Coherent Scatter Computed Tomography for Structural and Compositional Stone Analysis: A Prospective Comparison with Infrared Spectroscopy

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Coherent Scatter Computed Tomography for Structural and Compositional Stone Analysis: A Prospective Comparison with Infrared Spectroscopy

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Abstract

Introduction: Infrared spectroscopy (IRS) is a standard method of stone analysis yielding relative proportions of stone materials within a sample. IRS is destructive, using powdered samples with only a fraction of the stone being analyzed. This leads to sampling bias with components being over or underestimated or even missed entirely. IRS lacks the ability to provide structural composition such as that at the stone core. Coherent scatter computed tomography (CSCT) uses diagnostic x-rays to provide detailed structural and compositional analysis of intact specimens including detailed imaging of the stone core.

Methods: Consecutive patients undergoing surgical treatment for stone disease were recruited for the study. Stones or fragments were collected during surgery and underwent both CSCT and IRS analysis. The two methods were compared with respect to overall bulk composition and for the ability to identify the material at the stone core.

Results: CSCT and IRS agreed on the primary component in the majority (84.8%) of samples. CSCT detected additional compounds in 88.8% of stones identified as uniform by IRS. CSCT identified a distinct stone core in 78.8% of samples with IRS failing to detect the core compound in 21.2% of these stones. In 30.3% of the stones with a core component, IRS did not identify the core compound as the primary component.

Conclusion: CSCT provides superior quantitative stone analysis and is not prone to issues such as sampling error as the entire specimen is analyzed. CSCT offers excellent structural imaging of stone samples including detailed analysis of core composition.
Introduction

It has been estimated that the prevalence of urinary stone disease in the United States is roughly 10% to 15% with evidence it is on the rise.\(^1\) Although urolithiasis once represented a significant cause of renal loss and even mortality worldwide, innovations in surgical technique including the proliferation of shockwave lithotripsy (SWL), ureteroscopy (URS) and percutaneous nephrolithotomy (PCNL) have dramatically reduced this burden. Knowledge of stone composition provides clinicians with information that helps direct care including choice of treatment modality, dietary advice and medical therapy in an effort to render the patient stone-free and reduce the risk of recurrence.\(^2\) At present, standard laboratory stone analysis is performed by x-ray diffractometry (XRD) or infrared spectroscopy (IRS).\(^3\)\(^-\)\(^5\) Most stones are comprised of several mineral types, typically deposited in concentric laminations around a nucleus\(^4\) and factors triggering nucleation may be different to those promoting growth of peripheral layers.\(^6\) For example, the presence of struvite in the core of a stone suggests an infection-based triggering event, and recurrence prevention might target the cause of the infection, while struvite in only peripheral layers indicates an onset of infection subsequent to formation that would be treated differently. A calcium oxalate dihydrate (COD) calculus with its dehydrated chemical form, calcium oxalate monohydrate (COM), in the core indicates stone growth.\(^7\) It is thus generally accepted that composition – and in particular the nucleating event - is a key indicator of etiological processes and a critical factor in stone-disease management.\(^8,\)\(^9\) Unfortunately, XRD and IRS are destructive and analyze only powdered samples of the stone rather than intact stones or stone fragments. Standard laboratory stone analysis methods are inadequate with respect to providing information regarding the composition of the stone core. While radiographic techniques including computed tomography (CT) and micro CT offer
improvements over conventional radiography with respect to predicting stone composition, they fall short when analyzing different calcium components or small regions of a calculus.\textsuperscript{10-12}

Coherent scatter CT (CSCT) is a novel method developed in our laboratory that uses coherently scattered x-rays rather than the directly transmitted x-rays utilized by conventional radiography (Figure 1). Standard diagnostic energies are used to create specific coherent scatter patterns characteristic of, and unique to, each stone composition (Figure 2).\textsuperscript{13} CSCT has been shown to be accurate for the identification of stone components including COM, COD, uric acid (UA), calcium phosphate (CP/Apatite), calcium phosphate dihydrate (CPD/Brushite), magnesium ammonium phosphate (MAP/Struvite) and cystine.\textsuperscript{13} Davidson \textit{et al} demonstrated both compositional and structural analysis of intact urinary calculi using CSCT.\textsuperscript{14} The authors showed that CSCT accurately identified not only overall bulk composition of the calculi but also differentiated between regions of varying composition within non-uniform stones.

The objective of the present study was to prospectively evaluate CSCT for the structural and compositional analysis of human urinary calculi and to compare the results of this method with a standard technique of stone analysis (IRS). We hypothesize that CSCT will provide accurate overall compositional analysis and will prove superior to IRS for structural evaluation of stones including detailed information concerning the composition at the stone core.

\textbf{Patients and Methods}

Following institutional review board approval, we prospectively enrolled eligible patients into the trial. Patients were deemed eligible for the study if they were consented for either of two procedures (URS or PCNL) for the treatment of renal or ureteral calculi. The procedures were carried out as per standard surgeon protocol with no variation in technique for the purposes of this study. Calculi were retrieved based on the decision of the surgeon during the procedure.
Specimens were assigned a unique study number and were couriered to our laboratory for CSCT analysis. Following CSCT analysis the specimens were processed for IRS analysis as per standard institutional procedure.

Coherent scatter analysis was performed using a prototype CSCT system developed at our institution (Figure 1). Scans were performed using a 1mm² x-ray beam (70 kV) passed through a gadolinium filter to improve angular resolution of the scatter patterns. Intact stone samples were mounted in a secure holder to reduce movement artifact during the scan while allowing for tomographic slices in 2 and 3 dimensions. Low-angle x-ray scatter from the sample was detected using an x-ray image intensifier and charge-coupled device (CCD) camera. This generated a video signal that was digitized using a PC equipped with a PCI frame grabber (DT3155, Data Translation, MA). Captured scatter patterns were analyzed and compared to a chemical reference library obtained from pure chemical samples. A detailed explanation of the physical and mathematical approach used in this analysis is beyond the scope of this article and has previously been described by Davidson et al.

CSCT data was collected for each intact calculus or fragment at 0.25mm increments as the specimen was translated through the x-ray beams (70 kV, 200 mA). Raw data was reconstructed into tissue composition maps (Figures 3 and 4) as well as numerical proportion data. IRS was performed as per standard procedure. Stones were grouped into either uniform (single component) or non-uniform samples (two or more components) based on IRS analysis and compared to the data from CSCT analysis. Statistical analysis was performed using Graphpad Prism 4 (Graphpad Inc, CA).

Results
To date, 41 patients have been enrolled in the study with 33 of these having stone specimens collected during the procedure. The remaining 8 patients either had the stone(s) completely evacuated or the fragments were extremely small and left to pass spontaneously. All collected specimens have completed both IRS and CSCT analyses with the results summarized in Table 1.

Of the 33 samples, 9 were characterized as uniform and 24 as non-uniform composition based on IRS analysis. Of the 9 uniform stones, 8 (88.8%) were found to have at least one secondary component upon CSCT analysis. The most common secondary component identified by CSCT that was not identified on IRS was uric acid (6 of 8 specimens). The primary stone material identified on CSCT was the same as that identified by IRS in 28/33 specimens (84.8%). Due to the destructive nature of the technique, IRS was not able to distinguish components at the stone core while CSCT identified a distinct core in 26/33 specimens (78.8%). Approximately half of all stones identified as having uniform composition by IRS (5 of 9) showed a distinct core of a different mineral by CSCT. Of particular concern is that CSCT showed a core that was not identified at all by IRS in 7 samples (21.2%) and was not the primary IRS component in 10 specimens (30.3%)

Comparison of the two techniques for the identification of each stone component was assessed using the Bland-Altman method (Figure 5). This analysis illustrates the difference between relative concentrations of each mineral determined by IRS and CSCT as a function of the average concentration. General agreement was observed for each mineral, although significant differences existed in specific examples. It is believed this is due to the fact that CSCT gives the average concentration of each mineral for the entire stone while IRS analyses are based on selected fragments believed to be representative of the entire stone.
Discussion

Accurate stone analysis is essential to many aspects of stone management including treatment planning and prophylactic measures to reduce recurrence. IRS is an established technique for bulk stone analysis however it is limited in terms of structural imaging, particularly with respect to determining composition at the stone core. Davidson et al showed the accuracy of both IRS and CSCT when analyzing known quantities of compounds. Additionally, when areas of uniform composition identified by CSCT are analyzed by IRS there is also excellent agreement between the two methods. This suggests that both methods are technically accurate in determining the relative proportions of sampled materials. The two analyses differ, however, in that IRS samples only a fraction of the powdered stone leaving it susceptible to sampling error. For example, if a stone with a distinct core of UA surrounded by larger outer layers of COM is prepared for IRS in such a way as only the outer portion of the stone is sampled, there will likely be an underestimation of the UA component. In our study, IRS identified nearly one third of all specimens as being uniform in composition (consisting of 100% of one compound). In 88.8% of such cases, secondary (and sometimes tertiary and quaternary) components were identified by CSCT. This may be due, in part, to the IRS technique which assumes that values less than 5% of the volume are within the margin of error and are reported as zero. However, several of the uniform stones were found to have significant quantities of secondary compounds. For example, in one patient with a history of cystinuria (based on history and genetic investigation), IRS analysis determined the stone to be 100% cystine while CSCT showed a distinct core of UA comprising 38% of the intact specimen with the remainder being cystine and small amounts of struvite (figure 4b). The additional information provided by CSCT adds an element of insight into the formation of calculi and potentially assists with prophylactic measures.
In this study, IRS and CSCT agreed in 28 of the 33 stones (84.8%) in identifying the primary stone component. This makes intuitive sense as the component that is the greatest in volume will be determined as the primary component on CSCT and will also be more likely to be sampled during IRS preparation. The two methods are more likely to disagree when components are present in smaller quantities such as at the stone core. CSCT identified a distinct stone core in 26 (78.9%) of the samples, information that is not provided by IRS. If the bulk analysis provided by IRS were truly representative of the entire stone, one would expect that the core material identified by CSCT would be present in some quantity on the IRS analysis. In our series, the core material identified by CSCT was not the primary IRS mineral in 10 (30.3%) stones, and completely omitted from the IRS report in 7 (21.2%) stones.

Medical management of recurrent urolithiasis can be challenging and depends upon accurate identification of risk factors such as diet, lifestyle and metabolic abnormalities that may predispose a patient to the formation of stones. Stones may also form in layers with an initial core consisting of one material (i.e. UA) with another material such as COM encasing the core. While this information may be inferred from IRS by interpreting a bulk analysis or by selective sampling of the interior of a stone, CSCT offers a distinct advantage by providing accurate bulk analysis and structural imaging of the intact specimen. A situation where the information provided by CSCT may alter patient management is the previous example concerning a patient with known cystinuria and a history of multiple surgical interventions including PCNL and URS. IRS analysis identified this patient’s stone as 100% cystine while CSCT demonstrated a distinct uric acid core surrounded by cystine (Figure 4b). By targeting the uric acid component of this stone with dietary modification and, if necessary, medical therapy we hope to prevent the initial nucleation of the uric acid nidus and delay calculus formation. Of
course, with a history of cystinuria this patient remains at high risk for recurrence, however, merely reducing the rate of recurrence and prolonging the interval between stone episodes may spare this individual from numerous procedures.

A potential application of CSCT is the ability to accurately analyze stone composition in situ. Numerous studies have demonstrated the efficacy of SWL on stones of varying composition and efforts have been made to use various imaging modalities to predict SWL success.\textsuperscript{17, 23-25} No single technique has, as yet, distinguished itself as ideal for in situ stone analysis. At present, CSCT has not been used for in situ stone analysis primarily due to the issues of stone tracking and excess scatter from surrounding tissues. One potential solution to the issue of stone tracking would be to transmit an x-ray pencil beam through the stone and then collimate the detector along this beam. In situ imaging would involve transmitting the beam through the body which would result in scatter not only from the stone but from surrounding tissues. The use of multiple detector arrays to collect overlapping scatter and isolate just those from the stone is a potential solution although it has not yet been tested.

Coherent scatter CT offers accurate bulk stone analysis and provides structural imaging that is not available though standard laboratory techniques. In the future, we plan to conduct a prospective multicenter trial comparing both CSCT and IRS analyses as part of a management plan for stone-forming patients. We hope to demonstrate that the additional information provided by CSCT reduces recurrence rates by providing more accurate information to clinicians.

**Acknowledgments**

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References


Figure 1 – CSCT acquisition system

Coherent scatter is generated in the stone specimen when irradiated with a 1-mm pencil beam of x-rays. The resulting scatter pattern is characteristic of the mineral type.

254x190mm (96 x 96 DPI)
Figure 2. Coherent scatter patterns of a mixed urinary calculus. This stone has scatter patterns consistent with COM, CP and UA. The pattern on the right represents the composite of all three scatter patterns for the complete stone. Each of the three compounds creates a unique pattern that may be compared to a reference library and used to generate numerical proportion data as well as compositional maps (Figure 3).
Figure 3

Figure 3. CSCT analysis including a "stone map", numerical proportion data and graphical proportions of stone composition. The window at the top left represents CSCT transmission through the intact stone whereas each subsequent window shows strictly the stone component indicated.

190x254mm (96 x 96 DPI)
Figure 4. Composition images showing distributions of minerals in two intact stones. Each stone is approximately 1 cm in diameter. a) Stone with a struvite core (green) with subsequent layers of uric acid (red) and calcium oxalate monohydrate (blue). b) Three slices through a stone from a patient with a documented history of cystinuria. The IRS analysis reported 100% cystine while the CSCT analysis identified a distinct uric acid core (red) surrounded in cystine (blue) with small accumulations of struvite (green).
Figure 5. Bland-Altman plots of IRS and CSCT results for 33 stone samples. The dotted line represents the bias. Note that for lower average values (ie. 0.0 - 0.2) there is a tendency for the difference to be negative indicating a bias towards CSCT. This is likely due to the fact that IRS often disregards these smaller values reporting a value of 0 instead.

190x254mm (96 x 96 DPI)
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<th>Uniform by IRS</th>
<th>Non-Uniform by IRS</th>
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<tr>
<td>Number of patients</td>
<td></td>
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<td>41</td>
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<tr>
<td>Number of specimens</td>
<td>9</td>
<td>24</td>
<td>33</td>
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<tr>
<td>Number of specimens where IRS reported a uniform stone while CSCT identified one or more secondary components</td>
<td>8 (88.8%)</td>
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<td>Number of specimens where both IRS and CSCT identified the same primary component</td>
<td>9 (100%)</td>
<td>18 (75.0%)</td>
<td>28 (84.8%)</td>
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<td>Number of specimens where CSCT identified a distinct core</td>
<td>5 (55.6%)</td>
<td>21 (87.5%)</td>
<td>26 (78.8%)</td>
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<td>Number of specimens where CSCT identified a core mineral that was identified by IRS but not as the primary component</td>
<td>6 (66.7%)</td>
<td>4 (16.6%)</td>
<td>10 (30.3%)</td>
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<td>Number of specimens where the core mineral by CSCT was missed by IRS</td>
<td>4 (44.4%)</td>
<td>3 (12.5%)</td>
<td>7 (21.2%)</td>
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