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## Breast Imaging with the SoftVue Imaging system: First results

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### Abstract

For women with dense breast tissue, who are at much higher risk for developing breast cancer, the performance of mammography is at its worst. Consequently, many early cancers go undetected when they are the most treatable. Improved cancer detection for women with dense breasts would decrease the proportion of breast cancers diagnosed at later stages, which would significantly lower the mortality rate. The emergence of whole breast ultrasound provides good performance for women with dense breast tissue, and may eliminate the current trade-off between the cost effectiveness of mammography and the imaging performance of more expensive systems such as magnetic resonance imaging.

We report on the performance of SoftVue, a whole breast ultrasound imaging system, based on the principles of ultrasound tomography. SoftVue was developed by Delphinus Medical Technologies and builds on an early prototype developed at the Karmanos Cancer Institute. We present results from preliminary testing of the SoftVue system, performed both in the lab and in the clinic. These tests aimed to validate the expected improvements in image performance. Initial qualitative analyses showed major improvements in image quality, thereby validating the new imaging system design. Specifically, SoftVue's imaging performance was consistent across all breast density categories and had much better resolution and contrast. The implications of these results for clinical breast imaging are discussed and future work is described.

### Keywords

Breast imaging; tissue characterization; ultrasound tomography; ultrasound; SoftVue

## 1. INTRODUCTION

National cancer screening statistics indicate that only 51% of eligible women undergo annual mammograms<sup>1,2</sup>. Access, fear of radiation and discomfort are some of the factors that contribute to the low participation rate. Greater participation would lead to increased detection of breast cancer at an earlier stage, resulting in longer survival. Increased participation and improved breast cancer detection would have the greatest impact on the nearly 1 in 3 women who are diagnosed each year with later stage (regional or greater)

breast cancer, totaling approximately 60,000 women per year in the United States. The net effect would be an increase in survival and a corresponding decrease in mortality rates.

For women with dense breast tissue, who are at much higher risk for developing breast cancer<sup>3-7</sup>, the performance of mammography is at its worst<sup>7</sup>. Consequently many early cancers go undetected when they are the most treatable. Improved cancer detection for women with dense breasts would decrease the proportion of breast cancers diagnosed at later stages, which would significantly lower the mortality rate.

Although emerging technologies such as tomosynthesis and Positron Emission Mammography (PEM) may improve upon some of the limitations of standard mammography, they are unlikely to create a paradigm shift in performance because of their generation of ionizing radiation. On the other hand, magnetic resonance imaging (MRI) can significantly improve on these limitations by virtue of its volumetric, radiation-free imaging capability. Studies have shown that MR can have a positive impact in the breast management continuum ranging from risk assessment to diagnosis and treatment monitoring.<sup>8-18</sup> However, MR requires long exam times and intravenous contrast agents. Furthermore, MR has long been prohibitively expensive for routine use and there is a need for an equivalent low-cost alternative. Conventional sonography, which is inexpensive, comfortable and radiation-free, is not a practical alternative because of its operator dependence and the time needed to scan the whole breast. Therefore, it continues to play only an adjunctive role in breast imaging<sup>19</sup>. The emergence of whole breast ultrasound may eliminate the trade-off between the cost effectiveness of mammography and the imaging performance of MR.

We report on the performance of SoftVue, a whole breast ultrasound imaging system, based on the principles of ultrasound tomography (UST)<sup>20-27</sup>. SoftVue was developed by Delphinus Medical Technologies (DMT), and is based on an early prototype<sup>27-33</sup> developed at the Karmanos Cancer Institute (KCI). The SoftVue imaging system was designed to provide enhanced performance relative to the prototype. The new design was predicated upon the early prototype's clinical performance and pursued four aims for better image quality:

- (i) reducing the image slice thickness,
- (ii) improving the in-plane resolution,
- (iii) improving image contrast,
- (iv) artifact suppression.

The design goals were attained by increasing the transducer array density from 256 to 2048 and the central frequency from 2 to 3 MHz. Additional improvements focused on increasing patient throughput by integrating the reconstruction computer into the system, redesigning the water control system, increasing the number of transmit data channels from 11 to 512 and dramatically reducing the image reconstruction time from 9000 to 10 seconds per slice. The technical and clinical improvements are summarized in Table 1 below.

Testing of the SoftVue system has been performed in the lab to determine and confirm parameters such as data acquisition time, breast scan time and image reconstruction time. Testing at the KCI breast center assessed clinical performance parameters such as patient throughput and image quality. The purpose of this paper is to describe the initial technical and clinical performance of SoftVue and to present a qualitative assessment of its performance.

## 2. METHODS

The SoftVue imaging system was first tested in DMT laboratories during August and September of 2012. The SoftVue imaging system and the earlier prototype imaging system collected data from an anthropomorphic phantom, built by Ernest Madsen from the University of Wisconsin. The phantom was seeded with a number of inclusions (i.e. “masses”) ranging in size from 4 to 12 mm, as well as a group of microcalcifications. The phantom was designed to mimic a “dense” breast and challenge the imaging system performance to its operating limits.

Following laboratory testing, SoftVue was installed at the KCI’s, Alexander J. Walt Comprehensive Breast Center. SoftVue was initially co-located with the UST prototype to allow comparative clinical imaging. Clinical images were then obtained in the last quarter of 2012 to test the performance of SoftVue with human subjects. Participants were consented and data acquired under Wayne State University’s IRB (approval number #040912M1F). Fourteen healthy patient volunteers were scanned with SoftVue and with the UST prototype in order to assess relative performance differences. SoftVue’s image reconstruction algorithm was used to generate cross-sectional reflection B-Mode images of the phantom from both SoftVue and prototype data. For both systems, reflection images were corrected for refraction and attenuation effects to maximize image quality. A set of 45 tomograms (image slices) were generated for each patient. Overall image contrast and the presence of artifacts in each image stack was assessed using the software package ImageJ.

## 3. RESULTS

The SoftVue and prototype images produced from the phantom scans revealed the essential features of the phantom. Sample images are shown in Figure 1 with a schematic of the phantom components shown for comparison. The images shown reveal the skin, subcutaneous fat, glandular tissue, an 8mm cancer, a 12mm cyst, a 12mm fibroadenoma and a group of 500 micron sized microcalcifications. Both systems detected the relevant features but, as can be seen, in Figure 1, the SoftVue images have much greater contrast relative to background and greater signal to noise ratios for all 7 features. Furthermore, examination of the water background shows an almost complete elimination of artifacts relative to the prototype.

### In-Vivo Clinical Images

Figure 2 shows examples of reflection images obtained with the SoftVue imaging system. For increasing breast density on SoftVue reflection images, seen in Figure 2, underlying breast architecture of fibrous bands and/or Cooper’s ligaments become less and less visible

as the enveloping parenchymal tissue contributes to the increasing radiographic density. In more fatty breasts, the specular reflectors of the fibrous bands are thus readily identified while the non-specular echo signals from the extended denser tissues dominate the images of the denser breasts. As shown below, masses are not obscured by the dense parenchyma, as in standard ultrasound, due to their differences in biomechanical, and therefore acoustic, properties.

Figure 3 compares the reflection SoftVue images with those of the old prototype. The fibroglandular structures are revealed with greater sensitivity, contrast and resolution in the SoftVue images compared to the UST prototype. Despite the large contour of both breasts near the chest wall, the SoftVue images still visualize the entire breast with much better definition of the inner fibroglandular architecture. Even scanned at the same level per breast, the residual central parenchyma seen in the lower right SoftVue image is not even apparent on the degraded right prototype image. The 22cm diameter of the SoftVue ring array, compared with the 20cm prototype, allowed full visualization of breast skin boundary even near the chest wall. The much better noise reduction of the left SoftVue images also helps limit the near-field distortion that markedly degrades the prototype images.

#### 4. DISCUSSION

The above phantom imaging results generated high resolution scans of a breast phantom that was designed to push both SoftVue and the UST prototype to their limits. In clinical terms, the phantom was designed to represent a very dense breast, corresponding to BIRADS category IV breast density, or over 75% dense parenchyma by mammography. In acoustic terms, the glandular tissue represented in the phantom has a sound speed of 1550 m/s and attenuation of  $\sim 1$  dB/cm/MHz. At SoftVue's operating frequency of 3MHz, the total attenuation along a straight-line path passing through the center of the phantom, at its widest point (13 cm) is  $\sim 40$  dB. As indicated in Figure 1, this level of attenuation was a severe challenge for the UST prototype, despite operating at a lower frequency that should have allowed better penetration than SoftVue. Yet, the greater contrast resolution and noise reduction of SoftVue more than overcame any penetration deficit from the higher frequency. It is evident from SoftVue rendering of the glandular tissue, inclusions and the imbedded group of microcalcifications deep inside the phantom, that it performs well in this extreme case. The ability for whole breast ultrasound to perform well in dense breasts will be crucial for SoftVue to challenge mammography, which can miss up to 50% of cancers. Combined with the fact that women with dense breast tissue are much more likely to develop breast cancer, the clinical case for introducing whole breast ultrasound is compelling. If the SoftVue phantom results translate into the in-vivo domain for mass detection and discrimination above 5mm, the clinical case for SoftVue transitioning from diagnosis to screening may be made possible. We have begun scanning healthy volunteers and encouraging images were provided in the previous section.. These results demonstrated the ability to image breast architecture across the full range of breast density. Furthermore, it appears that the in-vivo images follow the phantom results, given the ability of SoftVue to penetrate even the densest breast tissues in a clinical setting.

A major gap in these initial results arise from not addressing SoftVue's clinical capability for mass detection and discrimination. To that end, we have begun a 300 patient study to quantify mass detectability and differentiation. The first cancer patient imaged thus far, presented with a 14 mm tumor (Figure 4). Figure 4 at least confirms that the cancer was detected within parenchymal tissue of a very dense breast. The reflection image was corrected using sound speed and attenuation data that was generated along with the reflection image. In the currently envisioned applications of SoftVue in the near term, reflection images will be used to provide diagnostic information using standard US-BIRADS criteria, pending FDA clearance to market. However, previous studies with the UST prototype suggest that sound speed and attenuation imaging can add diagnostic value that could augment the currently accepted US-BIRADS parameters. The ability of SoftVue to provide similar sound speed and attenuation information has not yet been tested but the 300 patient study will provide the needed clinical evaluation. A preliminary application of sound speed and attenuation data on the one cancer patient has successfully highlighted the mass and was based on a thresholding model that has been described fully in the literature<sup>32</sup>. The potential future of SoftVue imaging of breast cancer is shown in the right fusion image of Figure 4.

## 5. CONCLUSIONS

A new UST imaging system has been designed with the goal of achieving clinical relevance in the area of breast cancer detection and tissue characterization. The main design driver was to bridge the gap between research and clinical practice by building and improving upon an earlier research prototype. The resulting imaging system, named SoftVue, has now been tested on a worst-case-scenario phantom and clinical evaluation is starting in a 300 patient study. The phantom results and the preliminary in-vivo data indicate a major improvement over the previous prototype, particularly in the area of dense breast imaging where mammography's performance is at its weakest.

Successful implementation of this and other whole breast ultrasound technology will challenge existing paradigms. Current clinical practice is based on mammographic screening, with diagnostic follow-up and biopsy, frequently assisted by standard ultrasound and/or MR imaging. SoftVue has the potential to impact breast imaging and dramatically reduce the biopsy rate, which is the near term goal of SoftVue. In the long term, however, SoftVue may also challenge the screening paradigm and provide cost-efficacy by combining the screening and diagnostic steps. The current commercial version of SoftVue is the outcome of a platform UST technology whose performance could prove to be the equally effective, regardless of whether it is used for screening, diagnosis or future biopsy guidance. Furthermore, breast compression and use of ionizing radiation, or costly IV-enhanced MR would be averted.

Future near-term work is aimed at testing SoftVue's diagnostic performance through a 300 patient study that began in January, 2013. In the longer term, multi-center trials are planned that will test the suitability of SoftVue for screening of both the high-risk and general population.

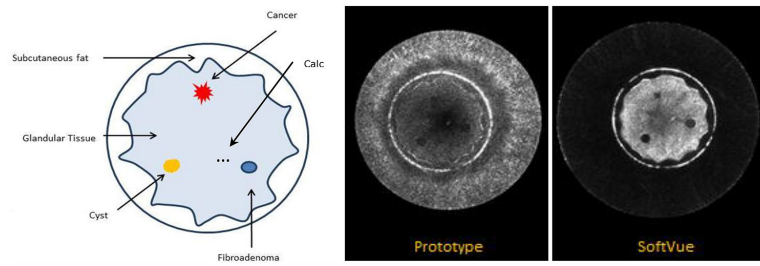
## 6. ACKNOWLEDGMENTS AND DISCLOSURES

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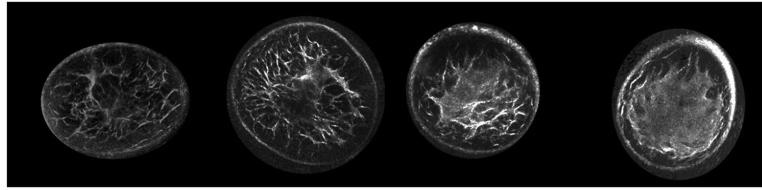
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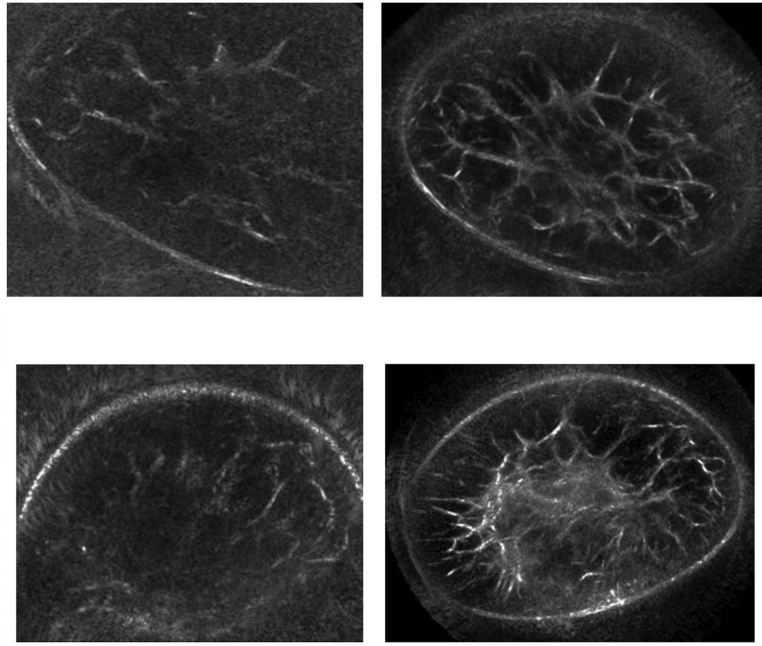


**Figure 1.** Cross-sectional schematic of anthropomorphic breast phantom (left). The reconstruction from the early prototype is shown in the center. The SoftVue B-mode reconstruction is on the right.

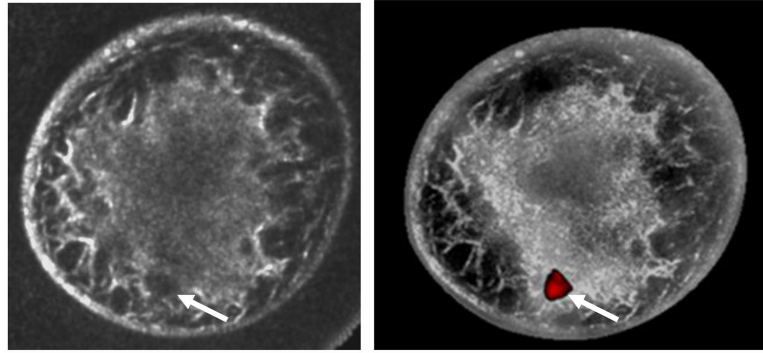




**Figure 2.**  
From left to right, cross-sectional coronal images of a fatty, scattered, heterogeneous and dense breast, as rendered by SoftVue.



**Figure 3.** Coronal breast images show SoftVue images on the right and prototype images on the left. A more fatty breast (top row) displays much better architectural detail, while the breast with more scattered central density (bottom row) is now clearly defined. Despite both breasts being scanned near the chest wall, the larger diameter of the SoftVue ring array than the prototype allowed clear boundary definition and much less near-field distortion from the breasts contacting the ring array (obscured upper and lower aspects of the top and bottom left images, respectively).



**Figure 4.** SoftVue images show reflection-only reconstruction on left with an irregular but ill-defined 1.4cm invasive ductal carcinoma at the 6-7 o'clock position (arrows). The fusion image on the right used previously established thresholds to create a grayscale overlay which highlights the distribution of dense parenchyma. Moreover, the cancer is well seen when mass sound speed and attenuation thresholds were applied. Further work is needed to validate this highly encouraging initial fusion performance with other masses or suspicious foci.

**Table 1**

SoftVue characteristics relative to prototype

<b>Technical Feature</b>	<b>UST prototype</b>	<b>SoftVue</b>	<b>Improvement</b>
Number of elements	256	2048	<b>8×</b>
Number of receive channels	256	512	<b>2×</b>
Number of transmit channels	11	512	<b>45×</b>
Data resolution	12 bits	14 bits	<b>4×</b>
Water usage	48 gal.	2.5-5 gal.	<b>10×</b>
Reconstruction time per slice	9,000 s	10 s	<b>900×</b>
Operating Frequency	2 MHz	3 MHz	<b>1.5×</b>
<b>Clinical Feature</b>	<b>UST prototype</b>	<b>SoftVue</b>	<b>Improvement</b>
Image resolution (volume)	$5 \times 0.5 \times 0.5$ mm	$2.5 \times 0.3 \times 0.3$ mm	<b>5×</b>
Max. breast diameter	20 cm	22 cm	<b>10%</b>
Patient Throughput	2/day	4/hour	<b>16×</b>

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