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Accuracy Evaluation in the Measurement of a Small Change in the Thickness of Arterial Walls and the Measurement of Elasticity of the Human Carotid Artery

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For the diagnosis of the early stages of atherosclerosis, it is important to evaluate the local acoustic characteristics of the arterial wall. For this purpose, it is necessary to increase the spatial resolution in the axial direction to several millimeters, which corresponds to the size of the macular lesion on the surface of the wall. We have proposed a method for measuring small velocity signals on the intima and adventitia of the arterial wall from the skin surface using pulsive ultrasonic waves. The small change in thickness of the arterial wall is obtained by integrating the difference between the two velocity signals on the intima and adventitia. The elastic property of the arterial wall is noninvasively evaluated from the change in thickness and the arterial inner pressure. In this paper, we evaluate the accuracy of the proposed method for measuring the small displacement. Moreover, we applied this method to evaluate the elastic property of the arterial wall of 50 patients and 8 healthy subjects.

KEYWORDS: small displacement, small velocity signal, small change in thickness, atherosclerosis

1. Introduction

The main cause of myocardial infarction and cerebral infarction is the rupture of the atheromatous plaque on and in the intima of the arterial wall. After the rupture, the vessel lumen narrows due to the thrombus formation including the subinitimal region and finally it becomes obstructed. Thus, for a noninvasive diagnosis of these serious diseases caused by atherosclerosis it is most significant to locally evaluate the elasticity of the surface tissue around the atheromatous plaque.

For this purpose, we have developed a method to simultaneously measure the small velocity signals on the surface of the intima and adventitia of the arterial wall.[1)] The change in the thickness of the arterial wall with an amplitude of several tenth micrometers, which is defined as the difference between the displacements of the intima and adventitia, is accurately obtained by integrating the difference between these two velocity signals.[2)] The spatial resolution in the axial direction of the artery of measurement is a few millimeters, which is determined by the width of the ultrasonic beam in its focal area. However, the change in thickness of several micrometers is accurately measured by the proposed method.

For the noninvasive measurement of the local elastic property of the arterial wall, we have proposed a method for measuring Poisson's ratio of the arterial wall.[2)] We have shown that Poisson's ratio is different in each artery.[3)] This result shows that it is important to evaluate locally the elastic property of the arterial wall. However, Poisson's ratio evaluates the average extension of the arterial wall in the circumferential direction, therefore, it is difficult to accurately evaluate the local elastic property of the arterial wall when a part of the arterial wall is deformed by atherosclerosis.

To solve this problem, the elastic property of the arterial wall is directly evaluated by the relationship between the change in thickness of the arterial wall and the arterial inner pressure.[4)] In this method, it is important to measure accurately the small velocity on the arterial wall, which is necessary to obtain the change in thickness of the arterial wall. The accuracy in measuring the small velocity is evaluated in the wide frequency band from d.c. to 1 kHz.[1)] From the experimental results, the minimum value of the measurable velocity is found to be about 0.5 mm/s.[5)] However, the accuracy of measurement of the small displacement has not been evaluated in the lower frequency band with a small amplitude.

In this paper, therefore, the accuracy of the measurement of the small displacement is evaluated in the lower frequency band from 5 Hz to 50 Hz with a small amplitude of about $\pm 30\,\mu$m. In the simulation experiment, the displacement obtained by the proposed method is compared with that obtained by a fiber optic displacement meter.

Furthermore, we evaluate the elastic properties of human carotid arteries. An atheromatous plaque has a large variance of elasticity in itself,[6)] however, the arterial wall, which has no remarkable deformation caused by atherosclerosis, generally has a tendency to harden with age.[7)] From this fact, it can be assumed that the elastic modulus obtained by the proposed method should have the same tendency when the arterial wall has no remarkable deformation. The correlation between the elastic modulus and age is evaluated from the experiments with respect to 50 patients and 8 healthy subjects with no remarkable deformation of the arterial walls.

2. Principle of Measuring Small Changes in Thickness of the Arterial Wall

To obtain a small change in thickness, $\Delta h(t)$, which is defined as the difference between the displacements, $x_{\rm in}(t)$ and $x_{\rm ad}(t)$, of the intima and adventitia, respectively, small velocity signals, $v_{\rm in}(t)$ and $v_{\rm ad}(t)$, on the intima and adventitia of the arterial wall are obtained using ultrasound by the following method.[1)] RF pulses with an angular frequency of $\omega_0 = 2\pi f_0$ are transmitted at time intervals of ΔT from an ultrasonic transducer on the surface of the skin. Defining the acoustic velocity as c_0, the instantaneous distance of an object from the ultrasonic transducer is denoted by $x(t) = c_0 \cdot \tau(t)$, where $\tau(t)$ is the instantaneous period required for a one-way transmission from the ultrasonic transducer to the object. The ultrasonic pulse reflected by the object is received by the same ultrasonic transducer. The output signal $z(t)$ is amplified and quadrature demodulation is applied to the signal. The resultant complex signal is A/D converted at a sampling period of T_s and then separated into the response signals, $\{y(x;t)\}$, for each transmitted pulse at a time t, where x denotes the distance of the object from the ultrasonic transducer.

The phase $\theta(x;t)$ of the resultant sectional complex signal $y(x;t)$ is given by the angular frequency ω_0 multiplied by twice the delay time $\tau(t)$ in the one-way propagation from the ultrasonic transducer to the object, as follows:

$$\begin{aligned}\theta(x;t) &= 2\omega_0\tau(t)\\ &= 2\omega_0\frac{x(t)}{c_0}.\end{aligned} \tag{2.1}$$

The phase difference $\Delta\theta(x;t)$ between the demodulated signals, $y(x;t)$ and $y(x;t+\Delta T)$, of the received signals for the successively transmitted pulses in the interval ΔT is given by

$$\begin{aligned}\Delta\theta(x;t) &= \theta(x;t+\Delta T) - \theta(x;t)\\ &= \frac{2\omega_0}{c_0}\Delta x(t),\end{aligned} \tag{2.2}$$

where $\Delta x(t) = x(t+\Delta T) - x(t)$ is the movement of the object in the period ΔT at a time t, where it can be assumed that the received interval almost coincides with the transmitted interval ΔT of the ultrasonic RF pulses. By dividing the movement Δx by the period ΔT the average velocity, denoted by $\widehat{v}(t+\frac{\Delta T}{2})$, of the object during the period ΔT is given by the phase difference $\Delta\theta(x;t)$ between the successively demodulated signals, $y(x;t)$ and $y(x;t+\Delta T)$, as

$$\begin{aligned}\widehat{v}(t+\frac{\Delta T}{2}) &= \frac{\Delta x(t)}{\Delta T}\\ &= c_0\cdot\frac{\Delta\theta(x;t)}{2\omega_0\cdot\Delta T}.\end{aligned} \tag{2.3}$$

We apply this method for the measurement of the small velocity signal on the wall of the human carotid artery. First, the initial depth positions, $d_{\mathrm{in}0}$ and $d_{\mathrm{ad}0}$, around the intima and adventitia, respectively, are manually preset at the end diastole by referring the M-mode image as shown in Fig. 1. The spatial resolution in determination of $d_{\mathrm{in}0}$ and $d_{\mathrm{ad}0}$ is equal to $T_s\cdot c_0/2 = 0.75\,\mathrm{mm}$ in the depth direction. Each displacement of the points A and B pointed out by $d_{\mathrm{in}0}$ and $d_{\mathrm{ad}0}$ is tracked by the method developed in .[1] Though the positions, $d_{\mathrm{in}0}$ and $d_{\mathrm{ad}0}$, do not corresponds respectively to the actual positions of the intima and adventitia, we define the thickness, h_{d}, of the arterial wall as the difference between $d_{\mathrm{in}0}$ and $d_{\mathrm{ad}0}$.

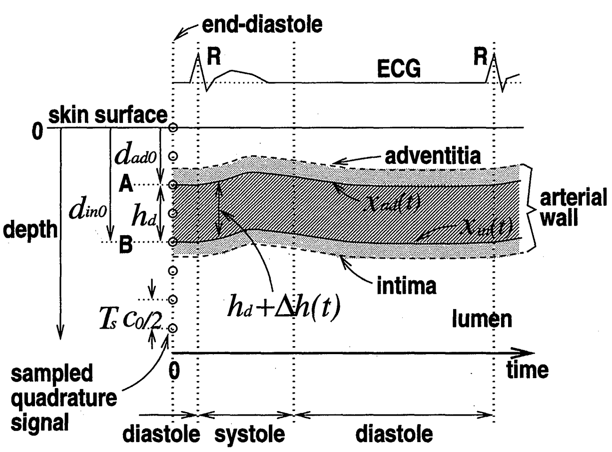

Fig. 1. Illustration for determining the initial position from where the velocity signals are obtained.

In addition, h_{d} is approximated by a constant during one cardiac cycle because $h_{\mathrm{d}} \gg$ the change in thickness, $\Delta h(t)$, of the arterial wall.

During the tracking process, the small velocity signals, $v_{\mathrm{in}}(t)$ and $v_{\mathrm{ad}}(t)$, of the intima and adventitia of the arterial wall are simultaneously obtained. By integrating the difference between the resultant velocity signals, $v_{\mathrm{in}}(t)$ and $v_{\mathrm{ad}}(t)$, the change in thickness, $\Delta h(t)$, of the arterial wall, which is defined by the difference between the displacements, $x_{\mathrm{in}}(t)$ and $x_{\mathrm{ad}}(t)$, on the intima and adventitia, is accurately obtained as[2]

$$\begin{aligned}\Delta h(t) &= x_{\mathrm{in}}(t) - x_{\mathrm{ad}}(t)\\ &= \int_{-\infty}^{t}\{v_{\mathrm{in}}(t) - v_{\mathrm{ad}}(t)\}dt.\end{aligned} \tag{2.4}$$

This change in thickness, $\Delta h(t)$, shows that the decrease of the wall thickness from $h_{\mathrm{d}} = d_{\mathrm{in}0} - d_{\mathrm{ad}0}$.

Since the amplitude of the change in thickness, $\Delta h(t)$, of the arterial wall is about $10\,\mu\mathrm{m}$, the resultant change in thickness, $\Delta h(t)$, cannot be measured by the B-mode or the M-mode images obtained by the standard ultrasonic diagnostic equipment.

3. Evaluation of the Elastic Property of the Arterial Wall

From the resultant change in thickness, $\Delta h(t)$, of the arterial wall, the maximum change of strain, $\Delta\varepsilon_{\mathrm{r}}$, in the radial direction of the arterial wall during one cardiac cycle is given by

$$\Delta\varepsilon_{\mathrm{r}} = \frac{\Delta h_{\mathrm{s}}}{h_{\mathrm{d}}}, \tag{3.1}$$

where Δh_{s} is the maximum amplitude of $\Delta h(t)$ in the systole, h_{d} is the thickness of the arterial wall at the end-diastole, which is determined by $d_{\mathrm{in}0} - d_{\mathrm{ad}0}$, $\Delta\varepsilon_{\mathrm{r}}$ shows the increase of the strain in the arterial wall when the blood pressure increases from the diastolic blood pressure, p_{d}, to the systolic blood pressure, p_{s}.

From the increase in strain, $\Delta\varepsilon_{\mathrm{r}}$, we define the following elastic modulus E by

$$E = \frac{p_{\mathrm{s}} - p_{\mathrm{d}}}{\Delta\varepsilon_{\mathrm{r}}}.\quad (\mathrm{Pa}) \tag{3.2}$$

4. Measurement System for Evaluating the Accuracy of the Proposed Method

Figure 2 shows an experimental setup for measuring a small displacement of the vibrating rubber plate in a water tank using ultrasound and a standard fiber optic displacement meter (IWATSU, ST-3711). The rubber plate is actuated by a vibrator (Brüel & Kjaer, Mini Shaker Type 4810) driven by a sinusoidal signal with various frequencies f from 5 Hz to 50 Hz. The maximum amplitude of the displacement is about $30\,\mu\mathrm{m}$. The displacement of the rubber plate actuated for each frequency f is simultaneously measured by the proposed method and the fiber optic displacement meter. From the resultant displacement signals, $x_{us}(t;f)$ and $x_{opt}(t;f)$, which are obtained respectively by the proposed method and the fiber optic displacement meter, the maximum, $r_0(f)$, of the correlation function, $r(\tau;f)$, and the minimum, $e_0(f)$, of the normalized average squared error, $e(\tau;f)$, defined by the following equations are evaluated at each actuated frequency f:

$$r_0(f) = \max_{\tau} r(\tau; f) \tag{4.1}$$

$$r(\tau; f) = \frac{\frac{1}{M}\sum_{t=1}^{M} x_{\mathrm{opt}}(t; f) \cdot x_{\mathrm{us}}(t+\tau; f) - \left\{\frac{1}{M}\sum_{t=1}^{M} x_{\mathrm{opt}}(t; f)\right\} \cdot \left\{\frac{1}{M}\sum_{t=1}^{M} x_{\mathrm{us}}(t+\tau; f)\right\}}{\sqrt{V_{\mathrm{opt}}(f)}\sqrt{V_{\mathrm{us}}(\tau; f)}}, \tag{4.2}$$

$$e_0(f) = \min_{\tau} e(\tau; f) \tag{4.3}$$

$$e(\tau; f) = \frac{\sqrt{\sum_{t=1}^{M} |x_{\mathrm{opt}}(t; f) - x_{\mathrm{us}}(t+\tau; f)|^2}}{\sqrt{\sum_{t=1}^{M} |x_{\mathrm{opt}}(t; f)|^2}} \times 100\,(\%), \tag{4.4}$$

where

$$V_{\mathrm{opt}}(f) = \frac{1}{M}\sum_{t=1}^{M} x_{\mathrm{opt}}(t; f)^2 - \left\{\frac{1}{M}\sum_{t=1}^{M} x_{\mathrm{opt}}(t; f)\right\}^2, \tag{4.5}$$

$$V_{\mathrm{us}}(\tau; f) = \frac{1}{M}\sum_{t=1}^{M} x_{\mathrm{us}}(t+\tau; f)^2 - \left\{\frac{1}{M}\sum_{t=1}^{M} x_{\mathrm{us}}(t+\tau; f)\right\}^2, \tag{4.6}$$

M is the number of data, and τ is the time lag between $x_{\mathrm{us}}(t; f)$ and $x_{\mathrm{opt}}(t; f)$.

For this measurement, a 12-bit A/D conversion is applied to the output of the fiber optic displacement meter, and the maximum amplitude of the A/D conversion is 40 μm, therefore, the digitized error is $\pm 40/2048 = \pm 0.02\,\mu$m, which is small enough for evaluation.

5. Experimental Results in Accuracy Evaluation

Figure 3(d) shows the small velocity signal, $v_{\mathrm{us}}(t; f)$, on the rubber plate obtained by the proposed method. The small velocity signal, $v_{\mathrm{us}}(t; f)$, has a high reproducibility. By integrating the resultant velocity signal, $v_{\mathrm{us}}(t; f)$, the displacement signal, $x_{\mathrm{us}}(t; f)$, is obtained as shown in Fig. 3(e). Figure 3(c) shows the displacement signal, $x_{\mathrm{opt}}(t; f)$, obtained by the fiber optic displacement meter.

Figure 4 shows the results of the displacements, $x_{\mathrm{us}}(t; f)$ and $x_{\mathrm{opt}}(t; f)$, of the rubber plate obtained by the proposed method and the fiber optic displacement meter respectively for each actuated frequency f from 5 Hz to 50 Hz. The displacement signals, $x_{\mathrm{us}}(t; f)$ and $x_{\mathrm{opt}}(t; f)$, are well correlated, and the average of the maximum, $r_0(f)$, of the correlation function, $r(\tau; f)$, is 0.99953 as shown in Fig. 5(a).

Moreover, the minimum, $e_0(f)$, of the normalized average squared error, $e(\tau; f)$, is shown in Fig. 5(b). Their average value is about 3% with respect to the small vibration with an amplitude of 30 μm. From these experiments, it is found that the displacement of the rubber plate is measured with high accuracy by the proposed method.

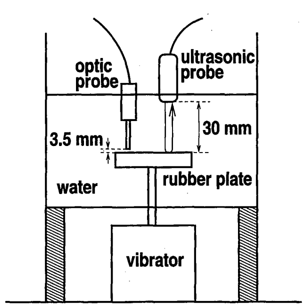

Fig. 2. Experimental setup for measuring a small displacement of a rubber plate on a small vibrator.

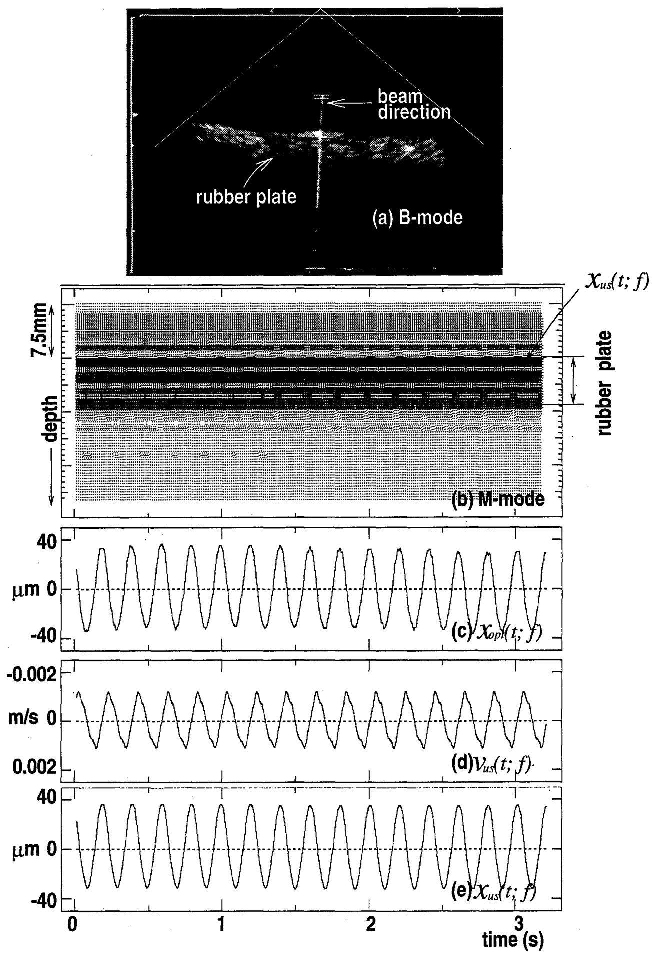

Fig. 3. Experimental results in accuracy evaluation. (a) B-mode image obtained by the standard ultrasonic diagnostic equipment. (b) M-mode image. (c) The displacement signal, $x_{\mathrm{opt}}(t; f)$, obtained by the fiber optic displacement meter. (d) The velocity signal, $v_{\mathrm{us}}(t; f)$, obtained by the proposed method. (e) The displacement signal, $x_{\mathrm{us}}(t; f)$, obtained by the proposed method.

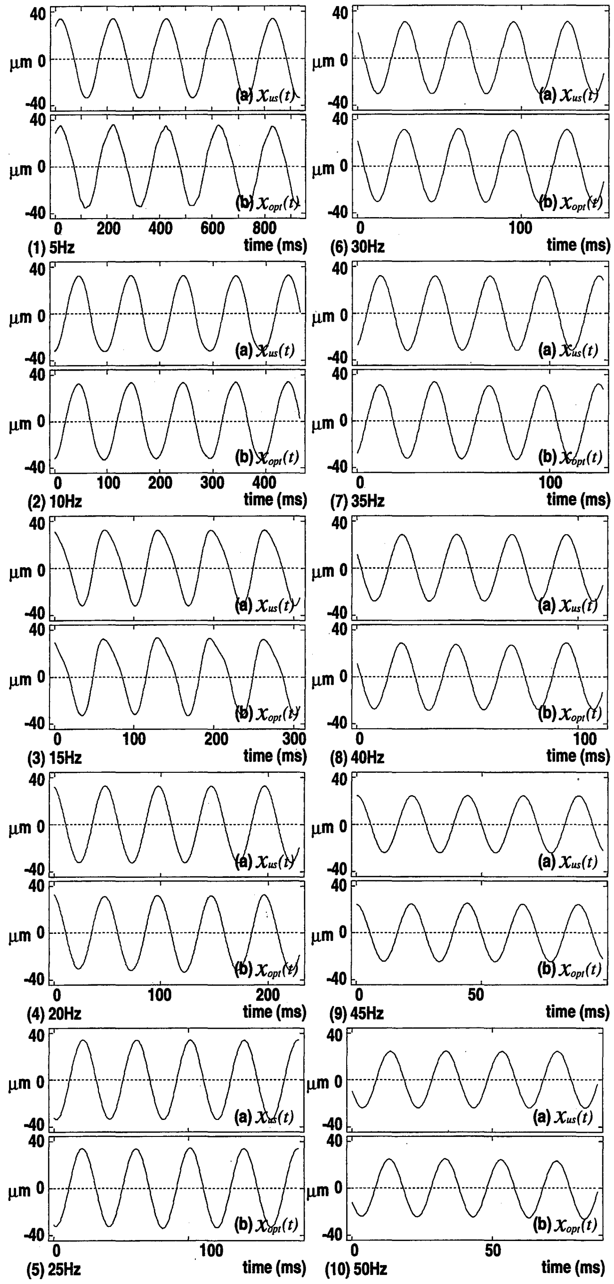

Fig. 4. (a) The displacement signals, $x_{us}(t; f)$, obtained by the proposed method for each actuated frequency f. (b) The displacement signals, $x_{opt}(t; f)$, obtained by the fiber optic displacement meter for each actuated frequency f.

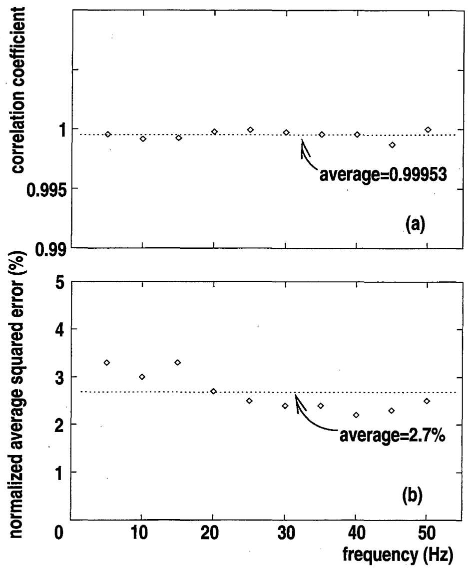

Fig. 5. Evaluation of the accuracy of measuring the displacement of the vibrating rubber plate by the proposed method. (a) The correlation coefficient, $r(\tau; f)$, between the displacement signals, $x_{us}(t; f)$ and $x_{opt}(t; f)$, obtained by the proposed method and the fiber optic displacement meter. (b) The normalized average squared error, $e(\tau; f)$, of the displacement signal, $x_{us}(t; f)$, obtained by the proposed method.

6. *In Vivo* Experimental Results

Figure 6 shows the *in vivo* experimental results obtained by applying the proposed method to the human carotid artery in a healthy young subject. The ultrasonic frequency is 7.5 MHz. Figures 6(e) and 6(f) show the velocity signals, $v_{in}(t)$ and $v_{ad}(t)$, respectively. Figure 6(g) shows the change in thickness, $\Delta h(t)$, from eq. (4.4) of the anterior wall. There is sufficient reproducibility even for such a minute change in thickness of about 10 μm.

Figure 7 shows the results of the evaluation of the elastic modulus of the arterial wall in 50 patients and 8 healthy subjects. The patients exhibited some risk factors for atherosclerosis, but all of the healthy subjects did not. In addition, there is no remarkable deformation of the arterial wall of the pa-

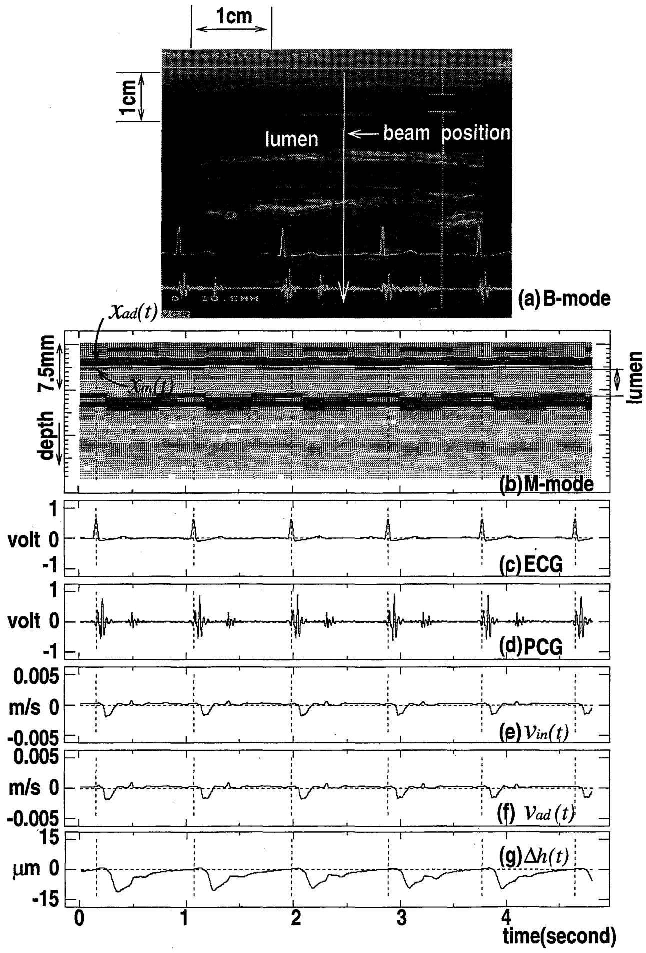

Fig. 6. *In vivo* experimental results of the human carotid artery in a healthy young subject. (a) B-mode image. (b) M-mode image. (c) Electrocardiogram. (d) Phonocardiogram. (e) The velocity signal, $v_{in}(t)$, on intima. (f) The velocity signal, $v_{ad}(t)$, on adventitia. (g) The change in thickness, $\Delta h(t)$, of the arterial wall.

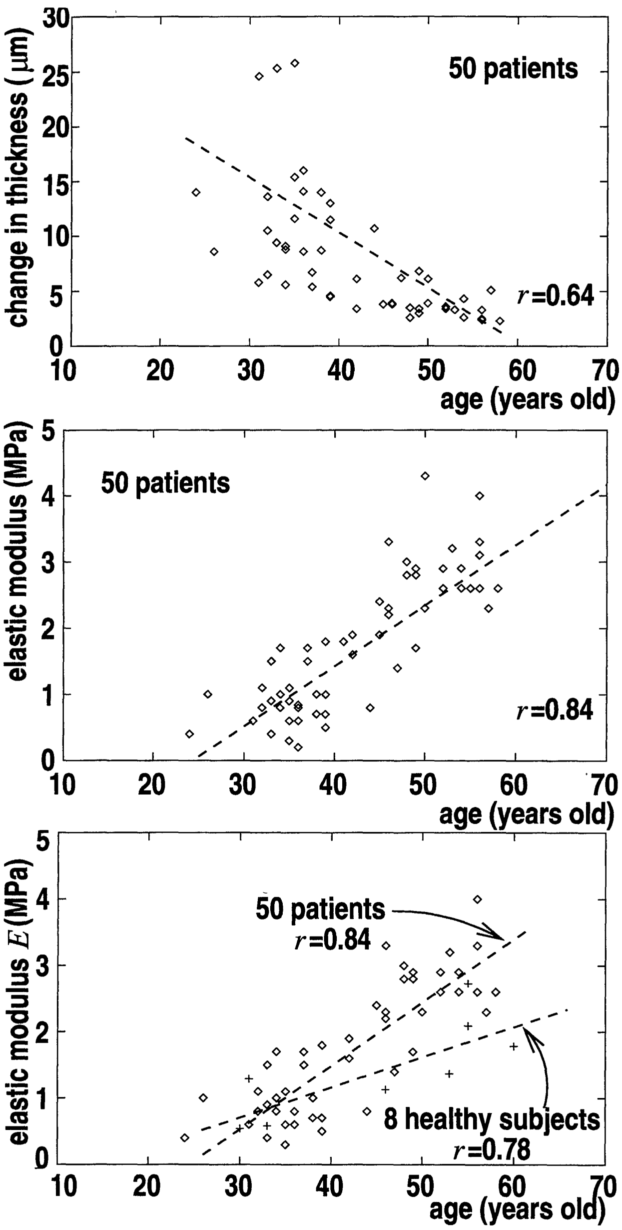

Fig. 7. *In vivo* experimental results for 50 patients and 8 healthy subjects. (a) The relationship between age and the maximum amplitude, Δh_s, of the change in thickness of the arterial wall. (b) The relationship between age and the elastic modulus E. (c) The elastic modulus E measured in patients and healthy subject.

tients. Figures 7(a) and 7(b) show the relationship between age and the maximum amplitude Δh_s of the change in thickness of the arterial wall and the relationship between age and the elastic modulus E, respectively. The maximum amplitude Δh_s of the change in thickness and the elastic modulus E are correlated with age. This tendency is also shown by the previous method such as the stiffness parameter β,[7] therefore, it can be said that the elastic property of the arterial wall is properly evaluated by measuring the elastic modulus E. The elastic modulus E of the patients are also compared to those of the healthy subjects as shown in Fig. 7(c). The patients have a relatively higher elastic modulus E after the age of 35.

The stiffness parameter β evaluates the average elasticity in the entire circumference because it is obtained by the change in diameter of the artery. On the other hand, using the elastic modulus E obtained by the change in thickness of the arterial wall, it is possible to evaluate the local elasticity of the arterial wall even when the arterial wall is deformed by atherosclerosis.

7. Conclusions

In this paper, the accuracy of the proposed method for measuring a small displacement is evaluated. The average error of the proposed method is determined to about 3% with respect to small vibrations from $-30\,\mu$m to $30\,\mu$m. These results show that the proposed method is sufficiently accurate for measuring small changes in thickness of the arterial wall with amplitudes of several tenth micrometers.

Moreover, this measurement was applied to the human carotid arteries of 50 patients and 8 healthy subjects. The results show that the elastic modulus of the arterial wall is positively correlated with age, which shows that the arterial wall hardens with age.

Such a local evaluation of the elastic property of the arterial wall will be useful in diagnosing whether the atheromatous plaque will rupture or not.

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