Ultrasonic tissue characterization of atherosclerosis by a speed-of-sound microscanning system

doi: 10.1109/TUFFC.2007.427

Ultrasonic Tissue Characterization of Atherosclerosis by a Speed-of-Sound Microscanning System

Yoshifumi Saijo, Esmeraldo Santos Filho, Hidehiko Sasaki, Tomoyuki Yambe, Motonao Tanaka, Naohiro Hozumi, *Member, IEEE*, Kazuto Kobayashi, and Nagaya Okada

***Abstract*—We have been developing a scanning acoustic microscope (SAM) system for medicine and biology featuring quantitative measurement of ultrasonic parameters of soft tissues. In the present study, we propose a new concept sound speed microscopy that can measure the thickness and speed of sound in the tissue using fast Fourier transform of a single pulsed wave instead of burst waves used in conventional SAM systems. Two coronary arteries were frozen and sectioned approximately 10 μm in thickness. They were mounted on glass slides without cover slips. The scanning time of a frame with 300 $\times$ 300 pixels was 90 s and two-dimensional distribution of speed of sound was obtained. The speed of sound was 1680 $\pm$ 30 m/s in the thickened intima with collagen fiber, 1520 $\pm$ 8 m/s in the lipid deposition underlying the fibrous cap, and 1810 $\pm$ 25 m/s in a calcified lesion in the intima. These basic measurements will help in the understanding of echo intensity and pattern in intravascular ultrasound images.**

I. Introduction

We have been developing a scanning acoustic microscopy (SAM) system for biomedical use since the 1980s [1]–[10]. We have been investigating the acoustic properties of various organs and disease states by using this SAM system. In the areas of medicine and biology, SAM has three main objectives. First, SAM is useful for intraoperative pathological examination because it does not require special staining. Second, SAM provides basic data for understanding lower-frequency medical ultrasound images such as in echocardiography or intravascular ultrasound. Third, SAM can be used to assess the biomechanics of tissues and cells at a microscopic level. The originality of the previous SAM system of Tohoku University lies in providing quantitative values of attenuation and speed of sound in thin slices of soft tissue. Although the system may still be in use, it was constructed using precise handcrafted technologies and analog signal acquisition circuits. In addition, the previous system needed repeated acquisitions for calculation of quantitative values because it used burst waves of different frequencies.

Recently, we proposed a prototype of a speed-of-sound microscanning system using a single pulsed wave instead of the burst waves used in conventional SAM systems [11]. In the present study, we constructed a compact speed-of-sound microscanning system and evaluated the system performance by measuring normal and atherosclerotic coronary arteries.

Manuscript received April 30, 2006; accepted October 18, 2006. This study was supported by Grants-in-Aid for Scientific Research (Scientific Research (B) 15300178, Scientific Research (B) 15360217) from the Japan Society for the Promotion of Science and Health and Labor Sciences Research Grants from the Ministry of Health, Labor and Welfare for the Research on Advanced Medical Technology (H17-Nano-001).

Y. Saijo, E. D. Santos Filho, H. Sasaki, T. Yambe, and M. Tanaka are with the Department of Medical Engineering and Cardiology, Institute of Development, Aging and Cancer, Tohoku University, Aobaku, Sendai 980-8575, Japan (e-mail: saijo@idac.tohoku.ac.jp).

N. Hozumi is with the Department of Electrical and Electronic Engineering, Aichi Institute of Technology, Yakusa, Toyota, 470-0392, Japan.

K. Kobayashi and N. Okada are with the Research and Development Headquarters, Honda Electronics Co. Ltd., Oiwa-cho, Toyohashi, 441-3193, Japan.

Digital Object Identifier 10.1109/TUFFC.2007.427

II. Methods

A. Principle of Acoustic Microscopy

In order to realize high-resolution imaging, the speed-of-sound microscanning system was designed to transmit and receive wide-frequency ultrasound up to 500 MHz. In our previous SAM system with burst waves, the central frequency was changed in 10-MHz steps between 100 and 200 MHz to obtain frequency-dependent characteristics of the amplitude and phase of the received signal. The spectrum for calculation of the thickness and sound speed of the material was approximated with the frequency-dependent characteristics. Fig. 1 shows an example of the frequency-dependent characteristics of the amplitude (a) and the phase (b).

Our previous SAM system was able to visualize quantitative acoustic properties of stable materials but it was not suitable for living biological materials because it required several measurements with different frequencies on the same position. Besides, the frequency range was not suitable for visualization of living cells because the spatial resolution was approximately 10 microns.

In the present method, a pulsed ultrasound with broadband frequency is captured in a time domain and the frequency domain analysis is performed by software. The data acquisition of each sampling point takes longer than with the conventional SAM, but only a single measurement on the observation plane is required in the proposed method.

First, considering the frequency characteristics of the high-frequency ultrasound transducer, the appropriate

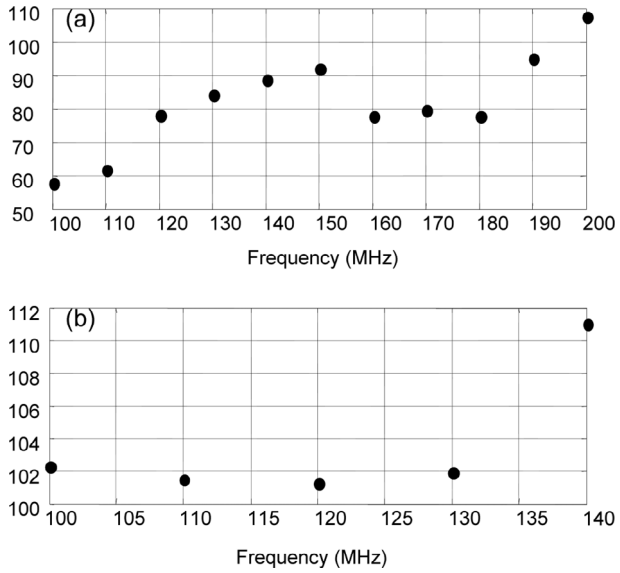

Fig. 1. Frequency-dependent characteristics of amplitude (a) and phase (b) obtained with our previous SAM system.

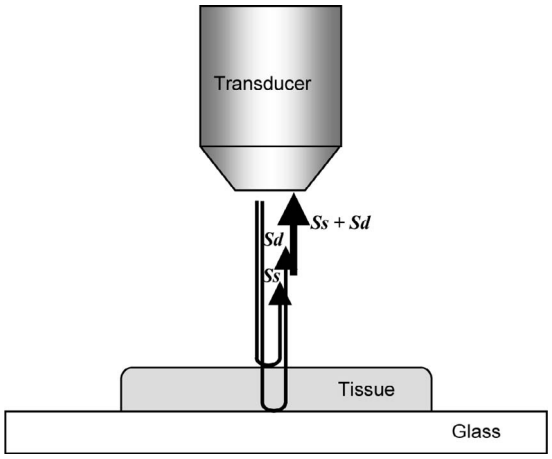

Fig. 2. Principle of quantitative measurement of acoustic properties by SAM.

pulse waveform and measurement system was designed. In order to analyze the signal in a frequency domain, the pulse width should be as short as possible and the pulse waveform should not contain many reverbs. Second, for realization of a compact system, integration of the scanner and signal acquisition was considered to design the whole acoustic microscope system.

Fig. 2 shows the principle of a scanning acoustic microscope. The soft biological material is attached to a substrate. Normal glass slides or high-molecular polymer materials used in dishes for cell culture can be used as the substrates. The biological material is sectioned at an appropriate thickness to separate the reflections from the tissue surface and from the interface between tissue and substrate. Single-layered cultured cells are also appropriate objects for SAM. The ultrasound is transmitted through a coupling medium and focused on the surface of the substrate. Transmitted ultrasound is reflected at both the surface of the biological material (S_s) and the interface between the biological material and the substrate (S_d). The transducer receives the sum of these two reflections. The interference of these two reflections is determined by the acoustic properties of the biological material. The determinants of the interference in the frequency (x-axis) are thickness and sound speed of the sample. The determinant of the interference of the intensity (y-axis) is the amplitude of the surface reflection and the attenuation of ultrasound propagating through the tissue. The concept of quantitative measurement of sound speed is based on the analysis of the interference frequency-dependent characteristics. In our previous SAM system, the frequency-dependent characteristics were obtained by serial measurements. The proposed sound speed SAM obtains the frequency-dependent characteristics by fast Fourier transform of a single broadband pulse.

B. Design of the Speed of Sound Microscanning System

An electric impulse was generated by a high-speed switching semiconductor. The start of the electric pulse was within 400 ps, the pulse width was 2 ns, and the pulse voltage was 40 V. Fig. 3(a) is the waveform of the electric pulse and Fig. 3(b) is the spectrum of the pulse. The spectrum extends to 500 MHz. The electric pulse was input to a transducer with a sapphire rod as an acoustic lens and with a central frequency of 300 MHz. Fig. 3(c) is the reflected wave form from the surface of the substrate. The ultrasonic pulse was changed from the electric pulse due to the frequency-dependent characteristics of the transducer, and it contained some oscillation components. The ultrasound spectrum is broad enough to cover 100–500 MHz [Fig. 3(d)].

The original electric pulse was almost an impulse, but the transmitted ultrasound contained oscillation components because of the thickness of the piezoelectric material of the transducer. The reflected wave also contained two components of reflections from the surface of the tissue and the interface between the tissue and the substrate. The waveform from the tissue and the glass was standardized by a reflection from the glass.

Fig. 3(e) shows the response to a singlet after this compensation. The reflections from the surface (front) and the interface (rear) are clearly seen in the waveform. These two peaks were separated by using proper window functions. The window function was originally a Gaussian function with 1 as its peak value, but the peak was flattened by splitting it at the peak point and inserting 1 with an appropriate length. Intensity and phase spectra of these separated waveforms were then calculated by Fourier transform.

Fig. 4 shows a block diagram of the speed-of-sound microscanning system for biological tissue characterization. A single ultrasound pulse with a pulse width of 2 ns was emitted and received by the same transducer above the specimen. The aperture diameter of the transducer was

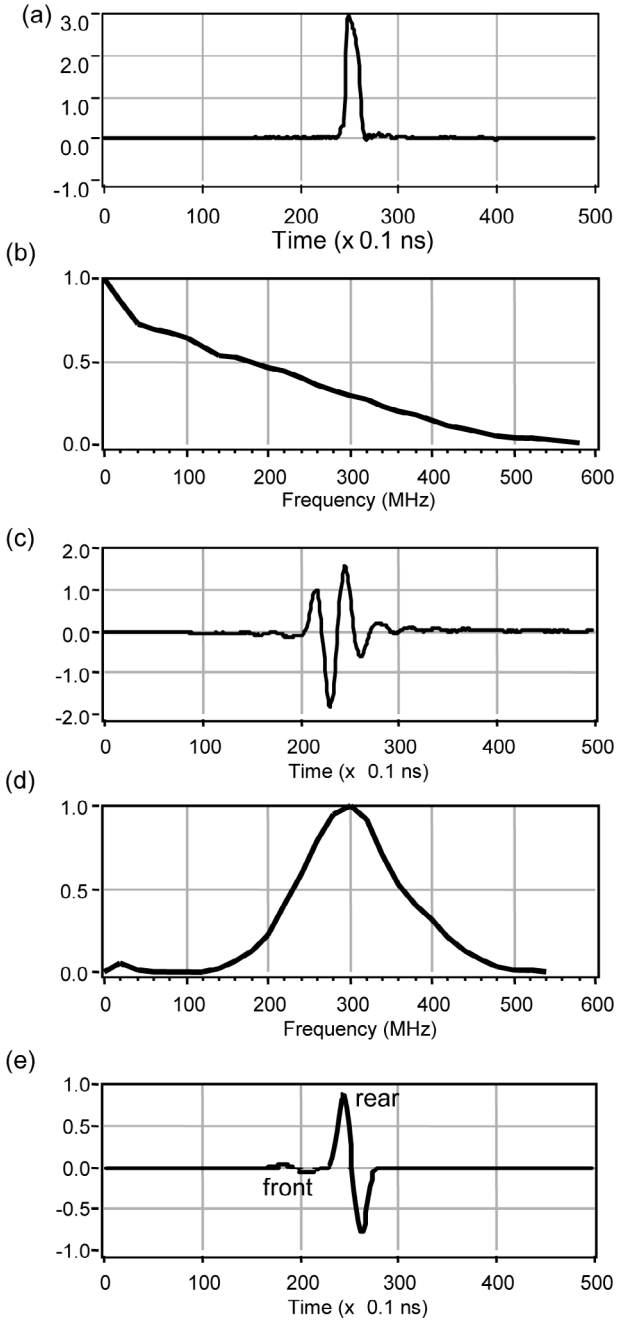

Fig. 3. (a) Waveform of the electric pulse; (b) the spectrum of the pulse; (c) the reflected wave form from the surface of the substrate; (d) ultrasound spectrum of the transducer; and (e) response to a singlet after standardization by a reflection from the glass. The reflections from the tissue surface (front) and the interface between the tissue and glass (rear) were separated in (e). The y-axis of each figure is normalized intensity (arbitrary units).

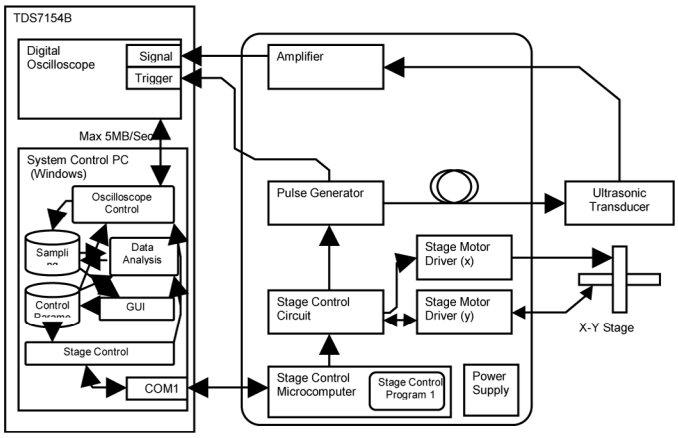

Fig. 4. Block diagram of sound speed microscopy.

1.2 mm, and the focal length was 1.5 mm. The central frequency was 300 MHz, the bandwidth was 100–500 MHz, and the pulse repetition rate was 10 kHz. The diameter of the focal spot was estimated to be 6.5 μm at 500 MHz by taking into account the focal distance and the sectional area of the transducer. Saline was used as the coupling medium between the transducer and the specimen. The reflections from the tissue surface and those from the interface between the tissue and glass were received by the transducer and were introduced into a Windows-based PC (Pentium D, 3.0 GHz, 2GB RAM, 250GB HDD) via a digital oscilloscope (Tektronix TDS7154B, Beaverton, OR). The frequency range was 1 GHz, and the sampling rate was 20 GS/s. Four consecutive values of the time taken for a pulse response were averaged in order to reduce random noise.

The transducer was mounted on an X-Y stage with a microcomputer board that was driven by the PC through an RS-232C interface. Both the X-scan and the Y-scan were driven by linear servo motors and the position was detected by an encoder. The scan was controlled to reduce the effects of acceleration at the start and deceleration at the end of the X-scan. Finally, two-dimensional distributions of ultrasonic intensity, speed of sound, attenuation coefficient, and thickness of a specimen measuring 2.4×2.4 mm were visualized using 300×300 pixels. The total scanning time was 90 s.

C. Signal Analysis

Denoting the standardized phase of the reflection wave at the tissue surface as ϕ_{front}, and the standardized phase at the interference between the tissue and the substrate as ϕ_{rear},

$$2\pi f \times \frac{2d}{c_o} = \phi_{\text{front}}, \tag{1}$$

$$2\pi f \times 2d\left(\frac{1}{c_o} - \frac{1}{c}\right) = \phi_{\text{rear}}, \tag{2}$$

where d is the tissue thickness, c_o is the sound speed in coupling medium, and c is the sound speed in the tissue.

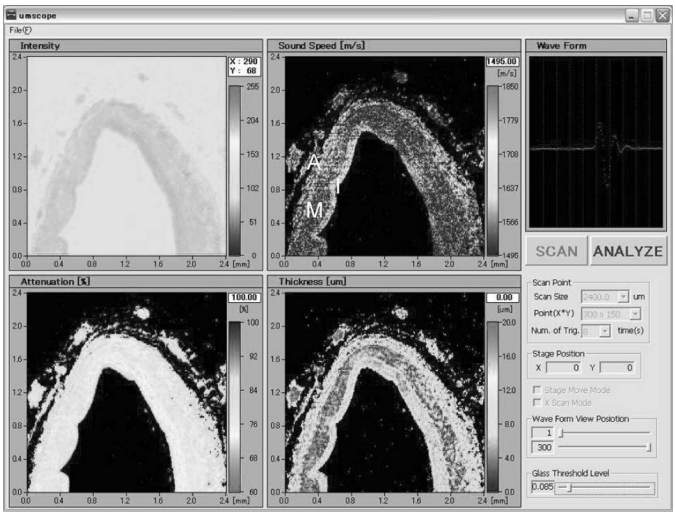

Fig. 5. PC window of speed of sound microscopy showing a normal coronary artery. Upper left: amplitude image; upper right: speed of sound image; lower left: attenuation image; and lower right: thickness. I: Intima; M: media; A: adventitia.

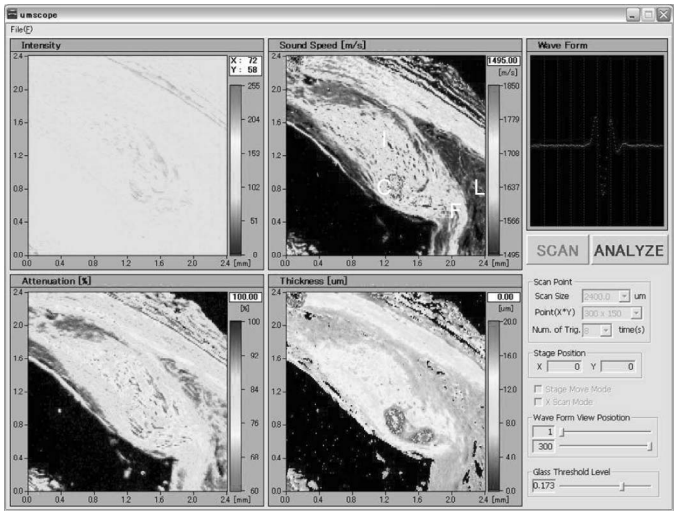

Fig. 6. PC window of speed-of-sound microscopy showing an atherosclerotic coronary artery. Upper left: amplitude image; upper right: speed of sound image; lower left: attenuation image; and lower right: thickness. I: intima; C: calcified lesion; F: fibrous cap; L: lipid.

Thickness is obtained as

$$d = \frac{c_o}{4\pi f}\phi_{\text{front}}. \tag{3}$$

Finally, sound speed is calculated as

$$c = \left(\frac{1}{c_o} - \frac{\phi_{\text{rear}}}{4\pi f d}\right)^{-1}. \tag{4}$$

After determination of the thickness, attenuation of ultrasound was then calculated by dividing the amplitude by the thickness and the frequency.

D. Tissue Preparation

Normal and atherosclerotic human coronary arteries were obtained from autopsy. The specimens were rinsed in phosphate buffer saline (PBS) and immersed in 10% to 30% sucrose solutions. Then the specimens were embedded in optimal cutting temperature (OCT) compound and rapidly frozen by liquid nitrogen at $-20°$C. The specimens were sliced at approximately 10 microns by a cryostat and mounted on silane-coated glass slides.

III. Results

Fig. 5 shows a PC window of the speed-of-sound microscanning system. The upper left is an intensity image, the upper right is a sound speed image, the lower left is an attenuation image, and the lower right is the thickness distribution of the normal coronary artery. In the present case, the attenuation image of the system means the intensity divided by the thickness. It is not quantitatively calculated as the attenuation coefficient. The intima was thin, and the sound speed was 1600 ± 20 m/s in the intima (I), 1560 ± 18 m/s in the medium (M), and 1590 ± 22 m/s in the adventitia (A). The thickness was 7.2 ± 0.1 μm in the intima, 4.8 ± 0.2 μm in the medium and 7.2 ± 0.1 μm in the adventitia. In qualitative analysis, the attenuation of the medium was slightly lower than that of either the intima or the adventitia.

Fig. 6 is an atherosclerotic coronary artery. The sound speed was 1680 ± 30 m/s in the thickened intima (I) with collagen fiber, 1520 ± 8 m/s in lipid deposition (L) underlying the fibrous cap (F), and 1810 ± 25 m/s in the calcified lesion (C) in the intima. The thickness was 11.8 ± 0.1 μm in the intima, 11.6 ± 0.2 μm in the medium and 14.8 ± 0.1 μm in the lipid deposition. In qualitative analysis, the attenuation of the calcified lesion was high and the attenuation in lipid deposition was low.

IV. Discussion

In the present study, speed of sound in the excised human coronary arteries was measured with the specially developed microscanning system. The results showed that the speed of sound in the intima and the adventitia, mainly consisting of collagen fiber, had higher values than that of the medium, mainly consisting of vascular smooth muscle. The difference of acoustic properties may lead to the classical three-layered appearance of a normal coronary artery in clinical intravascular ultrasound (IVUS) imaging. The findings indicate that the echo intensity is determined by the difference of acoustic impedance between neighboring layers because the specific acoustic impedance is the product of the speed of sound and the density. The distribution and the structure of materials with different acoustic properties may also contribute to the echo pattern in IVUS imaging.

The thick fibrous cap, consisting of collagen fiber in an atherosclerotic plaque, showed higher values of speed of

sound and attenuation than did normal medium. Generally, absorption and scattering are the two main factors of attenuation of ultrasound. Thus, the high scattering within the thickened intima or calcified lesion may lead to the high intensity echo in the clinical IVUS imaging. The region of lipid deposition showed low values of speed of sound. These values explain the low echo in the same manner as for renal cysts containing water-like fluid. Besides the absolute low values, the homogeneity of acoustic properties within the lipid pool may lead to the low scattering and consequently a lipid pool shows a low-intensity echo.

As ultrasound has the character of an elastic wave, ultrasound itself is closely related to the mechanical properties of tissues. The sound speed in a solid medium may be taken as

$$c = \sqrt{\frac{E(1-\sigma)}{\rho(1+\sigma)(1-2\sigma)}} \cdots , \tag{5}$$

where c is the speed of sound, E is the Young's elastic modulus, ρ is the density, and σ is the Poisson's ratio. The Poisson's ratio in biological soft materials is assumed to be nearly 0.5 and the density of these vary 3% [4]. Although these simple assumptions are not to be applied precisely, the information on the relative two-dimensional elasticity distribution can be assessed by sound speed image. A high value of sound speed means high elasticity of collagen which is the main component of the intimal thickening. Lipid is the main component of the lucent echogeneicity plaque, and the elasticity is low. The present study proved that the tissue component in the "hard plaque" was really hard and the component of "soft plaque" was really soft. Also, the intima mainly consisting of fibrotic tissues was harder than the normal intima-medium complex. The difference in the elasticity may explain why intimal tear often occurred at the junction of the thinnest plaque and adjacent normal arterial wall [12], [13]. Acoustic microscopy imaging, especially the sound speed image, is the interpretation of elasticity mapping, and it may also help in the understanding of the "elastography" [14] imaging of atherosclerotic plaques from a mechanical point of view.

There have been some time-resolved acoustic microscope systems [15], [16]. The most important feature of our sound speed microscope is that the system calculates the speed of sound and the thickness by frequency-domain analysis of the interference between the reflections from the tissue surface and from the interface between the tissue and glass. However, the error of the sound speed value is 15 m/s by the algorithm [17]. Besides, the system is not able to measure the speed of sound when the surface reflection is weak or the thickness is thinner than 3 μm because the two reflections cannot be separated.

V. Conclusions

An acoustic microscope system that can measure the sound speed of thin slices of biological material was developed. It is a unique acoustic microscope because it uses a single pulse and the Fourier transform to calculate the sound speed and the thickness at all measuring points. Although the data acquisition time of a single frame was greater than that in conventional SAM, the total time required for calculation was significantly shorter. The acoustic microscope system can be applied to intraoperative pathological examination, basic data for understanding lower-frequency medical ultrasound images, and assessment of biomechanics of tissues and cells at a microscopic level.

References

[1] M. Tanaka, H. Okawai, N. Chubachi, J. Kushibiki, and T. Sannomiya, "Propagation properties of ultrasound in acoustic microscopy through a double-layered specimen consisting of thin biological tissue and its holder," *Jpn. J. Appl. Phys.*, vol. 23, pp. 197–199, 1984.

[2] Y. Saijo, M. Tanaka, H. Okawai, and F. Dunn, "The ultrasonic properties of gastric cancer tissues obtained with a scanning acoustic microscope system," *Ultrasound Med. Biol.*, vol. 17, pp. 709–714, 1991.

[3] H. Sasaki, M. Tanaka, Y. Saijo, H. Okawai, Y. Terasawa, S. Nitta, and K. Suzuki, "Ultrasonic tissue characterization of renal cell carcinoma tissue," *Nephron*, vol. 74, pp. 125–130, 1996.

[4] Y. Saijo, M. Tanaka, H. Okawai, H. Sasaki, S. Nitta, and F. Dunn, "Ultrasonic tissue characterization of infarcted myocardium by scanning acoustic microscopy," *Ultrasound Med. Biol.*, vol. 23, pp. 77–85, 1997.

[5] Y. Saijo, H. Sasaki, H. Okawai, S. Nitta, and M. Tanaka, "Acoustic properties of atherosclerosis of human aorta obtained with high-frequency ultrasound," *Ultrasound Med. Biol.*, vol. 24, pp. 1061–1064, 1998.

[6] Y. Saijo, H. Sasaki, M. Sato, S. Nitta, and M. Tanaka, "Visualization of human umbilical vein endothelial cells by acoustic microscopy," *Ultrasonics*, vol. 38, pp. 396–399, 2000.

[7] Y. Saijo, T. Ohashi, H. Sasaki, M. Sato, C. S. Jorgensen, and S. Nitta, "Application of scanning acoustic microscopy for assessing stress distribution in atherosclerotic plaque," *Ann. Biomed. Eng.*, vol. 29, pp. 1048–1053, 2001.

[8] H. Sasaki, Y. Saijo, M. Tanaka, and S. Nitta, "Influence of tissue preparation on the acoustic properties of tissue sections at high frequencies," *Ultrasound Med. Biol.*, vol. 29, pp. 1367–1372, 2003.

[9] Y. Saijo, T. Miyakawa, H. Sasaki, M. Tanaka, and S. Nitta, "Acoustic properties of aortic aneurysm obtained with scanning acoustic microscopy," *Ultrasonics*, vol. 42, pp. 695–698, 2004.

[10] H. Sano, Y. Saijo, and S. Kokubun, "Material properties of the supraspinatus tendon at its insertion—A measurement with the scanning acoustic microscopy," *J. Musculoskeletal Res.*, vol. 8, pp. 29–34, 2004.

[11] N. Hozumi, R. Yamashita, C. K. Lee, M. Nagao, K. Kobayashi, Y. Saijo, M. Tanaka, N. Tanaka, and S. Ohtsuki, "Time-frequency analysis for pulse driven ultrasonic microscopy for biological tissue characterization," *Ultrasonics*, vol. 42, pp. 717–722, 2004.

[12] R. T. Lee and R. D. Kamm, "Vascular mechanics for the cardiologist," *J. Amer. Coll. Cardiol.*, vol. 23, pp. 1289–1295, 1994.

[13] A. Maehara, G. S. Mintz, A. B. Bui, M. T. Castagna, O. R. Walter, C. Pappas, E. E. Pinnow, A. D. Pichard, L. F. Satler, R. Waksman, W. O. Suddath, J. R. Laird , Jr., K. M. Kent, and N. J. Weissman, "Incidence, morphology, angiographic findings, and outcomes of intramural hematomas after percutaneous coronary interventions: An intravascular ultrasound study," *Circulation*, vol. 105, pp. 2037–2042, 2002.

[14] C. L. de Korte, G. Pasterkamp, A. F. van der Steen, H. A. Woutman, and N. Bom, "Characterization of plaque components with intravascular ultrasound elastography in human femoral and coronary arteries in vitro," *Circulation*, vol. 102, pp. 617–623, 2002.

[15] C. M. Daft and G. A. Briggs, "The elastic microstructure of various tissues," *J. Acoust. Soc. Amer.*, vol. 85, pp. 416–422, 1989.
[16] A. F. van der Steen, M. H. Cuypers, J. M. Thijssen, and P. C. de Wilde, "Influence of histochemical preparation on acoustic parameters of liver tissue: A 5-MHz study," *Ultrasound Med. Biol.*, vol. 17, pp. 879–891, 1991.
[17] N. Hozumi, "Development of sound speed acoustic microscopy for biological nano-imaging by picosecond evoked ultrasonic pulse," Research Accomplishment Report of Grants-in-aid for Scientific Research, 2006. (in Japanese)

Yoshifumi Saijo was born in Yokohama, Japan, on July 21, 1962. He received the M.D. and the Ph.D. degrees in 1988 and 1993, respectively, from Tohoku University.

He is currently an associate professor in the Department of Medical Engineering and Cardiology at the Institute of Development, Aging and Cancer, Tohoku University, and the Department of Cardiovascular Surgery, Tohoku University Hospital. His main research interests are assessment of biomechanics of cells and tissues by high-frequency ultrasound and clinical ultrasonic evaluation of cardiovascular system with intravascular ultrasound and transesophageal echocardiography. He received an award in 1997 for his outstanding research paper in *Ultrasound in Medicine and Biology*, the official journal of the World Federation of Ultrasound in Medicine and Biology. He is a member of the Japan Society of Ultrasonics in Medicine, the Japanese Society of Echocardiography, and the Japan Circulation Society.

Esmeraldo dos Santos Filho was born in 1971 in Sao Luis - MA, Brazil. He earned his bachelor and master degrees at the Federal University of Maranhao, in Brazil, in the years 1998 and 2000, respectively. In 2005, he earned his Ph.D. degree at Tohoku University in Japan.

During the academic year of 2001, he worked as a lecturer on digital systems at the Department of Electrical Engineering of the Federal University of Maranhao. Currently, he is a postdoctoral fellow of the Japan Association for Advancement of Medical Equipment at the Institute of Development, Aging, and Cancer, Tohoku University. His fields of interest are applications of artificial intelligence in biomedical image and signal processing. He is a member of the IEEE Signal Processing Society.

Hidehiko Sasaki received his M.D. degree from Yamagata University in 1990 and his Ph.D. degree from Tohoku University in 1996. He is currently Director of the Department of Cardiology at Miyagi Cardiovascular and Respiratory Center. His main research interest is acoustic microscopy evaluation of renal and cardiovascular diseases. He is a member of the Japan Society of Ultrasonics in Medicine and the Japanese Society of Interventional Cardiology.

Tomoyuki Yambe was born in May 7, 1959 in Sendai, Japan. He received the M.D. and the Ph.D. degrees in 1985 and 1989, respectively, from Tohoku University.

He is currently a professor in the Department of Medical Engineering and Cardiology at the Institute of Development, Aging and Cancer, Tohoku University. His main research interest includes development of artificial organs. He is a member of the Japanese Society for Artificial Organs.

Motonao Tanaka was born in Tokyo, Japan, on January 1, 1932. He received the M.D. and the Ph.D. degrees in 1958 and 1962, respectively, from Tohoku University. He was a professor in the Department of Medical Engineering and Cardiology at the Institute of Development, Aging and Cancer, Tohoku University from 1984 to 1996. He is currently Director of the Japan Anti-tuberculosis Association of Miyagi Prefecture. He invented one of the world's first B-mode echocardiographs in the early 60s. Since then he has been contributing to the development of medical ultrasound. He started developing acoustic microscopy for medicine and biology in 1985 and his current interest is "echodynamography" which enables visualization of stream lines and dynamic pressure distribution in heart chambers. He is a member of the Japan Society of Ultrasonics in Medicine, the Japanese Society of Echocardiography, and the Japan Circulation Society.

Naohiro Hozumi (M'94) was born in Kyoto, Japan, on April 2, 1957. He received his B.S., M.S., and Ph.D. degrees in 1981, 1983, and 1990, respectively, from Waseda University. He was employed at the Central Research Institute of Electric Power Industry (CRIEPI) from 1983 to 1999. He was an associate professor at Toyohashi University of Technology from 1999 to 2006. Since 2006, he has been a professor at Aichi Institute of Technology.

He has been engaged in research on insulating materials and diagnosis for high-voltage equipment, acoustic measurement for biological and medical applications, etc. He received awards in 1990 and 1999 from the IEE of Japan for his outstanding research papers. He is a member of IEEE, IEE of Japan, and the Acoustic Society of Japan.

Kazuto Kobayashi was born in Aichi, Japan, on June 8, 1952. He received his B.S. degree in electrical engineering from Shibaura Institute of Technology, Tokyo, Japan, in 1976.

He is currently Director of the Department of Research and Development at Honda Electronics Co. Ltd., Toyohashi, Japan. His research activities and interests include medical ultrasound imaging, signal processing, and high-frequency ultrasound transducers.

Nagaya Okada was born in Aichi, Japan, on January 27, 1964. He received the B.S. degree in electrical engineering from Shizuoka University, Shizuoka, Japan, in 1987, and the M.S. and Ph.D. degrees in electrical engineering from Shizuoka University, Shizuoka, Japan, in 1990 and 1993, respectively.

He is currently a manager of the Department of Research and Development at Honda Electronics Co. Ltd., Toyohashi, Japan. His research activities and interests include digital signal processing, ultrasound imaging and high-frequency ultrasound transducers.