Published in final edited form as:

Acad Radiol. 2018 October ; 25(10): 1270–1276. doi:10.1016/j.acra.2018.01.007.

Characterization of urinary stone composition by use of whole-body, photon-counting-detector CT

Andrea Ferrero, PhD¹, Ralf Gutjahr, BS², Ahmed F. Halaweish, PhD³, Shuai Leng, PhD¹, and Cynthia H. McCollough, PhD^{1,*}

¹Department of Radiology, Mayo Clinic, 200 First Street SW, Rochester, MN 55905

²Technische Universität München, Institut für Informatik, Boltzmannstr. 3, 85748 Garching bei München, Germany

³Siemens Healthcare, 40 Liberty Blvd, Malvern, PA 19355

Abstract

Rational and Objectives—To investigate the performance of a whole-body, photon-counting-detector (PCD) CT system in differentiating urinary stone composition.

Materials and Methods—Eighty-seven human urinary stones with pure mineral composition were placed in 4 anthropomorphic water phantoms (35 to 50 cm lateral dimension) and scanned on a PCD-CT system at 100, 120 and 140 kV. For each phantom size, tube current was selected to match CTDI_{vol} to our clinical practice. Energy thresholds at [25, 65], [25, 70] and [25, 75] keV for 100, 120 and 140 kV, respectively, were used to generate dual energy images. Each stone was automatically segmented using in-house software; CT number ratios were calculated and used to differentiate stone types in an ROC analysis. A comparison with second and third generation dual-source, dual-energy CT scanners with conventional energy integrating detectors (EID) was performed under matching conditions.

Results—For all investigated settings and smaller phantoms, perfect separation between uric acid (UA) and non-uric acid (NUA) stones was achieved (AUC = 1). For smaller phantoms, performance in differentiation of calcium oxalate (CaOx) and apatite (APA) stones was also similar between the 3 scanners: for the 35 cm phantom size, AUC values of 0.76, 0.79 and 0.80 were recorded for the second and third generation EID-CT and for the PCD-CT, respectively. For larger phantoms, PCD-CT and the third generation EID-CT outperformed the second generation EID-CT for both differentiation tasks: for a 50 cm phantom size and a UA/NUA differentiating task, AUC values of 0.63, 0.95 and 0.99 were recorded for the second and third generations EID-CT and for the PCD-CT, respectively.

Conclusion—PCD-CT provides comparable performance to state-of-the art EID-CT in differentiating urinary stone composition.

Keywords

CT; photon-counting-detector CT; spectral separation; urinary stones

*Corresponding Author: 200 First Street SW, Rochester, MN 55905, USA, Phone: (507) 284-2511, Fax: (507) 266-3661.

Introduction

Conventional x-ray CT systems rely on energy integrating detectors (EID), which generate an output signal that is proportional to the amount of energy deposited by the detected x-ray. Therefore, EID-CT systems inherently penalize the contribution of low-energy x-ray photons, which are the photons that carry the most contrast information for biological tissues and contrast media.

In recent years, a number of preclinical photon-counting-detector (PCD) CT systems were introduced [1–3]. Unlike EID-CT, PCD-CT systems directly convert each detected x-ray photon into individual pulses with amplitudes proportional to the energy of the incoming photon. Each individual pulse is counted separately through the use of fast electronics. The equal contribution of each detected photon regardless of their energy [4, 5], combined with a reduced influence of electronic noise, results in improved contrast-to-noise ratio (CNR) for PCD-CT when compared to EID-CT techniques [6]. Additionally, PCD-CT can provide acquisitions with full field-of-view (FOV), fully registered data, stability against motion artifacts, no cross scatter from a second x-ray tube, and the ability to configure more than two energy thresholds. Finally, all measurements provide multi-energy information, enabling the application of dual-energy or multi-energy post-processing algorithms for every scan.

The system utilized in this study is a whole-body PCD-CT research system (SOMATOM CounT, Siemens Healthcare, Forchheim, Germany) [7–9]. Preliminary *in vivo* animal and human studies demonstrated its ability to provide CT-images of diagnostic quality for several applications, including unenhanced and iodine-enhanced abdominal imaging [10, 11].

Renal stone characterization has been one of the most established clinical applications of dual-energy CT to date. Current state-of-the art dual energy CT systems can non-invasively separate uric acid (UA) from non-uric acid (NUA) stones with near 100% accuracy at the same radiation dose as routine, single-energy renal stone CT exams, providing valuable information to the ordering physician to guide treatment options [12]. Therefore, in this work we characterized *ex vivo* the performance of a PCD-CT system in differentiating the mineral composition of urinary stones and compared it to two commercial dual-energy EID-CT systems. As one of the potential advantages of PCD-CT is the ability to add spectral information to any CT exam, and since low tube potential imaging is a popular and effective method to reduce radiation dose, especially in contrast-enhanced abdominal CT scans, we extended the characterization to lower tube potential.

Materials and Methods

IRB protocol approval was not required for this non-patient study. However, biospecimen approval was obtained from the institutional biospecimen committee.

Stone Samples

A set of eighty-seven urinary stones was investigated, including uric acid (n = 17), cystine (n = 5), calcium oxalate (n = 30), brushite (n = 5), and apatite (n = 30). Reference composition

was given by microCT and infrared spectroscopy [13]. Only stones with purity higher than 90% were included in the cohort, with one stone sample selected from each individual patient. The stones were hydrated for 24 hours before being embedded in gelatin in two 60-well ice cube trays and placed in four torso-shaped water tanks with lateral dimensions of 35, 40, 45 and 50 cm, which were used to represent small, average, large, and obese adults, respectively. Figure 1 shows the experimental setup.

PCD-CT Data Acquisition and Reconstruction

All phantoms were scanned on a whole-body, PCD-CT research system. Three different tube potentials were investigated: 100, 120 and 140 kVp. For each tube potential, the threshold that resulted in the most uniform distributions of the detected x-rays between the low and high bin was selected. Figure 2 shows the detected energy spectra for the 3 settings used.

Since the scanned objects exceeded the 275 mm FOV of the PCD subsystem, a data-completion-scan (DCS) from the EID subsystem (500 mm FOV) was used to obtain artifact-free images. This additional scan has been shown to be successfully performed using very low radiation doses [14]. For each phantom size, the tube output was selected to match the volume CT dose index ($CTDI_{vol}$) to our clinical practice. Table 1 summarizes the PCD-CT acquisition parameters used for all scans.

Dual-energy PCD-CT data were obtained whereby the low energy image included x-rays with energies between the two detector thresholds (e.g., 25 to 65 keV), and the high energy image included x-rays with energies above the higher detector energy threshold (e.g. 65 to 100 keV). All images were reconstructed using the protocol parameters adopted in our clinical practice for renal stone composition: weighted filtered-backprojection (wFBP) reconstruction, 275-mm FOV, 1.0-mm thick slices with 0.8-mm slice interval, and a medium-sharp soft-tissue D30f reconstruction kernel.

Image processing and classification analysis

Kidney stones were automatically segmented using previously-validated in-house software [15]. Metrics describing morphological, volumetric and dual energy features were automatically extracted. Specifically, the CT number ratio (CTR) for each stone was quantitatively assessed as the ratio of the mean CT number within the stone in the low-energy to that in the high-energy image for each stone.

Receiver operating characteristic (ROC) curves were generated for each combination of phantom size and tube potential by varying values of the CTR threshold used to separate the stone types. Binary classifications between UA and NUA stones were investigated, as well as between calcium oxalate (CaOx) and apatite stones (APA). The area under the ROC curve (AUC) was used as the figure of merit to quantify the performance of the PCD-CT system to classify urinary stones based on their mineral composition.

Comparison with State of the Art DS-DECT

A comparison of second (SOMATOM Flash, Siemens Healthcare) and third (SOMATOM Force, Siemens Healthcare) generation dual-source, dual-energy CT systems for the task of

urinary stone composition was previously reported [16]. In that work, the same stone cohort and experimental setup as in the present study were used. Tube output and reconstruction parameters were also matched. Therefore, a thorough comparison between the three CT systems was possible. Hereafter, we refer to the three scanners as EID-CT1 (SOMATOM Flash), EID-CT2 (SOMATOM Force), and PCD-CT (SOMATOM Count). Figures of merit included the AUC as well as the absolute difference between mean CTR for the binary classifications that were investigated.

Results

Dose and image quality for PCD-CT system

As described in the methods, the $CTDI_{vol}$ was the same across all scanners for each phantom size (Table 2). No visible artifacts related to beam hardening or photon starvation were appreciated, even for the larger phantoms.

Differentiation of kidney stones

In Figure 3, the distribution of CTR values for UA and NUA stones across different CT systems and tube potentials is shown for the 35 cm phantom data. CTR – defined as the difference between the mean CTR for UA and NUA stones – varies significantly for the different scanners and tube potential pairs investigated, with the EID-CT2 outperforming the other two scanners at all energy pairs and phantom sizes (Figure 2 and Table 3). However, it is important to notice that the UA and NUA distributions were perfectly separated in all configurations, as shown in Figure 4, top-left panel. Data for the EID-CT1 AND EID-CT2 dual-energy CT systems were previously reported in Duan *et al* [16]. All scanners showed a degradation in separation between UA and NUA (i.e., decreased CTR) as phantom size increased. However, the degradation was significantly less pronounced for the PCD-CT, resulting in a better performance compared to the EID-CT1 for larger phantoms (Figure 4).

For smaller phantoms, AUC performance in differentiation of calcium oxalate (CaOx) and apatite (APA) stones was similar between the 3 scanners (Figure 5), despite the larger CTR recorded by EID-CT2 for all phantom sizes compared to the other two systems (Table 4). For the 35 cm phantom size, AUC values of 0.76, 0.79 and 0.80 were recorded for EID-CT1, EID-CT2 and PCD-CT, respectively. For larger phantoms, PCD-CT and EID-CT2 outperformed EID-CT1 (Figure 5). For the 35 cm phantom size, AUC values of 0.65, 0.78 and 0.76 were recorded for EID-CT1, EID-CT2 and PCD-CT, respectively.

Discussion

In this *ex-vivo* work, the performance of a whole-body, PCD-CT research system for the characterization of urinary stone composition was investigated. A wide range of patient sizes was mimicked through the use of anthropomorphic water tanks of different size, and used with different tube potential settings available on the CT system. A full comparison with existing dual-energy CT technology was also performed.

Compared to state-of-the-art dual-energy CT systems, reduced CTR differences between UA and NUA stones were measured. In principle, PCD-CT technology offers the possibility to separate the x-ray energy spectrum into two or more energy bins with no overlap.

However, a number of technology-inherent physical effects reduce the separation of distinct energy bins in PCD-CT, leading to spectral overlap and statistical correlations in the acquired CT images that could potentially negatively impact dual-energy CT applications. The most prominent effect is charge sharing, where several adjacent pixels may “fire-up” in response to x-ray deposited in a single pixel, causing a loss of both spectral and spatial information. For high photon fluxes, that are typical of clinical CT acquisitions, pulse pileup emerged as a substantial limitation for previous PCD-CT systems [1]. In this scenario, two or more low-energy x-ray photons detected within a short time interval create a single, high-energy pulse owing to the finite timing response of the detector in converting x-ray energy into electric pulses. These misclassifications in turn result in a certain degree of overlap between the two energy spectra used to generate the low- and high-energy images, as shown in the simulations presented in Figure 2, which modeled charge-sharing (but not pile-up).

Despite the reduced spectral separation, the investigated PCD-CT system was able to perfectly differentiate UA from NUA stones across all kV settings and phantoms sizes. Furthermore, PCD-CT was able to differentiate the two most common non-uric acid stone types, calcium oxalate and apatite stones, with good accuracy (AUC=0.8 at all three investigated kV for the 35 cm phantom). Unlike the second generation DECT system, the performance of the PCD-CT system was maintained for large patient sizes.

Different kV settings were investigated in this study for the PCD-CT, ranging from 100 to 140 kV. In PCD-CT, a single scan is performed and the recorded data are binned in two energy bins to mimic a low and a high-kV dual energy acquisition. Therefore, for the PCD-CT scan, a kV below 100 kV would not provide adequate spectral separation between the two energy bins. For reference, clinical EID-CT scanners across manufacturers use a minimum of 120 kV for their high-kV scan.

This study has limitations. Only pure stones were included in this study. Although quite common, in our experience pure (i.e. more than 90% of a single mineral) stones account for only approximately 50% of all stones encountered in a clinical setting. Finally, the data reported by Duan et al. defined the CTR for each stone as the average of the CTR computed for each pixel. In this work, however, we computed it as the ratio of the mean low- and high-CT numbers for each stone, as we believe this approach is less affected by noise in the acquired images. This difference could potentially explain the slightly higher variability in CTR for each subset of stones that was observed in the data from Duan *et al* compared to our measurements on the PCD-CT.

In conclusion, these *ex-vivo* results add to the developing body of literature showing how PCD-CT is a viable clinical alternative to conventional, EID-based CT for genitourinary applications, showing non-inferiority in several clinical trials [10, 11, 17]. The unique characteristics of PCD technology, including but not limited to the improved sensitivity to low-energy x-ray photons and reduced detector noise, may result in an increased use of

routine, multi-energy renal stone characterization CT protocols for the imaging of patients with suspected or established nephrolithiasis, including those with larger body habitus.

Acknowledgments

Funding: The project described was supported by grant number DK100227 from the National Institute of Diabetes and Digestive and Kidney Diseases and grant numbers EB016966 and RR018898 from the National Institute of Biomedical Imaging and Bioengineering of the National Institutes of Health. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Abbreviations

EID	energy integrating detectors
PCD	photon-counting-detector
CNR	contrast-to-noise ratio
FOV	field-of-view
UA	uric acid
NUA	non-uric acid
DCS	data-completion-scan
CTDI_{vol}	volume CT dose index
wFBP	weighted filtered-backprojection
CTR	CT number ratio
ROC	Receiver operating characteristic curves
CaOx	calcium oxalate stones
APA	apatite stones
AUC	area under the ROC curve

References

1. Shikhaliev PM. Computed tomography with energy-resolved detection: a feasibility study. *Physics in Medicine and Biology*. 2008; 53(5):1475. [PubMed: 18296774]
2. Taguchi K, Iwanczyk JS. Vision 20/20: Single photon counting x-ray detectors in medical imaging. *Medical physics*. 2013; 40(10):100901. [PubMed: 24089889]
3. Altman A, Carmi R. TU-E-210A-03: A Double-Layer Detector, Dual-Energy CT—Principles, Advantages and Applications. *Medical physics*. 2009; 36(6):2750–2750.
4. Giersch J, Niederlöhner D, Anton G. The influence of energy weighting on X-ray imaging quality. *Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment*. 2004; 531(1):68–74.
5. Schmidt TG. Optimal “image-based” weighting for energy-resolved CT. *Medical physics*. 2009; 36(7):3018–3027. [PubMed: 19673201]

6. Gutjahr R, Halaweish AF, Yu Z, et al. Human Imaging With Photon Counting–Based Computed Tomography at Clinical Dose Levels: Contrast-to-Noise Ratio and Cadaver Studies. *Investigative radiology*. 2016; 51(7):421–429. [PubMed: 26818529]
7. Kappler S, Glasser F, Janssen S. , et al. SPIE Medical Imaging. International Society for Optics and Photonics; 2010. A research prototype system for quantum-counting clinical CT.
8. Kappler S, Henning A, Krauss B. , et al. SPIE Medical Imaging. International Society for Optics and Photonics; 2013. Multi-energy performance of a research prototype CT scanner with small-pixel counting detector.
9. Yu Z, Leng S, Jorgensen SM, et al. Evaluation of conventional imaging performance in a research whole-body CT system with a photon-counting detector array. *Physics in Medicine and Biology*. 2016; 61(4):1572. [PubMed: 26835839]
10. Marcus R, Fletcher J, Sheedy S, Fidler J, Li Z, Yu Z, Enders F, Halaweish A, McCollough C. Photon-Counting-Detector CT for the Evaluation of Non-contrast Enhanced Abdominal Imaging in Patients. Radiological Society of North America 2016 Scientific Assembly and Annual Meeting; November 27 – December 2, 2016; Chicago IL. 2016
11. Pourmorteza A, Symons R, Sandfort V, et al. Abdominal Imaging with Contrast-enhanced Photon-counting CT: First Human Experience. *Radiology*. 2016; 279(1):239–245. [PubMed: 26840654]
12. Vrtiska TJ, Takahashi N, Fletcher JG, et al. Genitourinary applications of dual-energy CT. *American Journal of Roentgenology*. 2010; 194(6):1434–1442. [PubMed: 20489081]
13. Zarse CA, McAteer JA, Sommer AJ, et al. Nondestructive analysis of urinary calculi using micro computed tomography. *BMC urology*. 2004; 4(1):1. [PubMed: 15053832]
14. Yu Z, Leng S, Li Z, et al. How Low Can We Go in Radiation Dose for the Data-Completion Scan on a Research Whole-Body Photon-Counting Computed Tomography System. *Journal of Computer Assisted Tomography*. 2016; 40(4):663–70. [PubMed: 27096399]
15. Duan X, Wang J, Qu M, et al. Kidney stone volume estimation from computerized tomography images using a model based method of correcting for the point spread function. *The Journal of urology*. 2012; 188(3):989–995. [PubMed: 22819107]
16. Duan X, Li Z, Yu L, et al. Characterization of urinary stone composition by use of third-generation dual-source dual-energy CT with increased spectral separation. *AJR American journal of roentgenology*. 2015; 205(6):1203. [PubMed: 26587926]
17. Marcus R, Fletcher J, Vrtiska T, Wells M, Ferrero A, Montoya J, Huang A, Halaweish A, Enders F, Leng S, McCollough C. Detection and Characterization of Urinary Stones using Photon-Counting-Detector CT in a Clinical Setting. Radiological Society of North America 2016 Scientific Assembly and Annual Meeting; November 27 – December 2, 2016; Chicago IL. 2016.

Fig. 1.
Experimental setup.

Fig. 2.

Detected x-ray energy spectra for the different settings investigated. Spectra are simulated for a 35 cm reference phantom and include charge-sharing effects (see Discussion), which result in a finite chance for incoming x-rays of a certain energy to be misclassified and stored in the wrong (lower) energy bin.

Fig. 3.
Distribution of CTR values for uric acid and non-uric acid stones for all acquisitions settings tested in the 35 cm water phantom.

Fig. 4.

ROC analysis to differentiate uric acid from non-uric acid stones for different CT systems and phantom sizes. As phantom size increased, not all tube potential pairs could be used.

Fig. 5. ROC analysis to differentiate non-uric acid subtypes Calcium Oxalate and Hydroxyapatite for different CT systems and phantom sizes. As phantom size increased, not all tube potential pairs could be used.

Table 1

Acquisition parameters for PCD-CT scans.

	Tube potential (kVp)		
	100	120	140
Phantom sizes scanned[cm]	35, 40	35, 40, 45	35, 40, 45, 50
Energy Thresholds [keV]	25, 65	25, 70	25, 75
Detector collimation [mm]	32 × 0.5		
Rotation time [s]	0.5		
Helical pitch	0.6		

Table 2

CTDI_{vol} for each of the phantom sizes investigated. CTDI_{vol} was matched among all three CT systems investigated.

LAT Phantom Size (cm)	CTDI _{vol} (mGy)
35	13.5
40	19.9
45	33.4
50	45.0

Table 3

Absolute difference (CTR) between mean CTR for UA (N = 17) vs non-UA (N = 70) stones. As phantom size increased, not all tube potential pairs could be used.

CT System	Tube potential (kV)	phantom size (cm)			
		35	40	45	50
EID-CT1	80/Sn140	0.69	0.62		
	100/Sn140	0.42	0.30	0.23	0.05
EID-CT2	70/Sn150	1.03			
	80/Sn150	0.83	0.78		
	90/Sn150	0.70	0.64	0.62	
	100/Sn150	0.58	0.50	0.52	0.43
PCD-CT	100	0.30	0.30		
	120	0.39	0.35	0.35	
	140	0.44	0.41	0.37	0.35

absolute difference between mean CTR for CaOx (N = 35) vs APA (N = 30) stones. As phantom size increased, not all tube potential pairs could be used.

Table 4

CT System	Tube potential (kV)	phantom size (cm)			
		35	40	45	50
EID-CT1	80/Sn140	0.05	0.03		
	100/Sn140	0.04	0.03	0.01	0.01
	70/Sn150	0.11			
EID-CT2	80/Sn150	0.08	0.10		
	90/Sn150	0.08	0.09	0.07	
	100/Sn150	0.04	0.08	0.08	0.08
PCD-CT	100	0.02	0.03		
	120	0.04	0.03	0.04	
	140	0.03	0.05	0.05	0.03