Contrast-Enhanced Breast Tomosynthesis:
Combining the Best of Both Worlds for Better Breast-Cancer Diagnosis

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Introduction

Mammography is currently the most effective breast cancer screening technique. It has been shown by clinical studies that mammography has reduced the mortality by 30~50%. However, mammography is not a perfect technique in that about 30% of breast cancers are missed. A major limit to the sensitivity of conventional mammography is the superimposition of the breast tissue. A mammogram is a two-dimensional (2D) projection image from a three-dimensional breast volume. As a result, the various layers of the breast tissues are superimposed on each other in a single 2D image. For this reason, normal tissue may obscure more deeply buried tumors, making difficult to detect the tumor. Conversely, superimposed normal breast tissues have been known to sometimes produce "false lesions" that appear like a cancerous tumor on a mammogram. This is one reason for the unnecessary call-backs of the patient in 2D mammography. Digital breast tomosynthesis (DBT) is a technique that provides 3D structural information of the breast. By removing the superimposition of breast tissues, DBT potentially can improve the detection and diagnosis of breast cancers, as well as reducing unnecessary call-backs. The diagnostic capability of DBT may be further improved by the use of contrast agent. A contrast agent provides "functional" information of the breast lesion and its usage with 2D digital mammography is being investigated.

Digital Breast Tomosynthesis (DBT)

DBT is an exciting new development in breast imaging. It yields multiple high-resolution image slices that are located at different depth in a breast volume. As a result, it greatly reduces the problems of superimposed tissue that obscure tumors or create the illusion of cancer. Other researchers have investigated tomosynthesis for applications such as angiography, chest imaging, hand joint imaging and dental imaging. We have conducted the first clinical studies on using tomosynthesis for breast imaging. Our initial clinical studies showed compared with conventional mammography, DBT found more cancers (~16%) by removing the obscuring effects of superimposed normal tissue. It also reduced false-positive patient callbacks (85%) by eliminating "fake lesions" that appeared in mammograms caused by the superimposed normal structures projected on a 2D image.

Currently, DBT is at the research stage. A 3000-patient DBT screening study is being performed at the Massachusetts General Hospital (MGH). We believe the result will further prove the advantage of DBT. GE has obtained a license from MGH for building clinical DBT units. While
further FDA approval is still needed, there should not be any technological obstacles to the clinical use of DBT.

Figure 1. Schematic of a tomosynthesis setup for breast imaging.
Figure 2. Comparison of conventional mammography and breast tomosynthesis: potential of tomosynthesis to improve sensitivity. (A) The MLO-view mammogram of the left breast of a patient. A cancer (arrow) is obscured by superimposed breast tissues. (B) A tomosynthesis slice located 12 mm under the breast surface, which shows normal breast tissue. (C) A tomosynthesis slice located 28 mm under the breast surface that clearly shows the cancer (arrow).
Figure 3. Comparison of conventional mammography and breast tomosynthesis: potential of tomosynthesis to improve specificity. (A) Two mammogram views show a finding with ill-defined boundary (marked by arrows) in the left breast of a patient. (B) The finding is not shown in tomosynthesis slices from $Z = 10$ mm to 40 mm. The patient was called back and additional diagnostic mammograms proved that the finding in her original mammograms was caused by superimposed breast tissues.

Contrast-Enhanced Imaging

The "functional" information (i.e., the dynamics of tumor blood supply) of a lesion can be yielded by contrast agents. A contrast agent is usually required in breast MRI, which is approved by the FDA for use as a supplemental tool to mammography to help diagnose breast cancer. In the technique, patients get an injection of a gadolinium-based contrast agent that concentrates in abnormal breast tissue and lights up these regions. Although breast MR has very good sensitivity (detecting the abnormalities), its specificity (distinguishing between cancerous and non-cancerous findings) is relatively poor, which may lead to unnecessary breast biopsies. In addition, MRI is an expensive exam and takes longer time (>30 minutes) than mammography. Contrast-enhanced digital mammography is being investigated, but it is still a 2D imaging technique compromised by overlapping structures.

Combination of DBT and Contrast-Enhancement

Our goal is to combine the advantages of DBT and contrast imaging. DBT is a “3D mammography” technique while a contrast agent provides physiological information of the findings. Compared with 2D contrast-enhanced digital mammography, the superimposed enhanced breast tissue can be separated by DBT, so the morphology (shape) information of the enhanced lesion can be better characterized. Compared with breast MRI, contrast-enhanced DBT has significantly higher resolution (~0.1mm) than MRI (~1mm) because of the high spatial resolution of the digital detector used in DBT. The tumor can also be segmented from surrounding the tissue in order to measure the dynamic curve of the contrast as done in MR.

The current experiments on contrast-enhanced DBT study the capability of DBT in separating superimposed tissues that are enhanced by contrast agent, as well as the change in contrast enhancement over time. The experiments on specimens are different than in vivo imaging because contrast agent is injected and flow in interstitial spaces in the specimen, and the change in contrast enhancement in a specimen is different than that in a patient’s breast. Our result shows that DBT can separate superimposed tissues are enhanced by contrast agent and the borders of the enhanced features are much better characterized. The change in contrast enhancement over time (take-up and wash-out of the contrast agent) can also be qualitatively characterized. For in vivo imaging, some practical issues need to be studied such as breast compression, registration of pre- and post-injection images.
Figure 4B

Figure 4. An experiment in contrast-enhanced tomosynthesis was performed using a 52 mm thick mastectomy specimen. The pre-contrast and post-contrast subtraction can be easily performed since the specimen did not move during the injection. (A) The pre-contrast (left) and post-contrast (middle) projections and the subtraction image (right). (B) Pre-contrast (left column) and post-contrast (middle column) tomosynthesis slices, and the subtraction images (right column). The depths of the three slices are 15 mm (1st row), 25 mm (2nd row) and 33 mm (3rd row) respectively. Structures and spaces between tissues in the specimen are enhanced in both projection and reconstruction images, while the reconstruction images separate the enhanced tissues and spaces that are overlapped in projection images.
Figure 5. Magnified field of views (FOVs) (A) A FOV on a projection image after subtraction. (B) A FOV at the same in-plane location on a tomosynthesis slice 11 mm under the specimen surface. (C) A FOV on another tomosynthesis slice 15 mm under the specimen surface. Two features that are enhanced by the contrast agent are marked by circles in (A). The conspicuity of the features is compromised by the overlapping structures that are also enhanced by the contrast agent. The features are better perceived in tomosynthesis slices (B) and (C), with their borders clearly characterized.