Quantifying the impact of breast density on the lag-one coherence of hypoechoic masses

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***Abstract*—Ultrasound imaging is often used as a diagnostic tool to supplement mammography particularly in patients with dense breast tissue, because the ability of a mammogram to detect cancer is significantly lower in these patients. However, when breast tissue is dense, interactions between tissue layers can result in acoustic clutter in the ultrasound image, obscuring masses of interest and resulting in more false positives with increasing breast density. This work investigates the impact of breast density on a quantitative coherence-based metric, lag-one coherence (LOC). Greater separability was seen between fluid and solid masses within dense breast tissue compared to non-dense breast tissue. Specifically, the sensitivity and specificity for fluid-filled mass detection in non-dense breast tissue were 0.768 and 0.688, respectively, which improved to 0.911 and 0.898, respectively for masses within dense breast tissue. These insights support deployment of LOC as a quantitative differentiation tool, particularly for patients with dense breasts who are most commonly referred for ultrasound exams resulting in unnecessary biopsies due to the presence of acoustic clutter.**

I. Introduction

Breast cancer is the most common cancer among women and the second leading cause of cancer death [1]. Ultrasound imaging is often used as a supplement to mammography to diagnose breast cancer, particularly in patients with dense breast tissue, because mammographic sensitivity (i.e., the ability of a mammogram to detect cancer) is significantly lower in patients with dense breast tissue [2]. However, in the ACRIN 6666 trial, more false positives were seen in ultrasound with increasing breast density [3], which is indicative of an interaction between dense breast tissue and the effectiveness of ultrasound.

One potential cause of this decreasing performance of ultrasound with increasing breast density is acoustic clutter. Acoustic clutter is a noise artifact in ultrasound images that appears as diffuse echoes obscuring masses of interest [4] and is often caused by interactions between tissues layers. Due to the heterogeneity of breast tissue, breast ultrasound images are particularly susceptible to this noise caused by acoustic clutter.

To combat the effects of acoustic clutter, previous work has demonstrated that coherence-based beamforming can remove acoustic clutter and improve the differentiation between solid and fluid-filled breast masses [5], [6]. Rather than displaying traditional brightness information, coherence-based beamforming displays the spatial coherence of received signals across the ultrasound transducer, thereby removing contributions of incoherent clutter sources [7], [8]. This coherence information can be displayed as a clinical overlay to aid in diagnosis [9]. Focusing on one specific coherence-based feature, previous work investigated lag-one coherence (LOC) as a quantitative coherence-based metric to improve this differentiation between solid and fluid-filled breast masses [10]. LOC measures the spatial coherence of the backscattered ultrasound data from neighboring elements across the receive aperture [11] and is useful as a quantitative metric that does not require complete formation of an image or require reader input [10].

Drawing on the insights from this body of literature that dense breast tissue introduces increased levels of acoustic clutter, coherence-based beamforming can remove acoustic clutter, and LOC is effective at distinguishing solid from fluid breast masses, we hypothesize that breast tissue density will have an impact on the performance of LOC when distinguishing fluid from solid breast masses. To investigate this hypothesis, the work in this paper quantitatively assesses the LOC for several masses in both dense and non-dense breast tissue through a histogram analysis. In addition, we stratify the LOC values by breast density and compare the accuracy, sensitivity, and specificity of fluid-filled mass detection within each tissue type. Finally, we present LOC images to visualize qualitative differences between masses in both dense and non-dense breast tissue.

II. Methods

A. Data Acquisition

Twenty-four patients with twenty-seven suspicious hypoechoic breast masses were enrolled in our ongoing study after informed consent and approval from the Johns Hopkins Institutional Review Board. Patients were scanned immediately prior to their scheduled core-needle biopsy using an Alpinion ECUBE12R research ultrasound scanner connected to either an Alpinion L8-17 or Alpinion L3-8 linear ultrasound transducer. Raw radiofrequency (RF) data were acquired, saved, and processed offline.

In addition to the ultrasound data, the mammographic breast density of each patient was retrospectively determined from their most recent mammogram. Mammographic breast density is broken down into four categories [12]: (A) almost entirely fat, (B) scattered fibroglandular densities, (C) heterogeneously

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dense, and (D) extremely dense. These categories can be further reduced into non-dense breast tissue (combining A and B) and dense breast tissue (combining C and D). Patients with no prior mammogram were excluded from this analysis because mammographic breast density was unknown.

B. Lag-one Coherence

Raw RF data was processed off-line to measure lag-one coherence (LOC) [11], using the following equation to achieve a single coherence function:

$$\hat{R}[m] = \frac{1}{N-m}\sum_{i=1}^{N-m}\frac{\sum_{n=n_1}^{n_2} s_i[n]s_{i+m}[n]}{\sqrt{\sum_{n=n_1}^{n_2} s_i^2[n]\sum_{n=n_1}^{n_2} s_{i+m}^2[n]}} \quad (1)$$

where N is the number of elements in the transducer, m is the number of elements between two points in the aperture, or lag, $s_i[n]$ is a time-delayed, zero-mean signal received at element i from depth n. This calculation was performed with an axial correlation kernel of size $k = n_2 - n_1$ equal to one and a half wavelengths. To calculate LOC, Eq. 1 was evaluated at $m = 1$. LOC was calculated for each location n within a region of interest (ROI) at the center of each breast mass, resulting in multiple LOC values for each mass. The LOC values were then assessed based on mass type and stratified by mammographic breast density.

C. Statistical Analysis

Sensitivity and specificity of fluid-filled mass detection were measured by parameterizing the measured LOC values and varying the LOC threshold for fluid-filled mass detection. LOC values above the threshold were classified as solid and LOC values below the threshold were classified as fluid. Specifically, sensitivity and specificity were measured as follows:

$$\text{Sensitivity} = \frac{TP}{TP+FN} \quad (2)$$

$$\text{Specificity} = \frac{TN}{TN+FP} \quad (3)$$

where a true positive (TP) or false negative (FN) was defined as a pixel within a fluid-filled mass with an LOC value below or above a specific LOC threshold, respectively. A true negative (TN) or false positive (FP) was defined as a pixel within a solid mass with an LOC value above or below a specific LOC threshold, respectively. With these measurements, a receiver operating characteristic (ROC) curve was used to determine the optimal LOC threshold value by measuring the distance to the ideal operating point of (0,1).

TABLE I
SENSITIVITY, SPECIFICITY, AND OPTIMAL LOC THRESHOLD TO DISTINGUISH FLUID FROM SOLID MASSES.

Type	Number of Masses	Sensitivity	Specificity	LOC Threshold
Non-Dense	13	0.768	0.688	0.347
Dense	14	0.911	0.898	0.307
All	27	0.853	0.829	0.337

III. RESULTS & DISCUSSION

Table I shows the sensitivity, specificity, and optimal LOC threshold to distinguish fluid from solid masses for each stratification of breast density. The sensitivity and specificity of the optimal LOC threshold for the 27 masses included in this study were 0.853 and 0.829, respectively. Stratifying these results by breast density reveals greater separability between fluid and solid masses in dense breast tissue. Specifically, the sensitivity and specificity of the optimal LOC threshold in non-dense breast tissue (13 masses total) were 0.768 and 0.688, respectively, which improved to 0.911 and 0.898, respectively in dense breast tissue (14 masses total). Rounded to one significant figure, the optimal LOC thresholds reported in Table I were similar for both dense and non-dense breast tissue.

Fig. 2 shows example B-mode and LOC images for one fluid-filled and one solid mass within each dense and non-dense breast tissue. The center of the diverging colorbar was determined based on the optimal LOC threshold shown in Table I (i.e., 0.337 for all masses). Because the LOC images are displayed with the same colorbar, the improved separation between solid and fluid-filled masses can be visualized in Fig. 2(c) where the blue is darker inside the fluid-filled mass in dense breast tissue compared to Fig. 2(a) where the fluid-filled mass is in non-dense breast tissue.

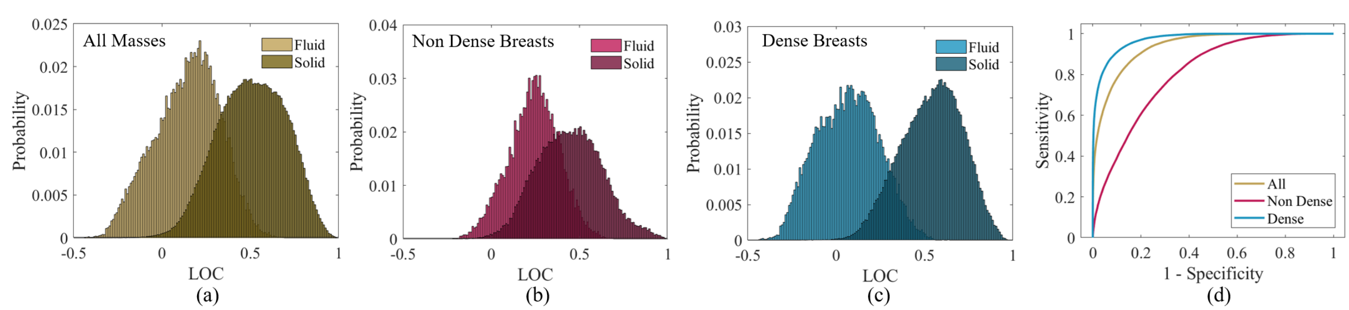

Fig. 1. Histograms of lag-one coherence (LOC) showing a distinction between solid and fluid in (a) all masses and masses in the two subsets of (b) non-dense and (c) dense breast tissue. (d) Associated ROC curves showing a greater area under the curve for masses surrounded by dense breast tissue (compared to masses surrounded by non dense breast tissue).

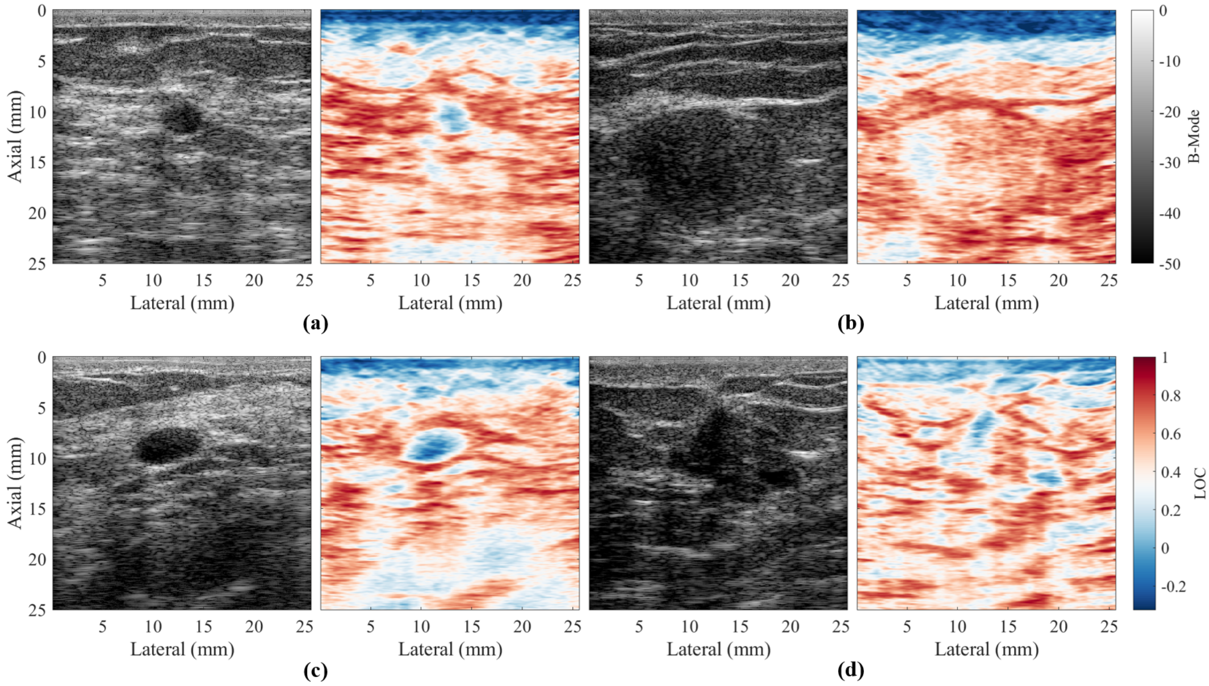

Fig. 2. Example (left) B-mode and (right) LOC images for fluid-filled (a,c) and solid (b,d) masses within (a,b) non-dense and (c,d) dense breast tissue.

These results demonstrate that the differentiation between fluid-filled and solid masses is improved when the mass is within dense breast tissue. When breast tissue is dense, the additional interactions between tissue layers increase the incoherent noise within fluid-filled masses, which corresponds to a decrease in LOC, and is likely responsible for the increased separability. These insights support deployment of LOC as a quantitative differentiation tool, particularly for patients with dense breasts who are most commonly referred for ultrasound exams and could generate confusing images (leading to uncertainty in diagnoses, unnecessary biopsies, and greater patient anxiety) due to the presence of acoustic clutter.

While the LOC images in Fig. 2 significantly differ from the typical B-mode ultrasound images, they could also be presented in the form of a clinical overlay similar to the coherence-based overlay presented in [9]. In addition, because LOC is a single quantitative tool, it can potentially add quantitative information to the diagnostic pipeline, similar to the quantification provided by some elastographic techniques such as supersonic shear imaging [13]. Although LOC was computed offline for this study, the same values can be computed in real-time by employing graphical processing units (GPUs) [14] or deep learning [15].

IV. Conclusion

This paper summarizes the impact of breast density on the lag-one coherence (LOC) of hypoechoic breast masses. When stratified by mammographic breast density, the LOC within fluid-filled masses is decreased, resulting in increased separation between fluid-filled and solid breast masses. These results are promising for the use of LOC as a quantitative differentiation tool, particularly for patients with dense breasts who are more often referred for ultrasound exams.

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References

[1] R. L. Siegel, K. D. Miller, and A. Jemal, "Cancer statistics, 2018," *CA: A Cancer Journal for Clinicians*, vol. 68, no. 1, pp. 7–30, 2018.

[2] M. T. Mandelson, N. Oestreicher, P. L. Porter, D. White, C. A. Finder, S. H. Taplin, and E. White, "Breast density as a predictor of mammographic detection: Comparison of interval- and screen-detected cancers," *JNCI: Journal of the National Cancer Institute*, vol. 92, no. 13, pp. 1081–1087, 2000.

[3] W. A. Berg, A. I. Bandos, E. B. Mendelson, D. Lehrer, R. A. Jong, and E. D. Pisano, "Ultrasound as the primary screening test for breast cancer: analysis from acrin 6666," *JNCI: Journal of the National Cancer Institute*, vol. 108, no. 4, 2016.

[4] M. A. Lediju, M. J. Pihl, J. J. Dahl, and G. E. Trahey, "Quantitative assessment of the magnitude, impact and spatial extent of ultrasonic clutter," *Ultrasonic Imaging*, vol. 30, no. 3, pp. 151–168, 2008.

[5] A. Wiacek, O. M. H. Rindal, E. Falomo, K. Myers, K. Fabrega-Foster, S. Harvey, and M. A. L. Bell, "Robust short-lag spatial coherence imaging of breast ultrasound data: Initial clinical results," *IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control*, vol. 66, no. 3, pp. 527–540, 2018.

[6] A. Wiacek, E. Oluyemi, K. Myers, L. Mullen, and M. A. L. Bell, "Coherence-based beamforming increases the diagnostic certainty of distinguishing fluid from solid masses in breast ultrasound exams," *Ultrasound in Medicine & Biology*, vol. 46, no. 6, pp. 1380–1394, 2020.

[7] M. A. Lediju, G. E. Trahey, B. C. Byram, and J. J. Dahl, "Short-lag spatial coherence of backscattered echoes: Imaging characteristics," *IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control*, vol. 58, no. 7, pp. 1377–1388, 2011.

[8] A. A. Nair, T. D. Tran, and M. A. L. Bell, "Robust short-lag spatial coherence imaging," *IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control*, 2017.

[9] A. Wiacek, E. Falomo, K. Myers, O. M. H. Rindal, K. Fabrega-Foster, S. Harvey, and M. A. L. Bell, "Clinical feasibility of coherence-based beamforming to distinguish solid from fluid hypoechoic breast masses," in *2018 IEEE International Ultrasonics Symposium (IUS)*. IEEE, 2018, pp. 1–4.

[10] A. Wiacek, E. Oluyemi, K. Myers, L. Mullen, and M. A. L. Bell, "Coherence-based beamforming improves the diagnostic certainty of breast ultrasound exams," in *2020 IEEE International Ultrasonics Symposium (IUS)*. IEEE, 2020, pp. 1–4.

[11] W. Long, N. Bottenus, and G. E. Trahey, "Lag-one coherence as a metric for ultrasonic image quality," *IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control*, vol. 65, no. 10, pp. 1768–1780, 2018.

[12] D. A. Spak, J. Plaxco, L. Santiago, M. Dryden, and B. Dogan, "Bi-rads® fifth edition: A summary of changes," *Diagnostic and interventional imaging*, vol. 98, no. 3, pp. 179–190, 2017.

[13] A. Athanasiou, A. Tardivon, M. Tanter, B. Sigal-Zafrani, J. Bercoff, T. Deffieux, J.-L. Gennisson, M. Fink, and S. Neuenschwander, "Breast lesions: quantitative elastography with supersonic shear imaging—preliminary results," *Radiology*, vol. 256, no. 1, pp. 297–303, 2010.

[14] D. Hyun, A. L. C. Crowley, and J. J. Dahl, "Efficient strategies for estimating the spatial coherence of backscatter," *IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control*, vol. 64, no. 3, pp. 500–513, 2017.

[15] A. Wiacek, E. González, and M. A. L. Bell, "CohereNet: A Deep Learning Architecture for Ultrasound Spatial Correlation Estimation and Coherence-Based Beamforming," *IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control*, 2020.