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Multi-covariate Imaging of Sub-resolution Targets

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Abstract

Conventional B-Mode ultrasound imaging assumes targets consist of collections of point scatterers. Diffraction, however, presents a fundamental limit on a scanner's ability to resolve individual scatterers in most clinical imaging environments. Well-known optics and ultrasound literature has characterized these diffuse scattering targets as spatially incoherent and statistically stationary. In this paper, we apply a piecewise-stationary statistical model to diffuse scattering targets, in which the covariance of backscattered echoes can be described as the linear superposition of constituent components corresponding to echoes from distinct spatial regions in the field. Using this framework, we present Multi-covariate Imaging of Sub-resolution Targets (MIST), a novel estimation-based method to image the statistical properties of diffuse scattering targets, based on a decomposition of aperture domain spatial covariance. The mathematical foundations of the estimator are analytically derived, and MIST is evaluated in phantom, simulation, and *in vivo* studies, demonstrating consistent improvements in CNR and speckle statistics across imaging targets, without an apparent loss in resolution.

Keywords

Ultrasound; probabilistic and statistical methods; quantification and estimation

I. INTRODUCTION

THE conventional approach to beamforming in diagnostic ultrasound imaging relies on a simple geometric model. Using the expected time of flight of acoustic waves in the field, delay-and-sum methods are employed to coherently combine echoes received at the array elements, providing a basis to spatially map the scattering strength of the imaging target.

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This fundamental paradigm of clinical ultrasound image formation has remained unchanged for many years.

With the advent of software-based processing of ultrasound echo data, many alternatives to the traditional delay-and-sum approach have been proposed to improve image quality over conventional B-Mode imaging. Many of these beamforming methods employ aperture domain spatial coherence as a contrast mechanism. In some cases, beamsummed data are weighted by a spatial coherence metric, as in the Generalized Coherence Factor [1] and Phase Coherence Factor [2]. Other methods directly map pixel brightness to measures of coherence. In short-lag spatial coherence (SLSC) imaging [3], pixel brightness is determined directly by the spatial coherence of received echoes, integrated up to a maximum lag in the receive aperture. The filtered-delay multiply and sum beamformer (F-DMAS) employs a pairwise multiplication and square root operation before summation, showing high sensitivity to spatial coherence [4], [5].

Another popular approach is to minimize incoherent noise through a constrained optimization problem. Various implementations of the minimum variance distortionless response (MVDR) beamformer [6], [7] have been adapted to diagnostic ultrasound [8]–[12], demonstrating reduced sidelobe levels and improved lateral resolution. Wiener filtering has also been applied to the beamforming process [13], and combined with coherence- and MVDR-based processing [14], [15]. Other approaches include aperture domain model image reconstruction (ADMIRE) [16] to model and remove the effects of multipath scattering in the aperture domain, and frequency-space prediction filtering (FXPF) [17] to filter out aperture domain incoherence using an autoregressive model.

Many of the above methods have been shown to improve image quality over conventional B-mode. However, to the extent that the above methods use spatial coherence as a mechanism to distinguish signal and noise, most rely on a general classification scheme to distinguish coherent and incoherent portions of the signal. SLSC and other methods take an *ad hoc* approach to image formation, only loosely based on a statistical model of ultrasound backscatter, and do not use the entire two-dimensional covariance matrix in the image formation process, thus discarding important statistical information which could be used to improve image quality.

In this paper, we apply a piecewise-stationary model to diffuse, sub-resolution targets, in which the covariance of backscattered echoes is the linear superposition of constituents from distinct spatial regions. Under this framework, we derive and validate an estimation-based imaging method to quantify and isolate the contributions of distinct components to the received echo data covariance. We have dubbed this method Multi-covariate Imaging of Sub-resolution Targets, or MIST. We hypothesize this approach to image formation is fundamentally better-suited to the diffuse scattering environments nearly universal in medical ultrasound imaging than conventional beamforming methods.

This paper is organized as follows. In Section II, we review the relevant theory of spatial covariance in medical ultrasound, and derive a mathematical framework to estimate the constituent components of the covariance matrix. Data acquisition methods are presented in

Section III. Simulation, experimental and *in vivo* data are presented and discussed in Sections IV and V, respectively. Conclusions are presented in Section VI.

II. THEORY

A. Spatial Covariance in Medical Ultrasound

The one-way sensitivity for a two-dimensional complex aperture function, $A(\mathbf{X}_a, f)$, located at $z = 0$, is given by the Fresnel diffraction integral [18]:

$$P(\mathbf{X}_s, z, f) = \frac{e^{jkz} e^{jk(\mathbf{X}_s' \mathbf{X}_s)/2z}}{j\lambda z} \times \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} \left\{ A(\mathbf{X}_a, f) e^{\frac{jk\mathbf{X}_a' \mathbf{X}_a}{2z}} \right\} e^{\frac{-2\pi j \mathbf{X}_s' \mathbf{X}_a}{\lambda z}} d\mathbf{X}_a, \quad (1)$$

where $P(\mathbf{X}_s, z, f)$ is the one-way sensitivity pattern for $A(\mathbf{X}_a, f)$, valid in the near field of the aperture. The aperture plane coordinates are given by $\mathbf{X}_a = [x_a, y_a]^T$, and the source (or field) plane coordinates are given by $\mathbf{X}_s = [x_s, y_s]^T$. The frequency is given by f and the wave number by $k = 2\pi/\lambda$, where λ is the wavelength. Equation (1) expresses the field pressure distribution as a scaled Fourier transform of the product of the complex aperture function and a quadratic phase term, evaluated at spatial frequencies $(f_x, f_y) = \left(\frac{x_s}{\lambda z}, \frac{y_s}{\lambda z}\right)$.

In medical ultrasound, the spatial covariance in the aperture domain can be related to the source pressure distribution through the van Cittert-Zernike (VCZ) theorem [19], [20]. For diffuse targets, ultrasonic backscatter can be considered an incoherent source, with intensity distribution equal to the squared magnitude of the product of the transmit beam amplitude (P) and the target distribution (χ) given by:

$$R(\Delta\mathbf{X}_a, z, f) = \int_{-\infty}^{+\infty} \int_{-\infty}^{+\infty} |P(\mathbf{X}_s, z, f) \chi(\mathbf{X}_s, z, f)|^2 \times e^{\frac{-2\pi j(\mathbf{X}_s' \Delta\mathbf{X}_a)}{\lambda z}} d\mathbf{X}_s, \quad (2)$$

where $\mathbf{X}_a$ represents the distance between two points $\mathbf{X}_1$ and $\mathbf{X}_2$ in the aperture plane. Equation (2) expresses a Fourier relationship between the measured spatial covariance and the field intensity distribution. Assuming a spatially incoherent target with uniform scattering strength, the predicted spatial covariance is simply the Fourier transform of the transmit intensity. At the transmit focal depth, this reduces to the autocorrelation of the transmitting aperture. For an unapodized linear array, the predicted spatial covariance is given by a triangle function, decreasing linearly with increasing element separation, or lag, up to the size of the transmitting aperture.

B. Piecewise-Stationarity of Diffuse Scattering Targets

In the optics and ultrasound literature, diffuse scattering targets have been traditionally modeled as spatially incoherent and statistically stationary [19]–[23]. Expanding this model to incorporate piecewise-stationary statistics, it can be shown that the covariance of

backscatter from diffuse targets is the linear superposition of constituents from distinct spatial regions. This result is given by:

$$\mathbf{R} = \sum_{p=1}^P \alpha_p^2 \mathbf{R}_p, \quad (3)$$

where the covariance $\mathbf{R}$ is represented as a superposition of P covariances $\mathbf{R}_p$, weighted by variances α_p^2 . Equation (3) implies the estimated data covariance matrix can be decomposed into a set of constituent components of echoes from distinct regions of the source distribution and from additive noise sources.

C. Estimation of the Constituent Components

The estimated data covariance matrix from an M -channel array at time sample t is given by:

$$\hat{\mathbf{R}}[t] = \mathbf{x}[t]\mathbf{x}^H[t], \quad (4)$$

where $\hat{\mathbf{R}}[t]$ represents the $M \times M$ covariance matrix, and $\mathbf{x}[t]$ is the $M \times 1$ vector of complex, time-delayed array data. The conjugate transpose operation is given by $(^H)$. In practice, the covariance matrix $\mathbf{R}$ is difficult to estimate from a point measurement at a single depth. Spatial averaging can be used to improve the conditioning of the estimate, given by:

$$\hat{\mathbf{R}}[t] = \frac{1}{T} \sum_{\tau=-T/2}^{T/2} \mathbf{x}[t+\tau]\mathbf{x}^H[t+\tau] \quad (5)$$

where T is a small axial window, or kernel, over which $\hat{\mathbf{R}}$ is averaged, typically on the order of a wavelength. The following derivation refers to a covariance estimate at a single sample. Accordingly, the sample index t has been removed for simplicity in notation, such that $\hat{\mathbf{R}} = \hat{\mathbf{R}}[t]$.

We consider the true data covariance matrix $\mathbf{R}$ to be a combination of constituent covariance models $\mathbf{A}_i$, weighted by scalar variances α_i^2 :

$$\mathbf{R} = \sum_{i=1}^P \alpha_i^2 \mathbf{A}_i + \mathbf{N}, \quad (6)$$

where $\mathbf{N}$ is a noise matrix to model the uncertainty in the observation. $\mathbf{R}$, $\mathbf{A}_i$, and $\mathbf{N}$ are of shape $M \times M$. The number of constituent models is given by P . The covariance $\mathbf{R}$ and model matrices $\mathbf{A}_i$ are assumed Hermitian symmetric.

A loss function is defined to minimize the squared error over the variances α_i^2 :

$$\epsilon = \left\| \hat{\mathbf{R}} - \sum_{i=1}^P \alpha_i^2 \mathbf{A}_i \right\|_F^2, \quad (7)$$

where the Frobenius norm is represented by $(\cdot)_F$. Additionally, let $\boldsymbol{\alpha}^2$ be the $P \times 1$ vector of variances:

$$\boldsymbol{\alpha}^2 = [\alpha_1^2, \alpha_2^2, \dots, \alpha_P^2]^T. \quad (8)$$

The least squares estimator is then defined as:

$$\hat{\boldsymbol{\alpha}}_{\text{ls}}^2 = \arg \min_{\boldsymbol{\alpha}^2} \left\| \hat{\mathbf{R}} - \sum_{i=1}^P \alpha_i^2 \mathbf{A}_i \right\|_F^2. \quad (9)$$

The variance estimates are calculated as the $\boldsymbol{\alpha}^2$ vector for which the gradient of the loss function is equal to zero ($\nabla_{\boldsymbol{\alpha}^2} \epsilon = 0$). A brief derivation is presented below.

The loss function first expanded using the definition of the Frobenius norm [24]–[26]:

$$\epsilon = \text{Tr} \left[\left(\hat{\mathbf{R}} - \sum_{i=1}^P \alpha_i^2 \mathbf{A}_i \right)^H \left(\hat{\mathbf{R}} - \sum_{j=1}^P \alpha_j^2 \mathbf{A}_j \right) \right], \quad (10)$$

where Tr is the trace operator and the conjugate transpose operation is represented by $(^H)$. The inner terms can be expanded as:

$$\epsilon = \text{Tr} \left[\hat{\mathbf{R}}^H \hat{\mathbf{R}} - \hat{\mathbf{R}}^H \left(\sum_{j=1}^P \alpha_j^2 \mathbf{A}_j \right) - \left(\sum_{i=1}^P \alpha_i^2 \mathbf{A}_i^H \right) \hat{\mathbf{R}} + \left(\sum_{i=1}^P \alpha_i^2 \mathbf{A}_i^H \right) \left(\sum_{j=1}^P \alpha_j^2 \mathbf{A}_j \right) \right]. \quad (11)$$

Given $\text{Tr} [\mathbf{A} + \mathbf{B}] = \text{Tr} [\mathbf{A}] + \text{Tr} [\mathbf{B}]$ and $\text{Tr} [\boldsymbol{\alpha}^2 \mathbf{A}] = \boldsymbol{\alpha}^2 \text{Tr} [\mathbf{A}]$ [24], and rearranging the order of summation, Eq. (11) can be represented as:

$$\epsilon = \text{Tr} [\hat{\mathbf{R}}^H \hat{\mathbf{R}}] - \sum_{j=1}^P \alpha_j^2 \text{Tr} [\hat{\mathbf{R}}^H \mathbf{A}_j] - \sum_{i=1}^P \alpha_i^2 \text{Tr} [\mathbf{A}_i^H \hat{\mathbf{R}}] + \sum_{i=1}^P \sum_{j=1}^P \alpha_i^2 \alpha_j^2 \text{Tr} [\mathbf{A}_i^H \mathbf{A}_j] \quad (12)$$

Assuming Hermitian symmetry of $\hat{\mathbf{R}}$ and $\mathbf{A}_i$, $\text{Tr} [\hat{\mathbf{R}}^H \mathbf{A}_i] = \text{Tr} [\mathbf{A}_i^H \hat{\mathbf{R}}]$ can be used to reduce Eq. (12) to:

$$\epsilon = \text{Tr}[\hat{\mathbf{R}}^H \hat{\mathbf{R}}] - 2 \sum_{i=1}^P \alpha_i^2 \text{Tr}[\mathbf{A}_i^H \hat{\mathbf{R}}] + \sum_{i=1}^P \sum_{j=1}^P \alpha_i^2 \alpha_j^2 \text{Tr}[\mathbf{A}_i^H \mathbf{A}_j] \quad (13)$$

Taking the derivative with respect to the individual weight α_k^2 :

$$\frac{\partial \epsilon}{\partial \alpha_k^2} = -2 \text{Tr}[\mathbf{A}_k^H \hat{\mathbf{R}}] + \sum_{j=1}^P \alpha_j^2 \text{Tr}[\mathbf{A}_k^H \mathbf{A}_j] + \sum_{i=1}^P \alpha_i^2 \text{Tr}[\mathbf{A}_i^H \mathbf{A}_k] \quad (14)$$

Given the Hermitian symmetry of $\mathbf{A}_j$, $\text{Tr}[\mathbf{A}_i^H \mathbf{A}_k] = \text{Tr}[\mathbf{A}_k^H \mathbf{A}_i]$ can be used to yield:

$$\frac{\partial \epsilon}{\partial \alpha_k^2} = -2 \text{Tr}[\mathbf{A}_k^H \hat{\mathbf{R}}] + 2 \sum_{i=1}^P \alpha_i^2 \text{Tr}[\mathbf{A}_i^H \mathbf{A}_k]. \quad (15)$$

Setting Eq. (15) equal to zero:

$$0 = -2 \text{Tr}[\mathbf{A}_k^H \hat{\mathbf{R}}] + 2 \sum_{i=1}^P \alpha_i^2 \text{Tr}[\mathbf{A}_i^H \mathbf{A}_k]. \quad (16)$$

The derivative can then be generalized with respect to the $P \times 1$ vector of component weights, $\boldsymbol{\alpha}^2$, such that:

$$\nabla_{\boldsymbol{\alpha}^2} \epsilon = \left[\frac{\partial \epsilon}{\partial \alpha_1^2}, \frac{\partial \epsilon}{\partial \alpha_2^2}, \dots, \frac{\partial \epsilon}{\partial \alpha_P^2} \right]^T, \quad (17)$$

where $\nabla_{\boldsymbol{\alpha}^2}$ represents the gradient with respect to the unknown parameter vector $\boldsymbol{\alpha}^2$. Letting $\mathbf{X}$ be the $P \times P$ Hermitian symmetric matrix of $\text{Tr}[\mathbf{A}_i^H \mathbf{A}_k]$,

$$\mathbf{X} = \begin{bmatrix} \text{Tr}[\mathbf{A}_1^H \mathbf{A}_1] & \text{Tr}[\mathbf{A}_1^H \mathbf{A}_2] & \dots & \text{Tr}[\mathbf{A}_1^H \mathbf{A}_P] \\ \text{Tr}[\mathbf{A}_2^H \mathbf{A}_1] & \text{Tr}[\mathbf{A}_2^H \mathbf{A}_2] & \dots & \text{Tr}[\mathbf{A}_2^H \mathbf{A}_P] \\ \vdots & \vdots & \ddots & \vdots \\ \text{Tr}[\mathbf{A}_P^H \mathbf{A}_1] & \text{Tr}[\mathbf{A}_P^H \mathbf{A}_2] & \dots & \text{Tr}[\mathbf{A}_P^H \mathbf{A}_P] \end{bmatrix} \quad (18)$$

and $\mathbf{Y}$ be the $P \times 1$ vector of $\text{Tr}[\mathbf{A}_i^H \hat{\mathbf{R}}]$,

$$Y = \begin{bmatrix} \text{Tr}[A_1^H \hat{R}] \\ \text{Tr}[A_2^H \hat{R}] \\ \vdots \\ \text{Tr}[A_P^H \hat{R}] \end{bmatrix}, \quad (19)$$

the generalized version of Eq. (15) is given by:

$$\nabla_{\alpha^2} \epsilon = -2Y + 2X\alpha^2. \quad (20)$$

Setting Eq. (20) equal to zero, the weights of the constitutive components can be estimated as:

$$\hat{\alpha}_{ls}^2 = X^{-1}Y, \quad (21)$$

where $\hat{\alpha}_{ls}^2$ defines the real vector of variance estimates of the contribution of each covariance constituent A_i to the estimated covariance matrix $\hat{R}$.

D. Application to Imaging

1) Selection of Constituent Covariance Models: From Eq. (3), the source intensity distribution can be segmented into a number of spatial regions of interest which contribute distinct components to the estimated covariance matrix. While these spatial regions can be chosen arbitrarily, for the purposes of imaging, an intuitive choice of spatial regions corresponds to the mainlobe and sidelobes of the predicted narrowband point spread function.

Additionally, a noise covariance model can also be defined. Acoustic clutter due to electronic noise and reverberation has been shown to be largely incoherent, with a coherence function well-approximated by delta-function at lag zero [27]–[29], or an identity matrix in the covariance domain. Given this noise model, a third constitutive covariance component corresponding to an identity matrix can be incorporated into the estimator formulation.

The mainlobe and sidelobe formulation, with and without the incoherent noise, are referred to as the 2- and 3-parameter MIST models, respectively. The 3-parameter model is shown in Fig. 1.

2) Image Formation: The variance estimates of Eq. (21) can yield negative values of $\hat{\alpha}_{ls}^2$, which have no physical meaning, as variances are necessarily positive. In practice, a non-negative least squares optimization is performed to calculate the weights, given by [30]:

$$\hat{\alpha}_{ls}^2 = \arg \min_{\alpha^2} \left\| X\alpha^2 - Y \right\|^2 \text{ subject to } \alpha^2 \geq 0. \quad (22)$$

Additionally, X is generally assumed invertible, which is determined by the orthogonality of the model matrices A_i . While the constituent covariance matrices presented in Fig. 1 are sufficiently separable, other covariance models may require diagonal loading to improve the matrix conditioning.

The variance estimates $\hat{\alpha}_{ls}^2 = \hat{\alpha}_{ls}^2(x, z)$ are calculated for each pixel location in the image, where x and z are the azimuthal and axial coordinates, respectively. The value of each pixel is calculated from a single model of interest, typically the mainlobe covariance estimate. The pixel value is given by $|\alpha_i(x, z)| = \sqrt{\alpha_i^2(x, z)}$, where i is the index of the desired constituent component, and the square root gives an estimate of magnitude. The spatial map of magnitude estimates is logarithmically compressed before display.

III. METHODS

To characterize the performance of the estimator, a number of simulation, phantom, and *in vivo* studies of various imaging targets were performed. Two formulations of the MIST estimator were used: (a) the 2-parameter method using the spatial mainlobe and sidelobe covariance models and (b) a 3-parameter method, using the mainlobe and sidelobe models, as well as an identity matrix to represent incoherent noise, shown in Fig. 1. The covariance contributions of the constituent components are referred to as the mainlobe, sidelobe, and noise estimates, respectively.

A. Simulation Studies

Simulation studies of a number of point and lesion targets were performed using Field II [31], [32], with a 64-element, 3 MHz linear array. The simulation parameters are presented in Table I.

1) Mainlobe-Sidelobe Separation: Simulations were performed of a single point target in an anechoic background, and a 1 cm anechoic, cylindrical cyst in a speckle-generating background. Radiofrequency (RF) echo data were collected, focused using dynamic receive processing, and in-phase and quadrature (I/Q) data were formed using the Hilbert transform. Images were formed using conventional B-Mode and the 2-parameter MIST estimator. No spatial averaging was used in the MIST covariance estimates.

2) Performance in Random Noise: To assess MIST performance in varying levels of noise, Field II was used to collect RF echo data from 10 speckle realizations of a 1 cm anechoic, cylindrical cyst. White noise was bandpass filtered to the transducer bandwidth, and added to the unfocused RF data prior to beamforming to simulate a specific channel signal-to-noise ratio (SNR), where channel SNR was defined as the ratio of the root-mean-square (RMS) echo amplitude from a speckle region at the focus to the RMS amplitude of

the noise. Previous work by our group has demonstrated typical SNR values encountered *in vivo* range from approximately -20 to $+20$ dB [29]. In this work, channel SNRs ranging from -40 to $+40$ dB were simulated.

The noisy echo data were then focused using dynamic receive processing, and converted to I/Q using the Hilbert transform. Images were formed at each channel SNR using conventional B-Mode, and both the 2- and 3-parameter MIST estimators, both of which employed a 1λ axial kernel in the covariance estimate.

3) Preservation of Native Target Contrast: To assess MIST performance across varying levels of native target contrast, 10 speckle realizations of a phantom target consisting of 1 cm cylindrical cysts of ± 6 , ± 12 , and ± 20 dB native contrast were simulated using Field II. The echo data were processed using conventional B-mode and the 3-parameter MIST estimator across channel SNRs ranging from -40 to $+40$ dB. The MIST estimator employed a 1λ axial kernel in the covariance estimate.

4) Edge Resolution: To evaluate the resolution performance of MIST, Field II simulations of a set of edge resolution phantoms containing two adjacent diffuse scattering regions with varying echogenicity. Simulations were performed with native contrast values of -6 , -12 , -20 , -30 , -40 , and $-\infty$ (anechoic) dB. The phantom targets measured $50 \times 50 \times 10$ mm in size. Echo data were processed using conventional B-Mode and the 3-parameter MIST estimator with a 1λ axial kernel. No noise was added to the simulated echo data. Lateral profiles of each phantom were averaged within ± 1 cm of the transmit focus, and plotted to comparatively evaluate B-Mode and MIST lateral resolution. A total of 10 speckle realizations were simulated for each native contrast value.

B. Phantom Studies

Phantom acquisitions of 2, 3, and 4 mm anechoic cyst targets (Model 549, ATS Laboratories, Bridgeport, CT) were acquired using the Verasonics Vantage 256 (Verasonics, Inc., Kirkland, WA, USA), and the 64-element P4-2v phased array transducer imaging at 4 MHz with a 4 cm transmit focus.

A matched model of the P4-2v and phantom target were also simulated using Field II. White noise was bandpass-filtered to the transducer bandwidth, and added to the simulated channel echo data to mimic the experimental channel SNR as predicted by the lag-one coherence measured in a speckle region at the focal depth [29].

B-Mode and MIST (3-parameter) images were formed of the phantom and matched simulation datasets. MIST images were formed using a single-sample estimate (0λ) of the covariance matrix, as well as a spatially-averaged covariance matrix over a wavelength (1λ) kernel.

C. In Vivo Studies

Channel echo data were collected from *in vivo* liver and fetal targets in accordance with IRB-approved protocols at the Duke University Medical Center. Data were acquired using the Verasonics Vantage 256 research scanner and a C5-2v curvilinear array. Pulse inversion

harmonic imaging sequences were used with a 2.4 MHz transmit frequency, a 4.8 MHz receive frequency, and a 60 element transmit and receive aperture. Channel I/Q data were collected, time-delayed, and processed using conventional B-Mode, receive spatial compounding (3 apertures, 50% overlap) [33]–[35], SLSC (Q=5%, 1λ axial kernel) [3], and MIST (1λ axial kernel). Correlation curves were calculated for a speckle-generating region at the transmit focus. The lag at which the correlation reached approximately zero was used to inform the effective transmitting aperture size when constructing the covariance models for the MIST estimator.

1) Liver: Images of the gallbladder and large liver vasculature were collected from a healthy male volunteer. The transmit focus was set to 85 mm.

2) Fetal: *In vivo* images of a 13 week fetus were collected from a 31-year-old patient in the Duke Fetal Diagnostic Center. The mother had a BMI of 24.5 prior to pregnancy. The transmit focus was set to 60 mm.

D. Performance Metrics

Image quality was evaluated using the following performance metrics:

$$\text{Contrast} = 20 \log_{10} \left(\frac{\mu_T}{\mu_B} \right), \quad (23)$$

$$\text{CNR} = \frac{|\mu_T - \mu_B|}{\sqrt{\sigma_T^2 + \sigma_B^2}}, \quad (24)$$

$$\text{Speckle SNR} = \frac{\mu_B}{\sigma_B}, \quad (25)$$

where μ and σ^2 represent the mean and variance, respectively, of the image magnitude in the target (T) and background (B) regions of interest (ROIs).

IV. RESULTS

A. Simulation Studies

1) Mainlobe-Sidelobe Separation: Conventional B-Mode and MIST estimator images are shown in Fig. 2. The reference B-mode images, as well as estimates of the mainlobe and sidelobe regions for the (a) point and (b) cyst target are shown at left. A 1-D lateral slice at the focal depth (50 mm) was taken from each image, and plotted at right.

a) Point Target: Much of the off-axis tails of the point spread function are reduced in the mainlobe image. The sidelobe estimate of the point target shows a significant drop (-250 dB) between $[-1, 1]$ mm, over which the mainlobe largely tracks with the B-mode profile, with significant loss in signal around ± 2 and ± 4 mm.

b) Cyst Target: The mainlobe estimate completely removes off-axis clutter written into the cyst center in the B-Mode image, decreasing the amplitude of the cyst center from approximately -50 dB to $-\infty$ dB, as the nonnegative least squares estimator returns exactly zero variance. This energy is captured in the sidelobe image, which shows a large number of dropouts in the background speckle, corresponding to peaks in the speckle pattern. Speckle texture in the mainlobe estimate is noticeably smoothed.

2) Performance in Random Noise: Sample B-Mode, and the 2- and 3-parameter MIST estimator images are shown in Fig. 3a for channel SNR values of -12 , 0 , $+12$ and $+40$ dB. Contrast, CNR and speckle SNR are plotted for each image formation method across the range of channel SNR values in Fig. 3b.

Image contrast is improved substantially at high SNRs for both estimator models. As SNR is decreased, the 3-parameter MIST model maintains improved contrast relative to B-Mode, whereas the 2-parameter model approaches that of conventional B-mode. CNR was comparable between the two estimators, consistently higher than B-mode above -12 dB SNR, and approaching the B-Mode value at very low SNRs. At high SNR, the speckle signal to noise ratio for both estimators was approximately 1.7 higher than B-Mode, though as SNR decreased, the 3-parameter estimator showed reduced speckle SNR, particularly. The loss in speckle SNR below -12 dB channel SNR appeared to offset the relative gains in contrast of the 3-parameter model relative to the 2-parameter model, resulting in virtually identical CNR curves.

3) Preservation of Native Target Contrast: B-Mode and MIST images of the negative and positive contrast targets are compared in Fig. 4a. The measured contrast for each image formation method across the six targets is plotted in (b). For all targets, MIST contrast approaches the native contrast measured by B-mode as channel SNR is increased, approaching the native contrast at a lower SNR than the corresponding B-Mode. In the high-contrast targets, the measured MIST contrast appears to slightly over- or undershoot before reaching the asymptote of the true native contrast.

4) Edge Resolution: The edge resolution simulations are presented in Fig. 5. Sample images of the anechoic phantom target are shown in (a), and the average lateral profile of B-Mode and MIST for each native contrast is shown in (b). At the boundary, the B-Mode and MIST curves overlap, indicating the MIST estimator preserves lateral resolution. The MIST lateral profiles for the low contrast targets (-30 and -40 dB) show a slight dip in contrast near the boundary before recovering to the native target contrast.

B. Phantom Studies

B-Mode and MIST images for the matched simulation and experimental datasets are shown in Fig. 6. In both datasets, the 0λ and 1λ MIST estimators demonstrated improved contrast

and CNR relative to B-Mode. CNR gains were much more pronounced with the 1λ estimator compared to the 0λ estimator. Speckle SNR across targets and image formation methods is presented in Table II.

C. In Vivo Studies

1) Liver Studies: B-Mode, spatially compounded, SLSC, and MIST images of the *in vivo* liver acquisition are shown in Fig. 7, showing the gallbladder at 50 mm, and large vasculature at 90 mm depth. The effective transmit aperture size measured as 20 elements, which was used to generate the MIST covariance model. Receive spatial compounding shows improved background speckle texture relative to B-Mode, increasing the CNR from 1.81 to 2.03. SLSC significantly improved the speckle SNR and CNR in the measured region, but results in a high-contrast image with regions of significantly darker speckle. The MIST image demonstrates significantly improved contrast and CNR relative to B-Mode and spatial compounding, while simultaneously preserving the background speckle brightness, and improving the speckle smoothness.

2) Fetal Studies: *In vivo* fetal images are shown in Fig. 8. The effective transmit aperture size measured as 12 elements, which was used to generate the MIST covariance model. Receive spatial compounding and SLSC demonstrate higher CNR and speckle SNR relative to B-Mode. Background speckle statistics and border delineation are much improved in the MIST image, without an apparent loss in resolution.

V. DISCUSSION

A. Imaging Performance

In simulation imaging environments, the MIST estimator was effective at delineating the mainlobe and sidelobe contributions to the covariance matrix. The estimator assumes a spatial covariance model corresponding to diffuse scatterers, so a highly-coherent point target is not well represented in the model. However, these results suggest stability in the presence of specular targets. There may also be a similarity between the sidelobe models for diffuse scatterers and point targets, as the estimator separates out a large portion of the sidelobe component.

The anechoic cyst represents a target aligned more closely with the estimator covariance model. In a pristine simulation environment, all signal mapped to the anechoic cyst interior arises from off-axis, sidelobe interference from scatterers outside the lesion boundary. The estimator is particularly effective at removing this signal, as the mainlobe image appears almost perfectly anechoic.

MIST was shown to be robust across a wide range of channel signal-to-noise ratios, demonstrating improved statistics relative to B-Mode for the anechoic cyst in a speckle-generating background. CNR was consistently improved using both the 2- and 3-parameter MIST estimators. The loss in speckle SNR for the 3-parameter estimator in high-noise environments is an intuitive result: as the noise amplitude greatly exceeds the background at low SNR, pixel values are increasingly attributed to the incoherent noise covariance matrix in the 3-parameter MIST model, improving contrast of the anechoic lesion, but at the

expense of background speckle statistics. This loss in speckle SNR may potentially be minimized through a larger spatial kernel, or post-processing techniques such as median filtering. These techniques may also improve image quality in other beamforming methods.

For targets with intrinsic positive and negative contrasts, MIST was shown to preserve the contrast measured by B-Mode, approaching the native target contrast values at a lower signal-to-noise ratio than the corresponding B-Mode, while simultaneously improving the background speckle texture. A subset of background pixels at the edges of the +20 dB target were attributed to the sidelobe region, resulting in dropouts in the mainlobe image, which may be similar behavior to the dark region artifact observed in many other coherence-based beamformers [36].

While most beamforming methods involving speckle reduction (such as spatial compounding) lead to a loss in lateral resolution, the edge resolution simulations demonstrated comparable lateral resolution between MIST and B-Mode imaging. Similar to the dropout artifacts of the high contrast edge in Fig. 4, the lateral profiles of the low-contrast targets undershot the native contrast before reaching an asymptote of the native target contrast.

Matched simulation and phantom studies demonstrated comparable MIST performance between anechoic targets of varying diameter. The spatially-averaged covariance estimate significantly improved imaging performance over B-Mode through gains in speckle SNR (+54% in simulation, and +39% in phantom) without a significant loss in resolution.

In vivo liver studies demonstrated qualitatively improved image quality of MIST relative to conventional image formation methods. MIST improved speckle smoothness significantly more than typical receive spatial compounding (3 apertures, 50% overlap) without an apparent loss in resolution. SLSC was implemented using a 1λ axial kernel, and a very short lag ($Q = 5\%$) was chosen in an attempt to maximize speckle statistics. Despite large gains in CNR, the liver SLSC image shows significant dark regions in the background speckle texture. MIST, by contrast, yields comparable contrast gains, while preserving speckle brightness and increasing the background smoothness significantly.

Similar results are observed in the fetal images. Qualitatively, MIST demonstrates smoothed background speckle texture relative to the other image formation methods, improved boundary definition in the abdomen, and improved delineation of multiple layers in the uterine wall, while preserving the native grayscale contrast. SLSC, however, amplifies high-contrast regions such as the stomach, while reducing detail in the head and boundary definition in the abdomen.

B. Limitations and Future Work

The performance of the estimator relies in part on the ability to distinguish contributions to the measured covariance matrix from a set of constituent components. The ability to distinguish the constituents may improve as the mainlobe and sidelobe covariance models become more orthogonal. While the data collected in this work used rectangular

apodization, alternate transmit apodization schemes, including those with deliberately higher sidelobes, may prove beneficial in this task.

The covariance model used in this paper relied on the narrowband prediction of the transmit intensity distribution at the focus. While the spatial covariance predicted by the van Cittert-Zernike theorem is independent of frequency, a model of the point spread function is necessary to define the predicted covariance matrices of the regions of interest (corresponding to the mainlobe and sidelobe in this work). The ideal cutoff point may vary as a function of frequency. Accordingly, it may be preferable to model a broadband point spread function, or alternatively, perform the estimation on narrow frequency subbands, in an approach analogous to frequency compounding.

The theoretical model of a sinc^2 intensity distribution for a rectangular aperture is only valid within the transmit depth of field, so the accuracy of the model degrades with distance from the transmit focus. This is evident in Fig. 7, in which the MIST image shows a number of dark pixels between 30 – 40 mm, where the model begins to fail. A depth-dependent covariance model using the transmit intensity as predicted by Eq. (1) may improve performance of MIST outside the depth of field.

The effectiveness of the estimator relies in part on the ability to model the spatial covariance of the echo data, which may deviate from the predictions of the VCZ theorem. The covariance in tissue harmonic imaging may vary substantially based on the imaging configuration and other parameters associated with nonlinear propagation, resembling an effective transmit apodization [37]. Acoustic clutter due to multiple scattering, aberration, or bright, off-axis targets may also degrade or alter the spatial covariance from the theoretical predictions, which may manifest as superimposed incoherent or partially coherent components, decreased correlation lengths resembling a smaller effective transmit aperture, or high correlations at long lags due to off-axis targets [27]–[29], [38], [39]. Similarly, spatial variations in target echogenicity may also affect the measured covariance. These deviations from the theory are typically unknown at the time of imaging, and the large parameter space of particular realizations is difficult to model, which may limit the effectiveness of the estimator. However, qualitative and quantitative results suggest MIST is quite robust to deviations from the predicted spatial covariance model.

Adaptive measurement of the data covariance matrix to inform the model may partially address this problem. In Figs. 7 and 8, the covariance model was defined based on the measured data covariance of a speckle region around the transmit focus. A spatially varying covariance model based on point or regional covariance measurements may improve on this framework.

While MIST has been shown to improve image statistics and maintain resolution relative to conventional methods, clinical feasibility of this method may depend on more than these quantitative metrics. Future work will involve clinical evaluation of MIST image quality through a blinded reader study involving trained radiologists and/or sonographers.

VI. CONCLUSION

Building on a mathematical framework describing diffuse scattering targets as piecewise-stationary, a novel estimation-based framework was presented to image the statistics of subresolution targets (Multi-covariate Imaging of Sub-resolution Targets, or MIST). Aperture domain spatial covariance was modeled as the linear superposition of constituents corresponding to a number of spatial regions of interest and noise sources, whose contributions to the echo data were estimated and imaged. MIST was demonstrated to improve CNR across simulation, phantom, and *in vivo* targets over conventional B-Mode. MIST was shown to preserve native target contrast while remaining stable in the presence of noise, and to improve speckle statistics without an apparent loss in resolution. These results suggest MIST may be better suited than conventional methods to image diffuse targets.

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Fig. 1:

Estimator framework using three constituent models. The predicted intensity distribution for a narrowband array is segmented into distinct mainlobe and sidelobe spatial regions. A third covariance model corresponding to incoherent noise is represented by an identity matrix.

The mainlobe, sidelobe, and incoherent noise covariance matrices are plotted at bottom, and a 1-D plot showing the average along the diagonal of each matrix is shown at right, with the superposition of the three components plotted in the dashed line.

Fig. 2:

MIST estimator images of simulated targets. A conventional B-mode image is compared to the main lobe estimate and side lobe estimate of a (a) point and (b) anechoic cyst target. 1-D lateral profiles at 50 mm depth are shown at right, where the y-axis has been split to display the full range of the lateral profiles.

Fig. 3:

B-Mode is compared to the 2-parameter (mainlobe + sidelobe) and 3-parameter (mainlobe + sidelobe + incoherent noise) MIST model across a range of channel signal-to-noise ratios for a 1 cm anechoic target. (a) Sample images at selected SNRs. (b) Contrast, CNR, and Speckle SNR are plotted against channel SNR.

Fig. 4:

(a) Comparison of B-Mode and MIST images across targets of varying native contrast at a channel SNR of 0 dB. (b) Plots of measured contrast vs. channel SNR demonstrate the stability of MIST across SNR. Across native contrast targets, MIST attains the true target contrast at a lower SNR than B-Mode.

Fig. 5:

Edge resolution simulations. (a) Sample B-Mode and MIST images of the edge phantom with a speckle generating and an anechoic region ($-\infty$ dB contrast). (b) Averaged lateral profiles of B-Mode and MIST images for each set of phantom simulations. The native contrast of the imaging phantom is indicated by the axis on the right.

Fig. 6:

Approximately matched B-Mode and MIST images using a single sample (0λ) and axial averaging of the covariance matrix over a wavelength (1λ). (a) Simulation and (b) phantom images are shown with contrast and CNR plotted to compare performance for each lesion.

Fig. 7:

In vivo liver images comparing B-Mode, receive spatial compounding (3 apertures, 50% overlap), SLSC ($Q=5\%$, 1λ kernel), and MIST (1λ). B-Mode, receive spatial compounding, and MIST images are shown on a 70 dB dynamic range. SLSC is shown on a [0-1] scale.

Fig. 8:

In vivo fetal images comparing B-Mode, receive spatial compounding (3 apertures, 50% overlap), SLSC ($Q=5\%$, 1λ kernel), and MIST (1λ). B-Mode, receive spatial compounding, and MIST images are shown on a 60 dB dynamic range. SLSC is shown on a [0-1] scale.

TABLE I:

Field II Simulation Parameters

Parameter	Value
f_0	3 MHz
Bandwidth	70%
f_s	200 MHz
Element Count	64
Element Pitch	300 μm
Array Footprint	$1.92 \times 1 \text{ cm}$
Transmit Focus	5 cm
Transmit F/#	2.6
Apodization	Rectangle
Scatterers/Res. Cell	20

TABLE II:

Matched Simulation and Phantom Speckle SNR

Image Former	Speckle SNR	
	Simulation	Phantom
B-Mode	1.82	1.95
MIST (0λ)	2.00	2.16
MIST (1λ)	2.80	2.72