical for convenience. For categories, calcium oxalate (CaOx), calcium phosphate (CaPhos), and uric acid (UA) were defined as either pure (100%) or majority ($\geq$ 51%) as noted. We also created a mixed CaOx/CaP category to compare with pure types. Brushite stones were included as a type of calcium phosphate stone for the purposes of this study. No struvite or cystine stones were included in this cohort.

HU were measured by use of the ellipsoid region of interest tool (e-ROI) and free hand ROI (f-ROI) by two independent urology graders using Philips iSite PACs. Axial abdominal-pelvic CT scans were utilized for measurements in the default, abdominal window (window width 400/window level 40). The application e-ROI was performed by creating the largest ellipse possible that would fill the stone, but not extend beyond the boundaries of the stone in the abdominal CT window. In contrast, f-ROI was applied by direct outline of the boundary of the stone. The obstructing or largest stone was measured when multiples were present. The stone was measured in its largest axial CT slice. HU density was calculated based on the measurement of the offending stone size as reported by the radiology report in the axial plane, again based on largest slice. HU reported by radiology were also included in the study, although the specific methods radiologists used to assess HU were not known.

Average interclass correlation was used to measure inter-rater reliability for the continuous variable of HU, Chi-square test was applied to compare patient demographics or other categorical variables, and student t-test used to compare continuous variables, such as HU measurements. ANOVA with Bonferroni correction was applied to ascertain presence or absence of differences amongst mean HU for different stone compositions. Correlations were analyzed between the percentage of stone components and HU. All statistics were performed using Stata 13 (Statacorp, College Station, TX, USA).

Results

One hundred twenty-five consecutive patients presented for ureteroscopic management of nephrolithiasis in 2014-2015. In total, 90 (72%) of the cohort had uploaded CT scans evaluated for HU and of those 94.4% also had corresponding stone analysis. The cohort had a median age of 54 (IQR 41-64) with 56% of the cohort female. Mean BMI was 30.2, ASA 2.5 and Cr 1.06 mg/dL. Fifty-two percent of the cohort had recurrent stones. For the 85 (73.9%) patients with complete data, there were no differences in terms of gender, race, stone-free rates, stone type, recurrence, baseline serum creatinine, or ASA score when compared to patients without complete data available (all $p > 0.05$). The most commons reasons for incomplete data included failure of outside hospital CT scan to be electronically reviewable or no stone fragment retrieved for analysis.

CT scan was the predominant mechanism of diagnosis for the cohort, with 94.2% of patients having had at least one scan in the weeks preceding

TABLE 1. **Breakdown of stone components in cohort**

Majority component	n	%	Mean f-ROI	SD f-ROI	Mean e-ROI	SD e-ROI
Calcium oxalate	45	52.4	673	251	793	195
Pure	26	30.6	619	234	733	177
Calcium phosphate	33	38.8	735	253	838	194
Pure	15	17.6	804	247	876	200
Brushite	4	4.7	773	319	861	261
Uric acid	7	8.3	435	123	480	108

f-ROI = free hand region of interest; e-ROI = ellipsoid region of interest; SD = standard deviation

ureteroscopic treatment. Ultrasound was used exclusively in 6 patients (5%). Stone composition in the cohort was predominated by calcium oxalate, Table 1. Mean grades for f-ROI versus e-ROI differed overall ($p = 0.006$) as e-ROI was consistently higher than f-ROI by an average of 107 units. An example can be seen in Figure 1. Measuring HU using either approach corrected for stone size in axial plane (HU density) was also significantly different, incurring an average difference of 138 units/cm ($p = 0.03$).

Based on majority stone type, either HU determination method could differentiate between uric acid stones and any calcium containing stone ($p \leq 0.004$). Bonferroni correction confirmed statistical power to differentiate between uric acid and CaP or uric acid and CaOx (all $p < 0.03$). After density correction, either method could differentiate uric acid from CaOx ($p < 0.007$), and CaP from uric acid ($p < 0.05$). Overall, there was a detectable difference in mean values when characterizing by pure stone types ($p < 0.002$). Bonferroni correction revealed a detectable difference between pure CaP and pure CaOx ($p = 0.03$), uric acid and pure CaP ($p = 0.001$), and uric acid and mixed stones ($p = 0.018$) using f-ROI. Findings for e-ROI were similar except it could not differentiate pure CaP from pure CaOx ($p = 0.30$).

In terms of HU variability, or standard deviation, uric acid was differentiated from other stone types whether mixed or pure. Specifically, f-ROI standard deviation for uric acid was 122.7 compared to 230-266 for other stone types. Likewise for e-ROI, standard deviation for Uric acid was 107.5 versus 177-210 for the other stone types. The four patients with brushite stones were analyzed separately, and median HU for the ellipse tool was 951 (IQR: 636-1026) versus 847 (IQR: 683-879) for the free-hand method ($p = 0.53$), Figure 2.

The radiology report provided HU measurements in 21 cases. In two situations, the highest value was annotated, whereas in one example a range of values of over 400 units was provided. In the remaining cases, a single measure was provided, but the exact methodology used by the radiologists creating the report was unknown. Comparing these 18 cases to f-ROI and e-ROI measurements, there were no significant differences ($p > 0.35$ for both). The mean difference between radiology derived value and f-ROI method was 90 units whereas for the e-ROI it was 35 units. In this limited cohort, the radiologic derived HU number was not able to differentiate between stone types.

Figure 1. Left example of HU using ellipsoid capture tool approximating shape. Right HU with free-hand capture tool, following contours of stone shape in the same patient.

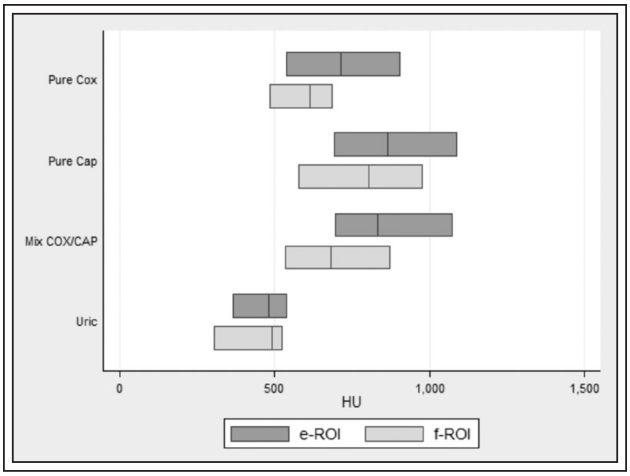

Figure 2. HU based on stone types.

In a separate analysis, we determined the relationship of percentage of each stone component with HU, given our patients with mixed stones. For example, we studied the relationship between increasing percentage of CaP and f-ROI density and found no significant association. Overall, correlation coefficients derived from HU measurements and percentage of stone components revealed patterns of weak to moderate correlations throughout, Table 2.

Excellent agreement was notable amongst the two graders for both e-ROI and f-ROI with average intraclass correlation of 89.9% (95%CI: 84.6%-93.4%) and 90.0% (95%CI: 84.7%-93.4%), respectively. The average time for graders to apply the free-hand tool was 5.5 seconds versus 4.9 seconds for ellipsoid ($p = 0.616$). In this experiment, one grader was slightly faster than the other on average, but this seems unlikely to impact overall efficiency given such short time expenditures overall ($p = 0.013$).

Discussion

HU determination is increasingly effecting management of nephrolithiasis. Key decisions which may be aided by HU determination include propensity for fragmentation with ESWL versus likelihood of resistance to fragmentation, or likely uric acid stone composition which could be treated medically. Urologists review imaging to aid in preoperative decision making and the additional step of HU determination adds little time and effort. Independent of the selected method, our graders took less than 6 seconds to perform this task. In a subset in which radiologists provided HU, there were no significant differences between their values and f-ROI or e-ROI. Either methodology seemingly provides the ability to discern a significant uric acid component of a stone despite a heterogeneous mix of CT scanners.

Our range of HU for each stone type is consistent with previous published values. HU density for any calcium containing stone has previously been estimated at 1050 HU/cm and uric acid 500 HU/cm, which are extremely similar to our values of HU density with e-FOI of 938 HU/cm and 414 HU/cm, respectively.[7] Others have reported uric acid stones to have HU of 338-500, consistent with our findings.[8,9] Likewise, in a study primarily powered to assess ESWL success based on attenuation values, ranges for various stone types included: 412-1585 for CaP, 371-1330 for CaOx and 136-402 for uric acid.[2] Some of these groups have even attempted to differentiate calcium monohydrate and dihydrate stones given potential clinical applications, but our cohort only included five calcium dihydrate majority stones. As such we were not powered to study this subgroup.

Various groups have published different methodology for estimating HU of stones: the average of distinct single pixel ROI measurements, using five pixel areas as estimates, a circular ROI 1 mm to 2 mm inside of a stone outline with a bone attenuation window, a hand-drawn ROI leaving 0.5 mm at the boundary, or by HU volume determination.[3,10-13] While all of these methods have demonstrated varied degrees of stone composition differentiating power, they are often tested in an ex-vivo setting, with specific settings and single CT scanners. Moreover, they are not necessarily intuitive or as quick as the method presented here and sometimes require radiology involvement. In summary, our method

TABLE 2. **Correlation between % stone component and HU by method**

Component	Free HU	Ellipse HU	Free HU density	Ellipse HU density
% CaOx	-0.15	-0.06	0.26*	0.30*
% CaP	0.32*	0.28*	0.04	0.01
% Uric	-0.32*	-0.34*	-0.32*	-0.31*

* $p < 0.05$; HU = Housefield units; CaOX = calcium oxalate; CaP = calcium phosphate

meets the differentiating power demonstrated by those previously published but it is efficient enough to incorporate into clinical practice.

Our cohort represents a heterogenous set of abdomino-pelvic CT scans, which can be viewed as a limitation or as a strength. We believe this study represents a realistic cohort of patients seen in a clinic setting. Upon discussion with radiology, the method of determination of HU at our center is currently at the discretion of each practicing radiologist. Our values were very similar to those provided by radiology, when available. Some in our radiology community believe spiral CT offers significant advantages beyond current techniques for stone composition determination and are hesitant for urologists to base treatment decisions on HU given the limitations of current technology.[14,15] We did not have radiologists actively participate in grading, by design as we aimed to pursue suitability of this approach for urologists for use in clinic

Certainly our findings indicate some measureable difference in stones when the full contour is included. We speculate the f-ROI tool, averages HU of the nucleus of the stone as well as outer rim components whereas e-ROI more accurately describes the nucleus of the stone alone. Anecdotally, urologists often observe the outer portion of stones fragment with ease while an inner hard nucleus requires more energy and time, even in cases of pure stone type. This is not unsurprising given newer stereomicroscopy techniques reveal very few stones to be purely composed of one mineral.[16] Given we observed the e-ROI tool was consistently higher, on average by 107 units, we are likely observing further evidence of this fact. It may be that e-ROI in capturing the core of the stone avoids volume averaging of surrounding soft tissue whereas f-ROI adds more variability given inclusion of irregular corners.

Indeed, previous studies have suggested concentric laminations may be involved in stone formation.[17] Zarse et al, eloquently demonstrated via micro-CT techniques that various portions of stones can be delineated and studied, each representing different mineral types in a heterogenous stone.[18] Likewise, standard deviation of HU determination has been shown to increase accuracy and differentiation between stone types.[19] Our findings indicate uric acid stone identification may be improved with inclusion of this data, although our standard deviation measurements for attenuation were increased from those previously reported.

New technology may ease the burden on urologists and offer increased accuracy for image-based stone composition determination. A novel automated system which accounts for abnormal shapes and applicable to low dose CT-scans was recently able to identify the main component of a kidney stone 52% of the time.[20] New dual source CT imaging may allow for further differentiation of stone type, although it is not yet widely available.[21] Moreover, even preliminary ex-vivo studies applying different levels of energy to stones offer conflicting and opposite results regarding values for CaP and CaOx.[10,12] MRI has may be able to identify stones of varied composition by application of ultra-short echo times.[22]

In terms of limitations, CT scanner type and settings were not standardized in any way. Likewise, attenuation windows were set to abdomen in an effort to maximize efficiency as this is the default setting and anecdotally the one most often used for surgical planning. Some groups advocate using bone windows or other settings to accurately see stone demarcation and limit volume averaging.[18,23] Also, larger image slices tend to increase attenuation averaging and we were unable to control image width in the heterogeneous cohort.[24] We did not have any cystine stones whose HU attenuation may overlap with other stone types, although this clinical dilemma is easily solved with urine pH determination. We have limited patient numbers, particularly for uric acid and brushite stones. Stone composition in this study was based on fragments and potentially open to sampling error given recent findings almost no stone is pure if analyzed in detail.[16]

We did not attempt to replicate the vigorous research methods used previously in lieu of efficiency.[3,10-13,23] In effect, we demonstrate for clinical urologists worldwide such rigorous methods are not fully required to apply HU to clinical practice. Despite our efforts, we believe it is unlikely HU alone can be used to diagnose stone type without additional clinical or metabolic information, no matter the methodology. At present, differentiating CaOx and CaP stones by imaging alone has limited clinical utility for the clinical urologists seeking to make treatment decisions with their patients.

Conclusion

For urologists lacking HU on their radiology reports, either free hand or ellipsoid measurement provides an efficient, additional tool to guide management. HU differentiates between any calcium containing stone and uric acid stones. Free-hand measurement may be more distinguishing than ellipsoid given the ability to account for non-spherical shape, but further investigation is needed to determine the clinical utility. □

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