Breast composition measurement with a cadmium-zinc-telluride based spectral computed tomography system

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Purpose: To investigate the feasibility of breast tissue composition in terms of water, lipid, and protein with a cadmium-zinc-telluride (CZT) based computed tomography (CT) system to help better characterize suspicious lesions.

Methods: Simulations and experimental studies were performed using a spectral CT system equipped with a CZT-based photon-counting detector with energy resolution. Simulations of the figure-of-merit (FOM), the signal-to-noise ratio (SNR) of the dual energy image with respect to the square root of mean glandular dose (MGD), were performed to find the optimal configuration of the experimental acquisition parameters. A calibration phantom 3.175 cm in diameter was constructed from polyoxymethylene plastic with cylindrical holes that were filled with water and oil. Similarly, sized samples of pure adipose and pure lean bovine tissues were used for the three-material decomposition. Tissue composition results computed from the images were compared to the chemical analysis data of the tissue samples.

Results: The beam energy was selected to be 100 kVp with a splitting energy of 40 keV. The tissue samples were successfully decomposed into water, lipid, and protein contents. The RMS error of the volumetric percentage for the three-material decomposition, as compared to data from the chemical analysis, was estimated to be approximately 5.7%.

Conclusions: The results of this study suggest that the CZT-based photon-counting detector may be employed in the CT system to quantify the water, lipid, and protein mass densities in tissue with a relatively good agreement. © 2012 American Association of Physicists in Medicine.

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Key words: breast imaging, material decomposition, CT, photon-counting detector

I. INTRODUCTION

In recent years, owed to the rapid development of improved detector technologies as well as fast readout electronics, photon-counting detectors suitable for spectral computed tomography (CT) applications have been intensively investigated. Different from conventional x-ray detectors that generally utilize the integrated electrical charge induced by x-ray radiation, photon-counting detectors are able to count individual photons. Since the amount of charge generated by a single x-ray photon is proportional to the photon energy, energy-resolved information can be obtained by means of selecting multiple energy thresholds. A proper selection of the background threshold can effectively reject the electronic noise, which cannot be easily removed from charge integrating detectors. In place of using a suboptimal energy-proportional weighting function, optimal weighting can be achieved for a photon-counting detector with its energy resolving ability to significantly improve the contrast-to-noise ratio of an image.^{1–8} More importantly, the energy resolving ability allows data acquisition to occur simultaneously for different energy ranges without potential spectral overlap, resulting in more efficient quantitative identification and material decomposition for spectral CT applications.

Currently, the most advanced photon-counting detectors are generally based on semiconductors, such as Si strips,^{9–11}

cadmium telluride (CdTe),^{12–19} and cadmium-zinc-telluride (CZT)^{1,2,20–27} crystals. To date, photon-counting mammography system using a Si strip detector with high quantum detection efficiency has already been used in the clinic.^{28,29} The feasibility to employ Si strip detector in a CT system, where photons of higher energy are involved, has also been studied.³⁰ At the same time, CdTe and CZT based detectors have exhibited promising potentials in detecting high energy photons; owing this to their excellent x-ray absorption efficiency, high energy and spatial resolution, and great stability at room temperature. Both theoretical and experimental investigations have been conducted by a number of groups,^{2,6,23,26,31–34} whose works reveal a promising future for CdTe and CZT-based photon-counting detectors. However, there are limitations such as low count rates,¹⁷ intensity-dependent artifacts induced by the pulse pile-up effect,³³ and limited energy resolution as a result of charge sharing.³⁴ In spite of these issues, CdTe and CZT-based photon-counting detectors can be competitive in some specific clinical applications, such as dedicated breast CT, where the composition of the sample is mainly dominated by low attenuating and relatively uniform tissue materials.²

One potential application for CZT-based photon-counting detectors in dedicated breast CT is material identification, which may provide additional information for evaluating

breast cancer risk. Currently, mammographic breast density, which is defined as the percentage of glandular tissue in the whole breast,³⁵ is the most commonly used parameter. A new approach was recently reported that proposed to extend the two-material segmentation of glandular and adipose tissues into a three-material compositional measurement of water, lipid, and protein contents for the entire breast using dual energy mammography.³⁶ The three-compartment model would allow lesions to be characterized according to their composition. A recent report suggests that, besides irregular mass shape, spiculated mass margin and patient age, high mass density (i.e., mammographic attenuation) increases the likelihood of malignancy.³⁷ Radiologists should consider a mass's mammographic attenuation as a valuable descriptor that can stratify risk. However, the authors also point out that by itself, the mammographic attenuation is not sufficiently accurate to avert the need for a biopsy. On the other hand, if a mass's quantitative composition could be obtained with dedicated breast CT measurements, the predictive capability might be improved. Since most cancers originate from the fibroglandular tissue, where most of the protein masses can be found, measurement of the protein fraction or "signature" would help to better categorize a suspicious finding as either malignant or benign.³⁶ It has also been reported that malignant tissues have a significantly higher water fraction compared to normal tissues.^{38,39} Additionally, lipid content can be used to identify certain benign lesions.⁴⁰ These reports indicate that sensitivity and specificity may be improved if the signals from water, lipid, and protein can be isolated to better characterize a lesion according to its composition. At the same time, reports have also suggested that water content of tissue can be affected by pathology.⁴¹ Mapping the water fraction in tissue may provide additional information during tumor progression and response. In order to achieve the goal of three-material decomposition in dual energy imaging, additional constraints have to be applied; in this case, it is the total thickness under each pixel.⁴² The approach proved to be successful in phantom studies with fixed thickness; however, it may meet significant challenges in clinical mammograms because an accurate estimate of breast thickness in mammography imaging is substantially difficult. Such difficulties can be eliminated with spectral CT where voxels of known sizes serve as additional constraints for the three-material decomposition. Thus, it is interesting to investigate the feasibility of breast composition measurement with a spectral CT system based on an energy-resolved photon-counting detector.

In this study, we used a prototype breast CT system based on a CZT detector. The energy resolving ability of the photon-counting detector could potentially improve the dose efficiency and image quality.¹ The purpose of this study was to test the feasibility of measuring *ex vivo* tissue composition, in terms of water, lipid, and protein mass densities, using data from a photon-counting CZT-based spectral CT system. With the analytical simulation mode, we determined (1) the optimal threshold needed to split the x-ray photons into low and high energy bins and (2) the proper beam energy for a CT scan. Phantom studies were carried out and

then followed by investigations of pure adipose and lean bovine tissues. Finally, in order to designate a gold standard for validation, the tissue samples were chemically decomposed into water, lipid, and protein contents under controlled laboratory conditions. Thus, the volumetric percentage of water, lipid, and protein contents obtained from spectral CT measurements can be directly compared with the results from the chemical analysis.

II. METHODS

II.A. Analytic simulation model

A previously reported analytical simulation model used for dual energy mammography studies⁴³ was modified for three-material decomposition.⁴⁴ This simulation follows the photon starting with its emission from the x-ray source, continuing on to its attenuation through the object and finally ending with its subsequent absorption in the detector. Using this information, the low and high energy attenuation coefficients were calculated for each material. Also, recorded were the detector signals and their uncertainties that resulted from statistical x-ray noise, which were then used to further calculate relevant quantities such as dual energy signal and uncertainty for the basis material (i.e., water, lipid, and protein) image.

At intervals of 1 kVp, the polyenergetic x-ray beams were stimulated from 40 to 140 kVp. Spectra were provided by the TASMIP code.⁴⁵ To be consistent with our experimental setup, the aluminum prefiltration was set at 1.0 mm to effectively remove the very low energy photons that cannot make their way to the detector while simultaneously providing a reasonably high flux for better quantum statistics, since the maximum tube current was limited by the experimental setup.

For the experiment, a composite of adipose and mammary gland tissues was used as the archetype for the breast anatomy. The stimulated breast sample was 14 cm in diameter, a value close to the average size of a breast obtained from published data.⁴⁶ The glandular percentage was set to 30%. According to the chemical composition data for adipose and mammary gland tissues from Woodard and White,⁴⁷ such percentage corresponds to the water, lipid, and protein volume fractions of 0.303, 0.611, and 0.083, respectively. The mean glandular dose (MGD) in the simulation was estimated for each kVp based on the Monte Carlo simulations obtained from previously reported data.⁴⁸

The quantum detection efficiency (QDE) of the CZT-based photon-counting detector was simulated for a 3 mm thick CZT crystal, which is what we have in our spectral CT system. No additive electronic noise was included in the simulation, due to the nature of photon-counting detectors. The splitting energy, which separates the low and high energy photons into two distinct datasets, was tested for each beam energy used in the simulation. For a given beam energy, the splitting energy varied from 22 keV, which was determined to be the noise level of our CZT detector, to the maximum energy of the spectrum in increments of 1 keV. The dose distributions between the low and high images

were thus determined by the splitting energy. For each combination of parameters tested, the dual energy signal-to-noise ratio (SNR) was calculated from the signal of lipid, as lipid accounts for the largest fraction of breast mass. We did not find significant differences if signals of water or protein were

used in the simulation. Since the signal will be normalized during the simulation, SNR is then determined by the variance of the lipid content thickness ($\sigma_{t_l}^2$), which can be represented by⁴⁴

$$\sigma_{t_l}^2 = \frac{\frac{(\overline{\mu_p(E_H)} - \overline{\mu_w(E_H)})^2}{SNR_{S_L}^2} + \frac{(\overline{\mu_p(E_L)} - \overline{\mu_w(E_L)})^2}{SNR_{S_H}^2}}{\left((\overline{\mu_p(E_L)} - \overline{\mu_w(E_L)}) (\overline{\mu_l(E_H)} - \overline{\mu_w(E_H)}) - (\overline{\mu_p(E_H)} - \overline{\mu_w(E_H)}) (\overline{\mu_l(E_L)} - \overline{\mu_w(E_L)}) \right)^2}, \quad (1)$$

where $\mu_i(E_j)$ is the energy-dependent attenuation coefficient, with the subscript i referring to water (w), lipid (l), or protein (p), and the subscript j referring to either the low (L) or high (H) energy bins, respectively. $SNR_{S_i}^2$ is the squared SNR with the subscript i referring to the low (L) or high (H) energy detector signal. Finally, a figure-of-merit (FOM), defined as the ratio between SNR of lipid and the square root of MGD, was calculated in order to optimize the dual energy SNR with respect to mean glandular dose. This definition permits an easy comparison between the image qualities of different configurations. More detailed descriptions regarding the derivation of SNR can be found in our earlier publication.⁴⁴

II.B. CZT CT system

The spectral CT system consisted of a tungsten target x-ray tube (Dynamax 78E) coupled with a Phillips Optimus M200 x-ray generator, and a CZT-based photon-counting detector (eV2500, eV Products, Saxonburg, PA) mounted onto an optical bench. A high precision motor (Kollmorgen Goldline DDR D062M, Danaher Motion, Wood Dale, IL) provided the rotational mechanism and also served as the platform upon, which the object was placed. The rotation motor was mounted on a translation stage controlled by two step motors, rendering both vertical and horizontal translations. The photon-counting detector consisted of a linear row of four CZT crystals each of 12.8 mm in length, 3 mm in height, and 3 mm in thickness. Each crystal was divided into 16 pixels, giving a total of 64 pixels with each pixel having an effective pitch of 0.8 mm. A brass collimator shaped the entrance beam to the detector, collimating the height of each pixel to 0.8 mm. To eliminate the scatter effect, fore and aft collimators were constructed out of lead sheets that were 3 mm thick. The slit widths of the fore and aft collimators were 0.3 and 0.8 mm, respectively. A simple sketch of the CZT CT system is presented in Fig. 1. The CZT detector communicated with the workstation through a USB interface. The signal integration time was 50 ms, yielding an effective frame rate of 20 fps. The energy resolving capability of the detector sorted the photons into five user-definable energy bins. The source-to-detector distance (SID) and the source-to-object distance (SOD) were 1.33 m and 0.93 m, respectively, leading to a magnification of 1.4 $\times$. The imag-

ing geometry was selected so that the field of view (FOV) is large enough to cover the calibration phantom and the tissue samples, while the spatial resolution can be maximized.

II.C. Calibration phantom and tissue sample preparation

With a polyoxymethylene plastic cylinder 3.175 cm in diameter, a calibration phantom was constructed with two holes (0.95 cm in diameter) that were subsequently filled with water and vegetable oil. The water, vegetable oil, and polyoxymethylene plastic represented water, lipid, and protein, in term of their x-ray attenuation properties, respectively. The justification for using polyoxymethylene as an equivalent for protein was reported in a previous study.³⁶

Prior to taking measurements, fresh pure lean muscle and pure fat tissue purchased from a local USDA compliant butcher were used to prepare two bovine tissue samples. Each sample was cut into regular cuboids that were approximately 3.0 $\times$ 3.0 $\times$ 2.0 cm³ in volume. The samples were stacked on top of one another and then wrapped with a thin, very low attenuation plastic film to prevent water loss. Samples were allowed to sit at room temperature for over 20 min before undergoing CT scans.

II.D. Image acquisition and processing

For all CT scans, the object was rotated at 1.0 rpm. Given that the frame rate was 20 fps, a full CT scan that covered 360 $^\circ$ of rotation yielded a total of 1229 frames. CT scans

FIG. 1. Schematic drawing of the spectral CT system based on CZT photon-counting detector.

were acquired at a beam energy of 100 kVp with a tube current of 1.00 mA. As prefiltration, a 1 mm Al foil was used. The total entrance skin air kerma (ESAK) under the current setting was estimated to be 5.8 mGy. The MGD as for a 14 cm breast of 30% glandularity is approximately 3.7 mGy according to the simulation.⁴⁸ All x-ray photons that interacted with the CZT detector were sorted into two energy bins. Preliminary tests showed that the lowest energy threshold to optimally eliminate electronic noise was 22 keV, which is used in the study as the lower threshold of the low energy bin. Another threshold of 40 keV was selected as the splitting energy between the low and high energy bins. All images were acquired with these settings. All data acquired with the CZT detector were corrected for nonuniformity across pixels, using a flat-field correction technique that was reported previously.¹ The flat-field correction was made using an open source image processing software package.⁴⁹ The projection images were then reconstructed using a filtered back-projection algorithm.

The CT images were reconstructed with a voxel size of $0.53 \times 0.53 \times 0.53$ mm³. Circular regions of interest (ROI) of identical diameters were carefully hand-delineated for each material in the calibration phantom to measure the mean values and variations of the reconstructed attenuation coefficients. To determine the size of the ROI, we completed the following tasks: (1) drew a large ROI to select the entire area containing the CT image's water region, (2) mean values were measured for the ROIs, and (3) this process was repeated while simultaneously decreasing the diameter each subsequent time until the mean values measured became constant. This can potentially help to eliminate the edge effect that results from partial volume effect. According to this method, the proper-sized ROI of water was determined to be 8 mm in diameter and contained 160 pixels; this was then designated as the standard measurement for all other materials. The mean values were further averaged over all slices for water, lipid, and protein before using it in calibrations. In the phantom decomposition, three large ROIs that each included more than one material were used. In the tissue study, 14 ROIs with the identical size were drawn at random from the lean and adipose tissue images, respectively. All ROI data were averaged to obtain the mean values of the reconstructed attenuation coefficients of pure lean and adipose tissues. Values from the individual ROIs were recorded to measure variation.

II.E. Image-based tissue composition measurement

A dual energy system of three equations and three unknowns was used to calculate the tissue compositions based on the measured linear attenuation^{36,42}

$$\begin{pmatrix} \mu_W^L & \mu_L^L & \mu_P^L \\ \mu_W^H & \mu_L^H & \mu_P^H \\ 1 & 1 & 1 \end{pmatrix} \begin{pmatrix} f_W \\ f_L \\ f_P \end{pmatrix} = \begin{pmatrix} -U^L \\ -U^H \\ 1 \end{pmatrix}, \quad (2)$$

where μ_W^L , μ_L^L , and μ_P^L are the linear attenuation coefficients of water, lipid, and protein, respectively. f_W , f_L , and f_P represented the volume fractions of water, lipid, and protein,

respectively. U^L and U^H were the measured attenuations of the images from the low and the high energy bins, respectively.

A means of linear numerical matrix inversion and least-squares fitting was used to solve for f_W , f_L , and f_P in a two-step process. Each material fraction can be represented as follows:

$$f_i = a_0 + a_1 U^L + a_2 U^H. \quad (3)$$

During the calibration process, the known fraction values (f_W , f_L , and f_P) and each respective image attenuation measurement at the low and high energies were substituted. Subsequently, the linear system of equations was solved to determine the system matrix calibration coefficients of a_0 , a_1 , and a_2 . In the decomposition process, we inputted the image attenuation measurements from the tissue samples with unknown compositions into the system to determine the image-based measurements (water, lipid, and protein contents).

II.F. Chemical analysis

Based on a standardized procedure devised by the United States Department of Agriculture, a chemical analysis was performed to measure the water, lipid, lean and mineral contents in the sample.⁵⁰ However, we did not separate the mineral ash content from the lean component in this experiment because the mineral ash's mass was assumed to be negligible. Samples were weighed before being placed into a vacuum (approximately 95 °C) for a minimum of 48 h to evaporate the water content before they were removed and reweighed. The change in mass was assumed to be purely water. Following, petroleum ether was mixed with the sample that was then grounded into slurry and agitated at 30 °C for approximately 1 h. This was performed to extract the lipid content from the tissue into the ether solvent. Sample

Fig. 2. A two axis contour plot showing the distribution of FOM values as a function of the beam energy and splitting energy. The values of FOM are normalized to the peak value, which was observed at beam energy of 103 kVp and splitting energy of 40 keV.

FIG. 3. (a) The simulated FOM as a function of splitting energy at the beam energy of 100 kVp. (b) The simulated FOM as a function of beam energy with a splitting energy at 40 keV.

was then cooled at approximately 20 °C (room temperature) for the next 24 h. After, the sample was vacuum filtered using a Buchner funnel of known weight. The residual lipid content was washed away with an additional 1 liter of pure petroleum ether. Remaining weight from reweighed sample was assumed to be purely protein mass with the lipid content assumed to be contained in the petroleum ether solution. The petroleum ether was then evaporated using heat under a vacuum distillation to isolate the lipid content and determine the lipid mass.

III. RESULTS

The contour plot of the FOM from the analytical simulation is shown as a function of beam energy and splitting energy in Fig. 2. Note that the values of FOM are normalized to the peak value. The simulation suggests that the best FOM can be found at a beam energy of 103 kVp and a splitting energy of 40 keV. The evaluation of the simulated FOM as a function of splitting energy for a given beam energy of 100 kVp is shown in Fig. 3(a). The simulated FOM peaked at the splitting energy of 40 keV. Figure 3(b) illustrates the relationship between simulated FOM and beam energy for a fixed splitting energy of 40 keV.

The x-ray spectra recorded with the CZT photon-counting detector are presented in Fig. 4. The tube voltage was set at 100 kVp, and the splitting energy of 40 keV is shown as a dashed line. The measured spectra with various fluxes, which were achieved by varying the tube current from 1.0 to 0.4

mA, are shown in Fig. 4(a) in unit of kilo-count per second per square millimeter (kcps/mm²). The k_{α} characteristic emission from the tungsten anode can be clearly identified (59.3 keV), which is in a good agreement with the expected value within an error of ± 1 keV.⁴⁵ The full width at half maximum (FWHM) of tungsten k_{α} peak was estimated to be approximately 5.5 keV. Although the overall shape of the measured spectrum agreed relatively well with what would be expected,⁴⁵ apparent spectral distortions can be easily observed. First, discernable count can be found above the tube voltage of 100 kVp, which can be attributed to the pulse pile-up artifact. Furthermore, the count in the low energy region was relatively high, which was caused primarily by the charge-sharing effect. In Fig. 4(b), the spectra with various fluxes were normalized to the maximum counts. It can be seen that the counts at the high energy region reduced for lower fluxes, due to the elimination of the pulse pile-up. However, the low energy regions of the spectra remained almost the same for various fluxes.

The CT image of the calibration phantom is shown in Fig. 5(a). Three representative ROIs were selected for material decomposition investigation using the calibration information from the same phantom. The expected volumetric fraction was estimated by an areal analysis of pixel numbers for the contents (i.e., water, lipid, and protein). The details are summarized in Table I. In Fig. 5(b), a direct comparison between image-based material decomposition and the expected values of ROI 3 in Fig. 5(a), which covered the entire calibration phantom, is presented for water, lipid, and

FIG. 4. Measured (a) and normalized (b) x-ray spectra at 100 kVp for various tube currents. The splitting energy of 40 keV is shown as the dashed lines.

FIG. 5. (a) A CT image of the calibration phantom, with three ROIs for decomposition study. (b) Water, lipid, and protein fractions in ROI3 estimated from image-based material decomposition based on CZT spectral CT measurement, in comparison with the expected values from area analysis. The RMS error of the image-based technique was found to be 2.7%.

protein contents. The combined RMS error is estimated to be 2.7%.

The results from the image-based tissue composition measurement are presented in Fig. 6. The fractions of water, lipid, and protein contents obtained from chemical decomposition were assumed to be the ground truth. The RMS error in comparison to the chemical analysis results was estimated to be 7.2% and 3.6% for adipose and lean tissues, respectively; leading to a combined RMS of 5.7% for tissue composition measurement with spectral CT technique based on CZT detector. The summary of the tissue decomposition results is also presented in Table I, which also details the errors for each individual data point in the study.

IV. DISCUSSIONS

The analytical simulation results suggested that the highest FOM could be obtained at a beam energy of 103 kVp with a splitting energy of 40 keV. However, the simulated FOM is not very sensitive to changes in beam energy after a certain threshold. The difference between the FOMs calculated at beam energies of 103 and 100 kVp is less than 0.1%. In fact, as shown in Fig. 3(b), the increase of FOM was almost saturated after 75 kVp, with only a slight reduction at high energies that can be attributed to dose penalty. Thus, the simulation suggested that there is a relatively large freedom in selecting beam energy for the CZT-based spectral CT system, rendering it possible for both micro and clinical CT applications. In order to simplify the technique without a significant FOM penalty, we chose a beam energy of 100

kVp for our experimental investigations. However, the selection of splitting energy turned out to be more critical. The optimal splitting energy for a wide range of beam energies (75–140 kVp) was estimated to be around 40 keV. A relatively narrow window where FOM is above 90% of the maximum (34–50 keV) can be estimated from Fig. 3(a). Outside that range, the FOM dropped abruptly.

The purpose of this study was to validate the feasibility of breast tissue composition in terms of water, lipid, and protein with a CZT based CT system. A very recent report⁵¹ suggested a significant association between mammographic attenuation of a mass and malignancy. Radiologists should consider high density masses as valuable descriptors that can stratify risk. Since the major contents in a breast are water and lipid, the ability to isolate water mass provides the most important and direct information about the composition of the high density masses in breast. Although this current study investigated bovine tissues instead of human breast tissues, our earlier study confirmed that the two tissues are very similar in term of water, lipid, and protein fractions.⁵² Investigations on the three-material decomposition of breast tissues are the matter of current research.

The preliminary results from this study suggested a good agreement between photon-counting-based spectral CT measurement and chemical analysis in term of water, lipid, and protein fractions. Sources of errors in the current study could have arisen for the following three reasons. First, the image-based material decomposition technique depends on a reliable measurement of the energy-dependent attenuation coefficient; therefore, it brings high requirements for the CT detectors. In spite of the attractive advantages in the spectral CT application, the CZT-based photon-counting detector is less mature than other techniques such as the flat panel detector. Issues regarding material properties and detector constructions of CZT detectors are currently under active investigations. Artifacts induced by pulse pile-up, field non-uniformity and charge sharing may lead to uncertainties in the measurement. Charge sharing may be attributed to charge diffusion, photoelectron range, and nonlocal reabsorption of the characteristic x-ray created in the detector volume. It typically results in abnormally high counts in low energy windows, as shown in Fig. 4.^{14,53} A previous report has suggested that the characteristic x-ray escape fraction is less than 20% for a pixel size of 1 mm at 120 kVp.⁵³ The presence of such effects will distort the incident spectrum. However, the normalized spectra in Fig. 4(b) suggested that

TABLE I. Summary of the water, lipid, and protein fractions derived from CZT-based spectral CT images for phantom and bovine tissues. The results from the area analysis of the phantom and the chemical analysis of the tissue were listed as the reference standard.

Studies	Water			Lipid			Protein			RMS error (%)
	Measured (%)	Known (%)	Error (%)	Measured (%)	Known (%)	Error (%)	Measured (%)	Known (%)	Error (%)	
ROI 1	55.5	50.0	5.5	−3.9	0.0	−3.9	48.3	50.0	−1.7	4.0
ROI 2	3.3	0.0	3.3	48.7	50.0	−1.3	47.9	50.0	−2.1	2.4
ROI 3	9.1	10.0	−0.9	13.7	10.0	3.7	77.3	80.0	−2.7	2.7
Lean	85.5	81.0	4.5	−3.0	1.2	−4.2	17.5	17.8	−0.3	3.6
Adipose	23.1	13.0	10.1	80.6	85.5	−4.9	−3.7	1.5	−5.2	7.2

FIG. 6. Comparison of composition fractions derived from the image-based technique with that obtained from chemical analysis for pure lean (a) and adipose (b) tissues. The RMS error was estimated to be 8.3% and 5.3% for lean and adipose tissues, respectively. Error bars represent the observed variation from different regions in the CT images.

the fraction of charge sharing does not depend on incident photon flux. Therefore, the spectral distortion induced by charge sharing can be calibrated during the phantom scan and should not contribute significantly to the decomposition error in tissue samples as long as the calibration phantom and tissue sample thicknesses are not significantly different. Nonuniformity causes ring artifacts in the reconstructed image, which increases the variance in the attenuation coefficient measurement. Different techniques for flat-field correction have been investigated, including multipoint corrections¹ and adaptive filter method.²³ In this study, we implemented a flat-field correction technique that has been reported previously to compensate for the nonuniformity across pixels.¹ Multipoint calibration was achieved by varying the photon fluence with polymethyl methacrylate (PMMA) slabs. For each flat-field image, the gain associated with each pixel is calculated with respect to the mean readout from all 64 pixels. The gains were linearly fitted in a piecewise manner for all calibration points of each pixel. During subsequent scan of the phantom and tissue samples, the gain for each pixel was used to calculate the flat-filed-corrected pixel value. It has been shown that the technique can effectively minimize the artifact induced by pixel nonuniformity.¹ One of the major challenges for a CZT detector is the pulse pile-up effect, which may significantly increase the count rate in high energy bins, as shown in Fig. 4. As a result, the attenuation coefficient measured at a high energy will be larger than it should be. The amount of increase depends on the degree of spectral distortion induced by dead time loss and pulse pile-up. Since our technique relies upon calibration, the artifact induced by pulse pile-up will be discernable when the level of pulse pile-up induced by the calibration phantom and the tissue sample differ substantially. The peaking time (τ) of our detector was set at 160 ns in this study. An estimation of the counting capability (I_{out}/I_{in}) can be done with

$$\frac{I_{out}}{I_{in}} = e^{-2\tau a} \quad (4)$$

where a is the count rate in unit of counts/second (cps). The count rates for the phantom and tissue samples were approximately 0.3 and 0.2×10^6 cps, respectively. The dead time

loss estimated from the above equation is about 10% and 6% for the phantom and tissue samples, respectively. Therefore, it is possible that the large relative error of protein measurement is mainly due to the effect of pulse pile-up. Simulation studies have been used to provide better understanding of the mechanism for pulse pile-up.³³ Development of the fast readout electronics can also reduce dead time and pulse pile-up effect, which may improve the accuracy of the technique.

Second, the use of polyoxymethylene plastic as a substitute for protein may introduce additional errors in material decomposition studies. Previous simulations suggested that error induced by such approach can be as high as 21%.⁵⁴ Interestingly, none of the errors we had in the current studies is comparable to that limit. One may also notice that the RMS error of phantom decomposition (2.7%) is much less than that of tissue decomposition (5.7%). This can be attributed to the fact that, in the phantom decomposition, calibration from polyoxymethylene plastic was used to measure the fraction of itself, whereas in tissue decomposition, the same calibration was used to measure protein content. Since the uncertainty from the material selection can be excluded in the phantom study, the RMS error we estimated here sets the limit of accuracy for quantitative three-material decomposition of breast tissue with the proposed technique. Finally, the MGD estimated from ESAK (Ref. 55) is expected to be 3.74 mGy for a 14 cm breast, which is about 60% of the dose from a dedicated breast CT system that is designed to match the dose of standard two view screening mammography.⁴⁶ This leaves room for further improvements in the measurement precision.

The analytical simulation was designed to estimate the optimal imaging parameters in a clinical situation. Therefore, an average breast diameter of 14 cm was used for simulation. The current results of small samples have suggested the possibility to quantify tissue composition into water, lipid, and protein contents using CT images obtained from a CZT photon-counting detector. It is thus interesting to see if this technique can be successfully applied to larger breast sizes. This study is currently under investigation in our group. Due to the difference in noise level, the imaging parameter obtained from our simulation may not be optimized to image the small samples in this study. However, this will

only result in reduced dose efficiency, which is not a major concern in a phantom study.

In conclusion, the results of this study suggest that the CZT-based photon-counting detector may be employed in the spectral CT system to quantify the water, lipid, and protein mass densities in tissue with a relatively good agreement with that obtained from chemical analysis. Therefore, the proposed technique can potentially be used in characterizing suspicious lesions by their chemical compositions.

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