Artificial Life and Robotics manuscript No.
(will be inserted by the editor)

Oxygen saturation of skin reflects blood flow and stagnation

Satoshi Yamamoto · Norimichi Tsumura · Tomokazu Yoshizaki · Keiko Ogawa-Ochiai

Received: date / Accepted: date

Abstract Skin is the largest organ of human body which can easily be observed non-invasively, but objective assessment of skin status is difficult. Therefore, we have focused on the oxygen saturation, and proposed the iterative optical path-length matrix method (OPLM) for estimating oxygen saturation of skin. Oxygen saturation of skin may help finding pre-disease state. In Kampo medicine (Japanese traditional herbal medicine), inspection of skin and tongue is one of the principal methods for diagnosis of the state. Kampo medicine contains a number of concepts which are useful for preventive medicine. The Oketsu status is a pathological concept in Kampo medicine, primarily denoting blood stasis / stagnation. In this study, we focused on oxygen saturation of skin as an objective index of skin properties, and studied correlation with the blood flow and the Oketsu score. First, we acquired Oketsu score of the patients, and measured oxygen saturation, hemoglobin concentration and blood flow of the patients at two locations: fingertip of the right first finger and dorsal surface of the right hand. Then, correlation among the values were calculated.

S. Yamamoto
Center for Kampo Medicine, School of Medicine, Keio University,
35 Shinanomachi, Shinjuku, Tokyo 160-8582, JAPAN
Tel.: +81-3-5366-3824
Fax: +81-3-5366-3825
E-mail: may-s@umin.net

N. Tsumura
Graduate School of Advanced Integration Science, Chiba University,
1-33 Yayoi-cho, Inage-ku, Chiba 263-8522, JAPAN

T. Yoshizaki
Department of Otorhinolaryngology & Head and Neck Surgery, Graduate School of Medical Science, Kanazawa University,
13-1 Takaramachi, Kanazawa, Ishikawa 920-8641, JAPAN

K. Ogawa-Ochiai
Clinic of Japanese–Oriental (Kampo) Medicine, Department of Otorhinolaryngology & Head and Neck Surgery, Kanazawa University Hospital,
13-1 Takaramachi, Kanazawa, Ishikawa 920-8640, JAPAN

As the result, the oxygen saturation showed large correlation with the blood flow and the Oketsu score at dorsal surface of hand. The oxygen saturation of skin will reflect systemic blood flow and Oketsu status, and it would help objective diagnosis by measuring skin color spectrum.

Keywords medical diagnosis · skin color spectrum · oxygen saturation · iterative optical path-length matrix method · Japanese traditional herbal medicine (Kampo Medicine) · blood flow

1 Introduction

Skin is the largest organ of human body which can easily be observed non-invasively, but objective assessment of skin status is difficult. Current diagnosis of dermatological disease is mainly dependent on subjective inspection by skillful physicians with macroscopic and microscopic view [1]. Skin should also reflect systemic change due to organic change. For example, heart or kidney failure causes edema, liver failure causes jaundice, and hormonal change in menopause sometimes causes so-called "hot flush". However, it is difficult to find onsets of the changes, as the observation is dependent on our subjective visual judgment.

Thermography has been proposed for assessment of skin lesion [2]. As it measures surface temperature of the skin, it is severely affected by the environment. Therefore, it is difficult to acquire an absolute value, while it is suitable to find a lesion in the intact skin. Blood flow imaging has also been proposed [3]. The system is resistant to environmental change. However, it is a little too large to install in the examination room of a clinic. Previously, we proposed the OPLM [4], and estimated oxygen saturation of skin using iterative OPLM [5]. OPLM is based on a Monte Carlo for multi-layered media (MCML), but can simulate skin spectral reflectance 27,000 times faster than MCML. As the inverse problem of MCML or OPLM is too complex to solve, iterating MCML or OPLM is necessary to estimate oxygen saturation. Hence, the OPLM was proposed as a faster alternative of MCML. With the algorithm, oxygen saturation can be estimated from a skin color spectrum, which is measured with a handheld device.

Oxygen saturation and blood flow of skin may help finding pre-disease state. Traditional visual examination can be milestones for finding the state. In Kampo medicine (Japanese traditional herbal medicine), the "four examinations", including inspection, listening / smelling examination, interview, and palpation, are defined as the methods for diagonsis [6]. Particularly, inspection of the skin and tongue is one of the principal methods for diagnosis. Additionally, Kampo medicine contains a number of useful concepts for preventive medicine. For example, "Mibyou" (disease-oriented state: not a disease, but can easily become one if no cure is applied) is one of the most important concepts for preserving health and preventing illnesses from developing by the early recognition of signs of abnormalities and their treatments. As a part of the Mibyou, the Oketsu status is denoted as the blood stagnation, and one

of the important pathological criteria in Kampo medicine. The Oketsu status reflects serum and blood viscosity [7] or aggregation of red blood cells in capillaries [8]. We previously developed a hyperspectral imaging system for tongue diagnosis [9,10]. The system revealed correlation between Oketsu score and tongue color spectrum. However, the system is too large, complex, and expensive for clinical use. Also, the tongue color is stable only for several seconds [11].

In this study, we focused on oxygen saturation of skin as an objective index of skin properties, and studied correlation among oxygen saturation, blood flow, and Oketsu score.

2 Materials and methods

2.1 Subjects

Thirteen data sets were acquired from 20 outpatients of the Clinic of Japanese–Oriental (Kampo) Medicine of Kanazawa University Hospital, or the Kampo Clinic of Japanese Red Cross Kanazawa Hospital (all Mongoloids, 2 males and 18 females, aged 50.1±14.4 years). All patients consented the study including measurements and examination in writing. None of the subjects had any serious skin disease. The Oketsu scores, diffuse reflectance of the skin, and laser speckle flowgraphy were taken from the participants. This study was approved by the Internal Review Board of Kanazawa University Hospital and Japanese Red Cross Kanazawa Hospital.

2.2 Measuring oxygen saturation of skin with iterative OPLM

Diffuse spectral reflectance was measured with a spectrophotometer CM-700d (KONICA MINOLTA, INC., Tokyo, Japan), with the 3-mm diameter aperture and the specular component excluded (SCE) mode. Reflectance measurements were performed at two locations: fingertip of the right first finger and dorsal surface of the right hand, where the spectrophotometer is stably measurable and can be easily localized on the image of laser speckle flowgraphy in the next subsection. Hemoglobin concentration and oxygen saturation at the two locations were estimated using the iterative OPLM as previously described [4,5]. First, we input arbitrary values to three variables, concentration of melanin, hemoglobin and deoxyhemoglobin, and compute skin spectral reflectance using OPLM. Then, we calculate the root mean square error (RMSE) between the measured spectral reflectance and the calculated spectral reflectance. Next, we revise the variables such that RMSE decreases. By repeating the steps, we estimate the three variables [12]. Figure 1 shows a scheme of the algorithm. Oxygen saturation is calculated as the fraction of oxyhemoglobin in hemoglobin.

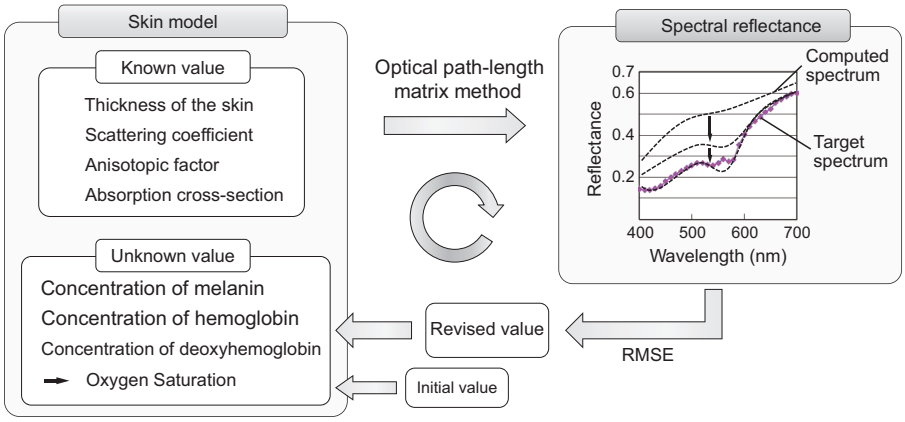

Fig. 1 Flow of the iterative OPLM
First, we input arbitrary values to the three unknown variables as the initial values, and calculate spectral reflectance using the OPLM. After comparing to the measurement value with the calculated value, the unknown values were input to the variables in the next cycle. By repeating this cycle, the unknown values are approximated.

This algorithm was implemented to retrieve the three unknown values: concentration of melanin, hemoglobin and deoxyhemoglobin, where oxygen saturation is calculated as the fraction of oxyhemoglobin in total hemoglobin [13].

2.3 Laser speckle flowgraphy

Blood flow of the skin was measured with a laser speckle flowgraphy LSFG-ANW-L (Softcare Ltd., Fukuoka, Japan). Blood flow images were taken from 19cm distance. Blood flow measurements were performed at two locations: fingertip of the right first finger and dorsal surface of the right hand. The measurement area of two locations were set manually avoiding blood vessels. Average values of the areas were calculated as the average of 10 seconds.

2.4 Oketsu score

The Oketsu status is defined as blood stagnation, one of the important pathological criteria in Kampo medicine, and the scoring system has been developed and frequently adopted [14]. The criteria for scoring are shown in Table 4. The Oketsu score was determined by an experienced clinician in Kampo medicine. The score was determined separately from two measurements above, and all measurement results were calculated together after finishing data collection to avoid biases from the results.

Table 1 Oketsu score
Oketsu score was previously determined by multivariate analysis conducted between symptoms described in the classics of Kampo medicine and clinical symptoms. Add full points for severe level of symptoms, and half points for moderate level. Oketsu is classified into the three levels by scores of <20 as non-Oketsu, <40 as moderate Oketsu, and ≥40 as severe Oketsu.

Symptoms	Male	Female
Dark-rimmed eyes	10	10
Areas of dark pigmentation of facial skin	2	2
Rough skin	2	5
Livid lips	2	2
Livid gingiva	10	5
Livid tongue	10	10
Telangiectasis / Vascular spider	5	5
Subcutaneous hemorrhage	2	10
Palmar erythema	2	5
Hemorrhoids	10	5
Dysmenorrhea	10	
Resistance and/or tenderness on pressure of:		
Right para-umbilical region	5	5
Left para-umbilical region	10	10
Umbilical region	5	5
Cecal region	5	2
Subcostal region	5	5
Right para-umbilical region	5	5

2.5 Correlation analysis

Correlation among the calculated values were computed by using the Pearson's product-moment correlation coefficient.

3 Results

The calculated values and correlation at fingertip of the right first finger are shown in Fig. 2 and Table 2, and at dorsal surface of the right hand are shown in Fig. 3 and Table 3. The values and correlation between two locations, fingertip and dorsal surface, are shown in Fig. 4 and Table 4. $0 \leq |r| < 0.1$: no correlation, $0.1 \leq |r| < 0.3$: small correlation, $0.3 \leq |r| < 0.5$: medium correlation, $0.5 \leq |r| \leq 1$: large correlation.

The hemoglobin concentration showed medium correlation with Oketsu score at dorsal surface of hand. The oxygen saturation showed large correlation with the blood flow and the Oketsu score at dorsal surface of hand, and medium correlation with the blood flow at fingertip. However, it showed small correlation with the Oketsu score at fingertip. The blood flow showed medium correlation with the Oketsu score at both locations. The hemoglobin concentration had small correlation with the oxygen saturation and the blood flow.

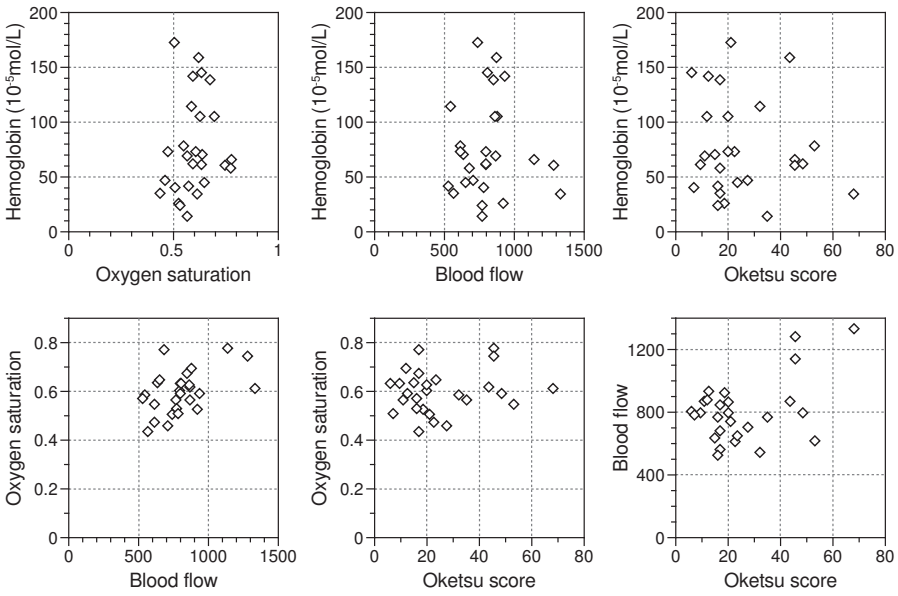

Fig. 2 Calculated values on fingertip

Table 2 Correlation at fingertip
Correlations among hemoglobin concentration, oxygen saturation, blood flow, and Oketsu score at fingertip of the right first finger are shown as r, Pearson's product-moment correlation coefficient.

	Oxygen saturation	Blood flow	Oketsu score
Hemoglobin	0.17	0.00	0.13
Oxygen saturation		0.47	0.16
Blood flow			0.45

Table 3 Correlation at dorsal surface of hand
Correlations among hemoglobin concentration, oxygen saturation, blood flow, and Oketsu score at dorsal surface of the right hand are shown as r, Pearson's product-moment correlation coefficient.

	Oxygen saturation	Blood flow	Oketsu score
Hemoglobin	0.26	0.20	0.42
Oxygen saturation		0.51	0.55
Blood flow			0.40

Table 4 Correlation between fingertip and dorsal surface of hand
Correlations between two locations are shown as r, Pearson's product-moment correlation coefficient.

Hemoglobin	Oxygen saturation	Blood flow
0.20	0.55	0.57

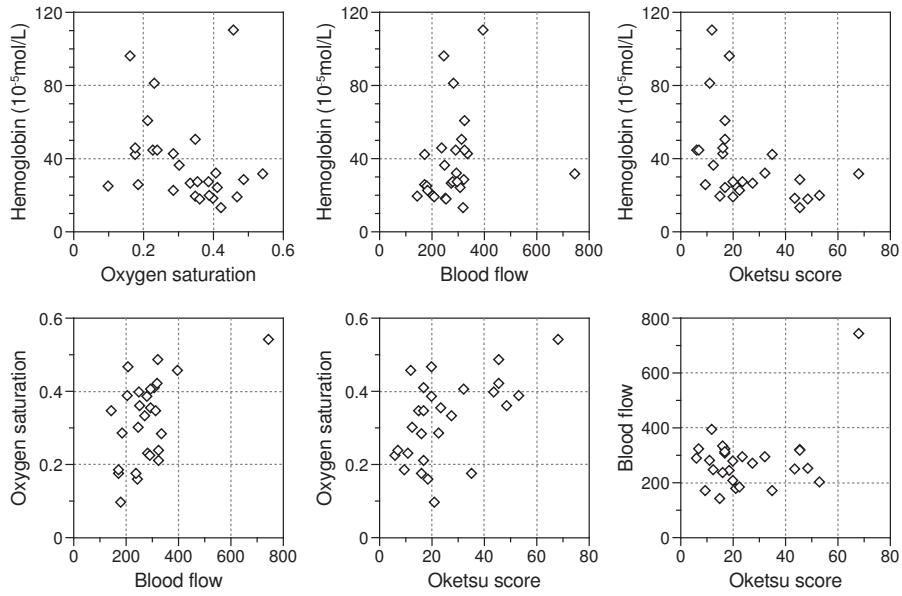

Fig. 3 Calculated values on dorsal surface of hand

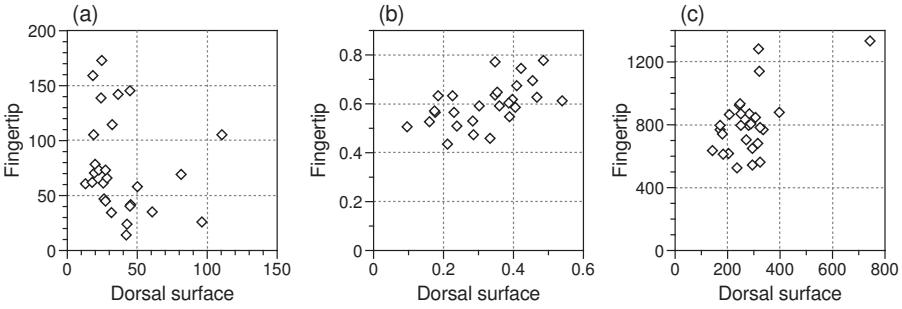

Fig. 4 Correlation between two locations

4 Discussion and conclusion

We measured blood flow and oxygen saturation of the fingertip and dorsal surface of the hand, and studied correlation among these values and Oketsu score. As the result, the blood flow and the Oketsu score showed large correlation with the oxygen saturation. The result indirectly revealed that the Oketsu score, traditionally defined as "blood stagnation" by its appearance, had been an actual phenomenon in the tissue. However, the Oketsu score showed small correlation with the oxygen saturation at fingertip. The difference between two locations is thought to be due to two physiological and anatomical differences. The first reason is that blood flow and sweating of palms and soles

are controlled by the autonomic nerves, mainly by the sympathetic nerve. Therefore, condition of fingertip can be easily affected by psychological status. Another reason is that the tips of fingers are sensitive to the environmental temperature, since its surface area is relatively wider. We need to measure more locations to find why this difference is caused.

For the future works, based on the trend of correlation acquired in this study, we need to study dispersion and the individual variation of the Oketsu score among the clinicians and patients to make the scores more precise. To discounting the variation, we need more subjects to average out the individual variations. Additionally, we need to determine the position where we can stably measure skin color spectrum to estimate oxygen saturation of systemic skin, or combining the results from the locations must be an another way to find better correlation. Difference among the locations maybe an indication for the systemic status. The oxygen saturation of systemic skin will reflect systemic blood flow and Oketsu status, which would help diagnosing a patient whose clinical feature is difficult to be acquired.

References

1. James, W. D., Berger, T., and Elston, D., [*Andrews' Diseases of the Skin: Clinical Dermatology*], Saunders, 11 ed. (3 2011).
2. Ring, E. and Ammer, K., "Infrared thermal imaging in medicine," *Physiological measurement* **33**(3), R33 (2012).
3. Nakagami, G., Sari, Y., Nagase, T., Iizaka, S., Ohta, Y., and Sanada, H., "Evaluation of the usefulness of skin blood flow measurements by laser speckle flowgraphy in pressure-induced ischemic wounds in rats," *Annals of plastic surgery* **64**(3), 351–354 (2010).
4. Yamamoto, S., Fujiwara, I., Yamauchi, M., Tsumura, N., and Ogawa-Ochiai, K., "Optical path-length matrix method for estimating skin spectrum," *Opt. Rev.* **19**(6), 361–365 (2012).
5. Yamamoto, S., Watanabe, S., Fujiwara, I., Tsumura, N., Akiba, T., and Ogawa-Ochiai, K., "Measuring oxygen saturation of skin with advancing age using iterative optical path-length matrix method," *Artif Life Robotics* **18**(3–4), 165–171 (2013).
6. Sato, Y., Hanawa, T., Arai, M., Cyong, J., Fukuzawa, M., Mitani, K., Ogihara, Y., Sakiyama, T., Shimada, Y., Toriizuka, K., et al., [*Introduction to Kampo — Japanese Traditional Medicine*], The Japan Society for Oriental Medicine. Tokyo: Elsevier Japan (2005).
7. Terasawa, K., Toriizuka, K., Tosa, H., Ueno, M., Hayashi, T., and Shimizu, M., "Rheological studies on 'Oketsu' syndrome: I. The blood viscosity and diagnostic criteria," *J Med Pharmaceut Soc WAKAN-YAKU* **3**, 98–104 (1986).
8. Terasawa, K., Itoh, T., Morimoto, Y., Hiyama, Y., and Tosa, H., "The characteristics of the microcirculation of bulbar conjunctiva in 'Oketsu' syndrome," *J Med Pharmaceut Soc WAKAN-YAKU* **5**, 200–205 (1988).
9. Yamamoto, S., Tsumura, N., Nakaguchi, T., Namiki, T., Kasahara, Y., Terasawa, K., and Miyake, Y., "Regional image analysis of the tongue color spectrum," *Int J Comput Assist Radiol Surg* **6**(1), 143–152 (2011).
10. Yamamoto, S., Tsumura, N., Nakaguchi, T., Namiki, T., Kasahara, Y., Ogawa-Ochiai, K., Terasawa, K., and Miyake, Y., "Principal component vector rotation of the tongue color spectrum to predict "mibyou"(disease-oriented state)," *Int J Comput Assist Radiol Surg* **6**(2), 209–215 (2011).
11. Yamamoto, S., Ishikawa, Y., Nakaguchi, T., Ogawa-Ochiai, K., Tsumura, N., Kasahara, Y., Namiki, T., and Miyake, Y., "Temporal changes in tongue color as criterion for tongue diagnosis in kampo medicine," *Forschende Komplementärmedizin/Research in Complementary Medicine* **19**(2), 80–85 (2012).
12. Tsumura, N., Kawabuchi, M., Haneishi, H., and Miyake, Y., "Mapping pigmentation in human skin from multi-channel visible spectrum image by inverse optical scattering technique," *J. Imaging Sci. Technol.* **45**(5), 444–450 (2001).
13. Young, A., "Chromophores in human skin," *Phys. Med. Biol.* **42**(5), 789–802 (1997).
14. Terasawa, K., [*KAMPO: Japanese–Oriental Medicine — Insights from clinical cases*], KK Standard Mclntyre (1993).