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Comprehensive backscattering characteristics analysis for quantitative ultrasound with an annular array: a basic study on homogeneous scattering phantom

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Abstract

High-frequency ultrasound (HFU, >20 MHz) and quantitative ultrasound (QUS) methods permit a means to understand the relationship between anatomical and acoustic characteristics. In our previous research, we showed that analyzing the acoustic scattering with HFU was an effective method for noninvasive diagnosis. However, the depth of field (DOF) of HFU transducers was limited, which constrains the range of QUS analysis. In this study, we seek to improve the accuracy of HFU, QUS-based parameters on the envelope statistics and frequency-based analysis by using an annular array that allows for an extended DOF. A 20-MHz annular-array transducer with five elements was employed to obtain signals which were beamformed in post-processing. Two kinds of low concentration scattering phantoms were scanned with 30- μ m step size. Two QUS analysis techniques were employed: the Nakagami distribution and the reflector method. The results demonstrated that the annular array provides a stable analysis over an extended axial range.

1. Introduction

Quantitative ultrasound (QUS) techniques provide a means to characterize soft tissue. Tissue characterization methods have been demonstrated in biological soft tissue based on the characteristics of the echo signal such as envelope statistics,¹⁻⁹⁾ frequency-based analysis¹⁰⁻¹⁶⁾ and shear wave elastography.^{17,18)} QUS techniques have already been applied to the diagnosis of some organs (i.e., liver, breast tumor, lymph node). In recent years, new research with a high-frequency ultrasound (HFU, >20 MHz) are progressing to better understand the intricate relationship between ultrasound scattering and tissue properties. Generally, HFU transducers provide high-resolution images because of the short wavelength

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and the small F-number. Thus, QUS techniques with HFU can give insight into tissue microstructure corresponding to the pathological information.

For single-element transducers, spatial resolution is determined by the center frequency and transducer geometry. Depth of field (DOF) is typically extremely limited unless the resolution is sacrificed. A few-millimeter DOF means decreasing the accuracy of the QUS parameter versus penetration depth and limits the range of the analysis. Multi-element array transducer, however, can improve the DOF and the spatial resolution by using a beamforming technique. In particular, standard instrumentation and fabrication methods may be employed to construct an annular array because the size of the individual elements is on the order of conventional HFU single-element focused transducers.^{19,20} An annular array that can provide the expanded DOF has been applied to HFU imaging for small animals^{21,22} and ophthalmology.^{23–26} However, there have been few reports that applied HFU annular arrays to tissue characterization with QUS.

The aim of this study is to improve the accuracy of HFU, QUS-based parameters on the envelope statistics and the frequency-based analysis by using an annular-array transducer that allows for an extended DOF. Two kinds of scattering phantoms with low attenuation and low concentration were employed to validate the approach. The accumulated radio frequency (RF) data were synthetically focused in post-processing. For the envelope statistics, we estimated the QUS parameters with the Nakagami distribution.²⁷ The Nakagami distribution can support the evaluation of a low scatterer concentration. For the frequency-based analysis, we estimated the scatterer diameter with the reflector method as a QUS-based parameter.

2. Materials and methods

2.1. Annular array and synthetic focusing

The 20-MHz annular array used in this study was fabricated using a previously described technique.¹⁹ A 25- μm -thick poly(vinylidene fluoride-tetrafluoroethylene) [P(VDF-TrFE)] film membrane was employed as the acoustic layer of the array. This membrane was metalized with one side and bonded to a copper-clad polyimide film (flex circuit) with degassed epoxy. The array has five equal-area annuli with a 10-mm total aperture and a 31-mm geometric focus. The spacing between the annuli was 100 μm .

To improve the spatial resolution and the DOF by using the annular array, a synthetic-focusing (SF)²⁸ technique was applied to post-process the 25 sets of the RF signal. SF was achieved by applying a round-trip delay to each transmit-receive (TR) pair for an arbitrary focal depth and then summing the data to create a locally focused area. To focus at the depth f , the delay t_n of each element is

$$t_n = \frac{a_n^2 \left(\frac{1}{R} - \frac{1}{f} \right)}{2c} \quad (1)$$

where a_n is the average radius of the n th element, R is the geometric focal length (i.e., 31 mm), and c is the speed of sound.

Synthetically focused data is formed by applying the delay and sum process to a series of focal depths, windowing the focal region of each focal depth and then splicing all of the focal-depth data. For a final image with q focal depths, the SF algorithm is defined as²⁰⁾

$$a(t) = \sum_{o=1}^q \left(\sum_{l=1}^n \sum_{m=1}^n E_{l,m}(\mathbf{r}, t - t_l^T - t_m^R) \right) w^o(t) \quad (2)$$

where $w^o(t)$ is the rectangular window cutting out focal zone o and $E_{l,m}$ is the RF echo signal for TR pair l and m . If the RF signals summed with no delay, the final data simulates a single-element focused transducer with the same total aperture and geometric focus as the annular array. Here, SF was performed at each pixel location of the final image. For example, Fig. 1 shows schematic figures of the focusing methods in the case for a three-element annular array. In Fig. 1, Ch. 1 is excited for transmitting the ultrasound, and all of the channels are used for receiving. In the fixed focusing case [Fig. 1(a)], echo from each depth on the sound axis of Ch.1 (shown as circles) to be added directly, and the focus of the annular array become single geometric focus determined by its curvature consequently. In the synthetic focus case [Fig. 1(b)], appropriate delays are added according to the combination of TR between each channel and the arbitrary position (distance), resulting in the convergence of the wavefront at a synthetic focal point closer than the geometric focus. Actually, this post-processing is performed for transmission on each channel.

The lateral beam profiles were measured by scanning the annular array across the wire.²⁹⁾ Figure 2 shows B-mode images from the echo data of a 50- μm stainless steel wire by using the annular array with the wire positioned 25 mm and 31 mm from the array surface. The four images were normalized by each maximum amplitude, and the dynamic range was 30 dB. The wire was scanned with a 15- μm step size in a lateral direction. Figures 2(a-1) and 2(b-1) represent the SF case, and the image seems almost the same at each depth. In contrast, the B-mode image in the fixed focusing (FF) case [Figs. 2(a-2) and 2(b-2)] had a wide lateral resolution off-focus. At the geometric focus, the acoustic field was the same as the SF and the FF case because the time shift is not valid. Figure 3 shows the magnitude of the signal and lateral resolution at each wire position. The DOF was determined within the range of -6 dB from the maximum intensity of the echo envelope. The DOF was expanded from 5 mm to 17 mm (solid lines), and the improvement of the lateral resolution was also evident (dashed lines) by applying the SF technique. The lateral and axial resolutions at the 31-mm focal depth were 200 and 100 μm , respectively. The power spectrums of the echo signal from an acrylic plate are shown in Fig. 4. The blue line is the case of using the SF technique, and the red dashed line is the summed case (FF). At 31-mm [Fig. 4(b)] there was no difference between each focusing method, but Fig. 4(a) shows the benefit of applying the SF technique; the power spectrum was similar to 31-mm depth.

2.2. Echo envelope statistics analysis

The Rayleigh distribution is one of the standard distributions that explain the envelope amplitude, but that follows a probability density function (PDF) of the echo signal amplitude from only homogeneous scattering mediums (i.e., >10 scatterers/resolution cell). In addition, there are some models that describe the envelope statistics of the RF signals and mainly are categorized into Rayleigh, pre-Rayleigh, and post-Rayleigh distributions.^{4,30,31)} Therefore, the Nakagami distribution was employed, which is a generalized two-parameter statistical model that exhibits computational simplicity and encompasses the three conditions.^{4,30,31)} When R was derived as a result of the Hilbert transform of the RF signal, $p(R)$ which shows the PDF of the echo envelope in the ROI under the Nakagami model is given by²⁷⁾

$$p(R) = \frac{2\mu^\mu R^{2\mu-1}}{\Gamma(\mu)\omega^\mu} \exp\left\{-\left(\frac{\mu}{\omega}\right)R^2\right\} U(R) \quad (3)$$

where Γ is the gamma function, and U is the unit step function, ω is a scaling parameter, and μ is the Nakagami parameter. In this statistical analysis, μ and ω were determined by maximizing the likelihood estimation using an ascent algorithm. At first, two parameters can be obtained from $\omega = E(R^2)$ and

$$\mu = \frac{(E[R^2])^2}{E[(R^2 - E[R^2])]} \quad (4)$$

as the initial value with the moment method.^{30,31)} In Eq. (4), E explains the expectation of the sample points within each ROI. In maximizing the likelihood estimation, the likelihood estimator ($\hat{\mu}$ and $\hat{\omega}$) were obtained by assuming that every envelope value within the ROI was independently and identically distributed based on the general maximum likelihood estimation method. The Nakagami parameter μ represents a shape parameter determined by the statistics of the backscattered signal. As the μ varies from 0.5 to 1, the envelope statistics change from a pre-Rayleigh to a Rayleigh distribution, which means low scatterer density, and the statistics of the backscattered signal conform to post-Rayleigh distributions when larger than 1. When μ is 0.5 to 1, the value reflects the scatterer density, especially the number of scatterers per the resolution cell. Moreover, when $\mu > 1$, the value reflects a scattering medium that contains a coherent signal component in addition to a speckle pattern component.

2.3. Backscatter coefficient (BSC) analysis

The frequency characteristics of the backscatter signals measured by a transducer include the characteristics of the measurement system (i.e., acoustic field and electrical circuit) and the scatterers in the scattering medium. To cancel the characteristics of the measurement systems and measure the BSC value, the reflector method was employed.³²⁾ In the case of an annular-array analysis, the measured BSC value σ_{meas} is estimated from the small ROI defined as^{10,32,33)}

$$\sigma_{meas} = 0.3625 \frac{A' \gamma^2 R^2 \langle |P_{meas}(k)|^2 \rangle}{A_0^2 L |P_{ref}(k)|^2} H(k) \quad (5)$$

where $\langle |P_{meas}(k)|^2 \rangle$ is the average of the power spectrum of several adjacent lines in the ROI, $|P_{ref}(k)|^2$ is the power spectrum from an acyclic plate for reference and k is the acoustic wave number ($k = 2\pi/\lambda$). γ is the pressure reflection coefficient of the planar reflector (water: 1.5 MRayl and acrylic plate: 3.0 MRayl), R is the distance from the transducer to the center of the ROI, A_0 is the area of the radiating surface, A' is the nominal area of the aperture, and L is the length of the ROI. The coefficient 0.3625 is the value derived in Refs. 10, 32, 33. The attenuation function $H(k)$ shown in Eq. (6) is a function which compensating for acoustic attenuation from the transducer surface to the upper part of the ROI and the attenuation in the ROI,³⁴⁾ and it is defined as

$$H(k) = e^{4\alpha_0(kc/2\pi)x_0} \left(\frac{2\alpha(kc/2\pi)L}{1 - e^{-2\alpha(kc/2\pi)L}} \right)^2 \times \left\{ 1 + \left(\frac{2\alpha(kc/2\pi)L}{2\pi} \right)^2 \right\}^2 \quad (6)$$

where α is the attenuation coefficient in the ROI, α_0 and x_0 are the attenuation coefficient and propagation distance, respectively.

In our previous study, the accuracy of the QUS parameter estimation assuming the spherical Gaussian model (SGM) case was low,³⁵⁾ and the results of the fluid-filled sphere (FFSM) and the structure factor model (SFM) was almost same under the low scattering condition.³⁶⁾ Thus, the QUS parameters were analyzed by the SFM in this study. By considering an ensemble of identical solid spheres independently and randomly distributed, the theoretical BSC using the FFSM model can be expressed as $BSC_{FFSM}(k) = \phi/V_s \sigma_b(k)$ where ϕ is the scatterer concentration, and V_s is the sphere volume. The ratio ϕ/V_s , corresponds to the number density of spheres. The differential backscattering cross section $\sigma_b(k)$ was calculated using the Faran theory.³⁷⁾ The SFM is based on the supposition that at high scatterer concentrations, interference effects are mainly caused by correlations between the spatial arrangements of individual scatterers. By considering an ensemble of identical solid spheres, the theoretical BSC for the SFM formulation is given by³⁸⁾

$$BSC_{SFM}(k) = \frac{\phi}{V_s} \sigma_b(k) S(k) \quad (7)$$

where $S(k)$ is the structure factor which depends on the pattern of the spatial arrangement of the scatterers and the scatterer concentration. $S(k)$ is explained as Eq. (8),

$$S(k) = 1 + m \int (g(r) - 1) e^{-2jkr} \quad (8)$$

where $g(r)$ represents the probability of finding two particles separated by a distance. Equation (8) cannot be computed for a complex spatial arrangement of the scatterers, however, for a medium of identical spheres homogeneously distributed, an expression for the $S(k)$ can be obtained. The version of the analytical expression for the $S(k)$ used here is described in detail in the Franceschini's report.³⁸⁾

The scatterer size was estimated by fitting the measured BSC σ_{meas} to the theoretical BSC $\sigma_{theo}(BSC_{SFM})$ by minimizing the cost function

$$F = \sum_j \left\| \log_{10} \sigma_{meas}(k_j) - \log_{10} \sigma_{theo}(k_j) \right\|^2 \quad (9)$$

where σ_{theo} is given by Eq. (7). The cost functions were minimized to the -20-dB frequency bandwidth of the measured spectrum, and the fitting procedure was computed using the minimization routine *fminresearch* in MATLAB (Math Works). In general frequency analysis, the -6 dB or -20 dB bandwidth is employed for the BSC analysis. In this research, -6 dB was narrow for the analysis because the pulse length of our annular array is more extended than general single-element transducers. Therefore, the -20 dB was employed in this paper.

2.4. Scattering phantom experiment

The RF echo data sets of all 25 TR ring pairs were acquired by scanning the annular array using our handmade ultrasound scanner (Fig. 5). To accomplish this task, one element was excited with a negative impulse, and the echo was received by one of the five elements (i.e., transmitting by Ch. 1 and receiving by Ch. 3) filtered with a 1 to 35 MHz band-pass filter by using the pulser/receiver (Model 5800, Panametrics-NDT). The switch was configured with the five array elements on input lines, the pulser/receiver on two output lines. The cross point (CXL/8X8, Cytec) switch permits any input to be connected to any output. Each echo signal was digitized to 12 bits/sample by a digital storage oscilloscope (HDO6104, Teledyne LeCroy) with a sampling frequency of 250 MHz. All data acquisition was controlled by using LabVIEW (National Instruments).

The scattering phantoms were a mixture of distilled water, 2% (w/w) agar powder, and 0.3 or 1% (w/w) acrylic monomer scatterer with a diameter of 20 μm (MX-2000, Soken Chemical). The image was taken with the optical microscope, and the scatterer size distributions were estimated from the optical image as shown in Fig. 6. The estimated scatterer size distribution for the scattering phantoms are explained in Fig. 6(b). The 20- μm diameter was the suitable estimation condition of scatterer characteristics for the range of ka values between 0.5 and 1.2 in the BSC analysis.³⁹⁾ Where k is the acoustic wave number ($k = 2\pi/\lambda$) and a is the scatterer radius. The wavelength λ is 75 μm at 20 MHz when the speed

of sound of propagation is 1500 m s^{-1} . Thus, the scatterer diameter can be estimated with high accuracy within 12.0 to $28.6 \mu\text{m}$ when the frequency is 20 MHz, and 12.0 to 28.6 MHz when the scatterer diameter is $20 \mu\text{m}$. Especially, $ka = 0.84$ when the measuring frequency and the scatterer size are 20 MHz and $20 \mu\text{m}$, respectively.

The attenuation coefficients of the two phantoms were determined using a standard substitution method⁴⁰⁾ with a 15-MHz single-element plane transducer (0.3 and 1% were 0.16 and $0.37 \text{ dB MHz}^{-1} \text{ cm}^{-1}$, respectively).

The phantoms were put in a water tank filled with degassed water and scanned with a $30 \mu\text{m}$ step size. After applying two beamforming algorithms to obtained 25 TR echo data, two QUS parameters were estimated with a small ROI that was $600 \mu\text{m}$ in the axial direction and $900 \mu\text{m}$ in the lateral direction. The axial size was defined as eight times the acoustic wavelength that was calculated at 20 MHz, and the lateral size was defined as five times the point spread function of the lateral direction. It has addressed that the size of ROI is encouraged to over five times from the size of resolution cell in the envelope statistics,^{3,31)} and 10 times of the wavelength of the center frequency is usually required for high accuracy analysis of BSC.^{11,15,38)} However, envelope statistics and BSC analysis were also performed with ROI size ten times wavelength, and its result was the same as eight times. Therefore, the axial ROI size which was smaller one was employed in this study.

3. Results and discussion

3.1. B-mode images

Figure 7 shows the B-mode images of the phantom for SF [Fig. 7(a-1) and 7(b-1)] and FF [Fig. 7(a-2) and 7(b-2)]. It can be confirmed that the resolution is enhanced over the wide range in SF, but only the geometric focal depth was focused in the FF case. The 0.3% phantom case showed the variation in brightness value reflecting the array's acoustic field. In contrast, the influence of attenuation became stronger, and the characteristics of the sound field were not noticeable (the power was decreasing linearly) in the 1% phantom condition.

3.2. Evaluation of Nakagami parameter

Figure 8 shows the mean values and the standard deviations of QUS parameters of μ on Nakagami model. Figures 8(a) and 8(b) means 0.3 and 1% phantom case, respectively. The blue lines and orange lines in Figs. 8(a) and 8(b) explain the results of SF and FF method, respectively. In the results of 0.3% phantom [Fig. 8(a)], the value of μ around the focal depth was almost the same on both cases of SF and FF. However, for SF, μ had a constant value even at a depth other than the focus, whereas the fluctuation of μ was large in the result of FF. The fluctuation in FF looks like the variation of the lateral resolution in Fig. 3. The value of μ was close to 1.0 near the transducer and at the extremely deep position. Generally, when $\mu = 1.0$, a certain condition could be met; the scatterers are randomly distributed with more than 10 scatterers per resolution cell and the amplitude and phase of the scattered signal is random. The 0.3% phantom with 1.22 scatterers/resolution cell at 25-mm depth and a theoretical value of $\mu \approx 0.6$. SF maintains this relationship at any depth, but the resolution decreases at a shallow depth and deep depth in FF, thus the apparent number of scatterers

changes and the PDF meets the condition of Rayleigh distribution (Sect. 2.2). In Fig. 8(b), which is the result of the 1% phantom, the same tendency as in the case of 0.3% phantom is shown. The 1% phantom with 4.05 scatterers/resolution cell at a 25-mm depth had a theoretical value of $\mu \approx 0.8$. The results of SF and FF had a value close to 0.8 at the around focal depth. However, in the case of FF, $\mu \approx 1.0$ as well as 0.3% phantom, especially near the array.

As a result of the analysis of the amplitude envelope characteristics of the two types of phantoms, the relation between the phantom scatterer density and the evaluated μ was consistent with the theory at the total depth of SF and the focal depth of FF. Based on the above relations, in the scatterer distribution condition in which there is one type of scatterer that was sparse and homogeneously distributed, it was suggested that the axial range that can evaluate the scatterer density of the echo source having scatterers smaller than the resolution cell could be improved by using an annular array with synthetic focusing.

3.3. Evaluation of BSC and scatterer diameter

An example of the result of fitting the theoretical BSC (dashed line) to the measured BSC (solid line) is shown in Fig. 9. In both phantoms, although small differences can be confirmed by each focusing method in the case of out of focus (i.e., 25 mm), a large difference cannot be confirmed as a whole. In the frequency-based analysis method, the echo signal from the planar reflector was used as a reference, and information other than the backscattering wave was pseudo canceled in a small ROI at each depth. By compensating the characteristics of the measurement system, it seems that there was little difference in the curves of BSC.

Figure 10 shows the mean values and standard deviations of the estimated scatterer diameter (ESD). Figures 10(a) and 10(b) shows the case of 0.3 and 1% phantoms. In the case of SF (blue line), the variation of the ESD value with respect to the depth direction was smaller than the result of FF (orange line) in both phantoms. The FF method shows a large value could be estimated out of the focal region. Because the annular array has directivity in each element, when the geometry is out of focus, if the phases of each acquired signal are not aligned, the synthesized signal from the flat plate may appear to be separated. It is thought that the characteristics of the system could not be canceled at depths where the estimation error in the FF was large (i.e., 26 mm) because the phase of each signal from the flat plate did not align well and the signal did not function as a reference. Except for the depth of the error value, there was little difference in the beamforming methods for the ESD value, because of being able to compensate for the characteristics of the measurement system and analyze only the backscattered signal simulated theoretically.

However, the matching accuracy between the actual scatterers size of the phantom and the ESD value was not sufficient. This was the result of using the reflector method because the method only applies to the focal region of the transducer where the wavefront is planar. In addition, it is considered that the compensation of the system characteristic as the circuit was performed excessively, based on the reflection from the plane, was used as a reference in the reflector method. Meanwhile, accurately transmitting and receiving conditions are required for sound field compensation, and in the actual calculation, there is a possibility that sound

pressure characteristics or beamforming characteristics are not compensated. On the other hand, in the reference-phantom method,⁴¹⁾ it can be assumed that the wavefront of the scattered wave is in contact with the surface of the transducer spherically since the reference becomes a sparse point sound source. Thus, it becomes possible to correct the characteristic and sound field of the system mathematically, and the reference-phantom method would be more appropriate to achieve a better estimation with the annular array.

4. Conclusions

An HFU annular array is effective for imaging biological tissue and for tissue characterization. In this study, we measured two kinds of low scatterer concentration phantom by using the 20-MHz annular-array transducer, estimated the two QUS parameters with envelope statistics and frequency-based analysis and examined the effect of the beamforming. This paper demonstrated a stable analysis of the axial range for the Nakagami parameter μ versus the depth in these low scattering media. For the BSC analysis, the result was almost stable, but there was room for improvement of the accuracy. In conclusion, applying the HFU annular array provides a wide-depth range to analyze QUS parameters.

In future work, we will apply the reference-phantom technique⁴¹⁾ for BSC analysis, which has been reported to permit higher accuracy than using the planar reflector method and improve the accuracy of estimation. Additionally, the data acquisition was per one-to-one path in this time. Therefore we will also re-component the pulser/receiver system for the rapid in-vivo measurements.

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References

- 1). Higuchi T, Hirata S, Yamaguchi T, and Hachiya H, Jpn. J. Appl. Phys 53, 07HF15 (2014).
- 2). Igarashi Y, Yamaguchi T, and Hachiya H, Jpn. J. Appl. Phys 50, 07HF02 (2011).
- 3). Omura M, Yoshida K, Kohta M, Kubo T, Ishiguro T, Kobayashi K, Hozumi N, and Yamaguchi T, Jpn. J. Appl. Phys 55, 07KF14 (2016).
- 4). Omura M, Yoshida K, Akita S, and Yamaguchi T, Jpn. J. Appl. Phys 57, 07LF15 (2018).
- 5). Tamura K, Yoshida K, Maruyama H, Hachiya H, and Yamaguchi T, Jpn. J. Appl. Phys 57, 07LD19 (2018).
- 6). Mori S, Hirata S, and Hachiya H, Jpn. J. Appl. Phys 53, 07KF23 (2014).
- 7). Yamaguchi T, Hachiya H, Kamiyama N, Ikeda K, and Moriyasu N, Jpn. J. Appl. Phys 40, 3900 (2001).
- 8). Mori S, Hirata S, Yamaguchi T, and Hachiya H, Jpn. J. Appl. Phys 57, 07LF17 (2018).
- 9). Bui TM, Coron A, Mamou J, Saegusa-Beecroft E, Yamaguchi T, Yanagihara E, Machi J, Bridal SL, and Feleppa EJ, IEEE Trans. Biomed. Eng 64, 1579 (2017). [PubMed: 28113305]
- 10). Insana MF, Wagner RF, Brown DG, and Hall TJ, J. Acoust. Sec. Am 87, 179 (1990).
- 11). Oelze ML, Zachary JF, and O'Brien WD, J Ultrasound Med 21, 1201 (2002). [PubMed: 12418761]
- 12). Mamou J, Coron A, Hata M, Machi J, Yanagihara E, Laugier P, and Feleppa EJ, Jpn. J. Appl. Phys 48, 07GK08 (2009).

- 13). Oguri T, Tamura K, Yoshida K, Mamou J, Hasegawa H, Maruyama H, Hachiya H, and Yamaguchi T, *Jpn. J. Appl. Phys* 54, 07HF14 (2015).
- 14). Fukushima T, Hasegawa H, and Kanai H, *Jpn. J. Appl. Phys* 50, 07HF02 (2011).
- 15). Muleki-Seya P, Guillermin R, Guglielmi J, Chen J, Pourcher T, Konofagou E, and Franceschini E, *IEEE Trans. Ultrason. Ferroelectr. Freq. Control* 63, 1335 (2016). [PubMed: 27164586]
- 16). Kurokawa Y, Taki H, Yashiro S, Nagasawa K, Ishigaki Y, and Kanai H, *Jpn. J. Appl. Phys* 55, 07KF12 (2016).
- 17). Minagawa M, Hasegawa H, Yamaguchi T, and Yagi S-I, *Jpn. J. Appl. Phys* 57, 07LF07 (2018).
- 18). Kitazaki T, Kondo K, Yamakawa M, and Shiina T, *Jpn. J. Appl. Phys* 55, 07KF10 (2016).
- 19). Ketterling JA, Aristizábal O, Turnbull DH, and Lizzi FL, *IEEE Trans. Ultrason. Ferroelectr. Freq. Control* 52, 672 (2005). [PubMed: 16060516]
- 20). Ketterling JA, Ramachandran S, and Aristizábal O, *IEEE Trans. Ultrason. Ferroelectr. Freq. Control* 53, 623 (2006). [PubMed: 16555771]
- 21). Filoux E, Mamou J, Moran C, Pye SD, and Ketterling JA, *IEEE Trans. Ultrason. Ferroelectr. Freq. Control* 59, 2825 (2012). [PubMed: 23221233]
- 22). Aristizábal O, Mamou J, Ketterling JA, and Turnbull DH, *Ultrasound Med. Biol* 39, 2321 (2013). [PubMed: 24035625]
- 23). Silverman RH, Ketterling JA, and Coleman DJ, *Ophthalmology* 114, 816 (2007). [PubMed: 17141314]
- 24). Mamou J, Ketterling JA, and Silverman RH, *IEEE Trans. Ultrason. Ferroelectr. Freq. Control* 55, 508 (2008). [PubMed: 18334358]
- 25). Silverman RH, *Clin. Ophthalmol* 10, 1865 (2016). [PubMed: 27757007]
- 26). Silverman RH, Ketterling JA, Mamou J, Lloyd HO, Filoux E, and Coleman DJ, *Ophthalmic Surgery, Lasers & Imaging* 43, 82 (2012).
- 27). Nakagami M, *Stat. Methods Wave Propag* (Pergamon, New York, 1960), p. 3.
- 28). Arditi M, Taylor WB, Foster FS, and Hunt JW, *Ultrason. Imaging* 4,1 (1982). [PubMed: 7199769]
- 29). Raum K and O'Brien WD, *IEEE Trans. Ultrason. Ferroelectr. Freq. Control* 44, 810 (1997).
- 30). Shankar PM, *IEEE Trans. Ultrason. Ferroelectr. Freq. Control* 47, 727 (2000). [PubMed: 18238602]
- 31). Tsui PH and Chang CC, *Ultrasound Med. Biol* 33, 608 (2007). [PubMed: 17343979]
- 32). Lavarello RJ, Ghoshal G, and Oelze ML, *J. Acoust. Soc. Am* 129, 2903 (2011). [PubMed: 21568393]
- 33). Insana MF, Hall TJ, and Cook LT, *IEEE Trans. Ultrason. Ferroelectr. Freq. Control* 41, 714 (1994). [PubMed: 18263260]
- 34). Oelze ML and O'Brien WD, *J. Acoust. Soc. Am* 111, 2308 (2002).
- 35). Mizoguchi T, Tamura K, Mamou J, Ketterling JA, Yoshida K, and Yamaguchi T, *Proc. Symp. Ultrason. Electron* 2018.
- 36). Mizoguchi T, Tamura K, Mamou J, Ketterling JA, Yoshida K, and Yamaguchi T, *Proc. IEEE Int. Ultrason. Symp.* 2018.
- 37). Faran JJ, *J. Acoust. Soc. Am* 23, 405 (1951).
- 38). Franceschini E and Guillermin R, *J. Acoust. Soc. Am* 132, 3735 (2012). [PubMed: 23231104]
- 39). Insana MF and Hall TJ, *Ultrason. Imaging* 12, 245 (1990). [PubMed: 1701584]
- 40). Roman K and Mischa S, *IEEE Trans. Sonics Ultrason* 26, 353 (1979).
- 41). Yao LX, Zagzebski JA, and Madsen EL, *Ultrason. Imaging* 12, 58 (1990). [PubMed: 2184569]

Fig. 1.
(Color online) Schematic figure operation of focusing in three arrays. (a) fixed focusing. (b) synthetic focus.

Fig. 2. The echo data from the 50- μm wire at (a) 25-mm (off-focus) and (b) 31-mm (on-focus) depth for the annular array processed with two methods. [(a-1) and (b-1)]; the B-mode image of SF using all 25 TR pair. [(a-2) and (b-2)]; 25 summed TR pair with no delay corrections.

Fig. 3.
 (Color online) The maximum amplitude of the echo signal from the wire and the lateral resolution, solid and dash line, respectively.

Fig. 4.
(Color online) The power spectrum of the echo signal from an acrylic plate from 25-mm depth (a) and 31-mm depth (b).

Fig. 5.
Experimental system diagram.

Fig. 6.
(Color online) (a) Optical microscope image. (b) The scatterer size distributions were estimated from the optical image.

Fig. 7.
B-mode image of the (a) 0.3% phantom and (b) 1% phantom. [(a-1) and (b-1)] the echo data were SF and [(a-2) and (b-2)] the echo data were FF.

Fig. 8.
(Color online) The fluctuation of the Nakagami parameter value versus depth for the two focusing methods.

Fig. 9.
(Color online) Examples of the measured BSC curves and fitted theoretical curves at 25-mm (off-focus) depth and 31-mm (on focus) depth. (a) The result of 0.3% case. (b) The result of 1% case.

Fig. 10.
(Color online) The fluctuation of the ESD value versus depth with two focusing methods.