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Monitoring of Peripheral Vascular Condition Using a Log-Linearized Arterial Viscoelastic index During Endoscopic Thoracic Sympathectomy

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Abstract— **This paper proposes a novel technique to support the monitoring of peripheral vascular conditions using biological signals such as electrocardiograms, arterial pressure values and pulse oximetry plethysmographic waveforms. In this approach, a second-order log-linearized model (referred to here as a log-linearized peripheral arterial viscoelastic model) is used to describe the non-linear viscoelastic relationship between blood pressure waveforms and photo-plethysmographic waveforms. The proposed index enables estimation of peripheral arterial wall stiffness changes induced by sympathetic nerve activity. The validity of the method is discussed here based on the results of peripheral vascular condition monitoring conducted during endoscopic thoracic sympathectomy (ETS). The results of ETS monitoring showed significant changes in stiffness variations between the periods before and during the procedures observed ($p < 0.01$) as well as during and after them ($p < 0.01$), so that it was confirmed that sympathetic nerve activity is drastically decreased in the area around the monitoring site after the thoracic sympathetic nerve trunk on the monitoring side is successfully blocked. In addition, no change was observed in the values of the proposed index during the ETS procedure on the side opposite that of the monitoring site. The experimental results obtained clearly show the proposed method can be used to assess changes in sympathetic nerve activity during ETS.**

I. INTRODUCTION

Hyperhidrosis is a condition characterized by excessive sweating unrelated to temperature elevation, and is caused by sympathetic nerve hyperactivity. It is known that such sweating affects areas of the body with high concentrations of sweat glands, such as the hands, peripheral legs and armpits. Patients with palmar hyperhidrosis tend to suffer particular distress from the condition. Japan's Ministry of Health, Labour and Welfare reports that the total number of people with serious hyperhidrosis is as high as 0.8 million [1]. The first stage of hyperhidrosis treatment involves a dermatological approach such as external application of aluminum chloride and electrical therapy on the skin surface. For severely affected patients who remain unresponsive to such treatment, an operation known as endoscopic thoracic sympathectomy (ETS) is performed in which the sympathetic trunk near the spine at the thorax is blocked [2]. The success of the surgery is evaluated by monitoring the sweating stages of the patient over a period of several weeks. If the sympathetic trunk cutoff procedure proves insufficiently effective, ETS needs be performed again. To support accurate assessment for the success or failure of ETS, it is therefore very important to be able to monitor sympathetic nerve activity beyond the distal area of the blocked part.

Several methods for quantitative evaluation of surgical results based on biological signals have previously been reported. For example, Zhang *et al.* monitored electrocardiograms (ECGs) using a Holter monitor on a round-the-clock basis before and after ETS, and extracted time domain and frequency domain parameters from heart rate variability data [3], [4]. However, it is fundamentally impossible to determine the success or failure of sympathetic trunk blocking in real time during ETS with this method because it involves the use of ECGs observed after surgery. Meanwhile, it is well known that arterioles and other peripheral arteries are controlled by the sympathetic nerve and acutely respond to disturbances such as coarctation and atony [5]. Leveraging such physiological responses, Sakane *et al.* proposed a method for estimating the dynamic characteristics of peripheral arterial walls, whose characteristics depend on linear stiffness, viscosity, inertia and other aspects of mechanical impedance [6]. A method of determining the vascular condition of patients during ETS based on estimated impedance parameters has also been proposed by Sakane *et al.*. However, as it is known that the relationship between intravascular pressure and arterial wall diameter is non-linear [7], [8], estimated parameters depend on blood pressure changes in this method.

This paper proposes a novel technique to support the monitoring of peripheral vascular condition in consideration of the non-linear relationship between blood pressure and vessel diameter, and reports on the results of patient monitoring conducted during ETS.

II. A LOG-LINEARIZED PERIPHERAL ARTERIAL VISCOELASTIC INDEX

A. A Peripheral Artery Mechanical Model

In quantitative evaluation for the mechanical characteristic of peripheral arteries during ETS, the following points should

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be considered: (i) arterial wall mechanical characteristics can be evaluated using mechanical impedance parameters such as stiffness, viscosity and inertia; (ii) stiffness that are considered influences (such as the non-linearity between intravascular pressure and arterial diameter) except sympathetic nerve activity can be estimated; (iii) distinctive information on peripheral arteries (such as data indicating the effects of veins and accumulation in arterioles) can be expressed. This paper introduces a novel mechanical peripheral arterial wall model designed in consideration of these three conditions (Fig 1). Here, the arterial wall's characteristics in an arbitrary radial direction are considered, and are shown from changes in force and arterial diameter as follows:

$$\begin{aligned} F(t) &= F_\mu(t) + F_\eta(t) + F_\beta(t) \\ &\approx \tilde{\mu}\ddot{r}(t) + \tilde{\eta}\dot{r}(t) + \tilde{F_{\tilde{\beta}}}(r(t)). \end{aligned} \quad (1)$$

Here, $F(t)$ is the normal force acting on the arterial wall at the arbitrary time t; $F_\mu(t)$, $F_\eta(t)$ and $F_\beta(t)$ are the forces originating from inertia, viscosity and stiffness, respectively; and $\tilde{\mu}$ and $\tilde{\eta}$ are the arterial wall inertia and viscosity, respectively. $r(t)$, $\dot{r}(t)$ and $\ddot{r}(t)$ represent arterial diameter, the speed of changes in arterial diameter and the acceleration of changes in arterial diameter, respectively. Taking into account the non-linearity between intravascular pressure and arterial diameter, the force originating from arterial wall stiffness is expressed as $\tilde{F_{\tilde{\beta}}}(r(t))$.

The relationship between blood pressure and arterial diameter has been extensively investigated in previous experiments. For example, Nagasawa *et al.* measured canine intravascular pressure and arterial outside diameter with a femoral artery on an *in vitro* basis to support examination of the artery's mechanical properties [7], [8]. The results indicated that the canine femoral artery exhibits distensibility in the range of 60 – 180 mmHg. It was also found that the relationship of the ratio of logarithm intravascular pressure to standard pressure and the ratio of arterial outside diameter to arterial outside diameter with standard intravascular pressure are linear. However, in a case with low blood pressure, it was observed that the artery stiffened significantly because the blood vessel diameter variation that accompanies increased intravascular pressure became very small. Due to this fact, this paper assumes that human peripheral arterial characteristic is also non-linear as the canine femoral artery in terms of arterial wall mechanical characteristics. Here, the logarithm force originating from arterial stiffness in consideration of the many arterioles in peripheral areas is expressed as follows:

$$\ln\{\tilde{F_{\tilde{\beta}}}(r(t))\} = \tilde{\beta}(r(t) - r_0) + F_{\tilde{\beta}_0} + F_{\tilde{\beta}_{nl}}(r(t)). \quad (2)$$

Here, $\tilde{\beta}$ is the arterial stiffness relating to logarithm force, $r(t) - r_0 = dr(t)$ is the arterial diameter change, r_0 is the equilibrium point, and $F_{\tilde{\beta}_0}$ is the constant of the arterial wall. $F_{\tilde{\beta}_{nl}}(r(t))$ is a force originating from stiffness that cannot be log-linearized and accrues when intravascular pressure falls below a certain threshold. Equation (2) can be substituted into Equation (1) after taking the exponent on both sides

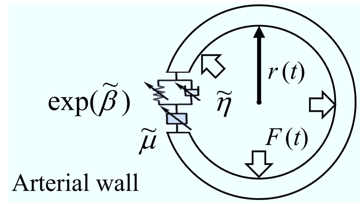

Fig. 1. Mechanical impedance model of a peripheral arterial wall

of Equation (2), and arterial impedance properties can be expressed as follows:

$$\begin{aligned} F(t) &\approx \tilde{\mu}\ddot{r}(t) + \tilde{\eta}\dot{r}(t) \\ &\quad + \exp\left\{\tilde{\beta}dr(t) + F_{\tilde{\beta}_0} + F_{\tilde{\beta}_{nl}}(r(t))\right\}. \end{aligned} \quad (3)$$

Here, for simplification and to support estimation of arterial wall non-linear impedance parameters, it is assumed that the blood pressure $P_b(t)$ is proportional to the force $F(t)$. Meanwhile, as it is difficult to measure vessel diameter changes $dr(t)$ directly *in vivo*, it is assumed that such changes can be approximated using photo-plethysmograms measured with a pulse oximeter [9]:

$$P_l(t) \cong k_p dr(t) + P_{l0}. \quad (4)$$

Here, $P_l(t)$ is the photo-plethysmogram, k_p is a constant of proportion, and P_{l0} is an offset constant. Equation (3) can be expressed using Equation (4) as follows:

$$\begin{aligned} P_b(t) &= \mu\ddot{P}_l(t) + \eta\dot{P}_l(t) \\ &\quad + \exp\left\{\beta P_l(t) + P_{b\beta_0} + P_{b\beta_{nl}}(P_l(t))\right\}, \end{aligned} \quad (5)$$

where,

$$\mu = \frac{\tilde{\mu}}{k_p}, \quad \eta = \frac{\tilde{\eta}}{k_p}, \quad \beta = \frac{\tilde{\beta}}{k_p}, \quad P_{b\beta_0} = F_{\tilde{\beta}_0} - \frac{\tilde{\beta}P_{l0}}{k_p},$$

and

$$P_{b\beta_{nl}}(P_l(t)) = F_{\tilde{\beta}_{nl}}(r(t))$$

represents blood pressure, which cannot be log-linearized and accrues when intravascular pressure decreases. Here, μ, η and β are the inertia, viscosity and stiffness of the arterial wall, respectively. Equation (5) represents the log-linearized peripheral arterial viscoelastic model, which can express peripheral arterial dynamic characteristics based on the mechanical impedance parameters of inertia μ, viscosity η and stiffness β.

B. Estimation Method of Proposed Indices

The method for estimating the impedance parameters of inertia μ, viscosity η and stiffness β in II-A is outlined here. It is difficult to estimate three impedance parameters at the same time due to the characteristic of $P_{b\beta_{nl}}(P_l(t))$, which cannot express linearity even if $P_{b\beta_{nl}}(P_l(t))$ is taken for the logarithm in the element originating with arterial stiffness (i.e., the stiffness element) in Equation (5). Accordingly, parameter estimation is performed in two stages. First, the stiffness element is approximated using Maclaurin series expansion. μ and η are estimated using the least squares method for each heartbeat. Second, substituting μ and η into Equation (5) gives an equation that can be used to separate the stiffness element from other elements. Subsequently, β can be estimated using the least squares method from the log-linearized stiffness element and measured photo-plethysmograms for each heartbeat in the range where the artery does not undergo significant stiffening. For the above, the impedance parameters of inertia μ, viscosity η and stiffness β for the arterial wall are estimated using the two-stage method. In this paper, the stiffness parameter β is proposed as a monitoring index value for peripheral vascular conditions.

III. Experiments

The proposed method was applied to support sympathetic nerve activity evaluation using biological signals measured during the T3 level of ETS on the right and left parts of the thorax for eight patients. During the ETS procedure, biomedical ECG signals, invasive right radial arterial blood pressure values (BP) and photo-plethysmograms (PPGs) of the right thumb were simultaneously measured at 125 Hz using a bedside monitor (BSS-9800, Nihon Kohden Corp., Tokyo, Japan) and entered into a computer via Transmission Control Protocol (TCP). As the biomedical signals were affected by various artifacts (such as light and mechanical stimulation of the patient's hand), the arterial pressure values and photo-plethysmograms were preprocessed using digital filters. The BP values and the PPG were filtered using a second-order IIR band-pass filter (0.3 – 10 Hz). Parameters with coefficients of determination of 0.95 or more between the measured and presumed blood pressure values were used to assess patient conditions.

First of all, the ETS was performed to block the right thoracic sympathetic trunk by clipping [10]. At this point, the stiffness parameter β in the vicinity of the measurement area (the right hand) rose with neural stimulus in line with the sympathetic nerve search, and the stiffness parameter β attenuated after the nerve was clipped because stimulation was cut off. Next, the sympathetic trunk of the left side was clipped. If the blocking of the sympathetic trunk on the right side with a clip was successful, the stiffness parameter β was not expected to change because the stimulus did not propagate from left to right. To check such changes in the stiffness parameter β associated with operation events, the value was normalized with the corresponding mean of values measured with the patient at rest, and focus was placed on a normalized stiffness β of 20 seconds as follows:

- rt-con: 400 seconds before the beginning of the search for the right thoracic sympathetic trunk for blockage
- rt-stim: 200 seconds before blockage of the right thoracic sympathetic trunk
- rt-post: 200 seconds after blockage of the right thoracic sympathetic trunk

Welch's t-test was used to determine the significance of differences between the stiffness parameter β of rt-con and that of rt-stim and between that of rt-stim and that of rt-post after the application of Bonferroni correction for each β, and differences were considered significant when results showing $p < 0.05$ were seen. The stiffness parameter β was also compared with the stiffness parameter $\tilde{K}$ for each event.

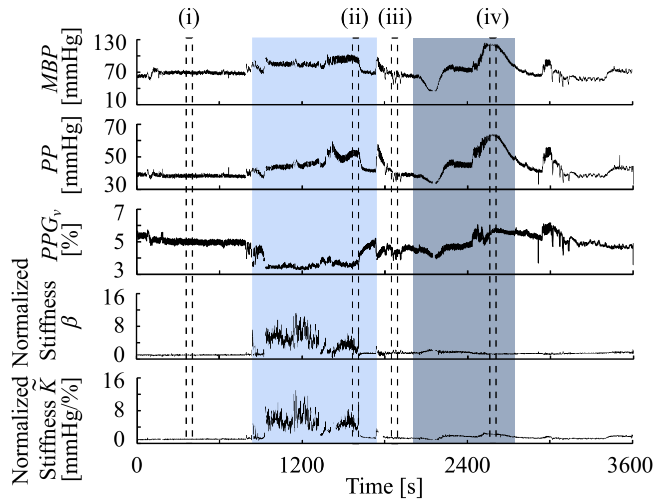

Fig. 2. Measured biosignals and estimated results for the stiffness parameters of the peripheral arterial wall in endoscopic thoracic sympathectomy (Patient A): (i) rt-con, (ii) rt-stim, (iii) rt-post and lt-con, and (iv) lt-stim

Informed consent was obtained from all study subjects before the experiments were performed based on the Declaration of Helsinki, and the approval of the Hiroshima University Ethics Committee was also obtained.

IV. Results

Figure 2 shows typical ETS data retrieved from Patient A. The figure plots mean blood pressure (MBP), pulse pressure (PP), photo-plethysmogram variation (PPG_v), the proposed stiffness parameter β and the conventional stiffness parameter $\tilde{K}$ [6]. The thick shaded area corresponds to the period during stimulation to search for the right thoracic sympathetic nerve, and the thin shaded area corresponds to the period during that for the left one.

Figure 3 shows averages of the proposed stiffness parameter β and the conventional stiffness parameter $\tilde{K}$ for rt-con, rt-stim and rt-post, respectively. The stiffness parameter β was 1.028 $\pm$ 0.028, 7.000 $\pm$ 2.785 and 1.173 $\pm$ 0.0.157 in the order of rt-con, rt-stim and rt-post, and the stiffness parameter $\tilde{K}$ was 1.035 $\pm$ 0.072, 8.001 $\pm$ 3.235 and 1.233 $\pm$ 0.276 in the same order. These results indicate a significant difference between rt-con and rt-stim for the stiffness parameters β and $\tilde{K}$, and between rt-stim and rt-post ($p < 0.01$). It is also seen that clipping of the right thoracic sympathetic trunk succeeded when PPG_v was stable or increased regardless of the rise in blood pressure seen during blocking of the left thoracic sympathetic nerve. The stiffness parameter β for lt-con (lt-con: 200 seconds before the beginning of the search for the left thoracic sympathetic trunk for blockage) and lt-stim (lt-stim: 200 seconds before the blockage of the left thoracic sympathetic

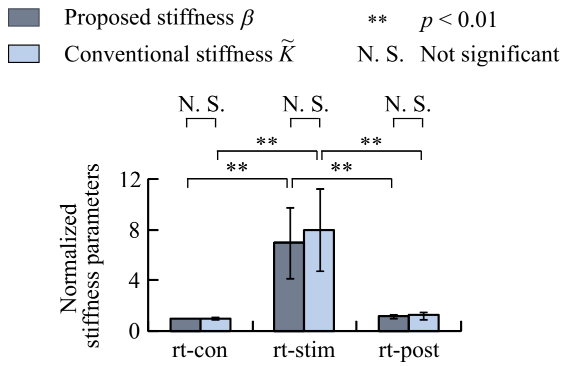

Fig. 3. Comparison of normalized stiffness parameters observed in endoscopic thoracic sympathectomy

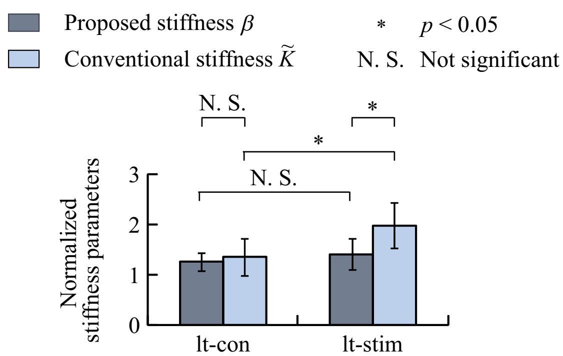

Fig. 4. Comparison of normalized stiffness parameters observed before and during left-side endoscopic thoracic sympathectomy

trunk) were then compared with the stiffness parameter $\tilde{K}$ of four patients for whom clipping of the right thoracic sympathetic trunk was considered successful. Figure 4 shows that the stiffness parameter β for lt-con was 1.266 ± 0.183, while that for lt-stim was 1.413 ± 0.313. In addition, the stiffness parameter $\tilde{K}$ for lt-con was 1.355 ± 0.368, while that for lt-stim was 1.989 ± 0.444. Here, it should be noted that blood pressure variations in some patients were not associated with blockage of the left thoracic sympathetic trunk because the anesthetic effect varies by individual. The results indicated a significant difference between the stiffness parameter $\tilde{K}$ of lt-con and that of lt-stim, and between the stiffness parameter β and $\tilde{K}$ for lt-stim ($p < 0.05$).

V. Discussion

Figure 3 indicates that the stiffness parameter β rapidly responded to stimulation associated with searching for the sympathetic nerve between rt-con and rt-stim. This suggests that the parameter increased because nerve stimulation constricted the peripheral arteries. Additionally, changes in the stiffness parameter β between rt-stim and rt-post were suppressed after clipping of the right thoracic sympathetic nerve. That is, the results suggest that the peripheral arteries relaxed rapidly from its previously tense condition. It is particularly worth noting that the estimated stiffness parameter β did not markedly increase around $t = 2550$ seconds during lt-stim (Fig. 2), although MBP was found to increase. At the same time, both the pulse pressure PP and the photoplethysmogram PPG_v variation increased. It was therefore concluded that the ETS on the right side was successful.

Figure 4 indicates that the conventional stiffness parameter $\tilde{K}$ (which is not considered the non-linear relationship between blood pressure and vessel diameter) changed during left-side ETS, while the proposed stiffness parameter β (which is considered non-linear relationship between intravascular pressure and arterial diameter) did not. This outcome strongly suggests that the proposed stiffness parameter β can be estimated for sympathetic nerve activity only without the effects of variations in peripheral arterial stiffness dependent on intravascular pressure.

VI. Conclusion

This paper presents a novel log-linearized peripheral arterial wall model in consideration of mechanical impedance, and also discusses the intravascular pressure dependence of arterial wall characteristics and an index for monitoring sympathetic nerve activity during ETS. Results obtained using the proposed index showed the feasibility of estimating changes in sympathetic nerve activity corresponding to operation events. The proposed index showed that the changes of sympathetic nerve activity corresponded with operating events could be estimated.

In future work, the authors plan to investigate the lack of linearity with blood pressure elements and to examine whether the model can be adjusted to other conditions such as pain testing and tilt testing.

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