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Award Number: W81XWH-11-1-0229

TITLE: Dynamic Contrast-Enhanced Digital Breast Tomosynthesis

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REPORT DATE: March 2012

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for public release; distribution unlimited

# REPORT DOCUMENTATION PAGE

*Form Approved*
*OMB No. 0704-0188*



**1. REPORT DATE** *(DD-MM-YYYY)*
01-03-2012

**2. REPORT TYPE**
Annual

**3. DATES COVERED** *(From - To)*
1 MAR 2011 - 29 FEB 2012

**4. TITLE AND SUBTITLE**
Dynamic Contrast-Enhanced Digital Breast Tomosynthesis

**5a. CONTRACT NUMBER**

**5b. GRANT NUMBER**
W81XWH-11-1-0229

**5c. PROGRAM ELEMENT NUMBER**

**6. AUTHOR(S)**
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**5d. PROJECT NUMBER**

**5e. TASK NUMBER**

**5f. WORK UNIT NUMBER**

**7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)**
The University of Pennsylvania
Philadelphia, PA 19104

**8. PERFORMING ORGANIZATION REPORT NUMBER**

**9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)**
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

**10. SPONSOR/MONITOR'S ACRONYM(S)**

**11. SPONSOR/MONITOR'S REPORT NUMBER(S)**

**12. DISTRIBUTION / AVAILABILITY STATEMENT**
Approved for Public Release; Distribution Unlimited

**13. SUPPLEMENTARY NOTES**

**14. ABSTRACT**
Contrast-enhanced digital breast tomosynthesis (CE-DBT) is a novel x-ray imaging technique that produces a 3D representation of the breast vasculature via an intravenous contrast agent. CE-DBT offers a combination of excellent spatial resolution and accurate functional information, suggesting a strong potential role in disease prognostication. We are developing an innovative technique for obtaining dynamic contrast-enhanced (DCE) images with high spatial and temporal resolution. Our objective is to demonstrate, in proof-of-principle, that 4D DCE-DBT is technically feasible and that the derived data accurately measures vascular dynamics. Current contrast-enhanced DBT systems produces images at 2-3 fixed time points. Our proposed acquisition technique is capable of producing perfusion images at 30-60 time points for the same radiation dose. The method is compatible with both temporal and dual-energy subtraction methods. Reconstruction is performed using one full set of sequentially-acquired images; however, unlike conventional DBT, the starting angle (and hence measurement time point) is arbitrary in our method. The resulting 4D data set consists of many time-resolved 3D functional measurements of tumor perfusion, offering the potential for superior lesion characterization and hence diagnostic accuracy.

**15. SUBJECT TERMS**
Breast Cancer, contrast-enhanced imaging, digital breast tomosynthesis, dynamic imaging, x-ray imaging

| 16. SECURITY CLASSIFICATION OF: | | | 17. LIMITATION OF ABSTRACT | 18. NUMBER OF PAGES | 19a. NAME OF RESPONSIBLE PERSON |
|---|---|---|---|---|---|
| **a. REPORT** | **b. ABSTRACT** | **c. THIS PAGE** | | | USAMRMC |
| U | U | U | UU | 9 | **19b. TELEPHONE NUMBER** *(include area code)* |

**Standard Form 298 (Rev. 8-98)**
**Prescribed by ANSI Std. Z39.18**

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## Introduction

We propose a new technique for obtaining 4D dynamic contrast-enhanced (DCE) digital breast tomosynthesis (DBT) images to measure tumor perfusion with improved accuracy. Current contrast-enhanced DBT systems produces images at 2-3 fixed time points. Our proposed acquisition technique is capable of producing perfusion images at 30-60 time points for the same radiation dose. The method is compatible with both temporal and dual-energy (DE) subtraction methods. In our proposed method a single projection image is acquired, for example, once every 5 seconds. One complete tomosynthesis projection series consists of a set of projection images acquired at distinct angles. In the proposed method, several complete tomosynthesis projection series are acquired sequentially. Reconstruction is performed using one full set of sequentially-acquired images; however, unlike conventional DBT, the starting angle (and hence measurement time point) is arbitrary in our. The resulting 4D data set consists of many time-resolved 3D functional measurements of tumor perfusion, offering the potential for superior lesion characterization and hence diagnostic accuracy.

**Body**

Overview

To date, we have excellent progress on this project. We presented some aspects of this research at the RSNA Annual Meeting in Chicago in November 2011.

The primary purpose of this grant is to demonstrate that dynamic 4D DCE-DBT is technologically feasible and results in superior measurements of tumor perfusion. Two objectives were proposed: (#1) Build a DBT prototype to demonstrate, in proof-of-principle, that 4D DCE-DBT is technically feasible. (#2) Develop techniques to derive accurate measures of breast tumor perfusion dynamics. With regard to aim 1, we have nearly completed the prototype, and will soon enter the testing phase. Aim 2 is largely complete.

Aim 1: System Design and Fabrication

A conceptual diagram of the imaging method is shown in Figure 1. Rather than making three rapid acquisitions of 13 projections each, thereby giving 3 discrete time points for which to perform contrast-enhanced imaging, we acquire the same number of images (and thus use the same dose); however, each projection image is delayed from the next by a finite period of time. For example, in the example shown, a delay of 5 seconds between each projection image would result in a total acquisition time of 190 sec [5 sec * (3*13 – 1)]. Reconstructions would then be made at 27 discrete time points [2*13 + 1]. In this aim, we proposed to build a proof-of-principle prototype for both the acquisition and reconstruction systems.

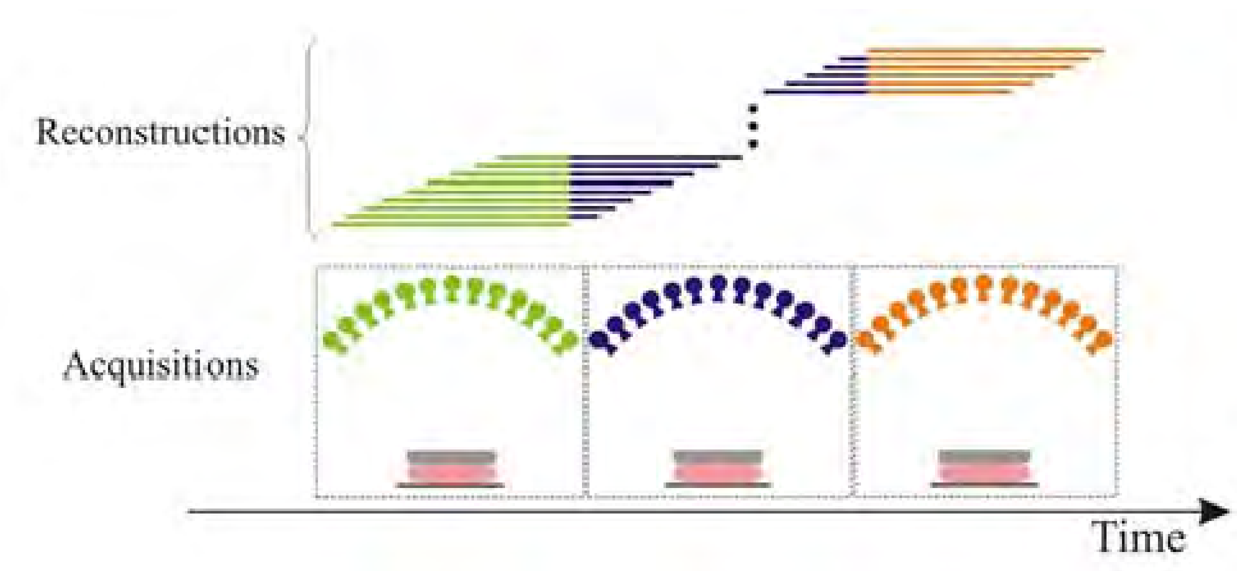



Figure 1: Illustration of the acquisition and reconstruction method

We have completed the design of the imaging system and are currently in the process of fabricating it. We have developed a computer-control interface to our existing x-ray generator. A computer controlled filter wheel has been designed and built. The filter wheel has positions for 8 filters to provide flexibility in altering the x-ray spectra. A computer-control phantoms motion stage has been assembled. The final elements of the computer software are also substantially complete. Currently, we are building our first dynamic flow phantoms and are working on the final design of our computer controlled pump and contrast agent circulation system.

We have also developed a method of preprocessing an existing reconstruction system (Piccolo, Real-time Tomography, LLC) available in our lab to enable reconstruction of the resultant images.

<u>Aim 2: Quantitation of Iodine Uptake</u>

We have had substantially more progress on Aim 2. We have developed a hybrid image subtraction method which performed temporal subtraction of the dual-energy images. This technique has several advantages, including the ability to suppress scatter and other artifacts in the dual energy images, insensitivity to motion artifacts, the ability to quantify contrast agent uptake, and good noise performance.

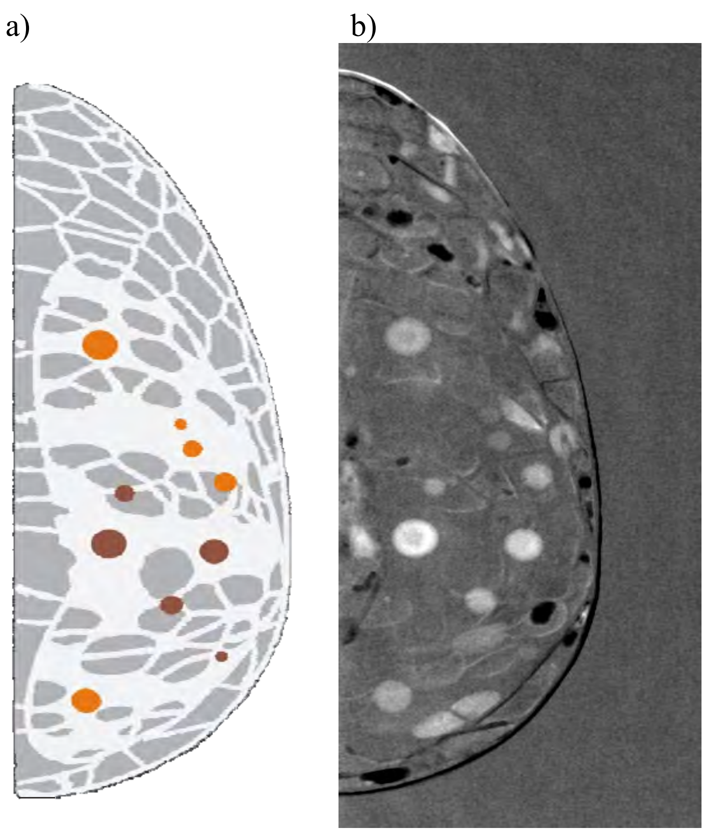


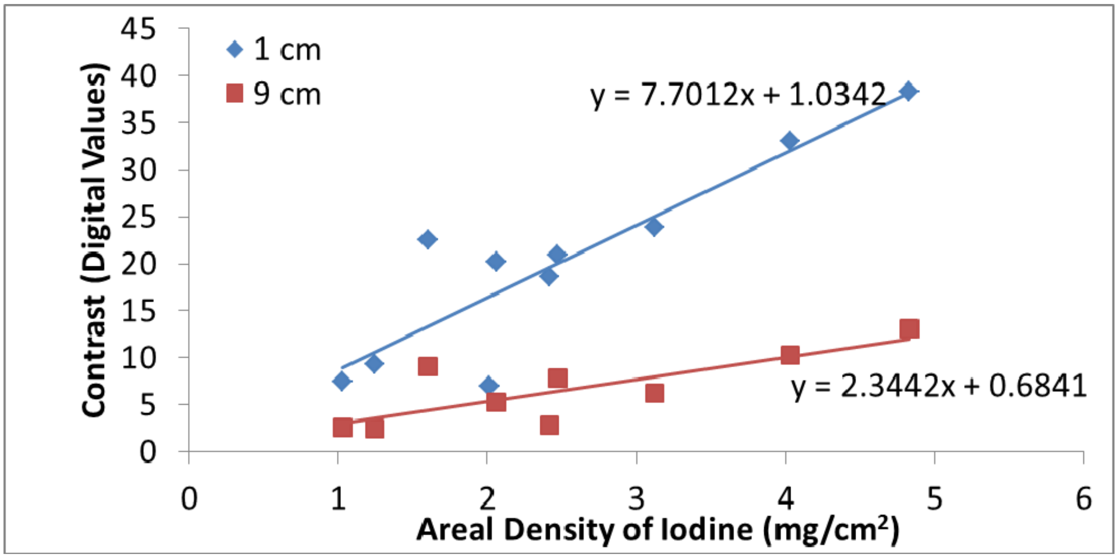

**Figure 2. (a)** A schematic diagram showing one layer of the contrast phantom. The inclusions are specified in Table 1. **(b)** A hybrid temporal dual-energy subtraction radiograph of the phantom showing the iodine inclusions.

The ability to quantify the iodine in terms of areal density is particularly important. The data, shown in Figure 2, illustrate this principle. Shown in Figure 2a is the subtracted signal as a function of the areal density of the contrast material in a static phantom already in use in the lab. The measurements are breast thickness dependent. Shown are the results for breasts 2 cm and 9 cm thick. The data for multiple thicknesses have been summarized in Fig 2b. These data allow us to quantify the uptake of tumors in absolute numbers for the first time. These results were presented at the 2011 Annual Meeting of the RSNA in Chicago in November 2011.

**Table 1:** The phantom illustrated in Figure 2 has 10 iodinated inclusions with the specified size and areal density.

| *Lesion depth [mm]* | *Lesion width [mm]* | *Areal density [mg I/cm$^2$]* | |
|---|---|---|---|
| | | 5.035 mg I/ml | 2.575 mg I/ml |
| *9.6* | 10.6 | 4.83 | 2.47 |
| *8* | 8.8 | 4.03 | 2.06 |
| *6.2* | 7.0 | 3.12 | 1.60 |
| *4.8* | 5.4 | 2.42 | 1.24 |
| *4* | 4.6 | 2.01 | 1.03 |

a)




b)

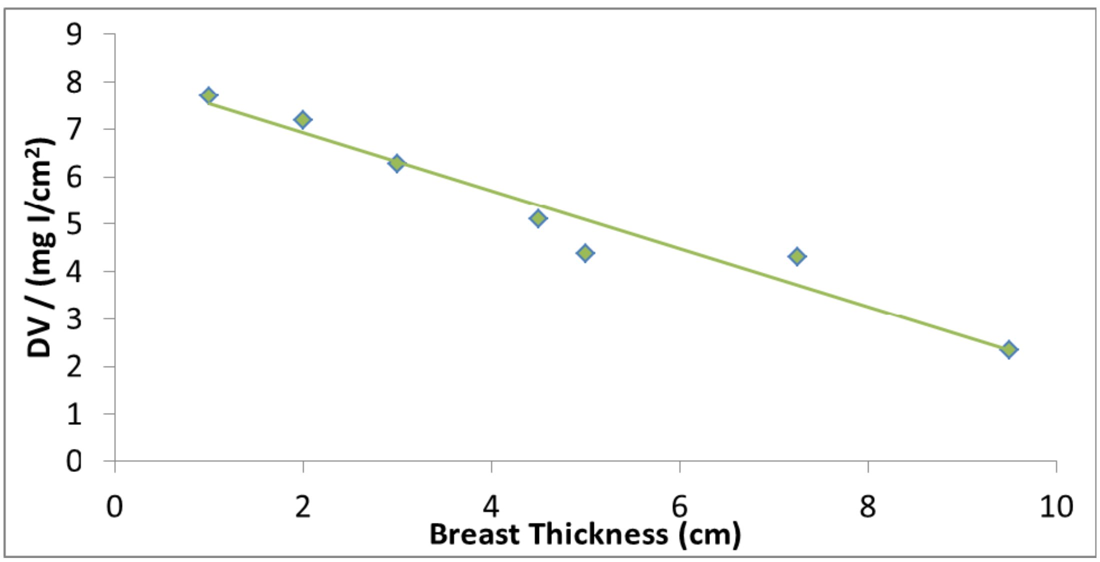



**Figure 3. (a)** Using static phantoms of different thickness, it is possible to quantify the signal as a function of areal density. Two thicknesses are shown for illustration. **(b)** The calibration coefficient (slope of lines in Fig 2a) can then be calculated for each breast thickness.

**Key Research Accomplishments**

- Designed prototype dynamic contrast enhanced imaging system intended for proof-of-principle experiments.
- Fabricated and/or assembled many key components, including main gantry, filter wheel, collimator, phantom holder and detector assembly.
- Fabricated x-ray generator interface, including dual-energy control
- In the process of writing image acquisition software, including integration of the x-ray generator, motor controllers and x-ray detector software
- Developed a method for quantitative reconstruction of contrast-enhanced images with scatter and thickness suppression.
- Performed initial experiments in quantifying the contrast agent uptake.

**Reportable Outcomes**

**Karunamuni; S C Gavenonis, MD; B Ren, PhD; C Ruth, PhD; A D Maidment, PhD**: *Technical Characterization of a Contrast-enhanced Digital Breast Tomosynthesis System*. Monday 11-28-2011 at RSNA 97th Scientific Assembly and Annual Meeting November 27-December 2 2011; Chicago, IL SSC15-06, Nov 2011.

**Conclusions**

As can be seen from the results to date, we are actively engaged in completing the various aspects of the proposed work in the grant. We will soon begin phantom experiments with the new 4D DCE-DBT prototype system. In the next year, as requested in our no-cost extension, we will be able to complete the system, characterize the system, and perform the necessary experiments to demonstrate proof-of-principle of 4D DCE-DBT. In addition, we will be able to write up these results for publication in the peer-reviewed literature, and we will seek patent protection for the acquisition, reconstruction and image processing methods. Finally, we anticipate that these data will enable us to submit a successful NIH R01 grant application.