# Breast Tissue Characterization with Sound Speed and Tissue Stiffness

Cuiping Li[1,2], Gursharan Singh Sandhu[1], Michael Boone[1], Neb Duric[1,2], Peter Littrup[1-4], Mark Sak[1], Kenneth Bergman[1]

[1]*Delphinus Medical Technologies, Inc., Novi, MI, USA,*
 *E-Mail: cli@delphinusmt.com*
[2]*Department of Oncology, Wayne State University, Detroit, MI., USA,*
[3]*Department of Radiology, Wayne State University, Detroit, MI., USA,*
[4]*Ascension Crittenton Hospital, Rochester, MI, USA*

## Abstract

Mammography is not sufficiently effective for women with dense breast tissue. At least in North America and Europe, womenwith dense breasts appear to be at much higher risk for developing breast cancer. Consequently, many breast cancers go undetected  at  a  treatable stage. Improved cancer detection and characterization for women with dense breast tissue is urgently  needed. Our clinical study has shown that ultrasound tomography (UST) is an emerging technique that moves beyond B-mode imaging by its transmission capabilities. Transmission ultrasound provides additional tissue parameters such as  sound speed, attenuation, and tissue stiffness information. For women with dense breasts, these parameters can be used to assist in detecting malignant masses within glandular or fatty tissue and differentiating malignant and benign masses. This  paper focuses on the use of waveform ultrasound sound speed imaging and tissue stiffness information generated using  transmission data to characterize different breast tissues and breast masses. In-vivo examples will be given to assess its effectiveness.

*Keywords:* Sound speed, stiffness, spiculation, BIRADS category

## 1    Introduction

SomoInsight was a breast screening study that used whole breast ultrasound as a supplement to mammography. It demonstrated that whole breast ultrasound plus mammography outperformed mammography alone [1], leading to the first FDA approval for ultrasound screening

for breast cancer. However, one drawback of ultrasound screening is that the call back rate increases significantly (up to a factor of 2 in case of the SomoInsight study) due to lack of efficient lesion characterization [2].

Ultrasound tomography (UST) is an emerging technique that moves beyond B-mode imaging by its transmission capabilities [3-18]. Complementary to B-mode imaging that uses pulse echo signals, transmission ultrasound takes advantage of transmitted signals to provide additional characterization by measuring tissue parameters such as sound speed (SS), attenuation and stiffness which not only can potentially improve detection of subtle suspicious masses but also can help differentiate lesions.

In this study, we are going to illustrate the ability of SoftVue's waveform SS and stiffness image to render a variety of breast tissue and masses. We analyzed in vivo breast sound speed and tissue stiffness images to demonstrate SS and stiffness features for different breast tissues and unique signatures for a variety of breast masses. We present results from our analysis and discuss the implications of these results for clinical breast imaging.

The purpose of this study is to demonstrate the efficacy of SoftVue to characterize breast masses with SS and tissue stiffness color mapping, aiming at additional lesion characterization for possible reduction in call back rates.

## 2 Method

The SoftVue system utilizes a ring-shaped ultrasound transducer that acquires both backscattered signals and transmitted signals [19]. Backscattered signals are used to produce SoftVue reflection images (B-mode), while transmission signals are used to reconstruct tissue SS, attenuation and stiffness distribution. The resulting tissue stiffness images are color coded and overlaid on the reflection images. All these parameters can be used to assist characterization of breast tissue and breast masses.

Validation of SoftVue tissue stiffness images to assist breast mass characterization has been shown [2], where one anthropomorphic breast phantom was used for initial technique validation, and 11 in vivo breast masses' stiffness images were compared with the standard elastography measurements. In this study, we focused on using SoftVue's SS image and tissue stiffness images to help detection and characterization of breast tissue and masses. Our measuring metric for SS imaging are based on both the quantitative SS values and BI-RADS criteria (Table 1) [19]. Different mass boundary scores are sketched in Figure 1. We use stiffness imaging to addresses potential improved characterization of subtle suspicious masses. The method is illustrated in Table 2. A total of 15 in vivo breasts were imaged, representing a variety of breast lesions in patients whose breast density ranges from fatty to dense.

| Mass/Tissue Type | | | |
|---|---|---|---|
| | Mass/Tissue Shape | Mass Margin | SS Value |
| Cyst | Oval/round | Well circumscribed with distinct margin | Cyst: similar to water SS |
| Fibroadenoma | usually oval | Usually circumscribed | Fibroadenoma: similar or higher than water SS |
| Cancer | Irregular | Microlobulated, Indistinct, angular, spiculated | Cancer: Varies, usually greater than water SS and dense parenchyma. |
| Fat | Any shape | n/a | Less that water SS |

Table 1: Quantative SS and BI-RADS Criteria for Different Masses

| Mass/Tissue Type | Possible measurements |
|---|---|
| Cyst | Soft (bluer than background on average) |
| Fibroadenoma | Mixed (can be stiff or soft) |
| Cancer | Stiff (redder than background on average) |
| Fatty Tissue | Soft (blueish) |
| Dense Parenchyma | Stiff (generally not as stiff/red as cancer) |

Table 2: SoftVue Stiffness Signatures for Different Masses



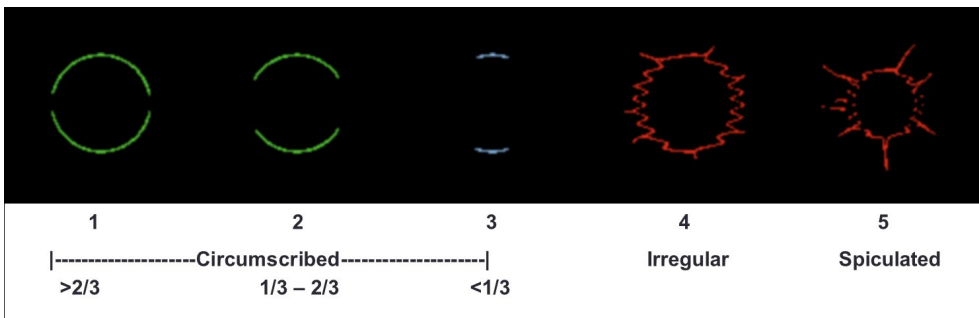| 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|
| |--------------------Circumscribed--------------------| | | Irregular | Spiculated |
| >2/3 | 1/3 – 2/3 | <1/3 | | |

Figure 1:   Mass boundary scores: 1-3: well to partially circumscribed; Score 4-5: irregular and spiculated, respectively.

SoftVue's SS and color stiffness images for the selected masses were analyzed and compared to the corresponding mammogram, standard ultrasound, and/or MRI, depending on their availability. A semi-transparent overlay of the SoftVue color stiffness images on the reflection image of the same coronal slice was used to ease the identification of the region of interest.

# 3    Results

The above metrics were applied to 15 in vivo breast images reconstructed with the SoftVue system. Results are  summarized in Table 3. All 5 cancers were characterized as stiff or moderately stiff (red) with mean SS range   from 1530-1571 m/s. Four fibroadenomas showed mixed stiffness (range of colors), one was stiff. Average SS  for these 5 fibroadenomas spans from 1534 m/s to 1563 m/s, which is greatly overlapping with the above cancers' SS. All 4 cysts had  mean SS from 1520 to 1534, which is very  close to water bath SS.

A few examples are presented below. A highly spiculated IDC is shown at 6 o'clock in figure 2 with an average SS of 1550 m/s and is stiffer than the surrounding dense breast tissue (Figure 2d). Spiculations of this IDC are better  presented in the zoom-in view (figure 2c). In standard B-mode (figure 2a), this mass shows strong shadowing, which   indicates high attenuation. Figure 3 shows a dense breast slice with a well circumscribed oval shaped fibroadenoma at 10:00 o'clock. In figure 3c we can clearly see the wall of the fibroadenoma. Figure 3d shows moderate stiffness compared   to adjacent dense parenchyma and an average SS of 1552 m/s. Again, standard B-model image is presented in  figure 3a for reference. An extremely dense breast slice is presented in figure 4, which has a well circumscribed cyst at  1:00 o'clock with an average SS of 1528 m/s. The stiffness image in figure 4d indicates that it is soft. In all three examples, fatty breast tissue has the lowest SS among normal breast tissue and breast masses, while breast  parenchyma generally has higher SS than cyst.

# 4    Discussion

The stiffness distribution of breast masses shows that cancers are generally stiffer compared to surrounding tissue, while cysts   appear soft. Fibroadenomas can be either soft, stiff or mixed of both. This trend is consistent with properties shown in   other modalities. SS values for cancers and fibroadenomas are greatly overlapping, while, as expected, cyst SS is consistently similar to water SS. The combination of SS, stiffness and mass margin   values demonstrates great potential to characterize benign from malignant breast masses.

However, there are some outlier cases that suggest we need additional pathology correlations. In this study, we analyzed two outlier cases. One case has scar tissue in the breast and the other case has benign non-fibroadenoma and non-cystic findings.  The scar tissue demonstrates spiculated boundary with high SS and stiffness. The benign finding in case 9 in Table

3 shows well circumscribed boundary, high SS and stiffness. SS and stiffness images for both cases are presented in figure 5a and 5b, respectively.

| Case # | Breast Density | Lesion Pathology | Average Lesion Size (cm) | Clock position | Mass Margin | Average Lesion SS compared to water SS | SoftVue stiffness assessment |
|---|---|---|---|---|---|---|---|
| 1 | Hetero-geneous | Cancer (ILC) | 0.93 | 5:00 | 5 | greater | Stiff |
| 2 | Scattered | Cancer (IDC) | 3.0 | 11:00 | 4 | greater | Stiff |
| 3 | Dense | Cancer (IDC) | 2 | 3:00 | 4 | greater | Moder-ately Stiff |
| 4 | Heteroge-neous | Cancer (IDC) | 1.23 | 6:00 | 5 | greater | Stiff |
| 5 | fatty | Cancer (DCIS) | | 11:00 | 4 | Moderately greater | stiff |
| 6 | Scattered | Fibroadeno-mas | 0.97, 1.38 | 4:00, 11:00 | 2, 1 | Greater, moderately greater | Mixed, Stiff |
| 7 | Dense | Fibroadenoma | 1.89 | 10:00 | 1 | greater | Mixed |
| 8 | Heteroge-neous | Scar | | 4:00 | 5 | greater | Stiff |
| 9 | Heteroge-neous | Solid Benign Mass | | 12:00 | 2 | greater | Stiff |
| 10 | Dense | Fibroade-noma | 2.19 | 3:00 | 2 | moderately greater | Mixed |
| 11 | Dense | Fibroade-noma | | 6:00 | 2 | greater | mixed |
| 12 | Dense | Cyst | | 10:00 | 2 | similar | soft |
| 13 | Extremely dense | Cyst | | 1:00 | 2 | similar | Soft |
| 14 | Heteroge-neous | Cyst | 1.66, 1.53 | 6:00, 9:00 | 2, 3 | similar, slightly greater | Moderately soft |
| 15 | Heteroge-neous | Cyst | 3.7 | 8:00 | 2 | similar | Soft |

Table 3: Summary table for all 15 cases

# 5    Conclusions

Our in vivo analyses show that, in addition to standard reflection ultrasound and margin-boundary considerations, combinations of SS and tissue stiffness information provide unique metrics to assist detection and characterization of different breast tissue and masses.

We have established detection/diagnosis metrics for waveform breast SS and through-transmission rendered tissue stiffness. A few examples demonstrate that a combination of SS and tissue stiffness  has great potential to assist detection and characterization of different breast tissues and breast masses.
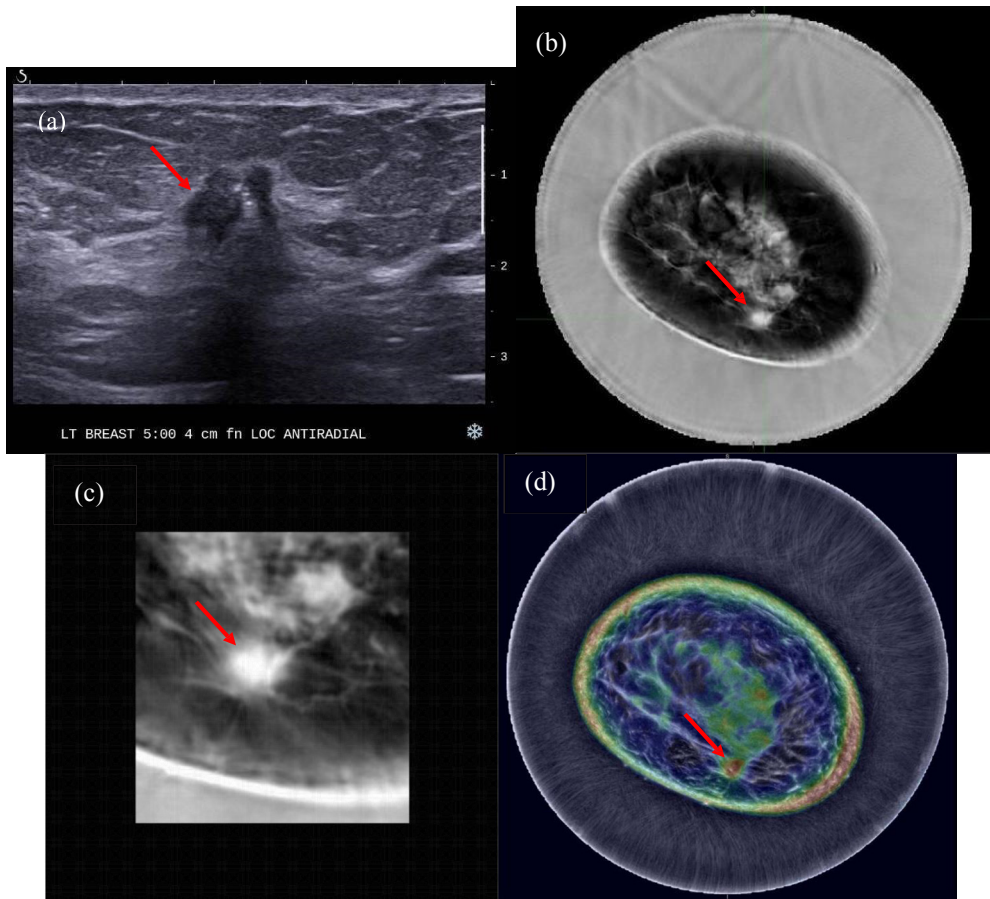


Figure 2:    Coronal slice with an IDC at 6:00 o'clock (red arrows). (a) Standard B-mode image for the IDC; (b) SoftVue SS image; (c) Zoomed-in SS view for the IDC; (d) Corresponding color-coded tissue stiffness overlay on reflection image (from blue to red color ~ soft to stiff).
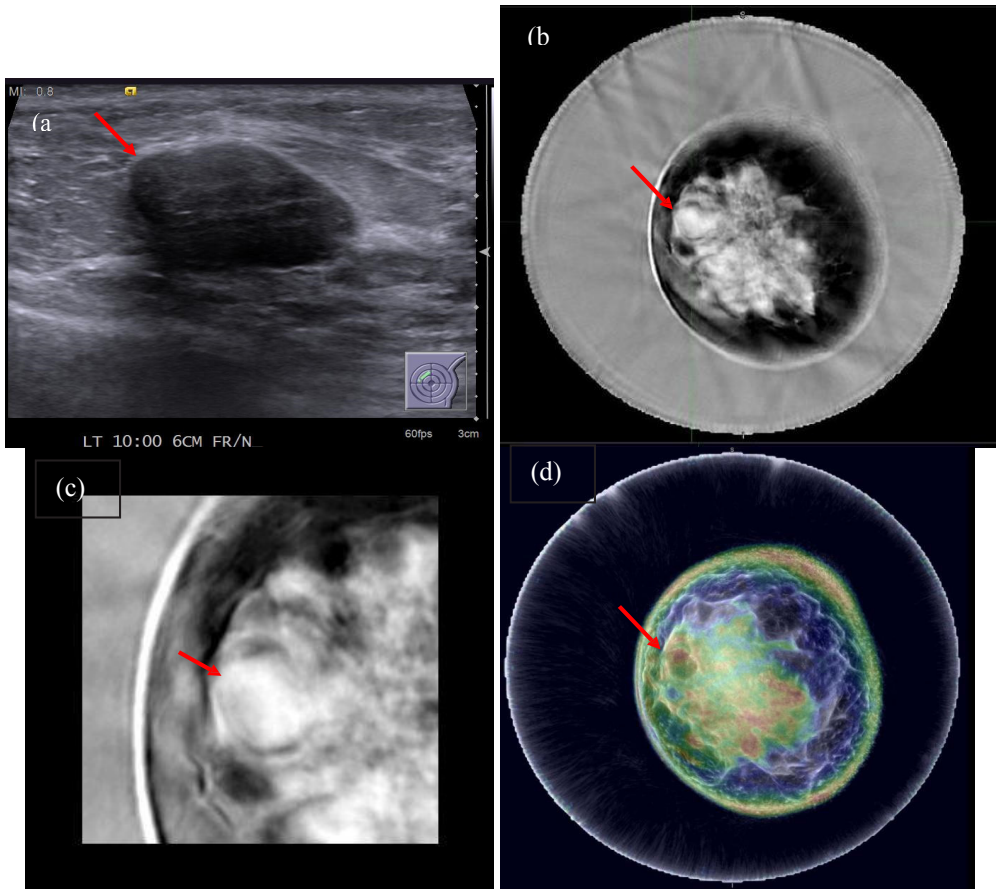
Figure 3: Coronal slice with a fibroadenoma at 10:00 o'clock (red arrows). (a) Standard B-mode image for the Fibroadenoma; (b) SoftVue SS image; (c) Zoomed-in SS view for the fibroadenoma; (d) Corresponding color-coded tissue stiffness overlay on reflection image.
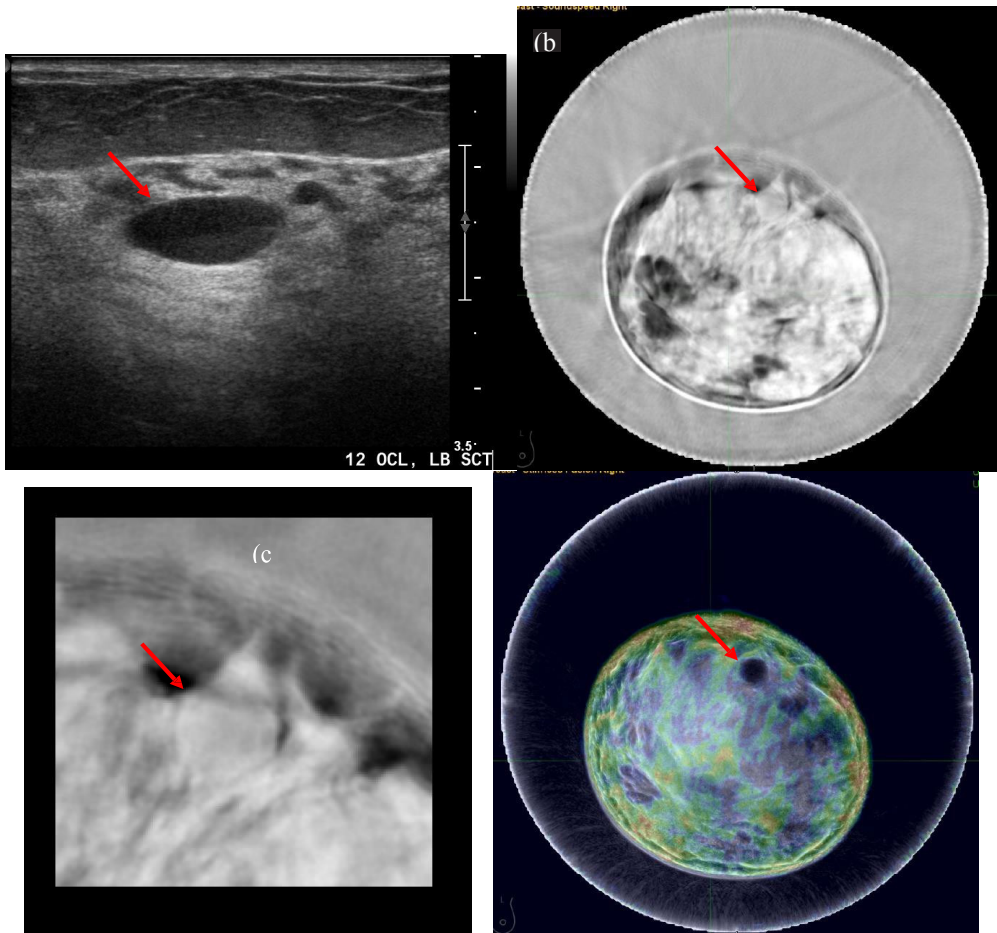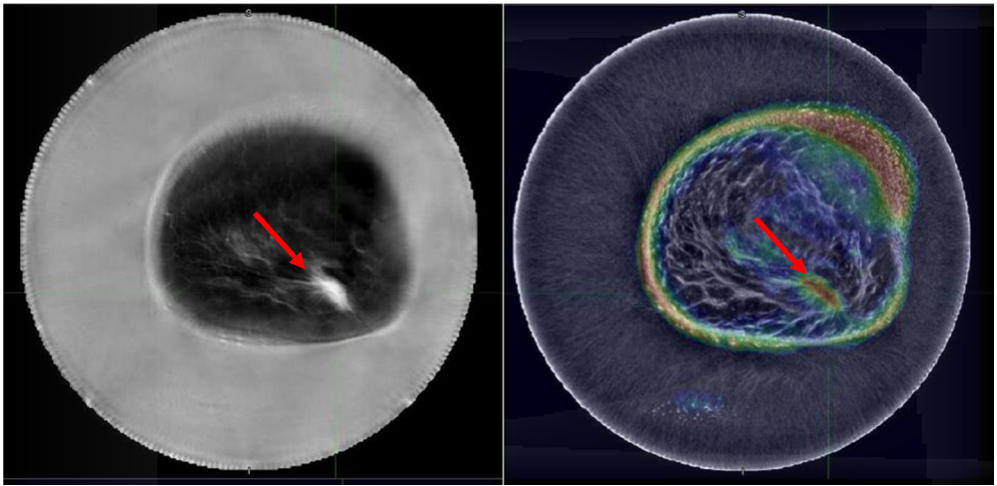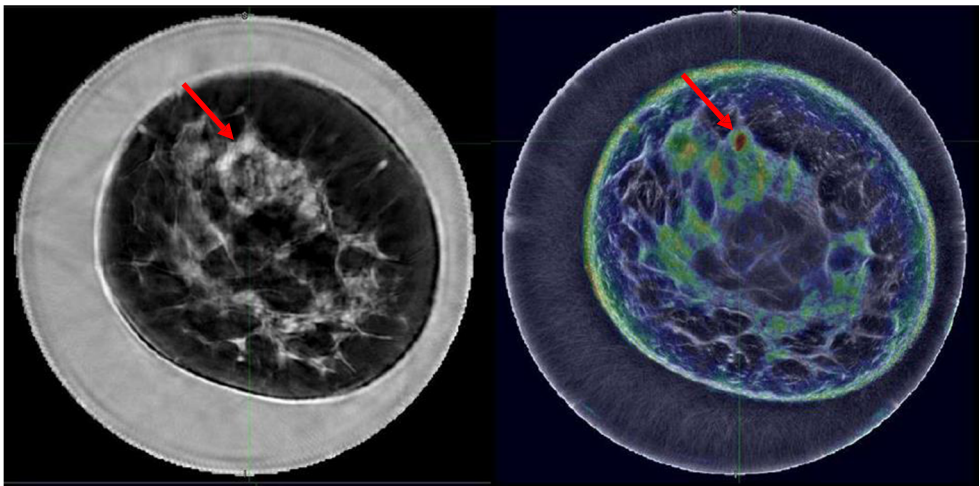
Figure 4: Coronal slice with a cyst at 1:00 o'clock (red arrows). (a) Standard B-mode image for the cyst; (b) SoftVue SS image; (c) Zoomed-in SS view for the cyst; (d) Corresponding color-coded tissue stiffness information overlay on reflection image.

(a)



(b)

Figure 5:    (a) Scar tissue. Left: SS; Right: Stiffness. (b)Benign finding – probable inspissated cyst. Left: SS; Right: Stiff-
ness. (Red arrows indicate masses).

# References

[1]     Brem, R. F., Tabár, L., Duffy, S. W., Inciardi, M. F., Guingrich, J. A., Hashimoto, B. E., ... & Miller, D. P. (2014). Assessing improvement in detection of breast cancer with three-dimensional automated breast US in women with dense breast tissue: The SomoInsight Study. Radiology.

[2]     Duric N, Littrup P., Li C., Roy O., Schmidt S., Seamans J., Wallen A. and Bei-Knight L.: Whole breast tissue characterization with ultrasound tomography, Proc. SPIE 9419, Medical Imaging, 94190G (2015).

[3]     Carson PL, Meyer CR, Scherzinger AL, Oughton TV. Breast imaging in coronal planes with simultaneous pulse echo and transmission ultrasound. Science 1981, Dec 4;214(4525):1141-3.

[4]     Andre MP, Janee HS, Martin PJ, Otto GP, Spivey BA, Palmer DA, "High-speed data acquisition in a diffraction tomography system employing large-scale toroidal arrays," International Journal of Imaging Systems and Technology 1997; Vol. 8, Issue 1:137-147.

[5]     Johnson SA, Borup DT, Wiskin JW, Natterer F, Wuebbling F, Zhang Y, Olsen C. Apparatus and Method for Imaging with Wavefields using Inverse Scattering Techniques. United States Patent 6,005,916 (1999).

[6]     Marmarelis VZ, Kim T, Shehada RE. Proceedings of the SPIE: Medical Imaging; Ultrasonic Imaging and Signal Processing 2003, Paper 5035-6.

[7]     Liu D-L, Waag RC. "Propagation and backpropagation for ultrasonic wavefront design," IEEE Trans. on Ultras.

[8]     Ferro. and Freq. Contr. 1997;44(1):1-13.

[9]     Gemmeke, H and Ruiter, N. "3D ultrasound computer tomography for medical imaging". Nuclear instruments and methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment, vol. 580, no. 2, pp 1057-1065, 2007.

[10]    Nicole V. Ruiter, Georg Göbel, Lutz Berger, Michael Zapf and Hartmut Gemmeke, "Realization of an optimized 3D USCT", Proc. SPIE 7968, 796805 (2011)

[11]    Duric N, Littrup P, Poulo L, Babkin A, Pevzner R, Holsapple E, Rama O, Glide C. Detection of Breast Cancer With Ultrasound Tomography: First Results with the Computerized Ultrasound Risk Evaluation (C.U.R.E) Prototype. Medical Physics Feb 2007; Vol 34 (2), pp. 773-785.

[12]    Glide-Hurst C, Duric N, Littrup P. Volumetric breast density evaluation from ultrasound tomography images. Med Phys. 2008; Vol. 35, Issue 9, pp. 3988-3997.

[13]    S. Schmidt, Z. Huang, N. Duric, C. Li and O. Roy. "Modification of Kirchhoff migration with variable sound speed and attenuation for acoustic imaging of media and application to tomographic imaging of the breast:. Med. Phys. 38, 998 (2011).

[14]  C. Li, N. Duric, P. Littrup, L. Huang. In vivo Breast Sound-Speed Imaging with Ultrasound Tomography.Ultrasound in Medicine & Biology, Volume 35, Issue 10, Pages 1615-1628. 2009.

[15]  Ranger B, Littrup P, Duric N, Chandiwala-Mody P, Li C, Schmidt S and Lupinacci J. Breast ultrasound tomography versus magnetic resonance imaging for clinical display of anatomy and tumor rendering: Preliminary results. AJR Am J Roentgenol Jan 2012; 198(1):233-9.

[16]  Duric, N. et al. Ultrasound Tomography Systems for Medical Imaging, in Emerging Imaging in Medical Diagnosis and Therapy. 2012. Taylor &Francis, Editors: Mark A. Anastasio; Patrick La Riviere. CRC Press.

[17]  Duric, N., Boyd, N., Littrup, P., Sak, M., Myc, L., Li, C., ... & Albrecht, T. (2013). Breast density measurements with ultrasound tomography: A comparison with film and digital mammography. Medical physics, 40, 013501

[18]  Duric, Neb, Peter Littrup, Cuiping Li, Olivier Roy, Steven Schmidt, Xiaoyang Cheng, John Seamans, Andrea Wallen, and Lisa Bey-Knight. "Breast imaging with SoftVue: initial clinical evaluation." In SPIE Medical Imaging, pp. 90400V-90400V. International Society for Optics and Photonics, 2014.

[19]  http://pubs.rsna.org/doi/pdf/10.1148/rg.305095144