Technical Note: Insertion of digital lesions in the projection domain for dual-source, dual-energy CT

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Purpose: To compare algorithms performing material decomposition and classification in dual-energy CT, it is desirable to know the ground truth of the lesion to be analyzed in real patient data. In this work, we developed and validated a framework to insert digital lesions of arbitrary chemical composition into patient projection data acquired on a dual-source, dual-energy CT system.

Methods: A model that takes into account beam-hardening effects was developed to predict the CT number of objects with known chemical composition. The model utilizes information about the x-ray energy spectra, the patient/phantom attenuation, and the x-ray detector energy response. The beam-hardening model was validated on samples of iodine (I) and calcium (Ca) for a second-generation dual-source, dual-energy CT scanner for all tube potentials available and a wide range of patient sizes. The seven most prevalent mineral components of renal stones were modeled and digital stones were created with CT numbers computed for each patient/phantom size and x-ray energy spectra using the developed beam-hardening model. Each digital stone was inserted in the dual-energy projection data of a water phantom scanned on a dual-source scanner and reconstructed with the routine algorithms in use in our practice. The geometry of the forward projection for dual-energy data was validated by comparing CT number accuracy and high-contrast resolution of simulated dual-energy CT data of the ACR phantom with experimentally acquired data.

Results: The beam-hardening model and forward projection method accurately predicted the CT number of I and Ca over a wide range of tube potentials and phantom sizes. The images reconstructed after the insertion of digital kidney stones were consistent with the images reconstructed from the scanner, and the CT number ratios for different kidney stone types were consistent with data in the literature. A sample application of the proposed tool was also demonstrated.

Conclusion: A framework was developed and validated for the creation of digital objects of known mineral composition, and for inserting the digital objects into projection data from a commercial dual-source, dual-energy CT scanner. Among other applications, it will allow a systematic investigation of the impact of scan and reconstruction parameters on kidney stone dual-energy properties under rigorously controlled conditions. © 2017 American Association of Physicists in Medicine [https://doi.org/10.1002/mp.12185]

Key words: computed tomography (CT), dual-energy CT, lesion insertion, material decomposition, projection domain

1. INTRODUCTION

In vivo assessment of renal stone composition can be performed using dual-energy CT (DECT),^{1,2} whereby the CT number ratio (CTR) of the stone at low and high energy is used as a surrogate metric for the effective atomic number, thus differentiating different materials. While dual-energy CT can accurately discriminate uric acid (UA) stones from non-uric acid (NUA) stones,³ only limited success has been reported in further separating NUA stones (calcium oxalate, hydroxyapatite, cystine, and struvite).^{3,4} A challenge in addressing this limitation is the lack of a reliable reference to use as ground truth. While *ex vivo* characterization of mineral composition of renal stones can be performed using a combination of micro-CT and infrared spectroscopy techniques,⁵ the heterogeneous composition of patient stones introduces uncertainty into the reference standard. In order to improve and expand the classification of renal stones using DECT

in vivo, a model that predicts the CTR for a stone of a given chemical composition and a specific CT acquisition protocol and patient size is needed. Such a model would take into account: (a) energy spectra of the x-ray beam; (b) attenuation properties of the patient; (c) energy response of the detector; (d) attenuation properties of the renal stone; and (e) image quality properties of the reconstructed data.

Chen et al.⁶ recently developed a lesion insertion tool that allows one to insert liver lesions and lung nodules into patient projection data. Inserting lesions in the projection domain rather than in image domain has several advantages, as it more accurately represents the impact of scan and reconstruction parameters on the appearance of lesion boundaries. In this work, we developed and validated a framework that accurately estimates the CT number for an object of known chemical composition and inserts it into dual-energy projection CT data. The model was tested in renal stone applications to showcase its flexibility and potential.

2. METHODS

2.A. Estimation of beam hardening and x-ray effective energy spectra

A second-generation dual-source, dual-energy CT scanner (Somatom Flash, Siemens Healthcare, Forchheim, Germany) was used throughout this investigation. The x-ray energy spectra past the tube filtration was provided by the manufacturer, together with the x-ray detector energy response.⁷ The beam hardening introduced by the patient and the CT table was modeled by computing the water equivalent diameter (WED) from the reconstructed CT images according to the methodology outlined by AAPM report 220:⁸

$$D_w = 2\sqrt{A_w/\pi} = 2\sqrt{\left[\frac{1}{1000} \overline{CT(x,y)_{ROI}} + 1\right] \left(\frac{A_{ROI}}{\pi}\right)} \quad (1)$$

where the ROI in the image is large enough to encompass both the table and the phantom.

The physics of x-ray attenuation allows us to model the x-ray energy spectrum exiting the patient and from there the energy spectrum detected by the x-ray detector:

$$spectrum_{det}(E) = spectrum_{post-filter}(E) \exp^{-\mu_{H_2O}(E)D_w} DQE(E) \quad (2)$$

where DQE is the x-ray detector energy response. From the detected x-ray energy spectra, the effective mass attenuation coefficient and CT number can be computed for any object whose chemical composition and density is known, using x-ray attenuation tables provided by the National Institute of Standards and Technology (NIST):⁹

$$\left(\frac{\mu}{\rho}\right)_{eff}(E) = \frac{\sum_{i=1}^M N_i A W_i \left(\frac{\mu}{\rho}\right)_i(E)}{MW} \quad (3)$$

where M is the number of elements in the compound, AW the atomic weight of each element, and MW the molecular weight of the compound.

Experimental validation of the accuracy of the developed beam-hardening model was performed using iodine (I) and calcium (Ca) inserts embedded in the center of torso-shaped water phantoms covering a clinically relevant range of patient sizes (25 to 50 cm lateral dimension). All available tube potential combinations were tested, (80/Sn140 kV and 100/Sn140 kV), where “Sn” refers to the additional tin filtration used for the 140 kV tube to better separate the low and high-energy spectra.¹⁰ The average CT number for each insert was recorded from the reconstructed images and compared with the corresponding values estimated from the developed model.

2.B. Generation of digital renal stones of known composition

Seven of the most prevalent renal stone types were included in this investigation. Their chemical composition and tabulated density is summarized in Table I. The effective

mass attenuation coefficient for each stone was computed according to Eq. (3) using the relative abundance of each element, and combined to the spectral model described in Eq. (2) for a 32 cm WED water phantom and 80/Sn140 kV energy spectra to generate the estimated CT numbers at high and low energy. The predicted CTR for each stone was compared to the measured values from a population of 43 renal stones scanned under similar parameters and previously reported in the literature.⁴

2.C. Insertion of digital lesions into dual-source, dual-energy CT projection data

The lesion insertion tool developed by Chen et al.⁶ was extended to dual-source CT projection data and integrated with the spectral model described above. The framework is summarized in Fig. 1.

The scanning geometry must be accurately reproduced during forward projection to ensure an accurate insertion of the desired lesion into sinogram data. The angular position of the two tubes and the table movements are especially critical in dual-source, spiral acquisition geometries, as even small errors can result in significant artifacts in images that contain data from low- and high-energy projections, hereafter referred to as mixed images. To validate the accuracy of our tube(s) position readout and forward projection geometry, we compared images reconstructed from the forward projection of a digitized version of the ACR phantom (performed on monochromatic energy spectrum as determined by Chen et al.⁶) to physically acquired dual-source CT images of the same phantom, in a procedure similar to the one employed by Chen et al.⁶ for a single tube. CT number accuracy (Modules 1 and 2 of the ACR phantom) as well as high-contrast resolution (Module 4) were used as figures of merit to validate our model. The ACR phantom was scanned at 80/Sn140 kV and 100/Sn140 kV energy pairs with a helical acquisition (pitch = 0.6), 32 × 0.6 collimation without flying focal spot, and CTDIvol of 12 and 39 mGy, respectively. Images were reconstructed on the scanner using a medium-sharp B40 kernel, 1 mm slice thickness and 22 cm field-of-view. We chose to compare the mixed images (composition fraction = 0.5)

TABLE I. Characteristics of the stone types used in this investigation.

Stone type	Chemical formula	Effective atomic number	Tabulated density (g/cm ³)
Uric acid (UA)	C ₅ H ₄ N ₄ O ₃	6.91	1.87
Cystine (CYS)	C ₆ H ₁₂ N ₂ O ₄ S ₂	10.78	1.57
Struvite (STR)	CaMgNH ₄ PO ₄ •6H ₂ O	12.17	1.71
Calcium oxalate dihydrate (COD)	CaC ₂ O ₄ •2H ₂ O	12.99	2.32
Calcium oxalate monohydrate (COM)	CaC ₂ O ₄ •H ₂ O	13.45	2.22
Brushite (BRU)	CaHPO ₄ •2H ₂ O	13.82	1.94
Hydroxyapatite (APA)	Ca ₁₀ (PO ₄) ₆ (OH) ₂	15.86	3.16

FIG. 1. The process of insertion of arbitrary lesions in dual-energy CT projections. In bold, the additional steps compared to the model developed by Chen et al.⁶

reconstructed from the forward-projected data and the physically acquired data, as they are the images most likely to show negative impact from any potential misregistration during the forward projection of the data from the two tubes.

2.D. Sample application

The developed framework for the insertion of arbitrary objects in dual-source, dual-energy CT projections was used to test the limits of a commercial postprocessing software for kidney stones using dual-energy CT data. Multiple digital kidney stones with UA and NUA components were created and inserted into the renal parenchyma of data from a patient scanned with the routine stone composition protocol at our institution. The features of the inserted stones are reported in Table II.

The forward-projected data were reconstructed with a medium-sharp D30 kernel and the reconstructed images evaluated using a commercial software (SyngoVia, Siemens Healthcare, Germany) with the default settings for its kidney stone composition application (resolution: 3; HU threshold: 200). Relevant metrics describing the stone properties, including volume, CTR, and composition classification were extracted and compared to the known information on the digital stones inserted.

TABLE II. Characteristics of the digital stones inserted in DECT projections from a patient scan using the developed framework.

Stone	Kidney	Shape	Volume (mm3)	Composition	CTR (100/Sn140 kV, 35 cm LAT patient)
#1	L	Sphere	65	UA	0.98
#2	R	Sphere	65	CYS	1.29
#3	L	Sphere	15	UA	0.98
#4	R	Sphere	15	CYS	1.29

UA, uric acid; CYS, cystine.

3. RESULTS

3.A. Validation of beam-hardening CT number estimation

The beam-hardening model used in our forward projection was validated with I and Ca test objects (virtual and real) in air and in phantoms from 24 to 45 cm WED. The predicted and measured CT numbers are shown in Fig. 2. At 80 kV, the percent differences between the measured and predicted CT numbers ranged from -2.2 to 0.1%. At 100 kV, the percent differences ranged from -0.5 to 7.5%, with the highest error occurring in the 45 cm WED phantom. At Sn140 kV, the percent differences ranged from -5.0 to 3.3%.

FIG. 2. Predicted vs measured CT numbers for the different tube voltage and phantom sizes tested. Left, Iodine insert. Right, Calcium insert. [Color figure can be viewed at wileyonlinelibrary.com]

3.B. Generation of digital renal stones of known composition

In Table III, we report the CT number ratio from the experimentally acquired renal stones and the simulated ones using the beam hardening and CT number estimation validated in III.A. The largest residual CTR error was well below 6%.

3.C. Validation of forward projection program in dual-source CT data

The largest average CT number difference for the four inserts in the CT number accuracy module of the phantom was 2 HU, as shown in Table IV.

In Fig. 3, we show the reconstructed mixed images from the high-contrast module of the ACR CT phantom for both the original reconstruction (Fig. 3(a)) and the forward-projected, digitized phantom at the two energies (Fig. 3(b)).

3.D. Sample application

In Table V, we report the results of the volume and composition assessment for the virtually inserted stones. A representative coronal view showing all stones is shown in Fig. 4. The small CYS stone (left kidney, lower pole) is not classified by the commercial software owing to its CTR value being too close to the built-in threshold used to discriminate UA from NUA stones, as well as the relatively small size of the stone itself.

4. DISCUSSION

A multistep model was developed in this work that allows for the accurate estimation of the x-ray attenuation of arbitrary objects of clinical interest and their insertion into dual-energy CT projection data, provided the knowledge of the chemical composition of the object, the size of the patient/phantom to insert the object into, the tube x-ray spectra and the x-ray detector energy response.

We validated the developed framework by comparing experimental and simulated CT numbers of iodine and

TABLE III. CT number ratio (CTR) from experimental acquisitions (80/Sn140 kV, 35 cm phantom) and matching simulated stones.

	UA	CYS	STR	BRU	COM	COD	APA
Experimental CTR ⁴	0.96	1.48	1.54	1.69	1.68	1.68	1.83
Simulated CTR	0.99	1.40	1.55	1.63	1.73	1.67	1.76
Difference (%)	2.9	-5.7	0.8	-3.7	3.1	-0.7	-4.0

Tube potential pair was 80/Sn140 kV.

TABLE IV. The CT numbers measured physically acquired ACR phantom image, “commercial”, and the CT numbers measured from the simulated ACR phantom image, “forward projection”. Unit: HU. The air, acrylic, bone, polyethylene, and solid water materials are provided by inserts in module 1 of the ACR phantom. Mixed images from both tubes used.

		Air	Acrylic	Bone	Polyethylene	Solid water
80/ Sn140 kV	Commercial	-1002	126	942	-96	-1
	Forward projection	-1002	124	942	-97	-1
100/ Sn140 kV	Commercial	-1004	133	843	-85	-1
	Forward projection	-1006	132	844	-87	-1

calcium, as well as CTRs for different kidney stones minerals, showing residual errors below 6%, well within the current experimental uncertainty in stone composition assessment. The geometry of forward projection for a dual-source CT scanner was also validated, showing no degradation in CT number accuracy is introduced by the dual-energy forward projection. Although no degradation in spatial resolution was observed, as shown by Fig. 3, small differences are noted in the reproduced bar patterns of the high-contrast resolution module of the ACR phantom, which show generally brighter edges than in the original data. We believe that these small differences are caused by the edge enhancement provided by the sharp reconstruction kernel in the images used to create the digital ACR phantom prior to forward projection. However, the achieved performance in terms of matching the spatial resolution of the original scan appears to be more than

FIG. 3. The high-resolution bar patterns from the mixed images in (a) the physically acquired ACR at 100/Sn140 kVp (b) the simulated ACR phantom for the same energy pair. The display window width setting is 300 HU and the level setting is 1000 HU.

TABLE V. Stone quantitation postreconstruction, as assessed by commercial software. The developed framework allows to evaluate the effect of scanning and acquisition parameters on stone quantitation and composition classification with known ground truth.

Stone	Kidney	Volume (mm ³)	Volume error (%)	CTR	CTR error (%)	Color-coding classification
#1	L	63.2	−2.8	1.0	+2.0	✓
#2	R	57.3	−11.8	1.23	−4.7	✓
#3	L	11.6	−22.7	0.96	−2.0	✓
#4	R	10.4	−30.7	1.11	−14.0	✗

FIG. 4. Coronal view of the four inserted stones in the renal parenchima. Color coding represents the stone classification (Red, UA; Blue, NUA) according to the commercial software.

sufficient for any clinical application using the proposed methodology.

The sample application investigated shows the advantages of using digital objects of known dimensions and chemical composition. Knowledge of grand truth in terms of stone volume and composition, combined with the developed ability to insert objects in dual-energy CT projection space enables the comparison of different reconstruction methods, noise

levels and quantitation algorithms. Moreover, the developed framework allows to test the accuracy of dual-energy postprocessing applications in ways that are not possible with experimental data alone, since ground truth is known.

This work builds on the previous work by Chen et al.⁶ in two aspects. First, it extends the previously developed methodology of inserting digital lesions to dual-source, dual-energy projection data. Additionally, it introduces the

modeling the properties of the detected x-ray spectra for a specific tube potential and patient size. This additional step is essential to enable the insertion of lesions, like kidney stones, that are not extracted from existing patient data but are rather created *ex-novo* and completely arbitrary in shape, chemical composition, and density. Moreover, it allows to adapt the appearance of the inserted lesions, whether in single or dual-energy CT data, to the specific habitus of the patient they are inserted into.

This study has limitations. The beam-hardening model used to estimate the CT number of an arbitrary object requires knowledge of the x-ray energy spectra as well as the x-ray detector energy response, which in our case were provided by the manufacturer. However, if this information were not available, it could be empirically derived from transmission measurements.¹¹ Additionally, the developed model assumes accurate beam hardening and scatter correction in the manufacturers' reconstruction algorithms. For larger phantoms, this is generally difficult to achieve. Insertion of objects into the CT projection data requires decoding of the commercial CT raw data, which is proprietary and therefore difficult to access. In this study, we utilized the vendor-specific reconstruction engine to perform the reconstruction since the data were acquired from a specific scanner. But in general, this methodology does not need the vendor-specific reconstruction engine. Our group developed a vendor-independent standardized raw data format, incorporating details of vendor-specific CT scanner geometries.^{12,13} After converting the vendor raw data format to that standardized format, a generic reconstruction engine can be used to perform the reconstruction.

To conclude, a framework that extends the previously developed lesion insertion tool in the projection domain⁶ to allow the insertion of virtual lesions of any chemical composition and to include dual-source, dual-energy CT acquisitions has been developed and validated.

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CONFLICT OF INTEREST

Potential Conflicts of Interest: Dr. McCollough receives industry grant support from Siemens Healthcare. All other authors have no conflicts to disclose.

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REFERENCES

1. Primak AN, Fletcher JG, Vrtiska TJ, et al. Noninvasive differentiation of uric acid versus non-uric acid kidney stones using dual-energy CT. *Acad Radiol.* 2007;14:1441–1447.
2. Stolzmann P, Kozomara M, Chuck N, et al. In vivo identification of uric acid stones with dual-energy CT: diagnostic performance evaluation in patients. *Abdom Imaging.* 2010;35:629–635.
3. 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 Am J Roentgenol.* 2015;205:1203.
4. Qu M, Ramirez-Giraldo JC, Leng S, et al. Dual-energy dual-source CT with additional spectral filtration can improve the differentiation of non-uric acid renal stones: an ex vivo phantom study. *AJR Am J Roentgenol.* 2011;196:1279–1287.
5. Krambeck AE, Lingeman JE, McAteer JA, Williams JC Jr. Analysis of mixed stones is prone to error: a study with US laboratories using micro CT for verification of sample content. *Urol Res.* 2010;38:469–475.
6. Chen B, Leng S, Yu L, Yu Z, Ma C, McCollough C. Lesion insertion in the projection domain: methods and initial results. *Med Phys.* 2015;42:7034–7042.
7. Fung GS, Stierstorfer K., Segars WP, Taguchi K, Flohr TG, Tsui BM. XCAT/DRASIM: a realistic CT/human-model simulation package. *Proc SPIE.* 2011; 7961:79613D-79613D-79616.
8. McCollough C, Bakalyar D, Bostani M. "AAPM report no. 220", Use of water equivalent diameter for calculating patient size and size-specific dose estimates (SSDE) in CT: the Report of AAPM Task Group. 2014;220.
9. Hubbell JH, Seltzer SM. *Tables of X-ray mass attenuation coefficients and mass energy-absorption coefficients 1 keV to 20 MeV for elements Z 1 to 92 and 48 additional substances of dosimetric interest.* Report for the National Institute of Standards and Technology;1995.
10. Primak A, Giraldo JR, Liu X, Yu L, McCollough CH. Improved dual-energy material discrimination for dual-source CT by means of additional spectral filtration. *Med Phys.* 2009;36:1359–1369.
11. Duan X, Wang J, Yu L, Leng S, McCollough CH. CT scanner x-ray spectrum estimation from transmission measurements. *Med Phys.* 2011;38:993–997.
12. Chen B, Duan X, Yu Z, Leng S, Yu L, McCollough C. Technical Note: development and validation of an open data format for CT projection data. *Med Phys.* 2015;42:6964–6972.
13. American Association of Physicists in Medicine. *Use of Water Equivalent Diameter for Calculating Patient Size and Size-specific Dose Estimates (SSDE) in CT: The Report of AAPM Task Group 220.* College Park, MD: American Association of Physicists in Medicine; 2014.