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Computed Tomography for Imaging the Breast

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Abstract Despite the success of screening mammography contributing to the reduction of cancer mortality, a number of other imaging techniques are being studied for breast cancer screening. In our laboratory, a dedicated breast computed tomography (CT) system has been developed and is currently undergoing patient testing. The breast CT system is capable of scanning the breast with the woman lying prone on a tabletop, with the breast in the pendant position. A 360° scan currently requires 16.6 s, and a second scanner with a 9-second scan time is nearly operational. Extensive effort was placed on computing the radiation dose to the breast under CT geometry, and the scan parameters are selected to utilize the same radiation dose levels as two-view mammography. A total of 55 women have been scanned, ten healthy volunteers in a Phase I trial, and 45 women with a high likelihood of having breast cancer in a Phase II trial. The breast CT process leads to the production of approximately three hundred 512 × 512 images for each breast. Subjective evaluation of the breast CT images reveals excellent anatomical detail, good depiction of microcalcifications, and exquisite visualization of the soft tissue components of the tumor when contrasted against adipose tissues. The use of iodine contrast injection dramatically enhances the visualization of tumors. While a thorough scientific investigation based upon observer performance studies is in progress, initial breast CT images do appear promising and it is likely that breast CT will play some role in breast cancer imaging.

Keywords Mammography · Cancer · Computed tomography · Radiation · Technology

Abbreviations

CT	computed tomography
MTF	modulation transfer function
BIRADS	breast imaging reporting and diagnosis system

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Introduction

The introduction of mammography as a screening test for mammography has led to a significant reduction in breast cancer mortality over the past two decades [1, 2]. Recent advancements in digital mammography have recently been shown to improve breast screening sensitivity for women with dense breasts [3], and these intermediate results should lead to greater reductions in mortality over the long term. Despite the apparent success of mammography (screen film and digital), most breast imaging experts agree that there is substantial room for improvement [4, 5]. With mammography, a three-dimensional object (the breast) is imaged, which results in two nearly orthogonal projection images, the cranial caudal (CC) view and the medial lateral oblique (MLO) view. With projection mammography, especially in women with dense breasts, the shadow of a breast tumor can easily be hidden within the complicated background structure of the glandular tissues of the breast. By getting two nearly orthogonal views of the breast, the rationale is that if the breast tumor is obscured in one view, then it will be apparent in the other. However, tumors which are superimposed with glandular anatomy in both views can be missed by even the most experienced radiologist. While mammography is imperfect, it remains the most practical and cost-effective approach for breast cancer screening at the present time. However, a number of investigators are developing alternative imaging procedures for breast cancer screening.

Ultrasound imaging of the breast is performed routinely as part of the diagnostic breast examination, which occurs typically after a suspicious lesion is identified by mammography screening or when a palpable mass presents. Ultrasound imaging is very useful for soft tissue lesions (masses) and is routinely used to differentiate between soft tissue masses and cysts, which have markedly different appearances under ultrasound. There are a number of studies which seek to improve breast ultrasound imaging to make it more practical for breast cancer screening [5–11]. However, ultrasound imaging as currently practiced clinically is a time intensive procedure which requires an experienced practitioner. This requirement substantially increases the actual costs of performing ultrasound-based breast cancer screening, and thus this modality is fiscally impractical for routine breast cancer screening. Furthermore, few studies have demonstrated that ultrasound imaging by itself can match the sensitivity of mammography.

Optical imaging techniques [12–18] have been explored as potential tools for breast cancer screening. Optical approaches to breast cancer screening are appealing due to potential cost effectiveness and the lack of ionizing radiation; however, no optical technique has demonstrated detection sensitivity approaching that of X-ray mammography. Optical techniques for imaging the breast are compromised by the fact that light in the optical wavelengths scatters significantly while propagating through the breast. It is estimated that the average light photon undergoes 10,000 scattering events while propagating through a typical breast. Consequently, the spatial resolution of optical breast imaging modalities is typically quite low, and thus tumors need to be quite large to be detected. Nevertheless, significant advancements in optical imaging techniques have occurred, and a number of investigators are still pursuing this appealing concept.

Magnetic resonance imaging (MRI) has recently been demonstrated to have superior sensitivity compared to mammography in younger, high-risk women [19–27]. While MRI technology makes use of fundamentally different physical properties of breast tissue to form the image than X-ray imaging does, the appearance of X-ray CT images and MRI images are similar at least subjectively, as both are sensitive to differences in mass density. Modern MRI breast imaging makes routine use of an injected contrast agent (gadolinium GTPA). The kinetics of this contrast agent are such that it tends to accumulate near many breast cancers, due to the reduced endotheliation of vessels within the tumor.

While the demonstrated higher sensitivity of contrast-enhanced MRI over mammography is encouraging, MR is probably not a cost-effective tool for breast cancer screening in the general population. MRI is significantly more expensive, the image acquisition process takes much longer than mammography, and a small fraction (~15%) of individuals do not tolerate MRI due to claustrophobia. Nevertheless, the apparent success of contrast-enhanced MRI demonstrates the added sensitivity that can be achieved by highlighting tumors using appropriate vascular targeting methods.

The benefit that ultrasound imaging, MRI, and many optical techniques (e.g., optical coherent tomography) have over mammography is that they are tomographic: the imaging procedure produces a number of virtual slices of the breast, instead of a two-dimensional projection image of the entire three-dimensional breast. The benefit of tomographic imaging procedures is that the overlying and underlying anatomical tissue can be effectively removed when viewing individual slices, and therefore the superposition problem which detrimentally affects mammography can be overcome. Recognizing the power of tomographic methods for potentially improving breast cancer detection, a number of investigators have pursued the development of X-ray CT techniques designed specifically for imaging the breast [28–30].

Ning and colleagues at the University of Rochester have developed a cone-beam CT scanner [31–33] and have reported on the potential of this technology for breast imaging [34–37]. Glick and his colleagues at the University of Massachusetts, Worcester, have developed a prototype breast CT scanner, and have reported a number of intriguing results comparing breast CT against mammography [38, 39]. Tornai and his colleagues at Duke University are also engaged in the development of a breast CT scanner and have proposed a hybrid system capable of both computed tomography and single-photon emission computed tomography (SPECT) [40–42]. Shaw and colleagues at MD Anderson Cancer Center have also built a working prototype scanner capable of imaging cadaver and mastectomy specimens [43]. A number of other investigators [44, 45] have also become interested in the potential of breast CT. The efforts of these groups to date have been primarily oriented toward technology development; moreover, most of these groups have worked with cadaver and mastectomy specimens to produce CT images of the breast.

Predating all of these efforts, Gisvold and his colleagues at the Mayo Clinic, working with scientists at General Electric, developed a breast CT scanner in the mid 1970s

[28, 46–48]. These investigators evaluated this technology by scanning several thousand women. The conclusion from these early clinical trials on breast CT was that iodinated contrast agent injection was necessary in breast CT to match the sensitivity of the mammography of that era. It should be noted that this early breast CT scanner produced a number of thick-slice (10 mm section thickness) images of relatively low resolution (1.53 × 1.53 mm picture element dimensions), and the technology available to these early investigators was limited in comparison to today's X-ray detectors, X-ray tubes, computers, and reconstruction algorithms.

While "breast CT" or "CT mammography" refers to true computed tomography of the breast, there has been much interest academically and commercially in the potential of limited angle tomography for breast imaging, usually referred to as "tomosynthesis" [49–52]. Tomosynthesis is capable of producing thick-section images with high in-plane spatial resolution. Probably the most significant advantages of tomosynthesis is that it can be performed on existing digital mammography systems with relatively minor modifications, and the in-plane resolution is generally superior to breast CT. Thus, tomosynthesis may outperform breast CT for microcalcification detection, while breast CT will likely outperform tomosynthesis for soft tissue (mass) lesion detection. Both breast CT and tomosynthesis are tomographic X-ray techniques for breast imaging, and it remains to be seen which technology is superior overall for breast cancer detection.

Computed Tomography of the Breast

A breast CT (bCT) scanner was designed, fabricated, characterized for image quality and radiation dose performance, and is currently undergoing testing in a Phase II clinical trial at our institution. [53–56]

Design and Fabrication

The bCT system made use of several off-the-shelf components, an X-ray generator (Pantak HF160, East Haven, CT) and X-ray tube system (Comet, Flamatt, Switzerland), a flat-panel digital detector system (Paxscan 4030CB, Varian Medical Systems, Palo Alto, CA), and a computer-controlled motor with integrated angle encoder (Kollmorgan, Radford, VA). The technical specifications for some of these components are listed in Table 1. For a bCT system to scan only the breast, the pendant geometry was utilized whereby the woman lies prone on a table with the breast to be imaged placed through a hole positioned at the center of the table. The X-ray tube and detector components of the CT scanner are mounted on a rotating *gantry*, and a number of projection images are acquired as the gantry rotates around the breast (Fig. 1a). Because it is essential to image all of the woman's breast tissue in a screening examination, good image coverage towards the posterior of the breast ("chest wall") is essential. To accommodate this constraint, the X-ray source and active detector elements need to be positioned immediately below the tabletop to insure coverage of breast tissue near the chest wall (Fig. 1b).

Given these basic design constraints, the bCT system was designed at our institution and fabricated at a local machine shop. A photograph of the first bCT prototype is shown in Fig. 1c.

Image Acquisition

Because the X-ray system takes a few moments to stabilize and achieve constant radiation output, an X-ray shutter system was developed to switch the X-ray beam between the on and off positions. A thick lead shutter system was developed with two opposing solenoids which were used to open the X-ray shutter under computer control. In addition to the moveable X-ray shutter, the X-ray tube assembly includes a lead collimator which focuses all primary radiation onto the rectangular detector, positioned approximately 90 cm away. With this geometry, the X-ray detector system becomes the primary barrier for radiation protection. For additional radiation shielding, the panels which surround the bCT gantry were fabricated to include an internal layer of lead, laminated to the external aluminum support. In addition to the floor and the 4 mm thick stainless steel table, these panels provide the secondary radiation shielding to reduce the scattered radiation levels in the room during the scan.

Table 1 Characteristics of the off-the-shelf components used in the breast CT scanner.

Component	Characteristics
X-ray tube	Focal spot: Water cooled W anode, beryllium window 0.4 × 0.4 mm 640 Watt, i.e., max mA at 80 kVp: 8 mA 0.3 mm Cu added filtration kVp range: 10–110 kVp
Detector	Detector: indirect detection (Csl scintillator) thin film transistor Native pixel matrix: 2048 × 1536 Native pixel dimension: 0.194 × 0.194 mm 2 × 2 pixel binned matrix: 1024 × 768 2 × 2 pixel size: 0.388 × 0.388 mm Frame rate: 30 frames per second at 2 × 2 binning
Motor	Torque: 13 ft–lbs continuous torque Minimum rotation speed: one RPM

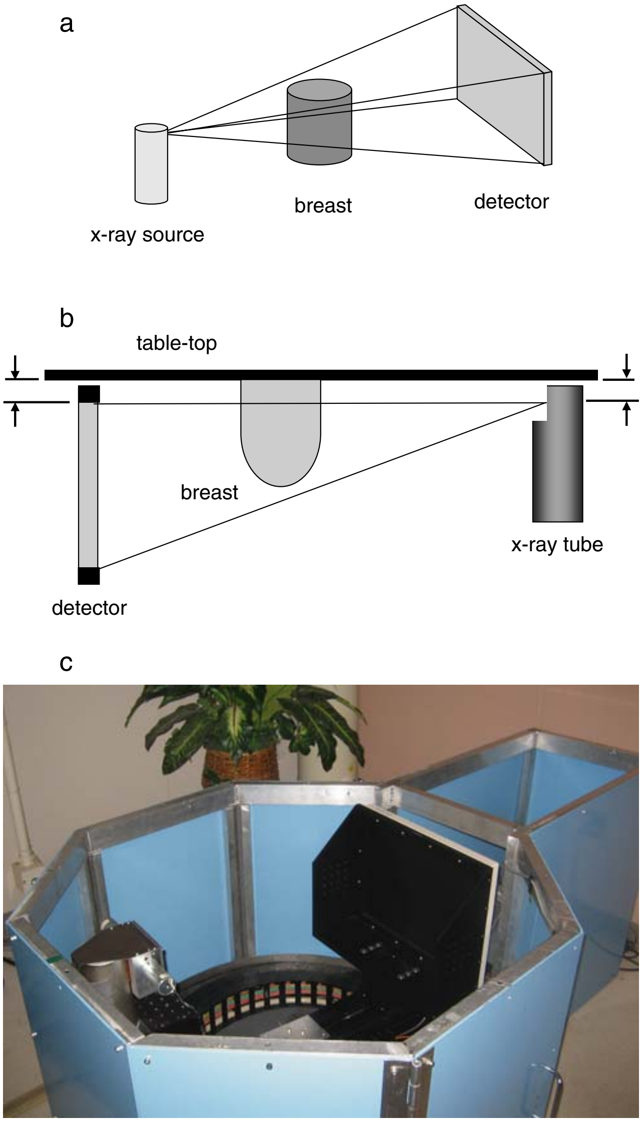

Figure 1 (a) The geometry of the X-ray source and detector of the breast CT scanner is illustrated. The large area detector results in a cone-beam geometry. The X-ray source and detector rotate on a moving gantry around the breast during acquisition. (b) This cross-section diagram illustrates the tabletop with pendant breast, and the position of the X-ray tube and detector, which must rotate freely under the table. To acquire image data as posteriorly as possible, the distances from the active detector to the bottom of the table, and from the X-ray source to the bottom of the table (shown with arrows), must be minimized. (c) An image of the breast CT scanner (first prototype) is illustrated, with the tabletop taken off. The X-ray tube and detector are mounted on a rotating, horizontal arm, and together these components comprise the rotating gantry. The spiral chain-link system which connects the stationary electronics to the rotating gantry is also seen.

The detector and the X-ray tube rotate approximately 420° around the breast during an acquisition procedure (this includes gantry acceleration and deceleration in addition to the 360° scan), and the electronics supporting these devices are mounted in the stationary laboratory frame. Consequently, a spiral chain mechanism was used to connect the stationary electronics to the rotating X-ray tube and detector subsystems. All wires, hoses, and cables connecting stationary to moving components were routed through a commercially available chain-link system, which is shown in Fig. 1c.

It was felt that 17 s was a reasonable amount of time to expect a woman to hold her breath while in the prone position for a prototype scanner. However, to reduce motion artifacts (which occur when the patient moves during the acquisition) the scan time should be reduced. To accommodate this, a second prototype breast CT scanner has been built which has an acquisition time of 9 s. It is expected that the reduction of the breast CT acquisition time from 17 to 9 s will result in far greater patient compliance and reduced motion artifacts.

A picture of a patient (model) is shown in Fig. 2 in the scanning position. It is extremely important in a breast cancer screen to image all of the breast tissue at risk. Therefore, the patient table was designed to have a 5 cm depression which spans the central region of the tabletop. This depression allows the woman's thoracic region to "slump" into the scan plane, such that the X-ray tube and detector can image up to the chest wall (pectoralis muscle). With the current tabletop design, we have achieved only marginal success in imaging up to the chest wall, with perhaps 10% of patients able to position themselves deep enough into the scanner for this. Consequently, trial and error has been required in order to study which tabletop designs are better capable of imaging the entire breast.

Radiation Dose

The radiation dose to the breast received during breast CT is of critical concern, and this technology would not be feasible if the radiation dose levels were too high. At the start of this project, the technology for computing radiation dose to the breast in the geometry of a dedicated breast CT scanner was not available. Consequently, a series of

Figure 2 A model is shown positioned on the breast CT scanner, with her right breast positioned in the pendant geometry and in the scanning position.

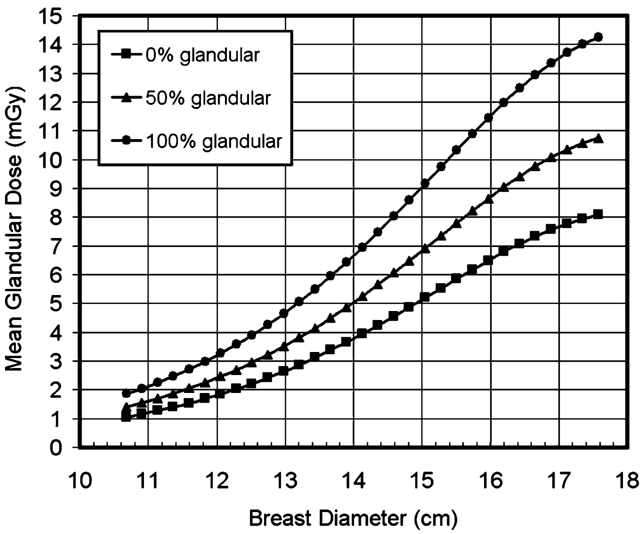

Figure 3 The mean glandular radiation dose to the breast is shown as a function of breast diameter, for three breast compositions. The mean glandular dose levels correspond to those of two-view (CC and MLO) mammography performed at our institution.

experiments involving validated Monte Carlo studies was undertaken. Exploiting knowledge gained in previous Monte Carlo simulations involving the computation of radiation dose coefficients in mammography [57], Monte Carlo simulations were designed specifically for the geometry of breast CT [54]. Coupled with a number of other physical measurements, including the determination of the radiation dose to the breast due to two-view (cranial caudal and medial lateral oblique) mammography and the radiation output characteristics of the scanner, technique factors were developed which allow the radiation dose from the breast CT procedure to be virtually equal to that of standard two-view mammography [55]. Women with larger breasts experience larger radiation doses in mammography, and this is true with breast CT as well. The image quality of both these modalities is highly dependent upon the amount of radiation striking the detector, and it requires higher levels of radiation (more dose) to penetrate larger breasts for both mammography and breast CT. The radiation levels of two view mammography are shown in Fig. 3 for three different breast compositions, and these are the calculated radiation doses for the breast CT examination as well.

Image Reconstruction

With computed tomography, a large number of projection images are acquired of the patient's anatomy as the rotating gantry circumnavigates the object being scanned. This raw dataset, after significant preprocessing, is used in a CT reconstruction algorithm to produce a number of tomographic images of the object. With the breast CT scanner, a total of five hundred 768 × 1024 projection images are acquired, and a cone beam CT reconstruction algorithm was written in order to reconstruct the breast CT images. In the current implementation of this algorithm, three hundred 512 × 512 tomographic images are produced from the raw acquired dataset. Figure 4 (top panels) illustrates five of the preprocessed acquired images, and Fig. 4 (bottom panels) illustrates five of the three hundred breast CT images.

Patient Imaging

One of the key features of breast CT is that the breast is imaged with the patient lying on the table, with the breast hanging in the pendant position. The optimal shape of the breast for CT scanning is cylindrical; no breast compression

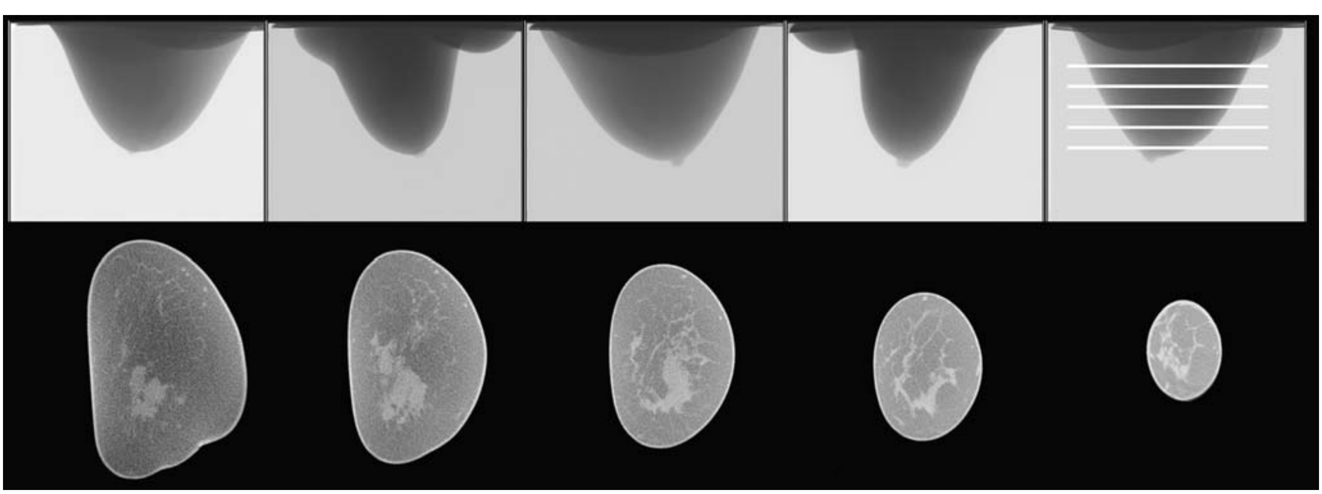

Figure 4 The top row of images illustrates five of the 500 "sinogram" images which are acquired by the breast CT hardware. These data represent the input to the CT reconstruction algorithm, which produces approximately 300 tomographic images. The reconstructed breast CT images are illustrated in the bottom panel (five of 300 images). The positions of the five breast CT images shown are indicated by the horizontal lines on the upper right sinogram image.

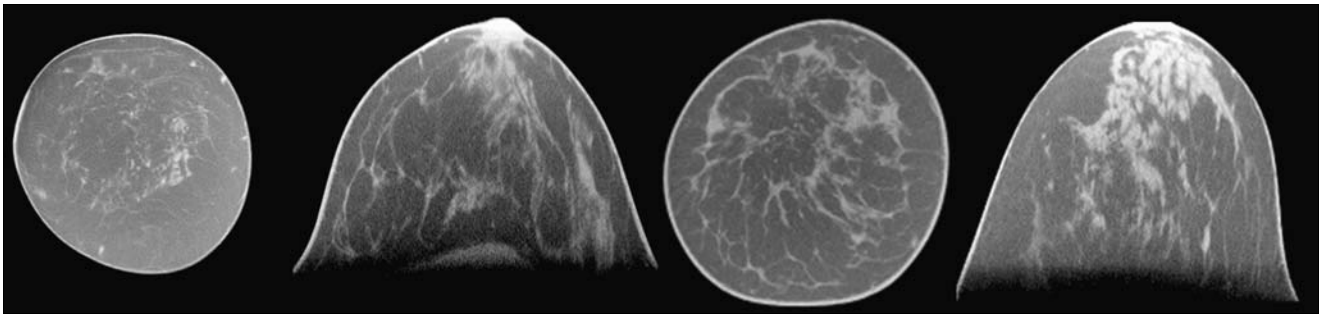

Figure 5 These four breast CT images were acquired from healthy volunteers. These images demonstrate anatomical detail not routinely seen in mammographic images.

is required nor is it desired. Therefore, this examination is thought to be far more comfortable than two-view mammography, which requires relatively aggressive compression of the breast to achieve good image quality.

Images produced on the first prototype breast CT scanner are illustrated in Fig. 5. This series of images illustrates some of the first in vivo images acquired on the breast CT scanner, and illustrate the complex normal anatomy associated with the breast. While print media only allow the depiction of a small number of images, the digital workstation for radiologist review of the breast CT images allows extremely rapid and flexible navigation through this large CT volume dataset. One of the fundamental limitations of projection mammography is that suspicious breast lesions (cancer) can be lost in the complex background of the normal breast anatomy; this is especially true for younger women who generally have greater breast density. The tomographic process, which breast CT enables, allows the radiologist to pan through the three-dimensional volume dataset slice by slice, essentially eliminating the complexity of the overlying and underlying glandular tissue which is so problematic in projection mammography imaging.

Breast CT images of breast cancer are illustrated in Fig. 6. This series of images depict noncontrast-enhanced breast cancers, demonstrating that there is intrinsic contrast between the biopsy-confirmed tumors and the surrounding (mostly adipose) tissues. X-ray contrast, which is also the basis of mammography screening, is dependent both on the effective atomic number (z) of the tissues, as well as the electron density (electrons/cm^3). While the difference in X-ray contrast between tumor and adipose tissues is high, if a tumor were completely imbedded within the normal glandular tissue of the breast, it is unclear whether there would be sufficient differential contrast to identify the lesion. As is visible in the images shown in Fig. 6, the identification of breast cancer using breast CT relies on anatomical changes which appear sufficiently different from the normal breast anatomy to raise suspicion. While the ability to separate tissues in a series of planes (the tomographic images) does eliminate the over- and underlying normal anatomical "noise", further studies (underway) are needed to evaluate the overall detection performance in breast CT, in comparison to mammography.

Contrast Agents

Figure 7 illustrates several biopsy-confirmed breast tumors which have been enhanced by the intravenous injection of iodine-based contrast agent. To produce these images, 100 ml of contrast agent was injected at the rate of 4 ml/second through the brachial vein. Imaging was performed 100 s after the initiation of contrast injection. The tumors

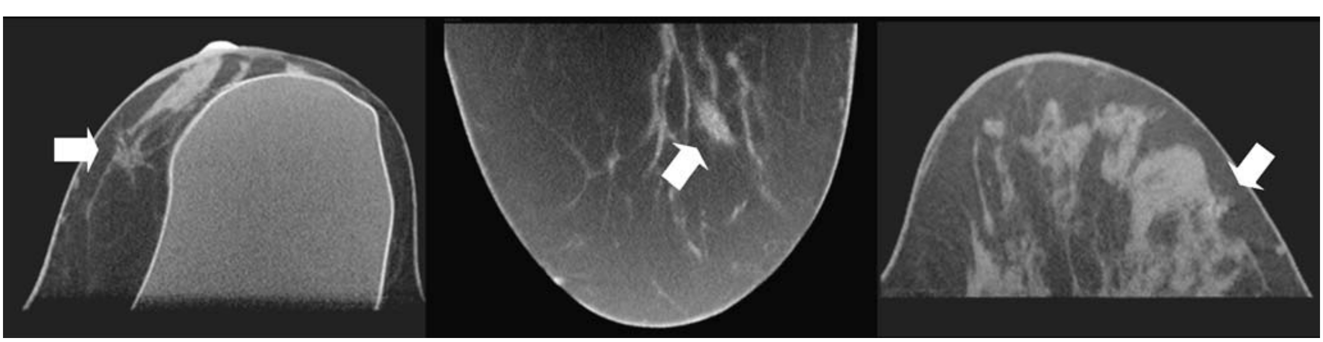

Figure 6 Three breast images are shown from different patients, with the arrows illustrating the location of breast cancers which were biopsy-confirmed after the breast CT imaging. (a) A spiculated lesion is seen, surrounded primarily by adipose tissue, just adjacent to the saline implant. (b) A ductal carcinoma in situ is illustrated, with numerous microcalcifications visible. (c) A cluster of microcalcifications is associated with this lesion, which is straddled between glandular and adipose tissue elements.

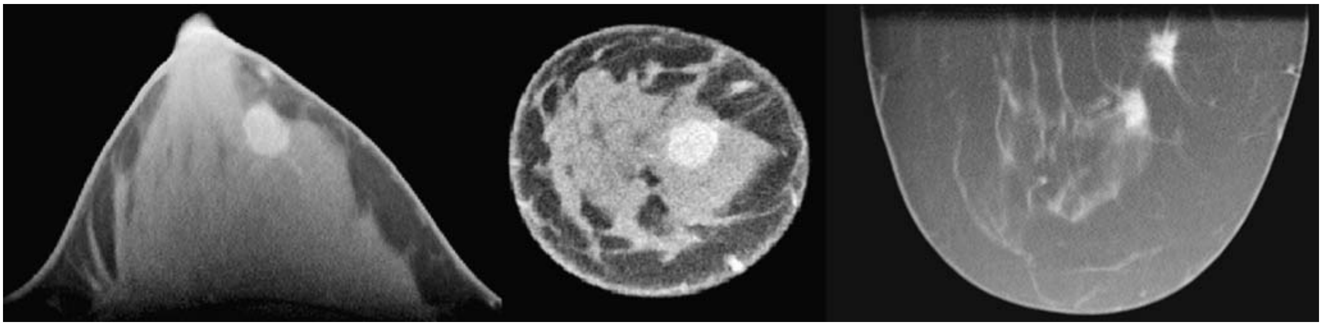

Figure 7 Breast images which were acquired after the injection of iodinated contrast are illustrated. The location of the tumors (all biopsy-confirmed) is evident without the need for arrows. The breast on the right has two lesions, one of which was not seen mammographically.

are well illuminated by the presence of contrast agent, which is thought to pool in the interstitial (extravascular) spaces due to the poorly constructed nascent vessels recruited by the tumor. The "leaky vessel" mechanism for contrast enhancement is the same mechanism underlying the success of contrast-enhanced breast MRI. Although breast CT obviously is associated with some exposure to ionizing radiation, under many circumstances breast CT would be more practical and cost-effective than breast MRI in a breast imaging clinic. It is estimated that breast CT on a dedicated system would be less than half the cost of an MRI-based biopsy, and could be performed in less time. If contrast-enhanced breast CT were shown to be equivalent to contrast-enhanced breast MRI, then the diagnostic mammography examination (not necessarily the screening mammography examination) may well take advantage of contrast-enhanced breast CT as an alternative to breast MRI. While a greater volume of contrast agent needs to be injected for CT (compared to MRI), the venous placement of the catheter is the same in the two procedures and this is the most uncomfortable aspect of the examination to the patient. Iodine-based X-ray contrast agent injection is associated with slightly higher risk of adverse reaction, but the vast majority of contrast reactions are minor (hives) and the documented risk is exceedingly low. In addition to issues of cost, some patients are unable to undergo MRI due to claustrophobia or due to metallic implants. X-ray CT also does not suffer from spatial distortion as does MRI (very important for biopsy), and regular metallic biopsy needles can be used in CT but not MRI. Therefore, as a method for biopsy needle guidance, breast CT has several advantages.

Summary

A prototype breast CT scanner has been designed, fabricated, and is currently undergoing clinical testing in our laboratory. A second prototype scanner is operational and will begin to be used for clinical studies shortly. The initial clinical images produced by the breast CT system demonstrate that high quality tomographic images can be produced in a dedicated pendant geometry at radiation levels identical to two-view mammography. While it is too early to predict the ultimate diagnostic potential of the breast CT modality, the excellent detail and anatomical complexity which is seen in these images are encouraging. We are currently accruing breast CT cases (along with mammograms), and will be performing an observer-performance study when more patient images have been acquired.

We are focusing on the potential of breast CT as a screening tool without contrast enhancement, which may accompany or possibly supplant screening mammography for some women. It is likely that women with dense breasts would benefit by the tomographic nature of breast CT more than women with adipose breasts. While it is unlikely that the use of contrast-enhanced breast CT will be practical in the screening environment, other investigators have demonstrated that contrast-enhanced breast MRI was superior in terms of sensitivity to mammography for screening women at high risk for breast cancer [58]. Thus, an additional role of breast CT may be to serve women with a family history or who are genetically predisposed (BRCA1 and BRCA2) to breast cancer. While the clinical efficacy of breast CT awaits observer-performance evaluation, it is likely that this technology will have some role to play in the breast imaging clinic, even if this is simply to replace stereotactic biopsy systems.

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