

# Real-time velocimetry for evaluation of change in thickness of arterial wall

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## Abstract

We previously developed a new method, namely, the phased tracking method, for accurately tracking the movement of the heart wall and arterial wall based on both the phase and magnitude of the demodulated signals to determine the instantaneous position of an object. By this method, the local change in wall thickness during one heartbeat can be determined. We have now developed a real-time system for measuring change in thickness of the myocardium and arterial wall. In this system, four high-speed digital signal processing (DSP) chips are employed for obtaining the initially developed method in real time. The tracking results for both sides of the wall are superimposed on the M (motion)-mode image in the workstation, and the thickness changes of the arterial wall are displayed in real time. Using this system, reported herein, velocity signals of the arterial wall with amplitudes less than several micrometers can be successfully detected in real time with sufficient reproducibility. The elasticity of the arterial wall is evaluated by referring to the blood pressure. In *in vivo* experiments, the rapid response of the change in wall thickness of the carotid artery to the dose of nitroglycerine (NTG) is evaluated for a young healthy subject and a young smoker. This new real-time system offers potential for quantitative diagnosis of early-stage atherosclerosis by the transient evaluation of the rapid response of the cardiovascular system to physiological stress. © 2000 Elsevier Science B.V. All rights reserved.

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## 1. Introduction

At the beginning of the ejection period, the arterial wall is affected by the pressure wave, which comes from the left ventricle (LV) and expands the lumen. Consequently, the arterial wall becomes slightly thin during the ejection period. In the literature, measurements of the change in diameter,  $\Delta d_{BA}(t)$ , of the lumen in Fig. 1 have been reported. From  $\Delta h_{AB}(t)$ , the elasticity of the arterial wall can be determined, but it is assumed that the arterial wall is homogeneously changed in the circumferential direction due to atherosclerosis.

However, measurement of the change in thickness of the wall makes it possible to evaluate the elasticity of the arterial wall in each local area, the locality in the circumferential direction being indispensable to diagnosis of the inner characteristics of atherosclerotic plaque. For this purpose, by tracking the instantaneous posi-

tions,  $x_A(t)$  and  $x_B(t)$ , which are respectively preset at  $x_A(t_0)$  and  $x_B(t_0)$  at the end-diastole along the ultrasonic beam in the arterial wall, as illustrated in Fig. 1(b), the small change in wall thickness,  $\Delta h_{AB}(t)$ , between these two points, *A* and *B*, is obtained [1], as illustrated in Fig. 1(c) when the ultrasonic beam is almost perpendicular to the wall. From the ratio of the change in thickness,  $\Delta h_{AB}(t)$ , to the thickness,  $h_{AB}(t_0)$ , between these points preset at the end-diastole, the deformation is obtained. If the deformation is sufficiently small and is in the linear regime, it shows the strain, and thus the regional elasticity of the wall can be approximately evaluated using the pulse pressure measured at the brachial artery. Therefore, the transcutaneous measurement of the change in thickness of the regional area of the arterial wall during each cardiac cycle provides the essential tools for diagnosis of atherosclerosis.

The accuracy required for the simultaneous measurement of the instantaneous positions  $x_A(t)$  and  $x_B(t)$  of points *A* and *B* is estimated as follows. For the carotid artery, the thickness of the wall is about 1 mm, and the

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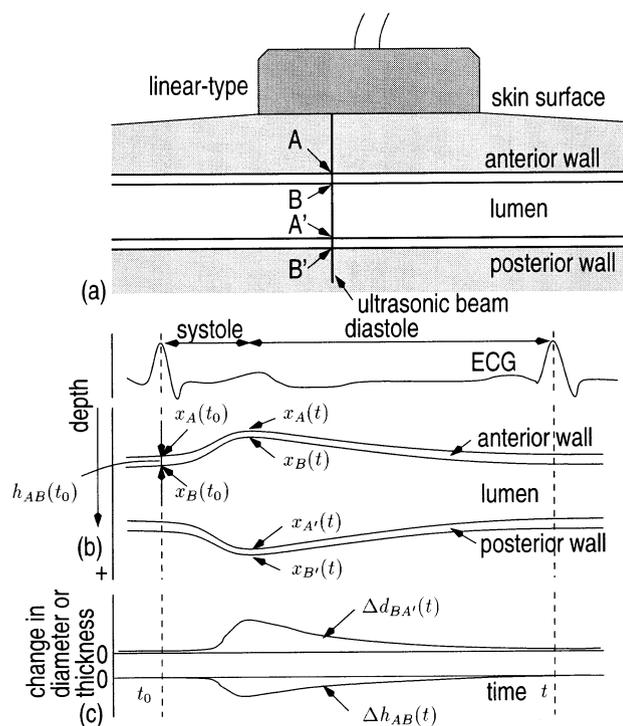


Fig. 1. Illustration explaining the procedure of measuring the change in thickness,  $\Delta h_{AB}(t)$ , of the arterial wall, and the change in diameter,  $\Delta d_{BA'}(t)$ , of the lumen by tracking the movement  $x_A(t)$  and  $x_B(t)$  of points A and B preset in the arterial wall along the ultrasonic beam [1]. (a) Cross-sectional image. (b) Displacement  $x_A(t)$  and  $x_B(t)$ . (c) Change in thickness,  $\Delta h_{AB}(t)$  of the arterial wall and change in diameter,  $\Delta d_{BA'}(t)$ .

change in thickness,  $\Delta h_{AB}(t)$ , is less than 100  $\mu\text{m}$  during one cardiac cycle in normal adults [1]. Therefore, the necessary spatial resolution in the measurement of instantaneous position as a waveform is at least 10  $\mu\text{m}$ . If the velocity signals,  $v_A(t)$  and  $v_B(t)$ , of these two points, A and B, are detected based on the pulse Doppler method, the necessary accuracy of the velocity measurement is about  $10 \mu\text{m}/200 \mu\text{s} = 0.05 \text{ m/s}$  when the pulse repetition frequency (PRF) of the transmission-pulse train is 5 kHz ( $=1/200 \mu\text{s}$ ). If the equivalent sampling period of the velocity signal,  $v_i(t)$ , is longer than 200  $\mu\text{s}$  as in the FFT (fast Fourier transform)-based standard Doppler system, for example, a more accurate velocity measurement is required.

Though M-mode echocardiography offers an advantage in critically examining the motion pattern of the wall, its spatial resolution along the ultrasonic beam is limited to a few wavelengths, namely, at most about several hundred micrometers for ultrasound of 7 MHz because an M-mode image is displayed based on the amplitude of the reflected ultrasound. However, numerous elaborate techniques have been proposed for non-invasive measurement of the velocity of the blood flow in the arteries based on the Doppler effect. Moreover, several methods, including the phase-locked-loop (PLL)

techniques, have been proposed to measure rough changes in the diameter of the arterial walls by tracking arterial wall displacement in real time.

For the accurate detection of the velocity signal, that is, the instantaneous movement, on or in the heart wall or arterial wall, we have developed the following phased tracking method [1]. In this method, by calculating the auto-correlation function with the constraint least-squares technique between the sequentially received echoes, the phase change caused by movement of the preset point ( $i$ ) during the pulse repetition period  $\Delta T$  ( $=1/\text{PRF}$ ) can be accurately determined, and the average velocity,  $v_i(t)$ , during the period can be obtained. By adding the product of  $v_i(t)$  and  $\Delta T$  to the previous object position  $x_i(t)$ , the next position,  $x_i(t + \Delta T)$ , is estimated as  $x_i(t) + v_i(t) \times \Delta T$ . This method has been confirmed by experiments using a water tank and has been applied to the in vivo detection of low-velocity signals, with sufficient reproducibility, at points in the interventricular septum (IVS) of the human heart [1]. The detected velocity signal shows rapid motion, including high-frequency components with small amplitudes, which cannot be recognized by M-mode echocardiography.

Moreover, the method has been applied to multiple points preset along an ultrasonic beam in the LV wall so that the instantaneous object positions  $\{x_i(t)\}$  and the velocity signals  $\{v_i(t)\}$  are obtained for these multiple points  $\{i\}$  in the LV wall [2]. The wall changes position and thickness with time. By making the location of the RV side of the IVS the reference point, the thickness change during myocardial contraction/relaxation can be detected. Then, their spatial distribution can be obtained and can be superimposed on the M-mode image using color coding.

The method of measurement herein described was developed by batch processing on an off-line system in our laboratory. However, the quantity of A/D converted data is considerable, and it is time-consuming to transfer the data from the A/D converter to a computer in the off-line system. Thus, real-time processing is indispensable in obtaining new clinical examination tools for an evaluation of transient change in the tolerance test.

The development and application of real-time processing significantly facilitate its use in clinical diagnosis and will offer a new tool for clinical examination. For example, nitroglycerine (NTG) is used medically as a vasodilator for rapid treatment of angina pectoris [3]. Real-time measurement of the transient change in thickness of the heart wall or the arterial wall just after the sublingual administration of NTG will be of use in a direct evaluation of the response of the heart wall or the arterial wall to the antianginal drug. At the same time, real-time monitoring during clinical intervention is essential for avoiding hyper-responses such as serious hypotension and/or arrhythmia.

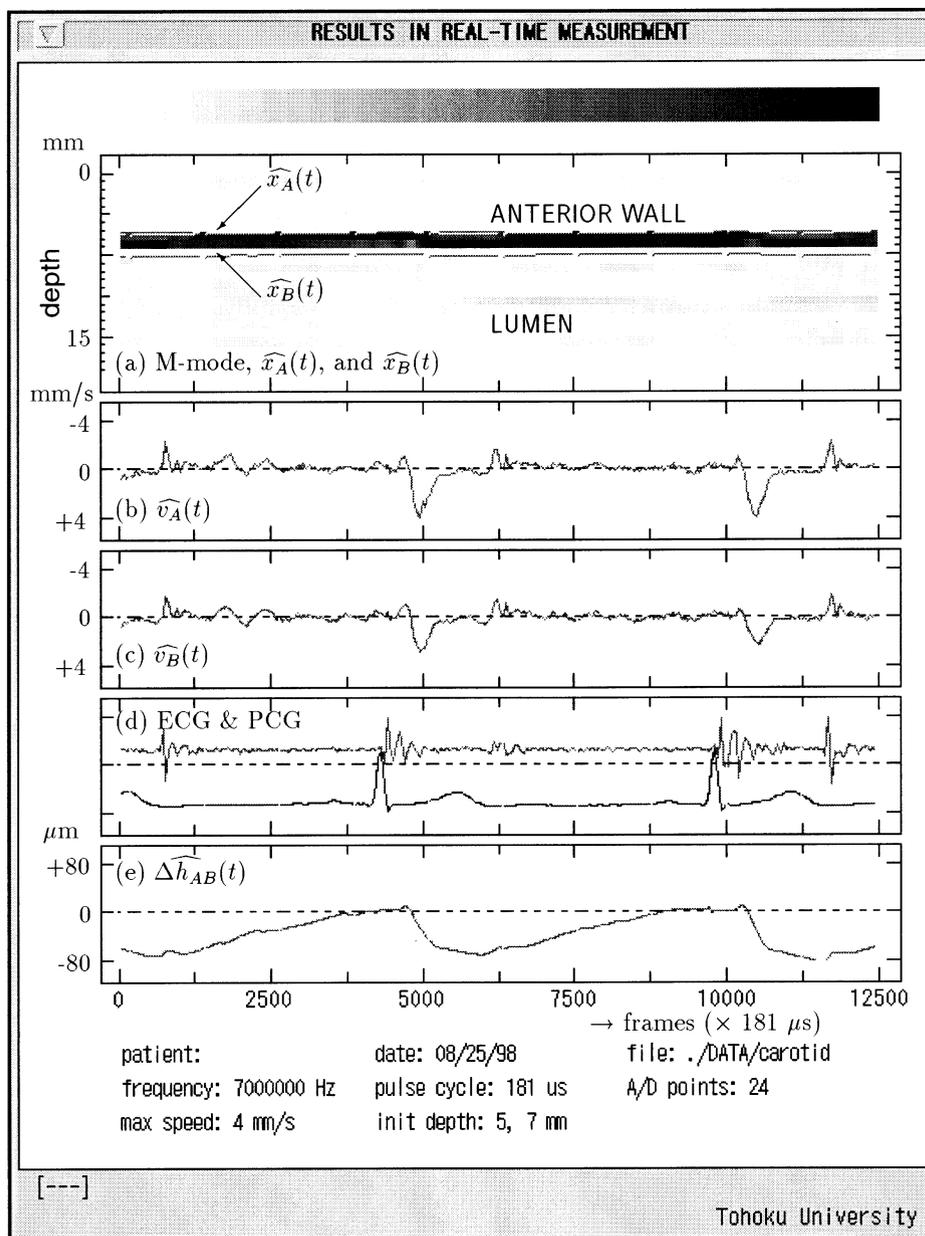


Fig. 2. In vivo experimental results of the vibration at points (A) on the adventitia side and (B) on the intima side of the anterior wall of the carotid artery [1]. (a) Tracking results  $\{\widehat{x}_A(t)\}$  and  $\{\widehat{x}_B(t)\}$  of points A and B, which are superimposed on the M-mode image. (b) and (c) Estimates of the vibration velocity signals  $\{\widehat{v}_A(t)\}$  and  $\{\widehat{v}_B(t)\}$  of points A and B. (d) ECG and the PCG. (e) Change in thickness,  $\Delta\{\widehat{h}_{AB}(t)\}$ , of the anterior wall of the artery.

In the process of tracking the instantaneous position, the object position is moved along the ultrasonic beam based on the previous results from the complex auto-correlator. For flexible processing, we have developed a real-time system based on high-speed floating-point digital signal processing (DSP) chips and a workstation (WS) [4].

In the hardware system employed, the received echo is quadrature-demodulated, and then the resultant in-phase and quadrature signals are simultaneously A/D-converted at a sampling frequency of 1 MHz with

a 12-bit accuracy. For these large-scale data, it is not possible to transfer them from the A/D converter to the DSP boards using the VME-bus (versa module European bus, the IEEE1024 standard) because its transfer speed is not so high. Much time-consuming processing is necessary from the A/D conversion to a real-time display of the M-mode image, the resultant waveforms, and the tracking results on the CRT (cathode-ray tube) of the WS. Thus, we employ four DSP chips. The A/D converter boards are directly connected to the DSP board. All of the processing in

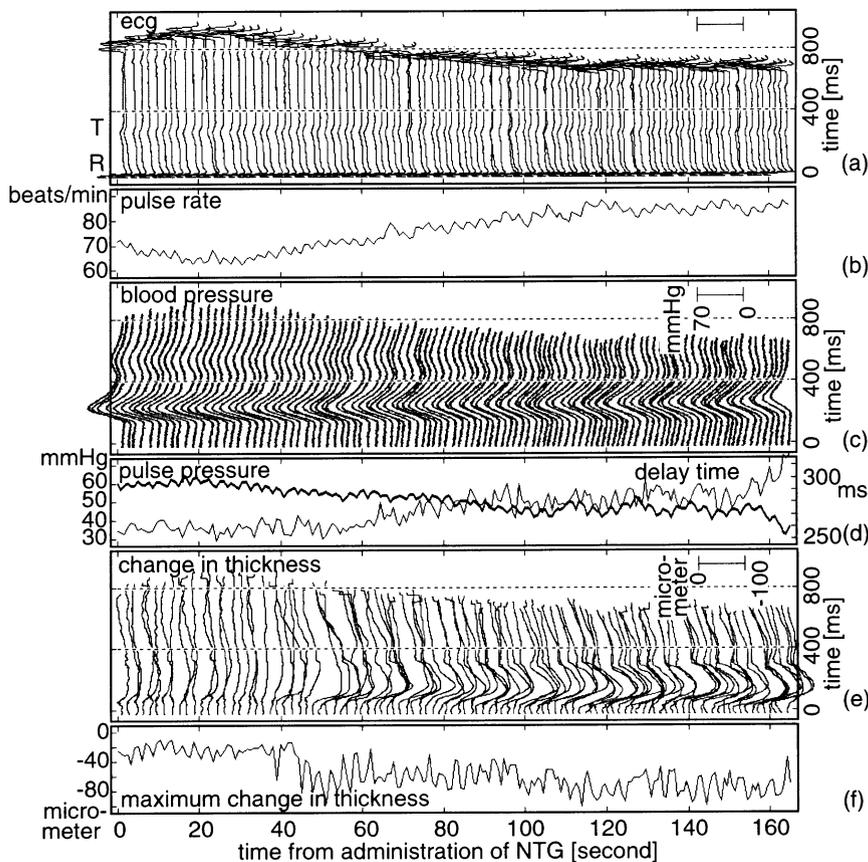


Fig. 3. Transient response of a 25 year old healthy male subject to the administration of nitroglycerine (NTG). (a) ECG for each heartbeat. (b) Pulse rate detected from the interval of the R-waves in the ECG. (c) Blood pressure continuously measured at the radial artery by the manometer. (d) Pulse pressure (bold line) and the delay time of peak pressure from the R-wave (thin line). (e) Change in thickness of the carotid arterial wall. (f) Maximum value of the change in thickness,  $\Delta h_{AB}(t)$ , of the CCA detected for each heartbeat.

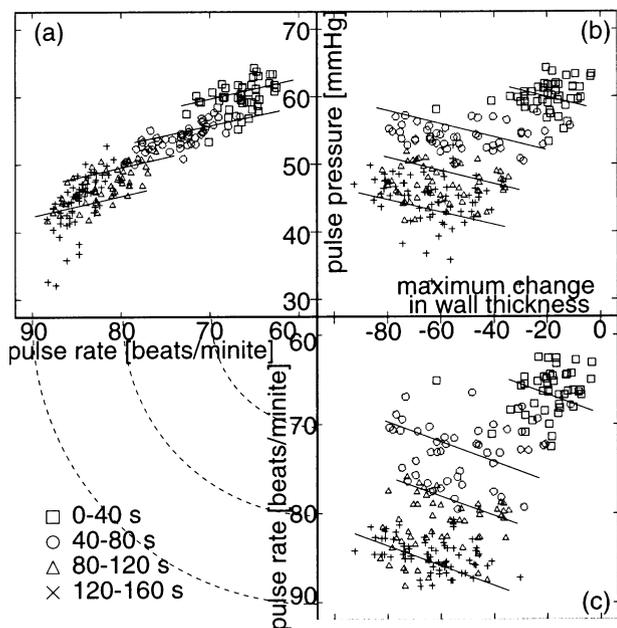


Fig. 4. Relationships among the maximum change in wall thickness in Fig. 3(f), the pulse pressure in Fig. 3(d), and the pulse rate in Fig. 3(b).

the four DSPs should be synchronized with the transmission timing of the ultrasonic pulse. By making free use of four DSP chips, pipelining and parallel processing are employed to increase the throughput. In this pipelining, each of the resultant tasks is completed within the pulse repetition period,  $\Delta T$ , which carries out the real-time processing, though these tasks cannot be performed in real time with a single DSP chip.

In this study, the real-time system was applied to in vivo experiments on the measurement of thickening and thinning in the human carotid arterial wall. Finally, the system was applied to the transient evaluation of the rapid response of the change in wall thickness of the artery to the dose of NTG.

## 2. In vivo results for the carotid artery

The developed real-time system in [4] is applied to the human common carotid artery (CCA) of a presumably healthy 39 year old male volunteer. The ultrasonic frequency is 7 MHz. Points (A) and (B) are set on the intima and adventitia of the anterior wall of the same

carotid artery, respectively. The ultrasonic beam passing through these two points is perpendicular to the wall during the measurements. Fig. 2(b) and (c) show the velocity signals,  $v_A(t)$  and  $v_B(t)$ , respectively. The change in thickness,  $\Delta h_{AB}(t)$ , of the anterior wall is estimated as shown in Fig. 2(e). A minute change in thickness of about 80  $\mu\text{m}$  is measured with sufficient reproducibility. In the waveforms of Fig. 2(b), (c) and (e), the dicotic notch is obviously observed at the radiation timing of the second heart sound (II).

### 3. Transient evaluation of arterial response to nitroglycerine

As described in Section 1, the real-time system to measure the change in thickness of the arterial wall will offer new tools for clinical examinations. In this study, the developed system is applied to evaluation of transient response of the change in thickness of the carotid artery for about the first 160 s after the sublingual administration of spray-type NTG.

The first subject is a 25 year old healthy male volunteer. The change in thickness,  $\Delta h_{AB}(t)$ , of the posterior wall of the CCA and the ECG are continuously measured by the developed real-time system. The blood

pressure,  $p(t)$ , is also continuously and non-invasively measured at the radial artery using a blood-pressure manometer (Japan Colin, Jentow-7700).

Fig. 3 shows the transient response to the sublingual administration of NTG. For each heartbeat, the waveform of the change in thickness,  $\Delta h_{AB}(t)$ , is measured as shown in Fig. 3(e), and the maximum of  $|\Delta h_{AB}(t)|$  during each heartbeat is detected and is shown in Fig. 3(f). From about 40 s after the administration of NTG, the pulse rate shown in Fig. 3(b), which is determined from the R–R interval of the ECG in Fig. 3(a), gradually increases, and the pulse pressure shown in Fig. 3(d) gradually decreases, where the pulse pressure is the difference between the maximal blood pressure and the diastolic pressure. At the same time, the maximum change in wall thickness increases. Thus, the arterial wall becomes compliant about 40 s after the dose of NTG. By assuming that the change in arterial compliance is one of the factors influencing the prolongation of the arrival time of the peak pressure at the radial artery, this observation is supported by the gradual increase of the delay — shown in Fig. 3(d) — between the peak blood pressure and the peak of the R-wave.

By contrast, the maximum change in wall thickness varies widely, especially from about 40 s after the NTG

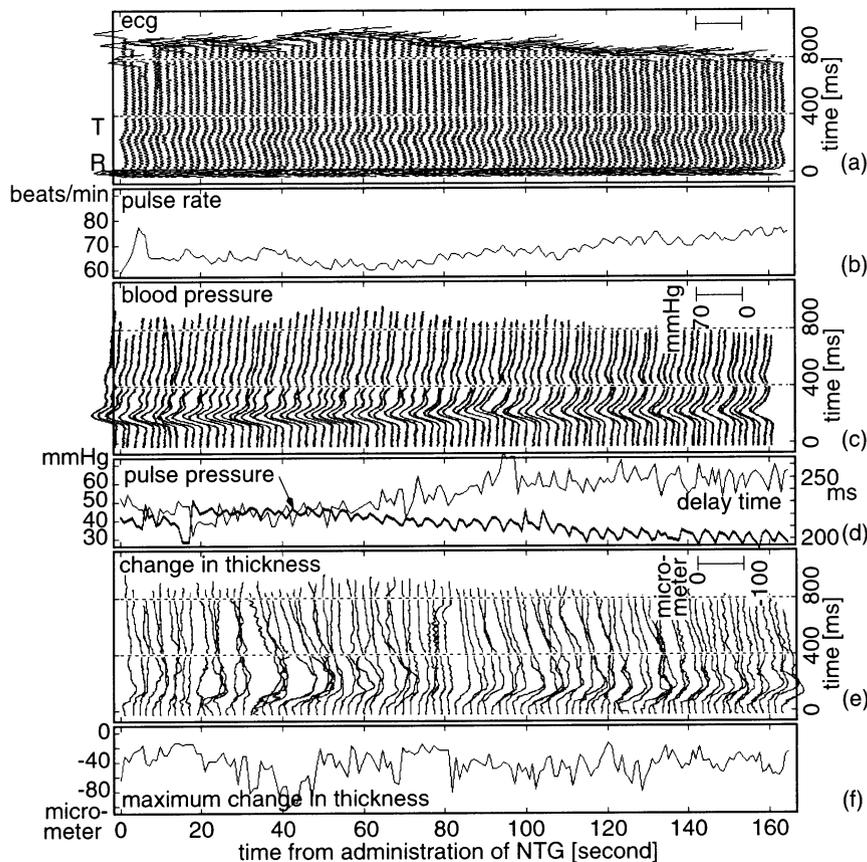


Fig. 5. Transient response of a 27 year old male smoker to the administration of nitroglycerine (NTG). For details, see Fig. 3.

administration [see the fluctuations in the trend of the change in thickness of Fig. 3(f)]. As shown in Fig. 4(b) and (c), however, there is a correlation between the maximum change in wall thickness of Fig. 3(f) and the pulse pressure of Fig. 3(c) or the pulse rate of Fig. 3(b). Thus, the scattering in the maximum change in wall thickness shown in Fig. 3(f) originates in the scattering in the pulse pressure shown in Fig. 3(d) or the pulse rate of Fig. 3(b).

Next, the same measurement was applied to the posterior wall of the CCA of a 27 year old male smoker consuming about 20 cigarettes per day for 7 years, and the results are shown in Fig. 5. The wall thickness is about 1.3 mm, which is almost same as the first subject in Fig. 3.

Even though there are fluctuations in Fig. 5, by comparing Fig. 5 with Fig. 3, the following observations were found:

1. The change in thickness during one heartbeat in Fig. 5(e) and (f) is relatively small for the smoker.
2. The changes in the pulse rate of Fig. 5(b), the pulse pressure of the bold line in Fig. 5(d), and the maximum change in thickness of Fig. 5(f) due to the response to the dose of NTG are also relatively small for the smoker.
3. These changes start about 60 s after the dose of NTG for the smoker in Fig. 5, while for the healthy subject in Fig. 3, the changes start after about 40 s. Similar results are obtained for other several healthy subjects.

Thus, the response to the dose of NTG is delayed and smaller for the smoker, compared to the young healthy volunteers.

#### 4. Conclusions

In this paper, we have demonstrated a novel real-time system for simultaneous measurement of velocity signals at two points preset on an ultrasonic beam by tracking the large movement of the object during the cardiac cycle. From the resultant velocity signals, the

local change in thickness of the arterial wall was evaluated in real time. In the preliminary clinical study, the response of the arterial wall to NTG is directly evaluated by the change in wall thickness for the first time. In such a measurement, the real-time measurement system is indispensable.

Further investigations are necessary to fully support the evaluation method of the response of the arterial wall to administration of NTG since the administration carries various side-effects such as the reduction of the preload for the heart. Detailed hemodynamic studies of the cardiac output flow, the ventricular stroke volume and associated pressure, as well as pressure build-up during the ventricular systole are also necessary for a more accurate evaluation of discriminatory effects of NTG on the arterial wall. Application of the measurement and evaluation to the response to NTG for the patients with arterial diseases also needs to be investigated.

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