HHS Public Access

Author manuscript

IEEE Trans Ultrason Ferroelectr Freq Control. Author manuscript; available in PMC 2017 September 01.

Published in final edited form as:

IEEE Trans Ultrason Ferroelectr Freq Control. 2016 September ; 63(9): 1306–1320. doi:10.1109/TUFFC.2016.2547341

Analysis of coherent and diffuse scattering using a reference phantom

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Abstract

The estimation of many spectral-based, Quantitative Ultrasound parameters assumes that backscattered echo signals are from a stationary, incoherent scattering process. The accuracy of these assumptions in real tissue can limit the diagnostic value of these parameters and the physical insight about tissue microstructure they can convey. This work presents an empirical decision test to determine the presence of significant coherent contributions to echo signals and whether they are caused by low scatterer number densities or the presence of specular reflectors or scatterers with periodic spacing. This is achieved by computing parameters from echo signals that quantify stationary or non-stationary features related to coherent scattering, and then comparing their values to thresholds determined from a reference material providing diffuse scattering.

The paper first presents a number of parameters with demonstrated sensitivity to coherent scattering and describes criteria to select those with highest sensitivity using simulated and phantom-based echo data. Results showed that the echo amplitude signal-to-noise ratio and the multitaper generalized spectrum were the parameters with highest sensitivity to coherent scattering with stationary and non-stationary features, respectively. These parameters were incorporated into the reference-based decision test, which successfully identified regions in simulated and tissue-mimicking phantoms with different incoherent and coherent scattering conditions. When scatterers with periodic organization were detected, the combination of stationary and non-stationary analysis permitted the estimation of the mean spacing below and above the resolution limit imposed by the pulse size. Preliminary applications of this algorithm to human cervical tissue ex vivo showed correspondence between regions of B-mode images showing bright reflectors, tissue interfaces, and hypoechoic regions with regions classified as specular reflectors and low scatterer number density. These results encourage further application of the algorithm to more structurally complex phantoms and tissue.

Keywords

Ultrasound backscatter; signal coherence; random media; nonrandom media; non-stationary; scatterer spacing; quantitative ultrasound; tissue characterization

I. Introduction

Quantitative Ultrasound (QUS) methods estimate values of tissue acoustic properties, such as the attenuation coefficient and the backscatter coefficient.¹ Parametric images based on

these methods display the spatial distribution of these properties. The aim of QUS is to augment the basic echo amplitude and flow information derived during conventional B-mode and Doppler examinations,² and to increase the objectivity of ultrasound as a diagnostic tool. The diagnostic value of QUS has been investigated for characterizing normal and abnormal breast, liver, kidney, and other tissues.^{1;3-6}

Because of the frequency dependence of backscatter and attenuation in soft tissues, many QUS methods rely on estimating the power spectral density (PSD) of radiofrequency (RF) echo signals.⁷ The PSD quantifies the expected value of the echo signal power detected at the transducer due to scattering from spatial variations in acoustic impedance within the ultrasound pulse volume.^{8;9} The *resolution cell* defines the basic sampling volume of the scattering process. It is defined laterally by the directivity function during transmission and reception, and axially by the pulse-echo pulse duration.⁸ This interpretation of the PSD assumes that echo signals are generated from a stationary scattering process and that scatterers are randomly distributed and in large concentration, leading to fully incoherent or “diffuse” scattering.¹⁰

The assumptions of a stationary, incoherent scattering process are not always attainable when working with biological tissue. Many tissues are composed of both spatially structured and randomly distributed scatterers, thus providing different levels of coherent and incoherent scattering.¹¹ Furthermore, scatterers might be present in such low concentrations that echoes coming from within the resolution cell only represent a very limited sample of the incoherent scattering process.^{12;13} These conditions can reduce the accuracy and precision of conventional QUS parameters as well as hinder the physical insight about the scattering sources.^{4;14-16} These problems arise, for example, when analyzing tissue with some level of scatterer organization, such as the liver and muscle.^{17;18} Also, the presence of sources of coherent scattering in the breast has been suggested to be a limitation for *in vivo* application of QUS in breast ultrasound.⁴ Thus, methods are needed that can detect these conditions so strategies can be implemented to deal with them. For example, if periodically-spaced scattering sources are present, the mean scatterer spacing can be estimated and reported as a parameter to describe the tissue.^{16;19;20} If specular reflectors are present, strategies have been developed to avoid them and continue processing typical diffuse-scattering QUS parameter estimates.^{14;15} Similarly, if low scatterer number density is present, strategies are available to increase the volume contributing to scattering. Testing for these conditions is more prudent than assuming they are not present.

The goal of this work is to develop an automatic algorithm that detects whether conditions of stationary, diffuse scattering are met within a QUS analysis region. In earlier work, Georgiou *et al.*^{13;21} used the WOLD decomposition²² and wavelet transforms^{23;24} to distinguish between echo signals arising from diffuse scattering and those from coherent scattering that cause line components in the signal power spectrum. Donohue *et al.*²⁵ applied the generalized spectrum to detect echo signals due to coherent scattering. More recently, Luchies *et al.*¹⁴ proposed a method for detecting specular reflectors by quantifying either the envelope signal-to-noise ratio or different metrics of the generalized spectrum. Here we propose a single tool to automatically detect various scattering conditions including diffuse scattering, low scatterer number density, and the presence of specular reflectors or periodic

scatterers with spacing either smaller or larger than the size of the resolution cell. This is achieved through an automated algorithm that quantifies parameters describing non-stationary and stationary features of the echo signals related to coherent scattering and then tests the statistical significance of the presence of coherent scattering.

The paper is organized as follows. Section II.A describes parameters used to quantify the presence of coherent scattering and presents criteria to select those with the highest detection performance. Section II.B describes automated empirical decision criteria that test for the presence of coherent scattering based on the parameters described in Section II.A. This is achieved by comparing the estimated parameter values to those obtained from echo signals from a reference material with diffuse scattering. Simulations and tissue mimicking phantoms used for parameter selection and for testing the algorithm are described in the corresponding sections. Section III presents the results for parameter selection and algorithm performance in both simulations and phantoms. In Section IV, a preliminary application of the algorithm on ultrasound echo data from the uterine cervix is presented as an example of the intent of the algorithm. In this case, the collagen structure is known to be pseudo-aligned in layers and it is not clear that the assumption of diffuse scattering is valid, so we test the assumption to determine if there is evidence for periodic scatterer spacing, strong isolated scatterers that should be avoided, or low scatterer number density that might lead to modifying how we acquire and process our data. Section V discusses the results as well as current work and future applications in the cervix. Section VI summarizes the findings and presents the conclusions.

II. Methods

The algorithm presented here is a two-step process: *Quantification* and *Decision*. In the *Quantification* step, a parameter “ q ” is used to quantify features in the echo signals related to coherent scattering. q can be any of a pool of parameters used to quantify the presence of coherent scattering “locally”, i.e., within a region known as the *Parameter Estimation Region* (PER).^{26;27} During the formation of parametric images, the PER is raster scanned over the field represented by RF echo signals.²⁶ From each location of the PER, an estimate of the parameter of interest is obtained. The PER is composed of a set of segments from adjacent RF echo signals. Features of these segments that are related to coherent scattering will depend on the spatial extent of the tissue organization, such as the spacing between periodic scatterers, with respect to the resolution cell. If the spatial extent is smaller than the size of the resolution cell, the statistics of the scattering process will be stationary. If larger, the echo signals will be non-stationary.

The *Decision* step compares q to a threshold defined from the distribution of values obtained in a reference material (designed to fulfill conditions of incoherent, diffuse scattering) to determine the probability of observing that value of q . The following subsections expand on the parameter selection for the *Quantification* step, as well as on the details about the *Decision* test and the complete algorithm.

A. Parameter Selection

Coherent scattering processes with different spatial extents with respect to the resolution cell size produce echo signals with either stationary or non-stationary features. In this section, we select those parameters that are most sensitive to the presence of coherent scattering over a wide range of scenarios. The selection of parameters was done by comparing their mean and variance under coherent scattering conditions to those under conditions of a stationary, diffuse scattering process. Effects of reducing the PER size are also investigated as small PERs are needed to study the spatial variability of the scattering process in a macroscopically heterogeneous tissue such as the cervix or the breast.^{4,28} Small PERs result in shorter and fewer echo signal segments for the analysis of the scattering process, thus possibly compromising the performance of the proposed algorithm. The analysis was tested with both simulations and experiments with well-characterized phantoms.

1) Data generation and acquisition—In each study, two types of echo data were simulated or acquired: sample data and reference data. Sample data consisted of simulated or experimental echo data from a medium potentially containing a source of coherent scattering. The reference data were obtained from a medium with only randomly positioned scatterers, providing stationary, diffuse scattering conditions.

The simulation tool was implemented in Matlab (The Math-Works Inc., Natick, MA) following a previously described one-dimensional model.²⁹ This model assumes backscattered echo signals result from the convolution of a mathematical acoustic pulse with a one dimensional array of point-like scatterers. The acoustic pulse was modeled as a Gaussian-modulated (75% –6dB bandwidth), 6MHz sine wave with a pulse length of 0.29mm and a wavelength λ of 0.26mm (sound speed $c=1540\text{m/s}$). Coherent scattering in the sample was simulated as an array of higher amplitude periodic scatterers with spacings between 0.2λ and 7.8λ embedded in a cloud of random scatterers (48 scatterers within a resolution cell). Each of these coherent scattering scenarios (e.g. one periodic spacing value) was independently generated and analyzed as described in Section II.A.2. The scattering amplitude of the periodic scatterers was adjusted to keep a constant coherent-to-incoherent power ratio of 1.5dB, computed as described by Varghese and Donohue.¹⁹ Previous work^{27,30} has shown that this value does not compromise the performance for detecting coherent scattering. The reference medium had similar random scattering properties. Ten RF echo frames were created for each sample condition and for the reference. Each frame consisted of 300 independent, one-dimensional simulated RF echo signals 77.2 μs in duration, corresponding to a depth range of 60mm.

In the experiments involving phantoms, the sample consisted of a mix of gel with 5–4 μm diameter glass bead scatterers (3000E, Potter Industries, Malvern, PA) with a concentration of 264mm^{-3} . It also contained a vertical (V) and a horizontal (H) plane of 0.10mm-diameter nylon fibers spaced 0.40mm apart and spanning 10mm axially and elevationally, respectively. Figure 1(a) shows the planes of fibers during the fabrication of the phantom. The reference phantom, with diffuse scattering conditions,³¹ consisted of a mixture of agarose gel media with the same type and concentration of glass beads as the sample phantom.

RF echo data were obtained from both phantoms with a Siemens Acuson S2000 (Siemens Healthcare, Ultrasound Business Unit, Mountain View, CA, USA) using the Axis Direct Ultrasound Research Interface.³² Two linear arrays were used: a 9L4 transducer operated at 4MHz, and a 18L6 transducer operated at 10MHz. Figure 1(b) shows a B-mode image of the phantom's vertical fiber plane acquired with the 18L6 transducer. Three independent planes of the sample phantom were scanned with the 9L4 transducer, and one with the 18L6 transducer. Using speckle correlation techniques,^{26;33–37} the axial and lateral correlation lengths, which are indirect assessments of the size of the resolution cell,^{8;38;39} were 0.51mm and 0.83mm respectively, for the 9L4 transducer, and 0.26mm and 0.99mm respectively, for the 18L6 transducer. Note that the spacing within fibers in the phantom was smaller than the 9L4's axial correlation length, but larger than the 18L6 axial correlation length, providing stationary and nonstationary conditions, respectively.

2) Criteria for Parameter Selection—In this section, parameters to quantify stationary and non-stationary features of echo signals related to coherent scattering are presented, and a criterion for selecting parameters based on their detection performance is described. This criterion is based on the detection strategy that compares values of the parameters under coherent scattering conditions to thresholds based on incoherent, diffuse scattering. The analysis of detection performance is based on two questions: 1. How sensitive is a parameter to the presence of coherent scattering? 2. How large is the difference in the value of the parameter with and without the presence of coherent scattering compared to its variance? To do this, a set of M independent PERs were defined in the sample and in the reference data. One estimate of each parameter was obtained from one PER. To assess question 1, each parameter's normalized contrast C_q with respect to the reference was quantified as:

$$C_q = \frac{\langle q \rangle_M - \langle q_{\text{Ref}} \rangle_M}{\langle q \rangle_M} \quad (1)$$

where q is a parameter that quantifies the presence of either stationary or non-stationary coherent scattering in one PER in one sample data frame. Subscript “Ref” indicates that the estimate is obtained from a reference data frame. The brackets indicate averaging over M independent PERs.

To assess question 2, we quantified the contrast-to-noise ratio CNR_q as:

$$\text{CNR}_q = \frac{\langle q \rangle_M - \langle q_{\text{Ref}} \rangle_M}{\sqrt{\hat{\sigma}_q^2 + \hat{\sigma}_{\text{Ref}}^2}} \quad (2)$$

where the hat indicates an estimate of the variance σ^2 of the parameter q . The number of PERs, M was set to 100 in the simulated data. For the phantom study, $M = 9$ for the sample while $M = 36$ for the reference. Error bars applied to C_q and CNR_q were obtained from error propagation analysis applied to estimates of the variance of each parameter, and they indicate one standard deviation of either C_q or CNR_q .

3) Stationary Parameters—Parameters describing stationary features of the echo signals are based on speckle statistics. These methods have been commonly focused at fitting a theoretical model to the probability density function of the echo amplitude. Under conditions of diffuse scattering, the density function of the echo amplitude follows a Rayleigh distribution.⁸ Shankar *et al.*^{12;40–45} proposed various versions of the K-distribution and the Nakagami distribution to characterize tissues with low scatterer number densities. These distributions have been used to classify benign and malignant breast lesions.^{44;46;47} Parameters of the Nakagami distribution provide enough sensitivity to discern normal livers from fibrotic ones with Metavir scores 3 and 4 ($p < 0.01$).⁴⁸ The most general model is the Homodyned-K distribution proposed by Jakeman and Pusey⁴⁹ and first applied in QUS by Dutt and Greenleaf.⁵⁰ It has been applied to differentiate breast sarcomas from carcinomas⁵¹ as well as to detect metastases in lymph nodes *ex vivo*.⁵²

Here we perform a systematic comparison of the performance of these parameters to detect coherent scattering with stationary features. These parameters were estimated by computing the echo signal amplitude, V and the intensity, $I = V^2$ from the magnitude and the squared magnitude, respectively, of each time sample of the Hilbert transform of each RF echo signal segment within the PER. Uncorrelated estimates of V and I within a PER were obtained by selecting samples separated by one axial correlation length and one lateral correlation length from each other.⁵³ Six parameters were investigated for detection purposes:

- **Model-free parameters:** These two parameters were the point-wise signal-to-noise ratio of the echo amplitude and of the intensity.⁸ Thus,

$$\text{SNR}_P = \langle P \rangle_N / \sqrt{\langle (P - \langle P \rangle_N)^2 \rangle_N} \quad (3)$$

where $P = V$ or I , and the brackets indicate averaging over the N samples within the PER. Use of these parameters is motivated by their well-known value under diffuse scattering conditions ($\text{SNR}_V = 1.91$, $\text{SNR}_I = 1$) corresponding to a Rayleigh amplitude distribution. Conditions with $\text{SNR}_V < 1.91$ or $\text{SNR}_V > 1.91$ are referred to as Pre-Rayleigh or Post-Rayleigh, respectively.^{29;38}

- **Homodyned-K model-based parameters:** These parameters are based on a model describing the scattering process as a random walk with a source of deterministic phase.⁵⁴ The model's "clustering parameter," α and the coherent-to-incoherent amplitude ratio,⁵¹ k were estimated using Destempes *et al.*'s method⁵⁵ based on minimizing differences between theoretical values and estimates of logarithmic moments of the intensity.
- **Nakagami model-based parameters:** These parameters include a maximum likelihood estimator of the "shape parameter" m ,^{42;55} and a generalized likelihood ratio test statistic, T that assumes as the null hypothesis the Rayleigh model for diffuse scattering conditions,³⁸ and the Nakagami model as an alternative hypothesis. Starting from the ratio of

the Nakagami and Rayleigh probability density functions, the resulting test statistic has the form:

$$T=2N\{\log \frac{m^m}{\Gamma(m)}+(m-1)[\langle \log I \rangle - \log \langle I \rangle - 1]\} \quad (4)$$

4) Non-stationary Parameters—Parameters related to the echo signal generalized spectrum (GS) have been shown to be promising tools for the detection of non-stationary features in echo signals related to coherent scattering.^{19;56} The GS quantifies the correlation among different frequency components of the echo signals.^{16;19} The GS has been widely investigated for breast cancer diagnosis by Donohue *et al.*^{20;25;57} It was found more useful for analysis of coherent scattering than the detection of peaks in the echo signal power spectral density¹⁷ or its cepstrum,^{19;58} and Singular Spectrum Analysis.^{59–61} Here we exploit the GS for the detection of unknown sources of non-stationary, coherent scattering, including the presence of specular reflectors and periodically-spaced scatterers with mean separation larger than the size of the resolution cell.

The echo-signal GS, $S(f_i, f_j)$ is the expected value of the correlation of the Fourier transform $Y(f)$ of a segment of RF signal $y(t)$ at frequencies f_i and f_j :

$$S(f_i, f_j)=E[Y(f_i)Y^*(f_j)] \quad (5)$$

where * indicates the complex conjugate.⁶² The GS is usually displayed in a bifrequency plane, where each point in the plane carries information about the correlation between frequency components f_i and f_j .^{19;56}

Three approaches to obtain the final GS for a particular parameter estimation region were investigated:

- **Single-taper GS (ST):** A single acoustic scanline estimate of the GS is obtained from the correlation of its Fourier transform with its complex conjugate after multiplying it with a low-leakage taper. The final GS estimate within a PER is the average of the individual scanline estimates.⁶³ In this work, we explore the use of two tapers: the boxcar taper (or no taper) and the first discrete prolate spheroidal sequence (DPSS) for a time-bandwidth product $N_f W=6$ (described below). The latter offers the minimum possible spectral leakage.^{9;64}
- **Weighted Overlapped Segment Average (WOSA):** RF signal segments from the acoustic scanlines within the PER are subdivided into overlapped subsegments. The final GS estimate is obtained by averaging all subsegment estimates.⁶³ This estimator reduces variance at the expense of poorer frequency resolution.^{65;66} In this work, we use an overlap ratio of 50% and a subsegment size of half the segment. This estimator has been widely used in many quantitative ultrasound applications.^{19;20;56;57;67}

- **Multitaper method (MTM):** A set of K GS estimates is obtained from the Fourier transforms of the RF echosignal segment when separately tapered by K DPSS. The final GS estimate is given by the weighted average of the K individual estimates.¹⁶ The number of tapers K and the time samples N_t of each RF echo segment define the local bias bandwidth W through $K = 2N_t W$.^{9;64} Increasing the number of tapers results in a reduction of variance due to the averaging of approximately uncorrelated spectral estimates.⁶⁴ Increasing the number of tapers also leads to more spectral leakage.

Figure 2 shows GS estimates resulting from applying (a) a single-taper estimator with the first DPSS for $W=1\text{MHz}$, and (b) the multitaper estimator with $W=1\text{MHz}$ to simulated echo signals from a medium with periodic scatterers, where the mean scatterer spacing, MSS is set to 0.4mm . If periodic scatterers are present, the GS will have non-zero values at $f = f_1 - f_2 = c/2\text{MSS}$, where c is the speed of sound in the medium.⁵⁶ We refer to each of the non-zero regions in the off-diagonals of the bifrequency display of the GS as *periodicity cells* (white squares in Fig. 2). In the case of the MTM estimator, the energy in the GS is concentrated along the secondary diagonals of each periodicity cell, as shown in Fig. 2(b).

To improve detection performance, the GS is normalized with respect to the values in the main diagonal ($f_i = f_j$) and phase aligned, as described by Huang *et al.*⁶³ This is shown in Fig. 3, where the values in the main diagonal are 1. The analysis of the GS can be simplified by computing its *Collapsed Average* (CAGS), i.e., the average of the diagonals of the GS within the useful bandwidth.⁶⁸ Computation of the Collapsed Average is also depicted in Fig. 3. Each value corresponds to a given f_i and the value at $f = 0$ (main diagonal of the GS) is always 1 as a result of normalization.⁶³ Most importantly, the presence of coherent scattering shows up as significant non-zero values outside the 0MHz peak.^{19;56;67} The useful frequency ranges of the GS are determined by the available signal bandwidth.

The detection of coherent scattering is based on finding the maximum value of the CAGS(f 0) (referred to as MaxCAGS) and comparing it to a threshold defined from the CAGS(f 0) values obtained from the reference echo signals. The performance of different estimators of the GS to detect a range of coherent scattering scenarios will depend on the tradeoff between their frequency resolution and their variance reduction efficiency. As the spacing among periodic scatterers increases, maxima in the CAGS are closer together and become more difficult to resolve. In addition, the use of limited data from small PERs can increase the variance of the CAGS estimate. To study these effects, the detection performance of each GS estimator was also quantified in terms of the contrast C_q and the contrast to noise ratio CNR_q described in Eqs. (1) and (2), where q is MaxCAGS.

To detect specular reflectors, we follow a strategy similar to that of Donohue *et al.*²⁰ and of Luchies *et al.*¹⁴ Specular reflectors introduce correlation among all frequency components of the echo signal. Thus, the frequency correlation bandwidth can be quantified as the width of the 0MHz peak of the CAGS, referred to here as the CAGS *main lobe width*, MLW. In this work, the MLW value measured in the sample was compared to a threshold, which was the MLW measured in the reference data.

B. Decision

As will be shown in the Results section, for our cases the signal to noise ratio of the echo amplitude, SNR_V and the maximum value of the collapsed average of the multitaper generalized spectrum, MaxCAGS produced the best detection performance for stationary and non-stationary features of the echo signals related to coherent scattering, respectively. We now describe a test to decide if the value of parameter q (either SNR_V or MaxCAGS) computed in the sample is significantly different from its value under conditions of stationary, diffuse scattering.

The decision test is based on the probability distribution of q under conditions of stationary, diffuse scattering. This probability distribution was empirically approximated from a set of values of q obtained from a reference material fabricated to provide conditions of stationary, diffuse and Rayleigh (backscatter coefficient proportional to f^4) scattering at each location of the PER. The design and use of such phantoms has been broadly investigated and design specifications are available in the literature.^{1;7;31;69–71} Backscattered echo data from the reference was obtained using the same system setup used to obtain the data from the sample. In addition, the reference material has a sound speed and attenuation close to those of the sample being classified.³¹

The set of reference values of the parameter q were obtained from M PERs in the reference echo data derived from the same depth as the PER in the sample echo data. These values were used to construct an empirical reference cumulative distribution, $F_E(q)$, which quantifies the probability that parameter q is smaller than, or equal to a particular value, q_0 under conditions of stationary, diffuse scattering.^{13;21;72} After ordering the reference values of the parameter q_m , $m = 1, \dots, M$, so that $q_1 < q_m < q_M$, $F_E(q)$ is constructed according to:¹³

$$F_E(q) = \begin{cases} 0 & q < q_1 \\ m/M & q_m \leq q < q_{m+1} \\ 1 & q \geq q_M \end{cases} \quad (6)$$

The diagram in Fig. 4 describes the automated algorithm that combines the *Quantification* and *Decision* stages. From the M estimates of reference MaxCAGS and SNR_V , $F_E(\text{MaxCAGS})$ and $F_E(\text{SNR}_V)$ are computed. A threshold q_a for MaxCAGS was chosen for a probability of false detection of 5%. If $\text{MaxCAGS} > q_a$, then the presence of a source of non-stationary coherent scattering is declared. Otherwise, echo signals within the PER are stationary. In the latter case, a two-tail test is used on the SNR_V to decide among pre-Rayleigh, Rayleigh, or post-Rayleigh conditions. For a total probability of false detection of 5%, we determine two thresholds: q_b , for which $F_E(\text{SNR}_V) > 97.5\%$, and q_c , for which $F_E(q) < 2.5\%$. If $\text{SNR}_V > q_b$, the presence of non-resolved periodic scatterers (associated with post-Rayleigh statistics)²⁹ is declared. If $\text{SNR}_V < q_c$, the presence of a low scatterer number density with pre-Rayleigh statistics^{8;12} is declared. Otherwise, diffuse scattering is present.

Zones with low scatterer number densities also cause an increase in the non-stationary coherence level as a consequence of insufficient averaging of the echo phase, as observed by Donohue *et al.*⁷³ Since this is not related to tissue organization, we refer to it as *false*

coherence. To distinguish it from coherent scattering due to organized scatterers, we analyzed the uniformity of the echo phase distribution within the PER, as suggested by Shankar *et al.*^{12;41} and Molthen *et al.*⁷⁴ Phase non-uniformity is quantified with the χ^2 metric of the phase histogram with N_{PB} phase bins:⁷⁴

$$\chi(f_d)^2 = \sum_{i=1}^{N_{PB}} \frac{(n_i - \langle n \rangle)^2}{\langle n \rangle} \quad (7)$$

where n_i is the number of phase estimates within the i^{th} phase bin of the histogram, and the brackets indicate the average of the number of phase estimates in all the bins. The frequency f_d is used to demodulate the RF signal and isolate the phase from echo interference. Its value is varied within the pulse bandwidth to probe for maximum constructive interference.⁷⁴ As the distribution of the phase approaches a uniform distribution, the χ^2 measure approaches zero. To determine if the departure from uniformity is statistically significant, an analysis similar to the one used to decide on the statistical significance of non-stationary features with the CAGS is performed. This implies looking for the maximum value in the sample χ^2 spectrum and comparing it with the empirical cumulative distribution from the reference material. An empirical threshold q_d is determined for the maximum of $\chi^2(f_d)$ for a probability of false detection of 5%: If the maximum of $\chi^2(f_d) > q_d$, then the phase within the PER is not classified as uniform; otherwise, the phase within the PER is taken to be uniform.

In cases where a periodic array of scatterers is present, the mean scatterer spacing (MSS) can be estimated.^{19;56} Different MSS estimation methods are required depending on whether the echo signals are stationary or not. Where the test for nonstationarity is positive, the frequency of MaxCAGS can be analyzed, as described by Huang *et al.*⁶³ In contrast, where signals are stationary, the phase χ^2 spectrum can be further analyzed to estimate the mean scatterer spacing, as proposed by Molthen *et al.*⁷⁴ Thus, the combination of both analyses can be used to estimate quasi-periodic spacing values below and above the resolution cell size. The analysis of post-Rayleigh statistics ($\text{SNR}_V > q_b$) can be used to decide between the χ^2 method (positive test) or the CAGS method (negative test).

C. Test of the algorithm

Once the complete algorithm, shown in Fig. 4, was defined, we tested its performance for detecting different scattering conditions in simulated and experimental phantoms.

1) Data acquisition and analysis—A simulated phantom containing eleven regions with different scattering properties, is shown in Fig. 5(a). Regions 1, 2 and 3, colored in green had only randomly positioned scatterers, with concentrations of 2, 16, and 32, scatterers per resolution cell. Region 4, colored in blue also had randomly positioned scatterers with a concentration equal to that of a simulated reference (48 scatterers per resolution cell). Regions 5 through 11, colored in red had, in addition to random scatterers with 48 scatterers per resolution cell, an array of periodic scatterers with spacings of 0.06mm, 0.12mm, 0.24mm, 0.3mm (about one axial correlation length under the simulated

conditions), 0.4mm, 0.8mm, and 1.20mm. Frames of RF echo data from the simulated phantom were created by laterally assembling one-dimensional simulated RF echo signal lines with simulated pulse conditions consistent with those used in previous sections (6MHz center frequency, 72% -6dB bandwidth). Adjacent scan lines were assumed to be separated by half the experimentally estimated beam width of the 18L6 transducer. Each region, with the exception of Region 4, included one hundred RF echo signal lines, yielding a total lateral span of 256mm. Sixty independent realizations of the scattering arrangements were created, leading to 60 independent frames of RF data from the phantom. A B-mode image shown in Fig. 5(b) was obtained by intensity modulating the display matrix proportional to the instantaneous echo amplitude.

A 4mm² PER was swept across the array of RF signals from the simulated phantom, with no overlap, to perform the characterization at uncorrelated positions. This generated a total of 715 (13 axial $\times$ 55 lateral) uncorrelated PERs. Within each PER, the MaxCAGS, SNR_V, MLW, and $\chi^2(f)$ were estimated as described above. The decision tests based on these parameters (non-stationary features, departure from Rayleigh statistics, and non-uniformity of the phase) were performed with parameter thresholding yielding a probability of false detection of 5%.

To quantify the adequacy of the decision process at a PER centered at a location (x, y) in the simulated phantom, we defined the *Detection Ratio* $DR(x, y; K)$ of scattering condition K (either diffuse scattering, low scatterer number density, periodic scatterers, or specular reflector) as the number of frames N_K in which the result of the algorithm was condition K , normalized to the total of frames, i.e., 60:

$$DR(x, y; K) = \frac{N_K}{60} \quad (8)$$

Thus, a detection ratio of 0% for scattering condition K at a particular PER indicates that such condition was not detected in any of the sixty independent frames, while a value of 100% indicates that the condition was detected in all sixty frames.

The experimental phantoms were the fiber and reference phantoms described in Section II.A. A 4mm² PER was swept across the phantom RF data array with 90% overlap. To improve the registration of the classification image, an adaptive trimming of echo signals within each PER was applied as described by Rosado-Mendez.²⁷

III. Results

A. Parameter selection for stationary features

1) Simulation Results—Figure 6(a) shows the normalized contrast, C_q as a function of the PER size for the six parameters of the stationary analysis, that is, SNR_V, SNR_F, α , k , m and T , derived for a source of coherent scattering surrounded by randomly distributed scatterers as described in Section II.A. The coherent component was produced by periodic scatterers with a 0.24mm spacing. The contrast from model-based parameters is larger than

the contrast from model-free parameters. The largest contrast is achieved with the Nakagami T statistic, followed by the parameters from the homodyned K model. No significant changes in the contrast of any of the parameters is observed when the PER size is equal to or larger than 25 axial correlation lengths $\times$ 25 uncorrelated scan lines.

Figure 6(b) shows the parameter contrast-to-noise ratio, CNR_q as function of the PER size for the same simulated phantom. Opposite to C_q results, the largest CNR_q is obtained with model-free parameters. In addition, CNR_q decreases as the PER size is reduced. Differences in CNR_q for SNR_V , SNR_I , the Nakagami m and the homodyned-K k become insignificant for PER sizes smaller than 10 axial correlation lengths $\times$ 10 uncorrelated scan lines. For this PER size, the CNR_q from the homodyned-K α and the Nakagami T remain about half the CNR_q values from the other parameters. Because of the similar performance of the Nakagami and the homodyne K parameters in terms of CNR_q and the relatively easy estimation of the former, further results and discussion will not include the parameters from the homodyned-K model.

Figure 7 compares CNR_q values for SNR_V , SNR_I , and the Nakagami m and T as the periodic scatterer spacing is varied in multiples of the wavelength. The PER size is 30 axial correlation lengths times 30 lateral correlation lengths. The most important result is that regardless of the spacing value, SNR_V produces the largest CNR_q values. The interplay between the pulse bandwidth and the interference pattern of scattered waves results in the trend of CNR_q as the MSS is varied. When $MSS < 0.3\lambda$, CNR_q values reduce to zero because the corresponding frequency $f = c/2MSS$ is larger than the maximum frequency of the pulse bandwidth. When the spacing is larger than approximately 1.13λ (the axial correlation length), CNR_q values for SNR_V , SNR_I , and the Nakagami m become negative as a consequence of the resolved scatterer periodicity that creates non-stationary echo signals and pre-Rayleigh statistics. Within $0.3\lambda < MSS < 1.13\lambda$, the statistics are post-Rayleigh,³⁸ and maxima CNR_q occur at integer multiples of 0.5λ due to constructive echo interference, as described by Tuthill *et al.*²⁹ The overall maximum at 0.5λ results from the proximity of the corresponding frequency to the maximum of the pulse spectrum.

2) Phantom Results—Figure 8 compares values of CNR_q from the four parameters estimated from simulated (Sim.) and experimental (Exp.) RF data from periodic scatterers with a 1.1λ spacing. The PER size was 12 axial correlation lengths times 12 lateral correlation lengths. In general, phantom-based results support the advantage of model-free parameters for detection purposes, in particular of the SNR_V , over model-based parameters.

B. Parameter selection for non-stationary features

1) Simulation Results—Figure 9(a) shows the normalized contrast C_q in panel (a) and the contrast to noise ratio CNR_q in panel (b) of the maximum value in the collapsed average of the generalized spectrum (MaxCAGS) as a function of the PER size expressed as the product of axial and lateral correlation lengths. Each color curve corresponds to a different GS estimator: single-taper with boxcar (blue) or the first ($k = 0$) DPSS taper for $N_t W = 6$ (red), WOSA (green), and multitaper, MTM, $N_t W = 6$ (black). The coherent component in the sample was a periodic array of scatterers separated by 0.4mm. Note that the contrast

from all the estimators approaches zero for PER sizes smaller than 5 axial correlation lengths $\times$ 5 lateral correlation lengths. When using larger PERs, the multitaper method offers the highest contrast of MaxCAGS. At a PER size of 15 axial correlation lengths $\times$ 15 lateral correlation lengths, the contrast from the multitaper estimator is about three times higher than that from any of the other methods. The CNR_q of MaxCAGS from the multitaper estimator is greater than the values from other estimators.

Fig. 10 shows the CNR_q of the periodicity peak in the CAGS as a function of the scatterer spacing in the simulated data. The CNR_q from all the estimators drops to zero when the scatterer spacing is smaller than 0.7λ .

2) Phantom Results—Figure 11 shows the CNR_q of MaxCAGS for the 0.4mm fiber spacing as a function of the PER size in units of axial correlation lengths times lateral correlation lengths. Each curve corresponds to a different estimator of the generalized spectrum. As expected, CNR_q increases as the PER size increases for all estimator methods. However, no significant difference was observed among the different estimators, with the exception of the single-taper estimator with the DPSS taper, which offered the lowest CNR_q over most of the analyzed PER sizes. Possible causes of this limited advantage of the multitaper estimator, as well as other factors motivating its selection for the algorithm, are addressed in the Discussion.

C. Detection performance of entire algorithm

1) Simulations Results—Figure 12 shows images of the detection ratio, defined in Section II.C.1, that result from applying the algorithm to 60 independent realizations of the simulated phantom, with zones of (a) stationary, incoherent scattering, (b) low scatterer density, (c) non-stationary scatterer periodicity, (d) stationary scatterer periodicity, and (e) specular reflector or dominant scatterer. Table I shows the average and standard deviation of the detection ratio within each region (see Fig. 5). Region 1 with only 2 scatterers per resolution cell, was classified $63 \pm 11\%$ of the time as a region of low-scatterer density; $26 \pm 12\%$ of the time as a region with periodic scatterers (possibly due to the presence of two scatterers within the resolution cell); and $11 \pm 4\%$ of the time as a region with a specular reflector (possibly due to the presence of a single scatterer per resolution cell). Most importantly, the detection ratio of diffuse scatterers within this region was 0%, thus completely excluding this region from any further analysis that assumes diffuse scattering conditions. In Regions 2, 3, 4, and 5 the detection ratio for stationary, incoherent scattering progressively increases as the scatterer number density increases, reaching a maximum of 95%. In particular, Region 4 has a detection ratio of $88 \pm 22\%$ due to the PERs being located at the transition with zones containing periodic scatterers, which were classified as containing a dominant scatterer or specular reflector. In Region 5, the frequency corresponding to the spacing of the periodic scatterers was beyond the sensitivity limits of the acoustic pulse and was therefore classified mainly as a zone with stationary incoherent scattering. Regions with periodic scatterers (excluding Region 5) were classified as such with detection ratios larger than $97 \pm 4\%$. Finally, Fig. 12(e) shows the detection ratio of the PERs classified as including a specular reflector. Most of the PERs exhibiting a high

detection ratio were located at the boundaries between regions. The highest detection rate occurs in the boundary between Region 4 and Regions 10 and 11.

Fig. 13 shows a parametric image of the mean scatterer spacing (MSS). In those cases where non-stationary periodicity was detected, the spacing was computed by automatically choosing either the non-stationary or the stationary estimators depending on the nature of the echo signals. Table I includes the average and the standard deviations of the MSS estimates for each of the regions. In Region 1, which was classified as containing periodic scatterers with a detection rate of 26%, the average of the mean scatterer spacing was about 0.20mm. The large standard deviation is caused by the spread of the frequencies detected by the generalized spectrum. Average scatterer spacings in Regions 6 to 11 agree with the expected values. The largest bias was observed in Region 9, which can be attributed to the PERs located at the boundary between the regions with 0.40mm and with 0.80mm spacing.

2) Phantom Results—Fig. 14 shows (a) a B-mode image of the data frame from the fiber phantom as well as (b) an image showing regions classified as diffuse scattering (blue), low scatterer density (green), specular reflectors (transparent), and periodic scatterers (red). In general, the classification achieved by the algorithm agrees with the structural composition of the phantom. In the top part, ranging in depth from 0 to 25mm, the phantom consisted of only randomly positioned scatterers. The algorithm classified 77% of this area as a region with diffuse scattering conditions, while 20% was classified as regions with low scatterer density. In the region of the periodically spaced nylon fibers, 84% of the area was classified as a region with scatterer spacing periodicity, while 16% was classified as a region containing specular reflectors. The area classified as containing specular reflectors is mainly the initial interface between the background and the fiber array.

Fig. 14(c) shows a Mean Scatterer Spacing (MSS) image of the phantom. To generate this image, the algorithm automatically detected the regions where periodic scatterers were present and then estimated the spacing only in these regions based on either the computed MaxCAGS or the phase χ^2 . A histogram of the MSS values estimated in those PERs classified as containing periodic scatterers is shown in Fig. 14(d). The vertical axis of this plot shows the occurrence, i.e., the number of PERs in which a particular MSS value was obtained expressed as a fraction of the total number of PERs classified as containing periodic scatterers. The MSS value corresponding to the fiber spacing (0.4mm) shows maximum occurrence (73%). The next highest occurrence values are close to the upper limit of the fiber region. These large spacing values, and the corresponding low frequencies, can be caused by the overall increase in the frequency correlation occurring when the fibers act as specular reflectors.

IV. Application to cervical tissue

To provide an example of the performance of the decision algorithm on echo signals from tissue, we applied it to backscatter data from human hysterectomy samples of the normal uterine cervix. The motivation to study the cervix is to understand changes in the microstructure of the uterine cervix during pregnancy. The collagen structure of the cervix is known to be pseudo-aligned in layers.^{28;75;76} This presents the reasonable possibility that

collagen fibers might be sufficiently aligned and periodically spaced to introduce a significant coherent component in the backscattered echo signals. This could influence criteria for accurate attenuation and backscatter coefficient estimation and could confound data interpretation. This algorithm provides a rigorous test to investigate that possibility.

Backscatter echo data was collected following Health Insurance Portability and Accountability Act compliant and Institutional Review Board approved protocols.^{77;78} Hysterectomy was indicated due to conditions not involving the cervix. Data were acquired using a Siemens S2000 ultrasound scanner and a 18L6 linear array transducer. Details about specimen preparation and ultrasound data acquisition can be found in Carlson *et al.*^{77;78} Samples were divided by slicing each one through the canal, forming an anterior (front) and a posterior (rear) half.

Figure 15(a) shows a B-mode image of the posterior (rear) half of one sample. The yellow box indicates the portion corresponding to the cervix, with a portion of uterine tissue to the right of the box. The left and right limits of the box indicate the vaginal and uterine ends of the cervix. Letters 'S', 'L', and 'D' designate specular reflectors, zones with low echogenicity, and what appears to be diffuse scattering in the B-mode image.

The algorithm was applied to RF echo data to detect zones with specular reflectors, low scatterer number density, diffuse scattering, and periodic scatterers, over 4×4mm PERs with an 85% overlap. Twenty frames of RF data from a phantom (equivalent to the reference phantom described in Section II.A) also were acquired to be used as reference. The results are shown in Fig. 15(b)–(e). In Fig. 15(b), PERs along the upper boundary of the sample corresponding the endocervical canal as well as those around bright reflectors (S) are detected as such. Normal QUS parameter estimation would avoid the boundaries of the tissue, and the specular reflections in those areas. However, as described by Luchies *et al.*,¹⁴ there is value in avoiding specular reflections within the PER. Figures 15(c) and (d) show regions classified as low-scatterer number density and diffuse scattering, respectively. These regions correspond to hypoechoic and isoechoic zones indicated by letters L and D. These areas could be processed with typical QUS parameter estimation procedures, or the PER could be increased in areas with low scatterer density to reduce bias and variance in QUS parameter estimates. Finally, Fig. 15(e) shows PERs classified as containing periodic scatterers, which were mostly concentrated at the bottom of the sample. Even though histology images demonstrate aligned collagen,¹⁸ apparently the extent to which the fibers are aligned, the irregularity in their spacing, or the dense packing of fibers results in little coherence in the echo signals at this frequency range and PER size. Therefore, based on this and equivalent analysis of other specimens, typical QUS parameter estimation in the cervix seems well-founded.

V. Discussion

The algorithm reported here tests the conventional assumptions of stationary echo signals and diffuse scattering, conditions that are commonly assumed in QUS, and offers a new starting point in the analysis of backscattered echo signals. This new starting point is centered on choosing an analysis that is appropriate for the scattering source instead of

simply making assumptions. In this way, the backscattered echo data and the valuable information it carries are fully exploited. The algorithm described here has four important properties: (1) It is based on carefully-optimized detection parameters. (2) It does not depend on segmentation stages performed by the user, making it a stand-alone method. (3) It automatically segments regions where the echo signals are consistent with a stationary diffuse scattering process and therefore suitable for the estimation of the attenuation coefficient and effective scatterer size. (4) When periodic scatterers are detected, it automatically decides on the best way to estimate the mean scatterer spacing depending on the properties of the echo signals.

Some of the parameters used in the classification strategy have been used as diagnostic tools for different diseases, as described by Shankar *et al.*^{12;40–45}, Dutt and Greenleaf⁵⁰, and Tsui *et al.*^{47;79;80} when dealing with stationary features, or in the series of papers by Donohue *et al.*^{20;25;57;67;73;81} dealing with non-stationary features.

In the case of stationary echo signals, our results showed a ubiquitous advantage of SNR_V regardless of the PER size (Fig. 6) and scatterer spacing (Fig. 7). The main limitation of model-based parameters is the large variance of their estimates, which leads to lower CNR_q values as shown in Figs. 6(b), 7 and 8. The variance of these parameters can be reduced by spatial (angular) or deformation compounding.^{37;51} However, when there is no interest in studying the spatial variations of the parameters within an ultrasound scan and large amounts of data are available for their estimation, their physical interpretation may offer a great advantage over model-free parameters. In addition, Fig. 8 showed that CNR_q values obtained from experimental data were about half the values obtained from simulated signals. This can be attributed to the larger variance in experimental data compared to simulated signals.

In the case of non-stationary echo signals, we investigated features related to coherent scattering in various estimators of the generalized spectrum.^{16;19;20;25;57} In general, it was found that the multitaper estimator of the generalized spectrum had a better detection performance than other estimators of the generalized spectrum (Figs. 9 and 10), which agrees with results of Rubert and Varghese.¹⁶ Figure 10 also showed that as the spacing between periodic scatterers increased, CNR_q decreased for all estimators of the generalized spectrum. The reduction of CNR_q from the WOSA and the multitaper estimators was more severe because, as the spacing increased, the separation among adjacent periodicity cells decreased and their overlap increased. This is a consequence of the larger size of the periodicity cell compared to those of single taper estimators. C_q could potentially be increased by reducing the $N_t W$ value (and hence number of tapers) in the multitaper estimator or by increasing the subsegment length in the WOSA estimator when trying to detect periodic scatterers with longer spacings. This would come at the expense of larger estimate variance and would require some prior knowledge about the scatterer spacing. Our results support the use multitaper estimator with $N_t W = 6$ for our algorithm, based on the larger CNR_q over other estimators and the accuracy of the mean scatterer spacing estimates over the relatively large range of spacing values that was studied.

Tissue-mimicking phantom results in Fig. 11 showed that the multitaper estimator produces similar CNR values to the WOSA and the single-taper with a rectangular window. This is different from what is observed in simulations (Fig. 9(b)). This can be attributed to experimental variations in the scatterer spacing, which has been shown to reduce the advantage of the multitaper estimator compared to other estimators.²⁷ In spite of this limitation, results reported elsewhere have shown that the multitaper estimator is less sensitive to spurious peaks in the collapsed average representation of the generalized spectrum, thus providing more accurate estimates of the mean scatterer spacing over a wide range of spacing values compared to other estimators of the generalized spectrum and to singular spectrum analysis.^{16;27;82} This further motivated the selection of the multitaper estimator for our algorithm.

The parameters from stationary and non-stationary features of the echo signals were combined in an algorithm based on comparing the detection parameters to their empirical cumulative distribution function obtained from echo signals from a reference material constructed to achieve conditions of stationary, diffuse scattering. The empirical cumulative distribution was previously used by Georgiou *et al.*¹³ to segment echo signals with pre-Rayleigh statistics by comparing with the theoretical K distribution. It is important to mention that the acquisition of the reference data is a standard of practice in our protocol to compensate for diffraction and system dependent factors when estimating the attenuation and the backscatter coefficients.⁷ Thus, it does not imply an additional workload during data acquisition with our clinical protocols.

The results of the application of the algorithm to a tissue mimicking phantom showed good agreement between its design and the classification of zones with different scattering conditions. An exception was a zone classified as having low scatterer number density in the area expected to show diffuse scattering conditions, representing a misclassification rate of 20%. Results from simulations showed that a 50% reduction in the scatterer number density (to that of the reference material) resulted in detection ratio of low scatterer density conditions of 20%. However, in the latter case, PERs within this category were randomly and uniformly distributed within the corresponding area instead of being congregated within a particular region of the simulated phantom. Whether the phantom really contains such a localized reduction in the glass bead concentration could only be tested destructively. Future work will investigate more complex phantoms to further test the specificity of the algorithm.

When applied to backscattered echo signals from *ex vivo* cervix tissue, the algorithm demonstrated significant specular scattering at the boundaries of the tissue as well as with the presence of bright point-like reflectors, as expected (Fig. 15(b)). Some regions along the upper boundary were not selected as specular reflectors due, in part, to the oblique incidence of the acoustic beam with the tissue boundary, causing lower backscatter. To increase the sensitivity of the algorithm, we are currently expanding our analysis to include multiple beam-steered views. It was also encouraging that zones of low echogenicity and similar echogenicity to the reference material were classified as zones with low scatterer density and diffuse scattering.

Backscatter from *ex vivo* cervix tissue demonstrated insignificant contribution from periodically-spaced scattering structures. Although collagen fiber (pseudo-)alignment is obvious in nonlinear optical microscopy imaging, their alignment might be too weak and/or their spacing too irregular to result in echo signal coherence (see, for example, Figs. 6 and 7 in Reusch *et al.*)¹⁸ We are currently performing a systematic comparison of collagen microstructure assessed through nonlinear optical microscopy with the results of the application of the algorithm in *ex vivo* cervix samples of humans and a Rhesus-macaque model. We are also improving the algorithm to provide a measure of the confidence of the classification. In the long term, we hypothesize that the algorithm could be used to track progressive collagen breakdown in the cervix that, at a normal rate, leads to a healthy delivery, but at a pathologically rapid rate, can lead to spontaneous preterm birth. For this purpose, parameters derived from the algorithm, such as the fraction of the cervix classified as having diffuse scattering, could be studied as a function of gestational age.

We are currently combining the use of the algorithm with the estimation of conventional QUS parameters. As previously stated, in those cases where periodic scatterers are detected, the mean scatterer spacing can be used as a parameter for tissue characterization. In those cases where specular reflectors or low scatterer concentrations are detected, different strategies could be followed to circumvent the problem. In the case of specular reflectors, Luchies and Oelze¹⁵ proposed to estimate the power spectral density using tapers with gaps at the locations of specular reflectors to avoid them. In the case of low scatterer number densities, the main problem is an increase in variance associated with the poorly sampled scattering process. This can be overcome by additional averaging techniques such as angular and deformation compounding,^{37;83} or increasing the area of the PER when possible. When no additional averaging is feasible, a multitaper power spectral density estimator can be used, where the number of tapers is chosen to reduce spectral variance without compromising accuracy.⁸⁴

A limitation of our study is the lack of consideration of diffraction in the simulations. The simple, diffraction-less simulation tool used in this work and elsewhere²⁹ allowed us to have a better understanding of the relationship between the values of the different parameters that were investigated and the phase relationships among the scatterers. This provided valuable insight into the strengths and weakness of the parameters for the task of detecting coherent scattering. The introduction of diffraction is not expected to significantly influence our observations. This is because the main effect of diffraction is a limitation of the lateral size of the resolution cell without affecting the phase relationship among scatterers.

Regarding the proposed algorithm, a limitation of our approach is that the size of the resolution cell in the reference material has to be close to that in the sample at a particular PER location. For the size of the resolution cell to be similar in the sample and the reference at a particular PER location, the diffraction field and the bandwidth of the acoustic pulse should be similar in both materials. This requires the phantoms to have similar sound speed and attenuation.³¹ An additional limitation could be the lack of echo signals within a PER, which can result from the presence of a highly reflective tissue interface or severely attenuating tissue above the PER, as well as from an absence of scattering sources (such as in a simple cyst). In this case, the result of the algorithm would not be representative of the

underlying tissue but a characterization of the detected noise. If the noise is white and Gaussian, the PER would be classified as meeting conditions of diffuse scattering. However, further estimation of parameters based on diffuse scattering would not proceed because of the low SNR of the power spectrum estimate.

VI. Conclusions

The manuscript reported a comprehensive approach to detecting and classifying stationary and nonstationary sources of coherent scattering in ultrasound echo signals. Our tests using simulated and phantom-based echo data from different scattering scenarios demonstrated that the algorithm was able to identify different sources of coherent scattering, such as periodic scatterers with subresolution or resolved spacing, as well as regions with low scatterer densities. When applied to echo signals from *ex vivo* cervix tissue, the algorithm found no significant periodically-spaced scattering sources. Specular reflection was demonstrated where it was expected, but much of the cervix was classified as likely having sparse scattering sources, which correlated well with low echogenicity in B-mode images.

Acknowledgments

The authors thank Ernest Madsen and Gary Frank for constructing the phantoms used in the study. We are grateful for the technical support from Siemens Ultrasound. This work was supported by grants R01CA111289 and T32CA009206 from the National Cancer Institute, and grants R21HD061896, R21HD063031, and R01HD072077 from the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. We also thank the Consejo Nacional de Ciencia y Tecnología de México for its support (I.R.-M., Reg. 206414).

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Fig. 1.

(a) A photograph of the fiber phantom during its construction showing a horizontal (H) and a vertical (V) plane of parallel, equally spaced, 100μm diameter nylon fibers. (b) B-mode image of the fiber plane with the 18L6 transducer.

Fig. 2.

Generalized spectrum obtained with (a) single-taper with first DPSS for $W=1$ MHz, and (b) multitaper for $W=1$ MHz from simulated backscatter echo data from a periodic array of scatterers separated by 0.4 mm within a cloud of 48 random scatterers/resolution cell.

Fig. 3. Computation of the Collapsed Average from the bifrequency plane of the generalized spectrum

Fig. 4.

Diagram describing the algorithm for detecting and classifying coherent scattering. Quantification parameters are SNR_V (signal to noise ratio of the echo amplitude), MaxCAGS and MLW (maximum value of the collapsed average and main lobe width of the multitaper generalized spectrum, respectively), and phase uniformity χ^2 metric. Those parameter values are individually compared to the empirical cumulative distribution of values obtained from the reference (diffuse scattering) phantom.

Fig. 5.

(a) Diagram and (b) B-mode image of the simulated phantom. Sc/RC is an abbreviation for "scatterers per resolution cell". Numbers in regions 5 to 11 indicate separation between periodic scatterers.

Fig. 6.

(a) Parameter contrast C_q and (b) contrast-to-noise ratio CNR_q of the investigated parameters as a function of the PER size in number of axial times lateral correlation lengths. Mean spacing 0.9λ . HK=Homodyned K.

Fig. 7.

Parameter contrast-to-noise ratio CNR_q of the investigated parameters as function of the scatterer spacing expressed in multiples of the wavelength ($\lambda=0.26\text{mm}$)

Fig. 8.

Parameter contrast-to-noise ratio CNR_q values of the four investigated parameters for simulated data (Sim.) and the phantom-based experiment (Exp.). Lines are visual guides to the data. Results from the simulations are also included in Fig. 7 (spacing of 1.1λ).

Fig. 9.

(a) Normalized contrast C_q and (b) contrast-to-noise ratio CNR_q of the periodicity peak in the Collapsed Average of the Generalized Spectrum as a function of the PER size. Curves correspond to different estimators: Single taper estimator with boxcar (blue) or first DPSS ($k=0$) for $N_t W = 6$ (red) tapers, Weighted Overlapped Segment Average estimator (WOSA, green) and multitaper estimator (MTM, black). The simulated sample phantom consisted of a random scatterer concentration of 48 scatterers per resolution cell and a periodic array of scatterers with spacing equal to 1.6λ . The simulated reference had a random scatterer concentration of 48 scatterers per resolution cell.

Fig. 10.

Contrast-to-noise ratio CNR_q of the periodicity peak in the Collapsed Average of the Generalized Spectrum as a function of the scatterer spacing in units of wavelengths ($\lambda=0.256\text{mm}$). Curves correspond to a different estimator: Single taper estimator with boxcar (blue) or first DPSS ($k=0$) for $N_t W=6$ (red) tapers, Weighted Overlapped Segment Average estimator (WOSA, green) and multitaper estimator (MTM, black). The simulated sample phantom consisted of a random scatterer concentration of 48 scatterers per resolution cell and a periodic array of scatterers. The simulated reference had a random scatterer concentration of 48 scatterers per resolution cell. The PER size was 15 axial correlation lengths times 15 lateral correlation lengths.

Fig. 11.

Contrast-to-noise ratio CNR_q of the periodicity peak in the Collapsed Average of the Generalized Spectrum corresponding to the 0.4mm spacing of the fibers in the tissue-mimicking phantom, plotted as a function of the PER size. Curves correspond to different estimators: Single taper estimator with boxcar (blue) or first DPSS ($k=0$) for $N_t W=6$ (red) tapers, Weighted Overlapped Segment Average estimator (WOSA, green) and multitaper estimator (MTM, black).

Fig. 12.

Detection ratio images for the final classification: (a) Stationary, incoherent scattering, (b) low scatterer density, (c) non-stationary scatterer periodicity, (c) stationary scatterer periodicity, and (e) specular reflectors or dominant scatterers.

Fig. 13.

Image of the mean scatterer spacing (MSS) from the simulated contrast phantom averaged over 60 independent frames overlaid over the B-mode image.

Fig. 14.

(a) B-mode image and (b) classification image of the fiber phantom showing zones of diffuse scattering (blue), low scatterer density (green) and scatterer periodicity (red). (c) Parametric image of the mean scatterer spacing (MSS) generated by the algorithm. (d) Histogram of MSS estimates in regions with periodic scatterers.

Fig. 15.

(a) B-mode and classification images (overlaid on top of the B-mode) of zones with (b) specular reflectors, (c) low scatterer number density, (d) incoherent, diffuse scattering, and (e) periodic scatterers of the posterior side of a hysterectomy sample (*ex vivo*). Letters point at S: specular reflectors, D: apparent diffuse scattering, L: apparent low echogenicity. The yellow box encloses the cervix.

TABLE I

Average and standard deviation (Std. Dev.) of the detection ratio and the mean scatterer spacing (MSS) values within each of the 11 regions of the contrast phantom.

Region	Detection Ratio				MSS (mm)		
	LSD	DS	P	SR	Exp.	Est.	
1	63±11%	0±0%	26±12%	11±4%	0	0.18±0.38	
2	20±7%	74±7%	0±1%	5±3%	0	0.00±0.05	
3	5±4%	92±4%	0±0%	3±3%	0	0.00±0.01	
4	3±3%	88±22%	0±1%	9±19%	0	0.00±0.06	
5	2±2%	95±3%	0±1%	3±2%	0	0.00±0.01	
6	0±0%	0±0%	100±1%	0±0%	0.12	0.12±0.02	
7	0±0%	2±3%	98±3%	0±0%	0.24	0.23±0.05	
8	0±0%	3±4%	97±4%	0±0%	0.30	0.29±0.05	
9	0±0%	0±0%	100±0%	0±0%	0.40	0.46±0.01	
10	0±0%	0±0%	100±0%	0±0%	0.80	0.81±0.06	
11	0±0%	0±0%	100±0%	0±0%	1.20	1.20±0.08	

Statistics were obtained from 60 independent frames and within each region.

LSD= Low scatterer density, DS= Diffuse scattering, P=Periodicity, SR=Specular Reflector, Exp=Expected, Est=Estimated