Dual-energy cone-beam CT with a flat-panel detector: Effect of reconstruction algorithm on material classification

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Purpose: Cone-beam CT (CBCT) with a flat-panel detector (FPD) is finding application in areas such as breast and musculoskeletal imaging, where dual-energy (DE) capabilities offer potential benefit. The authors investigate the accuracy of material classification in DE CBCT using filtered backprojection (FBP) and penalized likelihood (PL) reconstruction and optimize contrast-enhanced DE CBCT of the joints as a function of dose, material concentration, and detail size.

Methods: Phantoms consisting of a 15 cm diameter water cylinder with solid calcium inserts (50–200 mg/ml, 3–28.4 mm diameter) and solid iodine inserts (2–10 mg/ml, 3–28.4 mm diameter), as well as a cadaveric knee with intra-articular injection of iodine were imaged on a CBCT bench with a Varian 4343 FPD. The low energy (LE) beam was 70 kVp (+0.2 mm Cu), and the high energy (HE) beam was 120 kVp (+0.2 mm Cu, +0.5 mm Ag). Total dose (LE+HE) was varied from 3.1 to 15.6 mGy with equal dose allocation. Image-based DE classification involved a nearest distance classifier in the space of LE versus HE attenuation values. Recognizing the differences in noise between LE and HE beams, the LE and HE data were differentially filtered (in FBP) or regularized (in PL). Both a quadratic (PLQ) and a total-variation penalty (PLTV) were investigated for PL. The performance of DE CBCT material discrimination was quantified in terms of voxelwise specificity, sensitivity, and accuracy.

Results: Noise in the HE image was primarily responsible for classification errors within the contrast inserts, whereas noise in the LE image mainly influenced classification in the surrounding water. For inserts of diameter 28.4 mm, DE CBCT reconstructions were optimized to maximize the total combined accuracy across the range of calcium and iodine concentrations, yielding values of ~88% for FBP and PLQ, and ~95% for PLTV at 3.1 mGy total dose, increasing to ~95% for FBP and PLQ, and ~98% for PLTV at 15.6 mGy total dose. For a fixed iodine concentration of 5 mg/ml and reconstructions maximizing overall accuracy across the range of insert diameters, the minimum diameter classified with accuracy >80% was ~15 mm for FBP and PLQ and ~10 mm for PLTV, improving to ~7 mm for FBP and PLQ and ~3 mm for PLTV at 15.6 mGy. The results indicate similar performance for FBP and PLQ and showed improved classification accuracy with edge-preserving PLTV. A slight preference for increased smoothing of the HE data was found. DE CBCT discrimination of iodine and bone in the knee was demonstrated with FBP and PLTV at 6.2 mGy total dose.

Conclusions: For iodine concentrations >5 mg/ml and detail size ~20 mm, material classification accuracy of >90% was achieved in DE CBCT with both FBP and PL at total doses <10 mGy. Optimal performance was attained by selection of reconstruction parameters based on the differences in noise between HE and LE data, typically favoring stronger smoothing of the HE data, and by using penalties matched to the imaging task (e.g., edge-preserving PLTV in areas of uniform enhancement). © 2014 American Association of Physicists in Medicine. [<http://dx.doi.org/10.1118/1.4863598>]

Key words: cone-beam CT, dual-energy CT, model-based reconstruction, penalized likelihood, total variation, dose reduction, musculoskeletal imaging

1. INTRODUCTION

Dual-energy (DE) imaging is finding a variety of promising applications in diagnostic CT, both in imaging of endogenous materials (e.g., renal stones^{1,2}) and exogenous materials (e.g., iodine enhanced vessels^{3–5}) across a range of body sites.

Recent proliferation of flat-panel detector (FPD) cone-beam CT (CBCT) in areas ranging from dental and otolaryngology^{6–8} to breast^{9–11} and extremities imaging,^{12,13} raises the possibility for translation of DE imaging capabilities to such systems. Implementation of DE capabilities in CBCT has been demonstrated in preclinical (small animal)

systems.^{14–16} In clinical imaging, experience with conventional DE CT and radiographic DE modalities points to a number of promising DE applications in CBCT imaging of the breast and extremities. In mammography, DE imaging could improve the detection of calcifications by removing anatomical background clutter of adipose and glandular tissue,^{17,18} and initial implementation of DE CBCT has been presented.¹⁹ In extremities imaging, conventional DE CT demonstrates improved detection of uric acid crystals in gout,^{20–22} collagen differentiation of tendons and ligaments,^{4,22,23} and detection of bone marrow edema,^{22,24} while radiographic DE techniques have been the mainstay of bone densitometry (DXA).^{25,26} Contrast-enhanced CBCT imaging can similarly benefit from DE capabilities, as already investigated with conventional DE CT in discrimination of contrast agent (e.g., iodine) from endogenous tissue (e.g., bone or calcification)—e.g., arthrography²⁷ or vascular imaging.^{3–5} In this work, we investigate the implementation of DE CBCT in contrast-enhanced imaging, primarily in the context of musculoskeletal (joint) imaging, though the results may hold in other applications as well (e.g., contrast-enhanced breast, brain, or body imaging).

Previous work in technique optimization in DE radiography and DE CBCT provided a guide to technique selection in the current work. Simulation and experimental studies of DE radiographic imaging in mammography,^{18,28} chest imaging,^{29–31} and cardiac fluoroscopy³² show the dependence of DE image quality on energy separation (kVp and filtration), allocation of dose between low-energy (LE) and high-energy (HE) projections, and noise reduction algorithms. Recently, a cascaded systems analysis of DE CBCT was presented³³ as an extension of task-based modeling of single-energy CBCT (Ref. 34) providing an efficient analytical tool for task-based technique optimization in DE CBCT. Such studies indicate a number of considerations regarding the choice of the LE spectra (~ 60 – 70 kVp) and HE spectra (> 100 kVp) for maximizing discrimination of iodine and calcium.³³ Such work also indicates the benefit of additional high-Z filtration of the HE beam to increase spectral separation and dose allocation ascribing a larger proportion of dose ($\sim 60\%$ – 70%) to the HE beam.

The decomposition and reconstruction algorithm is similarly important to maximizing DE imaging performance. In DE CT and CBCT, reconstruction is either performed from sinograms of decomposition bases (e.g., photoelectric and Compton) computed from the LE and HE projections,^{35–38} or directly from the measured projections to yield LE and HE images as an input to (so-called “image-based”) DE processing.^{4,14,15,39–41} In both cases, the reconstruction algorithm imposes tradeoffs in noise and accuracy that can be optimized by recognizing not only the processing inherent to DE decomposition but also the differences in noise, contrast, and resolution intrinsic to the LE and HE projection data. For example, similar to differential smoothing in DE radiography,^{17,42} the differences in attenuation and detective quantum efficiency (DQE) between the LE and HE spectra suggest that different levels of noise reduction should be applied to the two datasets in the image-based DE paradigm—

subject, however, to artifacts that can be introduced by mismatch in spatial resolution (blur) imparted in the LE and HE data. Furthermore, growing interest in nonlinear, model-based image reconstruction (MBIR) and capability for dose reduction beyond that achievable with analytical methods^{43,44} suggest potential benefits of such methods applied to DE CT and CBCT. One possible approach uses MBIR to simultaneously solve DE decomposition and reconstruction by formulating an objective function that represents the object in terms of the DE basis functions and jointly models the acquisition of both the LE and HE beams.^{16,45–49} Alternatively, in the context of image-based DE CT, MBIR can be used as an alternative to filtered backprojection (FBP) to generate the input reconstructions. In addition to increased robustness to noise due to the built-in statistical weighting and capability to account for effects such as polyenergetic attenuation through appropriate extensions of the forward model, an additional advantage of MBIR is the ability to include a regularization term—i.e., a penalty that imposes specific blur properties onto the resulting reconstruction, such as piecewise-constant images with edge preservation as in the absolute value, total variation (TV) penalty.^{50–54} The effects of penalty selection in MBIR and differential filtration/regularization in both analytical reconstruction and MBIR in image-based DE CBCT are investigated below.

The experimental study presented below investigates the effects of reconstruction algorithm on the quality of material classification in contrast-enhanced DE CBCT. The impact of the reconstruction algorithm in image-based DE paradigm is studied for both analytical FBP and MBIR based on a penalized likelihood (PL) approach. In each case, the effect of differential noise reduction between LE and HE data is investigated: (i) for FBP, a separate degree of smoothing (reconstruction filter cutoff) between LE and HE projections is hypothesized to improve material classification by accounting for the different magnitude of noise in the LE and HE data; (ii) for PL, two variants are considered, each with differential regularization between the LE and HE data, including an edge-preserving total variation penalty hypothesized to improve material classification over a simple quadratic penalty. The performance of DE CBCT material classification is investigated across a range of material concentrations (iodine and calcium) and imaging dose. Finally, application to contrast-enhanced DE CBCT arthrography is demonstrated using a cadaveric knee.

2. MATERIALS AND METHODS

2.A. Imaging bench and phantoms

Experiments were conducted using the imaging bench illustrated in Fig. 1(a). The system employs a 14° anode angle DU694 x-ray tube in EA10 housing (Dunlee, Aurora, IL) and a PaxScan 4343R flat panel detector (Varian Imaging Products, Palo Alto, CA). Detectors with two types of screen were used in the experiments: a 100 mg/cm^2 DRZ-Plus $\text{Gd}_2\text{O}_2\text{S:Tb}$ scintillator in the study of the effects of material concentration and in the cadaver knee study (Secs. 3.A–3.C and 3.E), and a

FIG. 1. (a) Photograph of the imaging bench with a 16 cm CTDI phantom at isocenter for measurement of dose. (b) The Concentration phantom with various iodine and calcium inserts in a 15 cm diameter water cylinder. (c) The arrangement of the contrast inserts of variable diameter in the Detail phantom. The inserts were embedded in a water cylinder as in (b). (d) The Proximity phantom. The same inserts as in (c) were used.

250 mg/cm² CsI:Tl scintillator in the study of the effects of object size (Sec. 3.E). The native FPD pixel size was 0.139×0.139 mm² in both cases. There was no difference in classification procedures for the two detectors and no appreciable difference in the observed system calibration (e.g., material classification space illustrated in Fig. 2, below). The source and detector were positioned using an arrangement of linear translation stages (406XR and HLE60SR, Parker Hannifin, Cleveland, OH), and the object was rotated using a Dynaserv G3 servo drive coupled with a DR1060B motor (Parker Hannifin, Cleveland, OH)—each controlled by a Compumotor 6k8 (Parker Hannifin, Cleveland, OH). Motion, x-ray exposure, and FPD readout were synchronized using custom C++ software. All studies in the current work were performed with source-detector distance (SDD) of 120 cm and source-axis distance (SAD) of 60 cm. The method of Cho *et al.*⁵⁵ was employed for geometric calibration.

The LE and HE projection data were acquired at 70 kVp (+0.2 mm Cu, +2 mm Al) and 120 kVp (+0.2 mm Cu, +2 mm Al + 0.5 mm Ag), respectively. The additional high-Z filtration in the HE beam increases spectral separation from the LE beam.^{30,32,56,57} Each DE CBCT acquisition consisted of a

FIG. 2. DE CBCT calibration and material classification. The distribution of voxel values in varying concentration of iodine and calcium embedded in the water phantom of Fig. 1(b) is displayed with error bars indicating one standard deviation. For material decomposition, the HU_{LE} - HU_{HE} space is divided by assigning each point to the material of the closest calibration line. The dark gray region is classified as iodine, and the white as calcium. A region about the origin representing very low concentrations of contrast was assigned to water.

LE scan followed by a HE scan (without perturbing the object to be imaged), rather than computer-controlled kVp switching (and filter wheel). For both the LE and HE scans, 360 projections were collected with 1° angular step, detector pixels binned to 0.278×0.278 mm², and 0.8 mm focal spot size. The LE and HE projection data were processed with separate dark and flood-field corrections. The x-ray beam was axially collimated to 40 mm (measured at the detector) to reduce the effects of x-ray scatter.

The experiments included four objects: (i) The Concentration phantom illustrated in Fig. 1(b) consisted of a 15 cm water cylinder containing three solid 28.4 mm diameter iodine inserts (Gammex 472, Gammex, Middleton, WI) specified as 2, 5, and 10 mg/ml and three solid calcium inserts (Gammex 472) specified as 50, 100, and 200 mg/ml; (ii) the Detail phantom shown in Fig. 1(c) and consisting of the same 15 cm water cylinder as above, but with the 5 mg/ml Gammex 472 iodine inserts and the 50 mg/ml Gammex 472 calcium inserts precisely machined to the diameters of 28.4 (original size), 20, 15, 10, 5, and 3 mm; (iii) the Proximity phantom illustrated in Fig. 1(d) and made of the same materials as the Detail phantom, but with iodine and calcium inserts of the same diameter placed in direct contact; (iv) a cadaveric knee (~13 cm diameter, cut at midfemur and midtibia) injected with iodine solution following a standard protocol for iodine arthrography (20 ml of 175 mg/ml Omnipaque, GE Healthcare, Little Chalfont, UK). The x-ray tube current was adjusted such that equal dose was imparted by the LE and HE scans. Earlier studies in DE radiography^{30,31} and CBCT (Ref. 33) indicated a benefit to signal-to-noise-ratio and detectability by allocating ~60%–70% of the total DE dose to

the HE beam. We operated at the simpler, if slightly suboptimal, allocation of 50%, since the optima reported in previous work were typically broad and implied only a gradual deterioration such that a 50/50 split in dose between the LE and HE scans does not carry a major degradation in performance.

The Concentration phantom, the Contrast phantom, and the Proximity phantom were scanned at six values of total dose (i.e., the sum of the dose from the LE and HE scans): 3.1, 4.9, 6.2, 7.8, and 15.6 mGy. Dose was measured using a RadCal Accu-Pro 9096 multipurpose radiation meter (Radcal, Monrovia, CA) with a 0.6 cc ionization chamber at the center of a 16 cm CTDI phantom (Radcal 20CT6) placed at the isocenter [Fig. 1(a)].

2.B. Reconstruction algorithms

Projection data for all objects were acquired using a 2×2 FPD binning mode (pixel size of 0.278×0.278 mm²) and downsampled by 1×7 averaging, yielding 1.95 mm slice thickness. Axial slice reconstructions were computed from the processed projection data with voxel size of 0.15×0.15 mm² (sagittal $\times$ coronal). Although scatter conditions were fairly low by virtue of a fairly small object, an extended geometry, and narrow collimation, residual scatter was corrected using a simple method in which a constant fraction of the mean projection value (measured in a small square region in the center of the object shadow) was subtracted from each projection. Pixels exhibiting near zero signal (photon starvation with gain-normalized signal $< 5 \times 10^{-3}$) were corrected by median filtering across adjacent detector cells. The number of pixels requiring such correction was small (e.g., across all studies of the Concentration phantom, only one photon-starved pixel was found in the 3.1 mGy LE dataset), and thus no significant additional blur was introduced by the median filtering.

2.B.1. Filtered backprojection with differential filtering

The LE and HE projection data were treated with separate FBP filters to test the hypothesis that differences in attenuation and DQE between the LE and HE x-ray spectra would benefit from differential smoothing. Reconstructions were performed using FBP with a Ramp filter multiplied by a Hann apodization window. The filter cutoff frequency was varied from 0.09 to 0.81 mm⁻¹ [compared to the Nyquist frequency of the projection data, equal to $1/(2 \times 0.278$ mm) = 1.79 mm⁻¹] and the apodization window was defined so that it reached zero at the filter cutoff frequency. DE CBCT classifications were computed from each possible pairing of such differentially filtered projections.

2.B.2. Penalized likelihood reconstruction with differential regularization

In the PL approach, image reconstruction is posed as maximizing the objective function

$$\begin{aligned} \hat{\mu} &= \arg \max_{\mu} L(\mu; y) - \beta \cdot R(\mu) \\ &= \arg \max_{\mu} \sum_p \left\{ y_p \log \left[I_{0p} \exp \left(- \sum_j \mu_j l_{pj} \right) \right] \right. \\ &\quad \left. - I_{0p} \exp \left(- \sum_j \mu_j l_{pj} \right) \right\} - \beta \cdot R(\mu), \end{aligned} \quad (1)$$

where $L(\mu; y)$ is a likelihood term that encompasses the data fidelity (forward model) and a noise model, μ is the volume to be reconstructed, y are the measured projection data, index p encompasses all projection rays (all detector pixels for every projection angle), and index j enumerates all voxels in the volume. I_{0p} is the air scan value of the p th ray and l_{pj} is the length of intersection of the p th ray with the j th voxel. The familiar Poisson log-likelihood for the monoenergetic x-ray system model was used in Eq. (1) and throughout the current work. The $R(\mu)$ term is a penalty (regularization) that discourages noisy images that would result from maximization of the likelihood term alone. Typically, the penalty is defined as a function of neighboring voxel value differences

$$R(\mu) = \sum_i \sum_j f(\mu_i - \mu_j), \quad (2)$$

where index i runs through all voxels in the volume and j indicates first-order neighbors of voxel i .

The penalty functions were derived from the Huber function⁵⁸

$$f(x) = \begin{cases} \frac{1}{2\delta} x^2 & |x| < \delta \\ |x| - \frac{\delta}{2} & |x| \geq \delta \end{cases}. \quad (3)$$

Two forms of regularization were achieved by varying the size of the δ -neighborhood: (i) A quadratic penalty (denoted PLQ) was obtained by setting δ to 0.1 mm⁻¹, so the penalty carried a quadratic form across the range of voxel value differences for objects imaged in this study. Such a penalty results in uniform application of a blur across the image. (ii) A total variation penalty (denoted PLTV) was obtained by setting δ to 10^{-5} mm⁻¹, resulting in application of a one-norm penalty across most of the data. Such regularization favors piecewise-smooth images and introduces a degree of edge preservation.

The parameter β in Eq. (1) determines the strength of the penalty and thus the noise-resolution tradeoff in reconstructions, much like the filter cutoff in FBP. Increasing the value of β corresponds to stronger action of the penalty, increased blur, and reduced noise. Similar to FBP, the LE and HE projections of the three-material phantom were reconstructed with β varied from 3.125×10^3 to 1.6×10^6 for PLQ, and β varied from 50 to 4.096×10^5 for PLTV, and DE decompositions were computed for each pair of LE and HE images treated with such differential regularization. PL reconstructions were initialized with FBP reconstructions obtained at 0.9 mm⁻¹ cutoff frequency. The separable paraboloidal surrogates algorithm^{59,60} was used to maximize the PL objective function in Eq. (1). 100 iterations were carried out

for PLQ, and 200 iterations for PLTV, with visual inspection confirming negligible change in the reconstructions at further iterations.

2.C. DE calibration and material classification

In image-based DE CT, the concentration of basis materials can be solved by either a set of linear equations at each voxel (DE decomposition) (Refs. 14, 15, 41, and 61) or by clustering techniques for material classification of voxels based on the “position” in the 2D space of LE and HE attenuation values (HU_{LE} , HU_{HE}).^{62,63} A somewhat rudimentary form of material classification was used in this study to provide a useful lower bound on DE CBCT performance, while minimizing confounding factors and tradeoffs inherent in the design of more sophisticated decomposition and classification algorithms, e.g., those arising from noise amplification inherent in matrix inversion involved in DE decomposition. Furthermore, the classification approach presented below relies on the “separation angle” between the materials of interest in the (HU_{LE} , HU_{HE}) space, which underlies the fundamental performance characteristics of any image-based DE decomposition algorithm.^{14,40,64}

The DE material classification algorithm is illustrated in Fig. 2. First, a calibration was performed with the same 15 cm water cylinder phantom as described in Sec. 2.A, but with all six inserts representing iodine only (7.5–20 mg/ml) or all six inserts given by calcium (50–300 mg/ml). The calibration scans were acquired at a high total dose of 30 mGy (also with 50/50 split between LE and HE dose) to reduce noise and were reconstructed using FBP with a Ramp filter and Hann apodization with cutoff at the Nyquist frequency of the projection data (1.79 mm^{-1}). Regions of interest (ROIs) 22.5 mm in diameter were placed within each insert to measure the mean and standard deviation in voxel value. A scatter plot of the iodine and calcium LE and HE Hounsfield Unit (HU) values (denoted as HU_{LE} and HU_{HE} , respectively) is shown in Fig. 2 alongside a linear fit constrained to intercept the origin. Excellent linearity with concentration is observed for both materials. For any pair of LE and HE images, DE material classification was performed by assigning each voxel to the material (calcium or iodine) to which calibration line it was closer in the HU_{LE} - HU_{HE} space. The resulting division of the HU_{LE} - HU_{HE} space into two half-spaces representing the two materials is illustrated in Fig. 2 using a dark gray background for iodine and white for calcium.

In the Concentration phantom, the Detail phantom, and the Proximity phantom, voxels whose distance from the origin was shorter than the distance corresponding to 1 mg/ml iodine were assigned to water (shown by the white circle in Fig. 2). In the knee phantom, due to the presence of a variety of soft-tissues and high concentration of the injected iodine solution, voxels within a radius around the origin corresponding to 10 mg/ml iodine were classified as soft-tissue. In addition to DE decompositions, “composite images” given by an equally weighted linear combination of LE and HE reconstructions were also obtained.

2.D. Assessment of classification accuracy

A variety of metrics can be used to assess the effects of reconstruction algorithm on DE classification. The experiments below focused on the ability to accurately identify the distribution of materials within the object and produce a binary map for each material—viz., discrimination of iodine from calcium by binary classification. The fidelity of such maps are not well described in terms of usual image quality metrics, such as contrast-to-noise ratio (CNR) or modulation transfer function (MTF), since errors in material discrimination can arise from noise, blur, and artifacts in a complex interplay governed by the reconstruction and decomposition algorithm. The performance of such material discrimination was therefore evaluated as a classification task in terms of metrics of binary decision theory—i.e., true-positive (TP), false-positive (FP), true-negative (TN), and false-negative (FN) “decisions” for each voxel according to a known true distribution of materials in the object.

For both the Concentration phantom and the Detail phantom, two ROIs were defined for each insert (both calcium and iodine and for all insert diameters) as illustrated in the detail on the right of Fig. 3(a): a circular ROI_{in} completely within an insert and having a diameter of approx. 98% of the diameter of the insert (shown as gray overlay), and an annular ROI_{out} (white overlay) adjacent to the insert with the same area (number of voxels) as ROI_{in}. The ROIs were separated by a narrow annular region with thickness equal to $\sim 4\%$ of the insert diameter (measured radially from the outer edge of ROI_{in} to the inner edge of ROI_{out}) to avoid partial volume effects. Note that the excluded region is only a small fraction of the insert diameter, so that any significant blur from within the insert into the surrounding area is well captured by the ROIs. For a perfect classification, ROI_{in} should therefore contain only the material of the insert, and ROI_{out} should contain only water. Consequently, the number of voxels in ROI_{in} correctly identified by DE decomposition was counted as TP. Voxels in ROI_{in} not identified as the insert material [e.g., in Fig. 3(a), those identified as water or calcium] were counted as FN. Voxels in ROI_{out} correctly identified as water were counted as TN, and those identified as calcium or iodine were counted as FP. The simple phantom design allowed truth definition by simple segmentation of ROI_{in} and ROI_{out} containing only two of the three phantom materials, and the narrow boundary (4% of the insert diameter) rejected basic partial volume effects from the analysis. The DE classifier effectively describes a discrimination among three materials in that the “positive” population for ROI_{in} refers to the material of the insert (e.g., iodine), whereas for ROI_{out}, it refers to any material other than water (i.e., iodine or calcium). These terms TP, FN, TN, and FP therefore reflect a classification task (in any insert) of correctly identifying the insert material while avoiding misclassification of surrounding voxels and follow the expected arithmetic property: $(TP + FN) = (TN + FP) = V$, where V is the number of voxels in ROI_{in} (or ROI_{out}).

The performance of material classification was expressed in terms of sensitivity (Sens), specificity (Spec), and accuracy

FIG. 3. The effect of differential FBP filtering on DE CBCT material classification. (a) DE decompositions computed from differentially filtered LE and HE scans (total dose 6.2 mGy). The figure is a matrix of cropped regions about the 5 mg/ml iodine insert in the Concentration phantom decomposed with each combination of LE and HE reconstruction filter. Red overlay indicates voxels classified as iodine, blue indicates calcium, and the background (grayscale) is the composite image. ROIs of equal area (white and gray overlay in the insert detail on the right) are selected inside and outside each insert, and the fraction of voxels of each material type is used to compute metrics of (b) sensitivity, (c) specificity, and (d) accuracy. In (b), (c), and (d), the circle indicates the location of the maximum of the distribution, and the dashed line represents equal blur in the HE and LE images.

(Acc) defined as follows:

$$\text{Sens} = \frac{\text{TP}}{\text{TP} + \text{FN}}, \quad (4a)$$

$$\text{Spec} = \frac{\text{TN}}{\text{TN} + \text{FP}}, \quad (4b)$$

$$\text{Acc} = \frac{\text{Sens} + \text{Spec}}{2} = \frac{\text{TP} + \text{TN}}{2V}. \quad (4c)$$

The metrics in Eqs. (4a)–(4c) were analyzed separately for each of the iodine and calcium inserts. A combined metric describing the overall accuracy for all inserts (both calcium and iodine of various concentrations in the Concentration phantom and of various diameters in the Detail phantom) was denoted Acc_{comb}

$$\text{Acc}_{\text{comb}} = \frac{\sum_{i=1}^{N_{\text{ins}}} \text{TP}_i + \sum_{i=1}^{N_{\text{ins}}} \text{TN}_i}{2 \sum_{i=1}^{N_{\text{ins}}} V_i}, \quad (5)$$

where i runs through all six inserts of the Concentration phantom and all 12 inserts in the Detail phantom. The standard deviation of the metrics in Eqs. (4a)–(4c) and (5) was computed by randomly subdividing the ROI_{out} and ROI_{in} for a particular insert into nine subsets of equal size (number of voxels). This provided an ensemble of values from which the mean and standard deviation in a particular metric was computed.

3. RESULTS

Sections 3.A–3.C show the effects of differential filtering and regularization on the accuracy of DE CBCT material classification as a function of concentration and dose using the Concentration phantom of Fig. 1(b). Section 3.D extends the study to the effect of object size and spatial separation between the materials using the Detail phantom [Fig. 1(c)] and the Proximity phantom [Fig. 1(d)]. Finally, Sec. 3.E illustrates potential application of DE CBCT to iodine arthrography of the knee.

3.A. Differential FBP filtering in DE CBCT

Figure 3(a) shows DE classification of the 5 mg/ml iodine insert at total dose of 6.2 mGy (in each case, a color overlay on a composite FBP reconstruction at 0.81 mm^{-1} cutoff frequency) for differentially filtered LE and HE reconstructions of the Concentration phantom [Fig. 1(b)]. For a smooth LE image [e.g., top rows in Fig. 3(a)], increasing the sharpness (cutoff) of the HE reconstruction degrades classification within the insert [reduces sensitivity, Eq. (4a)]. Conversely, for a smooth HE image [e.g., first column in Fig. 3(a)], increasing the sharpness (cutoff) of the LE reconstruction degrades classification (of water) outside the insert [reduces specificity, Eq. (4b)]. The trends can be explained by considering Fig. 2. Because the inherent contrast for iodine and calcium is higher in the LE image, the material calibration lines are at a $>45^\circ$ angle from the HU_{HE} axis. The distance from any point in the $\text{HU}_{\text{LE}}\text{--}\text{HU}_{\text{HE}}$ space to the calibration line is

thus shorter along the HU_{HE} axis, and consequently noise in the HE image has a larger impact on discrimination of iodine and calcium. On the other hand, noise in the LE image is mitigated by the increased contrast of the material in the LE data. Conversely, in the circular region around the origin of the HU_{LE} - HU_{HE} space (classified as water), the inherent contrast is low in both images, and classification errors are primarily caused by the LE image, which carries higher noise than the HE image for a 50/50 dose allocation.³³

In Figs. 3(b)–3(d), the sensitivity, specificity, and accuracy are shown as a function of the cutoff frequencies of the LE and HE reconstructions for the same 5 mg/ml iodine insert. Sensitivity is maximized for low values of the HE cutoff, as expected based on the analysis of Fig. 3(a). Specificity shows a steeper dependence on the LE cutoff than the HE cutoff, also as expected from Fig. 3(a). Note also the region of decreased specificity for very low values of the LE cutoff [top row of Figs. 3(a) and 3(c)], where excessive blur leads to classification errors in ROI_{out}.

Figure 3(d) analyzes the same 5 mg/ml iodine insert in terms of classification accuracy (assigning equal weight to sensitivity and specificity). For FBP, accuracy is maximized at a LE filter cutoff of 0.25 mm^{-1} and a HE filter cutoff of 0.17 mm^{-1} , indicating a slight preference for more blur (i.e., stronger noise suppression) in the HE image. The benefit of

such differential filtering is evident by the off-diagonal location of the maximum Acc for almost any fixed LE or HE cutoff. For a given cutoff frequency in one of the (LE or HE) images, it is advantageous to use as low as possible a cutoff in the other (as long as the blur is not so large as to degrade specificity). There is no evidence of significant classification errors due to “edge effects” caused by such mismatch, except at the lowest LE cutoff [0.05 mm^{-1} in the top row of Figs. 3(a)–3(d)].

3.B. Differential PL regularization in DE CBCT

Extending the analysis to PL reconstruction methods and beyond the single material concentration shown in Fig. 3 [i.e., calculation of the aggregate Acc_{comb} in Eq. (5)], Fig. 4 shows Acc_{comb} measured as a function of the LE and HE cutoff frequencies (FBP) as well as the LE and HE penalty strengths, β , for PLQ and PLTV. The metric is computed across the inserts of varying concentration in the Concentration phantom of Fig. 1(b). The overall behavior of Acc_{comb} is similar for FBP and PLQ, with a broad region of optimal accuracy favoring increased smoothing overall and a slight preference for stronger blurring of the HE image. For both FBP and PLQ, when the blur parameter is increased for one of the (LE or HE) images, the accuracy in Fig. 4 indicates optimal operation at

FIG. 4. Overall accuracy (Acc_{comb}) of DE CBCT material classification for the Concentration phantom for various reconstruction algorithms (FBP, PLQ, and PLTV) at a total dose of 3.1 (top) and 6.2 mGy (bottom). The differential smoothing in FBP is controlled by the reconstruction filter cutoff applied to LE and HE data, while that in PL reconstruction is controlled by the penalty strength (β). Maxima of overall accuracy indicated with circles, equal blur in the LE and HE images represented with a dashed line.

an unmatched (and usually lower) value of the blur parameter for the other image, again demonstrating the benefit of differential filtering and regularization. Increasing the total dose from 3.1 mGy (top row of Fig. 4) to 6.2 mGy (bottom row of Fig. 4) broadens the region of optimal Acc_{comb} and increases the maximum achievable accuracy.

While the overall performance and general trends in combined accuracy of the DE classification are similar for PLQ and FBP, PLTV exhibits behavior that is qualitatively different than the other two methods. There is a broad region of high and almost constant Acc_{comb} , accompanied by a sharp drop in performance at lower penalty strengths. This behavior reflects the edge-preserving action of TV regularization. Once β reaches a certain magnitude, the PL reconstructor tends to enforce piecewise constant images that follow the boundaries of large, approximately uniform regions of attenuation separated by sharp edges. This greatly aids DE classification for the Concentration phantom, where the materials of interest (iodine and calcium) form such large areas of enhancement and thus very well match the piecewise-constant image model assumed by the TV regularizer.

3.C. Effect of dose and concentration on accuracy of material classification

Figures 5 and 6 show the dependence of classification accuracy on dose and material concentration, where each DE CBCT decomposition was obtained from FBP, PLQ, and PLTV reconstruction pairs that maximized the overall accuracy (Acc_{comb} , as in Fig. 4) for the Concentration phantom. Figure 5(a) shows the maximum Acc_{comb} as a function of dose for the three reconstruction algorithms. The performance of FBP and PLQ is similar and demonstrates an increase with dose reaching $\text{Acc}_{\text{comb}} > 90\%$ for total dose above ~ 4.9 mGy. On the other hand, PLTV achieves accuracy of $\sim 95\%$ at the lowest dose level (3.1 mGy), confirming the benefit of stronger edge-preserving regularization.

Figures 5(b)–5(d) show the accuracy (Acc) of each individual iodine insert for the same settings of DE decomposition that maximized the overall Acc_{comb} as in Fig. 4. For the lowest contrast case [2 mg/ml in Fig. 5(b)], PLTV clearly outperforms the other methods and maintains $\text{Acc} > 95\%$ across the complete range of dose. FBP and PLQ show a stronger dependence on dose and approach $\text{Acc} \sim 95\%$ for the 2 mg/ml iodine only at the highest dose (15.6 mGy). Interestingly, PLQ yields slightly lower accuracy than FBP, likely due to a combination of potentially unfavorable blur properties in the quadratic penalty for DE decomposition, including the induction of Gibbs-like ringing and the related difficulty in identifying the optimal value of penalty strength in the fairly flat domain of $(\beta_{\text{LE}}, \beta_{\text{HE}})$ in Fig. 4.

At higher iodine concentration, the accuracy achieved with the three reconstruction algorithms converge. A slight decrease in accuracy for the highest iodine concentration [10 mg/ml, Fig. 5(d)] compared to the medium concentration [5 mg/ml, Fig. 5(c)] is due to an increase in false positives arising from blur and artifacts from the high-contrast inserts.

FIG. 5. Effect of dose and material concentration on DE CBCT classification accuracy. (a) The maximum combined accuracy (Acc_{comb}) for iodine and calcium as a function of total dose for differentially filtered FBP (squares), PLQ (circles), and PLTV ("x"). The accuracy (Acc) in individual iodine inserts is shown in (b)–(d), measured for the same reconstruction parameter settings that maximize Acc_{comb} . Error bars represent $\pm$ three standard deviations around the mean, and fit lines are added as a simple representation of trends.

Figure 6 shows DE classifications obtained at maximum Acc_{comb} overlaid on the composite FBP images at total doses of 3.1, 6.2, and 15.6 mGy. As shown in Fig. 5, PLTV is seen to exhibit improved classification within the iodine and calcium regions and less blur into the surrounding water voxels. The reconstruction parameters (i.e., cutoff or regularization) correspond to those maximizing the plots in Fig. 4 and are displayed in the corner of each image. The trend toward

FIG. 6. DE CBCT classification of iodine (red) and calcium (blue) obtained using reconstruction parameters (FBP filter cutoff and PL regularization strength) corresponding to maximum Acc_{comb} . Decompositions are superimposed on composite FBP images for each dose.

increased blur (lower FBP cutoff value or higher value of β in PL) in the HE image illustrates again that the lower contrast of calcium and iodine in the HE data (compared to LE) results in increased sensitivity to HE noise in DE classification. PLQ images exhibit appreciable blur around the high-concentration iodine and calcium inserts, leading to an increase in false positive voxels, as discussed in relation to Fig. 5. Note also the slight increase in misclassified iodine voxels in the PLQ reconstructions compared to FBP, corroborating the lower Acc_{comb} for PLQ shown in Fig. 5. As mentioned above, this could be associated with unfavorable properties of the quadratic blur function and lack of a clear optimum in β for PLQ.

3.D. Effect of object size on accuracy of material classification

The studies summarized above were extended to investigate the influence of detail size using the Detail phantom [Fig. 1(c)] with iodine and calcium inserts of fixed concentration (5 and 50 mg/ml, respectively), but variable diameter (3–28.4 mm). Figure 7 illustrates the overall accuracy computed for the ensemble of all inserts of the Detail phantom for total dose of 6.2 mGy. The trends in Acc_{comb} are

similar to those observed for the Concentration phantom in Fig. 4. Slight preference for increased smoothing of the HE image is seen for FBP and PLQ. For a given value of one of the blur parameters, the maximum Acc_{comb} in FBP and PLQ is again achieved at a slightly unmatched value of the blur parameter in the other reconstruction in the DE pair. Similar to the results of Fig. 4, PLTV exhibits a broader area of elevated values of Acc_{comb} and achieves higher maximal accuracy than FBP and PLQ. However, the region of maximum PLTV accuracy is less uniform with a more distinct maximum than in Fig. 4. This reflects a more sensitive optimization of the TV penalty strength in the presence of smaller details compared to the large inserts in the Concentration phantom.

Figure 8 shows DE CBCT classification in the Detail phantom for 3.1, 6.2, and 15.6 mGy total dose. The blur parameters of the reconstruction algorithms were set to maximize Acc_{comb} in the contrast-detail phantom (corresponding to the maxima indicated with circles in Fig. 7 at total dose of 6.2 mGy). Similar to the Concentration phantom (Fig. 6), PLTV exhibits increased sensitivity (fewer misclassifications inside the inserts) and improved specificity (better delineation of insert edges) than FBP and PLQ. At the lowest dose (3.1 mGy), the increased smoothing required to reduce noise in the LE and HE images (maximize sensitivity) significantly

FIG. 7. Overall accuracy (Acc_{comb}) of DE CBCT material classification in the Detail phantom with a range of insert sizes (3–28.4 mm diameter) for various reconstruction algorithms (FBP, PLQ, and PLTV) at 6.2 mGy. Maxima of overall accuracy indicated with circles, equal blur in the LE and HE images represented with a dashed line.

FIG. 8. DE CBCT classification of the Detail phantom obtained using reconstruction parameters (FBP filter cutoff and PL regularization strength) corresponding to maximal Acc_{comb} . The values of the blur parameters and the corresponding Acc_{comb} are listed in the upper right corner of each decomposition. Iodine is shown as a red overlay and calcium as a blue overlay on composite FBP images for each dose.

FIG. 9. Effect of dose and detail size on DE CBCT classification accuracy. The accuracy of each individual iodine insert in the contrast-detail phantom is shown as a function of insert diameter for the reconstructions maximizing Acc_{comb} presented in Fig. 8. The total dose is 3.1 in (a), 6.2 in (b), and 15.6 mGy in (c). Differentially filtered FBP marked with squares, PLQ with circles, and PLTV with “x.”

reduced the accuracy for the 3 mm Ca insert for all reconstruction algorithms. This can again be understood in relation to the slope of the calibration lines in Fig. 2, where errors in the HE attenuation value have the stronger effect on classification. Reduction in HE attenuation due to blur leads to misclassification of calcium as iodine, but has less effect on iodine voxels. This is because reduction in the HU_{HE} value of voxels close to the iodine calibration line is less likely to result in a misclassification outside the iodine region of the $\text{HU}_{\text{LE}}\text{-}\text{HU}_{\text{HE}}$ space. With increase in dose, the classification improves across all inserts and reconstruction methods, reaching more than 90% for all three algorithms at a dose of 6.2 mGy.

The accuracy (Acc) of each individual iodine insert is analyzed as a function of insert diameter and dose in Fig. 9. The accuracy was measured in DE classifications that maximized Acc_{comb} in Fig. 8. Similar to the Concentration phantom and in agreement with Figs. 7 and 8, the performance of PLQ closely follows that of FBP, and PLTV provides the best accuracy for individual inserts across the range of diameters and imaging doses. However, even with PLTV, the accuracy remains below 90% for insert diameters smaller than ~ 15 mm at a total dose of 3.1 mGy, and smaller than ~ 10 mm at total dose of 6.2 and 15.6 mGy. This reflects the positioning of ROI_{out} , which is always located adjacent to the insert and has the same diameter as ROI_{in} and thus encompasses increasingly narrower annuli as the diameter of the insert decreases. The same absolute thickness of the blurred, misclassified edge therefore leads to stronger reduction in specificity for smaller inserts, as it encompasses a larger fraction of their ROI_{out} . This also leads to increased uncertainty ($\pm$ three standard deviations indicated by error bars) of the Acc values for the smaller inserts. In the procedure for estimating standard deviation explained in Sec. 2.D, an increasing number of subsets of ROI_{out} contained only misclassified voxels for these smaller inserts. Note also that the accuracy measured for the smaller inserts (less than 10 mm diameter) was typically smaller than Acc_{comb} for the same classification. This is due to implicit weighting by insert size in the definition of Acc_{comb} [Eq. (5)]. Depending on the imaging tasks, other metrics assigning larger weights to the contributions of smaller details could be devised within the same framework of binary decision theory.

The accuracy achieved with the three reconstruction methods converge with increased dose, especially for larger inserts (diameters greater than approx. 15 mm), similar to the case of the Concentration phantom. PLTV outperformed the other methods for the 3 and 5 mm inserts even at a dose of 15.6 mGy, reflecting the improved delineation of insert boundaries due to the edge-preserving penalty, also seen in Fig. 8.

To further examine the effects of differences in filtering (or regularization) of various reconstruction methods, Fig. 10 illustrates results in the Proximity phantom [Fig. 1(d)], where the calcium and iodine inserts of the Detail phantom were in direct contact. FBP and PLTV were compared at a dose of 6.2 mGy using reconstruction parameters maximizing Acc_{comb} in the Detail phantom. PLTV exhibits better delineation of the insert-water boundaries and improved sensitivity (decreased misclassification inside the inserts). However, while FBP presents fairly uniform blur around the entire perimeter of an insert, PLTV tended to introduce bridging between the neighboring inserts in each pair. This behavior is likely an effect of the edge-preserving action of the TV penalty in the area of contact between two regions of enhancement.

3.E. DE CBCT of a cadaveric knee

Initial application of DE CBCT to knee arthrography at a total dose of 6.2 mGy is illustrated in Fig. 11 for FBP and PLTV reconstruction techniques. (PLQ followed the

FIG. 10. Effects of proximity between regions of calcium and iodine in DE CBCT classification maximizing Acc_{comb} in the Detail phantom. The corresponding blur parameters shown in the upper left corner of each image.

FIG. 11. DE CBCT in a cadaveric knee iodine arthrography model at a total dose of 6.2 mGy. A composite “single-energy” image is shown on the left using a broad HU window to illustrate the difficulty in discriminating bone from iodine upon dilution of the contrast agent in the synovial fluid. Material classification was combined with a simple estimator of material concentration to yield FBP-based DE decomposition (center) and PLTV-based DE decomposition (right). Each DE decomposition gives clear discrimination of iodine and bone.

same level of performance as FBP, as detailed above.) The composite image of the iodinated knee (FBP with cutoff at 0.4 mm^{-1}) is shown on the left using a broad HU window to avoid saturation in iodine-enhanced voxels. Note that the standard 175 mg/ml iodine solution diluted with synovial fluid to a level of iodine enhancement with attenuation close to that of bone, challenging discrimination of the two materials in a single-energy (or composite) image. This is evident, e.g., in the Baker’s cyst. The DE CBCT images combine the classification approach outlined in Sec. 2.C with a simple estimator of material concentration, which was determined using the distance of voxels identified as iodine or bone from the center of the HU_{LE} - HU_{HE} space in Fig. 2. Reconstruction parameters such as slice thickness, pixel binning, and voxel size were matched between the phantom experiments and the knee study. The filter (or regularization) parameters were optimized according to the level of projection noise. While a more detailed study of this clinical application is the subject of ongoing work, the optimization in this initial experiment was performed via visual inspection of easily identifiable anatomical features, such as preservation of enhancement in the Baker’s cyst and minimization of misclassification inside the condyles. Optima were identified at LE cutoff of 0.49 mm^{-1} and HE cutoff of 0.17 mm^{-1} for FBP, and at $\beta_{LE} = 200$, and $\beta_{HE} = 800$ for PLTV. Note the preference for stronger filtering in the HE image. Clear discrimination of iodine and bone was achieved by DE CBCT using either FBP or PLTV. The results show dilution of iodine (mixing with synovial fluid) to concentration below $\sim 80 \text{ mg/ml}$. FBP exhibits reduced sensitivity in the condyles and in the tibial plateau, where areas of iodine are erroneously detected. In agreement with the phantom studies, PLTV exhibits less blur-induced classification error. At the same time, PLTV tends to present high-frequency “ridge-like” misclassification errors, likely related to the edge-preserving action of the penalty at strong gradients in material concentration. Similar to results in the Proximity phantom, PLTV introduces slight “bridging” for narrowly spaced regions of

iodine and calcium (e.g., low concentrations of calcium are erroneously detected in between the condyles and the enhanced joint space).

4. DISCUSSION AND CONCLUSIONS

The effect of reconstruction algorithm on performance of image-based DE classification in flat-panel detector CBCT was investigated, focusing on the application to contrast-enhanced extremities imaging. Optimal performance in the accuracy of material decomposition was achieved through differential filtration (or regularization) of the LE and HE reconstructions. Such differential filtration compensated for the differences in noise and contrast in the LE and HE images, consistent with various methods of noise reduction^{17,42} and as elucidated in cascaded systems analysis extended to DE CBCT.³³ Dose allocations other than the 50/50 partitioning employed here may yield additional improvement in decomposition performance if differential filtering/regularization were used to account for noise and contrast in a manner tailored to the classification algorithm.

The separation angle between materials did not significantly change between the two FPDs (i.e., employing a $\text{Gd}_2\text{O}_2\text{S:Tb}$ screen in the studies of the Concentration phantom versus employing a CsI:Tl scintillator in studies of the Detail phantom). Furthermore, both CsI:Tl and $\text{Gd}_2\text{O}_2\text{S:Tb}$ exhibit $\sim 60\%$ – 70% lower quantum detection efficiency for the HE beam compared to the LE beam, suggesting similar differential effect of the scintillator on noise in HE and LE data. Consequently, similar dose performance and comparable effects of differential filtering and regularization were observed with both FPDs, indicating the applicability of the current results for either type of x-ray converter.

The outcome of DE classification depends on the underlying fundamental properties of the LE and HE reconstruction (e.g., noise and resolution tradeoffs) and their complex interplay with the classification algorithm. This is especially true for nonlinear MBIR methods such as PLQ and

PLTV, where fundamental image properties are contrast and location-dependent. Metrics operating directly in the domain of the material distribution maps therefore provide a direct measure of DE imaging performance that is largely independent of both the reconstruction and the classification algorithms—i.e., avoiding pitfalls of CNR and/or MTF comparison between algorithms that may reflect little of the actual classification performance. Here, the quality of DE classification was assessed using metrics drawn from a binary decision framework, namely, sensitivity, specificity, and accuracy. Other imaging tasks and decomposition methods seeking local concentration of base materials through matrix inversion at each voxel^{14,15,40,61} may require different quality metrics. As mentioned in Sec. 2.C, however, the results presented here would be expected to hold as an estimate of baseline performance irrespective of the decomposition/classification method.

While the classification approach presented here does not provide an explicit estimate of material concentration, it can be easily augmented to do so using the same calibration data, as shown for knee arthrography in Sec. 3.E. Recognizing the need for further evaluation of this and other DE CBCT classification/decomposition strategies in clinical tasks, the framework utilized throughout this work is expected to be applicable to situations where the material of interest occupies a distinct region in the body (e.g., detection of contrast-enhanced vessels and joint spaces, or uric acid crystals), but is difficult to separate from surrounding tissues due to the similarity of their attenuation values, as opposed to the task of decomposing mixtures or overlapping materials into their components (e.g., in detection of bone marrow edema or bone densitometry).

For the range of imaging and reconstruction parameters studied here, both the quantitative metrics and qualitative visual inspection confirm the ability to form accurate material decomposition ($\text{Acc} > 90\%$) in DE CBCT down to 5 mg/ml iodine at detail size of 28.4 mm and total dose ~ 5 mGy using either analytical reconstruction (FBP) or iterative model-based PL methods. For a similar dose level (6.2 mGy), details down to ~ 10 mm diameter at iodine concentration of 5 mg/ml can be classified with $\text{Acc} > 75\%$ with either reconstruction method. Interestingly, PLQ reconstruction performed similarly to FBP across the range of conditions studies, and while further fine-tuning of the penalty strengths could potentially improve the quality of PLQ decomposition, the trends suggest little benefit from a simple quadratic penalty. Application of PLTV, on the other hand, resulted in quantitative and qualitative improvement in DE CBCT decomposition performance. Iodine concentrations as low as 2 mg/ml were detectable with accuracy of $>95\%$ at total dose of 3.1 mGy for insert diameter of 28.4 mm. For the same dose, almost 90% accuracy was achieved for 10 mm iodine details at 5 mg/ml. This underscores the value of an edge-preserving penalty function for the DE classification task involving continuous areas of contrast enhancement, as studied here. Reconstructions involving strong TV-type regularization can appear “patchy” and may not be ideally suited for visualization in general diagnosis, but in DE imaging this appearance may be beneficial for the clas-

sification/decomposition algorithm, and the final product (i.e., the map of material distribution) can be overlaid on a composite reconstruction obtained with a different algorithm—e.g., FBP—with a more favorable, familiar visual appearance of the surrounding anatomical context. The phantom studies reported here generally involved a contrast distribution well matched with the piecewise constant prior model invoked by the TV penalty. For cases where the regions of iodine and calcium were in very close proximity, the TV penalty was found to introduce a “bridging” of enhancement between the two regions, reducing specificity in the water background. While this could be controlled by further adjustment of the water threshold, it is likely that a less aggressively edge preserving form of the Huber penalty than the TV regularizer used here may prove beneficial for certain decomposition tasks. In general, a penalty function that is well matched to the “signature” of the DE decomposition task in the image domain (e.g., detection of calcifications or small crystals of uric acid) is likely to be generally beneficial over a generic blur function.

The phantom experiments provided a systematic exploration of the effects of concentration, detail size, dose, and reconstruction algorithm in contrast-enhanced DE CBCT. The clinical application of interest in this work (joint arthrography) currently involves relatively high concentrations of iodine, estimated to be in the 15–80 mg/ml range upon dilution in the synovial fluid. The phantom study investigated comparatively low concentrations of the contrast agent to provide insights applicable to a broader range of clinical scenarios and guide development of future imaging protocols. As such, the phantom study was not meant to optimize reconstruction parameters for any particular application, but rather to use an idealized imaging scenario to gain understanding of the major effects of the reconstruction algorithm, such as potential benefits of differential filtering/regularization and of edge-preserving penalties, and to establish the performance limits of DE CBCT with respect to physical factors such as material concentration and imaging dose. It is expected that future clinical applications of DE CBCT will require dedicated optimization of reconstruction and classification/decomposition methods, and the initial application of DE classification to a cadaveric knee injected with iodine demonstrated greatly enhanced discrimination of bone and iodine in the synovial space with DE decomposition by either FBP or PLTV.

The feasibility of contrast-enhanced DE extremities imaging on a CBCT platform was demonstrated here in benchtop studies, motivating implementation on dedicated musculoskeletal CBCT systems.^{12,13,65} While the current results demonstrate viable DE decomposition at total dose that is comparable to that reported for single-energy extremities CBCT,⁶⁵ additional practical issues need to be resolved for clinical implementation, most notably the potential for patient motion during a double scan (requiring ~ 20 – 40 s) and the need for high-quality scatter correction. Initial experience with the clinical prototype indicates that simple patient immobilization (viz., an air cast) is sufficient to eliminate motion artifacts even in imaging the standing knee and/or extended scan times.⁶⁶ Such mechanical approaches, coupled perhaps with increased FPD frame rate and/or reduction in angular

sampling in the LE and HE scans are therefore envisioned for translation of the work reported here to clinical studies. Accelerated GPU-based Monte Carlo scatter correction^{67,68} shows promise in efficient reduction of scatter artifacts and will be investigated for application in DE CBCT.

The results presented here, combined with previous studies of DE imaging technique optimization, lay the groundwork for more challenging DE imaging scenarios in FPD-based CBCT beyond discrimination of exogenous (iodine) contrast. In particular, ongoing work focused on extremities imaging includes DE CBCT classification of endogenous contrast such as tendons, bone marrow edema, and uric acid.

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