REVIEW PAPER

UROLITHIASIS

# Predicting stone composition before treatment – can it really drive clinical decisions?

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**Introduction** Determination of stone composition is considered to be crucial for the choice of an optimal treatment algorithm. It is especially important for uric acid stones, which can be dissolved by oral chemolysis and for renal stones smaller than 2 cm, which can be treated with extracorporeal shockwave lithotripsy (ESWL).

**Material and methods** This short review identifies the latest papers on radiological assessment of stone composition and presents a comprehensive evaluation of current scientific findings.

**Results** Stone chemical composition is difficult to predict using standard CT imaging, however, attenuation index measured in Hounsfield units (HU) is related to ESWL outcome. Stone density >1000 HU can be considered predictive for ESWL failure. It seems that stone composition is meaningless in determining the outcome of ureterolithotripsy and percutaneous surgery. Alternative imaging techniques such as Dual–Energy CT or analysis of shape, density and homogeneity of stones on plain X–rays are used as promising methods of predicting stone composition and ESWL outcome.

**Conclusions** New imaging techniques facilitate the identification of uric acid stones and ESWL–resistant stones. Therefore, they may help in selecting the best therapeutic option.

Key Words: urinary calculi ‹› chemical composition ‹› computed tomography ‹› ESWL ‹› percutaneous nephrolithotomy

## INTRODUCTION

Preoperative determination of stone composition seems to be essential for optimal stone management. It is important for three reasons. Firstly, composition is related to hardness, which in turn affects the outcome of extracorporeal shockwave lithotripsy (ESWL); hard stones may be resistant to ESWL treatment. Secondly, stones related to various metabolic syndromes, such as cysteine stones or uric acid stones may require systemic medical treatment. Finally, knowing the stone composition enables some preventive efforts (drug treatment, dietary restrictions) [1].

This is not an easy task. For years there have been many attempts to predict stone composition by analyzing metabolic status, searching for microcrystals in urine sediment, and finally by means of radiological examinations [2, 3]. In most cases minerals found in crystals from urine sediment corresponded to those found in stones [4]. However, the accuracy of these methods is not sufficient enough to use them in clinical practice. Additionally, stones are usually not composed of monocrystals and even two stones made up of the same minerals may differ in fragility because of their structural variability [5].

There are about eight minerals or substances that are frequent components of urinary stones and even more which occur sporadically. Chemical analysis, which is used in laboratory evaluation of extracted stones, is a complex process of reactions and requires the use of sophisticated techniques, such as X–ray diffraction or different types of spectroscopy [6]. None of these methods are able to define chemical composition of a stone *in vivo*. There is no simple and single radiological variable, such as attenuation index (Hounsfield units; HU), which can differentiate all of these substances.

Different imaging methods have been tested as predictors of stone composition, fragility, or treatment outcome. The question remains whether knowledge of chemical composition or fragility of stones can ac-

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tually influence our treatment decisions? And if so, whether this can apply to all patients?
This short review identifies the latest papers on radiological assessment of stone composition and presents a comprehensive evaluation of current scientific findings. The possibilities of currently available radiological examinations are discussed.

## Attenuation index and stone composition

CT remains the gold standard for diagnosis of urinary calculi. Stone density, which can be the indirect exponent of its chemical composition, is measured as CT stone attenuation value on non–contrast computed tomography (NCCT). So far, many studies focused on the predictive value of CT as a diagnostic tool for stone composition assessment [7, 8, 9]. However, this method is not helpful enough for certain differentiation of varying stone compositions. Moreover, in the study by Grosjean et al. the capability of four different computed tomography scanners to estimate urinary stone composition based on CT attenuation values was assessed. Direct comparison showed that there is a great variability between CT scanner models. The authors concluded that CT analysis and evaluation of Hounsfield units is not sufficient for the characterisation of renal stones [10].
Another issue is relatively high radiation dose associated with CT scanning. Therefore, low–dose stone protocols are used and are an excellent diagnostic tool. There are doubts whether the low–dose NCCT affects the evaluation of stone attenuation values. Alsyouf et al. analysed HU assessments in low– and conventional dose NCCT (from 5 to 140 mAs) on identical stones placed in various ureteral locations in cadavers. They have found that the reduced radiation dose is not associated with significant differences in stone HU values [11].
Dual–energy CT (DECT) is a newer technique, which can more accurately discriminate between different types of urinary calculi [12, 13]. Recently published studies have found that DECT can be used for *in vivo* characterisation of urinary calculi and sub–differentiation of calcium stones. It also enables the detection of lithotripsy–resistant calcium oxalate monohydrate stones [14]. DECT showed excellent accuracy in identification of stone chemical composition except for that of mixed stones [15].

## Uric acid stones

The main issue is identification of uric acid stones, because they can be dissolved by oral chemolysis. This is an argument for making efforts to determine this fact prior to any treatment. There is evidence that the combined use of CT attenuation index (<500 HU) and urine pH (<5.5) can result in high sensitivity and specificity in predicting stones composed of uric acid [16]. Another method is use of DECT. In contrast to other types of stones, uric acid stones are characterized by no change in attenuation when scanned with the two different X–ray energy spectra [17]. Thus, being radiolucent on plain X–ray and having specific properties under DECT, uric acid stones may be diagnosed *in vivo* and surgical treatment can be replaced by conservative measures. However, this does not apply in every case. Patients with ureteral and large renal uric acid stones are mostly candidates for interventional treatment because fragmentation resulting in increased stone surface area is essential for effective chemolysis. Therefore, in those cases oral chemolysis is used as an adjuvant to an ESWL or endourologic procedure and any actions taken to determine stone composition beforehand are pointless.

## Non–uric acid stones

It remains uncertain whether the type of non–uric acid stones can determine a treatment algorithm. According to the European Association of Urology Guidelines, identification of stone composition should be considered before selection of the stone removal procedure. This is mostly important in case of renal stones because of multiple treatment options available (FURS *vs.* PNL *vs.* ESWL).
Studies assessing the utility of stone CT attenuation as a predictor of flexible ureteroscopy with holmium laser lithotripsy outcome are limited. Ito et al. found that attenuation coefficients on NCCT were significantly related to the fragmentation efficiency and operative time, but they did not predict stone–free status [18]. Authors of another study did not observe differences in the operating time among the apatite, brushite, cystine, calcium oxalate monohydrate, calcium oxalate dihydrate, and uric acid stones [19].
Similarly, percutaneous lithotripsy dedicated studies are scarcely available. It seems that stone chemical composition is meaningless for the outcome of PNL. In the study concerning factors that affect bleeding during PNL, stone composition was not found as a predictor of total blood loss in a multivariate analysis [20]. In another study only struvite composition was an independent predictor for the development of complications [21].

## Predicting ESWL outcome

Contrary to invasive intracorporeal methods of lithotripsy, there is strong evidence that chemical stone composition is one of the factors determining ESWL success. Unfavourable stone composition (calcium oxalate monohydrate, brushite and cystine) is considered a major cause of ESWL failure [22]. For that reason, evaluation of stone composition before ESWL is clinically important. As stated previously, no imaging study can accurately predict chemical composition, however, stone fragility is related to its structure and density, which can be assessed by NCCT and expressed as an X–ray attenuation value. The relationship between stone density and ESWL outcome was evaluated in a number of studies (Table 1). Ouzaid et al. have prospectively analysed 50 patients with 5–22 mm renal stones to find the stone attenuation threshold predictive for ESWL failure [23]. In patients successfully treated with ESWL (stone–free or with only residual insignificant fragments four months after single ESWL session ) stone attenuation values were significantly lower than in patients with poor ESWL outcome (715 HU *vs.* 1196 HU, $p < 0.001$). The threshold of 970 HU was proposed by the authors as most sensitive (100%) and specific (81%), based on receiver–operating characteristic curves. The stone–free rate for patients with stones <970 HU was 96% *vs.* 38% for patients with stones ≥970 HU ($p < 0.001$). Other authors have obtained similar results with the threshold assessed from 612 to 1200 HU [24–31]. Therefore, based on results of those papers, stone density >1000 HU is commonly considered as strongly predictive for ESWL failure [33].

On the other hand, even a simpler method may be sufficient to predict the ESWL outcome. Some authors argue that plain radiography can predict renal stone fragmentation by ESWL [34]. Unlike CT–attenuations, the stone radiodensity is presented directly during ESWL. Hussein et al. found that nonhomogeneous stones with an irregular outline and density less than or equal to that of bone (for example the 12th rib) are easily fragmented by ESWL. Thus, CT would be necessary to predict success of ESWL only in cases of homogeneous and smooth stones with a density higher than bone [35].

## CONCLUSIONS

Analysis of stone images is crucial in selected groups of patients. Imaging techniques enable identification of uric acid stones and ESWL–resistant stones and therefore may lead to the selection of the best therapeutic option. Composition of non–uric acid stones, which need to be treated with invasive techniques, is very difficult to predict and the clinical value of this additional information is limited.

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**Table 1.** *Prediction of successful ESWL based on stone density*

| Study | N | Success definition | Results |
|---|---|---|---|
| Foda K, et al. [27] | 368 | Stone fragments <3 mm | Best discrimination value in ROC analysis:<br>≤934 HUs (94.4% sensitivity and 66.7% specificity) |
| Panah A, et al. [28] | 97 | Clearing of ureteral stone | Mean HU values for success *vs.* failure: 480 *vs.* 612 (P=0.004) |
| Choi JW, et al. [29] | 153 | Stone fragments ≤4 mm | Mean HU values for success *vs.* failure:<br>For stones ≤10 mm: 781 *vs.* 829 P=0.6<br>For stones >10 mm: 814 *vs.* 844 P=0.54 |
| Ouzaid I, et al. [23] | 50 | Stone fragments <4 mm | Best discrimination value in ROC analysis:<br>970 HU (100% sensitivity and 81% specificity) |
| El–Nahas AR, et al. [25] | 120 | Stone fragments <4 mm | Mean HU values for success *vs.* failure: 709 *vs.* 776 (P=0.2) |
| Weld KJ, et al. [30] | 200 | Stone fragments <4 mm | Mean HU values for success *vs.* failure in MVA: 638 *vs.* 801 (P=0.2) |
| Cheng G, et al. [31] | 52 | Stone fragments <3 mm | Mean HU values for success *vs.* failure: 579 *vs.* 1032 (P<0.01) |
| Gupta NP, et al. [24] | 112 | Stone fragments ≤5 mm | 72% of calculi >750 HU required three or more ESWL sessions |
| Pareek G, et al. [32] | 100 | Stone fragments ≤3 mm | Mean HU values for success *vs.* failure: 578 *vs.* 910 (P<0.05) |

N – number of patients in the study; ROC – receiver operating curve; MVA – multivariate analysis; HU – Hounsfield units

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