PREDICTING URINARY STONE COMPOSITION USING X-RAY COHERENT SCATTER: A NOVEL TECHNIQUE WITH POTENTIAL CLINICAL APPLICATIONS

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ABSTRACT

Purpose: Coherent scatter properties depend on the molecular structure of the scattering medium and measured scatter patterns are often characteristic of a chemical species. We explored the usefulness of coherent scatter analysis as a basis for identifying urinary calculus composition.

Materials and Methods: A laboratory system for collecting coherent scatter signals from biological specimens was developed. This technique uses a diagnostic x-ray tube and image intensifier, and measures coherent scatter from intact renal stones. The coherent scatter signatures of 6 common stone components (calcium oxalate monohydrate, calcium phosphate, calcium phosphate dihydrate, cystine, magnesium ammonium phosphate and uric acid) were acquired from pure chemical samples and stones identified by infrared spectroscopy as having a uniform composition. In addition, a sample of calculus identified as containing only calcium oxalate dihydrate was examined. The same fragmented stone samples analyzed by infrared spectroscopy were scanned using coherent scatter.

Results: In each case the scatter patterns from powdered chemicals and fragmented stones showed circular symmetry and consisted of a series of broad rings of various intensities. Each pure chemical sample produced a distinct coherent scatter pattern. The signatures of the stone specimens closely agreed with those of the chemical samples.

Conclusions: These initial results indicate that coherent scatter analysis using diagnostic x-rays has potential as a tool for urinary calculous composition identification. Further developments in this technique may have the potential for determining the composition of a calculus in vivo before therapy, thus, aiding in therapy planning.

Key Words: urinary tract, urinary calculi, lithotripsy, radiation, x-ray diffraction

Accurate preoperative prediction of urinary stone composition remains a challenge for the urologist. Knowledge of the stone composition is important since urate, calcium oxalate monohydrate (whewellite) and cystine stones are hard and less responsive to treatment with extracorporeal shock wave lithotripsy (ESWL) (Dornier Medical Systems, Inc., Marietta, Georgia). Stone composition influences the choice of treatment modality, followup schedule and preventive measures against recurrence. Currently stone analyses using methods such as infrared spectroscopy, x-ray crystallography and polarizing microscopy are done for stone fragments retrieved from the patient after treatment. However, what is needed is preoperative knowledge of stone composition while the stone is still in situ.

Predicting urinary stone composition based on some type of preoperative imaging has been studied by various investigators. In the simplest case of plain x-ray Ramakumar et al found that a panel of physicians specializing in stone disease could only correctly identify the composition of renal calculi 39% of the time.1 Spiral computerized tomography (CT) has been found that a panel of physicians specializing in stone disease could only correctly identify the composition of renal calculi 39% of the time.1 Spiral computerized tomography (CT) has been used to identify accurately calculus composition in vitro.2,3 However, when spiral CT was applied in vivo, only calcium oxalate and uric acid stones could reliably be differentiated.4 In another in vitro study magnetic resonance imaging was able to separate struvite stones from apatite stones using T1-weighted imaging as well as struvite and uric acid using a proton density sequence.5 While some modalities appear promising, they generally lack sufficient discriminating power. We developed a system that combines the discriminating power of x-ray diffraction with the clinical preoperative usefulness of diagnostic imaging.

X-ray diffraction is a special case of an interaction known as coherent scatter. This type of scatter arises from the interaction of an x-ray beam with the electric field associated with the electron distribution of the scatterer. Electrons thus affected subsequently emit radiation of the same energy as the incident x-rays (fig. 1). Radiation produced by neighboring electrons interact, resulting in patterns of constructive and destructive interference (scatter patterns) (fig. 2). These patterns appear as characteristic diffraction patterns when produced from atoms that are rigidly fixed with respect to each other.6 The angle through which photons scatter depends on their energy. Therefore, x-ray diffraction is typically performed with a monoenergetic beam, which results in sharp diffraction peaks.7 Mono-energetic beams can be obtained using characteristic scatter from a secondary source, such as an 8 keV, Cu source, but this energy is too low to consider using it in situ due to insufficient penetration. Synchrotron sources produce mono-energetic beams in the diagnostic energy range with adequate penetration but these
facilities are expensive and not appropriate for general clinical use.

We developed a system for collecting low angle (less than 10 degrees) scatter from biological specimens that uses a conventional diagnostic (polyenergetic) x-ray source and x-ray image intensifier. In the diagnostic energy range low angle scatter is primarily coherent. We show that it is possible to differentiate hard and soft stone components based on their coherent scatter patterns despite the broadening of these patterns due to the polyenergetic source.  

An alternative approach using low angle x-ray scatter to identify calculi was proposed by Dawson et al using an x-ray tube operating at 70 kVp. and 1 mA. Scatter is detected by an energy resolving germanium detector set at a fixed angle to the primary beam and a multi-channel analyzer. While this method demonstrates differences in the spectra of x-rays scattered from different components, it is time-consuming (180-second acquisition per stone) and provides no mechanism for analyzing mixed stones. In contrast, exposures for the current method are less than 10 seconds in duration and could be optimized further. Scatter patterns of aggregate materials are linear superpositions of each constituent pattern. Pure chemicals possibly present in a sample are analyzed and result in a set of library patterns. Coherent scatter signals from unknown specimens are identified by fitting this library to the unknowns using a nonnegative least squares algorithm. The fit parameters reveal the relative proportions of each material present in the specimen. We have previously demonstrated that this technique can be used to decompose conglomerates into their constituents.  

In this study we explored the usefulness of coherent scatter analysis as a basis for classifying urinary calculus composition. We present a library of common stone constituents and demonstrate similarities in the coherent scatter from pure chemicals and that from urinary calculi collected postoperatively. Because our scanner uses diagnostic equipment, coherent scatter analysis may eventually be developed to determine the composition of stones in situ.
beam, thus, reducing the broadening of scatter peaks due to the polychromatic source. After filtration the beam is collimated to 1 mm\(^2\) using a triple aperture, parallel plate collimator. The stone is mounted on a specimen stage 30 cm. from the x-ray source. The transmitted primary beam is blocked by 3 mm. Pb, while coherent scatter from the object is detected by the CFS x-ray image intensifier (Precise Optics, Bay Shore, New York) mounted 30 cm. from the specimen and centered on the beam axis. The output phosphor of the x-ray image intensifier is read by a charge coupled device video camera (Cohu, Poway, California) operating at 30 frames per second and processed on an O2 work station (Silicon Graphics, Mountain View, California).

Chemical reference library. Chemically pure samples of calcium oxalate monohydrate, calcium phosphate (apatite), calcium phosphate dihydrate (brushite), cystine, magnesium ammonium phosphate (struvite) and uric acid served as standards. Each sample was mounted in the beam and exposed for 5.3 seconds.

Clinical stone samples. This process was repeated with a set of powdered calculi all of which were identified by infrared spectroscopy as containing only calcium oxalate monohydrate, calcium phosphate, calcium phosphate dihydrate, cystine or uric acid plus a stone identified as 60% magnesium ammonium phosphate and 40% calcium phosphate, and a calcium oxalate dihydrate stone. Information was extracted from the resulting scatter patterns by segmenting them into a series of concentric annuli, integrating the signal in each ring and normalizing the result to the solid angle subtended by the ring (fig. 4). The curve obtained in this manner is referred to as the cross section since it is proportional to the differential coherent scatter cross section.

RESULTS

Figure 2 shows scatter patterns for pure chemicals and stone samples. Each pattern had the circular symmetry characteristic of polycrystalline materials, although calcium oxalate dihydrate, cystine and magnesium ammonium phosphate-calcium phosphate stone samples had various degrees of additional structure in their patterns due to preferential scattering from aligned crystal planes. The patterns were segmented and integrated in whole rings and, hence, this structure had a limited effect on analysis. It was easily observed that each stone component had a distinct scatter pattern and stone patterns were consistent with pure chemical patterns.

Figure 5 shows graphs of differential coherent scatter cross sections obtained from the scatter patterns normalized to peak height (fig. 2). Again it was observed that each stone type had a distinct coherent scatter signature. Figure 6 shows direct comparisons of cross sections derived from pure powdered samples and those from powdered stones for each chemical species. The major features in each curve showed good agreement of pure chemicals and stone samples even in the cases of cystine and magnesium ammonium phosphate-calcium phosphate, indicating that structure in diffraction patterns does not impede component identification.

DISCUSSION

To our knowledge there is currently no reliable method in clinical practice to determine the composition of urinary calculi before proposed therapy. There are many treatment options for urinary calculi and optimal treatment often depends on stone size, location and composition. Stone size and location may be determined by radiography before treatment. However, stone composition is difficult to determine unless the patient has a history of recurrent urolithiasis and even this history is often unlikely to be predictive of stone composition.

The treatment modalities available for upper tract urinary calculi include ESWL, percutaneous nephrolithotripsy, ureteroscopic manipulation and rarely open renal surgery. ESWL is often the first line therapeutic modality used but unfortunately it is not applicable to all stone compositions. For example, calcium oxalate dihydrate, uric acid and magnesium ammonium phosphate stones are usually successfully fragmented by ESWL whereas cystine, calcium oxalate monohydrate, calcium phosphate and urate stones are less likely to fragment using ESWL.\(^{12}\) Thus, many patients undergo ESWL therapy unsuccessfully due to the unknown composition of the stone. If one were able to determine stone composition before treatment, treatment failures and the need for re-treatment could be minimized or possibly even eliminated.

Multiple methods have been used in an attempt to determine stone composition preoperatively, including previous stone analysis, urinary pH\(^{13}\), urine microscopy,\(^{14}\) plain x-ray,\(^{2}\) conventional CT,\(^{15}\) spiral CT,\(^{2\text{-}4}\) magnetic resonance imaging\(^{5,16}\) and bone densitometry.\(^{17}\) Although some of these modalities appear promising, currently there is no available modality in clinical use to determine stone composition before proposed therapy.
The current study indicates that coherent scatter analysis can be used as a basis for identifying urinary calculi by composition. This technique relies on establishing a library of cross sections obtained from pure chemical samples of materials known to be present in biological specimens of interest. We have previously shown in a bone imaging context that when such a library exists, it is possible to identify the composition of a conglomerate. The current study provides the collection of cross sections required to identify the most common components of urinary calculi. Figure 5 shows that each chemical component of a urinary calculus has a unique pattern of peaks in its cross section, signifying that components can be distinguished from each other.

Comparing cross sections of pure chemicals with those of stones encourages the development of coherent scatter analysis for calculous classification. Figure 6 shows that in each case stone curves agreed with all major features of the standard cross sections. However, there were differences in some instances. This finding was not unexpected because truly pure stones rarely occur. The discrepancy in pure uric acid powder and the stone identified as 100% uric acid by infrared spectroscopy is believed to be due to the presence of materials undetected or unreported by infrared spectroscopy. Human urinary calculi are known to be conglomerates of a mineral phase and organic matrix. Calciferous stones contain only 2% to 3% matrix by dry mass but the proportion is much higher in uric acid stones. Thus, the organic matrix likely explains discrepancies in the stone and pure chemical. There was also a divergence in the calcium phosphate standard and stone, which was also due to the presence of unidentified compounds. This discrepancy may be resolved by the second phase of our study, in which the composition of stones determined by coherent scatter analysis are planned to be compared to infrared spectroscopy and a third independent technique. Notably although we used fragmented stones in this study, the technique does not rely on small powdered homogenous specimens. Crushed stones were used only to facilitate direct comparison with infrared results.

We have determined the feasibility of applying coherent scatter techniques to the problem of identifying the composition of urinary calculi. It has been demonstrated that using a relatively simple apparatus constructed from diagnostic radiology equipment coherent scatter signals can be acquired that provide a characteristic signature for each stone type. The use of an imaging detector rather than a spectrometer, such as the Ge detector used by Dawson et al., enables the use of higher x-ray tube current settings, thereby reducing exposure time by a factor of 30. Although a Ge detector allows for finer energy resolution than is possible with the polyenergetic approach, distinctive curves are still obtained. Because the coherent scatter method is based on fitting unknown curves with standard curves obtained in the same

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Fig. 5. Cross sections from chemically pure samples of calcium oxalate monohydrate (COM), calcium phosphate (CP), calcium phosphate dihydrate (CPD), cystine (CYS), magnesium ammonium phosphate (MAP), uric acid (UA) and stone identified as 95% calcium oxalate dihydrate (COD) by infrared spectroscopy. Scatter intensity (I) at each scatter-angle was normalized to peak height.
manner, having cross sections that differ from each other is more important than any single chemical producing a single strong and easily recognizable feature.

CONCLUSIONS

This study shows that coherent scatter analysis can be used to determine the chemical composition of urinary calculi. Each chemical species examined demonstrated a distinct scatter pattern and, moreover, the scatter patterns of stones were shown to match pure chemical patterns. Study of a larger set of calculi is in progress to confirm these early results and investigate the predictive power of coherent scatter analysis with stones containing many components. Coherent scatter analysis uses standard diagnostic x-ray equipment and with appropriate collimation it may be adapted for use in the preoperative in vivo setting.

Calcium oxalate monohydrate, calcium phosphate, calcium phosphate dihydrate, cystine, magnesium ammonium phosphate and uric acid were obtained from Sigma-Aldrich Co., St. Louis, Missouri and Fluka Chemika, Buchs, Switzerland.

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Fig. 6. Normalized scatter intensity of calcium oxalate monohydrate (COM), calcium phosphate (CP), calcium phosphate dihydrate (CPD), cystine (CYS), magnesium ammonium phosphate (MAP) and calcium phosphate, and uric acid (UA) pure chemical (solid line) and stone (dotted line) cross sections.