Effect of attenuation correction on backscattering coefficient evaluation of lymphedema

リンパ浮腫組織の後方散乱係数評価における減衰補正の影響

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1. Introduction

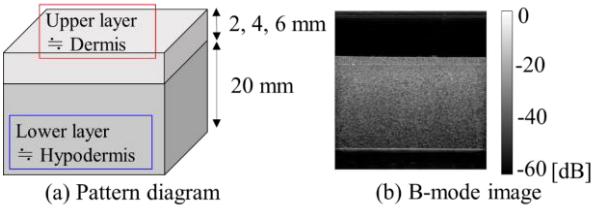
Lymphedema (LE) has complex tissue properties such as inflammation, fibrosis, and edema for the progress of the disease, and the current standard methods are the International Society of Lymphedema (ISL) stage finding from scintigraphy and palpation. It is assumed that quantitative ultrasound (QUS) parameters have different features related to different backscattering properties between LE stages. Our previous studies indicated the relationship between acoustic impedance of *ex vivo* skin dermis, backscatter coefficient (BSC) and scatterer density, was obtained between without and with LE [1,2].

In this study, we clarified the variation of the same physical properties with different thickness of phantom to varify the effect of attenuation correction on BSC evaluation of LE. The proposed attenuation correction method was then applied to the clinical data and the evaluated BSC and ISL stages were compared.

2. Materials and Methods

2.1 Homogeneous layer phantom

The two layers agar-gel phantoms were a mixture of distilled water, 2% (w/w) agar powder, and 5 wt% acrylic particles with mean diameters of 10 μm for upper layer and 20 μm for lower layer (MX-1000 and MX-2000; Soken Chemical). **Figures 1(a) and 1(b)** shows the schematic diagram and the B-mode image of a layer phantom, respectively. The upper layer of the phantom expresses dermis and becomes thicker as LE progresses. The lower layer is hypodermis. A single layar phantom with the same composition as the lower layer was also created as a reference phantom.



(a) Pattern diagram (b) B-mode image

Fig. 1 Two layers phantom images

2.2 Data acquisition

Two-dimensional RF data sets of phantoms were acquired using a modified clinical scanner (AplioXG, Toshiba Medical Systems) and a linear probe (PLT-1204AT, Toshiba Medical Systems) with the center frequency of 8 MHz. The RF echo data were sampled and digitized with 40 MHz and 14-bits/sample, respectively.

2.3 Attenuation coefficient analysis

In the process of sound wave propagation, attenuation occurs due to absorption and scattering. The local attenuation α [dB/m] calculated from average power spectrum of the reference and analysis medium at any depth d_1 and d_2 [3,4]. The local attenuation was calculated as

$$\alpha(f) = \alpha_{ref}(f) + 8.686\frac{\ln\left(\frac{P(d,f)}{P_{ref}(d,f)}\right)\Big|_{d_2} - \ln\left(\frac{P(d,f)}{P_{ref}(d,f)}\right)\Big|_{d_1}}{4(d_2 - d_1)}. \quad (1)$$

where the P and P_{ref} are the power spectra for the sample and reference, at frequency f, respectively, and d_1 and d_2 are depths in the ROI, where $d_2 > d_1$. The BSC was assumed to have a constant difference at any depth. The AC was calculated by linearly approximating of local attenuation. The distance difference $d_2 - d_1$ was set to 2.5 mm.

2.4 Backscattering coefficient analysis

The reference phantom method was employed to compensate the properties of transmission-reception sound field and attenuation [3]. The BSC was calculated in the domain of wavenumber k as

$$BSC(k) = \frac{P(k)}{P_{ref}(k)} BSC_{ref}(k) \exp\left[\frac{4dkc(\alpha - \alpha_{ref})}{8.686 \cdot 2\pi}\right]. \quad (2)$$

where the P and P_{ref} are the power spectra obtained from the analysis and the reference phantom, respectively, BSC_{ref} is the theoretical BSC, d is the distance between the transducer and central position of the analysis window, and α and α_{ref} are the AC of the analysis and reference phantoms, respectively. As ACs of dermis (upper layer) and hypodermis (lower layer), 2.0, 1,8

[dB/cm/MHz] [5] or average of AC calculated from each data were employed in α. The theoretical values were calculated by setting the physical conditions of the reference medium in the Faran model [6]. Furthermore, effective scatterer diameter (ESD) and effective acoustic concentration (EAC) were estimated by Gaussian form factor model [7].

The bandwidth used for estimation of BSC was 3-14 MHz, which corresponds to the range of -6 dB from the power spectra of the center frequency. A 2D ROI (1.2 mm × 2.0 mm; 64 × 20 pixels) was set with 80% overlap. The constant false alarm rate (CFAR) process was applied to eliminate connective fibers in the hypodermis.

2.5 Classification of lymphedema severity

The number of cases was stage 0 (n = 49), I (n = 15), early II (n = 13), late II (n = 9), III (n = 3). It was performed using ROC curves by a logistic regression model whether the subjects can be distinguished with normal and early condition of the LE.

3. Results

Figure 2 shows the calculated BSCs of phantoms and the theoretical BSCs. Regardless of the thickness of the dermis, BSC when using the measured AC was the closest to the theoretical value in both layers, and the same accuracy was obtained for the AC obtained by Log-difference method.

Figure 3 shows the average of calculated BSCs from each data at each ISL stage. In the dermis, BSCs of ISL stage ≥ early II tends to be smaller

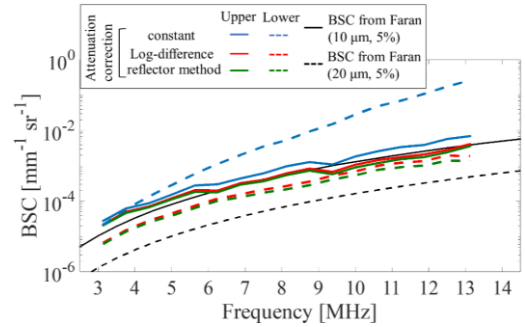


Fig. 2 The mean BSC curves of phantoms

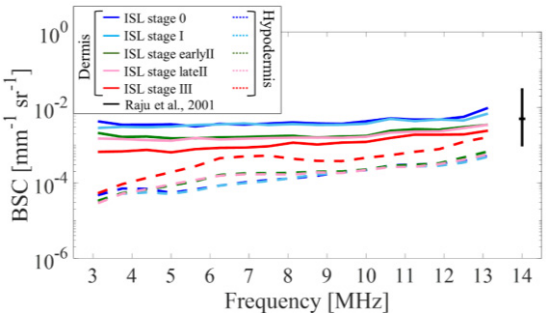


Fig. 3 The mean BSC curves of LEs

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Tab. 1 Results of classification performance

	ISL stage 0 or stage ≥I			ISL stage ≤ I or stage ≥ earlyII		
	AUC	Sensi-tivity	Speci-ficity	AUC	Sensi-tivity	Speci-ficity
Thickness	0.916	77.5	91.8	0.943	96.0	90.6
Fiber ratio	0.727	77.5	71.4	0.812	44.0	90.6
AC	0.609	35.0	83.7	0.723	56.0	81.3
ESD	0.619	72.5	55.1	0.639	0	98.4
EAC	0.813	62.5	95.9	0.921	64.0	98.4
All parameters	0.938	85.0	85.7	0.958	76.0	93.8

than those of stage ≤ I. This tendency is consistent with the findings of the previous *ex vivo* study using extracted tissues [1]. In the hypodermis, BSCs after stage early II tends to be larger than those of stage ≤ I. This tendency is also consistent with qualitative evaluation results of previous study [8].

Table 1 shows the classification performance that were obtained by using QUS parameters individually and in combination. Performance of the classification in combination were 85.0% sensitivity and 85.7% specificity for the extremely early stage, and 76.0% sensitivity and 93.8% sensitivity for early stage.

4. Conclusions

QUS assessment might excel in distinguishing the early stage of the LE easily and continuously characterization against the scintigraphy imaging. The possibility of *in vivo* quantitative assessment of the severity of LE in the dermis and hypodermis was proposed by applying the attenuation coefficient measured in backscattering analysis.

The next step is to use multiple clinical data from the same stage to identify differences in QUS parameters depending on patient background.

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