Experimentally determined spectral optimization for dedicated breast computed tomography

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Purpose: The current study aimed to experimentally identify the optimal technique factors (x-ray tube potential and added filtration material/thickness) to maximize soft-tissue contrast, microcalcification contrast, and iodine contrast enhancement using cadaveric breast specimens imaged with dedicated breast computed tomography (bCT). Secondly, the study aimed to evaluate the accuracy of phantom materials as tissue surrogates and to characterize the change in accuracy with varying bCT technique factors.

Methods: A cadaveric breast specimen was acquired under appropriate approval and scanned using a prototype bCT scanner. Inserted into the specimen were cylindrical inserts of polyethylene, water, iodine contrast medium (iodixanol, 2.5 mg/ml), and calcium hydroxyapatite (100 mg/ml). Six x-ray tube potentials (50, 60, 70, 80, 90, and 100 kVp) and three different filters (0.2 mm Cu, 1.5 mm Al, and 0.2 mm Sn) were tested. For each set of technique factors, the intensity (linear attenuation coefficient) and noise were measured within six regions of interest (ROIs): Glandular tissue, adipose tissue, polyethylene, water, iodine contrast medium, and calcium hydroxyapatite. Dose-normalized contrast to noise ratio (CNRD) was measured for pairwise comparisons among the six ROIs. Regression models were used to estimate the effect of tube potential and added filtration on intensity, noise, and CNRD.

Results: Iodine contrast enhancement was maximized using 60 kVp and 0.2 mm Cu. Microcalcification contrast and soft-tissue contrast were maximized at 60 kVp. The 0.2 mm Cu filter achieved significantly higher CNRD for iodine contrast enhancement than the other two filters ($p=0.01$), but microcalcification contrast and soft-tissue contrast were similar using the copper and aluminum filters. The average percent difference in linear attenuation coefficient, across all tube potentials, for polyethylene versus adipose tissue was 1.8%, 1.7%, and 1.3% for 0.2 mm Cu, 1.5 mm Al, and 0.2 mm Sn, respectively. For water versus glandular tissue, the average percent difference was 2.7%, 3.9%, and 4.2% for the three filter types.

Conclusions: Contrast-enhanced bCT, using injected iodine contrast medium, may be optimized for maximum contrast of enhancing lesions at 60 kVp with 0.2 mm Cu filtration. Soft-tissue contrast and microcalcification contrast may also benefit from lower tube potentials (60 kVp). The linear attenuation coefficients of water and polyethylene slightly overestimate the values of their corresponding tissues, but the reported differences may serve as guidance for dosimetry and quality assurance using tissue equivalent phantoms. © 2011 American Association of Physicists in Medicine. [DOI: [10.1118/1.3537077](https://doi.org/10.1118/1.3537077)]

I. INTRODUCTION

Carcinoma of the breast is the most frequently diagnosed cancer in women, with more than 192 000 new cases of the invasive disease estimated to occur among women in the United States in 2009, leading to an estimated 40 000 breast cancer deaths.¹ Mammography is currently the gold standard imaging modality for early detection of breast carcinoma. Screen-film and digital mammography are particularly adept at visualizing microcalcifications and soft tissue masses embedded in an adipose background;² however, mammographic visualization of lesions in denser breasts is hindered by the superimposition effects found in projection imaging. The summation of overlying breast tissue in a projection image can obscure the visualization of a malignant lesion, leading to a false negative reading, or can cause summation artifacts,

yielding a false positive and possibly unnecessary follow-up imaging procedures, biopsies, and anxiety for the patient.

Several groups have developed experimental, flat-panel detector, cone-beam x-ray-based imaging systems to acquire fully tomographic, three-dimensional images of the entire breast volume, overcoming the superimposition issues of projection imaging.³⁻⁶ Initial clinical experience with dedicated breast computed tomography (bCT) confirms that bCT is better at visualizing breast lesions associated with a soft tissue mass, while mammography is still better at visualizing microcalcifications.⁷ Further studies have employed the use of injected, iodinated contrast agents to improve bCT visualization of malignant lesions, specifically malignant lesions manifested mammographically as microcalcifications.⁸ However, these studies have evaluated lesion visualization on bCT and contrast-enhanced bCT (CE-bCT) using a single

predetermined combination of bCT technique factors that are not necessarily optimized to achieve maximum signal difference between materials/tissues of interest in breast imaging.

Important material signal differences in breast imaging and bCT include (i) soft-tissue contrast (glandular tissue against an adipose background), (ii) microcalcification contrast (microcalcifications against a glandular tissue background), and (iii) iodine contrast enhancement (iodine contrast medium against a glandular background). Previous studies have explored varying bCT technique factors, specifically x-ray tube potential, filter material, and filter thickness, to generate different x-ray spectra⁹ and to evaluate the effects of those spectra on image quality.^{3,10–13} However, many of these studies focused on soft-tissue contrast or microcalcification contrast, but not iodine contrast enhancement, and have mainly used computer simulations or experimental measurements with idealized phantoms to evaluate image quality.

The purpose of this study was to experimentally identify the optimal combinations of x-ray tube potential and filtration material/thickness to maximize soft-tissue contrast, microcalcification contrast, and iodine contrast enhancement using cadaveric breast specimens imaged with bCT. A secondary purpose was to evaluate the accuracy of phantom materials as tissue surrogates and to characterize the change in accuracy with varying bCT technique factors.

II. MATERIALS AND METHODS

II.A. Phantoms and materials

A cadaveric breast specimen was obtained under approval by the Body Donation Program at our institution. The specimen was an embalmed left breast (approximately 12 cm in diameter) including pectoralis major and skin from a 76 yr old woman who died from acute myocardial infarction secondary to coronary artery disease. The subject had no history of breast pathology. Three hollow cylindrical inserts were constructed from polymethylmethacrylate measuring 1.3 cm in diameter and 6.6 cm in length. The inserts were filled with water, iodine contrast medium (2.5 mg/ml iodixanol; Visipaque, GE Healthcare, Waukesha, WI), or a calcium hydroxyapatite (CaHA) suspension (100 mg/ml; Berkeley Advanced Biomaterials Inc., Berkeley, CA). A similarly sized cylindrical insert of solid ultrahigh molecular weight polyethylene (PE) was also constructed.

The concentration of CaHA was selected as per a previous study.¹³ The concentration of iodine was chosen by estimating the mean iodine concentration in 29 malignant breast lesions imaged as a part of an ongoing, Institutional Review Board approved clinical trial of CE-bCT, using the same bCT scanner as in this study.⁸ Patients undergoing CE-bCT received a 100 ml intravenous injection of iodixanol (320 mg/ml) at 4 ml/s using a power injector. The mean time from the start of contrast injection until the postcontrast scan was 96 s (range: 52–219 s). To develop a calibration curve using known iodine concentrations, 12 cuvettes containing varying concentrations of iodixanol (1.4–189 mg/ml) were placed in a previously described 7.5 cm box phantom filled with water

FIG. 1. Cadaveric breast specimen with inserts. Coronal bCT image (80 kVp, 0.2 mm Cu) of cadaveric breast specimen with regions of glandular tissue (G), adipose tissue (A), PE, water (H_2O), iodine contrast medium (I), and CaHA delineated by dotted lines.

and polyethylene slabs.¹⁴ The phantom was scanned on the bCT scanner at 80 kVp and 7 mA. Five hundred projections were acquired in all scans (16.7 s exposure at 30 frames per second) and reconstructed using filtered backprojection with a Shepp–Logan filter. The mean intensity, in Hounsfield units, of each iodine concentration was measured in a region of interest (ROI) within each cuvette and fit to the known iodine concentration using a second order polynomial. The intensity of iodine in the malignant lesions was measured from patient CE-bCT images by manually segmenting the lesions from precontrast and postcontrast images. The iodine intensity was measured as the difference in mean voxel intensity in the precontrast and postcontrast lesion volumes. Iodine concentration within the lesion was then estimated using the measured iodine intensity from the patient scans and the polynomial fit to the iodine cuvette calibration. The calibration curve did not take into account the differential contribution of scatter between a patient breast scan (14 cm mean diameter) and that when imaging the cuvette phantom (7.5 cm), which may lead to inaccuracy.

II.B. Specimen imaging

The cadaveric breast, with the four cylindrical inserts embedded centrally within, was scanned (Fig. 1) using a previously described prototype bCT scanner (Table I).^{7,15} Six different x-ray tube potentials (50, 60, 70, 80, 90, and 100 kVp) and three different filter types [0.2 mm copper (Cu), 1.5 mm aluminum (Al), and 0.2 mm tin (Sn)] were tested to generate various photon spectra (Fig. 2). For each tube potential and filter combination, the tube current and detector frame rate were selected to satisfy detector limitations. Air scans were performed to select these technique factors (Table II), maximizing the detector pixel intensity counts without saturating the detector. The detector was operated in a low-gain mode with 2×2 pixel binning to achieve an effective pixel pitch of $388 \mu\text{m}$ with 1024×768 pixels per frame. A complete scan consisted of 500 images over a 360° rotation with a $197 \times 197 \text{ mm}^2$ field of view.

TABLE I. Specifications of bCT scanner. All images were acquired using a prototype cone beam computed tomography scanner with the given specifications.

X-ray tube	Comet, Flamatt, Switzerland
Power	1000 W
Anode	Water-cooled tungsten
Focal spot	0.40×0.40 mm
X-ray detector	Paxscan 4030CB, Varian Imaging Systems, Palo Alto, CA
Type	Indirect, thin-film-transistor array
Size	40 cm×30 cm
Scintillator	CsI
Detector element pitch	388 μ m (with 2×2 binning to achieve 1024×768 pixels)
CT pixel pitch	208 μ m
Source to detector distance	1037 mm
Source to isocenter distance	511 mm

For each scan, the breast specimen was positioned on a stack of foam rings in a prone pendant geometry at the scanner isocenter, with the superior aspect of the specimen oriented toward the head of the scanner, as would be done for a patient scan. Scans were reconstructed by means of a filtered backprojection based, cone-beam reconstruction algorithm¹⁶ using a Shepp–Logan reconstruction filter and a 512×512 matrix. Two consecutive bCT scans were performed for each combination of technique factors and the subtraction of the two scans was used for noise measurements.

II.C. Dose calculation

For dose calculations, the fibroglandular density of the cadaveric breast specimen was assumed to be 50%. The mean glandular dose (D_g) from each scan was calculated as

$$D_g = D_g N_{CT} \times X_{Iso}, \quad (1)$$

where X_{Iso} is the exposure in air measured at isocenter and $D_g N_{CT}$ is the polyenergetic normalized glandular dose coefficient used in dedicated breast CT.¹⁷ Exposure was derived from the product of scan time and the exposure rate, measured using a general purpose, in-beam chamber (RadCal Corporation, Monrovia, CA). The polyenergetic $D_g N_{CT}$ coefficients were computed as

$$D_g N_{CT} = \frac{\int_0^{E_{max}} \Phi(E) F(E) dE}{\int_0^{E_{max}} \Phi(E) K(E) dE} \quad (2)$$

for a photon fluence $\Phi(E)$ in photons/mm², Monte Carlo derived glandular dose per fluence $F(E)$ in μ Gy/(10⁶ photons/mm²), and air kerma per fluence $K(E)$ in μ Gy/(10⁶ photons/mm²). The photon fluence $\Phi(E)$ for each combination of technique factors was derived using tungsten anode spectral model interpolating polynomials¹⁸ (TASMIP) assuming a 0.15% x-ray generator ripple. The model was modified by adding additional aluminum filtration to match half-value layer measurements performed on our scanner for each pair of x-ray tube energy and filter. The glandular dose per fluence $F(E)$ was generated using the pre-

FIG. 2. Photon spectra. A total of 18 different photon spectra were generated through combinations of x-ray tube potential and filter type. Shown here are the 50 (solid line), 80 (thick dashes), and 100 kVp (thin dashes) spectra using 0.2 mm Cu, 1.5 mm Al, and 0.2 mm Sn filtration, derived using TASMIP (Ref. 18).

viously validated SIERRA Monte Carlo code system.^{19,20} The air kerma per fluence $K(E)$ was calculated as the product of energy fluence and mass energy transfer coefficient.

II.D. Image analysis and spectral optimization

Each image data set was evaluated using IMAGEJ version 1.41 (U.S. National Institutes of Health, Bethesda, MD). Mean intensity (linear attenuation coefficient) measurements

TABLE II. bCT technique factors. X-ray tube current (mA) and detector frame rate [frames per second (fps)] used with three filter types and six tube potentials (kVp). Half value layers and air kerma rate measurements are also given for each pair of technique factors.

kVp	0.2 mm Cu				1.5 mm Al				0.2 mm Sn			
	mA	fps	HVL (mm Al)	Air kerma rate (mGy/min)	mA	fps	HVL (mm Al)	Air kerma rate (mGy/min)	mA	fps	HVL (mm Al)	Air kerma rate (mGy/min)
50	16	9	3.11	34.0	16	30	1.34	226.9	17	6	1.32	53.1
60	11	15	3.77	42.6	9	30	1.53	179.5	13	9	1.47	56.9
70	11	30	4.43	66.0	5.5	30	1.75	142.5	10	12	1.68	58.4
80	6	30	4.96	51.4	4	30	2.02	129.3	8	18	1.97	61.2
90	5	30	5.66	57.7	2.7	30	2.17	104.6	6	22	2.45	58.6
100	3.5	30	6.31	49.1	2.2	30	2.47	100.1	4.5	22	2.98	54.9

were made for six representative regions (glandular tissue, adipose tissue, PE insert, water insert, iodine insert, and CaHA insert) using a 306 pixel ROI. The six measurements were repeated on three noncontiguous slices. For noise measurements, the bCT image data set for a given combination of technique factors was subtracted from an identical repeat scan, removing the cupping artifact and structural information and leaving behind only noise. Noise was measured on the subtraction images as the standard deviation in pixel intensity using the same 18 ROIs (6 ROIs over 3 slices) as described above. Due to the propagation of error from the subtraction of two identical images, the actual noise is given by the reported noise divided by the square root of two.

Signal difference between pairs of regions was calculated as the difference in mean intensity (averaged over the three slices measured). Signal difference to noise ratio (SDNR) was calculated as

$$\text{SDNR} = \sqrt{2} \frac{|I_1 - I_2|}{\sqrt{\sigma_1^2 + \sigma_2^2}}, \quad (3)$$

where I represents the mean intensity for the three repeat ROIs of a region and σ is the mean standard deviation in pixel intensity over the three ROI measurements for a region. We assumed that noise is inversely proportional to the square root of dose. Thus, the optimization metric used in this study was the dose-normalized contrast (signal difference) to noise ratio (CNRD)

$$\text{CNRD} = \sqrt{2} \frac{|I_1 - I_2|}{\sqrt{\sigma_1^2 + \sigma_2^2} \sqrt{D_g}}, \quad (4)$$

where D_g is given by Eq. (1). The regions compared were iodine against water (as a surrogate for enhancing lesions on CE-bCT), CaHA against water (as a surrogate for microcalcification visualization), and glandular tissue against adipose tissue (native tissue contrast). Water was compared against PE as phantom surrogate materials for native tissue contrast. Water and PE were also compared to glandular tissue and adipose tissue, respectively, to evaluate the effects of different photon spectra on the use of these materials as tissue surrogates.

II.E. Statistical analysis

All intensity and noise measurements represent the mean over three repeat ROIs from noncontiguous slices. Thus, error in these measurements is reported as the standard deviation over the three ROIs. Mixed-effect linear regression models adjusting for multiple comparisons were designed to test the effects of tube potential and filter material on the intensity and noise of each ROI as well as for the CNRD between pairs of ROIs.

The accuracy of water and PE as surrogate phantom materials for adipose tissue and glandular tissue, respectively, was evaluated. The mean linear attenuation coefficients measured over the three ROIs for each material were compared directly and as a percent difference.

Univariate statistical summaries and comparative tests were performed using standard spreadsheet software (Microsoft Excel, Microsoft Corporation, Redmond, WA) and Stata 11 (StataCorp, College Station, TX). Statistical significance was assumed at a two-sided $p < 0.05$.

III. RESULTS

III.A. Iodine concentration

Figure 3 shows an iodine calibration curve derived from bCT scans of cuvettes containing known concentrations of

FIG. 3. Iodine calibration curve. Cuvettes containing known concentrations of iodine contrast medium were scanned and the measured intensity (Hounsfield units) was fit to a second order polynomial.

iodine contrast medium and CE-bCT scans of patients with malignant breast lesions. The mean iodine concentration in 29 malignant lesions was 1.6 ± 0.76 (standard deviation) mg/ml. The iodine concentration in the iodine insert used for this study (2.5 mg/ml) was 1.18 standard deviations above the mean lesion iodine concentration.

III.B. Intensity (linear attenuation coefficient)

Overall, the CaHA ROI had the highest intensity (linear attenuation coefficient), followed by iodine, then water and glandular tissue, and finally PE and adipose tissue (Fig. 4). At 80 kVp using the 0.2 mm Cu filter, the CaHA, iodine, water, glandular, PE, and adipose ROIs had attenuation coefficients ($\pm$ standard deviation) of 0.243 ± 0.020 , 0.227 ± 0.011 , 0.198 ± 0.007 , 0.193 ± 0.010 , 0.186 ± 0.009 , and 0.183 ± 0.006 cm^{-1} , respectively. The intensity for all ROIs showed an energy dependency with intensity decreasing as x-ray tube potential increased.

Mixed-effect linear regression models of intensity for each ROI showed similar findings (Table III). There was a significant decrease in intensity for all ROIs with increasing tube potential ($p \leq 0.003$). The 1.5 mm Al filter had significantly higher intensity measurements than the 0.2 mm Cu filter for all ROIs ($p \leq 0.013$), while the 0.2 mm Sn filter had an even larger increase in intensity over the 0.2 mm Cu filter ($p < 0.001$). As per the interaction terms, the drop in intensity with increasing energy was amplified when using the 0.2 mm Sn filter ($p \leq 0.001$), but was not modified by the 1.5 mm Al filter.

III.C. Noise

Glandular tissue generally had the highest noise, followed by water, iodine, CaHA, and PE, and adipose tissue had the lowest noise (Fig. 5). At 80 kVp using the 0.2 mm Cu filter, these ROIs had noise measurements of 0.0167 ± 0.0004 , 0.0153 ± 0.0002 , 0.0164 ± 0.0005 , 0.0136 ± 0.0003 , 0.0143 ± 0.0004 , and 0.0108 ± 0.0008 cm^{-1} , respectively. Noise appeared to follow an energy dependency with noise decreasing as tube potential increased, but this trend was not statistically significant in most ROIs (Table III). Regression models suggested the noise using 0.2 mm Cu and 1.5 mm Al were similar, while the 0.2 mm Sn filter had significantly higher noise for all ROIs ($p \leq 0.003$).

III.D. Dose-normalized contrast to noise ratio

CNRD was calculated for eight pairwise ROI comparisons: CaHA-glandular tissue, CaHA-water, iodine-glandular tissue, iodine-water, glandular tissue-adipose tissue, water-PE, water-glandular tissue, and PE-adipose tissue (Fig. 6). Iodine contrast enhancement (CNRD for iodine-glandular tissue) was maximized using 60 kVp and 0.2 mm Cu. Microcalcification contrast (CNRD for CaHA-glandular tissue) was maximized using 60 kVp and 1.5 mm Al filtration. Native soft-tissue contrast (glandular tissue-adipose tissue) was maximized using 60 kVp and 1.5 mm Al.

FIG. 4. Mean intensity. The intensity (linear attenuation coefficient) of six ROIs was measured for each combination of x-ray tube potential and filter material/thickness. Error bars represent the standard deviation for three repeated measurements from nonadjacent slices.

Regression models estimated the 0.2 mm Cu filter and 1.5 mm Al filter to achieve similar CNRD measurements for most ROI comparisons; however, the 0.2 mm Cu filter achieved a higher estimated CNRD than the 1.5 mm Al filter when comparing iodine versus glandular tissue ($p=0.01$) and versus water ($p=0.04$). The 0.2 mm Sn filter had significantly lower CNRD than the 0.2 mm Cu filter for all ROI comparisons ($p \leq 0.014$) except when comparing water to PE and tissues to their surrogate phantom materials (Table III).

TABLE III. Mixed-effect regression models. Linear regression models were generated for intensity (linear attenuation coefficient), noise, and CNRD measurements with tube potential, filter, and their interaction set as model parameters. Model coefficients are reported for each region of interest (polyethylene, water, iodine, CaHA, glandular tissue, and adipose tissue) and each pairwise comparison of CNRD. The intercept (comparison group) for the models used a tube potential of 50 kVp and 0.2 mm Cu filtration. Statistical significance at $p < 0.05$, $p < 0.01$, and $p < 0.001$ is given by one, two, and three asterisks, respectively.

Measured variable	Coefficient	PE	Water	Iodine	CaHA	Glandular	Adipose		
Intensity (linear attenuation coefficient, cm^{-1})	kVp	-0.0004**	-0.0007***	-0.0011***	-0.0014***	-0.0006**	-0.0004**		
	1.5 mm Al	0.0236***	0.0220**	0.0200*	0.0421**	0.0210**	0.0223***		
	0.2 mm Sn	0.0412***	0.0464***	0.0303***	0.0631***	0.0421***	0.0433***		
	kVp $\times$ 1.5 mm Al	-0.0003	-0.0002	-0.0001	-0.0005	-0.0002	-0.0002		
	kVp $\times$ 0.2 mm Sn	-0.0009***	-0.0009***	-0.0009**	-0.0017**	-0.0009***	-0.0009***		
Noise	kVp	-3.20×10^{-5}	-7.22×10^{-5} *	-3.72×10^{-5}	-6.87×10^{-5}	-5.83×10^{-5}	-2.98×10^{-5}		
	1.5 mm Al	7.26×10^{-4}	-3.50×10^{-5}	1.23×10^{-3}	6.73×10^{-4}	9.10×10^{-4}	7.37×10^{-4}		
	0.2 mm Sn	4.02×10^{-3} **	4.45×10^{-3} **	4.83×10^{-3} **	5.41×10^{-3} **	5.55×10^{-3} **	3.80×10^{-3} **		
CNRD			CaHA-glandular	CaHA-water	Iodine-glandular	Iodine-water	Glandular-adipose	Water-PE	Water-glandular
	kVp		-0.0042*	-0.0014	-0.0032*	-0.0007	-0.0005	-0.0034***	-0.0019**
	1.5 mm Al		0.0539	0.1032	-0.1573*	-0.1275*	-0.0597	-0.0698	-0.0083
	0.2 mm Sn		-0.2172**	-0.1854**	-0.3720***	-0.3565***	-0.0982*	-0.0550	-0.0032
									PE-adipose
									0.0003
									0.0150
									-0.0273

III.E. Tissue surrogate accuracy

Using water as a surrogate for glandular tissue, microcalcification contrast (CaHA-water) and iodine contrast enhancement (iodine-water) were maximized with the same technique factors found to maximize CNRD using the actual tissue ROI; however, native soft-tissue contrast using surrogate materials (water-PE) suggested 50 kVp and 0.2 mm Cu maximizes CNRD.

The linear attenuation coefficients for glandular tissue and adipose tissue, as well as for their phantom surrogates (water and PE, respectively), were measured and plotted for all combinations of tube potential and filter type (Fig. 7). For all three filter types, linear attenuation decreased with increasing tube potential. The linear attenuation coefficient for water, across all tube potentials, had a range of 0.042 cm^{-1} (median, 0.201 cm^{-1}) for 0.2 mm Cu, 0.047 cm^{-1} (median, 0.220 cm^{-1}) for 1.5 mm Al, and 0.084 cm^{-1} (median, 0.221 cm^{-1}) for 0.2 mm Sn. Adipose tissue, glandular tissue, and PE showed similar trends with the median value and range in values increasing from a minimum using the 0.2 mm Cu filter to a maximum using the 0.2 mm Sn filter.

The percent difference in linear attenuation coefficient between PE and adipose tissue was smaller than the percent difference between water and glandular tissue (Fig. 8). The average percent difference in linear attenuation coefficient, across all tube potentials, for PE versus adipose tissue was $1.8 \pm 0.3\%$, $1.7 \pm 0.9\%$, and $1.3 \pm 0.3\%$ for 0.2 mm Cu, 1.5 mm Al, and 0.2 mm Sn, respectively. For water versus glandular tissue, the average percent difference was $2.7 \pm 1.6\%$, $3.9 \pm 0.8\%$, and $4.2 \pm 1.2\%$ for the three filter types.

IV. DISCUSSION

Iodine contrast enhancement is maximized at 60 kVp with 0.2 mm Cu filtration. Soft-tissue contrast and microcalcifica-

tion contrast may be optimized at 60 kVp, with 0.2 mm Cu and 1.5 mm Al filtration providing similar contrast performance.

Of the three filter types used, the copper filter produced the hardest photon spectra, followed by the aluminum filter, and the tin filter produced the softest photon spectra, largely due to its K-edge at 29.2 keV. As expected, intensity (linear attenuation coefficient) decreased as the hardness of the photon spectrum increased (increasing tube potential or filtration of low energy photons). While the CaHA had the highest intensity, it must be mentioned that microcalcification contrast is not the major challenge in microcalcification detection. It is their small size that poses a larger challenge. Future studies must be directed toward improving the spatial resolution of bCT and minimizing blur from patient or gantry motion that confounds microcalcification detection, issues that are not the focus of this study.

Since dose was not held constant (varying mA) among image acquisitions, direct comparisons of noise levels among photon spectra are difficult to make. It was necessary to vary dose in order to maximize the x-ray tube output and thus the photon counts at the detector, particularly for low energy spectra and when using the tin filter. The power output of the x-ray tube used in this study was limited to 1000 W, but use of a more powerful tube may allow for larger photon fluence with highly filtered or very low kVp spectra. By maximizing x-ray tube output, we ensured that noise measurements were quantum limited and not limited by the inherent electronic noise of the detector. The resultant mean glandular doses calculated from the exposure levels used in this study are clinically unacceptable (11.3–27.7 mGy), but were necessary to achieve reasonable signal at low x-ray tube potentials. When performing scans at clinically relevant doses to the breast, the use of dynamic gain detector modes may be necessary to overcome the expected dominance of electronic noise.²¹

FIG. 5. Noise. The noise (standard deviation in linear attenuation coefficient) of six ROIs was measured for each combination of x-ray tube potential and filter material/thickness. Measurements were made on subtraction images from two identical scans to remove cupping artifact and anatomical structures. Error bars represent the standard deviation for three repeated measurements from nonadjacent slices.

The primary outcome measure (CNRD) was normalized per unit dose in order to make valid comparisons across spectra. The main findings suggest that different technique factors may be ideal for each of the three most relevant viewing tasks in breast imaging (soft-tissue contrast, microcalcification contrast, and iodine contrast enhancement). Iodine contrast enhancement on bCT is optimized using 0.2 mm Cu filtration and a tube potential of 60 kVp, with 0.2 mm Cu

FIG. 6. Dose-normalized contrast to noise ratio. Signal difference (contrast) to noise ratio was normalized per unit dose for pairs of ROIs. Error bars represent the standard deviation for three repeated measurements from nonadjacent slices.

filtration providing significantly greater “iodine contrast enhancement” than 1.5 mm Al filtration ($p=0.01$). Microcalcification contrast and native soft-tissue contrast were maximized at 60 kVp and were similar using the 0.2 mm Cu filter and 1.5 mm Al filter, but were significantly lower using the 0.2 mm Sn filter ($p \leq 0.014$). With recent studies suggesting that CE-bCT is more effective at lesion visualization than unenhanced bCT,⁸ it may be optimal to perform a single CE-bCT scan on a system tuned for iodine based imaging (60 kVp, 0.2 mm Cu).

Other limitations to this study pertain to the use of cadaveric breast specimens. The effect of embalming on the linear attenuation coefficients of breast tissues is unknown. Further-

FIG. 7. Tissue surrogate linear attenuation coefficient. Linear attenuation coefficients were measured as a function of x-ray tube potential and filter material/thickness for adipose tissue, glandular tissue and their surrogates, polyethylene, and water, respectively. Shaded regions represent the difference in linear attenuation coefficient for adipose tissue versus polyethylene and glandular tissue versus water.

more, during embalming, the cadaveric specimen was cleared of all blood plasma, red blood cells, and the iron-rich ($Z_{Fe}=26$) hemoglobin within. The soft-tissue contrast measured in this study, using cadaveric breast tissue, likely underestimates the soft-tissue contrast that would be expected from *in vivo* measurements of fully perfused glandular tissue. Lastly, dose calculations were made assuming a glandular fraction of 50%, but the glandularity of the specimen was

FIG. 8. Tissue surrogate accuracy. Percent difference in linear attenuation coefficient for adipose tissue versus polyethylene and glandular tissue versus water across each combination of technique factors. Error bars represent the standard deviation for three repeated measurements from nonadjacent slices.

closer to 0%. The resultant overestimation of mean glandular dose suggests that the CNRD measurements are underestimates; however, only the relative CNRD measurements are of importance, making this limitation minor.

Water and polyethylene were found to have energy-dependent and filter-dependent inaccuracies in linear attenuation coefficient when used as surrogates of glandular tissue

and adipose tissue, respectively. Water and polyethylene overestimate the linear attenuation coefficients of glandular tissue and adipose tissue, respectively, with 0.2 mm Cu filtration providing the least variation in linear attenuation measurement over the tested x-ray tube potentials. Polyethylene is a more accurate surrogate for adipose tissue than water is for glandular tissue. Water had up to a 5.6% difference in linear attenuation coefficient from glandular tissue. Such inaccuracies have implications on image quality and dose estimation when phantoms of these materials are used in quality assurance and tuning of imaging systems. More specifically, when assessing dose experimentally, such as when using the techniques described by Hammerstein *et al.*,²² care must be taken to recognize the inaccuracy in using these tissue equivalent materials. Several studies have reported the linear attenuation coefficients of tissue equivalent materials,²³ particularly in the context of mammography.²⁴ In this study, the large cone angle geometry and beam hardening may have impacted the absolute accuracy of the linear attenuation coefficients reported; however, our findings suggest that water and polyethylene have relatively higher linear attenuation coefficients than glandular tissue and adipose tissue, respectively, which may lead to overestimation of dose deposition when these materials are used as tissue surrogates in dosimetry phantoms. The results presented in this study may serve as initial guidance, or even as correction factors, for more accurate phantom-based dosimetry, particularly in dedicated breast CT.

V. CONCLUSIONS

In conclusion, bCT technique factors, specifically x-ray tube potential and filtration material/thickness, were varied in order to identify the optimal photon spectra for maximum soft-tissue contrast, microcalcification contrast, and iodine contrast enhancement. Iodine contrast enhancement is maximized at 60 kVp with 0.2 mm Cu filtration. Soft-tissue contrast and microcalcification contrast may be optimized at 60 kVp, with 0.2 mm Cu and 1.5 mm Al filtration providing similar contrast performance. The use of tin filtration produced suboptimal contrast in all cases and is to be avoided, given the current hardware constraints.

The linear attenuation coefficients of water and polyethylene were measured across all combinations of technique factors and compared to glandular tissue and adipose tissue, respectively. For all technique factors, the tissue surrogates had higher linear attenuation coefficients than their true corresponding tissue. These differences have implications on mean glandular dose and image quality when using phantoms for dosimetry and quality assurance.

The results from this study suggest that CE-bCT can be optimized by selecting the appropriate technique factors. The resulting improvement in the contrast of enhancing lesions may lead to better lesion conspicuity and thus, improved lesion detection. Future large scale studies of CE-bCT, using the optimal technique factors proposed in this study, are needed to establish the sensitivity and specificity of this modality in breast cancer detection.

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