Sensors and Actuators A 297 (2019) 111487

Contents lists available at ScienceDirect

Sensors and Actuators A: Physical

journal homepage: www.elsevier.com/locate/sna

Development of an ultrasonic probe to measure both radial arterial pressure and diameter change at the same position for early diagnosis of vascular endothelial function: Preliminary study

Mototaka Arakawa [a,b,*], Takumi Saito [a], Shohei Mori [b], Shigeo Ohba [b], Kazuto Kobayashi [c], Hiroshi Kanai [a,b]

[a] Graduate School of Biomedical Engineering, Tohoku University, Sendai, Miyagi 980-8579, Japan
[b] Graduate School of Engineering, Tohoku University, Sendai, Miyagi 980-8579, Japan
[c] Honda Electronics Co. Ltd., Toyohashi 441-3193, Japan

ARTICLE INFO

Article history:
Received 20 January 2019
Received in revised form 5 June 2019
Accepted 4 July 2019
Available online 24 July 2019

Keywords:
Radial artery
Blood pressure
Diameter
Piezoelectric effect
Viscoelasticity
Ultrasonic probe

ABSTRACT

We have evaluated the viscoelastic properties of arterial walls by measuring the relationship from radial arterial pressure to the change in arterial diameter to evaluate vascular endothelial functions. In our previous study, these parameters were measured at different positions, which caused timing errors. In the present study, a novel probe was developed to measure both radial arterial pressure and the change in arterial diameter at the same position. The central piezoelectric element of the linear array probe was disconnected from the ultrasonic diagnostic equipment and used to measure the arterial pressure. To obtain the blood pressure waveform, the output was integrated and calibrated using the systolic and diastolic pressures measured by a conventional sphygmomanometer. The arterial diameter was measured using the other 191 elements of the ultrasonic diagnostic apparatus via the phased-tracking method. The hysteresis loop, which is the relationship between the change in diameter and instantaneous pressure during a heartbeat, and thus reflects the viscoelasticity of the arterial wall, was measured successfully. The reproducibility for successive two heartbeats was confirmed for two subjects.

1. Introduction

Arteriosclerosis is the main cause of cardiovascular diseases. Vascular endothelial function decreases in the early stages of arteriosclerosis, followed by thickening of the intima-media complex, plaque formation, coarctation, and occlusion as arteriosclerosis advances.

Intravascular ultrasound and X-ray imaging have been used to diagnose arteriosclerosis; however, these techniques are invasive and unsuitable for repeated diagnoses. Noninvasive methods such as the pulse wave velocity (PWV) [1,2] and the ankle branchial index (ABI) [3] have been proposed. However, these indices yield only average values over a wide range, which may cause late decisions in the case of locally advancing lesions. Intima-media complex thickness (IMT) of the common carotid artery has been used for local diagnosis of arteriosclerosis. However, a conventional B-mode image provides information on only the shape; it cannot be used to evaluate the elasticity.

In the early stage of arteriosclerosis, lesions appear on vascular endothelial functions and the generation of vasodepressor material decreases. It is important to evaluate these functions as early as possible because the lesions are still reversible [4]. The conventional way to evaluate vascular endothelial functions is to measure the change in the inner diameter of the brachial artery using the flow-mediated dilation (FMD) method [5]. However, it is difficult to evaluate the vascular endothelial function accurately using the FMD method because the rate of change in diameter is only approximately 6% in healthy subjects [6,7].

We have proposed evaluating the viscoelastic properties of the blood vessel wall by measuring the arterial pressure and change in arterial wall thickness [8–13] or the arterial pressure and change in arterial diameter [14]. To measure the arterial pressure and change in diameter, an ultrasonic probe was placed between two pressure sensors, and the time delay between the ultrasonic probe and the pressure sensors was corrected using the PWV estimated by the two pressure sensors. However, it is difficult to accurately correct the time delay because the PWV, caused by changes in blood pressure, varies during a heartbeat.

* Corresponding author at: Graduate School of Biomedical Engineering, Tohoku University, Sendai, Miyagi 980-8579, Japan.
E-mail address: arakawa@ecei.tohoku.ac.jp (M. Arakawa).

https://doi.org/10.1016/j.sna.2019.07.011
0924-4247/

We believed that measuring the arterial pressure and change in diameter at the same position could be realized if blood pressure was measured using the piezoelectric element of an ultrasonic probe. However, the main frequency components of blood pressure waveforms exist below 12 Hz [15], which is much lower than the several to 10-MHz frequency range of the ultrasonic probe. Thus, we investigated a method for measuring blood pressure via the piezoelectric effect using the piezoelectric element of an ultrasonic probe [16]. Blood pressure waveforms with a high enough signal-to-noise ratio (S/N) were obtained by integrating the output from the piezoelectric element.

In the present study, we developed an ultrasonic probe for measuring both radial arterial pressure and the change in arterial diameter at the same position simultaneously, which were used to estimate the hysteresis characteristic of the arterial wall. We investigated the reproducibility of the hysteresis characteristic for successive heartbeats. In addition, viscoelastic parameters were estimated on the basis of the Voigt model.

2. Principle

The main frequency components of a blood pressure waveform are below approximately 12 Hz [15], much lower than the bandwidth (usually several to 10 MHz) of the ultrasonic probes. When a piezoelectric element is used to measure blood pressure, the measured waveform is derivation of the blood pressure waveform because the electric charges generated by the piezoelectric effect are extracted as current by the external circuit. Therefore, the blood pressure waveform is obtained by integrating the voltage waveform at the load resistance in the output circuit. For lead zirconate titanate (PZT) ceramics, which belong to the class *6 mm* of the hexagonal crystal system, the force $f(t)$ applied to the direction of spontaneous polarization is expressed as follows [16]:

$$f(t) = \frac{c_{33}^{E}}{Re_{33}} \int_0^t V(\tau)\,d\tau, \tag{1}$$

where c_{33}^{E} and e_{33} are the elastic constant under a constant electric field and the piezoelectric constant, respectively, and $V(\tau)$ is the voltage at the load resistance R. The force $f(t)$ is the product of the area of the piezoelectric element and the pressure applied to it, and the voltage generated increases as the area of the piezoelectric element increases. The force waveform $f(t)$ is obtained by integrating the voltage waveform $V(\tau)$ from $\tau = 0$ to t.

To obtain the blood pressure waveform $\hat{p}(t)$, $f(t)$ in Eq. (1) is calibrated using the systolic blood pressure p_{sys} and the diastolic blood pressure p_{dia}, measured using a conventional manometer, as follows:

$$\hat{p}(t) = \frac{p_{sys} - p_{dia}}{f_{max} - f_{min}} \left\{ f(t) - f_{min} \right\} + p_{dia}\,, \tag{2}$$

where f_{max} and f_{min} are the maximum and minimum values of $f(t)$.

We investigated the voltage output from a piezoelectric element (area = 0.8 mm^2, thickness = 3.2 mm) of the linear probe, the operating frequency of which was 7.5 MHz, where $c_{33}^{E} = 1.28 \times 10^{11}$ N/m^2, $e_{33} = 25.9$ C/m^2, relative permittivity $\varepsilon_{33}^{S}/\varepsilon_0 = 2,021$, and density $\rho = 7,500$ kg/m^3, and the input resistance R of the output circuit was 1 MΩ [16]. The voltage was estimated as 0.03 mV at 5 Hz via a pressure difference of 50 mmHg. Furthermore, we experimentally confirmed that the voltage was on the same order as the theoretical voltage and the integrated waveform $\hat{p}(t)$ resembled the typical waveform measured by a tonometer in the radial artery [16].

In the present study, we developed an ultrasonic probe for measuring both radial arterial pressure and arterial diameter at the same position simultaneously to estimate the hysteresis characteristic of the arterial wall.

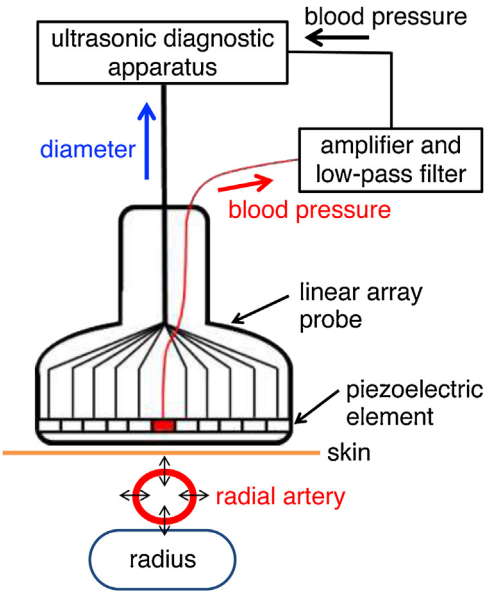

Fig. 1. Schematic view of the experimental setup.

3. Method

The schematic view of the experimental setup is shown in Fig. 1. A commercial linear array probe (Honda Electronics) with a center frequency of 7.5 MHz was prepared. The probe has 192 channels and each piezoelectric element was $0.2 \times 4 \times 3.2$ mm^3. The probe was customized by cutting the connection of the one center piezoelectric element from the transmitting and receiving unit of the ultrasonic diagnostic apparatus. The center piezoelectric element was used to detect the blood pressure and the other 191 channels were used to measure the diameter by ultrasound. The output voltage increases with the area of the piezoelectric element, that is, as the number of elements used for blood pressure measurement increases. Thus, a larger area is preferred to measure only the blood pressure. However, the accuracy of the diameter change could decrease if the number of elements for the diameter-change measurement is decreased by increasing the number of elements for the blood pressure measurement. Therefore, lower number of elements for blood pressure measurement is desirable if the S/N of the blood pressure waveform is sufficient. The customized probe was connected to an ultrasonic diagnostic apparatus (ProSound F75, Hitachi Aloka). The phased-tracking method was used to determine the boundary of the artery to estimate the change in its diameter [17]. In this method, the average velocity of the blood wall during the pulse transmission interval was obtained. The position of the wall was estimated from the velocity. The method is described in detail in Ref. [17]. The diameter was measured at a sampling frequency of 40 MHz and a frame rate of 252 Hz. An electrocardiogram was also measured with three leads by the ultrasonic diagnostic apparatus.

To measure the blood pressure, the output voltage from the center piezoelectric element went through an amplifier with an amplification factor of 100, and a low-pass filter with a cutoff frequency of 30 Hz, and then to the external pulse input port of the ultrasonic diagnostic apparatus. The cutoff frequency of the low-pass filter was determined to suppress the commercial power supply component with a frequency of 50 Hz, and to get through the blood pressure component with a frequency below 12 Hz [15]. Therefore, the diameter and the blood pressure were measured simultaneously. The blood pressure waveform was obtained by

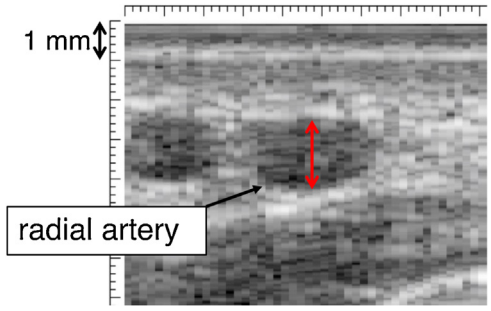

Fig. 2. B-mode image of the left radial artery for subject A.

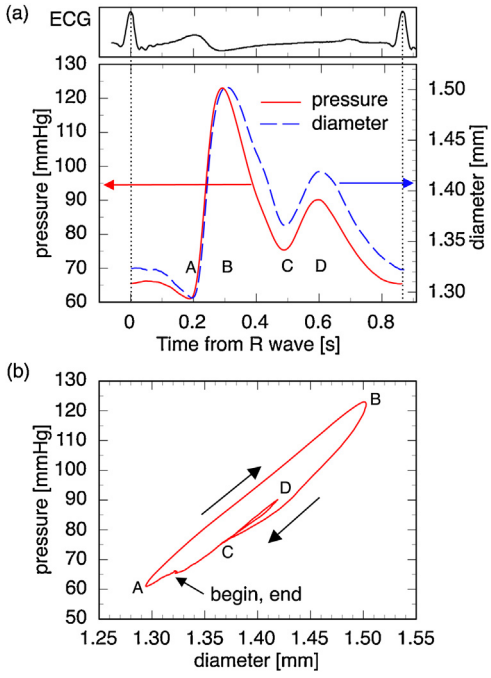

Fig. 3. (a) Waveforms of arterial pressure and diameter for subject A. (b) Relationship between arterial pressure and diameter for subject A.

integrating the measured waveform. To obtain absolute blood pressure values, the voltage measured by the piezoelectric element was calibrated using Eq. (2) with the systolic and diastolic blood pressures measured with a conventional sphygmomanometer.

We used our probe to measure the blood pressure and arterial diameter simultaneously in the left radial artery of two males (subjects A and B) in their twenties. The output voltage from the piezoelectric element strongly depends on the position of the blood vessel. Upon departing from the upper position, the output decreases. The probe enables confirmation of the position of the blood pressure measurement via the B-mode image in the ultrasonic diagnostic apparatus. Therefore, the position of the center element can be easily adjusted to be just above the blood vessel.

4. Results and discussion

Fig. 2 shows the B-mode image of the left radial artery for subject A. Any effect caused by removing the center piezoelectric element was not observed on the B-mode image, which was produced using the data from the other 191 elements.

Fig. 3(a) shows the electrocardiogram, measured blood pressure waveform $\hat{p}(t)$ of Eq. (2), and the change in diameter for subject A. The blood pressure waveform $\hat{p}(t)$ obtained by the single piezoelectric element had a sufficient signal-to-noise ratio. The increase

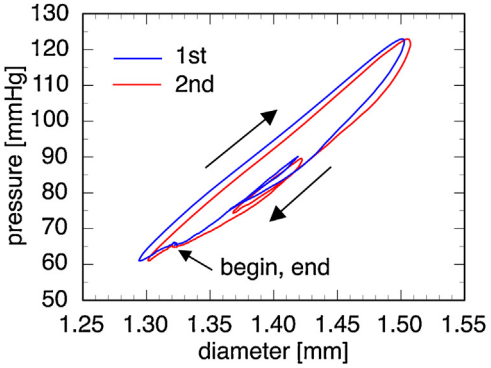

Fig. 4. Relationship between arterial pressure and diameter for two successive heartbeats for subject A.

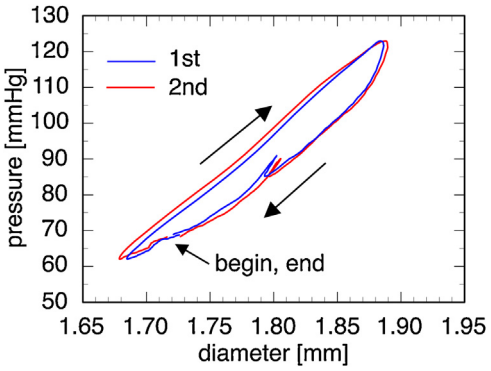

Fig. 5. Relationship between arterial pressure and diameter for two successive heartbeats for subject B.

in both arterial pressure and the change in arterial diameter during systole was almost simultaneous. p_{sys} and p_{dia} were measured as 123 and 61 mmHg, respectively. Both blood pressure and diameter returned to their initial values after a heartbeat. The effect of ultrasound signals with a frequency of 7.5 MHz was not observed for the blood pressure waveform because the main frequency of the blood pressure waveform is much lower than the ultrasound signals and a low-pass filter with cut-off frequency of 30 Hz was used to obtain the blood pressure waveform.

Fig. 3(b) shows the relationship between blood pressure and arterial diameter between the two R-waves on the ECG shown in Fig. 3(a). The times labeled A, B, C, and D are the same in Fig. 3(a) and (b). The diameter expanded linearly with an increase in blood pressure and then gradually returned to its initial size with viscosity as the blood pressure decreased. The results were similar to those obtained using pressure sensors and an ultrasonic probe [14]. Therefore, we were successful in showing the relationship between blood pressure and the change in diameter using only an ultrasonic probe.

Next, we measured arterial pressure and diameter for two successive heartbeats. The waveforms showing the relationship between arterial pressure and diameter for subject A are shown in Fig. 4. The similarity between the two waveforms confirms reproducibility.

Finally, the viscoelastic parameters pressure-strain elastic modulus E_p and pressure-strain viscosity η_p were estimated using the least-squares method based on the Voigt model, which is the most fundamental viscoelastic model of biological tissues [14,18,19]. The estimation method is described in detail in Ref. 14. We found that E_p was 1.43×10^2 and 1.47×10^2 kPa and η_p was 0.65 and 0.62 kPa·s for the first and second heartbeats, respectively. The reproducibil-

ity of results was also confirmed on the basis of the estimated viscoelastic parameters.

To confirm the reproducibility of the measurements, we applied the method to subject B. The relationships between arterial pressure and diameter are shown in Fig. 5. E_p was 1.83×10^2 and 1.97×10^2 kPa while η_p was 1.36 and 0.82 kPa·s for the first and second heartbeats, respectively. Similar hysteresis properties were also obtained.

In the present study, the linear array probe was customized. Using other types of probes, such as a sector probe, is also possible because the blood pressure can be obtained by the piezoelectric effect.

5. Conclusions

In this paper, we presented our newly developed ultrasonic probe that simultaneously measures radial blood pressure and change in arterial diameter. The relationship between blood pressure and change in diameter during a heartbeat was measured and the hysteresis characteristics caused by the viscoelasticity of the blood wall were confirmed. The reproducibility of results using the probe was confirmed from the measured waveforms and the estimated parameters. In a future study, we intend to check the reproducibility using multiple subjects and evaluate vascular endothelial functions by measuring the changes in viscoelasticity caused by an FMD reaction as shown in our previous paper [14].

Acknowledgments

This work was supported in part by JSPS KAKENHI17H02105 and the Murata Science Foundation.

References

[1] E. Wetter, T. Kenner, Grundlagen der Dynamik des Arterienpulses, Springer, Berlin, 1968, p. 379 (in German).
[2] D.A. McDonald, Blood Flow in Arteries, 2nd ed., Edward Arnold, London, 1974, p. 284.
[3] J.I. Weitz, J. Byrne, G.P. Clagett, M.E. Farkouh, J.M. Porter, D.L. Sackett, D.E. Strandness Jr., L.M. Taylor, Diagnosis and treatment of chronic arterial insufficiency of the lower extremities: a critical review, Circulation 94 (1996) 3026–3049, http://dx.doi.org/10.1161/01.CIR.94.11.3026.
[4] R. Ross, Atherosclerosis—an inflammatory disease, N. Engl. J. Med. 340 (1999) 115–126, http://dx.doi.org/10.1056/NEJM199901143400207.
[5] M.C. Corretti, T.J. Anderson, E.J. Benjamin, D. Celermajer, F. Charbonneau, M.A. Creager, J. Deanfield, H. Drexler, M. Gerhard-Herman, D. Herrington, P. Vallance, J. Vita, R. Vogel, Guidelines for the ultrasound assessment of endothelial-dependent flow-mediated vasodilation of the brachial artery, J. Am. Coll. Cardiol. 39 (2002) 257–265, http://dx.doi.org/10.1016/S0735-1097(01)01746-6.
[6] C.D. Black, B. Vickerson, K.K. McCully, Noninvasive assessment of vascular function in the posterior tibial artery of healthy humans, Dyn. Med. 2 (2003) 1, http://dx.doi.org/10.1186/1476-5918-2-1.
[7] Ø. Rognmo, T.H. Bjørnstad, C. Kahrs, A.E. Tjønna, A. Bye, P.M. Haram, T. Stølen, S.A. Slørdahl, U. Wisløff, Endothelial function in highly endurance-trained men: effects of acute exercise, J. Strength Cond. Res. 22 (2008) 535–542, http://dx.doi.org/10.1519/JSC.0b013e31816354b1.
[8] T. Kaneko, H. Hasegawa, H. Kanai, Ultrasonic measurement of change in elasticity due to endothelium dependent relaxation response by accurate detection of artery-wall boundary, Jpn. J. Appl. Phys. 46 (2007) 4881–4888, http://dx.doi.org/10.1143/JJAP.46.4881.
[9] K. Ikeshita, H. Hasegawa, H. Kanai, Ultrasonic measurement of transient change in stress–strain property of radial arterial wall caused by endothelium-dependent vasodilation, Jpn. J. Appl. Phys. 47 (2008) 4165–4169, http://dx.doi.org/10.1143/JJAP.47.4165.
[10] K. Ikeshita, H. Hasegawa, H. Kanai, Flow-mediated change in viscoelastic property of radial arterial wall measured by 22 MHz ultrasound, Jpn. J. Appl. Phys. 48 (2009) 07GJ10, http://dx.doi.org/10.1143/JJAP.48.07GJ10.
[11] K. Ikeshita, H. Hasegawa, H. Kanai, Noninvasive measurement of transient change in viscoelasticity due to flow-mediated dilation using automated detection of arterial wall boundaries, Jpn. J. Appl. Phys. 50 (2011) 07HF08, http://dx.doi.org/10.1143/JJAP.50.07HF08.
[12] K. Ikeshita, H. Hasegawa, H. Kanai, Improvement in accuracy of ultrasonic measurement of transient change in viscoelasticity of radial arterial wall due to flow-mediated dilation by adaptive low-pass filtering, Jpn. J. Appl. Phys. 51 (2012) 07GF14, http://dx.doi.org/10.1143/JJAP.51.07GF14.
[13] M. Sato, H. Hasegawa, H. Kanai, Correction of change in propagation time delay of pulse wave during flow-mediated dilation in ultrasonic measurement of arterial wall viscoelasticity, Jpn. J. Appl. Phys. 53 (2014) 07KF03, http://dx.doi.org/10.7567/JJAP.53.07KF03.
[14] Y. Sakai, H. Taki, H. Kanai, Accurate evaluation of viscoelasticity of radial artery wall during flow-mediated dilation in ultrasound measurement, Jpn. J. Appl. Phys. 55 (2016) 07KF11, http://dx.doi.org/10.7567/JJAP.55.07KF11.
[15] D.W. Holdsworth, C.J.D. Norley, R. Frayne, D.A. Steinman, B.K. Rutt, Characterization of common carotid artery blood-flow waveforms in normal human subjects, Physiol. Meas. 20 (1999) 219–240.
[16] M. Arakawa, K. Kudo, K. Kobayashi, H. Kanai, Blood pressure measurement using piezoelectric effect by an ultrasonic probe, Sens. Actuators A: Phys. 286 (2019) 146–151, http://dx.doi.org/10.1016/j.sna.2018.12.019.
[17] H. Kanai, M. Sato, Y. Koiwa, N. Chubachi, Transcutaneous measurement and spectrum analysis of heart wall vibrations, IEEE Trans. Ultrason. Ferroelectr. Freq. Control 43 (1996) 791–810, http://dx.doi.org/10.1109/58.535480.
[18] J. Alastruey, A.W. Khir, K.S. Matthys, P. Segers, S.J. Sherwin, P.R. Verdonck, K.H. Parker, J. Peiró, Pulse wave propagation in a model human arterial network: assessment of 1-D visco-elastic simulations against *in vitro* measurements, J. Biomech. 44 (2011) 2250–2258, http://dx.doi.org/10.1016/j.jbiomech.2011.05.041.
[19] K. Niki, M. Sugawara, D. Chang, A. Harada, T. Okada, R. Sakai, K. Uchida, R. Tanaka, C.E. Mumford, A new noninvasive measurement system for wave intensity: evaluation of carotid arterial wave intensity and reproducibility, Heart Vess. 17 (2002) 12–21, http://dx.doi.org/10.1007/s003800200037.

Biographies

Mototaka Arakawa received the B.E., M.E., and Ph.D. degrees in electrical engineering from Tohoku University, Sendai, Japan, in 1993, 1995, and 2000, respectively. He is currently an associate professor at the Graduate School of Biomedical Engineering, Tohoku University. His research interests include developments of the ultrasonic transducer and the acoustic microscopy for tissue and cell characterization and the application of the line-focus-beam ultrasonic material characterization system.

Takumi Saito received the B.E. degree in electronic engineering from Tohoku University, Sendai, Japan, in 2018. He is currently studying toward the M.E. degree at Tohoku University. His research interests include the evaluation of vascular endothelial functions using the ultrasonic probe developed in the present paper.

Shohei Mori received the B.E., M.E., and Ph.D. degrees in Mechanical and Control Engineering from Tokyo Institute of Technology, in 2013, 2015, and 2017, respectively. He is a currently an assistant professor at the Graduate School of Engineering, Tohoku University. His research interests include the ultrasonic tissue characterization of liver disease and the measurement of arterial wall movement.

Shigeo Ohba graduated from Shiroishi technical high school, in 1969, and he received the Ph.D. degree in Electronic Engineering from Tohoku University, in 2002. From 1969, he has been with the Tohoku University, Sendai, Japan, where he is currently a technical expert in the experimental laboratory for students on Department of Electrical, Information and Physics Engineering, Tohoku University. His research interest includes biomedical electrodes and instrumentation for the physiological signal measurement.

Kazuto Kobayashi received B.E. degree in electrical engineering from Shibaura Institute of Technology, in 1976. He received Ph.D. degrees in 2011 from Tohoku University. He is currently a director of Department of Research and Development at Honda Electronics Co. Ltd. in Toyohashi, Japan. His research activities and interests include medical ultrasound imaging, signal processing and high frequency ultrasound transducers.

Hiroshi Kanai received a B.E. degree from Tohoku University, Sendai, Japan, in 1981, and M.E. and the Ph. D. degrees, also from Tohoku University, in 1983 and in 1986, both in electrical engineering. He is currently a professor in the Department of Electronic Engineering, Graduate School of Engineering, Tohoku University. His present interests are in transcutaneous measurement of the heart wall vibrations and myocardial response to propagation of electrical potential and cross-sectional imaging of elasticity around atherosclerotic plaque with transcutaneous ultrasound for tissue characterization of the arterial wall.