Stiffness Estimation from Arterial Wall Vibration and its Application:
A new earphone for examining arteriosclerosis between music and next music

Fumio Nogata
Emeritus professor
Gifu University
Gifu, Japan
Email: nogata [AT] gifu-u.ac.jp

Yasunai Yokota
Professor, Faculty of Engineering
Gifu University
Gifu, Japan

Yoko Kawamura
Faculty of Engineering
Gifu University
Gifu, Japan

William R. Walsh
Professor
Prince of Wales Hospital, UNSW
Australia, Kensington

Taro Goto
Wisteria Y.K. Co. LTD..
Kiyosu Aichi Japan

Kenji Kagechika
Professor
Department of Rehabilitation medicine
Kanazawa Medical University
Kanazawa, Japan

Abstract—**The purpose of this report is establishment of technique and new device that lead to health guidance early to measure the progress of arteriosclerosis from childhood. We proposed a new measurement method for estimating sclerosis from the bulge vibration of arterial wall due to the heartbeat as like taking a heart rate on the body surface by fingertip. Basic concept of the technique is measurement of the natural frequency of artery. The development of a trial device for sensing the natural frequency and stiffness estimation from arterial wall's free vibration, and its application for the development of a new earphone type device to measure between music and the next music were described. By finding early lesion of arteriosclerosis on the basis of the long-term examination data with health guidance from a childhood, a scheme was also proposed to promote that the production age is 80s with health longevity up to 100s.**

Keywords- arterial stiffness; arteriosclerosis; early lesion; ultrasonic image; natural frequency; pulse wave.

I. INTRODUCTION

The latest report indicated that cardiac and cerebrovascular diseases are a major cause of one-third of Japanese mortality in 2015 [1]. Cardiac disease such as myocardial infraction and cerebrovascular diseases are directly related to the arteriosclerosis [2, 3]. It is also known that the process of atherosclerosis can begin early in childhood but its progression is slow, and a disease of the arterial wall of which the particularity is to give clinical symptoms only when advanced. There are some diagnostic tests depending on the results of the physical examination to find signs and symptoms of arteriosclerosis and atherosclerosis such as electrocardiogram (ECG), ankle-brachial index, Doppler ultrasound, imaging tests using ultrasound, X-ray computer tomography (CT), magnetic resonance angiography (MRA) and so on [4].

On the other hand, recent diversified diet, lack of exercise, obesity, and smoking can cause the risk factors for these diseases, as the results individual difference and the progression at early age of the disease have been observed in clinical data [2, 5, 6, and 7]. The study of cardiovascular risk in Young Finns were performed in detail on socioeconomic status in young adults is associated with cardiovascular risk factor levels and carotid intima-media thickness (IMT), which showed higher cumulative risk score in childhood was expected to be associated with higher IMT and its progression [6,7,8]. Also in Korea, it was reported on atherosclerotic cardiovascular disease beginning in childhood and proposed about risk-stratification and treatment algorithm [9]. From the view point of mechanical properties, the studies on examinations of arteriosclerosis and atherosclerosis are of arterial strengths [5, 10, 11, 12, 13] and cross-sectional elasticity distribution [14], aortic compliance [15], common carotid artery [5, 16], abdominal aortic [17], pulmonary artery elastic modulus using ultrasound [18]. Therefore, it is worldwide problem and urgent task that is indispensably required to detect arteriosclerosis by early diagnosis method to prevent such diseases beforehand, e.g., a technique available regular screening with non-invasive, easy handling, and inexpensive device.

The purpose of this report is the establishment of technique and new device that lead to health guidance early to measure the progress of arteriosclerosis from childhood. We proposed a new measurement method for estimating sclerosis from the bulge vibration of arterial wall due to the heartbeat, like taking our heart rate at the body surface by fingertip. Basic concept of the technique is measurement of natural frequency of artery: All structure has the natural frequency which depends only on mass and stiffness of the system that is deformation resistance in response to an applied force. Therefore, stiffness can be measured from the natural frequency of bulge vibration generated by variation of blood pressure. The developments of a trial device for sensing vibration and stiffness estimation from arterial wall, and as its application to a new earphone-type devise to examine arteriosclerosis between music and next music were presented.

II. EXPERIMENTAL PROCESURES

Slight bulge vibration of arterial wall caused by the heartbeat propagates toward peripheral artery, and then the vibration attenuates while free vibration. If it is considered that free vibration of a spring-mass system with one degree of freedom, the natural frequency is dependent on stiffness and mass. Therefore, it is possible to estimate stiffness of arterial wall by analysis of the free vibration system. The prototype measurement device was made for analyzing the arterial wall vibration.

The device consists of a vibration sensor (piezoelectric transducer) from the skin surface, an operational amplifier (S/N=10~28dB), and a frequency analysis tool (high-pass filter=2.8Hz and low-pass filter=500Hz). To examine validation of the device, natural frequency analysis and stiffness estimation were conducted by the use of tuning fork and some man-made pipes.

A. Frequency analysis using tuning fork

Figure 1 shows the results of natural frequency (fn) using the prototype device for two different tuning forks, 128 and 440Hz.

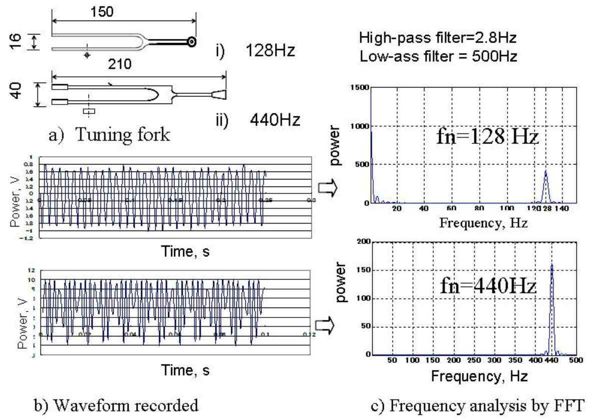


Figure 1. Free vibration waveforms and its natural frequency (fn) of two kinds of tuning forks analyzed using the prototype device.

The result shows that each frequency of both tuning forks was obtained with the correct value. This means that the device and frequency analysis software are working properly.

B. Frequency analysis and stiffness estimation using some pipes

The natural frequency of a horizontal cantilever-fixed pipe and stiffness were examined for three kinds of materials such as aluminum, polyvinyl chloride (PVC) and steel. In the measurement, weak impact load was repeatedly applied to the free end.

Figure 2 shows dimensions of the specimen used for the stiffness measurement from natural frequency.

In the cantilever support model, basic equations of free vibration are

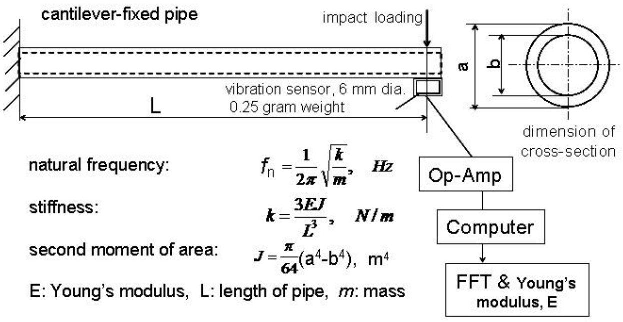
natural frequency: $$f_n = \frac{1}{2\pi}\sqrt{\frac{k}{m}}, \quad (Hz) \qquad (1)$$

stiffness (k>0): $$k = \frac{3EJ}{L^3}, \quad (N/m) \qquad (2)$$

second moment of area:

$$J = \frac{\pi}{64}\left(a^4 - b^4\right), \quad (m^4) \qquad (3)$$

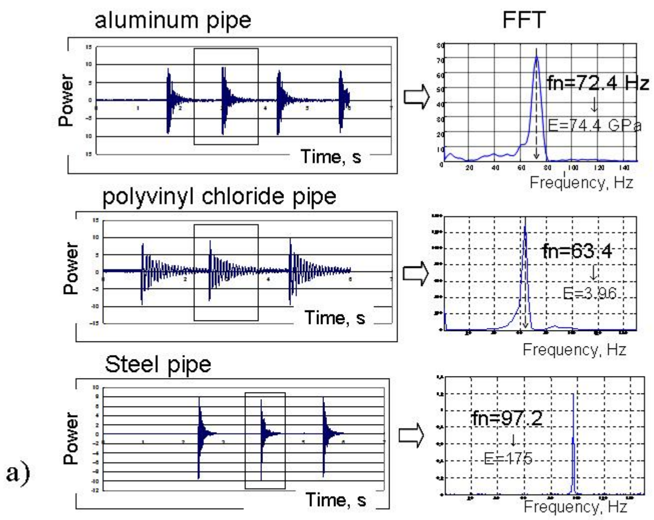
where E =Young's modulus, L=length of pipe, and m= mass.



Materials	Diameter of cross-section, a b (mm)	Specimen length, L (m)	Specimen mass, m (kg)
Aluminum	20 14	0.6	0.026
Polyvinyl chloride (PVC)	21 12	0.4	0.010
Steel	20 13	0.5	0.073

Figure 2. Dimensions of three materials used for the stiffness estimation based on vibration characteristics.

Figure 3 shows oscillation waveforms of three materials and those natural frequencies (fn) from the FFT analysis. Young's modulus (E) estimated using the equations (1) - (3) and the specification strengths of the materials were compared in tabular form (Fig. 3b). In the case of steel, %error was greater though, we considered that stiffness of material can be properly evaluated using the prototype device.



b)

Materials	Measured frequency fn (Hz)	Young's modulus E: (GPa) from fn. (%error)	Young's modulus : ISO specification, E :(GPa)
Aluminum	72.4	74.4 (+4.3%)	71.3
Polyvinyl chloride (PVC)	63.4	3.96 (in range)	2.5 - 4.2
Steel	97.2	175 (-12.5%)	200

Figure 3. Experimental results of thee materials: a) measured wave forms, natural frequency (fn), and estimated Young's modulus (E) using eqs.(1) ~ (3). b) Comparison of the estimated Young's modulus with the specification of materials

III. RESULTS AND DISSCUSION

STIFFNESS ESTIMATION FROM ARTERIAL WALL VIBRATION

Vibration of the arteries of the human body is influenced by surrounding several tissues such as soft tissue, muscle, and bone. Therefore, the relation between the stiffness from the vibration measured on the skin surface and the stiffness from the arterial bulging deformation of the ultrasonic moving image was investigated.

A. Arterial wall vibration of the upper extremity

There are some spots on the body at which an artery is close to the surface and a pulse can be felt. Artery of the upper arm is one of the pulse measurement locations.

Figure 4 shows an example of the radial and brachial arteries: a) female, 22-year, b) male, 64-year. As can be seen from the figure, strong pulse wave were recorded and it indicates clear age dependency between two examinees. That is, large value of the fn means larger Young's modulus (greater progression of arteriosclerosis) from equation (1). In this experiment, 19 subjects were measured.

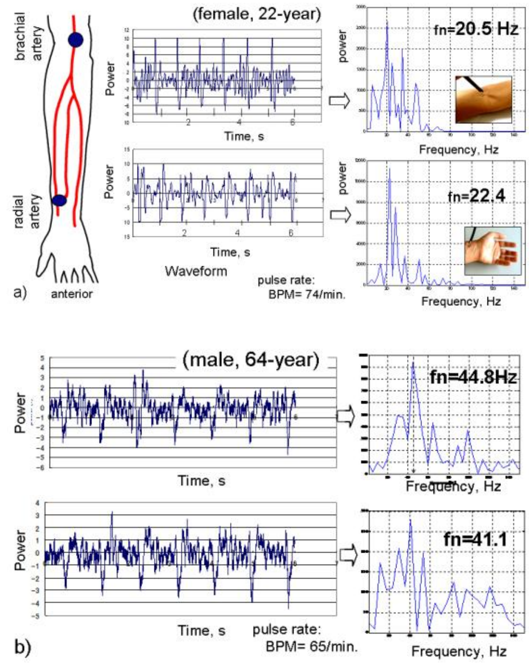


Figure 4. An example of vibration estimation of arteries of the upper extremity: a) female, 22-year, b) male, 64-year.

B. Superficial temporal artery and common carotid artery

The superficial temporal artery (STA) is a distal artery of the external carotid located in the head. We can easily detect a pulse wave at some spots e.g., at the external auditory canal and at the upper root of the ear crus. In the measurement, five locations (both side of the arteries and the heart) were recorded as follows:

1) A trial earphone-type vibration sensor was inserted into the both external auditory canal (Fig. 5a).

2) The vibration sensor was directly pasted at skin surface of around middle of the neck for the common carotid artery.

3) The vibration sensor was inserted into the tube of stethoscope (Fig. 5b) and was fixed on the chest surface near apex of the heart.

The simultaneous measurements of five locations and only both side carotid arteries were 9-subject, respectively (a total of 18-examinee).

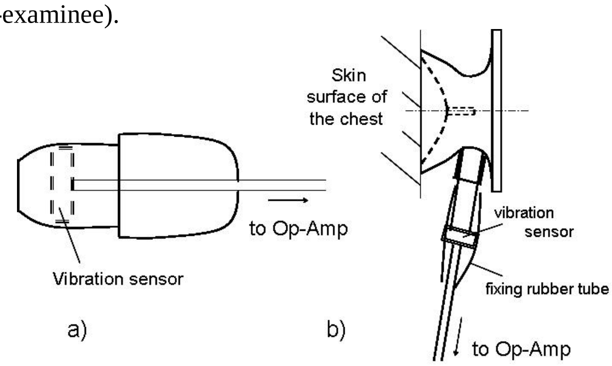


Figure 5. Measurement components used: a) earphone type sensor for the ear canal, b) sensor using a stethoscope for heartbeat.

Figure 6 shows an example of simultaneous recorded arteries at the five locations aged 65 years, male. The pulsatile blood flow and pressure by the heart beats dilates arterial wall and its bulge propagates to distal portion. The propagation velocity was calculated using the time until each location of arterial waveforms. In an adult human, the distance from the heart to the ear is approximately 30 cm (typical value). Therefore, it takes (0.3 m/0.14s) = 2.14 m/s to reach the STA from the heart. Note that this is the propagation speed of bulge deformation of arterial wall.

On the other hand, assuming a thin-walled and linear elastic material (Hookean solid), and the elastic wave propagation in artery can be calculated by the equation (Kortweg-Moens wave velocity [19]) as:

$$V= ([E_{th\,t}/\rho)\,(t/a)]^{1/2}. \qquad (4)$$

Thus, V=7.52 m/s from Eth=0.6 MPa (60's), $\rho=1.06\text{x}10^3$ kg/m^3 (blood density), t= 0.8 mm (wall thickness) and a=8 mm (outer diameter). Note that the velocity is water hammer (pressure wave) speed, and this is equivalent to the PWV (pulse wave velocity) which is generally used as a marker of cardiovascular risk [20, 21, 22]. From the viewpoint of physics, if arterial wall is stiffer and/or thicker due to in aging, the pressure wave propagates higher velocity because the wall would become almost no bulge. Furthermore, since the velocity V is expressed as a function of the square root of the Eth (Young's modulus), when Eth is quadrupled, V is doubled, which means that it is a low sensitivity inspection method.

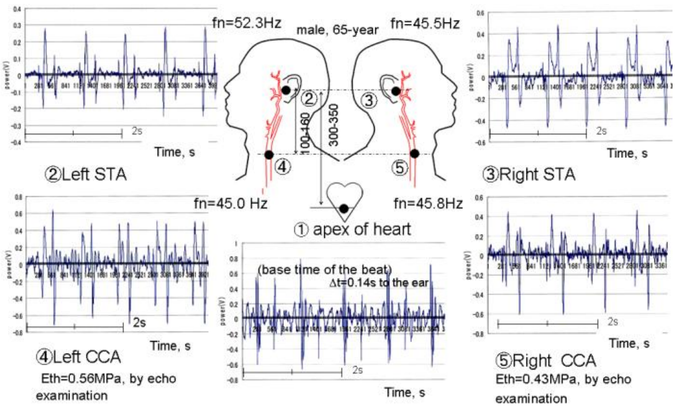


Figure 6. An example of simultaneous recorded free vibration of arteries at the five locations aged 65 years, male.at.

Figure 7 shows the graph of a relation between the fn and age of four arteries: upper extremity (radial and brachial arteries), superficial temporal artery (STA) and common carotid artery (CCA). Those regression equations are given as follows:

For brachial and radial arteries,

$$fn =19\,ln\,(age) - 36,\ R^2=0.78,$$

where R is the correlation coefficient, and

$$\text{for STA, } fn =21.3\,ln\,(age) - 39,\ R^2=0.87,$$

$$\text{for CCA, } fn =18.5\,ln\,(age) - 29.5,\ R^2=0.76.$$

As can be seen above results, it shows that those fn equations have a similar age dependency. Then, the regression equation for all arteries (48-examinee) was

$$fn=19\ln (age) -33,\ R^2=0.75.$$

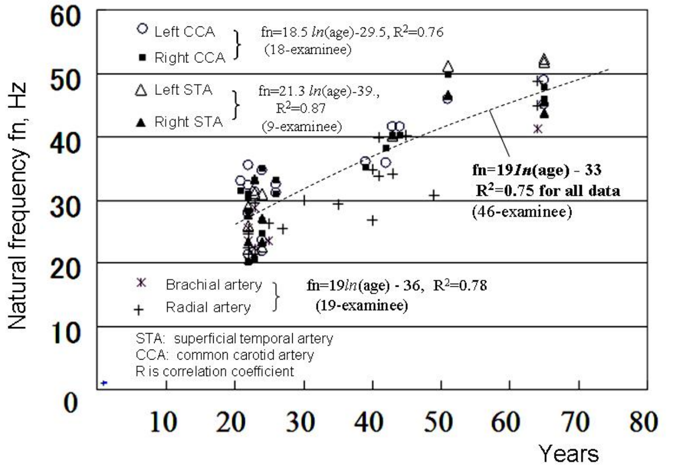


Figure 7. A relation between the fn and age for four kinds of arteries: upper-extremity (radial and brachial arteries), superficial temporal artery (STA) and common carotid artery (CCA).

C. Young's modulus estimation using carotid ultrasonic imaging

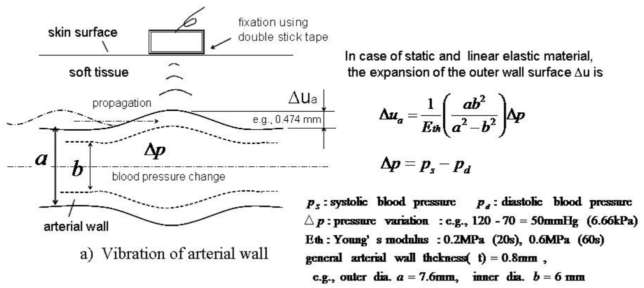
In the section, the procedure for estimating Young's modulus was discussed from arterial wall movement due to pulsatile blood flow. And then a relation between the fn and Young's modulus estimated from arterial wall movement using ultrasonic echo moving image (30-frame/s, and 0.0713 mm/pixel) was examined. Arterial wall is viscoelastic material which exhibits a non-linear relation between elongation and external force (e.g., blood pressure). On the other hand, the difference between Ps (a systolic blood pressure) and Pd (a diastolic blood pressure) is 30 to 50 mmHg (4k to 6.66kPa) in general. From the viewpoint, we considered that bulge deformation of the artery is in the linear range approximately. On the basis of the linear elastostatics, we can calculate bulge deformation of arterial wall.

Figure 8 shows a schematic representation of arterial wall bulge deformation. The expansion (Δu_a) on the outer wall surface from a textbook of material mechanics is

$$\Delta u_a = (1/Eth)\,[ab^2/(a^2-b^2)]\,\Delta p. \qquad (5)$$

Where ΔP is blood pressure difference (ΔP=Pd - Ps), e.g., 120-70=50 mmHg (6.66kPa), and diameter of the common carotid artery, e.g., a=7.6 and b=6.0 mm, the wall thickness is 0.8 mm (typical adult), Eth is Young's modulus of arterial wall, e.g., 0.2MPa (20s) and 0.6MPa (60s) [5, 23], and also see Fig. 10.

From equation (4), we obtain that Δu_a = 0.474 mm for age of 20s, and Δu_a = 0.158 mm for age of 60s. That is, %diameter of the vibration amplitude ($2\Delta u_a$ /a) is 12.5% and 4.16 % of the outer diameter, respectively. And the bulge deformation propagates to distal portion while its deformation energy attenuates.



a) Vibration of arterial wall

Aged 20s: Eth=0.2 MPa	60s: Eth=0.6 MPa
Δu_a: 0.474 mm	0.158 mm
%dia. : $2\Delta u_a/a$ =12.5	4.16

b) Calculated expansion of the outer surface (Δu_a) and %diameter

Figure 8. A schematic representation of arterial wall bulge deformation and the calculation based on homogeneous material and linear elastostatics: a) vibration of arterial wall, b) calculated expansion of the outer surface Δu_a and %diameter.

Figure 9 shows a typical example of ultrasonic image of the common carotid artery for a young adult at age 16 (male) for estimating Young's modulus. As seen in the echo image, the inner wall is sharper than the other places. And the maximum hoop stress (σ_θ) occurs at this inner wall. A graph of the inner diameter variation with time was obtained using the software developed in our laboratory. The stress (σ_θ) at the inner wall is

$$\sigma_\theta = [(a^2+b^2)/(a^2-b^2)]\Delta p, \tag{6}$$

and the strain is

$$\varepsilon_b = (\Delta b/b), \tag{7}$$

where Δb is the diameter variation of the inner wall caused by the ΔP. Therefore, the equation based on the definition of Young's modulus is

$$Eth = \sigma_\theta/\varepsilon_b . \tag{8}$$

From the measurement data in Fig. 9, we can obtain that Eth=0.154 MPa, where a= b+2t=6.95 mm, b=5.35 mm at Pd, Δp=43 mmHg (5.73kPa), Δb=0.8 mm, and the wall thickness is 0.8 mm (typical adult value). If the expansion (Δu_b) of the outer surface is same to that of the inner wall ($\Delta u_a = \Delta u_b = \Delta b$), we obtain that Eth=0.145 MPa from the equation (5). Therefore, both values of calculated Eth using equations (5) and (6) are the same.

The above discussion was carried out as homogeneous material and linear elastostatics. However, actual arterial wall consists of three layers (tunica intima, tunica media and tunica externa) which have different stiffness. That is, arterial wall would show slight different movement with time. From the viewpoint of practical examination, it would require the measurement at stable body temperature state and in the resting state, e.g., measurements after exercise and/or after bathing should be avoided.

Figure 10 shows the age dependence of *in vivo* Young's modulus (Eth) of the common carotid artery for adult (male 159 and female 51 subjects) using the measurement system shown in Fig. 9. The result shows age dependency as well as individual difference and right-and-left differences of the CCA. In addition, note that there is a possibility that sclerosis is progressing more than the age in some young adults. And also note that there are some people who are a large difference between the left and right of carotid artery. These results might be related to the possibility that lead to stroke. A correlation equation was obtained as:

$$Eth = 0.0085(age) + 0.076, \quad R^2 = 0.31, \tag{9}$$

for the range of application is that 20≦age≦70.

In general, it is unfamiliar with numerical value of Young's modulus, but we can find some materials in daily life. For example, Young's modulus of a long-shaped toy balloon subjected to internal pressure of water was Eth=0.36 MPa approximately [24], which is equivalent to 30s~40s as seen in Fig.10: the burst pressure of a balloon was at 266 mmHg (35.56kPa). This indicates the importance of the use of mechanical characteristics as an index of arteriosclerosis.

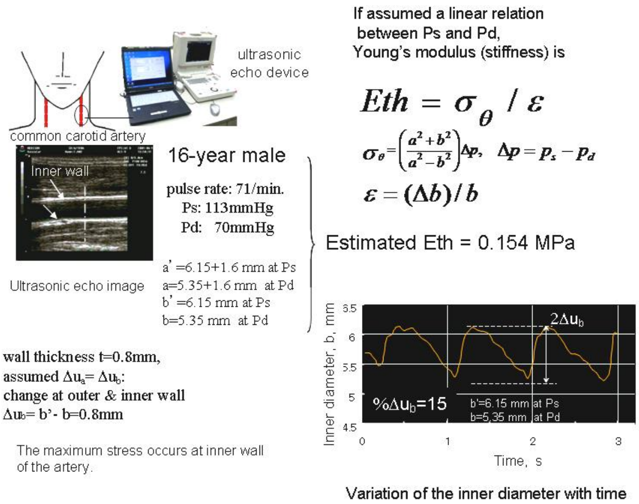


Figure 9. Measurement system for estimating Young's modulus (Eth) and an example of ultrasonic image of the common carotid artery of a young adult.

.

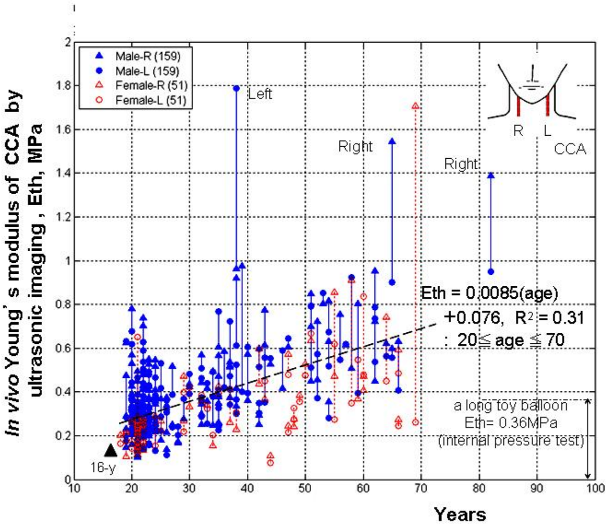


Figure 10. Age dependence of *in vivo* Young's modulus (Eth) of common carotid artery

Figure 11 shows the relation between the natural frequencies measured at the skin surface (fn) and Young's modulus estimated (Eth) using ultrasonic imaging of the CCA. From the data, we obtained the following regression equation:

$$Eth=0.014\ (fn) - 0.13, \quad R^2= 0.66. \tag{10}$$

As an actual data of Eth=0,5 MPa, it was equivalent to 0.8MPa of the tensile strength and burst internal pressure was 800 mmHg (106.6kPa) approximately, using the CCA of human specimen (authors' test data at the UNSW). Therefore, a simple technique for estimating Young's modulus (Eth) of the CCA could be established from the frequency (fn) and the equation (10).

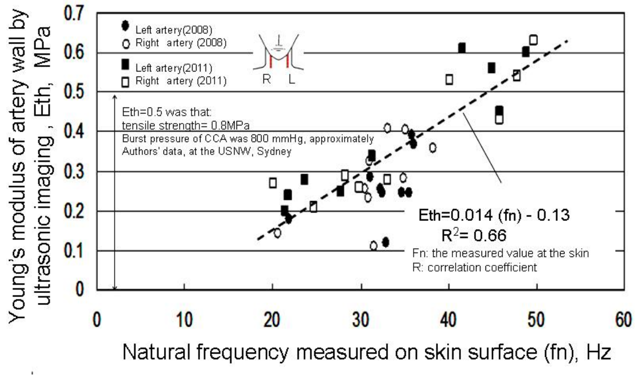


Figure 11. The relation between the natural frequencies measured (fn) on the skin surface and estimated Young's modulus (Eth) using ultrasonic imaging of the CCA.

VISION OF A NEW EARPHONE FOR EXAMINING ARTERIOSCLEROSIS BETWEEN MUSIC AND NEXT MUSIC

We discussed in the previous section the feasibility of stiffness estimation of the arterial wall on the basis of vibration analysis. On the other hand, in recent diversified diet, one of the urgent problems to be solved is that arteriosclerosis at an early age which leads to the seriousness of health as cardiovascular diseases. That is, the technique can be expected application to young adult.

Figure 12 shows our vision of new earphones for examining arteriosclerosis between music and music. A pair of sensors inserts both of the ear canal, and it can be accomplished by measuring the arterial vibration between music and the next music in a relaxed state for a few seconds with relaxing. This plan would be expected as a new earphone with easy-to-use approach, low cost, and data recording and/or telemedicine through such as smart phone.

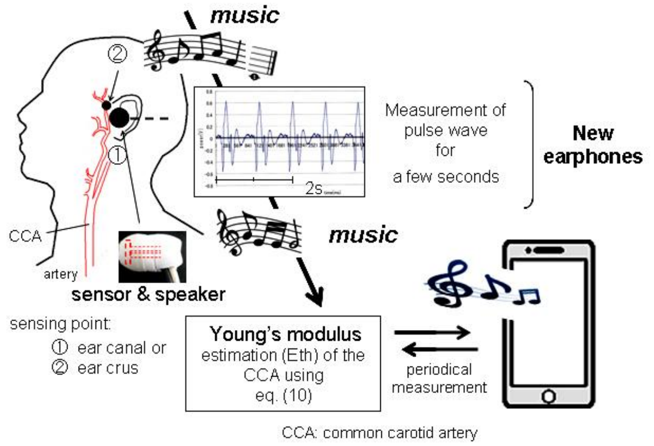


Figure 12. A vision of new earphones for examining arteriosclerosis between music and next music.

Figure 13 shows our scheme drawing of artery inspection and health guidance at an early stage to promote the 80-year-old productive age and the 100-year-old health longevity using the personal artery management records: the value of burst blood pressure of the CCA was plotted from the figure 5 in [5]. We hope that the procedures would be assist health longevity on the basis of long-term examination data from childhood.

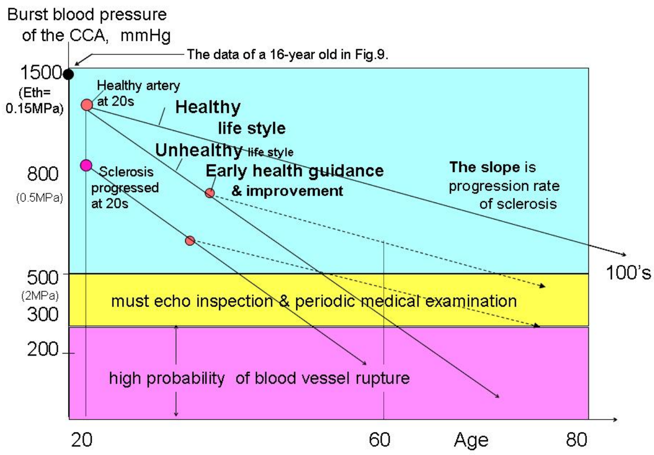


Figure 13. A scheme of early-stage artery examination and health guidance promoting healthy life and productive age up to age 80 using individual records

IV. CONCLUDING REMARKS

We proposed a new measurement method for estimating sclerosis from the bulge vibration of arterial wall due to the heartbeat as like taking our heart rate at the body surface by fingertip. Basic concept of the technique is measurement of natural frequency of artery. All structure has a natural frequency which is depend only on mass and stiffness of the system that is deformation resistance in response to an applied force. Therefore, stiffness of artery can be measured from the natural frequency of bulge vibration generated by variation of blood pressure. The results were summarized as follows:

1) From the results of the upper extremity, superficial temporal artery and common carotid artery, the regression equation between the natural frequency (fn) and age was:
fn=19*ln* (age) - 33, R^2=0.75.

2) The equation between Young's modulus (Eth) and the fn was Eth=0.014 (fn) - 0.13, R^2= 0.66.
Therefore, the Eth can be estimated from the natural frequency (fn) of arterial wall measured at skin surface.

3) A new earphone-type device to measure sclerosis of the superficial temporal artery during music and next music was made.

The new measurement method allows long examination from childhood with easy use cheaply and efficiently. Therefore, by finding early lesion of arteriosclerosis on the basis of long-term examination data from a childhood, it would be expected to promote 80-year-old productive age and the 100-year-old health longevity with periodical health guidance.

ACKNOWLEDGMENTS

The authors express appreciation to all students and organizations cooperated in research from 2007 to 2012. The clinical investigations were performed according to the rules of the Ethics Committees of Gifu University Hospital and other participating hospitals.The work was partially supported by the Chiteki Cluster Project (Gifu-Ohgaki Area) of the Ministry of Education, Science, Sports, and Culture of Japan.

REFERENCES

[1] Japanese Government Statistics on Annual Report of Ministry of Health, Labor and Welfare, Annual estimates of demographic statistics (2015), Japan :http://www.mhlw.go.jp/toukei/saikin/hw/jinkou/suikei15/

[2] For example, The department of health of Australian Government on Cardiovascular. disease: https://www.health.gov.au/internet/main/publishing.nsf/Content/chronic-cardio

[3] G. Gamble, "B-mode ultrasound image of the carotid artery wall, Correlation of ultrasound with histological measurement", Arteriosclerosis, Vol. 102, 1993, pp.163-173.

[4] For example, diagnostic tests at the Mayo clinic in U.S., http://www.mayoclinic.org/diseases-conditions/arteriosclerosis-atherosclerosis/diagnosis-treatment/

[5] F. Nogata, Y. Yokota, Y. Kawamura, W.R Walsh, H. Morita, Y. Uno, T. Kawamura, M. Nagashima, and N. Hotta, A Technique for Estimating Sclerosis of Carotid Artery with Ultrasonic Echo, WC 2009, IFMBE Proceedings25/IV (2009)pp.655-658.

[6] Juho R.H. Raiko, Conventional and novel cardiovascular risk factors in young Finns and their associations with structural and functional vascular changes of sub clinical atherosclerosis, The cardiovascular risk in young Finns study, Sarja - Ser. D OSA –TOM. 981,

[7] T Laitinen, Cardiovascular health from childhood to adulthood –with special reference to early vascular changes, the cardiovascular risk in Young Finns Study, Medica - Odontologica,Turku 2015.

[8] Christian Hakulinen, Laura Pulkki-Råback, Marko Elovainio, Laura D. Kubzansky, Markus Jokela, Mirka Hintsanen, Markus Juonala, Mika Kivimäki, Kim Josefsson, Nina Hutri-Kähönen, Mika Kähönen, Jorma Viikari, Liisa Keltikangas-Järvinen, and Olli T Raitakari, Childhood Psychosocial Cumulative Risks and Carotid Intima-Media Thickness in Adulthood: The Cardiovascular Risk in Young Finns Study, Psychosom Med. 2016 Feb-Mar; 78(2): pp. 171–181.

[9] Young Mi Hong, Atherosclerotic Cardiovascular Disease Beginning in Childhood, Korean Circ J., The Korean Society of Cardiology, 2010 Jan; 40(1): pp. 1–9.

[10] R. H. Peterson, R. E. Jensen, R. Parnell: "Mechanical properties of arteries in vivo," Circulation Research, Vol. 8, 622-639,1960.

[11] A.G., Hudetz, "Incremental elastic modulus for orthotropic incompressible arteries," J. Biomechanics, Vol. 12,1979, pp.651-65.

[12] F.Hansen, et al., "Diameter and compliance in the human common carotid artery variations with age and sex," Ultrasound in Med. & Bio. Vol. 21,1995, pp. 1-9.

[13] D. H. Bergel: "The Static Elastic Properties of the Arterial Wall. J. Physiol,"1961, 156,pp.445-457.

[14] Hiroshi Kanai, Hideyuki Hasegawa, Masataka Ichiki, Fumiaki Tezuka and Yoshiro Koiwa, Elasticity imaging of atheroma with transcutaneous, Ultrasound, Circulation, American Heart Association, 107, 3018-3021,2003.

[15] A. Lalande, V.K. Khau, N. Salve, D. Ben Salem, L. Legrand, P.M. Walker, Automatic determination of aortic compliance with cine-magnetic resonance imaging: an application of fuzzy logic theory, Invest Radiol, 37 (2002), pp. 685–691

[16] T. Khamdaeng, J. Luo, J. Vappou, P. Terdtoon, E.E. Konofagou, Arterial stiffness identification of the human carotid artery using the stress-strain relationshop in vivo, Ultrasonics. 2012 Mar;52(3):402-411.

[17] Marcel van 't Veer, Jaap Buth, Maarten Merkx, Pim Tonino, Harrie van den Bosch, Nico Pijls, Frans van de Vosse, Biomechanical properties of abdominal aortic aneurysms assessed by simultaneously measured pressure and volume changes in humans, Journal of Vascular Surgery, Volume 48, Issue 6, December 2008, pp. 1401–1407.

[18] Kendall S. Hunter, Joseph A. Albietz, Po-Feng Lee, Craig J. Lanning, Steven R. Lammers, Stephen H. Hofmeister, Philip H. Kao, H. Jerry Qi, Kurt R. Stenmark, Robin Shandas, In vivo measurement of proximal pulmonary artery elastic modulus in the neonatal calf model of pulmonary hypertension: development and ex vivo validation, Journal of Applied Physiology Published 1 April 2010 **Vol.** 108, 4, pp. 968-975.

[19] C. Ross Ethier and Craig A. Simmons, "Introductory Biomechanics from cells to organisms," Cambridge texts in biomedical engineering, Cambridge University press, 2007, pp.186-194..

[20] Asmar R., Pulse wave velocity, Principles and measurements. In: Safar ME, editor. Arterial stiffness and pulse wave velocity – clinical applications. Paris: Elsevier; 1999. pp. 25–53, Chap. III ,pp. 143–157.

[21] Meaume S, Rudnichi A, Lynch A, et al. Aortic pulse wave velocity: an independent marker of cardiovascular risk. J Hypertension. 2001;19, pp871-877.

[22] Safar ME, Henry O, Meaume S., Aortic pulse wave velocity: an independent marker of cardiovascular risk, Am. J of Geriatric Cardiology, 2002 Sep-Oct;11(5):295-298.

[23] C. Ross Ethier and Craig A. Simmons, "Introductory Biomechanics from cells to organisms," Cambridge texts in biomedical engineering, Cambridge University press, 2007, Table 4.2 on p.187.

[24] The undergraduate student's projects performed on 2007-2009 at Gifu University,unpublish