Breast tissue composition and breast density measurements from ultrasound tomography

Mark Sak[1], Neb Duric[1,3], Norman Boyd[2], Peter Littrup[1,3], Erik West[3], Cuiping Li[1,3]

[1]Karmanos Cancer Institute, Wayne State University, 4100 John R Street, Detroit MI 48201

[2]Princess Margaret Hospital, 610 University Ave., Toronto, Ontario, Canada M5G 2M9

[3]Delphinus Medical Technologies, 46701 Commerce Center Dr, Plymouth, MI, 48170

ABSTRACT

It is known that breast cancer risk is greater in women with higher breast densities. Currently, breast density is measured using mammographic percent density, defined as the ratio of fibroglandular to total breast area on a two dimensional mammogram. Alternatively, systems that use ultrasound tomography (UST) create tomographic sound speed images of the patient's breast. These volumetric images can be useful as a diagnostic aid because it is also known that sound speed of tissue is proportional to the density of the tissue. The purpose of this work is to expand on the comparisons of the two imaging modalities by introducing new ultrasound tomography measurements that separate and quantify the fatty and dense tissue distributions within the breast. A total of 249 patients were imaged using both imaging modalities. By using k-means clustering, correlations beyond the volume averaged sound speed of the ultrasound images and the mammographic percent density were investigated. Both the ultrasound and mammographic images were separated into dense and fatty regions. Various associations between the global breast properties as well as separate tissue components were found.

Keywords: Ultrasound tomography. Breast density. Breast cancer risk.

1. INTRODUCTION

Over the course of their lifetime, 1 out of every 8 women will develop breast cancer. Fortunately, with early detection, breast cancer is not a lethal disease[1]. Early detection is accomplished through the use of predictive models, which identify risk factors. It is known that women with higher breast densities have an increased risk of developing breast cancer, up to a six-fold increase in incidence rate compared to women with fatty breasts[2-4]. Because of this increased risk, some recent predictive models now incorporate breast density[5-6].

The current gold standard in the early detection of breast cancer is the use of mammography screening. The use of mammography screening has been shown to reduce the mortality rate in multiple trials[1]. Yet, mammography may have difficulties in detecting breast cancer in very dense breasts, or people with the highest risk. Also, many abnormal findings not related to cancer are also generated. These abnormal findings can lead to additional, costly images and unnecessary biopsies[7-10]. The use of ionizing radiation to create mammographic images can also lead to an increased risk of developing breast cancer.

Breast density can be measured from a mammogram by the calculation of a computer-generated value known as mammographic percent density (MPD). One program that calculates MPD in this way is Cumulus[11]. MPD is simply the ratio of fibroglandular to total breast area as measured on a mammogram. MPD is likely to bear some relationship to the actual density of the breast, but the relationship is not direct.

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Mammography is a two dimensional representation of three dimensional anatomy and this can limit how effective a tool for predicting breast cancer risk that MPD can be.

Ultrasound tomography (UST) uses non-ionizing ultrasound waves to create three dimensional sound speed images of the breast anatomy. The longitudinal sound speed of any material is given by:

$$v = \sqrt{\frac{C}{\rho}}$$

where C is the bulk modulus and ρ is the density of the material in question. Studies have shown[12-16] that the bulk modulus of breast tissue scales with the cube of its density. This suggests that for breast tissue, the velocity has a direct relationship with density. Therefore, the average density of the breast can be measured by calculating the volume averaged sound speed (VASS), which is a quantitative measurement of breast density.

Previous work focused on the use of an ultrasound tomography clinical prototype at the Karmanos Cancer Institute's (KCI) breast center[16-20]. In particular, the relationship between the VASS and the MPD for each breast was examined. It was shown[21] that a significant correlation existed between the two density measurements. This suggests that UST's ability to measure density is comparable to that of mammography. Building on this work requires the segmentation of the UST sound speed images into regions of dense and fatty tissue.

Applying a k-means clustering algorithm to the sound speed image allows for segmentation of the breast. The segmentation is similar to the segmentation that can be achieved in mammography. Therefore, UST percent density can be calculated in a similar manner to MPD, by finding the ratio of the dense volume to the total volume of tissue. However, because of the quantitative nature of the sound speed images, further analysis of the dense and fatty volumes can also be performed.

2. METHODS AND MATERIALS

2.1 Patient dataset - Mammography

Patient data were acquired from patients recruited into ongoing studies in accord with a Karmanos Cancer Institute and Wayne State University approved protocol. A cohort of 249 patients were examined with the UST device to create sound speed images of the breast. Of this cohort, 85 patients received digital mammograms and 164 patients received film mammograms. The mammographic percent density of each patient was analyzed by one reader (NFB) using the CUMULUS 4 Software. This software allowed for measurements of dense and total breast area which was then used to calculate the percent density and non-dense areas[22].

2.2 Patient dataset – Ultrasound Tomography sound speed measurements

Tomographic breast sound speed images were created using the UST system. During these exams, the patient lies prone on a canvas with the breast of interest suspended pendulously through a hole in the canvas into the imaging tank. The tank is filled with water and contains an acoustic transducer ring of 256 elements that moves from the chest wall to the nipple region on a motorized gantry. Sound speed images are based on the arrival times of the acoustic signals as they travel through the patient anatomy. Patients were scanned at 1 mm intervals, which resulted in approximately 40-100 positions per patient. Sound speed tomograms were then reconstructed at each position to produce an image stack. Each image is composed of a matrix of values that stores the sound speed value of each pixel in km/s.

Analysis of the images was done with the public domain software package *ImageJ*. The volume averaged sound speed of each patient was measured by first removing the surrounding water bath from the image using a semi-automated elliptical approximation of the breast. Once this mask of the breast was created, the remaining pixel values were then averaged to produce the VASS.

Further analysis of the images was done using a k-means clustering algorithm to segment the breast into dense and fatty volumes. Ultrasound percent density (USTPD) could be calculated by comparing the volume of dense tissue to the total volume measured. Using the segmented volumes also allows for a more in depth study of breast density. These techniques allowed for a thorough comparison of the two different imaging modalities in their ability to measure breast density.

3. RESULTS AND DISCUSSION

Figure 1 shows the plot of volume averaged sound speed (VASS), obtained using the UST device, versus the mammographic percent density, obtained using mammography, for both the digital and film mammograms respectively. Both plots are shown with their corresponding Pearson correlation coefficients (0.79 for digital and 0.72 for film) which indicate that a strong and positive correlation exists between the sound speed and mammographic percent density. The correlation is slightly stronger for digital mammograms than for film mammograms.

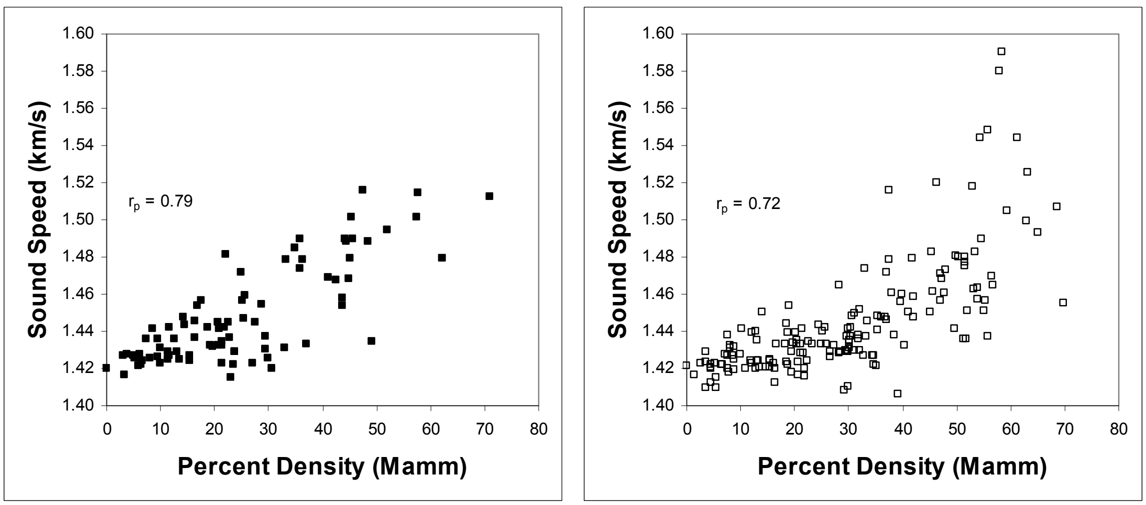

Figure 1 – Plots of volume averaged sound speed (VASS) versus mammographic percent density (MPD) for both digital and film mammograms.

The relationship for digital mammograms appears to be linear, while the relationship for the film mammograms appears to be more curvilinear. This may be due to the sigmoidal response of film mammograms to x-rays compared to the linear response of digital mammograms. However, some studies[23] have also suggested that the relationship between a volumetric and area-based density measurement, may in fact be curvilinear. When both liner and non-linear regression was performed, a 2nd degree polynomial fit seems to indicate a slightly stronger fit than a linear fit. The R^2 value for the digital mammograms increases from 0.63 to 0.64 when going from a linear fit to a 2nd degree polynomial, while the R^2 value for film increases from 0.52 to 0.57.

Figure 2 shows the relationship between the VASS and the dense area measured on the mammogram for both digital and film respectively. The Pearson coefficient is shown with the plot (0.45 for digital and 0.43 for film) and suggests that as the breast sound speed increases, the total area of dense tissue on a mammogram also increases. This suggests that the anatomy of breasts with high average sound speeds is composed of more dense tissue than breasts with low average sound speeds. The variation in the data occurs because the entire volume of the breast is not considered. A large, but fatty breast may actually show more dense area on a mammogram than a small, but dense breast.

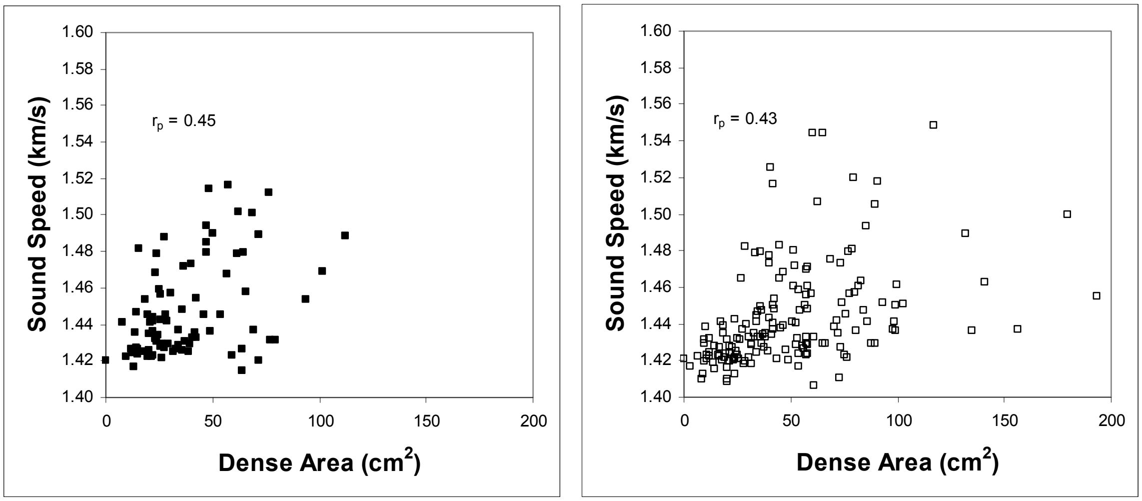

Figure 2 – The plots of volume averaged sound speed versus dense area on a mammogram as measured for both digital and film mammograms respectively.

With the use of the k-means clustering algorithm, regions of dense and fatty tissues within the volume were segmented. This allowed for the calculation of a volumetric percent density (USTPD), which is shown below in Figure 3, plotted against the VASS. Since the measurement of this UST percent density does not depend on the mammographic groups, the plot includes all 249 patients. The Pearson correlation coefficient is 0.68 which suggests there is a correlation, but not as strong as that for the relationship between sound speed and mammographic percent density. This is likely because the algorithm that segments the sound speed images chooses the regions differently and perhaps less effectively than the Cumulus software.

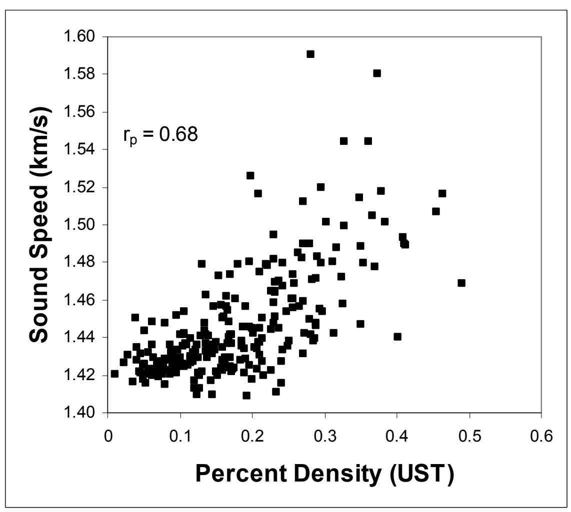

Figure 3 – The plot of volume averaged sound speed versus UST percent density for the entire cohort of patients.

A more direct comparison of the two imaging modalities can be performed by plotting the relationship between the UST percent density and the mammographic percent density. This relationship is shown in Figure 4 for both digital and film mammograms. The Pearson coefficients for these plots are 0.72 and 0.62 respectively, which suggests a correlation on par with that of VASS versus MPD. However, this is a more direct comparison of the two imaging modalities as both values measure the same characteristic, density, in a different manner. It shows the relationship between the three dimensional volumetric analysis of the breast versus the two dimensional compressed analysis of the breast.

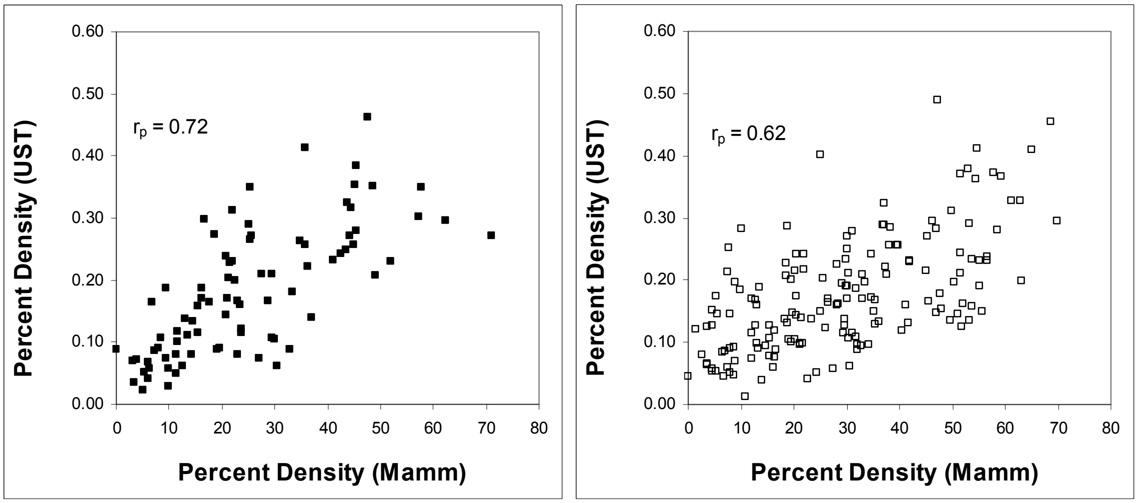

Figure 4 – Plots of UST percent density versus MPD for both digital and film mammograms respectively.

Further analysis with the k-means clustering algorithm is possible by measuring the average sound speed of the dense and fatty regions separately. Figure 5 below shows the relationship between the VASS against the average sound speed of the dense and non-dense regions respectively for the entire cohort of patients. Since this plot was obtained entirely from the measurements made with the clustering algorithm, the mammographic groups are not shown. The Pearson correlation coefficients of 0.79 and 0.96 suggest that there is a relationship between overall density of the breast and the density of the sub-regions.

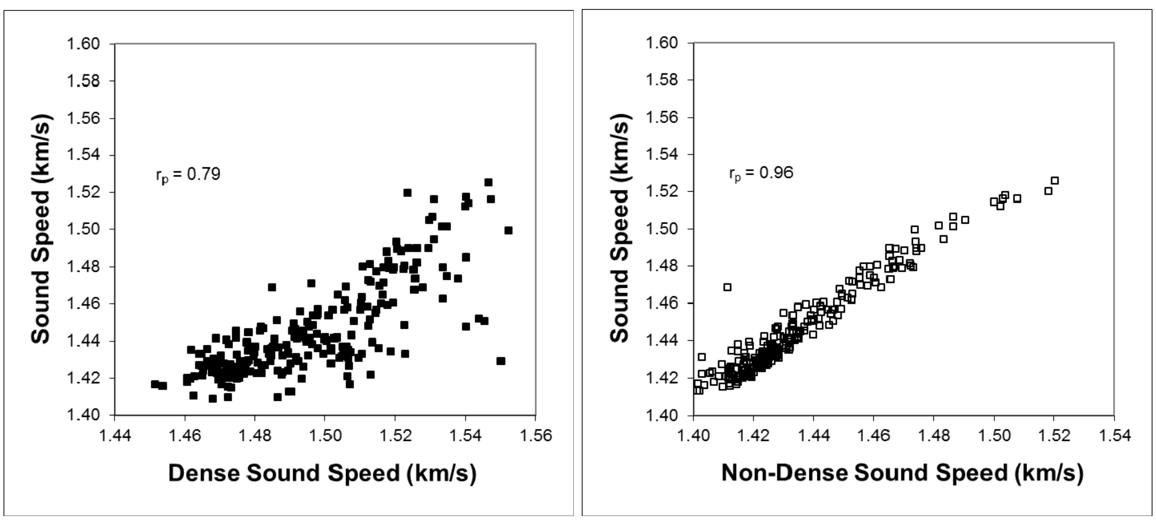

Figure 5 – Plot of VASS versus the average sound speed of the dense and non-dense regions for the entire cohort of patients.

Although Figure 2 above shows the relationship between the overall density and the dense tissue, it suffers from the fact that the dense area on a mammogram varies depending on the size of the breast. By measuring the average sound speed of the dense regions directly, the volume is normalized and the size of the breast is no longer a variable in the relationship. The correlation improves as a result of this normalization.

These results suggest there are some potential characteristics about breast anatomy. It could suggest that dense breasts are more uniformly dense throughout. It appears to be unlikely that a breast will have a very dense region surrounded by very fatty tissue. The dense and fatty regions both tend to be denser throughout in these breasts. However, this result could also be explained by the algorithm's limited ability to identify true regions of fat in the presence of very dense tissue. More analysis still needs to be completed to determine if this is a true characteristic of breast anatomy.

4. CONCLUSIONS

Ultrasound tomography was used to create sound speed images of the breast for 249 subjects who also received either digital or film mammograms. A k-means clustering algorithm was also used to further examine the UST images. It was found that the volume averaged sound speed associated strongly with both mammographic percent density and UST percent density. It was also found that the UST percent density correlates strongly with mammographic percent density. This suggests that UST's ability to measure breast density is consistent with the current standard of care, mammography. Characteristics regarding breast anatomy and tissue composition have also been viewed using UST, but further investigation is still required to determine the nature of this relationship. Still, UST shows promise to become a quantitative, cost-effective non-ionizing alternative for measuring breast density and even compositional characteristics of the breast.

5. ACKNOWLEDGMENTS

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