Development of Noninvasive Measurement of Peripheral Circulation and its Medical Application

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Abstract

Surveys were carried out on tissue blood flow measurement based on the thermal diffusion method and on the assessment of peripheral circulatory function using photosensors.

Regarding the thermal diffusion method, first noninvasive measurement using a Peltier stack was carried out. Then, measurements using a thermal clearance curve at various temperatures were performed.

For noninvasive measurement of the mechanical properties of peripheral arteries using photosensors, the author determined the vascular volume ratio and/or the relative vascular volume.

For clinical application in field studies, it is necessary to develop an apparatus with which absolute evaluation of the intravascular volume can be carried out using the blood volume around the unit volume as an indicator. Therefore, an apparatus that removes a signal constituent from tissue other than the blood using two-wavelength photosensors is required.

If a noninvasive method to accurately measure the intravascular volume is established, changes in the mechanical properties of the peripheral arteries that correspond to functional and organic changes in the normal response can be observed more directly. Moreover, quantitative assessment of peripheral circulatory function will become possible, and diagnosis of the severity of peripheral circulatory disorders will be facilitated.

Key words: Noninvasive measurement, Tissue blood flow, Thermal diffusion method, Photosensor, Mechanical properties of peripheral arteries

1. Introduction

It is important to carry out early diagnosis of peripheral circulatory disorders by examining the effects of physical environmental stimuli on peripheral circulation. For this purpose, it is necessary for us to observe both peripheral blood flow and functional and organic changes in the blood vessels by a noninvasive method^{1,2)}. Thus, the purpose of this series of studies is to evaluate the effects of physical environment stimuli on peripheral circulation, and to clarify the pathogenesis of peripheral circulatory disorders.

The author has examined not only the assessment of peripheral circulatory function using blood flow measurements based on

the thermal diffusion method but also the assessment of the mechanical properties of digital arteries using photosensors. The thermal diffusion method using a Peltier stack was assessed for the purpose of continuous monitoring under various conditions. The use of a thermal clearance curve at various temperatures was also evaluated. Assessment by these methods was compared to the classical method using a temperature-controlled thermocouple.

The author has also carried out preliminary examination of the assessment of peripheral circulatory function using photosensors. The apparatus, the principle involved in measurement, the assessment of elasticity and nonlinear characteristics of the digital arteries, the measurement of tissue blood volume and the progress in these studies will be discussed. The author also wants to highlight the possibility of measuring techniques using photosensors in medical science and the future direction of peripheral circulatory measurement.

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2. Peripheral circulatory indices and their characteristic

1) Blood flow and its related indices

The types of indices of peripheral circulation being used until now and their characteristics, using the blood flow and its related indices, are summarized in Table 1. Various methods have gained popularity for measuring blood flow³⁾, and the thermal diffusion method, clearance methods using hydrogen gas^{4, 5)} or ¹³³Xe⁶⁻⁹⁾, the plethysmography method¹⁰⁻¹²⁾, the laser Doppler method¹³⁻¹⁵⁾, and so on have been widely used in various clinical fields. These methods are recently being used for clinical diagnosis of peripheral circulatory disorders of the lower limbs caused by diabetes mellitus and others diseases^{8, 9, 14, 15)} as well as for the assessment of peripheral circulation in neonates¹²⁾. However, the method that is used must be selected according to the application as each method has its own merits and demerits. When used for human measurement, it is necessary to monitor peripheral circulatory movement during exposure to stimulation such as local vibration of the exposed hand. In such tests, it is important to know whether signals from the sensor may change due to such as vibrations. Skin temperature and the volume of the pulse wave at the fingertip can be measured noninvasively and continuously. Though these can be measured on the side exposed to stimuli, there are limitations in the assessment of blood flow or quantitative measurement. The plethysmography and clearance methods show problems in continuity, while the laser Doppler method is limited, not only in that determination of an absolute value is difficult but also in that it cannot be used on the side exposed to stimuli.

On the other hand, measurement by the thermal diffusion

method can be carried out continuously on the side exposed to stimuli and absolute values can be determined by the clearance method using hydrogen gas, etc. Thermal diffusion apparatuses can be divided roughly into two types. One is the classical type using a temperature-controlled thermocouple¹⁶⁻¹⁸⁾, and the other uses a Peltier stack, a method begun by Carter in the neurosurgical field in the 1980s¹⁹⁻²³⁾.

2) Peripheral circulatory indices using photosensors

Recently, it has become possible to noninvasively measure the oxygen saturation level of arterial blood^{24, 25)}, finger arterial pressure (FINAP)²⁶⁻³²⁾, and the elasticity of digital arteries using photosensors and light-emitting diodes (LED)³³⁻³⁵⁾. Photosensors have also been used to measure the mechanical properties of digital arteries and indices such as the blood volume in peripheral tissue³⁶⁾. FINAP using strain-gauge plethysmography has been used to diagnose hand-arm vibration syndrome and to elucidate the mechanism of its pathogenesis by noting changes in FINAP measurement after finger cooling³⁷⁻⁴²⁾. Futatsuka et al.³²⁾ have examined the effects of noise and vibration on peripheral circulation through FINAP measured by sphygmomanometer using photosensors.

There are various peripheral circulatory indices that can be obtained using a laser beam and near infrared light from the LED (Table 2). Though these indices can be obtained noninvasively or minimally invasively by application of short-term pressure, the continuity of measurement is lost when cuff pressure is applied. Measurement is insufficient using light of only 1 wavelength in this method. Determination of an absolute value can be improved if 2 or 3 wavelengths are used^{36, 43, 44)}. Oxygen satura-

Table 1 Peripheral circulatory indices and their characteristics
(1) Blood flow and its related indices

	Invasion	Continuity	Assessment of absolute value	Observation of blood flow	Object · Site	Use under temperature condition	Use under impact	Use in exposed side under handgrip	Usage
1. Skin temperature	no	good	possible	impossible	human, animal surface of organ	possible	possible	possible	Experiment/Diagnosis
2. Volume pulse wave	no	good	possible	impossible	human, animal finger, etc.	possible	possible	impossible	Experiment
3. Plethysmograph	pressure	poor	possible	possible	human, animal finger, etc.	possible	possible	impossible	Experiment
4. Clearance method (¹³³ Xe, H ₂)	severe	poor	possible	possible	animal, human many organs	possible	impossible	impossible	Experiment
5. Thermal diffusion using classical thermocouple	no	good	impossible	possible	human, animal surface of organ	impossible	possible	possible	Experiment
6. Thermal diffusion using a Peltier stack	no	good	possible*	possible	human, animal surface of organ	impossible	possible	possible	Experiment
7. Thermal diffusion using a thermal clearance curve	no	poor	possible*	possible	human, animal surface of organ	impossible	possible	possible	Experiment
8. Laser Doppler flowmetry	no	good	impossible	possible	human, animal surface of organ	possible	impossible	impossible	Experiment

possible* means that it requires comparison with the clearance method.

Table 2 Peripheral circulatory indices and their characteristics
(2) Peripheral circulatory indices using photosensors

	Invasion	Continuity	Assessment of absolute value	Observation of blood flow or vascular response	Object · Site	Use under temperature condition	Use under impact condition	Use in exposed side under handgrip	Usage
A) Laser beam									
1. Laser Doppler flowmetry	no	good	impossible	blood flow	human, animal body surface	possible	impossible	impossible	Experiment
B) Near infrared light									
2. oxygen saturation of arterial blood (2 wavelengths)	no	good	possible	impossible	human, animal body surface	impossible	possible	possible	Diagnosis/ Experiment
3. tissue hemoglobin (2 or 3 wavelengths)	no	good	possible	impossible	human, animal body surface	impossible	possible	possible	Experiment
4. tissue blood volume (2 or 3 wavelengths)	no	good	possible	vascular response	human, animal body surface	impossible	possible	possible	Experiment
5. local blood flow (2 or 3 wavelengths)	pressure by cuff	poor	possible	vascular response	human, animal body surface	impossible	possible	impossible	Experiment/ Diagnosis
6. finger arterial pressure (1 wavelength)	pressure by cuff	poor	possible	vascular response	human, animal finger, etc.	impossible	possible	impossible	Experiment
7. finger arterial mechanical property (1 wavelength)	pressure by cuff	poor	impossible	vascular response	human, animal finger, etc.	impossible	possible	impossible	Experiment/ Diagnosis
8. finger arterial mechanical property (2 or 3 wavelengths)	pressure by cuff	poor	possible	vascular response	human, animal finger, etc.	impossible	possible	impossible	Experiment
9. tissue oxygen metabolism (2 or 3 wavelengths)	no	good	possible	impossible	human, animal brain, etc.	impossible	possible	possible	Experiment

tion and blood volume are indirect indices of the blood flow response. However, other indices can be said to be direct indices. Moreover, measurement of tissue oxygen metabolism has been attempted in the brain^{45, 46)} and the skeletal muscle^{47, 48)}.

Most of the above-mentioned blood flow measurements were obtained during experimental research. However, the method using photosensors can be used for diagnosis in humans. With this method there is a possibility that measurement values can change greatly if the location of the sensor moves during the measurement. Because use of a cuff is necessary, this method cannot be used for continuous measurement during exposure to stimuli. Use in measurement of the mechanical properties of peripheral arteries using 1 wavelength is discussed later.

3. Noninvasive blood flow measurement using the thermal diffusion method

1) Skin blood flow measurement using the hydrogen clearance method

The author used the hydrogen clearance method for the purpose of absolute value estimation in the thermal diffusion method. Preliminary examination of the hydrogen clearance method was carried out using inhaled hydrogen gas and hydrogen gas generated by electrolysis. The measurement of skin blood flow by the hydrogen clearance method is established in humans⁴⁹⁻⁵¹⁾.

Assessment of the absolute value for blood flow became possible by estimation of the thermal diffusion using the hydrogen clearance method.

The hydrogen clearance method using hydrogen gas generated by electrolysis was used to measure gastric mucosal blood flow. Research has been carried out on the mechanism of development of acute gastric mucosal lesions of rats, which are induced by exposure of whole body vibration or noise^{52, 53)}.

2) Blood flow measurement using a Peltier stack

The measuring principle of the thermal diffusion method is that the thermal conductivity of tissues such as skin responds simultaneously to changes in blood flow. Therefore, the basis of this measurement method is the precise monitoring of thermal conductivity. A temperature-controlled-type blood flow meter, in which a classical thermocouple is used, is currently on the market¹⁸⁾. In this classical system, current is changed to regulate the temperature difference of the thermocouple. The changes of blood flow are measured through changes in the current. The response is insufficient for increases in blood flow beyond a certain blood flow level and the determination of absolute values is limited because the actual values are different when estimated at two different times. Therefore, the absolute value cannot be estimated in this classical method.

On the other hand, current is fixed in the method using a

Fig. 1 Schematic diagram of tissue blood flow measurement apparatus for the thermal diffusion method using a Peltier stack. One gold plate is heated and the other cooled by the Peltier stack.

Fig. 2 Principle of skin blood flow measurement by the thermal diffusion method. Hydrogen SBF and Thermal SBF = skin blood flow by the hydrogen clearance method and the thermal diffusion method, respectively. V is the temperature difference of two gold plates with flow and V_0 is that with no flow. Φ is the constant determined by the thermal conductivity of the tissue.

Peltier stack, and blood flow is evaluated from the temperature difference of two gold plates (V) when blood flow exists and the temperature difference (V_0) when there is no blood flow (Fig. 1)^{51, 55}. The difference between V and V_0 ($V_0 - V$) corresponds to the absolute value of the clearance method. This result is proved by the theoretical equation derived from Fourier's law of thermal conduction. Blood flow is in proportion to the reciprocal of V in this equation (Fig. 2). The thermal diffusion flow probe used by the author is shown in Fig. 1. The author has developed a system where, when a current of 200 mA was applied to a Peltier stack, was measured precisely with 1 mV as the thermo-electromotive force. The thermal conductivities of 10 kinds of boards which were close to that of the skin tissue of humans were measured using a thermal diffusion flow probe. A linear relationship was seen in the reciprocal of V from the thermal diffusion flow probe and the thermal conductivity, and the thermal conductivity could almost be determined. The hydrogen clearance method was used for absolute value estimation-based theory. V_0 at no flow and the coefficient Φ were determined, and the absolute value was estimated (Fig. 2).

The author examined the effects of handgrip and local vibration on peripheral circulation using this measurement system in healthy subjects and vibratory tool operators^{56, 57}. When the effect of five-minute handgrip in healthy subjects was observed, the decline of finger blood flow occurred early, and that of skin temperature was delayed. This result showed that skin temperature depends on the thermal capacity of a large area.

Fig. 3 Finger blood flow response patterns determined for vibratory tool operators by the 30% Handgrip Test. Δ FBF means finger blood flow change from the initial value. A, group with no symptoms. B, group with numbness and/or pain. C, group with vibration-induced white finger (VWF).

After the blood flow became stable with a handgrip of 5 Kg, a vibration of 60Hz at 5G was applied. The response of the blood flow was observed in the vibratory tool operators. Though blood flow increased in the group without symptoms, this increase was not observed in the group with vibration-induced white finger (VWF). In addition, a 30% handgrip test, which is an examination of autonomic nerve function, was carried out, and the blood flow response was observed⁵⁸. The decline in the blood flow in the handgrip was large, and it was found that the recovery of blood flow of responsive hyperemia after the handgrip was also large in the group without symptoms. On the other hand, it was found that the decline in blood flow was small in the group with VWF, as was the recovery of blood flow. A difference in the decrease of blood flow during handgrip and in its subsequent recovery was therefore observed between the group without symptoms and the group with VWF. The degree of the responsive hyperemia and the compliance of the tissue were evaluated from the size of the blood flow decrease during the handgrip test and from the size of the recovery, respectively (Fig. 3). There was no case in which both a decline in responsive hyperemia and in tissue compliance were seen in the group without symptoms. Responsive hyperemia declined in 6 of 10 cases in the group with VWF, compliance declined in 8 cases, and both declined in 5 cases. Moreover, the author applied this system to observation of the effects of handgrip, hand-arm vibration, noise and combined effects of these stimuli on peripheral circulation, and observed that the effects of handgrip and hand-arm vibration were large.

Fig. 4 Schematic diagram of tissue blood flow measurement apparatus for the thermal diffusion method using a thermal clearance curve.

3) Blood flow measurement using a thermal clearance curve

The method using a Peltier stack was affected by large or rapid changes of the environmental temperature such as cold water immersion. To remove the effect of the environmental temperature change, a method which corrected the baseline before each measurement was devised using a thermal clearance curve⁵⁹⁾. This can be measured almost every minute, though it cannot be measured continuously. Though the flow probe is larger in size than the probes using a Peltier stack because the probe for thermal clearance curve utilizes heat insulation by air, it can be attached to the finger (Fig.4). Heater lines were wound around one side of the thermocouple and a temperature difference was established. Substances with different thermal conductivities could be distinguished from the gradient of the thermal clearance curve. The probe was attached to a polyethylene board, and put into water at 24 °C, the same temperature as surrounding air. Next, the water temperature was gradually decreased to 4 °C, and then raised again to 40 °C. Measurement was performed under these large changes of temperature. The coefficient of variation was 2.8%, and the precision was good. If the baseline was adjusted before each measurement, it was found that the thermal conductivity could be determined from the gradient of the thermal clearance curve at various temperatures. Moreover, when a tourniquet was wound around the upper arm, the blood flow at rest, ischemia under pressure and the responsive hyperemia could be distinguished clearly from the gradient of the thermal clearance curve (Fig.5). Peripheral circulatory movement during the cold water immersion of hands of vibratory tool operators was observed by using this system⁶⁰⁾. The author observed that there was little vasoconstriction after cold water immersion in the group with VWF and that the cold-induced vasodilatative response during and after cold water immersion was also lacking.

4) Clinical application of the thermal diffusion method

The measurement of tissue blood flow based on the thermal diffusion method has been mainly used to study cortical blood flow of the brain and skin blood flow. This method has been recently been used to measure blood flow in the liver and kidney in animals and blood flow in tumor tissue of humans^{61, 62)}.

Regarding cortical blood flow measurement in the brain, recently, preliminary examination of the relationship between intracranial pressure and blood flow has been carried out with the aim of clinical application⁶³⁻⁶⁵⁾. This method is also being utilized for neurosurgical patients. It is being used for postoperative monitoring of blood flow and for the monitoring of blood flow

Fig. 5 Comparison between the thermal clearance curve in the finger skin at rest and that in the ischemic or hyperemic state induced by a tourniquet up to 300 mmHg.

in arterial occlusions during operations on cerebral aneurysms^{66, 67)}. Moreover, the continuous measurement of cortical blood flow of the brain has also been attempted in head injury cases⁶⁸⁾. Recently, the use of this method in head injury and aneurysm patients in intensive care units has also been reported⁶⁹⁻⁷²⁾.

This method has also been used to measure finger blood flow in experimental research in humans^{56-58, 73, 74)}. Miyakita et al.⁷³⁾ have observed the influence of noise, vibration and static load on peripheral circulation while healthy subjects operated a chainsaw. Furuta et al.⁷⁴⁾ examined the influence on finger blood flow of hand-arm vibration at seven frequencies from 16 Hz to 1000 Hz. By the above series of experiments, it was possible to obtain information on the influence of handgrip, noise and hand-arm vibration on peripheral circulation, that could not be obtained from skin temperature measurement only.

4. Assessment of peripheral circulatory function using photosensors

1) Observation of the mechanical properties of peripheral arteries

a) measuring principle

Measurement of the mechanical properties of peripheral arteries using photosensors became possible with the advent of noninvasive methods of measuring blood pressure such as the oscillometric method^{36, 75-79)}. The system, which uses light of 940 nm in the oscillometric method and the volume pulse wave of the finger, is based on the same principle as the sphygmomanometer of the finger arteries (Fig.6)^{36, 80)}. When light passes through the finger, its intensity decreases due to absorption²⁴⁾. When the finger is subjected to external pressure, the capillary vessels and veins collapse under the comparatively low pressure. On the other hand, the tissue is thought to maintain constant optical characteristics under external pressure. Therefore, the intensity of trans-

Fig. 6 Schematic diagram of the measuring apparatus for the peripheral circulatory function using a photo-sensor. LED and PD stand for the light-emitting diodes (light source) and the photodiodes (photodetector).

Fig. 7 Vascular volume ratio (V/V_0) plotted against transmural pressure (P_{tr}) in the middle finger for healthy controls and a chain saw operator without VWF symptoms. V_0 is the volume at $P_{tr} = 0$.

mitted light (I) will change in accordance with the change in vascular volume in the digital artery when cuff pressure (P_c) rises above venous pressure. The light path length (L) through the artery is given by the following equation based on the Lambert-Beer law³³⁾:

$$L = (-K \cdot Ca)^{-1} \cdot \ln(I/I_0).$$

Ca and K represent the concentrations of optical absorptive material in arterial blood and its absorption coefficient, respectively³³⁾. Thus, $K \cdot Ca$ gives the absorption rate of arterial blood. I_0 is the intensity of transmitted light decreased by absorption only in the non-blood tissue area when P_c rises above the systolic blood pressure (SBP), and the arteries, capillary vessels, and veins all collapse. The light path length (L) in arterial blood is hereafter presumed to be proportional to the vascular volume (V).

Even though $K \cdot Ca$ is not constant among different subjects due to individual differences in the optical characteristics of arterial blood, this problem can be eliminated by calculating the ratio of vascular volume (V/V_0) to the volume (V_0) when P_c is equal to the mean blood pressure (MBP), or the ratio of the relative vascular volume (V/V_c) to the volume (V_c) when P_c reaches a constant low level.³⁴⁾ However, arteries normally show intrinsic nonlinearity in the pressure-volume (P - V) relationship³³⁾.

We can evaluate the nonlinearity of an artery using the V/V_0 - P relation curve. This nonlinearity can also be evaluated by observing the changes in the relative vascular volume (V/V_c). Systolic blood pressure and mean blood pressure are measured by using the system with photosensors to detect the change of the intensity of transmitted light under pressure from the cuff.

b) application

To study the elastic properties of arteries, I calculated V_{30}/V_0 by V_0 at $P_{tr} = 0$ and V_{30} at $P_{tr} = 30$ when the transmural pressure (P_{tr} : MBP- P_c) reached 0 mmHg and 30 mmHg, respectively^{34-36, 81-83)}. V_{30}/V_0 tended to decline with aging^{36,80)}. This result agreed with the finding of Ando³⁴⁾. It also suggested that V_{30}/V_0 reflects the arteriosclerotic changes associated with aging.

However, we also observed an abnormally high V_{30}/V_0 , an

unclear SBP, and an unclear MBP in a number of the chain saw operators. In these cases, it was impossible to evaluate the elasticity of the artery or to use V_{30}/V_0 to ascertain the nonlinearity of the digital arteries (Fig.7)⁸⁰⁾.

The aim of this study was to evaluate the mechanical properties of digital arteries by observing the closed or open condition of these arteries using photosensors when cuff pressure was applied. For this purpose, we examined the relative vascular volume (V/V_c) on the basis of the vascular volume at a constant low level of P_c ⁸⁰⁾. The evaluation of the nonlinearity of the digital arteries of chain saw operators was thus performed using V/V_{40} . As shown in Fig.8, the changes in vascular volume were evaluated through changes in V/V_{40} in relation to the P_c reduction rate in the chain saw operators. The fingers of healthy controls, the asymptomatic fingers of chain saw operators without VWF, the fingers of chain saw operators with mild VWF, and the fingers of chain saw operators with severe VWF could be distinguished by changes in V/V_{40} .

The author established a standard for the decrease in the opening of the digital arteries when the reduction rate of P_c was 25%, 50%, and 75% (Table 3)⁸⁰⁾. We also classified the decrease in the opening of the digital arteries into four grades: 0, 1, 2, and 3. Table 3 shows the relationship between this classification and the severity of VWF. Of the 20 fingers examined for the ten asymptomatic chain saw operators 12 were classified as grade 0, five as grade 1, and three as grade 2 or 3. By contrast, there were no grade 0 fingers among 23 fingers of chain saw operators with VWF. Among 20 fingers with VWF, 17 were classified as grade 2 or 3. Of 12 fingers with severe VWF, seven were classified as grade 3, four as grade 2 and one as grade 1. Middle fingers with no VWF on the left hand of three subjects with mild VWF of right-hand fingers were classified as follows: one finger as grade 1, one as grade 2, and one as grade 3. Thus, this classification of the delay in opening was clearly related to the severity of VWF. Therefore, our observations indicated that changes in the nonlinearity of the arteries increased with the severity of VWF.

The author also classified the pattern of mechanical proper-

Table 3 Classification of the arterial opening disturbance in fingers of workers using chain saws.

Group Grade		Number of fingers				Total
		Group with no VWF no symptoms	Group with VWF Severity			
		no attacks	mild	severe		
Grade 0	V(25)≥0.05 V(50)≥0.25 V(75)≥0.50	12	0	0	0	12
Grade 1	V(25)<0.05 V(50)≥0.25 V(75)≥0.50	5	1	2	1	9
Grade 2	V(25)<0.05 V(50)<0.25 V(75)≥0.50	2	1	5	4	12
Grade 3	V(25)<0.05 V(50)<0.25 V(75)<0.50	1	1	1	7	10
Total		20	3	8	12	43

V(25), V(50) and V(75) are the relative volumes at 25%, 50%, and 75% reduction of cuff pressure (Pc) from SBP to 40 mmHg, respectively.

Mild and severe VWF mean several VWF attacks in the last year (once a month in the winter) and frequent VWF attacks in the last year (at least once a week during the winter), respectively.

ties (Table 4). Grade 1 signifies degeneration and hardening of the tissue surrounding the blood vessel, as well as slight functional changes in the vessel walls. V_{30}/V_0 appears to be abnormally high because the nonlinearity of peripheral arteries has changed slightly (Fig.8). In Grade 2, in which the delay in the opening of the artery lasted until the Pc reduction rate reached 50%, we suggest that an organic change occurs in the blood vessel walls resulting in stricture in the central portion of measurement and in decreased blood inflow. These changes suggest that MBP could not be determined and the increase in vascular volume was delayed because the nonlinearity of the digital arteries had already changed. In grade 3, in which the delay in the opening of the artery lasted until the Pc reduction rate reached 75%, we posit that the blood inflow decreases greatly due to advanced organic changes accompanied by severe stricture. This severe organic change suggests that SBP became unclear, and that the increase in vascular volume was delayed because the nonlinearity of the digital arteries had changed greatly.

The mechanical properties examined here were considered to be useful for the assessment of vasodilation following collapse or constriction of digital arteries induced by various loads other than external pressure. The delay in the opening of the digital arteries observed in VWF patients suggests a vasodilative disorder, and implies a relationship between changes in the mechanical properties and the vasodilation of the digital arteries. Thus, the same delay can be expected during recovery from other transient circulatory disorders.

There have recently been reports that a β -adrenergic vasodilating mechanism exists in peripheral arteries with arteriovenous anastomosis (AVA) and that it is involved in the onset of Raynaud's phenomenon in primary Raynaud's disease^{84, 85}. Nazzari et al. reported that the opening rate of AVA is important

Table 4 Hypothesis of the relationship between arterial mechanical property patterns and classification of the arterial opening disturbance.

Grade	Detection of Ps from the AC component	Detection of Pm from the AC component	Nonlinearity of the pressure-volume relationship	Calculation of the vascular volume ratio (V/V ₀)
Grade 0	+	+	→ (normal)	+
Grade 1	+	+/- (not clear)	↓ (slight change)	+
Grade 2	+	-	↓ (moderate change)	-
Grade 3	-	-	↓ (severe change)	-

See Table 3 for the grades. Ps: systolic blood pressure; Pm: mean blood pressure See Fig. 7 for V/V₀.

Fig. 8 Relative vascular volume (V/V_{40}) plotted against the rate of reduction in cuff pressure (Pc) from systolic blood pressure (SBP) in the middle fingers of healthy subjects without exposure to vibration and in those of chain saw operators with and without VWF symptoms. Fingers without symptoms did not include the middle finger on the left hand of three chain saw operators with mild VWF. V_{40} is the vascular volume at $P_c = 40$ mmHg. Values are mean and 2SEM (double standard error). The statistical significance was low compared to the corresponding values of fingers of healthy subjects: * $p < 0.01$; ** $p < 0.001$, of fingers without symptoms: a, $p < 0.05$; b, $p < 0.01$.

in recovery from transient circulatory disorders induced by exposure to cold⁸⁶.

If one wavelength is used, we must take the intensity of the transmitted light for blood vessels collapsed by pressure into consideration in the signal treatment. It is expected that this problem can be solved if two wavelengths of light in the absorption range where reduced hemoglobin is the same as oxidized hemoglobin, which corresponds to total hemoglobin, are used. Intravascular volume can be seen as the movement of the absolute value by the improvement of such signal treatment. I think that slight, moderate and severe changes can be evaluated quantitatively. As mentioned, if 2 wavelengths are used, I believe that there is a diagnostic application in the measurement of the mechanical properties of arteries.

Fig. 9 Extinction coefficient of HbO₂ and Hb in each light wavelength.

2) The observation of tissue blood volume

PDs which utilized 2 wavelengths around 570 nm and 800 nm, which correspond to all hemoglobin, were used for the observation of tissue blood volume (Fig.9)^{36, 43}. The blood volume measured by photosensors and the blood flow measured by the laser Doppler method at the fingertip were determined at the same time when the proximal part of the finger was placed under pressure by the cuff. Blood volume increased together with a decline in blood flow due to the pressure. This is thought to be due to the inhibition of the venous return to the center. Arterial blood flow started again with the decline of the cuff pressure. The blood volume of the tissue increased at the same time. This increase is thought to be due to the fact that only the inflow of the blood to the finger began in the state where there was no venous return. When cuff pressure decreased further, venous return started again, and the blood volume decreased (Fig.10).

In this way, the congestive state of the fingertip which is different from the movement of blood flow, can be observed from the change in blood volume. The blood volume of the fingertip in cold water immersion was observed in healthy subjects. Blood volume became lowest in the fourth minute following immersion about two minutes earlier than the peak of skin temperature. Following this, the blood volume recovered earlier than skin temperature with changes that showed cold-induced vasodilation, and recovered promptly after the stop of immersion. This result indicates that blood volume reflects blood flow, and shows an earlier response than skin temperature^{36, 43}.

3) Problems of measurement using photosensors

The permeability of living body tissue to light with wavelengths of 700-1,200 nm is large, and the light is able to easily pass through it^{87, 88}. This characteristic has been utilized, and an attempt to see through a living body has been made^{89, 90}. While information about the structure could be obtained, there was a problem in that resolution was poor due to dispersion. Recently, attempts to detect breast cancer have been reported⁹¹⁻⁹³. On the other hand, changes in the blood flow and functional information such as oxygen state and metabolic information can be obtained by continuous measurement of oxidized Hb, reduced Hb and all Hbs^{43, 51}. If the cuff pressure and other factors are combined, we can also get indices such as the mechanical properties of peripheral arteries^{36, 80}. Though it has the advantage of being a noninvasive measurement, it has weak points in that there is a limit to the optical depth and an absolute value for the

Fig. 10 Comparison of blood flow movement by the laser Doppler flowmeter and blood volume movement by the two-wavelength spectrometric method during pressure by the cuff.

absorption intensity can not be obtained. If such technical problems as these can be overcome in the future, we can expect to see development of noninvasive measurements such as light-CT.

5. Ending remarks

The author attempted to clarify the development of medical techniques for the measurement of peripheral circulation in the living body. Methods using photosensors will result in techniques with (1) high sensitivity, (2) low invasion or noninvasion and (3) image processing. In image processing, especially two-dimensional measurement has been attempted by scanning of the laser beam in the laser Doppler method and the image measurement of skin blood flow distribution is possible⁹⁴. A new technique where the thermal conductivity of the skin was treated as an image using a thermograph has also been reported⁹⁵.

There will also be improvements resulting in (4) high precision, (5) miniaturization and (6) increased speed, which will influence peripheral circulatory measurement directly. In other words, with these techniques we will be able to get more accurate absolute values with small sensors of dynamic objects such as blood flow.

From this point, the ideas of medical researchers become more important. That is, it becomes important how we improve the engineering techniques and how we introduce them to clinical practice.

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