Relationship between breast sound speed and mammographic percent density

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ABSTRACT

Despite some shortcomings, mammography is currently the standard of care for breast cancer screening and diagnosis. However, breast ultrasound tomography is a rapidly developing imaging modality that has the potential to overcome the drawbacks of mammography. It is known that women with high breast densities have a greater risk of developing breast cancer. Measuring breast density is accomplished through the use of mammographic percent density, defined as the ratio of fibroglandular to total breast area. Using an ultrasound tomography (UST) prototype, we created sound speed images of the patient's breast, motivated by the fact that sound speed in a tissue is proportional to the density of the tissue. The purpose of this work is to compare the acoustic performance of the UST system with the measurement of mammographic percent density. A cohort of 251 patients was studied using both imaging modalities and the results suggest that the volume averaged breast sound speed is significantly related to mammographic percent density. The Spearman correlation coefficient was found to be 0.73 for the 175 film mammograms and 0.69 for the 76 digital mammograms obtained. Since sound speed measurements do not require ionizing radiation or physical compression, they have the potential to form the basis of a safe, more accurate surrogate marker of breast density.

Keywords: Ultrasound tomography, mammographic percent density, breast imaging

1. INTRODUCTION

Every 2 minutes in the United States, a woman is diagnosed with breast cancer. Over the course of their lifetime, 1 out of every 8 women will develop breast cancer. Fortunately, with early detection, breast cancer is a far from lethal disease[1]. Early detection is accomplished through the identification of risk factors and the use of screening.

Most models that predict the development of breast cancer[2-3] use risk factors that include the patient's current age, their age at menarche, their age at the birth of their first child, their family history of the disease and their menopause status. In addition to these risk factors, women with higher breast densities have an increased risk of developing breast cancer. Women with the highest breast densities have upwards of a six-fold higher incidence of breast cancer compared to women with fatty breasts[4-6]. More recent predictive models have also included breast density[7-8].

Mammography screening, the current gold standard for breast cancer detection, has been shown to reduce the mortality rate in multiple screening trials[1]. However, many abnormal findings not related to cancer are also generated. This leads to additional, costly imaging procedures and unnecessary biopsies[9-12]. Furthermore, mammography requires ionizing radiation to create images which may increase the risk of developing breast cancer. It may however be difficult to detect breast cancer by mammography in the presence of extensive density.

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When using mammography, breast density is usually measured using one of two separate methods. The first is an estimation requiring a radiologist's visual assessment of the mammogram. The radiologist uses the four-category Breast Imaging Reporting and Data System (BIRADS) lexicon to rank the density of the breast. This is a highly subjective density classification and it is limited in use due to the considerable intra- and inter-observer reader variability[13-14]. Nevertheless the BIRADS classification does identify groups of women with substantially different risks of breast cancer and is recorded on a large number of women having mammograms in the United States[15].

The second technique is the calculation of a computer-generated value known as mammographic percent density (MPD). One example of this approach is a program called Cumulus[16]. MPD is defined as the ratio of fibroglandular to total breast area. MPD is likely to bear some relationship with actual breast density, but that relationship is not direct. It also has to overcome the fact that MPD uses a two dimensional projection of three dimensional anatomy. The definition of the cutoff between dense tissue and fatty tissue is also dependent on the observer. These factors limit the ability of MPD to be used as an effective tool for predicting the risk of breast cancer.

Ultrasound tomography (UST) has the potential to overcome many of the shortcomings of mammography in the measurement of breast density. It uses non-ionizing ultrasound waves to create 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 of the material and ρ is the density. Studies have shown[17-21] that for breast tissue, the bulk modulus scales with the cube of density. This leaves a direct relationship between sound speed and tissue density.

Ultrasound tomography can be used to directly measure volumetric breast density through the measurement of the volume averaged sound speed (VASS). This volume averaged sound speed is a quantitative measure of breast density. Through the use of an ultrasound tomography clinical prototype in KCI's breast center[21-25], we have been able to test the performance of the volume averaged sound speed measurements versus the more conventional measure, mammographic percent density.

2. METHODS AND MATERIALS

2.1 Patient dataset

Patient data were acquired from patients recruited into ongoing studies in accord with a Karmanos Cancer Institute (KCI) and Wayne State University approved protocol. A cohort of 251 patients were examined using the UST system to produce breast sound speed images. Of the 251 patients, 175 also received film mammograms and the remaining 76 received digital mammograms. The mammographic percent density was measured by one reader (NFB) using the CUMULUS 4 software. The interactive computer assisted method was used to generate measurements of the areas of dense tissue and total area, and percent density and non-dense area derived from these measurements[26].

2.2 UST 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 of each pixel in km/s.

All analysis on the images was done with the public domain software package *ImageJ*. Each sound speed image included both reconstructions of the patient anatomy and of the surrounding water bath. The first step was to crop out the water bath in each image using a semi-automated elliptical approximation of the breast region. The first slice was defined as the image obtained closest to the chest wall while the last slice was defined as the final slice in the areolar region. The first slice usually coincided with the first slice of the exam while the last slice may have excluded some peri-areolar slices due to the limited out-of-plane resolution of the UST device. Once these masks were created, the volume averaged sound speed could be measured by calculating the mean pixel value of the remaining breast anatomy. This was easily done by using *ImageJ*'s built-in "Histogram" function which also gave the standard deviation and the standard error of the mean of the distribution.

3. RESULTS AND DISCUSSION

Figure 1 shows the relationship between the volume averaged sound speed and the mammographic percent density for both the film and digital mammograms. Sound speed was strongly and positively correlated with mammographic percent density for both film and digital. The Spearman's correlation coefficient (r_s) for sound speed was 0.69 for the digital mammography and 0.73 for film mammography. The relationship of sound speed with digital mammography was approximately linear, while with film mammography it was more curvilinear. This difference may be related to the respective linear and sigmoidal response characteristics of digital and film mammography and is the subject of ongoing studies.

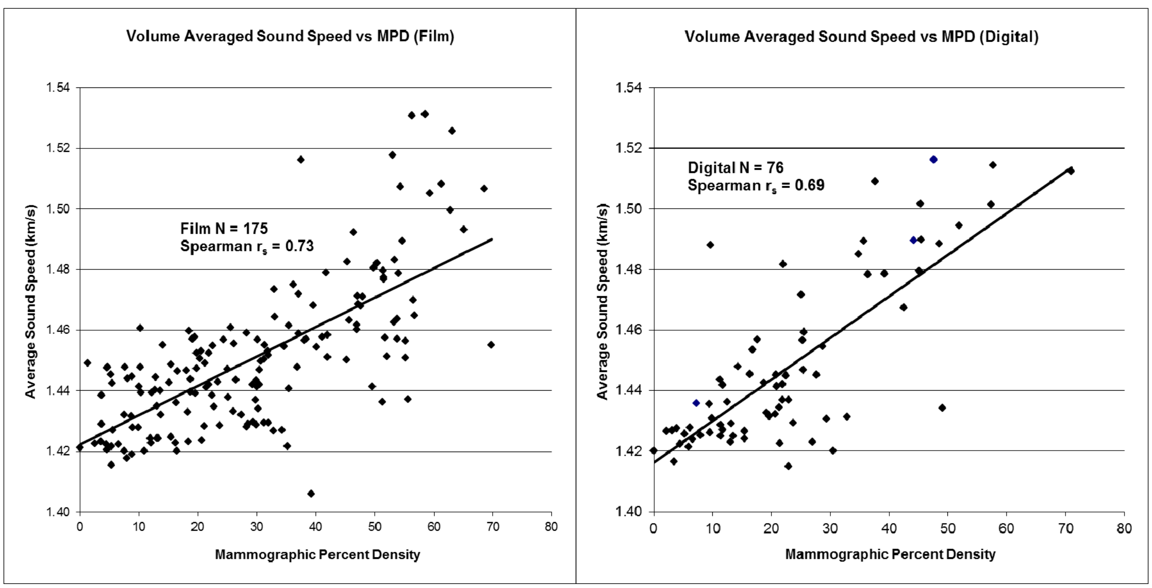

Figure 1 – The plots of volume averaged sound speed versus mammographic percent density for both film (left) and digital (right) mammograms. A strong correlation, indicated by the Spearman correlation coefficient (r_s), is evident.

For denser breasts, the data appears to be more scattered. One possible explanation is that the extra scatter is due to the limitations of mammography. By creating a two-dimensional projection of three-dimensional anatomy, it is possible that there may be geometric misrepresentation of denser regions of the breast. The three-dimensional analysis of the UST sound speed images may therefore provide a more accurate portrayal of the actual density of the breast.

Anomalous anatomy can also affect the average sound speed of the breast which can affect the scatter in the above correlations. Fatty tissue has lower sound speed while dense tissue, breast implants, benign masses and malignant masses have higher sound speeds. It is possible that a large tumor, implant or mass may have a high enough sound speed to significantly affect the overall average sound speed of the entire breast. This may have also affected the amount of scatter visible in the data since many of the study subjects had either benign or malignant lesions. The presence of such lesions is a confounding factor in our study since breast cancer risk is related to the VASS of the healthy tissue, not the VASS of the mass or implant.

Fortunately, the UST sound speed images give us the ability to easily analyze and distinguish different volumes within the breast and thereby segment out masses that are large enough to significantly affect the results. Several patients presenting large tumors and implants were analyzed and it was found that removing these regions from the calculations reduced the VASS. Removing the largest masses (volume of about 30 cc) reduced the VASS by less than 0.75% (about 10 m/s), while removing the breast implants reduced the VASS by 1.2% (about 18 m/s) although the latter represents only 2 cases. The current study is ongoing and will adopt such corrections in the future. Ultimately, studies involving only the contralateral breast will be carried out.

During the usage of the clinical prototype, several different ring transducer arrays were installed. Each new array introduced slightly different time delays based on the exact geometry and location of each array element. These time delays also introduced slight systematic shifts in the reconstructed sound speeds. This can be seen in figure 2. The shifts can be corrected with a proper calibration of the device which is still a source of ongoing investigation. The calibration does not affect the correlation when the array is not changed, as was the case for the digital mammograms.

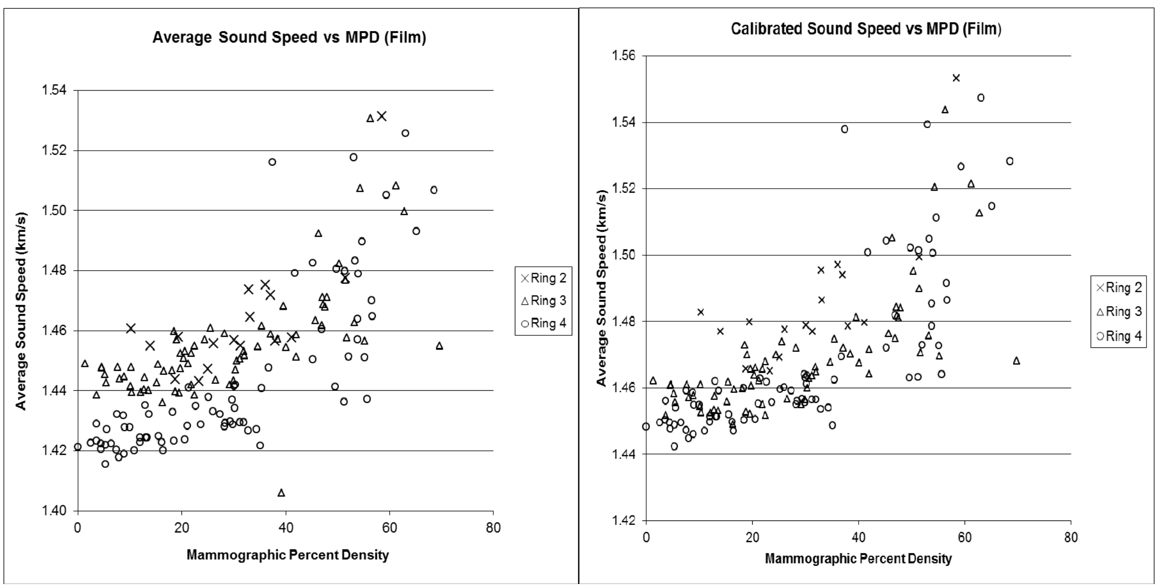

Figure 2 – The uncalibrated volume averaged sound speed versus mammographic percent density for the film mammograms (left). Here, the systematic shifts between sound speed values are apparent when different ring transducers were used. The shifts can be accounted for with proper calibration of the device (right), which is still an area of ongoing investigation.

4. CONCLUSIONS

Ultrasound tomography was used to create sound speed images of the breast for 251 subjects. The volume averaged sound speed of the breast was shown to significantly correlate with mammographic percent density obtained through the use of both film and digital mammography. This suggests that the UST system's ability to evaluate breast density is consistent with the current standard of care. Since UST does not use ionizing radiation, it could therefore also be used more frequently on women with denser breasts who already have a higher risk of developing breast cancer. UST shows promise to become a quantitative, cost-effective, non-ionizing alternative for measuring breast density measurement thereby impacting the field of breast cancer prevention. Future studies will assess the direct correlation of UST measurements of breast density with breast cancer risk.

5. ACKNOWLEDGMENTS

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