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Quantification Method of Vascular Conditions by Capillaroscopy

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Abstract In this study, we proposed and examined the evaluation method for image processing of capillary vessels in the fingertips. Objectification of an image has many problems; especially, it is difficult to evaluate meandering of a blood vessel. Therefore we extracted the vessel shape from a clinical image, and simplified it to numeric data representing the characteristics of the shape. Using clinical illustration of the nailfold capillary, we investigated the characteristics of the nailfold capillary by feature point extraction techniques. We created a simplified program that automatically calculates the parameters of fingertip blood vessels from clinical images. This technique may be potentially useful to evaluate the status of capillaries after intake of supplements, by measuring the parameters of the microcapillary shape.

Keywords: microscope, nailfold capillary, image processing, radar chart.

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1. Introduction

According to the 2012 vital statistics report published by the Ministry of Health, Labour, and Welfare of Japan, vascular disorders such as heart disease and cerebrovascular disease are the causes of death in approximately 30% of the Japanese population. Blood vessels have been studied by various methods such as digitization using change in temperature obtained from thermography, blood flow measurement using infrared rays, pulse wave, and blood pressure [1, 2].

Microcirculation has been suggested as a contributing factor to vascular pathology. Impaired blood flow in lifestyle-related diseases suggests an involvement of the vasa vasorum, which are perivascular capillaries. Changes in the capillary structure are assumed to be the initial lesion of impaired blood flow. Observation of the nailfold capillaries by capillaroscopy is a simple, noninvasive technique and blood sampling is not required. In collagen diseases such as scleroderma, involvement of impaired blood flow is evident [3]. The contribution of impaired capillary to hyperlipidemia and other diseases with high prevalence is also becoming apparent.

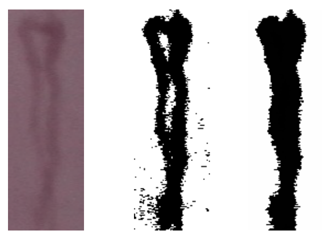
The health status of the capillaries has been conventionally determined through observation by experts in this field [4]. Although data on the relation between symptoms and shape of blood vessel have been reported [5], the data did not allow quantitative evaluation of the blood vessel. The need for the development of quantitative techniques is increasingly recognized. In this study, we developed a novel processing method for capillary fingertip imaging using microscopes. There were no studies that estimate morphological abnormalities of capillary image quantitatively, so our trial that digitize and evaluate the capillaries has originality.

Microcapillary parameters such as thickness, width, length and bend can be quantified using microscopic images. Our final objective is to contribute to the advancement of preventive medicine for vascular conditions in future.

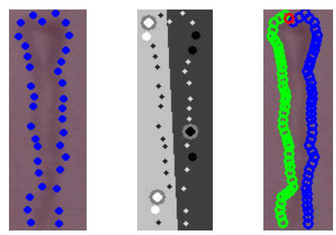
2. Method

2.1 Image processing example

Figure 1 shows serial processing of images of a capillary vessel in the fingertip. After binarization of the clinical image of **Fig. 1a**, the image contained noise, making further image processing difficult (**Fig. 1b**). Therefore, background noise was removed as shown in **Fig. 1c**. Noise processing was performed using raster scan labeling. This method examines the connected components in all pixels. If the area of connected component is small, the connected component is removed. As a result, noise such as small holes and connected components are removed from the image.



(a) clinical image; (b) binarization; (c) noise rejection



(d) feature extraction; (e) SVM (f) output

Fig. 1 Image processing flow.

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We deleted the bright internal domain to detect only the external shape of the blood vessel. In order to extract the contour of the capillary blood vessels from the image after noise processing, the Harris corner detection method was used to determine feature points on the blood vessel image (**Fig. 1d**). Corner detection is used because detection of the external shape of the blood vessels is easier than detection of the internal shape. Among several methods such as Harris method, KLT method and Hesse method, we chose Harris method because it is well known for corner detection. Using this method, feature points can be detected from a grayscale image using a smoothing process. To prevent erroneous detection due to noise contained in the image, a binary image was used.

There was no relationship between the feature points because they were discontinuous and only show position matching information. Therefore, to calculate parameters such as the bend, length, and width, the feature points classified into two classes; on the left or right side of the image, were subjected to numbering by the shortest distance of each feature point based on class. Classification was performed using the Support Vector Machine (SVM) method [6] (**Fig. 1e**). The SVM input is a coordinate, and the Kernel function is the straight line obtained from the mid-point, which classifies characteristic points into arterial side and venous side. Although polynomial kernel is more appropriate for blood vessels with complex shapes, a straight line is chosen as the first stage in the present study. Using this series of image processing, feature extraction was successfully performed, as shown in **Fig. 1f**.

2.2 Quantification

The normal profile for nailfold capillaries is a hairpin shape with thin lines, as observed in previous studies. In microcapillary blood flow disorders, the length of the nailfold capillaries is short, the width and vessel diameter are large, and the image is unclear with a meandering shape. Therefore, we selected six parameters for indexing (**Fig. 2**): bending frequency, vessel diameter, clearness, capillary width, blood velocity, and non-ellipticity. We quantified these parameters and examined their usefulness. In addition, we quantitatively evaluated changes in the microcapillaries after intake of supplement.

Vessel diameter and sharpness were measured from the capillary image, and length and bending were calculated from the feature points that were classified into two classes. Width was defined as the maximum distance between the arterial and venous sides, and thickness was measured in the artery, the bend, and venous sections. Clearness was defined as the difference in luminosity between a blood vessel and the background of the image. Velocity was calculated using the CapiScope [7].

Velocity was defined as the maximum blood flow. The vessel length (L), bending (q), and non-ellipticity (R) were calculated using equations 1, 2, and 3, respectively (**Fig. 2**). The location of point (i) was at x_i, y_i, and subsequent point (i + 1) was defined as x_{i+1}, y_{i+1}. The length L was obtained by integrating the distance of the extraction point. Bending q was obtained by integrating the angular change of the vector in length. q/L became the bending frequency. Non-ellipticity R was calculated from the surrounding area (S) and capillary width (W). The diameter ratio was defined as the ratio of the diameter of the blood vessel on the arterial side to that on the venous side.

$$l = \sum_{i-1}^{n-1} \sqrt{(x_{i+1} - x_i)^2 + (y_{i+1} - y_i)^2} \tag{1}$$

$$q = \sum_{i=2}^{n-1} \left(\pi - \cos^{-1} \left(\frac{(x_{i-1,i}^2 + y_{i-1,i}^2) + (x_{i,i+1}^2 + y_{i,i+1}^2) - (x_{i-1,i+1}^2 + y_{i-1,i+1}^2)}{2\sqrt{(x_{i-1,i}^2 + y_{i-1,i}^2)(x_{i,i+1}^2 + y_{i,i+1}^2)}} \right) \right) \tag{2}$$

$$R = \frac{\pi W^2}{4S} \tag{3}$$

3. Results

3.1 Image processing

Twenty-five persons were recruited by our institute to quantitatively evaluate nailfold capillary images before and after intake of a supplement. **Figure 3** shows the images of microcapillary from one subject. The outline of the vessel in **Fig. 3** was determined by the feature point extraction technique. We were able to quantify the parameters of the two capillaries shown as an example by microscopic observation. After eight weeks of supplement intake, meandering of the blood vessel improved slightly and the difference was well reflected in the quantification data. The degrees of hairpin turn and non-ellipticity decreased, and the length and flow velocity improved sharply (**Table 1**). In contrast, clearness, thickness, and width did not change. With our technique, the quantitative results were expressed as a radar chart in order to determine health condition (**Fig. 4**). The measured values were converted to radar chart values using the formula shown in **Table 1**. A radar chart value of 50 is standard, 100 is the best (scale of 50 is three times the standard deviation), and 0 is the worst. In addition, the area of the plot on the radar chart shows a wide area when blood flow is good.

The radar chart for one subject shown in **Fig. 4** shows that velocity, non-ellipticity, and degree of hairpin turn had improved

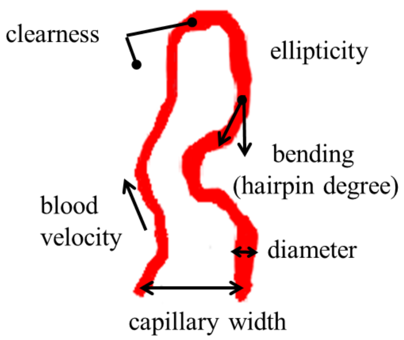

Fig. 2 Evaluation parameters.

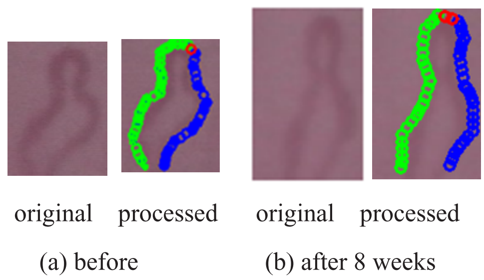

Fig. 3 Image processing of a fingertip blood vessel.

after intake of supplement. Improvement of mean blood velocity at four weeks or eight weeks suggested that the state of the blood vessel was improved, which probably led to the decrease in degree of hairpin turn, and the improvement of non-ellipticity. As for the reason why blood velocity increased, we propose three factors: decreased adhesiveness of blood cells including white blood cells and red blood cells, lowered plasma viscosity, and lowered coagulation factor activities. The contribution of each factor may be different among individuals.

In the example shown in **Fig. 4**, clearness, thickness, and width did not change. We confirmed the validity of the analysis, because increasing velocity, decrease in degree of hairpin turn and non-ellipticity are consistent with change in morphology of the capillary. Additionally, we have previously reported that three factors; the width of capillary, the diameter ratio and clarity, depicted on a radar chart were associated with serum triglyceride level [4]. The vessel width increases in diabetes, the clearness decreases in worse metabolism. The diameter ratio of the artery/vein is aggravated by the venous return failure.

Table 1 Quantification example.

	before	after	to radar chart
NE: non-ellipticity	0.42	0.22	100(1-NE/1.2)
B: bending (rot/mm)	4.44	3.17	100(1-B/7)
C: clearness	11.9	12.4	100C/24
W: capillary width (mm)	42.5	43.1	100(1-W/72)
D: diameter ratio	0.79	0.84	100D
V: blood velocity (mm/s)	414	1195	100V/1200

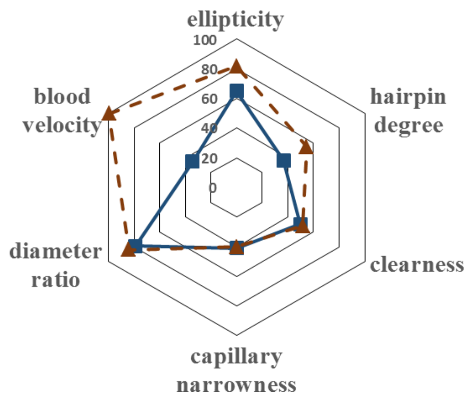

Fig. 4 Radar chart.

Table 2 Correlation coefficients of shape parameters (n = 25).

	hairpin degree	non-ellipticity	width	velocity	clearness	diameter ratio
hairpin degree		0.36	0.49	−0.23	0.12	0.22
non-ellipticity	0.36		0.68	−0.27	0.18	−0.06
width	0.49	0.68		−0.04	0.34	−0.01
velocity	−0.23	−0.27	−0.04		0.05	0.01
clearness	0.12	0.18	0.34	0.05		−0.02
diameter ratio	0.22	−0.06	−0.01	0.01	−0.02	

Table 3 Correlation coefficients of clinical parameters and shape (n = 25).

	hairpin degree	non-ellipticity	width	velocity	clearness	diameter ratio
total protein	−0.08	−0.06	0.00	0.30	0.12	−0.03
creatinine	0.16	0.22	0.09	−0.42	0.17	−0.04
uric acid	0.15	0.08	−0.01	−0.20	0.16	0.09
γ-GTP	0.23	0.13	0.26	−0.11	−0.02	−0.05
total cholesterol	−0.15	−0.20	0.00	0.38	0.26	−0.02
neutral fat	−0.19	0.08	−0.08	−0.12	0.02	−0.21
LDL cholesterol	−0.07	0.19	0.16	0.00	0.21	−0.03
HDL cholesterol	−0.10	−0.19	0.03	0.35	−0.02	0.00
blood glucose level	0.30	0.15	0.14	−0.15	−0.04	0.19
white blood cell	−0.12	−0.05	−0.12	−0.12	−0.22	0.00
red blood cell	0.10	0.01	−0.07	−0.16	−0.01	−0.07
hemoglobin	0.22	0.20	0.16	−0.33	0.11	0.02
hematocrit	0.20	0.18	0.13	−0.32	0.12	0.02
systolic blood pressure	−0.10	0.01	−0.22	−0.09	−0.09	0.06
diastolic blood pressure	−0.08	−0.05	−0.16	−0.10	−0.04	−0.04
pulse	−0.05	0.13	0.05	0.11	−0.10	−0.01

3.2 Correlation coefficients

When examining health indicators by radar chart, it is necessary to quantitatively evaluate the relationship between the parameters. Therefore, we calculated the correlation coefficients of each parameter with clinical laboratory test results (**Tables 2 and 3**). By tests of significance between shape parameters (**Table 2**), for parameters with correlation coefficients more than 0.3, no correlation was rejected and correlation was confirmed. The correlation coefficients between blood components and shape parameters were low (**Table 3**). Tests of significance confirmed low correlation. The correlation coefficients of the parameters were arranged on a radar chart in **Fig. 4** according to the magnitude of correlation in **Table 2**. Although non-ellipticity and crookedness have a negative correlation, two or more indices determine the bending conditions of a blood vessel. Hairpin degree and width has a positive correlation, which is considered an index for lipid metabolism. Moreover, a relation with other parameter such as metabolism, fatigue, and edema is suggested based on the correlation and clinical information of clearness.

It is unlikely that various blood chemistry values correlate with the shape parameters on an one-to-one basis. In the future, by correlating integrated factors with the shape parameters, it is expected that indicator of the overall condition can be obtained. However, the correlation was poor between various biochemical data and the shape parameter. Further studies should investigate conditions to obtain high correlation and identify the index indicating the overall status.

4. Discussion

The shape of the nailfold microcapillary is straight in a normal person. However, a variety of nailfold structures are observed in patients with diseases. Structures that are associated with inflammation and oxidation are known and are very useful for the early detection of the advanced stages of collagen disease such as scleroderma. However, the relationship between inflammation and oxidation, which is the cause of bending and thickening of the capillaries, has not been revealed. In this study, we aimed to determine the cause using several indicators based on imaging findings and flow velocity in capillaries. Flow rate and clarity changed easily, but bending and thickness did not change after a few hours. It is necessary to be objective using multiple indicators that reflect the status over several weeks, and express the results using a radar chart to be perceived intuitively. Capillary images as well as changes in blood flow are captured well by microscopic images. Moreover, the changes are easily visualized in a radar chart.

Although the width and diameter of the blood vessel have been suggested to be related to triglyceride levels [8], we observed a low correlation. In our study, vessel diameter was not included in the radar chart, because vessel diameter on the venous side increased when blood flow improved. Therefore, the software computed the ratio of the diameter of the vessel on the arterial side to that on the venous side (considered to be in a precongestion state), and used vessel diameter as one of the indices on the radar chart. We have already demonstrated a possibility of determining heart failure at a very early stage [9] based on the deformation of the nailfold capillary.

In this study, we showed a low correlation between non-ellipticity and degree of hairpin turn, and this issue requires further research.

5. Conclusion

We established an evaluation method of vascular conditions by processing images of the blood vessels in the fingertip. Using clinical images of the nailfold capillaries, we characterized fingertip capillaries by the feature point extraction techniques. We created a simplified program that automatically calculates parameters of fingertip blood vessels from the clinical images. This technique may be useful to evaluate the status of the capillaries after supplement intake, by measuring parameters of the microcapillary shape.

In the future, development of image processing with high accuracy is indispensable, and may be used to clarify the relationship between nailfold microcapillary deformation and vascular disease.

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We have no conflicts of interest relationship with any companies or commercial organizations based on the definition of Japanese Society of Medical and Biological Engineering.

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