Temporal Subtraction Versus Dual-Energy Contrast-Enhanced Digital Breast Tomosynthesis: A Pilot Study

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Abstract. In contrast-enhanced DBT (CE-DBT), breast lesion vascularity is characterized by administrating an iodinated vascular contrast agent. In this work, a combined temporal and dual-energy (DE) subtraction CE-DBT technique was performed in 4 women with mammographic findings that warranted biopsy. Lesion enhancement characteristics and morphology obtained with both CE-DBT techniques are correlated to lesion enhancement characteristics and morphology obtained with CE-MRI. The findings are compared to the clinical outcome of the regular DBT exam. Preliminary results show that both temporal and DE CE-DBT provide morphologic and qualitative vascular information concordant with CE-MRI. Temporal subtraction is the most sensitive method since background breast tissue can be completely canceled while with DE CE-DBT tissue background can only be partially canceled. However, the temporal CE-DBT image data suffer from significantly more motion artifacts and therefore possible misdiagnosis.

Keywords: Contrast-Enhanced Digital Breast Tomosynthesis, Dual Energy Subtraction, Temporal Subtraction, vascular contrast agent.

1 Introduction

Breast tumor growth and metastasis are accompanied by the development of new blood vessels that have abnormally increased permeability [1]. As a result, the absorption of vascular contrast agents is often different in cancerous breast tissue than in benign and normal tissues. Today, MRI using gadolinium as a vascular contrast agent is the standard for providing tomographical functional images of breast tumor vasculature. Preliminary studies have demonstrated that contrast-enhanced digital breast tomosynthesis (CE-DBT) using an iodinated vascular contrast agent has the potential to rival CE-MRI [2]. The high spatial resolution of DBT results in superior depiction of breast morphology than MRI and importantly, CE-DBT is based on a technology that is fundamentally less expensive than MRI and thus has the potential to become more widely available.

Two CE-DBT techniques have been proposed: temporal and dual-energy (DE) subtraction [2-4]. In temporal subtraction, one pre- and one or more post-contrast tomosynthesis time-points are acquired using a spectrum beyond the K-edge of iodine

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(33.2 keV). Pre- and post-contrast image series are then logarithmically subtracted yielding iodine enhanced images. DE CE-DBT requires only post-contrast DBT series at two energies that closely bracket the K-edge of iodine. At each time point, iodine-enhanced images are calculated by weighted logarithmic subtraction of the low- and high-energy (LE and HE) images.

In the absence of breast motion, temporal subtraction is the more sensitive method since background breast tissue can be completely canceled while with DE CE-DBT tissue background can only be partially canceled. Any breast motion between DBT series, however, will result in registration artifacts in the subtraction images resulting in an erroneous estimate of the iodine uptake. Temporal subtraction CE-DBT has demonstrated significant breast-motion artifacts due to the extended time delay (up to 10 minutes) between pre- and post-contrast series [2]. With DE CE-DBT breast motion can be significantly reduced because the two image series at each time point can be acquired simultaneously or in rapid succession.

The objectives of this study were to compare lesion enhancement characteristics and morphology obtained with a temporal and a DE subtracted CE-DBT technique and to correlate lesion enhancement characteristics and morphology with CE-MRI. The findings were also compared with the regular DBT exam.

2 Material and Methods

Eligibility Criteria

IRB approval was obtained for a pilot project to assess the clinical feasibility of temporal and DE subtraction CE-DBT. The CE-DBT pilot study was part of a National Cancer Institute-funded grant (NIH P01 CA85484-01A2) evaluating multimodality breast imaging. Patients with BI-RADS 4 and 5 lesions scheduled for biopsy were imaged with both CE-DBT techniques and with CE-MRI. We present the findings from our four initial patients.

Imaging Protocol

Temporal and DE subtraction CE-DBT imaging were performed with a General Electric Senographe DS DBT system (GE Medical Systems, Chalfont St. Giles, U.K.) that was designed for conventional DBT. The system was modified under IRB approval to allow HE image acquisition by adding a 0.25 mm Cu filter (Alfa Aesar, Ward Hill, MA) to the x-ray beam path. The affected breast of each patient underwent CE-DBT using a single breast compression in the medio lateral oblique (MLO) view. Light to moderate compression was applied to immobilize the breast and to reduce the dose, latitude, and scatter. The patients were seated for the duration of the exam. The timing of the DBT image sequence is shown in Fig. 1. First, a pre-contrast HE DBT projection image series was acquired. After contrast agent administration, HE and LE DBT projection image series were acquired twice. The technical parameters for the HE and LE image series are specified in Table 1. The technique was optimized as a compromise between image quality, the heating and cooling limitations of the x-ray tube, the patient radiation dose and the speed of the image read-out.

Each DBT projection series consists of seven images acquired in 6.7-degree increments over a 40-degree arc and the tube motion is motorized from head to toe; between each image series there is a need to reset the x-ray tube to the original start position.

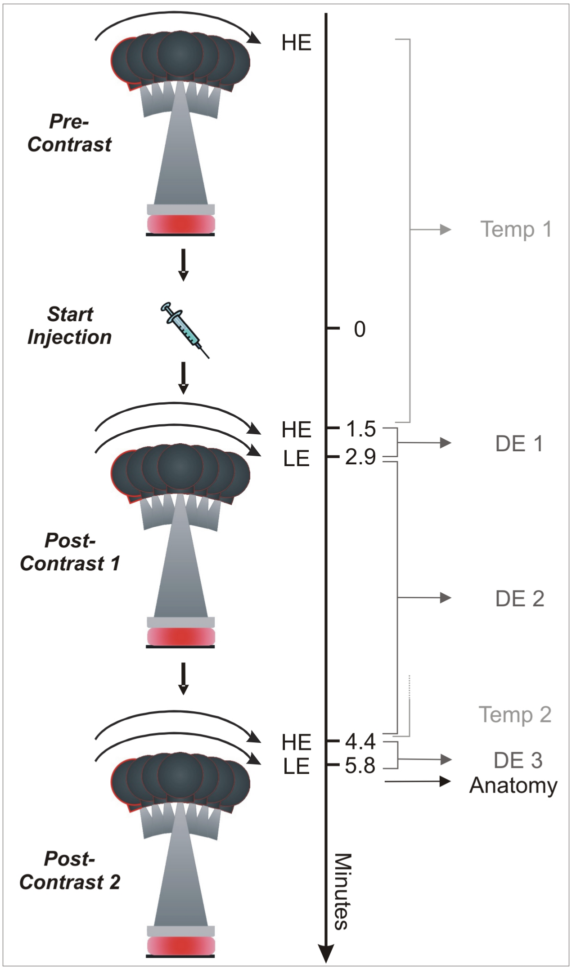

Fig. 1. Illustration of the imaging sequence and timing of acquisition. The affected breast is compressed, then a HE pre-contrast DBT image series is acquired. After injection, two HE/LE DBT image series are acquired. After image processing and tomographic reconstruction, the following image sets are available: temporal-subtraction contrast-enhanced images at 2 time points (Temp1 and Temp2); DE contrast-enhanced images at 3 time points (DE1, DE2 and DE3); and anatomic images.

The contrast agent was Visipaque-320® (320 mg I/ml iodixanol, Amersham, Princeton, NJ) with a dosage of 1.0 ml/kg bodyweight. The contrast agent injection was followed by a 60 ml saline flush. The contrast agent and saline were administrated manually at a rate of ~2 ml/second.

Typically, the total procedure time was 8 minutes. The time delay between the post-contrast series was due to the time required for the image read-out.

The total mean glandular dose (MGD) of the entire exam was 5.3 mGy for a breast of thickness 5 cm (the mean compressed breast thickness of the patients in this pilot study); this is comparable to the MGD of two conventional mammographic views. MGD were calculated using a model published by Boone [5].

Table 1. Technical parameters used to acquire the HE and LE tomosynthesis series. The MGD is specified as a function of breast thickness (indicated between round brackets).

	Target	*Filter*	*kVp*	*HVL [mm Al]*	*mAs*	MGD_{Total} *[mSv]*
HE	Rh	25 µm Rh + 0.25 mm Cu	49	3.355	160	0.60 (4 cm)
						0.58 (5 cm)
						0.57 (6 cm)
LE	Rh	25 µm Rh	30	0.440	63	2.05 (4 cm)
					71	1.76 (5 cm)
					80	1.53 (6 cm)

Image Processing

Temporal and DE subtraction iodine-enhanced images were produced from the recorded projection images; these images are corrected for detector non-uniformity. The data are linear with detector dose.

Temporal subtraction projection series were obtained at two time points (Fig. 1). At each time point a logarithmic subtraction was performed between the HE pre-contrast series and the respective post-contrast image series.

DE subtraction projection series were obtained at three time points (Fig. 1). At each time point, a weighted logarithmic subtraction was applied to the HE and LE image series. For each breast, a constant weighting factor, w_t, was applied; w_t was optimized for the region of the breast with constant compressed thickness. Optimal weights for the subtraction are obtained using the method described in [4].

Tomographic Reconstruction

Each subtracted projection image series was reconstructed using a custom filtered-backprojection algorithm. This reconstruction algorithm was also applied to the final LE image series to provide a 3D image of the breast anatomy. A 20.5×20.5×T cm^3 volume of interest was reconstructed in each instance, where T is equal to the thickness of the breast as measured by the compression device and recorded in the source image DICOM header. The images were reconstructed in planes parallel to the detector in 1-mm increments, images were reconstructed with an in-plane voxel pitch of 220 µm. Each reconstructed image series was written as DICOM CT object to the departmental PACS and a MIRC research database.

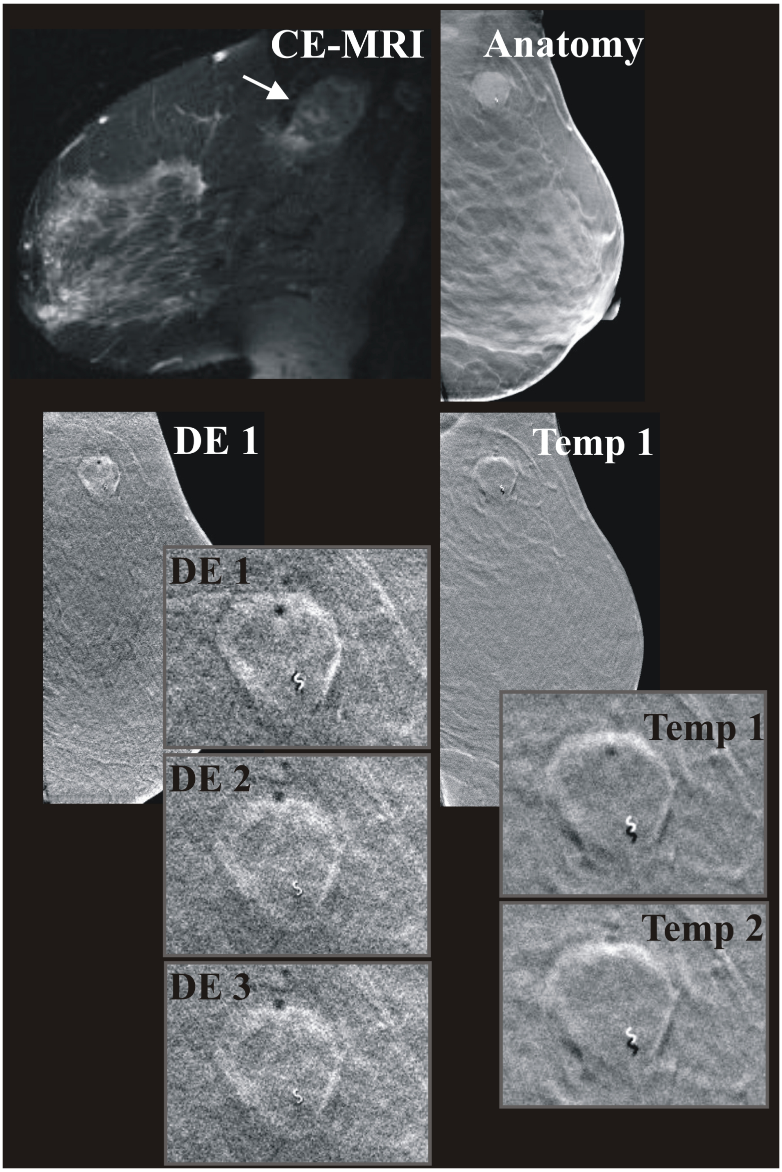

Fig. 2. CE-MRI slice, anatomy DBT slice, DE and temporal subtraction CE-DBT slices. The zoomed images highlight the lesion with DE and temporal subtraction CE-DBT at the various time points (indicated by the numbers). Highly suspicious rim enhancement is seen with CE-MRI and both CE-DBT techniques. Note however significant motion artifacts in the temporal subtracted CE-DBT slice: A clip inside the lesion shows a displacement of approximately 2 mm. All images show consistent lesion morphology but there is more detail of the internal architecture of the lesion in the dual energy images than the temporal subtraction images, again due to less motion artifacts.

MRI and Pathology Report

Prior to CE-DBT imaging the women underwent CE-MRI using previously described procedures [6]. All four patients had a tissue diagnosis established either before or after multimodality imaging, depending on the stage of patient work-up at the time of study recruitment.

Image Display

The DBT and MRI images were displayed with Efilm (V1.5.3; Merge Healthcare, Milwaukee, WI) at full resolution on two 21” 1200×1600 grayscale monitors

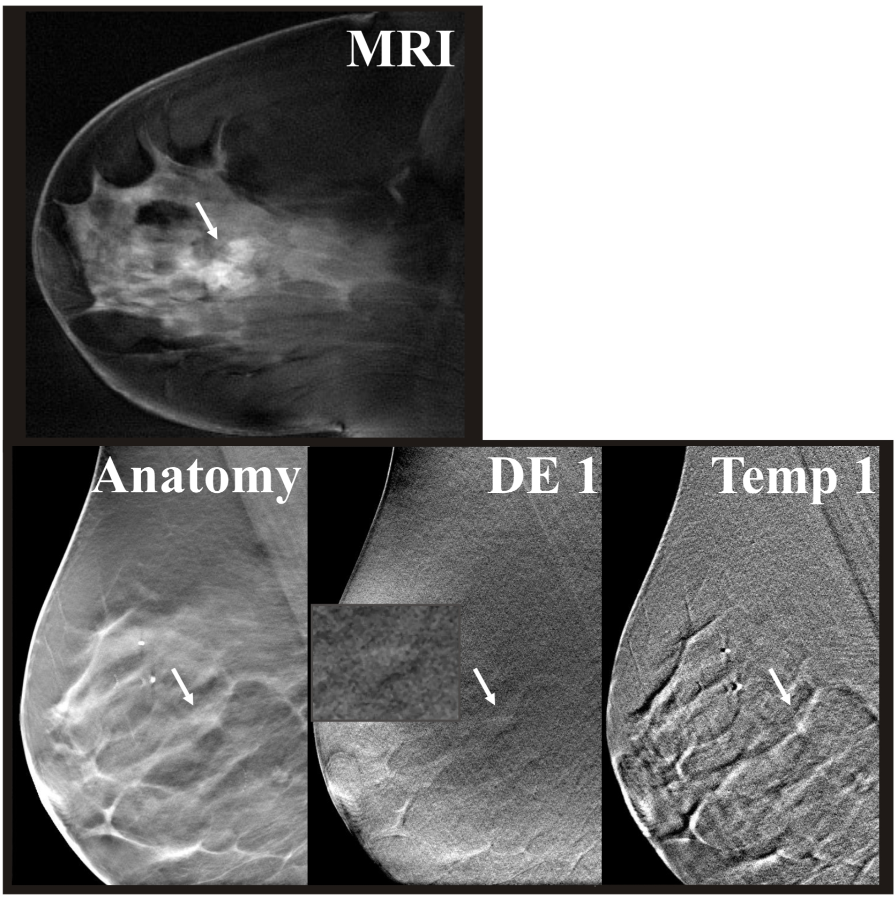

Fig. 3. CE-MRI slice, anatomy DBT slice, DE and temporal subtraction CE-DBT slices at the first time point. The patient has invasive ductal and lobular carcinoma with an extensive insitu component. There is only slight contrast agent uptake. Note however significant motion artifacts in the temporal subtracted CE-DBT slice: the iodine uptake is swamped by motion artifacts. The CE-MRI subtraction image is not shown because it did not show significant contrast enhancement.

(Siemens SMM-21125P, Karlsruhe, Germany) in stack mode. Monitor luminance was calibrated to the DICOM GSDF using the AAPM TG18 protocol (ref).

3 Results

The mean age of the four women was 53.5 years (age range, 45-57 years). Two of the four patients had pathology-proven invasive carcinomas and the other two had benign pathology results (fibroadenoma and papillomatosis). The patient shown in Fig. 2 had a 3 cm poorly differentiated invasive ductal carcinoma that had undergone an ultrasound guided core biopsy with clip placement. The biopsy clip allows a precise marker of the motion between the image series with more motion evident on the temporal series. Suspicious enhancement was demonstrated with CE-MRI and with both CE-DBT techniques. The internal enhancing architecture of the tumor is sharper on the DE CE-DBT than on the temporal CE-DBT images due to the extended time between temporal series and the resultant motion artifact. The patient shown in Fig. 3 had a 2.3 cm mixed invasive ductal and lobular carcinoma with an extensive in situ component. There are two coarse benign calcifications in the breast tissue centrally and the degree of displacement on the temporal images again demonstrates the magnitude of motion. The DE CE-DBT images show an area of slight enhancement in the superior breast that represents the malignancy. A similar enhancement pattern was observed in the CE-MRI images. The zone of enhancement is also present in the temporal subtraction images, however it is swamped by motion artifacts. The two benign cases had insignificant enhancement detected after contrast administration with CE-MRI, DE CE-DBT and temporal subtraction CE-DBT but motion artifacts were apparent.

4 Discussion

The purpose of the current study is to compare the clinical feasibility of temporal subtraction CE-DBT versus DE CE-DBT on a small number of patients. Lesion morphology and enhancement characteristics are consistent between both CE-DBT techniques and CE-MRI for all four cases. At this time, DE CE-DBT appears to be superior overall because it is less sensitive to patient motion. However, we postulate that with appropriate motion correction algorithms temporal subtraction may prove to be superior because it allows to completely cancel tissue background and because its images are less noisy. To the best of our knowledge, no such motion correction algorithms are available yet.

Acknowledgments

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