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1 Verification of effect of interference between multiple scatterers

2 on the evaluation of backscattering coefficient

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- 13
- 14 Abstract

15Backscattering coefficient (BSC) analysis methods for biological tissues have been clinically applied, but they are based on the theory of a homogeneous scattering medium. In this paper, 16 the effect of spatial correlation of waves between scatterers on the backscattering properties 17of inhomogeneous mediums containing two types of scattering sources with different 18 acoustic properties was investigated. In the echo data of a phantoms containing two types of 19 20scatterers acquired by multiple sensors, the power and frequency dependence of the BSC 21were different from theoretical calculations due to the interference effects of each scatterer. 22The effect of interference between the two types of scatterers was confirmed to be 23particularly strong for echoes acquired by the sensor at high intensity and high frequency, or 24for higher number densities of strong scatterers.

1. Introduction

Quantitative ultrasound (QUS) is useful for noninvasive evaluation of diseases of various biological tissues such as liver, breast, lymph nodes, skin, and bone. In particular, amplitude envelope statistics,¹⁻⁶⁾ attenuation coefficients (AC),⁷⁻¹⁰⁾ backscatter coefficients (BSC),¹¹⁻¹⁵⁾ and elastography¹⁶⁻²¹⁾ have attracted attention in clinical practice, and tools for evaluating QUS parameters which were obtained from these techniques have been implemented in clinical ultrasound systems.

Since backscatter coefficient depends on physical quantities such as the scatterer diameter, volume fraction, and acoustic impedance ratio of the scatterer and surrounding medium, the physical quantity to be evaluated can be estimated by comparing the measured backscatter coefficient with a theoretical model.^{22,23)} It has been reported that evaluation of fatty liver,^{24,25)} dermal lymphedema,²⁶⁻²⁸⁾ thyroid tumors,^{29,30)} and trabecular bone³¹⁾ is possible using the backscatter coefficient as an indicator. BSC evaluations using singleelement concave transducers have been widely used in these basic studies.

There are also reports of evaluation using multiple frequency bands,^{32,33)} plane wave compound imaging,³⁴⁻³⁶⁾ and spatial synthesis^{11,13)} to improve evaluation accuracy. Omura et al. used multiple ultrasound scanners to acquire signals with two different beamforming methods, line-by-line beamforming with focused imaging and parallel beamforming with plane-wave imaging, and verified the variation of BSC.³⁶⁾ The calculated BSC was independent of either the system setting or the beamforming method, and the feasibility of BSC analysis using plane wave imaging was demonstrated.

47However, the accuracy of quantitative evaluation is limited even when plane waves 48 are also used, because multiple types of scattering sources are mixed in biological tissues. 49There is a trend to consider the influence of structures in the tissue and interference between scatterers as the main causes of this problem. Scattering sources in biological tissue are 50densely intermingled, with multiple sources within the point spread function (PSF) of the 51transducer. Therefore, backscatter characterization is usually based on the speckle signal, 52which is the interference between the scatterers. In other words, it is necessary to understand 53the spatial correlation between scatterers. The effect of spatial correlation in a 54homogeneously distributed medium with one type of scatterer is well understood. E. 55Franceschini et al. investigated a scattering model from the perspective of explaining 56experimental BSCs from cell pellet biophantoms with a single structural and acoustic 57parameter set.³⁷⁾ They reported that the impedance and size estimated from the scattering 58model were satisfactory. On the other hand, spatial correlations between scatterers in 59

heterogeneous media containing a mixture of scatterers with different acoustic properties have not been well studied. Therefore, the interpretation of backscatter coefficients from complex biological tissues first requires an understanding of ultrasonic backscatter from a biological phantom with known scattering conditions, especially the effects of wave interference caused by the positional correlation of scatterers.

In this study, we focused on the effect of interference between scatterers and compared the backscatter coefficients of phantoms with two different types of scatterers at different scattering ratios. Using a self-made ultrasonic scanner and a single concave transducer, the backscatter coefficients at low and high frequencies were evaluated. We also evaluated them using a research platform scanner and a very high-frequency linear array probe. In particular, signals were acquired using the parallel beamforming method with plane wave imaging and BSC analysis was performed.

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73 **2. Materials and Methods**

74 **2.1** Tissue-mimicking phantoms of multiple types of scatterers

75Seven different rectangular phantoms (8 cm in width \times 2 cm in length \times 4 cm in 76 height) were prepared as reference and evaluate phantoms. The solvents of each phantom 77were 2 wt% agar (A1296; Sigma-Aldrich, MO, USA) and distilled water. The weak scatterers were nylon spheres with an average particle size of 5 µm (ORGASOL 2001 EXD 7879 NAT 1; Arkema, Colombes, France), and the strong scatterers were acrylic spheres with an average particle size of 20 µm (MX-2000; Soken, Aichi, Japan). The intrinsic acoustic 80 81 impedances are 1.493 and 1.665 Mrayl, respectively. These scatterers were mixed at various 82 volume fractions as shown in Table I.

83 Phantom A and B are homogeneous media with only one type of scatterer. They were created as reference medium which the spatial correlations between scatterers are 84 known for comparison with phantoms which contain two types of scatterers. Phantom A was 85 86 created so that the scattering intensity was equivalent to that of a normal liver. Phantom B is a case in which only fat droplets are present, which is not possible in actual living tissue. 87 88 Phantoms C, D, and E are groups in which fat droplets (strong scatterers) are mixed in different fractions within the normal liver (weak scatterers),³⁸⁾ while phantoms D, F, and G 89 90 are groups in which fat droplets are constant and liver components are different fractions. By comparing the BSCs of these phantoms, the fraction (distribution) of the two types of 91 92scatterers and the effects of scattering and mutual interference from each scatterer can be evaluated. 93

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95 **2.2 Data acquisition using the laboratory-made scanner**

Three-dimensional RF echo signals were observed using a laboratory-made 9697 ultrasonic scanner and two types of single-element concave transducers [transducer I (V327; Olympus, Tokyo, Japan) and transducer II (PT35; TORAY, Tokyo, Japan)]. The center 98 frequency and -6 dB bandwidth are 10 MHz \pm 3 MHz and 30 MHz \pm 10 MHz, respectively. 99 100 The depth of focus and f-number are 19.7 mm, 10mm, and 2.10, 1.85, respectively. For echo data acquisition, pulser receiver I (Model 5800; Olympus, Tokyo, Japan) for V327 and 101 102 pulser receiver II (DPR500; JSR Ultrasonics, NY, USA) for PT35] for PT32 were used to 103 excite negative impulses to the element for transmission. After the echo signals were 104received, they were band-pass filtered at 1-35 MHz and 30-300 MHz, respectively, by the receiver circuit in each pulser receiver. Each echo signal was quantized at 12-bits by the 105oscilloscope (HDO6104; Teledyne LeCroy, NY, USA) set to the sampling frequency of 250 106 107 MHz. The PSF near the focus of each transducer is shown in Table II. The transducer was fixed to a triaxial linear rail (MTN100CC, Newport) and mechanically scanned in the lateral 108 109 and slice directions. The phantom was fixed in degassed water at 22-24°C. Echo signals were 110 acquired by irradiating ultrasound from the top surface. The depth of field of each transducer was 17.8-21.5 mm for V327 and 9.7-10.7 mm for PT35, so the phantom surfaces were set to 111 11217 mm and 9 mm, respectively, in order to cover the analysis area within the depth of field. The scan pitch was 30 µm in both lateral and slice directions. Three-dimensional RF echo 113signals of 4096 in depth \times 501 in latetal \times 101 in slice pixels were acquired for all phantoms. 114 All data acquisition and motor stage control were controlled by LabVIEW (National 115116 Instruments, TX, USA).

117

118 2.3 Data acquisition using the research-platform scanner

Two-dimensional RF echo signals were acquired using the research-platform 119 scanner (Vantage256; Verasonics, WA, USA) and a linear array probe (L39-21gD; 120Verasonics, WA, USA). The center frequency and -6 dB bandwidth were 25 MHz \pm 9 MHz. 121122The element pitch and the number of elements were 0.055 mm 128 channels, respectively. 123The focus depth in the elevation direction was approximately 6.5 mm. Each echo signal was 124quantized at 14-bits with the sampling frequency set to 4/3 times the center frequency. In 125addition, the acquired data were up-sampled by a factor of 3 in the depth direction to produce 126 data with a sampling frequency that is effectively 4 times the center frequency. The PSF at the highest resolution point is shown in Table II. RF data of each B-mode plane of each 127

phantom were acquired by plane wave imaging with parallel beamforming. Plane waves were steered at 11 angles (0° , $\pm 1^\circ$, $\pm 2^\circ$, $\pm 3^\circ$, $\pm 4^\circ$, and $\pm 5^\circ$), and the analysis signal was generated by combining them after delay and sum (DAS).

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132 **2.4 Speed of sound and attenuation coefficient calculation**

The speed of sound and the attenuation of each phantom were evaluated by the 133134reflection method before BSC analysis. 3-D RF echo signals were acquired using a singleelement plane transducer III (V312; Olympus, Tokyo, Japan) in the same setting as 135transducer I in 2.2. The center frequency and -6 dB frequency bandwidth are 10 MHz \pm 3 136 137 MHz. Echo signals were also acquired using transducer II under similar conditions. An acrylic plate was placed on top of the sound absorber, and the echo signals were acquired 138139with and without the sample while maintaining the positional relationship between the transducer and the acrylic plate.³⁹⁾ The transducer was set at the depth at which the signal 140141from the acrylic plate was maximum. The speed of sound was calculated from the time of 142flight (TOF) based on the time difference between the maximum amplitude returned from 143the sample and the acrylic plate as follows:

$$c_p = c_0 \left(1 + \frac{t_{ref} - t_r}{t_b - t_s} \right),$$
 (1)

144 where t_s is the TOF from the sample surface, t_b is the TOF from the back, t_r is the TOF 145 from the acrylic plate after the sample passed through, and t_{ref} is the TOF from the acrylic 146 plate at the same position as during the measurement. c_0 is the speed of sound of water. The 147 thickness d of the sample was calculated by $d = c_0(t_b - t_s)/2$. The attenuation rate of the 148 phantom, α [dB/cm], was calculated using the power spectra with and without the sample 149 as follows:

$$\alpha(d, f) = \frac{8.686}{4d} \ln \frac{P_s}{P_{ref}},$$
(2)

where P_s is the power spectrum through the phantom and P_{ref} is the power spectrum 150without the sample. α is the total attenuation at an arbitrary frequency f. The attenuation 151rate can be considered to be the same as the absorption rate when the frequency is somewhat 152low, when absorption attenuation can be considered to be dominant, or when scattering is 153ignorable in a relatively homogeneous medium. In particular, in the frequency band between 1541 MHz and 10 MHz used in clinical used ultrasonic diagnostic equipment, it can often be 155156approximated as proportional to the first power of the frequency. Therefore, the attenuation coefficient α_0 [dB/cm/MHz] can be written as $\alpha(f) = \alpha_0 f + b$. On the other hand, the 157

158 frequency dependence of attenuation is considered to be an important characteristic in the 159 frequency band above 10 MHz, and the dependence of attenuation on frequency is described 160 as $\alpha(f) = \alpha_0 f^n + b$, where n as well as α_0 is considered to vary.⁴⁰⁾ Therefore, the 161 parameters when approximated by the equations $\alpha(f) = \alpha_0 f + b$ and $\alpha(f) = \alpha_0 f^n + b$ 162 were calculated for the signals measured with transducer III and transducer II, respectively, 163 using the least-squares method with a -6 dB bandwidth.

164

2.5 Backscatter coefficient analysis using reference phantom method

Backscatter coefficient was calculated using the reference phantom method.⁴¹⁾ The 166 167 reference phantom method assumes that the attenuation properties and backscatter coefficient of the phantom used as the reference medium and the attenuation properties of 168 169the analysis medium are known. By using a medium with known scattering conditions as a 170reference signal, the backscatter coefficient can be evaluated robustly by correcting the 171sound field of the transmitting and receiving systems when evaluating a medium with 172complex beam diffraction effects such as a linear array probe or a medium with complex scatterer structures such as biological tissue. The array probe can be used to evaluate 173backscatter coefficient with high robustness. For this reason, array probes are widely used. 174In this study, a region of interest (ROI) was set up to analyze local RF signal characteristics, 175and the backscatter coefficient for each ROI was estimated. The ROI size was 10 times the 176177wavelength at the center frequency of the transducer in the depth direction and 10 uncorrelated echo lines in the lateral direction. Backscatter coefficient was estimated as 178

$$BSC(f) = \frac{\overline{P(f)}}{\overline{P_r(f)}}BSC_r(f)\exp\left\{\frac{4(\alpha - \alpha_{ref})f\left(x_0 + \frac{\Delta z}{2}\right)}{8.686}\right\}$$
(3)

179 where $\overline{P(f)}$ represents the average of the power spectrum of the analyte in the ROI and 180 $\overline{P_r(f)}$ represents the power spectrum of the reference medium. The frequency response of 181 the measured echo signal includes a component of attenuation that occurs during ultrasonic 182 wave propagation. Therefore, the last section corrects for the attenuation up to the analysis 183 window. α and α_{ref} are attenuation coefficients, x_0 is the distance from the scattering 184 medium surface to the start of the analysis window, and Δz is the size of the analysis 185 window.⁴²⁾

In the frequency range from 1 MHz to 10 MHz, n = 1, since the attenuation can be assumed to be proportional to the power of one of the frequencies. $BSC_r(f)$ is the theoretical value of the backscatter coefficient of the reference medium. In this study, the reference phantom was evaluated as Phantom A. The theoretical values were calculated bythe mathematical model as follows:

$$BSC_r = m \int_0^\infty p(r) \sigma_{b_{\text{elastic}}}(k, r, \gamma) S(k, r, \varphi) dr, \qquad (4)$$

where m is the number density of scatterers. p(r) is the probability density function of 191 scatterers, which can be assumed by performing calculations for each scatterer diameter 192193 when there is a distribution of scatterer diameters and finally performing weighted integrals. $\sigma_{h \text{ elastic}}(k, r, \gamma)$ is the Faran model⁴³, which assumes that the scatterers are elastic and 194 transverse waves propagate. It assumes that the scattering body is elastic and shear waves 195propagate. $S(k, r, \varphi)$ is the structure factor and assumes that the scatterer is dense and the 196 randomness of the scatterer's position is impaired. r, k, γ and ϕ are the particle size, 197198 wavenumber, acoustic impedance ratio, and volume fraction of the scatterer, respectively.

In order to verify the effect of interference between the two types of scatterers, the deviation between the evaluated backscatter coefficient and the theoretical value of the backscatter coefficient was calculated. The theoretical value of the backscatter coefficient was calculated in the same way as in equation (4). The average deviation was defined as

Deviation =
$$\frac{1}{BW} \sum_{f \text{ in } BW} \{BSC(f) - BSC_{ref}(f)\},$$
 (5)

where BW indicates the frequency band used in the analysis.

204

205 **3. Results**

3.1 BSC evaluation of phantoms with one type of scatterer

To understand the characteristics of the phantoms used for reference, phantom A and B which contain only one type of scatterer were measured with three single-element concave transducers and linear probe. B-mode images of phantom A and B acquired using transducer I, transducer II, and the linear array probe are shown in Fig. 1. Each B-mode image was normalized by the maximum value of phantom B. Because the acoustic impedance of scatterer 2 is higher than that of scatterer 1, the amplitude of phantom B is larger in each transducer.

- In phantom A, the number of scatterers present is 749, 28.9, and 88 relative to the PSFs of the transducer I, transducer II, and linear array probe, respectively, which is confirmed to be speckle (Fig. 1(a-1)-(c-1)).
- In phantom B, on the other hand, the number of scatterers present is 7.02, 0.27, and 0.82, respectively, so that scatters acquired with transducer I are speckles, while those

acquired with transducer II and the linear array probe can be identified as point sources (Fig.
2(a-2)-(c-2)).

The amplitude envelopes of phantom A and B acquired by each sensor are shown in Fig. 2. The F-values of transducers I and II are 2.10 and 1.85, respectively, and the sound pressure gradient of transducer II is steep. Therefore, the signal below 12 mm is equivalent to the amplitude value in the water region, and the S/N ratio is not sufficiently high (Fig. 2(b)). On the other hand, the data measured by the linear array probe shows a high signal intensity, and a high S/N ratio is guaranteed even in deep areas (Fig. 2(c)).

The frequency spectrum of phantom A and B acquired by each sensor are shown in Fig. 3. Each frequency spectrum is normalized by the maximum value of each phantom. Transducer I has a narrow effective bandwidth (Fig. 3(a)), while transducers II and linear array probes have a wide effective frequency band in the very high frequency range (Fig. 3 (b), (c)).

232The results of the backscatter coefficient estimation for phantom A and B using each 233single-element transducer and their respective theoretical values are shown in Fig. 4. 234Phantom A is self-referencing, so the sound field and attenuation corrections can be performed with high accuracy, and the results are in agreement with theoretical values. For 235236Phantom B, the results for transducer I agreed with the theoretical values, confirming the 237high precision of the evaluation (Fig. 4(a)). However, in the high-frequency band, there was 238no complex frequency dependence as in the theoretical values, and the deviation was large. 239(Fig. 4(b), (c)).

240

3.2 BSC evaluation of phantoms with two types of scatterers

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3.2.1 Effects of increasing strong scatterers

243Based on the trend of the backscatter coefficient evaluation results for phantoms 244with only one type of scatterer mixed in, the effect of the number density of strong scatterers 245on the backscattering characteristics was confirmed. B-mode images of phantom C, D, and 246E acquired using transducer I, transducer II, and linear array probe are shown in Fig. 5. 247Normalization method of B-mode images was the same as in Fig. 1(a-2)-(c-2). Comparing phantom C, D, and E in transducer I, the amplitude increases as the scatterer number density 248249increases (Fig. 5(a)). In transducer II, the amplitude did not change as the number density increased (Fig. 5(b)). On the other hand, in the linear array probe, the amplitude of the 250251phantom decreases as the number density increases. In particular, strong scatterers are 252recognizable as point sources, and the amplitude of strong scatterers decreases gradually

253 (Fig.5(c)).

The amplitude envelopes of phantom A, B, C, D, and E in each sensor are shown in 254Fig. 6. For comparison, Figure 6 also presents results for phantom A and B. Since the signal 255intensity from the surface waves is similar for both phantoms, it can be assumed that the 256257intensity of the incident ultrasound signal of the phantoms in this study is similar (Fig. 6 (a), 258(b)). This is because the number density of scatterers in the phantom in this study is 259sufficiently small, and the reflected wave signal from the phantom surface does not include 260 the reflected wave from the scatterers, but is considered to be the reflection from the 261surrounding medium, the agar phantom. In the amplitudes acquired by the linear array probe, the scatterer number density increases in the order of phantom B, D, and E, but the 262263amplitudes are lower in the order of phantom B, D, and E (Fig. 6 (c)).

264The frequency spectrums of phantom A, B, C, D, and E observed with transducer I, 265II, linear array probe are shown in Fig. 7. The power was normalized by the maximum value of each phantom. The bandwidth widens as the scatterer number density increases in 266267transducer I. Both phantoms were speckle signals, and the total power of the signal increased 268as the number density increased (Fig. 7 (a)). In transducer II and the linear array probe, the bandwidth is narrower than in phantom A because the signal from the strong scatterer is 269270acquired as a point scattering source. In phantom C and D and E, the higher number density 271of scatterers in the PSF increases the signal at lower frequencies, while the signal at higher 272frequencies decreases due to greater scattering attenuation (Fig. 7 (b), (c)).

The estimated and theoretical backscatter coefficients for phantom C, D, and E at 273274each transducer are shown in Fig. 8. The theoretical value of the two-scatterer mixed 275phantom is the value obtained by substituting the probability density function of the scatterer particle size for each phantom into the probability density function in eq. 5. In other words, 276277it is the sum of the theoretical values of the backscattering coefficients of each scatterer. That 278is, it is the sum of the theoretical values of the backscattering coefficients of each scatterer. 279Thus, interference between each scatterer is taken into account, but the effect of mutual 280interference between the two types of scatterers is not taken into account. There was no 281difference in the frequency dependence of each phantom in transducer I. As the number of strong scatterers increases, the value of the backscatter coefficient is higher, and the values 282283for phantom C and D are consistent with the theoretical values (Fig. 8 (a)). In transducer II, the estimation results are similar for the phantom with two mixed scatterers, as in phantom 284B, with a large deviation from the theoretical value. In particular, the properties of phantom 285D are strongly consistent with phantom B (Fig. 8 (b)).³⁸⁾ The results of the evaluation with 286

the linear array probe show a lower value compared to Phantom B, although the deviation from the theoretical value is large. Comparing phantom C, D, and E, the backscatter coefficients show lower values as the scatterer number density increases (Fig. 8 (c)).

The deviation between the estimated backscatter coefficient and the theoretical 290291value calculated by the mathematical model is shown in Fig. 9. Although Phantom B has 292 only one type of scatterer, the deviation from the theoretical value is so large that it is difficult 293to compare with the deviation calculated by eq. 7. Therefore, the deviations of the other 294phantoms were normalized at each frequency so that the deviation of phantom B was zero, 295and the mean and standard deviation were calculated. The theoretical value of the backscatter 296 coefficient is a model that does not take into account the interference between the two types 297 of scatterers, whereas the measured evaluation results include their effects, and the deviation 298indicates the degree of such interference. A smaller standard deviation indicates a smaller 299frequency-dependent deviation. Since the evaluation of phantom A is self-referencing and 300 the evaluation is highly accurate in all modalities, the deviation of phantom A is not 301 calculated. The mean and standard deviation of the deviation in transducer I are within 3 dB, 302 indicating a high degree of agreement with the theoretical values. The mean deviation for 303 transducer II and the linear array probe was lower with increasing scatterer number density, 304 and the standard deviation of the deviation was larger for the linear array probe.

305

306 3.2.2 Effects of increasing weak scatterers

307 To confirm the effect of increasing of week scatterers, phantom D, F, and G were 308 compared. B-mode images of phantom D, F, and G acquired using transducer I, II, and the 309 linear array probe are shown in Fig. 10. Normalization method of B-mode images was the same as in Fig. 1(a-2)-(c-2). In Fig. 10, it is confirmed the amplitudes of transducer I are 310311similar for an increasing number of weak scattering sources (Fig. 10(a)). B-mode images 312 acquired with the transducer II and linear array probes show a low-contrast image with a 313 small amplitude of the strong scattering source as the weak scatterer increases (Fig. 10(b), 314 (c)).

The amplitude envelopes of phantom D, F, and G using transducer I, transducer II, and linear array probes are shown in Fig. 11. The amplitude envelopes of phantom A and B are also shown for comparison. The similarity of phantom B, D, and F in the signals acquired with transducer I indicates that the strong scatterer is dominant in the reflected signal. Phantom G has a sufficiently high number density of weak scatterers, and many scatterers are mixed in near the phantom surface. Because the reflected waves from the scatterers are

321included in the surface wave signal of the phantom, the surface waves are larger than those 322 of other phantoms and the signal inside the phantom is also lower (Fig. 11(a)). The signal intensities of phantom B, D, F, and G acquired with transducer II are comparable, and the 323 amplitude gradient of the signal below the focus is steeper as the number density increases 324325due to scattering attenuation (Fig. 11(b)). Signals acquired with the linear array probe show an increase in scatterer number density but lower amplitude when compared to phantom B, 326 327 D, and F. Phantom G is difficult to compare with other phantoms, because the intensity of the incident signal is smaller than the other phantoms due to the larger surface waves in Fig. 328 329 11(a). However, comparison of phantom B, D, and F suggests that the scattering intensities 330 are not simply additive (Fig. 11(c)).

The frequency spectrums of phantom A, B, D, F, and G acquired using each sensor 331332 are shown in Fig. 12. For transducer I, the frequency bandwidth tended to narrow as the 333 number of weak scatterers increased (Fig. 12(a)). For the transducer II and linear array 334probes, as in Fig. 7(b),(c), the low-frequency signal increased with each increase in scatterer 335 number density, but the high-frequency signal decreased due to high-frequency attenuation 336 (Fig. 12(b),(c)).

The estimated backscatter coefficients of phantom D, F, and G acquired by each 337 338 sensor and the theoretical values calculated by the mathematical model are shown in Fig. 13. 339 The theoretical values for a phantom with two mixed scatterers are calculated in the same 340 way as in chapter 3.2.1. Phantom B, D, F and G were similar in transducer I (Fig. 13(a)). 341The deviation from the theoretical value was large for transducer II, while results for B, D, 342and F were similar. On the other hand, phantom G shows lower values than the other phantoms, and the difference is larger than the difference between the theoretical values (Fig. 343 13(b)). In the linear array probe, as in transducer II, the deviation from the theoretical value 344345is large but low as the scatterer number density increases. The frequency dependence is also 346 different in the frequency range from 25 MHz to 35 MHz, where the slope becomes smaller 347 as the number density increases (Fig. 13(c)).

348

The deviation between the estimated backscatter coefficient and the theoretical value calculated by the mathematical model is shown in Fig. 14. The same as in Fig. 9, 349 normalized by Phantom II. For all modalities, the mean value of the deviation was higher as 350351the scatterer number density increased. In addition, the standard deviations of the deviations are larger for transducer I, transducer II, and the linear array probe, in that order. 352

353

4. Discussion 354

355 In this study, the effect of the interference state between different scatterers on the 356 backscattering characteristics was examined by changing the ratio of the scatterers in a medium with multiple types of scatterers. The amplitudes were evaluated for the medium 357358 with a fixed amount of weak scatterers and an increased amount of strong scatterers, and for 359 the medium with a fixed amount of strong scatterers and an increased amount of weak 360 scatterers, as shown in Figs. 5(c) and 10(c). The amplitude is low even in shallow areas as 361 the number density increases due to the weaker interference caused by the mixture of two types of scatterers. As shown in Fig. 5(a) and Fig. 10(a), the intensity of the surface wave 362 363 does not change between phantoms, indicating that it is not due to the reflection of the surface wave. 364

365As shown in Fig. 8(a) and Fig. 13(a), the theoretical model for a phantom with two 366 types of scatterers does not consider the interference between the two types of scatterers. 367 Therefore, the mutual influence between the two types of scatterers is small in the theoretical 368 value. On the other hand, in the actual measurements, as shown in Figs. 8(b) and 13(b), the 369 scattering from the strong scatterer is sufficiently larger than that from the weak scatterer, 370 and the signal from the strong scatterer is dominant in the two-scatterer mixed phantom. Therefore, the interference signal between the weak scatterers is small, and it is assumed that 371372 the backscattering coefficient is estimated low in Figure 8(c) because the strong scatterers in 373 the analysis region are weakened by the interference with the surrounding weak scatterers 374and the contrast is reduced. This can be understood from the fact that the slope as well as the power is smaller, as shown in Fig. 13(c). In other words, it is due to the effect of weaker 375376 interference from strong scatterers and more dominant signals from weak scatterers.

377 As shown in Fig. 9 and Fig. 14, the standard deviation of the deviation is larger for each increase in the number density of scatterers in the order of transducer I, transducer II, 378 379 and the linear array probe, and the data acquired with the linear array probe shows the largest deviation from the frequency dependence, indicating the influence of interference. The 380 381 deviation in transducer II shows the difference between the theoretical values and is not due 382 to the effect of interference, because the difference between the phantoms in the backscatter 383 coefficient evaluation results is small as shown in Fig. 8(b) and Fig. 13(b). The standard deviation of the deviation in transducer I is small, indicating that the frequency dependence 384385of the deviation is highly consistent despite the difference in power. Thus, interference between the two types of scatterers has a significant effect on the backscattering 386387 characteristics when evaluated with a high intensity and high frequency sensor.

5. Conclusions

390 In order to understand the influence of wave interference caused by the correlation 391 of scatterer positions, we compared the backscattering characteristics of a phantom with a mixture of two types of scatterers when the ratio of the scatterers was changed, using several 392 393 sensors. The signal acquired with a single transducer showed only a small influence of interference, while the signal acquired with a linear array probe of high intensity and high 394 395 frequency showed a weaker influence of interference, which became more pronounced as the number density of scatterers increased. However, the scattering intensity of actual 396 397 biological tissue differs significantly from that of the simulated biological samples used in this study and has a more complex scatterer distribution, so the frequency dependence of the 398 BSC is also assumed to have more diverse variations. In future works, we will evaluate the 399 scattering intensity of real biological tissue as well as media with heterogeneous scatterer 400 401 distribution and structure, which are closer to the scattering intensity of biological tissue.

402

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Figure Captions

Fig. 1. (Color Online) B-mode images of (a-1)-(c-1) phantom A and (a-2)-(c-2) phantom B acquired with (a) transducer I, (b) transducer II, and (c) linear array probe

Fig. 2. (Color Online) Amplitude envelopes of phantom A and B acquired using (a) transducer I, (b) transducer II, and (c) linear array probe

Fig. 3. (Color Online) Power spectrums of phantom A and B acquired using (a) transducer I, (b) transducer II, and (c) linear array probe

Fig. 4. (Color Online) Backscatter coefficients of phantom A and B acquired using (a) transducer I, (b) transducer II, and (c) linear array probe and theoretical values

Fig. 5. (Color Online) B-mode images of (a-1)-(c-1) phantom C, (a-2)-(c-2) phantom D and (a-3)-(c-3) phantom E acquired with (a) transducer I, (b) transducer II, and (c) linear array probe

Fig. 6. (Color Online) Amplitude envelopes of phantom A, B, C, D and E acquired using (a) transducer I, (b) transducer II, and (c) linear array probe

Fig. 7. (Color Online) Power spectrums of phantom A, B, C, D and E acquired using (a) transducer I, (b) transducer II, and (c) linear array probe

Fig. 8. (Color Online) Backscatter coefficients of phantom A, B, C, D and E acquired using

(a) transducer I, (b) transducer II, and (c) linear array probe and theoretical values

Fig. 9. (Color Online) Deviation between the estimated backscatter coefficients for phantom B, C, D, and E and the theoretical values calculated by the mathematical model

Fig. 10. (Color Online) B-mode images of (a-1)-(c-1) phantom D, (a-2)-(c-2) phantom F and (a-3)-(c-3) phantom G acquired with (a) transducer I, (b) transducer II, and (c) linear array probe

Fig. 11. (Color Online) Amplitude envelopes of phantom A, B, D, F and G acquired using (a) transducer I, (b) transducer II, and (c) linear array probe

Fig. 12. (Color Online) Power spectrums of phantom A, B, D, F and G acquired using (a) transducer I, (b) transducer II, and (c) linear array probe

Fig. 13. (Color Online) Backscatter coefficients of phantom A, B, D, F and G acquired using (a) transducer I, (b) transducer II, and (c) linear array probe and theoretical values

Fig. 14. (Color Online) Deviation between the estimated backscatter coefficients for phantom B, D, F, and G and the theoretical values calculated by the mathematical model

Phantom	А	В	С	D	E	F	G
Volume fraction of scatter 1 [%]	0.5	-	0.5	0.5	0.5	2	5
Volume fraction of scatter 2 [%]	-	0.3	0.1	0.3	0.5	0.3	0.3

 Table I. Phantom composition and acoustic properties

Scatterer 1: nylon with diameter of 5 µm, scatterer 2: acrylic with diameter of 20 µm.

Table II.PSF near focus for each sensor

	Axial [µm]	Lateral [µm]
V327	109	300
PT35	42	95
L39-21gD	80	120



Fig. 1











Fig. 4



Fig. 5



Fig. 6



Fig. 7







Fig. 9



Fig. 10







Fig. 12



Fig. 13



Fig.14