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Possibility of Extracting Feature Value from the Changes in Brightness over Time of Blood Coagulation in the Extracorporeal Circuit

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Abstract: Blood clotting is measured by using a pressure sensor in a blood circuit, but the sensor doesn't respond quick enough because the blood clotting can only be detected by an increase of the pressure caused by the clotting itself. This research is to evaluate predictive maintenance on MATLAB, based on our report at SEIA'2019 Conference for imaging data from a new sensing method for blood clotting (photoacoustic imaging with LED light). When the luminance of the imaging data (0-255 levels) was randomly analysed from photoacoustic imaging in a grid pattern, an increase or decrease of the luminance was seen at certain levels before and after the clotting. These important changes suggest that it may lead to a reduction in the amount of data handled during predictive maintenance of blood coagulation status.

Keywords: Blood clotting, Photoacoustic imaging, LED, Circuit in an extracorporeal device, Temporal observation, MATLAB, Predictive maintenance.

1. Introduction

Blood purification therapy is a method of treatments represented by haemodialysis and cardiopulmonary bypass (CBP). As the technology of a blood purification therapy advances, an apheresis treatment for autoimmune diseases and liver failure covers more indications and there are more cases that require a high-level management of an extracorporeal circulation device [1-3]. The therapy is a method of treatment that uses extracorporeal circulation, and a schematic diagram of the blood flow in the blood purification circuit is shown in Fig. 1. The blood is drawn out of the body by a roller pump during the treatment and comes into contact with artificial foreign materials such as a blood circuit and dialyzer. The blood that makes contact with an extracorporeal circulation device causes an acceleration of blood clotting.

Heparin was discovered as an anticoagulant treatment in 1915 and a sustainable anticoagulation therapy was established. At present Heparin is commonly used as an anticoagulant for a blood purification therapy [4-9]. However, because Heparin that is one of the anticoagulants behaves as a foreign body against blood, it's difficult to prevent the blood clotting completely on the surface of the circuit or in the dialyzer.

A pressure sensor is used to detect blood clotting in an existing extracorporeal circulation circuit. The

sensor reacts only after the circuit is clogged due to the blood clotting or when the pressure rises because the blood is difficult to flow. Therefore, a more sensitive method than conventional ones is needed to be able to observe the change of blood clotting state in an extracorporeal circulation circuit.

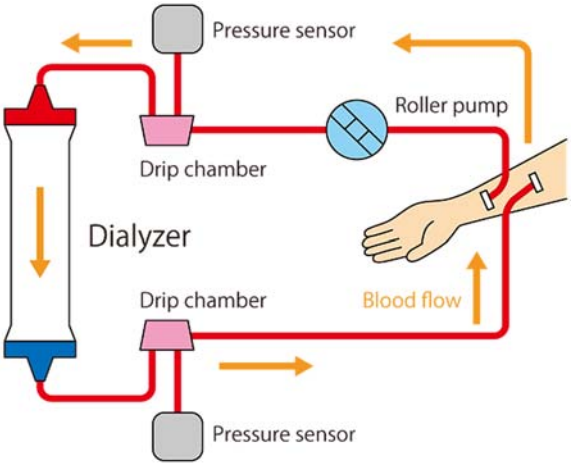


Fig. 1. Schematic diagram of the blood flow in the blood purification circuit.

Recently photoacoustic method was tried out as a measuring method to solve the aforementioned problem [10-12]. However, no report is available yet about the process of thrombus growth during the blood clotting in the blood purification circuit [13-15].

Photoacoustic imaging is a promising, structural, functional and molecular imaging technique for a wide range of biomedical applications, with the potential for high contrast and high spatial resolution.

Elastic waves, generated by volume expansion due to the heat, are received and imaged by an ultrasound probe. Recently, its application to blood flow has been reported [16]. Our research aims to observe the change of blood clotting over time that occurs in the extracorporeal circulation circuit during the blood purification therapy. When measuring the extracorporeal circulation circuit over time, a solid laser device that's conventionally used in photoacoustic measurement isn't suitable to use as a light source, because of its weight and size in order to constantly attach it to the extracorporeal circulation device and to monitor blood clotting over time. Therefore, this research used photoacoustic imaging with LED as a light source.

The extracorporeal circuit includes an air trap to prevent air contamination. In addition, a mesh filter is installed to prevent generated blood clots from flowing into the body from the external circuit. The air trap and mesh filter are installed in a drip chamber. Blood flow in the drip chamber is almost stationary due to the presence of the air trap and mesh filter as shown in Fig. 2. As a basic experiment, a microtube simulating the condition of the drip chamber is used.

Similarly to the previous research [17-19], blood was drawn from a mouse and put it into a microtube simulating the drip chamber and we performed photoacoustic measurement on blood clotting over time by the Acoustic X using an LED light as a light source.

In this paper, we propose a method for converting images from photoacoustic imaging that was obtained by the photoacoustic phenomenon to a smaller size. And we also show the result that was obtained the change of the luminance level before and after clotting on mode B from the results of photoacoustic imaging analysis is able to use machine learning.

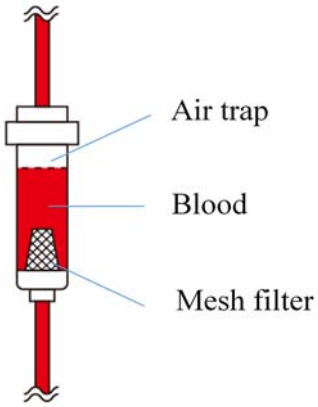


Fig. 2. The drip chamber.

2. Method

The setup for the experiment is the same condition as reported in SEIA2019. The wavelength on LED was 850 nm to obtain sufficient volume expansion of the light absorber. The light energy at the time was about 200 μJ/pulse. We used a 10 MHz ultrasonic probe and also ImageJ was used to convert images from photoacoustic imaging to luminance data [18, 20, 21]. Blood to be measured was put into a microtube simulating the drip chamber after it was taken out of a Mouse, and we observed the change of blood clotting state through a transparent plastic.

Fig. 3 (a), (b) and (c) show the results – (a) immediately, (b) 5 minutes after, (c) 10 minutes after mouse blood was filled and the state of blood clotting being confirmed. On the image of mode B, when photoacoustic phenomenon responds stronger, the image goes white, on the other hand, when it responds weaker, it goes black. We divided the luminance into 256 levels – the brightest photoacoustic phenomenon level is set as 255 and no response at all is set as 0.

If the observation of the changes on blood clotting state in the extracorporeal circulation circuit was carried on continuously, the data volume would be enormous. To avoid that and in order to reduce the data volume, we selected narrow area that has particular changes on luminance level before and after the blood clotting. Extraction of the luminance level was performed as follows.

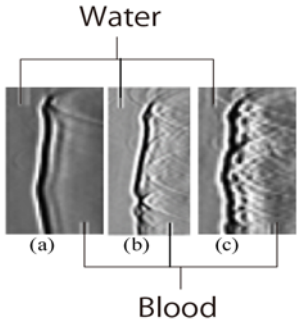


Fig. 3. Images from photoacoustic imaging (a) 0 mins after blood injection (b) 5 min (c) 10 min.

Using ImageJ to enlarge Fig. 3, the grid line (in green) and the analyzing range (red window) were established as shown in Fig. 4. By enlarging the image the most, a square (in green grid line) consists of 4×4 pixel. The area where the photoacoustic phenomenon remarkably appeared was set as the analysis range. In this analysis range (in the red window), 11 grid lines are arranged side by side, which is 176 pixels. Luminance per pixel sets the 256 levels from 0 to 255. The points where the photoacoustic phenomenon reaction was prominent were connected, it became 11 blocks from the outside of the wall surface of the microtube.

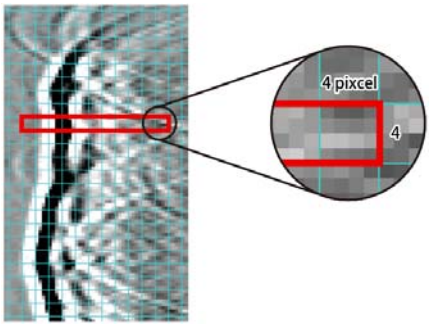


Fig. 4. Method of luminance level measurements at each pixel.

Histograms were created from the images in Fig. 3 (a), (b), and (c), and the change in brightness was analyzed and shown in Fig. 5. Fig. 3 consists of 1024×128 pixels. The horizontal axis in Fig. 5 is each brightness (0 to 255). The vertical axis is within 1024×128 pixels, which is the position of counts representing each brightness.

In the histogram of (a), the peak brightness was 128 and the position of pixels was 7887, in (b), the peak brightness was 139 and the number of pixels was 6831 and (c) after 10 minutes, the peak brightness was 148 and the position of pixels was 3792. For comparison of the graphs, the confidence interval was defined as the brightness value of confidence interval of 70 %. The brightness with more than the confidence interval of 70 % is 114 to 140 in (a) (confidence interval: 27), 123 to 155 in (b) (confidence interval: 33), and 126 to 170 in (c) (confidence interval: 45). As the coagulation progressed, the height of the peak and the position of the mountain moved to the higher brightness side. Therefore, as a reaction of the photoacoustic phenomenon due to blood coagulation became stronger, the brightness changed with time.

To make it easier to compare the temporal changes in Fig. 5, the peak positions and confidence intervals are shown in Fig. 6. The vertical axis (left side) is the peak brightness, and the vertical axis (right side) represents the brightness width of 70 % or more of the number of pixels of the image in the reliability range. The horizontal axis is the time (seconds) after encapsulation in the microtube. Since an approximate line of the transition between the peak and the confidence range becomes linear 120 seconds after encapsulation, it can be inferred that an exponential element is included. Especially at the peak, as shown in the log-log graph of Fig. 7, it becomes a straight line from (b) to (d), the mechanism needs to be considered.

Next, Table 1 shows the brightness level of each pixel in the measurement range shown in the red window.

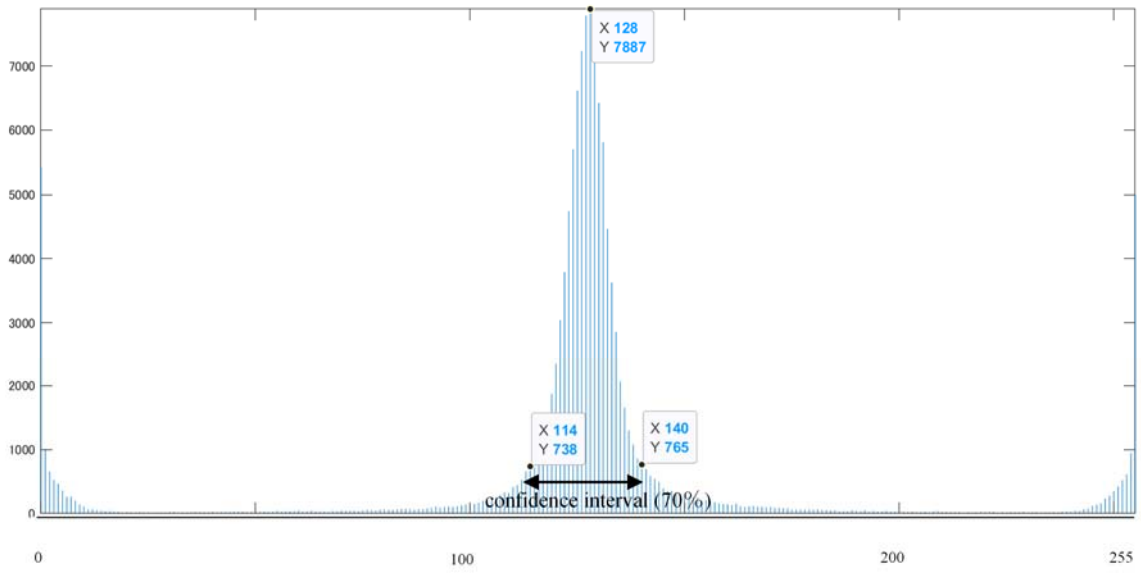
Table 1. Luminance analysis on the pixels of pictures obtained by photoacoustic imaging (a) Before blood clotting (0 mins after blood was filled) (b) after blood clotting (10 mins after blood was filled).

	Point of measurements							
Luminance	1	2	3	4	5	6	7	…
0	6	1	6	7	6	8	10	…
1	0	1	1	2	1	0	0	…
2	1	0	2	1	1	2	1	…
3	0	1	1	1	0	1	1	…
4	0	0	1	2	2	0	0	…
5	1	1	0	0	0	0	0	…
250	0	0	0	0	1	1	0	…
251	0	0	0	0	1	1	1	…
252	0	0	0	2	1	1	2	…
253	0	0	0	2	1	1	1	…
254	0	0	2	1	0	3	0	…
255	1	1	2	6	9	8	9	…
Total	176	176	176	176	176	176	176	…

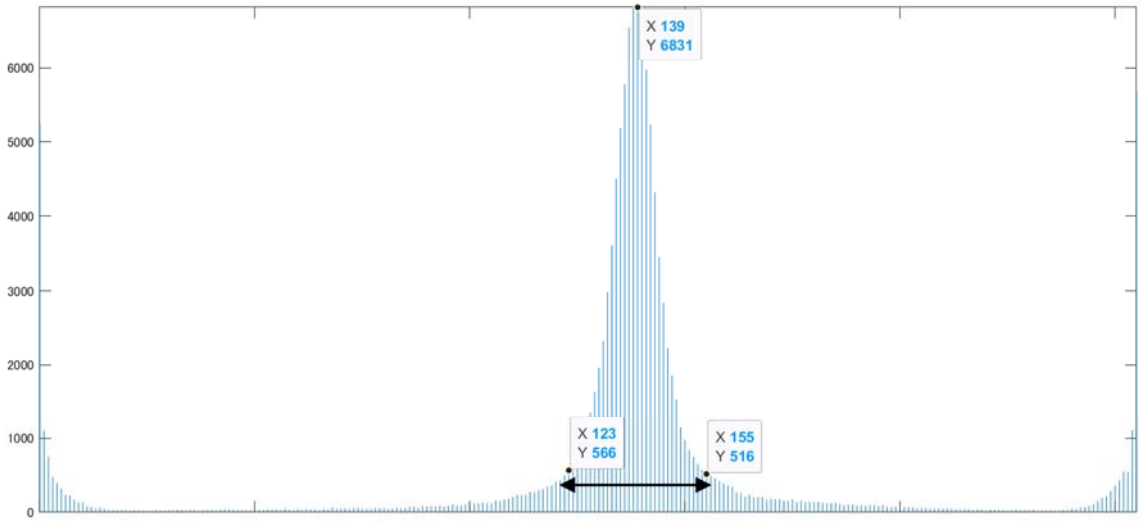
(a) Luminance analysis immediately after the mouse blood was filled into microtube. (Luminance levels: 0 to 5, 250 to 255).

	Point of measurements							
Luminance	1	2	3	4	5	6	7	…
0	8	8	8	9	11	11	7	…
1	1	2	1	1	1	2	3	…
2	0	1	2	2	2	2	2	…
3	0	3	1	2	0	0	0	…
4	0	2	0	1	1	1	2	…
5	2	3	2	0	2	1	0	…
250	2	3	1	3	1	2	2	…
251	0	0	0	2	1	1	0	…
252	4	1	1	0	4	5	4	…
253	2	2	3	3	4	6	5	…
254	1	2	0	2	4	3	5	…
255	18	15	17	20	23	14	14	…
Total	176	176	176	176	176	176	176	…

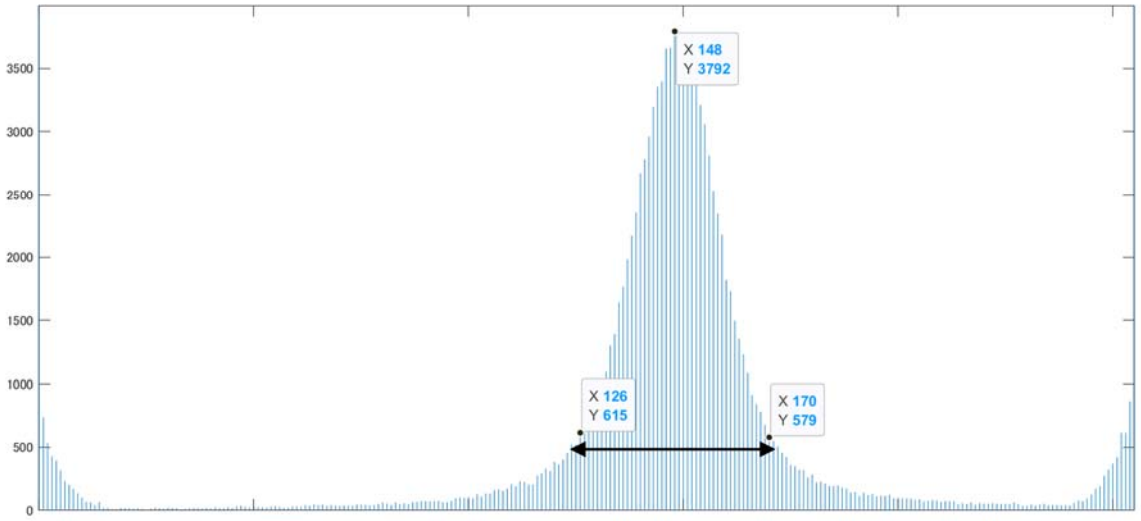
b) Luminance analysis immediately after the mouse blood was filled into microtube. (Luminance levels: 0 to 5, 250 to 255).



(a) Before blood clotting (0 mins after blood was filled)



(b) After blood clotting (5 mins after blood was filled)



(c) After blood clotting (10 mins after blood was filled)

Fig. 5. Luminance variation of the entire image obtained by photoacoustic imaging.

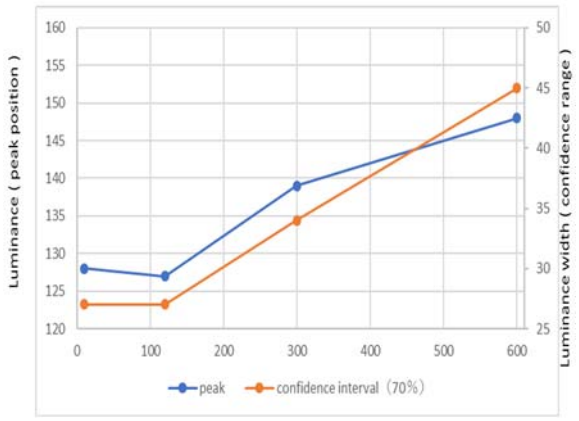


Fig. 6. Transition of peak and confidence range width (0 s, 120 s, 300 s, 600 s).

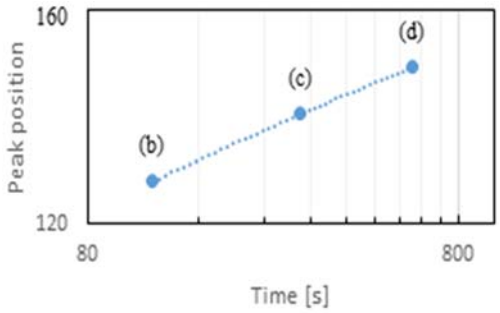


Fig. 7. Log-log graph of peak changes over time in Fig. 6.

Measurement was performed at 24 points along the microtube. In creating Table 1, MATLAB Diagnostic Feature Designer (MATHWORKS) was used to extract a feature value from the temporal change of the obtained mode B image.

Based on Table 1 measured as described on Fig. 4 and Fig. 5 shows a comparison of the counts at each luminance Table 1 (a) before blood clotting and (b) after blood clotting.

The creation process of Fig. 5 is as follows:

1) As shown in Fig. 4, one measurement range (red window) is divided into 176 pixels;
2) specify the brightness of each pixel and count them at 24 points in the microtube;
3) graph the counts at each measuring point as shown in Fig. 8;

and the vertical axis is the probability of each total count in 0 mins and 10 mins after blood injection graph (contribution ratio). The contribution ratio is by dividing each graph in Fig. 8 by total position. The contribution ratio shows how much each primary element accounts the rate of variation of the total. Graphs in orange and in blue show (a) before blood clotting (0 mins) and (b) after blood clotting (10 mins), respectively. It shows that the greater the difference between graphs in colored by orange and blue, which represented before and after the blood clotting. As an example, Fig. 8 shows a graph of luminance level at 255 and 254.

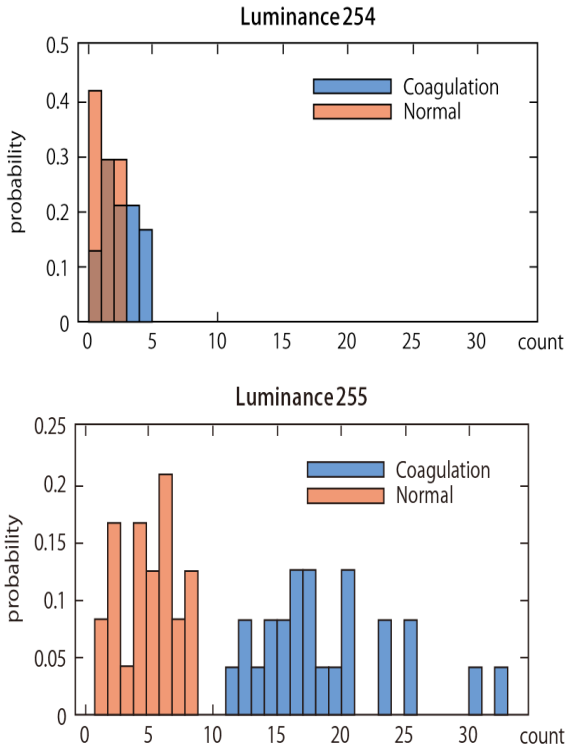


Fig. 8. Photoacoustic imaging at each luminance (comparison before blood clotting to after blood clotting in Fig. 3).

3. Results

In order to identify notable luminance levels for using future values for machine learning, Fig. 8 was subjected to T-test in MATLAB and ranked. T-test is a test that identifies the difference between the means of samples taken from two independent populations. Based on the ranking, Fig. 9 shows results of analysis by 5-point moving average to compare changes at each luminance level (0 ～ 255). The vertical axis and horizontal axis are the T-test and luminance, respectively. It can confirm that the larger the T-test values are, the more remarkable the changes are.

Also, Fig. 10 shows the result of T-test for a feature extraction. Results of the T-test at each luminance are colour-coded. 4 to 5 is in blue; 5 to 6 is in dark green; 6 to 7 is in light green; 7 to 8 is in yellow and 8 or more is in orange.

If the luminance of 6 or more on the T-test is considered as a feature value of blood clotting, the data would be too spread and it's difficult to comprehend, but with the luminance of 4 or more on the T-test, there would be more data avaialble to analyze. Therefore, 4 or more on the T-test and the range where luminance is gathered to some extent was used as a targeted data for analysis so that the volume of analysis data could be reduced.

As a result on this research, photoacoustic phenomenon at luminance level of 109 to 169 before and after blood clotting is likely to produce particluar changes.

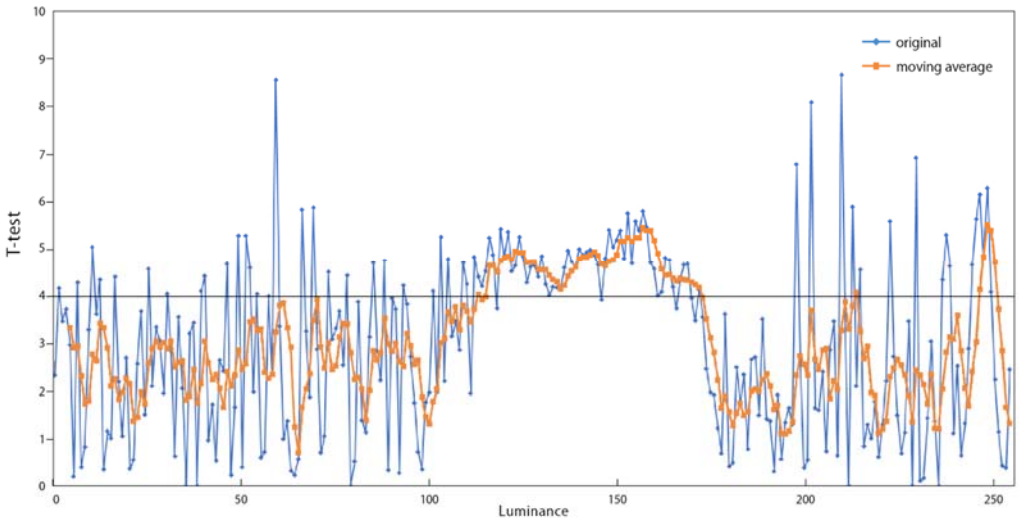


Fig. 9. 5-point moving average (based on Fig. 4).

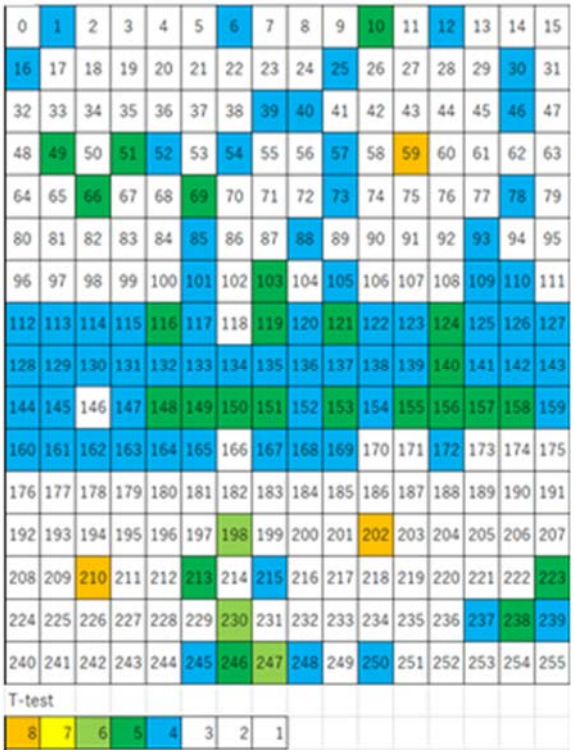


Fig. 10. Summary of T-test of before and after blood clotting on each luminance (0 to 255).

4. Conclusion

In the process of blood clotting within a microtube simulating an extracorporeal circulation circuit in a blood purification therapy, we extracted the feature values from volume of changes in photoacoustic phenomenon and identified the large range of luminance for the contribution ratio. The result shows possibility that when a temporal that when a temporal change of blood clotting in an extracorporeal circulation circuit is measured, the volume of the data handled is reduced.

In the extracorporeal circulation circuit, the drip chamber is used as a measuring site because the blood flow becomes extremely slow due to a filter for preventing coagulated blood from flowing into a human body. The drip chamber has a length of 12.5 cm (blood level: Approximately 7 cm) and a diameter of 7.5 cm, and the one that is used as a blood coagulation sensor by the bedside should be as a small size as possible. For that purpose, it is necessary to reduce the size of the light source and ultrasonic probe, and to select a measuring point where the photoacoustic phenomenon due to blood coagulation is prominent, instead of measuring the entire drip chamber in order to further reduce the amount of data to be handled.

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