Initial Experience with Dual-Energy Contrast-Enhanced Digital Breast Tomosynthesis in the Characterization of Breast Cancer

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Abstract. An assessment is ongoing of the ability of dual energy contrast-enhanced digital breast tomosynthesis (CE-DBT) to depict the morphologic and vascular characteristics of breast cancer in comparison with breast MRI and digital mammography (DM). Eight patients with newly diagnosed breast cancer were imaged with an automated dual-energy CE-DBT system. High energy/low energy image pairs of the index breast were obtained at 1 pre- and 3 post-contrast timepoints. Post-contrast images were obtained after intravenous administration of Visipaque (1 mL/kg). Anatomic images were reconstructed using filtered backprojection, and contrast-enhanced images were generated using simple backprojection followed by temporal or dual-energy subtraction. Dual-energy CE-DBT was able to demonstrate the index malignant lesion in 7 of 8 patients (9 of 10 lesions). Morphologic characteristics including margin detail and associated microcalcifications were qualitatively concordant with DM. Vascular characteristics were identifiable qualitatively on post-processed images in some cases, and judged to be qualitative concordant with breast MRI.

1 Introduction

On imaging, malignant breast lesions are characterized by both structural and functional features[1-4]. Currently, multimodality imaging provides complementary information that is useful in the assessment and staging of breast cancer. However, while MRI can provide vascular information about breast lesions [5-6], it has lower spatial resolution than digital mammography and microcalcifications are not directly visible on MRI. Conversely, projection digital mammography can demonstrate morphology with high spatial resolution, but is susceptible to artifacts from superimposed tissues and does not provide functional information about breast lesions.

CE-DBT can potentially integrate into one breast imaging tool many of the strengths of existing multimodality imaging while also avoiding some limitations of existing modalities. The unique combination into a single imaging modality of the ability to

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acquire functional characteristics of breast lesions together with high spatial resolution similar to digital mammography results in a potentially powerful breast imaging tool. An additional strength of CE-DBT lies in the underlying technology of digital breast tomosynthesis (DBT), which circumvents the limitations of two-dimensional projection mammography. DBT is an emerging x-ray based breast imaging technique in which high resolution tomographic images of the breast are obtained at a dose comparable to projection mammography [11, 12]. In clinical trials, DBT provides improved sensitivity and specificity relative to projection mammography[12].

Thus, the purpose of this study was to assess the ability of dual-energy CE-DBT to demonstrate morphologic and vascular characteristics of breast cancer in comparison with breast MRI and digital mammography. Our hypothesis is that these features of breast cancers will be demonstrable on CE-DBT images.

2 Methods

2.1 Acquisition Protocol

This prospective research study received IRB approval and is HIPAA compliant. After informed consent was obtained, 8 patients (age range 48 – 68 years) with newly diagnosed breast cancer were imaged with an automated dual-energy CE-DBT system (Hologic, Bedford MA). High energy/Low energy image pairs of the index breast were obtained at 1 pre and 3 post-contrast timepoints. Dynamic post-contrast images were obtained after intravenous administration of Visipaque (1 mL/kg) using a power injector (2-3 ml/sec). Images were reconstructed using backprojection (Figure 1). Subtraction images were generated and reviewed (dual energy and temporal). In this preliminary study, no motion correction processing was applied. Qualitative comparison with breast MRI and DM in each case was performed.

DM: DM was obtained as part of the standard clinical workup, prior to diagnosis.

MRI: The breast MRI was performed either before or after the CE-DBT exam (6 on the same day, 1 the day after MRI, and one 12 days after MRI.) MRI was performed with the patient prone in a 1.5-T scanner (Siemens) with a dedicated surface breast coil array. For contrast imaging, a rapid bolus injection of 0.1 mmol/kg gadobenate dimeglumine (MulitHance, Bracco Diagnostics Inc, Princeton, NJ) followed by a saline flush was administered (via peripheral intravenous access). The clinical breast MRI protocol includes the following series: pre-contrast T1-weighted, pre-contrast T2-weighted fat suppressed, pre-contrast T1-weighted fat suppressed, dynamic post-contrast T1-weighted fat suppressed (3 timepoints, 90 second intervals), delayed axial T1-weighted fat suppressed. Sagittal subtraction images are generated.

CE-DBT: Each patient underwent unilateral CE-DBT using the Hologic Selenia Dimensions CE-DBT prototype system (Table 1). Patients were seated for the duration of the exam. Initial pre-contrast DBT high and low energy pair in the MLO projection (or optimal projection for visualization of the index lesion) was obtained (7 MLO, 1 XCCL). The low energy series was used as an unenhanced anatomic

baseline for tomographic assessment of microcalcifications and margin analysis. The high energy series was used as the tomographic mask for temporal subtraction. The breast remained in this compression for the remainder of the study. Then, a contrast injection of 1ml/kg iodixanol (Visipaque-320,GE Healthcare Inc., Princeton, NJ) was made(via peripheral intravenous access) using a power injector followed by a saline flush. Three post-contrast high energy/low energy (HE/LE) image sets were obtained (20 seconds, 1 minute 25 seconds, and 3 minutes 25 seconds after injection commencement.) The timing of the post-injection CE-DBT images is based on prior work for breast MRI with multiple post-contrast time points [10]. The breast with the index lesion was then decompressed. Our current technique results in a mean glandular dose of approximately 3.0 mGy per HE/LE image set for a 4.5 cm breast. Current total procedure time is less than 8 minutes.

Table 1. Hologic Prototype CE-DBT system

Target	W
kVp	49 (HE) / 32 (LE)
Filter	Cu (HE) / Al (LE)
SID	70 cm
Detector	3 fps, 2x2 binning
Angular Range	15°
Scan Time	7.3 seconds
Projections	22, 11(HE), 11(LE) interleaved

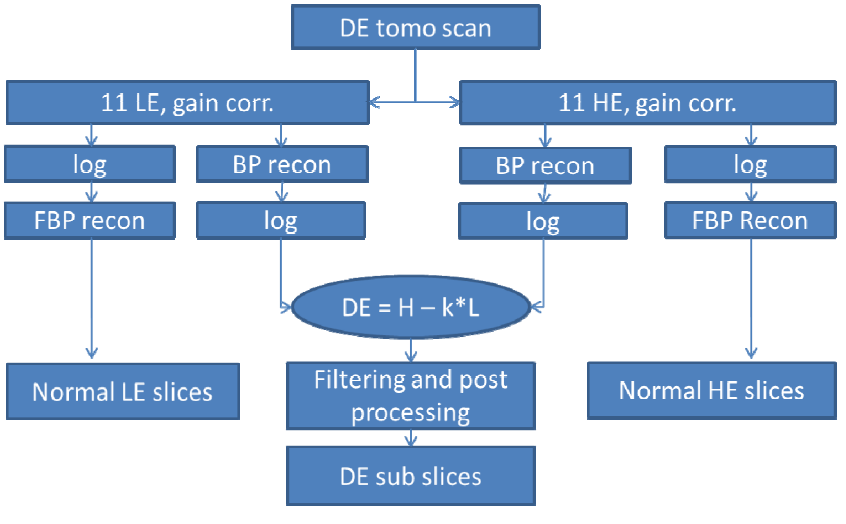

Fig. 1. Dual Energy Processing. FBP = Filtered Back Projection, BP = Back Projection. Source DE tomosynthesis images were post processed per this schematic to create the images for clinical interpretation.

2.2 Image Interpretation

Images were reviewed by a fellowship-trained breast imager. The size of the index lesion (at least the greatest linear dimension) was measured. Findings regarding the margins of the index lesion were recorded using descriptors in the ACR BIRADS lexicon. Vascular enhancement kinetics were assessed and characterized as Persistent, Plateau, or Washout for the index lesion (as per the BI-RADS lexicon[1]).

Ratings on a 10-point scale (10 = best, equivalent to DM) of the conspicuity of margins on CE-DBT relative to DM and on MRI relative to DM were recorded. Similarly, the visibility of any associated microcalcifications on CE-DBT and MRI were separately evaluated relative to DM and recorded.

3 Results

Dual-energy CE-DBT was able to demonstrate the index malignant lesion in 7 of 8 patients (9 of 10 lesions). The one lesion in one patient that was not demonstrated was secondary to a far posterior location of the tumor, which was not an area that could be imaged mammographically (the finding had been detected on physical exam and evaluated with ultrasound).

Morphologic characteristics including margin detail were visualized on CE-DBT. Presence of associated microcalcifications were visualized on CE-DBT processed images in 4/4 lesions with associated microcalcifications. Benign microcalcifications away from the index lesion were visualized and characterized as benign on tomosynthesis images in 1 case. Qualitative concordance with digital mammography was judged to be achieved. Vascular characteristics were identifiable qualitatively on post-processed dual energy subtraction images in 4 cases. Qualitative concordance with breast MRI was judged to be achieved in those cases. (Table 2) (Figures 2 and 3)

4 Discussion

CE-DBT can potentially integrate into one breast imaging tool many of the strengths of existing multimodality imaging while also avoiding some limitations of existing modalities. The unique combination into a single imaging modality of the ability to acquire functional characteristics of breast lesions together with high spatial resolution similar to digital mammography results in a potentially powerful breast imaging tool. An additional strength of CE-DBT lies in the underlying technology of digital breast tomosynthesis (DBT), which circumvents the limitations of two-dimensional projection mammography. DBT is an emerging x-ray based breast imaging technique in which high resolution tomographic images of the breast are obtained at a dose comparable to projection mammography [11, 12]. In clinical trials, DBT provides improved sensitivity and specificity relative to projection mammography[12].

Table 2. Case Summary. For numerical scales, 10 = best, equivalent to DM

Case	*Lesion*	*Size (mm) ML, SI, AP if available*		*Margins*		*Enhancement Kinetics (if available)*		*Margin conspicuity relative to DM*		*Microcalcification conspicuity relative to DM*	
		CE-DBT	MRI	CE-DBT	MRI	CE-DBT	MRI	CEDBT	MRI	CE-DBT	MRI
1		9 x 5 x 6	14 (AP)	Indistinct, irregular	Irregular	Persistent	Persistent	7	6	-	-
2		24 (SI) x 59 (AP)	50 (AP)	Segmental non-mass like	Segmental non-mass like	Persistent	Persistent	-	-	9	1
3		15 (SI) x 13 (AP)		Spiculated	Spiculated	Not seen	Present, No descriptor reported	10	8	9 (benign)	1
4		Not seen, too far posterior	13 (SI)x 15 (AP)	-	Irregular	Not seen	Present, No descriptor reported	-	7	-	-
5	1	6 x 12	9	Linear	Linear	Not seen	Present, No descriptor reported	-	-	8	1
	2	6 x 13	10	Indistinct, irregular	Irregular, associated non-mass like	Not seen	Avid	10	10	8	1
6		24 x 21	25 AP (index)	Spiculated	Spiculated, associated non-mass like	Rapid, persistent	Rapid, persistent	10	8	-	-
7	1	8 x 27	88 x 38 both findings	Calcifications	N/A	Not seen	Present, No descriptor reported	-	-	10	1
	2	9 x 14		Irregular	-	Not seen	Present, No descriptor reported	10	8	-	-
8		20 x 31	23 x 25	Spiculated	Irregular	Rapid washout	Rapid	10	7	-	-

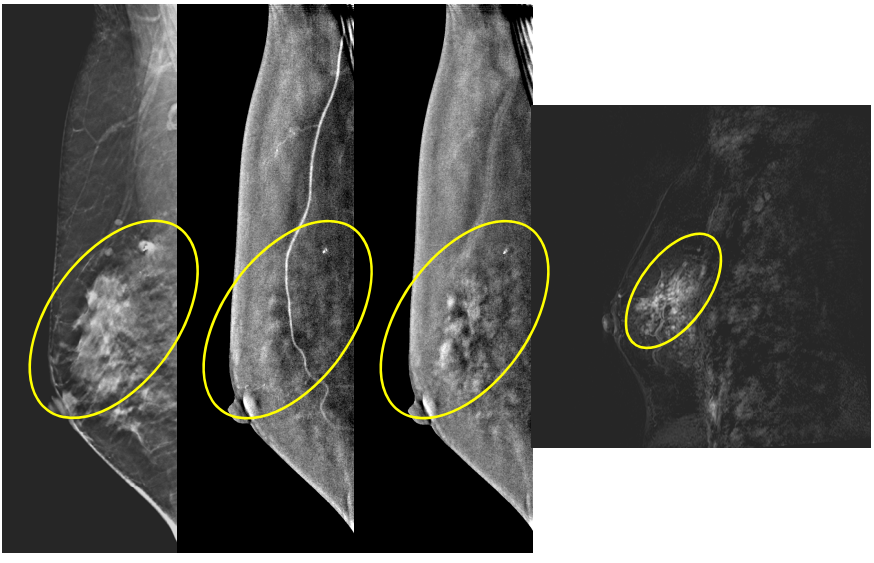

Fig. 2. DCIS. Segmental clumped enhancement in the upper breast. From left to right: Pre-contrast low energy DBT, Post-contrast DE subtraction at 20 s, Post-contrast DE subtraction at 3 m 25 s, and subtraction image from breast MRI at 3 min. Clip at site of prior biopsy.

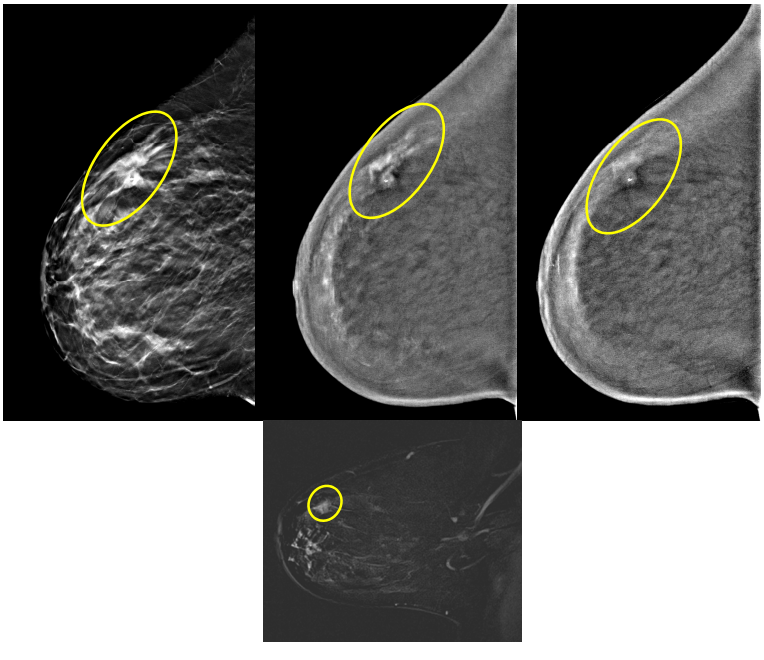

Fig. 3. Invasive ductal carcinoma. Irregular enhancing mass in the upper breast, with washout kinetics. From left to right: Pre-contrast low energy DBT, Post-contrast DE subtraction at 20 s, Post-contrast DE subtraction at 3 m 25 s, and (bottom) subtraction MRI at 3 min.

Early preliminary studies[7] have demonstrated that CE-DBT using an iodinated vascular contrast agent has the potential to demonstrate morphology and vascular enhancement information of malignant breast lesions concordant with that of MRI. A temporal subtraction CE-DBT technique was performed in 13 patients, where one pre- and one or more post-contrast tomosynthesis time-points are acquired using a spectrum beyond the K-edge of iodine (32.3 keV). Logarithmic subtraction yields iodine-enhanced images. In this early pilot group, 11 of 13 patients had malignancy [6 invasive ductal carcinoma; 4 DCIS; and 1 invasive lobular carcinoma]. Suspicious enhancing lesions were demonstrated in 10 of 11 cases of pathology proven breast cancer using this temporal subtraction CE-DBT technique. Also, when present, spiculated margins were more conspicuous on CE-DBT than on breast MRI. Furthermore, one case of breast cancer was initially detected by CE-DBT, and was only demonstrated on MRI on repeat imaging.

Additional early investigations into a dual-energy technique for CE-DBT have been performed[8]. At each time point, iodine-enhanced images are calculated by weighted logarithmic subtraction of the low-energy and high-energy (LE and HE) images[9, 10, 13, 14]. In a pilot study of one patient[8] with a known malignancy, a combined temporal and dual-energy CEDBT technique was performed with a total mean glandular radiation dose within prescribed limits for x-ray breast imaging (6.48mSv for this patient with a breast thickness of 5 cm in compression). In addition to providing morphologic and vascular information about the malignant lesion, dual energy CE-DBT also appeared more resilient to motion artifacts when compared with temporal subtraction CE-DBT in this one case.

Thus, the purpose of the current study was to assess more fully the ability of dual-energy CE-DBT to demonstrate morphologic and vascular characteristics of breast cancer in comparison with breast MRI and digital mammography. Our hypothesis that these features of breast cancers will be demonstrable on CE-DBT images is supported by the qualitative results obtained to date.

One of the technical factors that may have led to nonvisualization of the index lesion is the location of the finding. In one case, the finding was far posterior and could not be visualized on mammographic techniques, as the region could not be included in the image. This is not a limitation that is unique to tomosynthesis or CE-DBT.

Another factor that may have influenced contrast agent uptake is that in this current series, the breast remained in compression for the injection in order to allow for temporal subtraction of the pre image from the post images. This compression force may have impeded vascular flow through the breast and to the lesion. This factor is under consideration as further studies are planned. Thus, future work would include optimizing the compression force used (if any) during contrast injection.

In addition, visualization of uptake may be affected by the timing of image acquisition post-contrast. Either imaging too early or too late could affect this. Future work also includes optimizing the image acquisition timing post contrast injection.

If there were associated microcalcifications, these findings were very well demonstrated on the CE-DBT study. In future work, if vascular enhancement visualization can be optimized, then this would facilitate correlation of any visualized enhancement with the calcifications.

5 Significance and Future Directions

The results from this pilot study support the hypothesis that CE-DBT can demonstrate both high-resolution morphologic features of breast cancers (including microcalcifications) and vascular characteristics that are qualitatively concordant with DM and breast MRI. Additional reader studies are planned. Furthermore, CE-DBT may also theoretically offer quantitative evaluation of contrast uptake and perfusion given the linear relationship between attenuation and contrast-agent concentration. Additional work in this exciting direction is also planned.

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