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Reduction of Influence of Decrease in Signal-to-Noise Ratio in Measurement of Change in Thickness of Arterial Wall Due to Heartbeat

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To diagnose early-stage atherosclerosis, for the local evaluation of the elasticity of the arterial wall it is necessary to increase the spatial resolution in the axial direction of the artery to several millimeters, which corresponds to the size of the lesion on the surface of the arterial wall. For this purpose, we previously proposed a method for measuring the small change in thickness of the arterial wall during the cardiac cycle [H. Kanai *et al.*: IEEE Trans. UFFC **43** (1996) 791, H. Kanai *et al.*: IEEE Trans. UFFC **44** (1997) 752 and H. Hasegawa *et al.*: Electron. Lett. **33** (1997) 340]. The change in thickness cannot be measured from conventional B-mode or M-mode images because of its small amplitude of less than 100 micrometers. Though the change in thickness is useful for *in vivo* assessment of the local elasticity of the arterial wall, in some cases successful measurements based on only two consecutive echos fail because of the low signal-to-noise ratio (SNR) of the echos. To realize the practical use of the proposed method, this problem must be overcome. In this paper, we propose a method that is more robust in the presence of noise. In this method, more than two echos are employed to estimate their phase shift for reducing the influence of low SNR. Simulations provide an optimal value of the estimation period for each SNR. By evaluating the SNR of *in vivo* experimental data, the optimal estimation period is determined. In *in vivo* experiments using an optimal estimation period of 20 ms, the change in thickness can be measured with good reproducibility even in the case of a low SNR of 28 dB.

KEYWORDS: atherosclerosis, change in thickness of arterial wall, phase shift, signal-to-noise ratio (SNR)

1. Introduction

The steady increase in the number of patients with myocardial infarction or cerebral infarction, which are considered mainly to be caused by atherosclerosis, is becoming a serious problem. Therefore, it is important to diagnose atherosclerosis in an early stage. However, the methods employed for the diagnosis of atherosclerosis such as computed tomography (CT) and magnetic resonance imaging (MRI) cause great physical and mental hardship to patients.

The pulse wave velocity (PWV) method has been developed as a technique for the noninvasive diagnosis of atherosclerosis.[1] In this method, the elasticity of the arterial wall is evaluated by measuring the velocity of the pressure wave propagating from the heart to the femoral artery. It is useful in terms of the noninvasive evaluation of elasticity, however, elasticity cannot be evaluated locally due to a low spatial resolution of several tenths of a centimeter, which corresponds to the distance from the heart to the femoral artery.

To increase the spatial resolution in the measurement of PWV, we previously proposed a method to accurately measure the propagation velocity of vibrations on the arterial wall using ultrasound.[2] Using this method, the PWV between two adjacent points which are several centimeters apart is noninvasively evaluated by estimating the time delay between the resultant vibrations at these two points.[3]

In this study, we evaluated the elasticity in each local region of a few millimeters not only to diagnose early-stage atherosclerosis but also to measure the spatial distribution of the elasticity, which is useful to diagnose vulnerability of the atherosclerotic plaque. For this purpose, the small change in the thickness of the arterial wall due to the heartbeat is accurately measured in each local region which corresponds to the focal area of the ultrasonic beam.[4,5] From the resultant change in thickness, the local strain and the elasticity of the arterial wall are noninvasively evaluated.

To obtain the change in thickness of the arterial wall in the previously proposed method,[2] each displacement of the intimal side and of the adventitial side is obtained by estimating the phase shift between two consecutively received echos, and the phase shift can be estimated with high accuracy when the echo is measured under good conditions of SNR. From the basic experiments, the accuracy in the estimation of the displacement is less than 1 μm.[4,6,7]

However, under *in vivo* conditions, the SNR of the received echo signal is not always high mainly because there is not a large difference in the acoustic impedance between the arterial wall and blood. In the case of low SNR, the accuracy decreases when only two consecutive echos are employed to determine the phase shift between them. In this paper, we propose a method for reducing the influence of a decrease in the SNR of the echo in the estimation of its phase shift using more than two consecutive echo signals.

2. The Previous Method for Measurement of Small Change in Thickness of the Arterial Wall

As illustrated in Fig. 1, for accurate measurement of small changes in thickness, the phase shift of the echo due to its propagation back and forth between the object and the ultrasonic transducer is estimated from two consecutive echos.[2] For this purpose, quadrature demodulation is applied to the received echo reflected by the object, and then the in-phase and the quadrature signals are A/D converted. From the demodulated signal, $z(t; d)$ reflected at a depth d at a time t, the phase shift, $\Delta\theta(t)$, between two consecutive echos is obtained from the complex cross correlation function computed for $M + 1$ samples in the depth direction as follows:

$$e^{j\Delta\theta(t)} = \frac{\sum_{m=-M/2}^{M/2} z(t+T; d+mD) \cdot z^*(t; d+mD)}{\sum_{m=-M/2}^{M/2} |z(t+T; d+mD) \cdot z^*(t; d+mD)|}, \quad (1)$$

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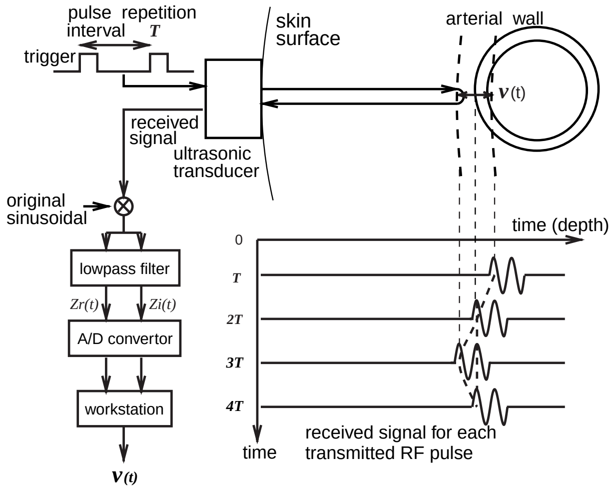

Fig. 1. Illustration of measurement of a small vibration on the arterial wall.

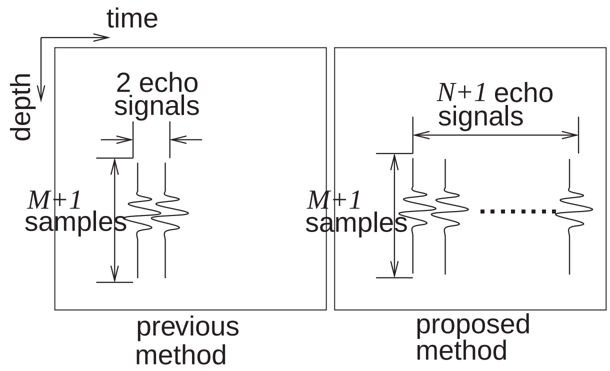

Fig. 2. Difference in the length of time used in the estimation between the new method and the previously proposed method.

where D and T are the interval of sample points in the depth direction and the pulse repetition interval, respectively, and $*$ represents the complex conjugate. From the phase shift accurately estimated by eq. (1), the small velocity signal at time $t + T/2$ is obtained as follows:

$$v\left(t + \frac{T}{2}\right) = -\frac{c_0}{2\omega_0}\frac{\Delta\theta(t)}{T}, \qquad (2)$$

where ω_0 and c_0 are the angular frequency of the ultrasonic pulse and the speed of sound, respectively.

By subtracting the displacement, $x_{in}(t)$, of the intimal side of the arterial wall from that of the adventitial side, $x_{ad}(t)$, a small change in thickness, $\Delta h(t)$, of the arterial wall is obtained as follows:

$$\begin{aligned}\Delta h(t) &= x_{ad}(t) - x_{in}(t)\\ &= \int_{-\infty}^{t}\{v_{ad}(t) - v_{in}(t)\}dt. \qquad (3)\end{aligned}$$

3. A Method for Reducing Influence of Decrease in SNR in Measurement of Small Change in Thickness of the Arterial Wall

In the previously proposed method,[2)] the accuracy in the measurement of the displacement is less than 1 μm from the basic experiments.[4,6,7)] However, under *in vivo* condition, the SNR of the received echo is not always high in comparison with that in the basic experiments. In the case of the lower SNR, the accuracy in the estimation decreases when only two consecutively received echos are employed for the estimation of their phase shift.

In this paper, we propose a method for reducing the influence of the decrease in the SNR in the estimation of the phase shift of the echo signals using more than two echos as illustrated in Fig. 2. An accuracy is improved in the case of the lower SNR using the proposed method. The principle is as follows.

Let us assume that the amplitudes of two consecutively received echo signals are equal because the pulse repetition interval, T, is sufficiently short. In addition, we assume that the phase shift, $\Delta\theta(t)$, of the echos due to the wall motion is constant during the short period $\Delta T = (N+1)T$. Thus, the estimator, $\widehat{z}(t + nT; d)$, of the quadrature modulated signal, $z(t+nT; d)$, at the time $t+nT$ expected by $z(t+(n-1)T; d)$ is defined as follows:

$$\widehat{z}(t + nT; d) = z(t + (n-1)T; d) \cdot e^{j\Delta\theta(t)}. \qquad (4)$$

The normalized mean squared difference, $\alpha(\Delta\theta(t))$, between $z(t + nT; d)$ and $\widehat{z}(t + nT; d)$ is defined as follows:

$$\alpha(\Delta\theta(t)) = \frac{\displaystyle\sum_{n=-N/2}^{N/2}\sum_{m=-M/2}^{M/2}|z(t+nT; d+mD) - z(t+(n-1)T; d+mD)\cdot e^{j\Delta\theta(t)}|^2}{\displaystyle\sum_{n=-N/2}^{N/2}\sum_{m=-M/2}^{M/2}|z(t+nT; d+mD)|^2}, \qquad (5)$$

where M and N are the number of samples in the depth direction and the number of echos used for calculating the difference $\alpha(\Delta\theta(t))$. By replacing the denominator of eq. (5) by A, eq. (5) can be rewritten as

$$\begin{aligned}A\alpha(\Delta\theta(t)) = \sum_{n=-N/2}^{N/2}\sum_{m=-M/2}^{M/2}&\{|z(t+nT; d+mD)|^2\\ &- z(t+nT; d+mD)\cdot z^*(t+(n-1)T; d+mD)\cdot e^{-j\Delta\theta(t)}\\ &- z^*(t+nT; d+mD)\cdot z(t+(n-1)T; d+mD)\cdot e^{j\Delta\theta(t)}\\ &+ |z(t+(n-1)T; d+mD)|^2\}. \qquad (6)\end{aligned}$$

By taking the partial derivative of eq. (6) with respect to $\Delta\theta(t)$, the following equation is obtained.

$$A \cdot \frac{\partial \alpha(\Delta\theta(t))}{\partial \Delta\theta(t)} = \sum_{n=-N/2}^{N/2} \sum_{m=-M/2}^{M/2} \{jz(t+nT; d+mD) \cdot z^*(t+(n-1)T; d+mD) \cdot e^{-j\Delta\theta(t)} - jz^*(t+nT; d+mD) \cdot z(t+(n-1)T; d+mD) \cdot e^{j\Delta\theta(t)}\}. \quad (7)$$

By setting the right hand side of eq. (7) to zero, the phase shift of the echo is determined by the following normalized complex cross-correlation function.

$$e^{j\Delta\theta(t)} = \frac{\displaystyle\sum_{n=-N/2}^{N/2} \sum_{m=-M/2}^{M/2} z(t+nT; d+mD) \cdot z^*(t+(n-1)T; d+mD)}{\left|\displaystyle\sum_{n=-N/2}^{N/2} \sum_{m=-M/2}^{M/2} z(t+nT; d+mD) \cdot z^*(t+(n-1)T; d+mD)\right|}. \quad (8)$$

Such averaging has been employed in conventional pulsed Doppler systems.[8)] Though the accuracy is improved using multiple echo signals, when the estimation period becomes long, the accuracy worsens because the time resolution is poorer. For this reason, the estimation period should be set to an optimum for each SNR condition. However, in conventional pulsed Doppler systems, the estimation period is fixed to a certain length. In this paper, the optimal estimation period is determined by simulations, and in *in vivo* experiments the optimal estimation period is used by evaluating SNR of *in vivo* experimental data.

4. Accuracy Evaluation by Simulations

In the case of the lower SNR, accuracy in the estimation of the phase shift is improved by increasing the time period, $\Delta T = (N+1)T$, used for the phase estimation. However, the time resolution worsens when the estimation period, ΔT, becomes long. In this section, in the following simulations, the accuracy of the proposed method is evaluated for different SNRs and estimation periods, ΔT, to determine the optimal estimation period for each SNR.

Figure 3 shows the waveform of the ultrasonic pulse used for simulating the echos. Its center frequency is 7.5 MHz and the pulse duration is 5 wavelength. In this simulation, the received echo signal is described by the summation of two pulses reflected by the interfaces of the intima and adventitia of the arterial wall, and the distance between these two interfaces is 0.6 mm at the R-wave of an electrocardiogram (ECG). The pulse repetition frequency and the sampling frequency of the simulated echo are 1 kHz and 1 GHz, respectively. The phase shifts due to the wall motion, which corresponds to the displacements of intima and adventitia shown in Fig. 4, are introduced into the echos reflected by the interfaces of the intima and adventitia. After quadrature demodulation, the modulated signals are extrapolated to a sampling frequency of 10 MHz, which is used in the actual measurement system, and Gaussian white noise is added to them to adjust the SNR of the demodulated signal.

The phase shifts between consecutively transmitted and received echo signals at the intimal side and adventitial side are estimated by the proposed method for each SNR and each estimation period ΔT. The change in thickness, $\Delta h(t)$, obtained by estimating the phase shift between two consecutively received echo is shown in Fig. 5(a) for different SNRs. The time axis in Fig. 5(a) corresponds to one heartbeat. Under each condition, the root mean squared (RMS) error, $e_{\mathrm{RMS}}(\mathrm{snr}; \Delta T)$, of the estimated instantaneous change in thickness, $\hat{v}_h(t; \Delta T) = \hat{v}_{ad}(t; \Delta T) - \hat{v}_{in}(t; \Delta T)$, from its true value, $v_h(t; \Delta T)$, is computed to evaluate the accuracy of the estimation of the phase shift as follows:

$$e_{\mathrm{RMS}}(\mathrm{snr}; \Delta T) = \sqrt{\frac{1}{N}\sum_{n=1}^{N} |\hat{v}_h(t; \Delta T) - v_h(t; \Delta T)|^2}, \quad (9)$$

From Fig. 5(b), it can be observed that the error curves have minima at different locations, depending on the SNR.

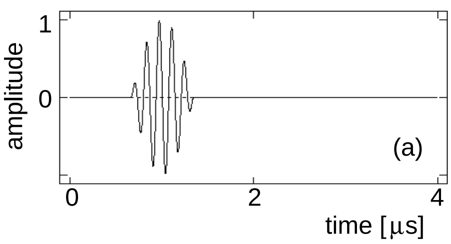

Fig. 3. Waveform of the ultrasonic pulse used for simulating the echos.

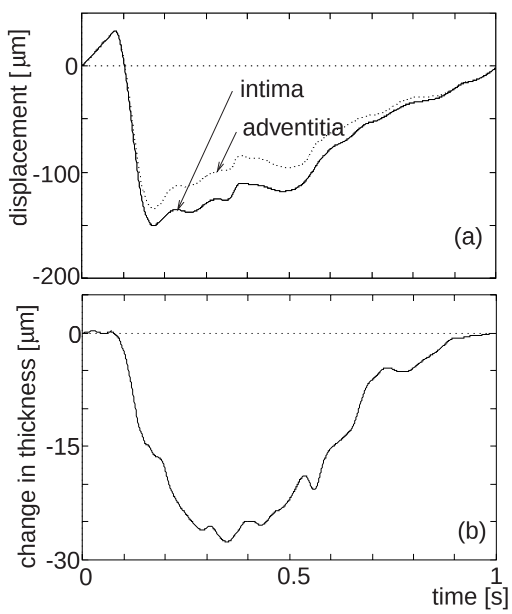

Fig. 4. (a) Displacements of the intimal side and the adventitial side, which correspond to the phase shifts of the simulated echos. (b) Change in thickness (difference between the displacements shown in (a)).

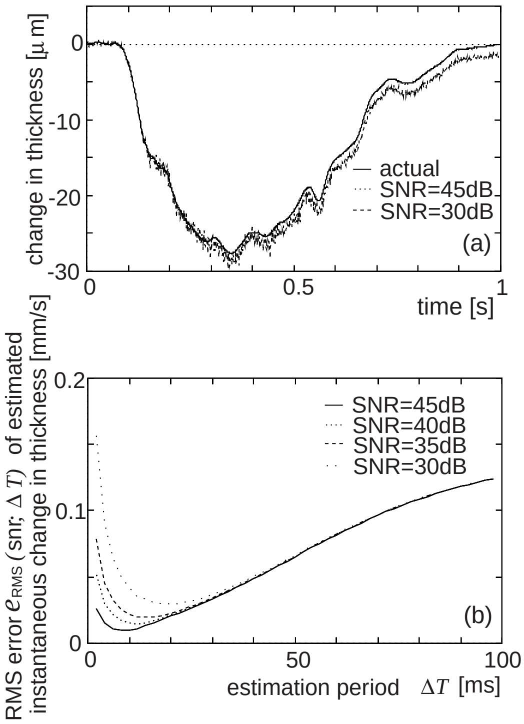

Fig. 5. (a) The change in thickness, $\Delta h(t)$, estimated by the previously proposed method for different SNRs. (b) The RMS error of the estimated instantaneous change in thickness from the true one as a function of SNR and the estimation period.

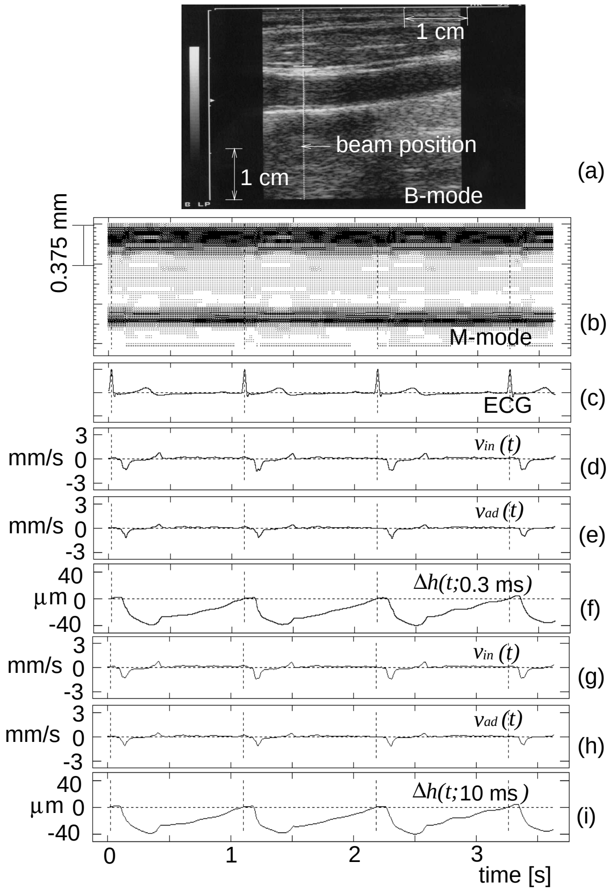

Fig. 6. *In vivo* experimental results for the human carotid artery of a 50-year-old male subject (SNR = 39 dB). (a) B-mode image. (b) M-mode image. (c) Electrocardiogram. (d), (e), and (f) Velocity signals, $v_{in}(t)$ and $v_{ad}(t)$, on the intima and adventitia, and the change in thickness, $\Delta h(t)$, estimated with an estimation period of 333 μs (2 frames). (g), (h), and (i) Velocity signals, $v_{in}(t)$ and $v_{ad}(t)$, on the intima and adventitia, and the change in thickness, $\Delta h(t)$, estimated with an optimal estimation period of 10 ms.

5. *In vivo* Experimental Results for the Human Common Carotid artery

Two sets of data were measured from the common carotid artery of a 50-year-old male subject and a 25-year-old male subject as shown in Figs. 6 and 7, respectively. The data sets are acquired along the ultrasonic beam shown in Figs. 6(a) and 7(a). The velocity signals, $v_{in}(t)$ and $v_{ad}(t)$, on the intimal side and adventitial side are obtained by tracking points preset at the beginning of the M-mode image as shown in Figs. 6(d) and 6(e). Velocity signals are also obtained in the same manner as shown in Figs. 7(d) and 7(e). The change in thickness, $\Delta h(t)$, of the arterial wall is obtained by integrating the difference between $v_{in}(t)$ and $v_{ad}(t)$ as shown in Figs. 6(f) and 7(f). There are some differences between the change in thickness, $\Delta h(t)$, in Fig. 6 and that in Fig. 7. In Fig. 6, $\Delta h(t)$ is reproducible from heartbeat to heartbeat. This is not the case in Fig. 7. One reason for these differences is the decrease in the SNR from Fig. 6 to Fig. 7.

To determine the optimal estimation period ΔT, the SNR of these two sets of data are evaluated. For this purpose, the echo signal reflected by the interface of the rubber plate fixed in the water tank is measured many times. The difference between the average and each echo represents the noise. The noise estimate is extracted this way: First, the average, μ, of the absolute amplitude of the received signal, $z(t; d)$, reflected at the depth d, is obtained by

$$\hat{\mu} = \frac{1}{N}\sum_{n=1}^{N} |z(t + nT; d)|, \tag{10}$$

where the period for averaging is 1 second, that is, $N = 1000$ ($T = 1$ ms). The noise power, σ_n^2, is evaluated by

$$\hat{\sigma}_n^2 = \frac{1}{N}\sum_{n=1}^{N} \{|z(t + nT; d)| - \hat{\mu}\}^2. \tag{11}$$

Second, the signal power, σ_s^2, in an *in vivo* experiment is obtained by

$$\hat{\sigma}_s^2 = \frac{1}{N}\sum_{n=1}^{N} |z(t + nT; d + \hat{x}(t + nT))|^2, \tag{12}$$

where $\hat{x}(t+nT)$ is the estimated displacement of the wall due to its motion estimated by the *phased tracking method*.[2)]

Finally, the SNR in an *in vivo* experiment is obtained by

$$\mathrm{SNR} = 10 \log_{10} \frac{\hat{\sigma}_s^2}{\hat{\sigma}_n^2} [\mathrm{dB}]. \tag{13}$$

For the data in Figs. 6 and 7, the SNRs are evaluated as 39 dB and 28 dB, respectively. The optimal estimation periods for Figs. 6 and 7 are 10 ms and 20 ms, respectively, according to the results of the simulation experiment in Fig. 5(b).

Using the optimal estimation period ΔT, the change in thickness is obtained as shown in Figs. 6(i) and 7(i). In the case of the relatively high SNR (Fig. 6), the waveforms are hardly changed due to this new method in Figs. 6(f) and 6(i).

On the other hand, clear improvement is obtained in the case of lower SNR as shown in Figs. 7(f) and 7(i).

In Fig. 8, the improvement in reproducibility, γ, between heart cycles is plotted as a function of SNR. The improvement in reproducibility is defined by the difference between standard deviations, σ_{2fr} and σ_{opt}, evaluated for each estimation based on two echos and the optimal estimation period as follows:

$$\gamma = \sigma_{2fr} - \sigma_{opt}. \tag{14}$$

The standard deviations, σ_{2fr} and σ_{opt}, between M heartbeats are computed during one cardiac cycle, which corresponds to the time period NT, as follows:

$$\sigma_{2fr} = \frac{1}{N}\sum_{n=1}^{N}\sqrt{\frac{1}{M}\sum_{m=1}^{M}\{\Delta h(nT + T_r(m); T) - \frac{1}{M}\sum_{m=1}^{M}\Delta h(nT + T_r(m); T)\}^2}, \tag{15}$$

$$\sigma_{opt} = \frac{1}{N}\sum_{n=1}^{N}\sqrt{\frac{1}{M}\sum_{m=1}^{M}\{\Delta h(nT + T_r(m); \Delta T_{opt}) - \frac{1}{M}\sum_{m=1}^{M}\Delta h(nT + T_r(m); \Delta T_{opt})\}^2}, \tag{16}$$

where $T_r(m)$ and ΔT_{opt} are the time of mth R-wave of the electrocardiogram and the optimal estimation period. Figure 8 shows that the proposed method is effective, especially in the case of the lower SNR.

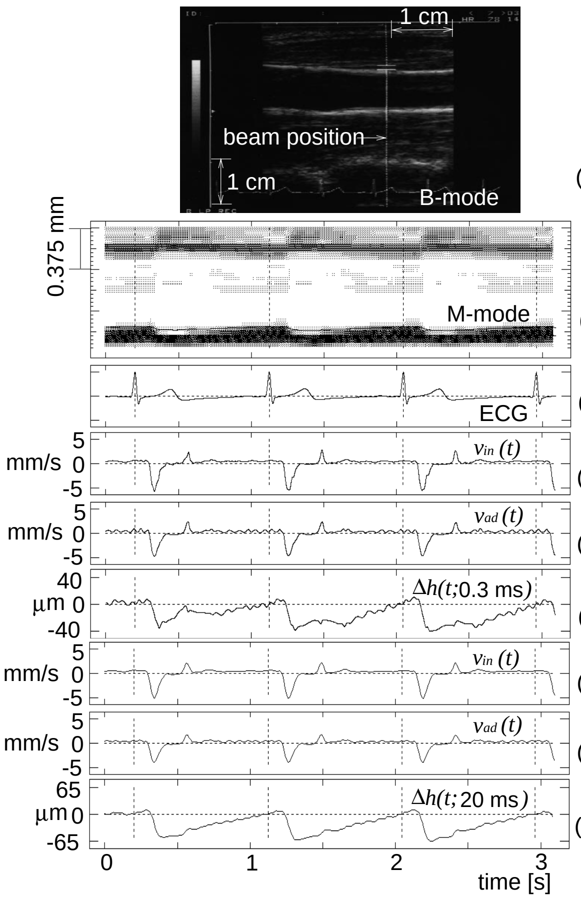

Fig. 7. *In vivo* experimental results for the human carotid artery of a 25-year-old male subject (SNR = 28 dB). (a) B-mode image. (b) M-mode image. (c) Electrocardiogram. (d), (e), and (f) Velocity signals, $v_{in}(t)$ and $v_{ad}(t)$, on the intima and adventitia, and the change in thickness, $\Delta h(t)$, estimated with an estimation period of 333 μs (2 frames). (g), (h), and (i) Velocity signals, $v_{in}(t)$ and $v_{ad}(t)$, on the intima and adventitia, and the change in thickness, $\Delta h(t)$, estimated with an optimal estimation period of 20 ms.

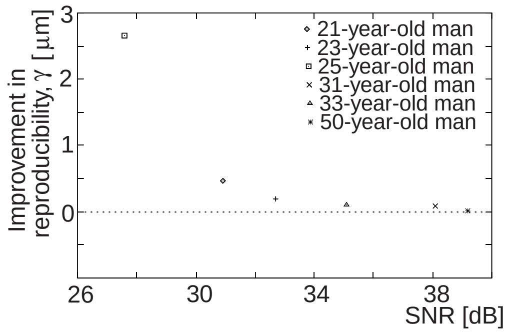

Fig. 8. Improvement in the reproducibility of the change in thickness plotted as a function of SNR.

6. Conclusions

We have already proposed a method for the accurate measurement of displacement by estimating the phase shift of two consecutive echo signals. However, the accuracy decreases with the SNR of the received signal. In this paper, a method is proposed for reducing the influence of the decrease in the SNR using multiple echos. Using this method, a small change in thickness of the arterial wall is obtained with good reproducibility even in the case of low SNR.

Acknowledgement

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