Breast imaging with acoustic tomography: a comparative study with MRI

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ABSTRACT

The objective of this study is to investigate a potential low-cost-alternative to MRI, based on acoustic tomography. Using MRI as the gold standard, our goals are to assess the performance of acoustic tomography in (i) depicting normal breast anatomy, (ii) imaging cancerous lesions and (iii) accentuating lesions relative to background tissue using thresholding techniques. Fifteen patients were imaged with MRI and with an acoustic tomography prototype. A qualitative visual comparison of the MRI and prototype images was used to verify anatomical similarities. These similarities suggest that the prototype can image fibrous stroma, parenchyma and fatty tissues, with similar sensitivity to MRI. The prototype was also shown to be able to image masses but equivalency in mass sensitivity with MRI could not be established because of the small numbers of patients and the prototype's limited scanning range. The range of thresholds required to establish tumor volume equivalency suggests that a universal threshold for isolating masses relative to background tissue is possible with acoustic tomography. Thresholding techniques promise to accentuate masses relative to background anatomy which may prove clinically useful in potential screening applications. Future work will utilize larger trials to verify these preliminary conclusions.

Keywords: breast, lesion, cancer, ultrasound tomography, MRI

1. INTRODUCTION

One in eight women born today will be diagnosed with cancer of the breast at some time during their lifetime[1]. Today, mammography is the conventional imaging modality most widely used to generate an understanding of the extent of tumor involvement in breast tissue[2]. Although it plays a vital role in early detection of invasive carcinomas in the breast, reading mammograms is challenging because the appearance of the breast varies significantly from woman to woman. It also involves breast compression, which can be uncomfortable for some patients. Furthermore, some forms of breast cancer are harder to notice in a mammogram, especially in women that have denser breast tissue. Diagnostic mammography also detects abnormalities that are not related to cancer, leading to additional imaging procedures and biopsies that turn out to be costly and unneccessary[3]. Due to the inconsistency of mammograms, breast screenings are often complemented with ultrasound (US), which is both cost-effective and patient friendly. Ultrasound allows for further differentiation between solid and non-solid masses in the breasts, which in turn leads to fewer false positives[4]. Unfortunately, the conventional ultrasound scan is quite operator dependent and, like mammography, screening ultrasound has a low positive predictive value in cases where biopsy is performed[5].

Breast magnetic resonance imaging (MRI) is now recognized as an important adjunctive examination to mammography and ultrasound[6]. It is an important tool for investigating breast cancer because it has the capability to detect cancers that mammograms miss in many high-risk women[7]. Breast MRI has shown a very high sensitivity for invasive carcinoma. MRI can also differentiate well between benign and cancerous lesions by analyzing morphology and enhancement characteristics[8]. However, MRI is extremely costly to operate and to house and requires a specialized staff for operation. Scans are relatively long in duration ranging from 30-60 minutes depending on the type of scan. Contrast enhancements may be used to highlight vascular structures (magnetic resonance angiography) which can emphasize a cancerous mass. The most common contrast agents used are gadolinium derivatives, which have magnetic properties that

Medical Imaging 2009: Ultrasonic Imaging and Signal Processing, edited by Stephen A. McAleavey, Jan D'hooge
Proc. of SPIE Vol. 7265, 726510 · © 2009 SPIE · CCC code: 1605-7422/09/$18 · doi: 10.1117/12.813350

affect proton relaxation times. However, such agents make the procedure fundamentally invasive and can cause uncomfortable side-effects.

The above disadvantages have stood in the way of the universal adoption of MRI, limiting its role in both screening and diagnosis. Consequently, a modality that can rival MRI's image quality while obviating these difficulties could potentially have greater societal impact. The experimental approach we discuss in this paper is based on acoustic tomography, which utilizes ultrasound transducer arrays to construct whole breast images from measurements of scattered acoustic pulses interacting with breast tissue.[9] One embodiment of this approach is our Computed Ultrasound Risk Evaluation (CURE) device, a clinical prototype at the Karmanos Cancer Institute. Our goal is to determine whether CURE can generate images comparable to MRI but at a much lower cost and much more quickly. The ultimate goal is to provide diagnostic accuracy to reduce the rate of biopsies for benign lesions and provide a means of characterizing masses within high-risk women that have denser breast tissue or have fibrocystic changes. The scan is comfortable, in contrast to the breast compression associated with mammography or injections associated with MRI. The CURE prototype also offers several additional benefits relative to conventional imaging. This includes whole-breast analysis in a single scan, which allows for the extraction of diagnostic information from the entire volume of the breast. It uses non-ionizing scanning techniques, which makes multiple, frequent scans possible so that it would be feasible to monitor changes in the breast over time. The scan is completely non-invasive because it does not require contrast enhancements.

This paper reports on a study that compares MRI imaging with CURE for a set of 15 patients. The goals of the study are to establish quantitative CURE thresholds for its new imaging parameters and to assess its clinical potential relative to MRI. To accomplish this, we have examined similarities and differences between suspicious lesions and anatomical structures found in both of the imaging modalities through qualitative and quantitative analysis, as described below.

2. METHODS

2.1 Patient Recruitment

Fifteen patients were recruited at KCI's Alexander J. Walt Comprehensive Cancer Center and given both MRI and CURE breast exams. MRI was chosen as the gold standard for comparison because of its accuracy and its ability to image the whole breast in a geometry very similar to that of the acoustic prototype. MRI scans were received in axial-sliced stacks and were then re-sliced in *ImageJ* into coronal views to match the native format of the CURE acquisitions. The dataset included all MRI data, including T1- and T2-weighted, fat-subtracted, and contrast enhanced images. We used gadolinium-enhanced, fat-subtracted T1-weighted images to define the volume and extent of cancer in this study. T2-weighted images also helped define benign lesions such as cysts. The dataset represents a variety of breast shapes, patient ages, breast densities, and contains both benign and cancerous lesions. All imaging procedures were performed under an institutional review board-approved protocol, and in compliance with the Health Insurance Portability and Accountability Act.

2.2 CURE Data Acquisition

The principles and techniques of the CURE device were described in detail previously[9]. The device is markedly different than that of other imaging modalities such as mammography and conventional ultrasound. The patient is positioned face-down on the examination bed with the breast situated through a hole leading to a water tank. The breast is suspended into the water tank where it is scanned by a ring-array US transducer. Water, because it has a well-defined sound speed close to that of breast tissue, serves as the coupling medium between the breast and transducer. A 20-cm-diameter ring transducer, which operates at a frequency of 2 MHz, encircles the breast and scans from the patient's chest wall to nipple region by the means of a motorized gantry. The ring consists of 256 elements that both emit and receive

the ultrasound signals. One complete scan consists of approximately 45-75 tomographic slices of the breast at 1 mm separation. The scanning process takes approximately 1 minute.

Three types of images were produced from the raw data using tomographic reconstruction algorithms. *Sound speed image*s are based on the arrival times of acoustic signals. Previous studies have shown that cancerous tumors have enhanced sound speed relative to normal breast tissue (e.g., Greenleaf[10] *et al*). This allows for potential differentiation of masses, normal tissue, and fat in these types of images. *Attenuation Images* are tomographic reconstructions based on amplitude changes. Higher attenuation in cancer causes greater absorption or scatter of the US wave, so attenuation in conjunction with sound speed provides a potentially effective means of determining malignancy. *Reflection images,* based on changes in acoustic impedance*,* provide echo-texture data and anatomical detail for the entire breast. These three types of images can be combined by means of image fusion, allowing for multi-parameter visual characterization of masses.

Image manipulations and calculations were performed with *ImageJ*, a public-domain, java-based image processing program whose development was supported by the National Institutes of Health[11]. CURE images are constructed from the same data and can be fused together without any geometric discrepancies. A macro in *ImageJ* was developed and used to fuse images and adjust thresholds. Adjusting thresholds regulates the visibility of masses relative to general anatomy thereby enabling the suppression of background tissue. Image fusion allowed for improved visualization so that multiple characteristics could be viewed within one fused image and different breast tissue features could be evaluated more effectively. In addition, colors are used to enhance the visualization of lesions and architecture in the fused image. In our images, we arbitrarily chose colors to represent different features. Conversion to gray-scale provided another means of comparison with MRI.

2.3 Image Analysis

We fused the reflection, attenuation and sound speed CURE images and compared them with the various MRI image sequences. This process was enabled by the similarities in the sensitivity and resolution of the two imaging modalities. The spatial resolution of the MRI data was ~ 1 mm and the images slices were typically 1 mm thick. The CURE images were characterized with a spatial of resolution of 1 to 2 mm with a slice thickness of ~ 4mm. All fused CURE images were converted to gray-scale to better match the MRI image presentation.. All comparisons were made with the assistance of an experienced radiologist and a radiology resident. During the comparison process, the MR imaging parameters that we paid particular attention to were the estimated size of the primary tumor and the detection of additional suspicious lesions. There were some discrepancies between the CURE and MRI images because the MRI scan was done in air, while the CURE scan was done in water. These discrepancies were minor and included a slightly different volume distribution, and a different length in the axial plane. Furthermore, 3D projections of the lesions were created from the thresholded MRI and CURE stacks for additional visual comparison. This function allowed us to rotate the masses in 3-dimensions so that the morphology and volume distribution of the lesions could be compared more effectively.

Once a preliminary relationship was confirmed from a visual assessment, a more quantitative technique was used to verify that CURE was producing accurate images. A quantitative analysis also eliminated the subjectivity associated with visual analysis, and showed that our techniques were reproducible. First, we obtained US and MRI reports to determine the umber of reported masses. We then sought corresponding masses in the CURE images, with the help of an experienced radiologist and radiology resident. US and pathology data were used in order to calibrate any systematic effects in tumor size caused by MRI's tendency to overestimate tumor sizes relative to US.

To estimate the volumes of the lesions, we obtained mass dimensions from the pathology report of the patient with a date closest to that of the MRI scan. Using the ellipsoid formula: (π/6 x Length x Width x Height), we determined a rough estimate of the volume of the tumor. To get dimensions from MRI and CURE, we used coronal views to get the dimensions in the x-y plane, and an axial re-slice of the coronal image to get the depth in the z-plane. From CURE, we utilized sound speed, attenuation and reflection images to get a dimensional volume. Again, this was done with the help of an experienced radiologist and radiology resident. Upon the completion of the volume calculations and threshold determinations, we averaged all of the thresholds in an attempt to determine the uniqueness of a potential universal

threshold. Using the average thresholds for sound speed and attenuation that we collected, we re-calculated the volumes of each mass using the average thresholds to determine how much the newly calculated volumes varied from the actual volume.

3. RESULTS AND DISCUSSION

The fused CURE images were most comparable the T1 fat-subtracted MRI sequences. A visual assessment of the images led to the identification of parenchyma, fibrous stroma, masses and fatty tissues in both the CURE and MRI images. Furthermore, these components of breast anatomy were distributed in a similar, though not exact, manner in the two sets of images. Figure 1 shows images that depict similar breast architecture. The gray scale in the fused image correspond directly to the fat-subtracted MRI image. Dark gray represents fat, light gray depicts parenchyma, and the white bands are fibrous stroma. Anatomical differences can be accounted for by (i) the dissimilar breast deformation under MRI (air) and CURE (Water) exams, (ii) the lower spatial resolution of the CURE images and (iii) the greater slice thickness associated with the CURE images.

In order to compare the depiction of masses rather than overall breast architecture we relied on the observation that masses tend to have higher sound speeds relative to background tissue. Starting with the threshold that emphaiszed anatomical equivalence between CURE and MRI, we progressively increased the sound speed threshold until masses could be maximally isolated relative to background tissue. The procedure was repeated for the attenuation images. The thresholded images were then fused with the reflection image to show the isolated mass in relation to the breast architecture. In this study the thresholded sound speed and attenuation images were color coded in red (R) and blue (B), respectively while the reflection images were depicted with a grey scale (Gr). The three images were then fused to create a composite RBGr image . In this depiction masses with high sound speed and attenuation would appear magenta in color. which would be consistent with a mass that is dense and stiff, characteristics often noted for cancerous masses[10]. Figure 2 shows such images of a patient with an invasive carcinoma. The mass in both the CURE and MRI images are approximately the same size and extent within the same quadrant of the breast. It is quite evident that a suspicious lesion is present in the CURE images, more so than in the T1 weighted MRI images. Comparison with contrast-enhanced, fat-subtracted MRI images shows that the CURE identified mass does indeed correspond to the MRI identified mass. This type of imaging paves the way for further study exploring the possibility of detecting masses within radiographically dense breast tissue, and locating masses within parenchyma without the use of MRI and contrast agents.

A mass detection by CURE was defined as a distinct feature appearing in one or more CURE modalities that coincides in location and size with masses identified in the MRI images. In this study, The CURE exams may miss some of the unknown (secondary) masses if they fall outside of its scanning range which occasionally occurs for women with large breasts for whom the scanning range has to be centered on the known mass location, leading to some parts of the breast not being scanned, usually the chest wall and nipple areas. This limitation is brought about by CURE's initial storage memory of 11 Gb which limits the number of scans that can be acquired. This limitation has now been removed (memory is now 22Gb) and will improve future studies. Future scans will have the capability to detect additional lesions beyond what could be found in this study. Table 1 shows the number of masses found by CURE relative to the number reported in the initial Mammography and US reports. It also tabulates the number of secondary masses seen by CURE, and verified with MRI, that were not originally reported. Patients that have masses outside CURE's scan range are labeled appropriately. The degree to which CURE matches up to MRI performance will be answered in future studies.

Using the methodology described above for isolating a region of interest, we calculated mass volumes from CURE data by thresholding. The average we obtained for sound speed from this quantitative assessment was 1.48 km/s. Attenuation yielded an average value of 0.17 dB/cm. To determine if the average thresholds could produce accurate results and possibly act as a universal threshold, we re-calculated all of the volumes using the average thresholds. Overall, most of the volumes were not significantly affected. The volumes deviated from the mean in sound speed and attenuation images by 2.64 cm^3 and 1.44 cm^3 respectively. This shows that for the most part, a universal threshold should be able to determine a tumor volume that is quite accurate with moderate variance. However, further study with more patients would be necessary in order to determine whether the average threshold is indeed universal.

4. CONCLUSIONS

Fused CURE images, rendered in grey-scale, show similar breast architecture seen on T1 weighted MRI images. Minor differences can be accounted for by the differing breast geometries and the lower spatial resolution of the CURE images. Color-coded thresholding of CURE images was shown to enhance the visibility of breast masses. The thresholded CURE images are more effective in identifying masses than the T1 weighted MRI images and are more similar to the contrast-enhanced, fat-subtracted MRI images. Out of 15 patients who had 22 total masses reported, CURE was able to find 18 of them, as well as an additional 5 that were not originally reported. The 4 that were missed were out of CURE scanning range. Recent upgrades to the device should lead to detection of masses that this study may have missed. Although this study is limited in scope it suggests that CURE has the potential to find additional masses missed in standard US and mammography exams. Future studies will be carried out with larger cohort of patients to determine the sensitivity to breast masses relative to MRI.

ACKNOWLEDGMENTS

The authors acknowledge that this work was support by a grant from the Michigan Economic Development Corporation (Grant Number 06-1-P1-0653). For correspondence regarding this paper, contact Neb Duric at *duric@karmanos.org*.

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Table 1: Number of masses found with CURE

Patient Number	# of masses reported	# of corresponding masses found with CURE	# of additional masses found with CURE (confirmed with MRI)
147	2	2	
152	1	1	
160	3	3	5
161*	2	1	
172	1	1	
177*	2	1	
180*	1	1	
182*	2	0	
191	3	3	
198	1	1	
206	1	1	
238	1	1	
239	1	1	
250	1	1	
252	1	1	
Total	23	19	5

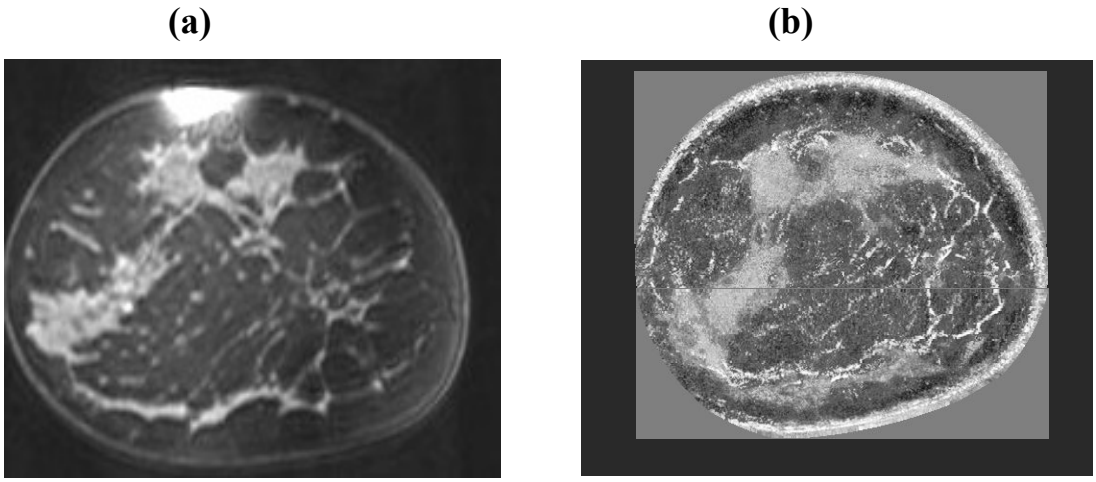

Figure 2: (a) Coronal fat-subtracted MRI image of breast. (b) Fused image, created using ImageJ, of the same patient. The anatomical features of the breast, especially the shape of the parenchyma, in the CURE image and in the MRI image is almost identical. The dark gray corresponds to fat, the lighter gray represents the parenchyma, and the thin white bands are fibrous stroma.

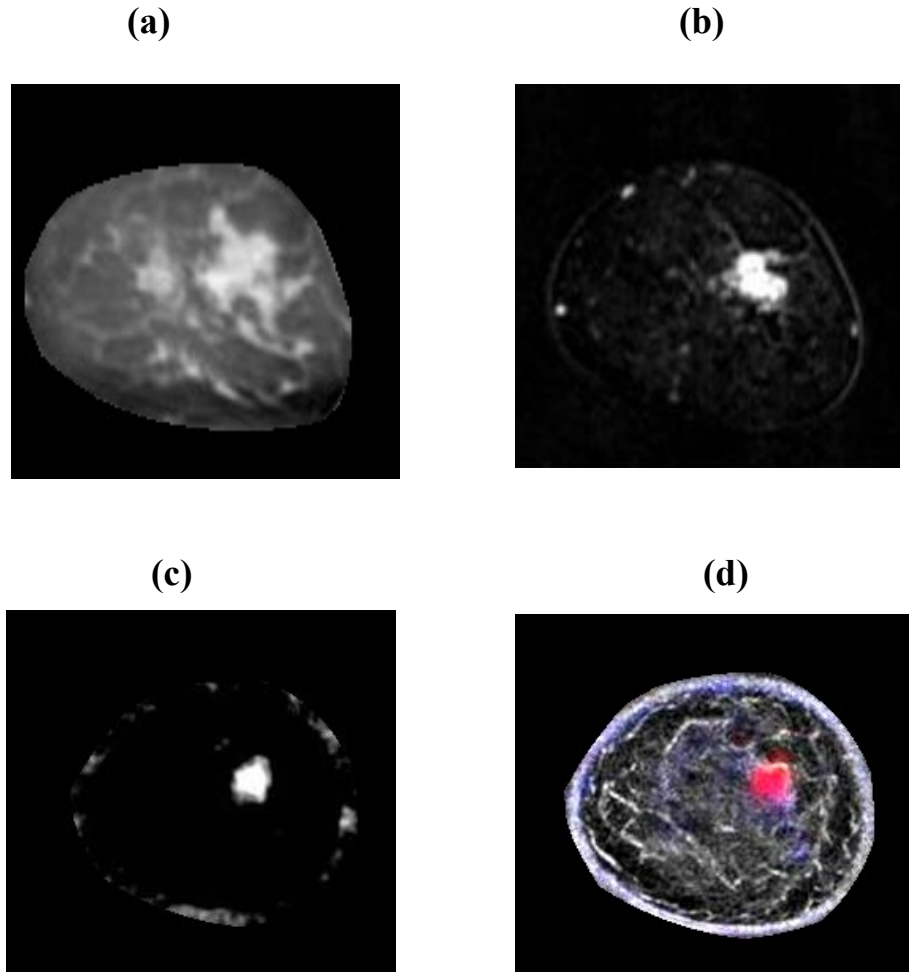

Figure 3: (a) Coronal T1 fat-subtracted gadolinium-enhanced MRI image of breast. (b) Contrast enhanced, fat-subtracted MRI image highlighting a mass at 2:00 o'clock. (c) Thresholded CURE sound speed image showing the same mass (no contrast agent). (d) Fused image. The magenta area on the CURE image shows that the mass has high sound speed and attenuation.