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FULL PAPER

Determining the composition of urinary tract calculi using stone-targeted dual-energy CT: evaluation of a low-dose scanning protocol in a clinical environment

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Objective: This study will evaluate the accuracy of dual-energy CT (DECT) in characterizing urinary tract stone composition on patients presenting to a UK hospital with renal colic. The study will also assess the additional radiation dose burden of DECT over standard protocol.

Methods: Data from 106 DECTs between October 2011 and October 2015 were retrospectively analyzed. Patients were imaged using a Toshiba Aquilion ONE™ CT scanner (Toshiba Medical Systems, Otawara-shi, Japan). All patients received a low-dose non-contrast CT of the abdomen and pelvis prior to stone-targeted DECT at 80 and 135 kVp and 40-mm field of view. Radiation dose output was evaluated using dose-length product (DLP). 19 stones were recovered and their compositions were analyzed using Fourier transform infrared spectroscopy.

Results: 137 stones were characterized. Mean stone diameter was 8.8 mm (range 3–48 mm). There was an 18.7% increase in mean DLP for DECT over standard CT protocol (319.4 vs 269.1 mGy cm; $p < 0.001$). Infrared spectroscopy analysis of 19 recovered stones identified 15 stones as calcium, 2 stones as cystine and 2 stones as mixed composition. Dual energy correctly predicted 11 (78.6%) of 14 calcium stones, 2 (100%) of 2 mixed composition stones and 0 (0%) of 2 cystine stones, resulting in a fair agreement (Cohen's $\kappa = 0.374$, $p = 0.009$).

Conclusion: DECT is able to determine the composition of urinary tract stones with fair accuracy. Its utility is offset by a small but significant supplementary radiation exposure.

Advances in knowledge: DECT can provide urological surgeons with useful diagnostic stone material information prior to planning optimal management of stone disease.

INTRODUCTION

Urinary tract calculi are a common cause of attendance to emergency departments and referral to secondary health care systems; the lifetime prevalence is estimated at 10–14%, with a 50–70% risk of recurrence.¹ Stones are associated with significant morbidity including acute and chronic abdominal pain and renal failure.² As a consequence, stone disease is responsible for considerable economic burden on health care systems worldwide.³

Non-contrast CT is considered the gold standard in the diagnosis of urinary tract stones.⁴ Low-dose protocols are becoming increasingly widespread as a means of reducing the risk of cumulative lifetime radiation exposure with minimal loss of diagnostic quality, which is beneficial for young individuals who require multiple CT scanning for recurrent disease.⁵ While CT has numerous advantages (rapid acquisition, no contrast material, high sensitivity

for detecting stone burden, diagnosis of alternative abnormalities), it had not been able to reliably analyze the chemical composition of stones using single-energy protocols.⁶

Urologists are able to determine the chemical composition of retrieved stones post-operatively using crystallography (e.g. infrared spectroscopy); however, knowledge of stone composition prior to treatment can help guide optimal management. Firm stones, such as cystine and calcium oxalate monohydrate, are less likely to be successfully fragmented *via* extracorporeal shock-wave lithotripsy (ESWL), instead necessitating invasive endourological treatment such as ureterorenoscopy or percutaneous nephrolithotomy (PCNL). Uric acid stones can be dissolved medically with urinary alkalinization therapy, such as oral potassium citrate solution $\pm$ allopurinol. Patients with familial metabolic stone diseases may also benefit

from medical therapy; for example, captopril in patients with cystinuria.

Recent technological advances in dual-energy CT (DECT) have paved the way for new clinical applications. The principle of DECT is simultaneous acquisition of high- and low-energy data sets of the same anatomical location. Specific changes in attenuation [Hounsfield units (HU)] between high- and low-energy spectra allow DECT to differentiate between materials containing similar electron densities but differing photon absorption.⁷ Using software, DECT scanners can create attenuation profiles of stones including uric acid and calcium and assign colour to different materials. *In vivo* studies have demonstrated accurate pre-operative prediction of urinary tract stone material with DECT in agreement with crystallography analysis.^{8–10}

The aim of this study was to further evaluate the utility of DECT to predict urinary tract stone composition on a cohort of patients presenting to a UK National Health Service (NHS) hospital against a gold standard (infrared spectroscopy). The study will also compare ionizing radiation dose output of the DECT protocol with standard non-contrast single-energy CT protocol.

METHODS AND MATERIALS

Patients and study design

Acquisition data were retrospectively collected from 106 DECT scans performed on 102 patients presenting to Morriston Hospital (Abertawe Bro Morgannwg University Health Board, Swansea, Wales, UK) with urinary tract stones between October 2011 and October 2015. Both inpatient and outpatient cohorts were scanned *via* identical DECT protocols. Patients were predominantly male (ratio = 70 males:32 females), and mean patient age was 53.4 years (range = 14–87 years; standard deviation = 15.9).

Dual-energy CT protocol

All patients were imaged using a Toshiba Aquilion ONE™ CT scanner (Toshiba Medical Systems, Otawara-shi, Japan) following

a standardized dual-energy protocol: a single-energy low-dose non-contrast CT of the abdomen and pelvis is initially performed (Figure 1). The CT dose output is controlled for individual patients through automatic exposure regulation and tube current modulation. If a urinary tract stone is identified on the raw CT data by a radiographer trained in dual-energy acquisition, then stone-targeted DECT with 40-mm field of view is subsequently performed. The Aquilion ONE mechanism of acquisition involves fast-switching of both peak kilovoltage and tube current to provide images with similar noise characteristics. High-energy parameters were 135 kVp/37 mAs and low-energy parameters were 80 kVp/217 mAs. Full technical parameters are shown in Table 1. Two temporally uniform scans are acquired in a single synchronized rotation with no couch top movement.

Stone material characterization

Dual-energy software built into the CT scanner post-processed the data in an automated fashion. The region of interest (*i.e.* the stone) is initially identified by the radiographer. Following this, the attenuation profile of the stone is presented as a plot on a graph, featuring the attenuation value for low and high peak kilovoltage as *x*- and *y*-axes, respectively. A red line and a blue line are superimposed onto the graph to indicate the attenuation profiles for uric acid and calcium stones, respectively (Figure 2). The software also characterizes the stone by labelling it with a red colour for uric acid, blue for calcium and pink for a mixed stone (Figure 2). Images were evaluated by a single assessor for the following parameters: number of stones, location, maximal diameter and characterization of material.

19 stones were collected from 19 patients following DECT. Stones were retrieved either following invasive procedures including ureterorenoscopy and PCNL or after spontaneous passing of a stone. All stones were sent to the biochemistry laboratory at Royal Gwent Hospital (Aneurin Bevan University Health Board, Newport, Wales) for analysis of material composition using a Fourier transform infrared spectroscopy technique.

Dosimetry

CT dose index (CTDI) and dose-length product (DLP) values were obtained from all 106 DECTs as a measure of radiation dose output. Separate CTDI and DLP values for the single-energy CT and DECT acquisitions were recorded. For each scan, the single-energy DLP and dual-energy DLP were combined to calculate a total cumulative DLP per investigation.

Statistical analysis

The mean single-energy DLP and mean total cumulative DLP were statistically evaluated. Shapiro–Wilk testing revealed that the data were not normally distributed; therefore, non-parametric statistical analysis was adopted. A Wilcoxon signed-ranks test assessed the difference in mean DLP.

For characterization of stone material composition, agreement between DECT and infrared spectroscopy was evaluated using the Cohen's kappa coefficient. This statistical method has been previously used to assess agreement between DECT and crystallography.¹⁰ All statistical analyses were performed using SPSS® v. 22 (IBM Corp., New York, NY; formerly SPSS Inc., Chicago, IL).

Figure 1. Non-contrast low-dose CT abdomen and pelvis demonstrating a stone in the right pelvi-ureteric junction.

Table 1. Technical data for dual-energy CT protocol

Technical Parameter	Low energy	High energy
Kilovoltage (kVp)	80	135
Tube current (mAs)	217	37
Rotation time (s)	0.75	0.75
Field of view (mm)	40	40
Reconstruction slice thickness (mm)	0.8	0.8
Scanning time (s)	0.75 (simultaneous)	

RESULTS

Urinary tract stones

From 106 DECT acquisitions, 137 stones were characterized. 84 scans characterized a single stone, 16 scans characterized 2 stones, 4 scans characterized 3 stones, 1 scan characterized 4 stones and 1 scan characterized 5 stones. Mean maximal stone diameter was 8.8 mm (range = 3–48 mm; standard deviation = 6.1 mm). 116 (84.7%) stones were located in the kidney; 21 (15.3%) stones were located in the ureter. DECT determined 79 (57.7%) stones as calcium, 17 (12.4%) stones as uric acid and 41 (29.9%) stones as mixed composition.

Infrared spectroscopy

Infrared spectroscopy analysis of 19 recovered stones identified 15 (78.9%) stones as calcium, 2 (10.5%) stones as cystine and 2 (10.5%) stones as mixed composition. DECT correctly predicted

11 (73.3%) of 15 calcium stones, 2 (100%) of 2 mixed stones and 0 (0%) of 2 cystine stones. Cohen's kappa measure of agreement between DECT and spectroscopy revealed a fair agreement that was statistically significant (Cohen's $\kappa = 0.374$, $p = 0.009$). Tables 2 and 3 outline the agreement between DECT and infrared spectroscopy.

Dosimetry

The calculated mean CT radiation dose outputs are provided in Table 4. The mean DLP for standard single-energy low-dose protocol was 269.1 mGycm, with a range between 98.5 and 1304.5 mGycm. Dual energy contributed on an average an additional 50.3 mGycm (18.7%) DLP to the standard low-dose CT protocol; the total mean DLP was 319.4 mGycm, with a range between 143.5 and 1347.4 mGycm. The increase in mean DLP between standard single-energy low-dose CT and

Figure 2. Dual-energy CT (DECT) prediction of urinary tract stone composition: (a) DECT prediction of uric acid stone in the right pelvi-ureteric junction and (b) DECT prediction of calcium stone in left renal pelvis. The upper left panels are showing low kVp data. The upper right panels are showing high kVp data. The lower left panels are graphs depicting attenuation profile of the stone (dot). The lower right panels are showing high kVp data with superimposed colour over the stone indicating DECT prediction (see online article for colour figures).

Table 2. Retrieved stone size, location, dual-energy CT (DECT)-predicted material and infrared spectroscopy-confirmed material

Patient number	Stone size (mm)	Stone location	DECT-predicted stone material	Infrared spectroscopy-confirmed material	Agreement?
1	5	Kidney	Mixed	Calcium (100% oxalate)	No
2	22	Kidney	Mixed	Mixed (50% calcium phosphate, 50% struvite)	Yes
3	3	Kidney	Calcium	Calcium (100% oxalate)	Yes
4	20	Kidney	Uric acid	Calcium (75% oxalate, 25% phosphate)	No
5	8	Kidney	Calcium	Calcium (100% oxalate)	Yes
6	4	Kidney	Calcium	Calcium (100% oxalate)	Yes
7	20	Ureter	Mixed	Mixed (70% calcium phosphate, 30% struvite)	Yes
8	8	Kidney	Mixed	Calcium (80% oxalate, 20% phosphate)	No
9	6	Kidney	Mixed	Calcium (80% phosphate, 20% oxalate)	No
10	15	Kidney	Calcium	Calcium (80% oxalate, 20% phosphate)	Yes
11	12	Kidney	Mixed	Cystine 100%	No
12	10	Kidney	Calcium	Calcium (90% phosphate, 10% oxalate)	Yes
13	6	Kidney	Calcium	Calcium (79% oxalate, 21% phosphate)	Yes
14	9	Ureter	Calcium	Calcium (100% oxalate)	Yes
15	8	Kidney	Calcium	Calcium (60% oxalate, 40% phosphate)	Yes
16	5	Kidney	Calcium	Calcium (81% oxalate, 19% phosphate)	Yes
17	10	Ureter	Calcium	Calcium (60% oxalate, 40% phosphate)	Yes
18	3	Kidney	Calcium	Calcium (100% oxalate)	Yes
19	48	Kidney	Mixed	Cystine 100%	No

DECT protocols was significant (269.1 vs 319.4 mGy cm; $Z = 9.567$; $p < 0.001$).

DISCUSSION

DECT has recently begun to establish its efficacy in predicting urinary tract stone material composition, both *in vitro* and

in vivo, prior to clinical management.^{8–11} The purpose of this study was to discover whether the benefits of a low-dose DECT protocol could be applied to patients presenting to a UK NHS hospital with urinary tract stones, while endeavouring to avoid additional accumulation of significant ionizing radiation.

Table 3. Agreement between dual-energy CT and infrared spectroscopy for determination of urinary tract stone composition

Dual energy	Infrared spectroscopy			
	Calcium	Mixed	Uric acid	Cystine
Calcium	11	0	0	0
Mixed	3	2	0	2
Uric acid	1	0	0	0

Table 4. Mean radiation dose output data ($\pm$ standard deviation)

Non-contrast CT urinary tract (single-energy)		Stone-targeted dual-energy CT		Total dose output per investigation
CTDI/vol	DLP (mGy cm)	CTDI/vol	DLP (mGy cm)	DLP (mGy cm)
6.02 (± 3.95)	269.10 (± 190.63)	11.17 (± 1.08)	50.30 (± 13.05)	319.40 (± 191.57)

CTDI, CT dose index; DLP, dose-length product.

In our study, we correctly predicted 68% of urinary tract stones *in vivo* using a low-dose DECT protocol on a Toshiba Aquilion ONE™ scanner. Cohen's kappa confirmed significant agreement between DECT and infrared spectroscopy; however, the magnitude of agreement ($\kappa = 0.374$) suggests that this agreement is merely "fair".¹² Recent *in vivo* studies have demonstrated greater accuracy in determining stone composition *via* DECT. Hidas et al⁹ prospectively performed stone-targeted DECT using a Philips Orion N (Philips Healthcare, Cleveland, OH) prior to performing PCNL on 27 patients and demonstrated an 81% (22 of 27 stones) success rate after confirmation with X-ray diffraction. Manglaviti et al¹⁰ retrospectively compared DECT acquisitions from a Siemens Somatom Definition scanner (Siemens Medical Solutions, Forchheim, Germany) with crystallography in 40 patients with suspected stone disease and showed high accuracy in determining the chemical composition [(92%) 45 of 49 stones]. Inconsistency between different manufacturers and models of CT scanners could potentially explain the differences in accuracy between the studies. When comparing the capability of four major brands of CT scanners to predict urinary tract stone composition *in vitro via* dual energy, Grosjean et al¹³ found not only intense overlapping of attenuation profiles (making stone identification difficult), but also significant variability in HU values between CT scanners manufactured by different companies. The DECT protocol used in our hospital is recommended by the manufacturer, although we do not know whether the company determined stone material attenuation profiles from the same model or extrapolated predetermined acquisition parameters from alternative CT models.

Uric acid stones are composed of low-molecular weight elements (carbon, hydrogen, oxygen and nitrogen). At high- and low-CT voltage outputs, uric acid stones exhibit different CT attenuation properties in comparison with other stone materials (calcium oxalate/phosphate, cystine and struvite), which are composed of elements with higher molecular weights (calcium, phosphorus, magnesium and sulfur).¹⁰ Uric acid stones demonstrate higher HU values at high voltages, in comparison with calcium and other stone materials, which demonstrate higher HU values at low voltages.

None of the 19 retrieved stones in our study were confirmed on infrared spectroscopy to be uric acid. In addition, one confirmed calcium stone was incorrectly predicted to be uric acid by DECT. Therefore, we are unable to discuss the accuracy of DECT to determine uric acid stones from our results, which is disappointing, since the identification of a uric acid calculus is potentially the greatest advantage of DECT, as patients can avoid invasive and expensive procedures in favour of medical dissolution therapy.^{14,15} Primak et al¹¹ demonstrated the ability of

DECT to discriminate uric acid from other stone materials *in vitro via* phantoms with 92–100% accuracy. Thomas et al,⁸ Hidas et al⁹ and Manglaviti et al¹⁰ all demonstrated 100% accuracy for DECT to pre-operatively identify uric acid stones *in vivo*. In our department, all patients within whom uric acid stones are identified, including DECT, will have been commenced on potassium citrate medical dissolution therapy as standard protocol, which could potentially explain the paucity of uric acid stones retrieved in the study. As our patients have not been followed up in this study, we are unable to comment on the success of medical dissolution therapy to prevent additional invasive procedures.

The Toshiba Aquilion ONE™ DECT system unfortunately does not facilitate the identification of cystine calculi. Knowledge of a cystine stone can be useful to the surgical team when planning treatment, as the firm composition of cystine means it is less likely to be successfully fragmented by ESWL.¹⁶ These patients can therefore avoid exposure to complications of ESWL (including pain and renal bleeding) and are more likely to benefit from endourological interventions as first line. The attenuation ratio of cystine stones lies in between the attenuation ratios of calcium and uric acid,⁹ which may explain why two cystine stones retrieved in our study were predicted to be of mixed composition by DECT. *In vivo* studies evaluating prediction of cystine stones have previously yielded variable results: Manglaviti et al¹⁰ correctly identified 100% (7 of 7) of cystine stones pre-operatively *via* DECT. However, of the six stones predicted by DECT to be composed of cystine by Hidas et al,⁹ only one stone was confirmed to be cystine *via* X-ray diffraction; the other five stones were composed of either calcium or struvite (magnesium ammonium phosphate). There is potential for the manufacturer to update the dual-energy software on its scanners to incorporate the attenuation ratio of cystine, in line with alternative medical imaging providers. This would, however, require additional assessment of validity and reliability to ensure accurate differentiation between stones of mixed composition (*i.e.* calcium and/or struvite) and cystine, prior to clinical implementation.

There is strong evidence in the literature that reduced-dose protocols for urinary tract CTs are comparable with traditional protocols, offering no loss of confidence in diagnosis.^{17–19} Because of this, low-dose protocols are becoming more widely implemented as the gold standard and have become the standard within our local radiology department. Our study reveals a small but statistically significant increase in radiation dose in patients undergoing DECT over single-energy CT. This result was expected, given that the dual-energy protocol is essentially a single-energy CT protocol followed by the addition of stone-

targeted dual-energy acquisition. Despite this, our mean DLP result of 319.4 mGycm for a diagnostic single-energy CT and DECT investigation performs well in comparison with published radiation doses for urinary tract CT in developed countries. Thomas et al⁸ displayed reliable *in vivo* determination of calcified and non-calcified stones using a low-dose DECT protocol, demonstrating a mean DLP of 340 mGycm. In addition, the US Dose Imaging Registry reviewed over 49,000 single-energy urinary tract CT scans and found a mean DLP and effective dose of 746 mGycm and 11.2 mSv, respectively, a huge increase in ionizing radiation burden in comparison with our results.¹⁸ Our data showed that 28 (26.4%) acquisitions produced a total DLP of under 200 mGycm and only 23 (21.2%) acquisitions produced a total DLP of over 400 mGycm, in comparison with USA, in which only 10% of institutions kept DLP at 400 mGycm or less in at least 50% of patients.¹⁸

Using the abdominal conversion factor reported by the European Guidelines for Multislice Computed Tomography, the mean effective doses for single-energy CT and DECT investigations from our study were calculated as 4.6 and 5.4 mSv, respectively.²⁰ While these doses suggest a successful low-dose DECT protocol, it is important to note the difficulty in estimating individual patient dose from the CT output data (CTDI and DLP), as absorbed doses will be significantly affected by the

height, weight and width of individual patients, which we did not record in this study.²¹

Our study had some limitations. As previously mentioned, we were unable to analyze any retrieved uric acid stones, which is likely due to a combination of (a) medical dissolution therapy and (b) a relatively small sample size. Further research may aim to evaluate a larger population *via* invasive endourological management (generating a higher yield of retrieved stones), although ethical considerations must be considered if patients with uric acid stones could be exposed to a potentially unnecessary surgical risk if managed surgically instead of medically.

In conclusion, evaluation of urinary tract stone composition *via* DECT is feasible for patients presenting to a UK NHS hospital with stone disease. Dual energy has demonstrated fair accuracy at determining calcified and mixed calculi using a low-dose protocol. Despite a small but significant supplementary radiation exposure, the additional diagnostic evidence is beneficial for urologists to determine optimal definitive management.

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