

博士論文（要約）

Development of tissue circulation monitoring algorithm
and system based on multifunctional wearable device
(多機能ウェアラブルデバイスを用いた組織血流モニタ
リングのアルゴリズムとシステムの開発)

令和元年5月31日提出

指導教員 関野 正樹准教授

東京大学大学院工学系研究科

電気系工学専攻

37-167295

顧 剣

With the increasing expectance on quality of life of patients, plastic surgeries like tissue transplantation have been wide performed in recent years. However, a risk of compromised circulation due to thrombus in seven postoperative days required a regular checkup of medical staffs, which was labor consuming. Tissue circulation monitoring devices were developed to detect compromised circulation after tissue transplantation instead of medical staffs. Nevertheless, the real-time tissue monitoring is still challenging, because the conventional monitoring devices are incapable of one-week continuous monitoring due to the limitations of system size. In addition, the sensitivity and specificity of the system did not meet the demands of doctors.

This study proposed a multifunctional measurement system based on pulse wave, color and temperature signal for flap circulation monitoring using wearable flexible sensor probe. Thus, the aim of our system (TTM-3) was to realize continuous real-time monitoring at any position by improving the attachment and usability of the sensor probe, and to provide tissue information that is similar to clinical checkups to doctors by multifunctional probe. Two main tasks I solved were the evaluation of feasibility of measuring compromised circulation by proposed sensors and the development of algorithm that meet the needs of one-week real-time monitoring. To be specific, the principle of pulse wave, color and temperature signal change for normal and compromised circulation tissue is assessed. Furthermore, an algorithm that discriminates between three states -- normal circulation, compromised circulation, and artifacts is developed. The effectiveness of the system was accessed by rat experiment, healthy volunteer assessment and clinical study.

In rat experiment, simplified models for light tissue interaction and temperature change after blood occlusion are proposed based on Lambert Beer's Law and Gauge's two node model. The proposed model only focuses on the relationship between signal and change of blood volume in tissue structure. The epigastric flap rat model was used to provoke ischemia and congestion events by ligating artery and vein, respectively. The sensor probe measured both signals on the flap and reference control tissue at the same time. The raw pulse wave signal showed that the intensity of pulse wave had a steep decline after both arterial and venous ligation. The raw color signal showed that the red, green and blue light components decreased after venous ligation. The green and blue components increased after arterial ligation but the red component kept stable. The raw temperature signal did not change after ligation in most trials, but the one of the trails showed a decrease after arterial ligation. The results proved that raw pulse wave and color signal matched with the suggested model, but the temperature transition might not change in a short-term according to the position of flap and attachment of sensor.

Pulse power, lightness, temperature transition were used for evaluating intensity and speed of response for pulse wave signal, color signal and temperature signal respectively. Pulse power was the maximum peak value of spectrum, lightness of color signal was calculated by transform red, green, blue, and infrared component into XYZ colorimetric system. The continuous signal was evaluated by fitting exponential function. The intensity and speed of

response were corresponding to the amplitude of signal change and time constant transition parameters. Statistic study for both pulse power and lightness transitions showed significant differences between normal and compromised circulation group. The amplitude of lightness change yielded significant difference between ischemia and congestion group, which was the superiority of our monitoring system compared to the conventional devices. Speed of response of the pulse power and lightness was approximately 10 to 100s. The result proved that continuous measurement was feasible to verify existence and type of compromised circulation within a short period. Thus, signal of our device could be delivered to medical staff at real-time.

The safeness of TTM-3 monitoring system was required before being applied to healthy volunteers and patient. The electrical, mechanical, biological safety and EMC influence on other devices were basically evaluated or managed following standard written in JIS T 0601. The durability of the water-proof coating for flexible probe was assessed by our original 1000-time-bending and saline-soaking test because the existed standard did not match the situation. The result proved that 30 μm parylene coated probe could endure load of curvature radius down to 1 cm, a bending curve like cuffing on the wrist. Therefore, the probe was qualified to monitor most of the position on human. The mechanical test ensured that the cable and connector would not be teared off if the data transmitter fell on the ground. The biological precipitation test proved that the toxic materials would not be dissolved in organic resolution with 30 μm coating. And the electromagnetic wave produced from the device would not interfere with other medical devices.

The proposed algorithm solves two main problems for the application of flexible sensor. On one hand, the serious motion artifact would yield strong noise larger than pulse wave signal in spectrum, resulting in false calculation of pulse power. On the other hand, the slight unconscious motion would not yield a strong noise, but it still affects weakened pulse power during compromised circulation. The concept of the algorithm was to extract pulse wave signal by the counting the rate rather than by using the largest periodic signal of spectrum. Given the hypothesis that heartrate would not shift within a short period, the algorithm analyzes the convolution windows of the sample data. All possible peak of spectrum are extracted and the peaks from all windows are counted. The low count indicates a serious artifact, and the highest count indicates a pulse wave signal. The weakened pulse power hidden in the spectrum could be extracted by the proposed method. The useable pulse power data was then verified by its intensity value. The sample data would be judged as normal circulation If the intensity was larger than the threshold, and would be judged as compromised circulation if the opposite situation. The threshold was calculated by ROC method, applying data from all volunteers measured at rest. The judgement of circulation or motion artifact output could be obtained soon after loading the sample data.

Healthy volunteer assessment involved eight subjects. Algorithm for pulse wave alone was evaluated following rules of ethic in human study. Provocation of ischemia and congestion events was to change the pressure of forearm by sphygmomanometer. The measurement of

signal on different body position indicated that the pulse power varies one another. For all volunteers, the sensitivity and specificity of the algorithm when verifying normal and compromised circulation signals were 96.7% and 99.4% even when the signal was partially corrupted due to motion artifacts. Seriously corrupted data were identified as artifacts. The sensor probe cohesively attached to the body endured one-week load of daily life motion. The sensor probes were attached to volunteers even when they were taking a shower. Data usage and specificity during one-week monitoring on volunteers were $89.7 \pm 3.0 \%$ and $99.3 \pm 0.6 \%$, respectively. The results implied that the proposed algorithm was feasible to monitor the healthy subject continuously in one-week.

Clinical study further evaluated the performance of the system and algorithm in terms of judging a much natural procedure of compromised circulation event. Twenty-seven clinical cases including tissue transplantation at 8 parts of body were operated in within five facilities, and five of the cases were diagnosed as compromised circulation by doctors. Medical checkups twice a day were randomly picked up as reference of tissue circulation, and 221 references were obtained in the study. The distribution of pulse power for all doctor-judged results revealed that normal pulse power was significantly higher than that of compromised circulation. A threshold calculated by ROC could verify 27 cases including approximately 200,000 data with high accuracy. The risk value calculating the ratio of compromised circulation within a time period provided a user-friendly assessment of tissue. The algorithm outputs “risky” judgement when risk value exceeded 50%. The judgement outputs were compared with reference points one on one, and the sensitivity and specificity of patient monitoring are 85.0% and 97.5% respectively. Those results showed that the system and algorithm of pulse wave signal yield good result in verifying circulation compared with conventional manual methods, and was capable of assisting doctors in postoperative monitoring.

The algorithm of color and temperature signal based on the hypothesis that transition of the signal followed primary delay response after compromised circulation in clinical study. The convolution samples were fitted to exponential function, and the parameter of amplitude, time constant and goodness of fit were applied to make an index for risk of compromised circulation. The results showed that the algorithm for color signal could verify compromised circulation, but yielded false positive judgement due to the serious interference of artifacts as well. The algorithm for temperature signal could not verify compromised circulation effectively. It revealed that the condition we suggested for temperature signal should be reconsidered, and artifacts on color sensor should be solved for further application.