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Comparison of Antera 3D® and TcPO2 for Evaluation of Blood Flow in Skin

Kento Ikuta,* Kohei Fukuoka,* Yoshiko Suyama,* Maki Morita,* Yuka Kimura,* Ryunosuke Umeda,* Haruka Kanayama,*† Makoto Ohga,* Makoto Nakagaki* and Shunjiro Yagi*

**Department of Plastic and Reconstructive Surgery, Tottori University Hospital, Yonago 683-8504, Japan and †Department of Plastic and Reconstructive Surgery, Nagoya University, Graduate School of Medicine, Nagoya 466-8560, Japan*

ABSTRACT

Background There is a need for quick skin blood flow tests that can be performed in the wound healing field. Antera 3D® is a compact scanner using multispectral imaging. It can perform quick assessment of skin conditions. The purpose of the present study was to investigate the ability of the Antera 3D® to assess skin blood flow in comparison with transcutaneous partial pressure of oxygen (TcPO2) measurements.

Methods This study was conducted on 13 patients with a history of lower extremity ulcers. Measurements of hemoglobin average level (hereafter, Hb score) measured by Antera 3D® and TcPO2 measured by a transcutaneous blood gas monitor were obtained at the same sites on the dorsal foot and lower leg. Differences in Hb score and TcPO2 were analyzed by t-test for each measurement site and for the presence of peripheral arterial disease (PAD). The correlation between TcPO2 and Hb score was analyzed by Pearson's correlation coefficient.

Results Twenty-four limbs were tested. Hb score was higher ($P < 0.001$) and TcPO2 was lower ($P = 0.056$) in the dorsal foot compared to the lower leg. In the dorsal foot, Hb score was higher ($P = 0.023$) and TcPO2 was lower ($P = 0.046$) in patients with PAD compared to those without PAD. A significant negative correlation ($r = –0.68$; 95% confidence interval –0.85 to –0.38, $P < 0.001$) between TcPO2 and Hb score was observed in the dorsal foot.

Conclusion The negative correlation between TcPO2 and Hb score may reflect compensatory peripheral vasodilation due to occlusion or stenosis of central arteries. This study showed that Hb score measured by Antera 3D® may be related to skin blood flow.

Corresponding author: Shunjiro Yagi, MD, PhD
yagishun68@gmail.com
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Abbreviations: a.u., arbitrary unit; CI, Confidence Interval; CLTI, Chronic Limb-threatening Ischemia; Hb score, hemoglobin average level; IFU, instruction for use; LED, Light Emitting Diode; MSI, Multispectral Imaging; PAD, Peripheral Arterial Disease; TcPO2, Transcutaneous Partial Pressure of Oxygen

Key words blood gas monitoring, transcutaneous; diabetic foot; foot ulcer; microcirculation; peripheral arterial disease

Lower extremity ulcers occur against a background of various factors, including diabetes mellitus and impaired circulation. In the treatment of lower extremity ulcers, it is important to evaluate blood flow when wound healing is delayed due to insufficient blood flow. Transcutaneous partial pressure of oxygen (TcPO2) measurement, a commonly used skin blood flow test, is reliable but takes a long time to perform. Because lower extremity ulcers have a high risk of recurrence, frequent follow-up is recommended even after the ulcer has healed.[1] Therefore, a blood flow evaluation test that can be performed in a short time is required in clinical practice. Antera 3D® is a compact scanner that can quickly assess skin surface hemoglobin by multispectral imaging (MSI). In recent years, many reports on the clinical usefulness of MSI in the wound healing field have been published, but reports in Japan are limited.[2] Antera 3D®, which utilizes MSI, is a device mainly used in the aesthetic field, but has never been reported in the wound healing field.[3, 4] We conducted this study to investigate the potential application of Antera 3D® in wound healing by comparing it with TcPO2.

MATERIAL AND METHODS

Research Approval

This single-center observational study was approved by the Ethical Review Committee of Tottori University Hospital (No. 21A189). A summary of the study was made publicly available at the outpatient clinic and on the hospital website, which provided study subjects with the opportunity to opt out of the study.

Instruments

TCM400 transcutaneous blood gas monitor (Radiometer Limited, Copenhagen, Denmark)

TCM400 transcutaneous blood gas monitor is an instrument to measure TcPO2. TcPO2 is a method used to evaluate the cutaneous microcirculatory system, in which heating an electrode attached to the skin increases capillary blood flow and enables the partial pressure

Fig. 1. Antera 3D®. (**A**) Photograph showing the size and portability of the Antera 3D® device. (**B**) The 5.6 × 5.6 cm flat surface of the device is placed against the skin for imaging. (**C**) Diagram shows the application of visible light LED to the skin surface from multiple directions to analyze the concentration and scatter of hemoglobin. All images were sourced from Miravex Limited with the permission. LED, Light Emitting Diode.

of oxygen gas to be measured transcutaneously. This method is used to diagnose and evaluate the severity of lower extremity ulcers, determine the effectiveness of revascularization procedures, and predict wound healing.[5, 6] Normal TcPO2 values are ≥ 60 mmHg; values below 60 mmHg indicate impaired blood flow (40-59 mmHg: mild, 30-39: moderate, < 30: severe).[7] Its advantages include the ability to measure the area surrounding the ulcer painlessly, but the test takes a long time (approximately 30 minutes).

Antera 3D® (Miravex Limited, Dublin, Ireland)

Antera 3D® is a compact scanner designed for skin analysis (Figs. 1a and b). Skin was irradiated by seven visible-light Light Emitting Diodes (LEDs), and hemoglobin concentration and scattering from the epidermis to the dermis were analyzed by MSI (Fig. 1c), and output as an image of skin reflectance in different wavelength bands in the visible regions. MSI is a technology that analyzes images invisible to the naked eye by splitting light into multiple narrow bands. Spectral light irradiated on biological tissue undergoes multiple scattering and is absorbed by hemoglobin, water, and other substances in the tissue. This reflected light from this tissue is analyzed for quantitative evaluation of the hemoglobin in the tissue.[2] Specific measurement algorithms of MSI instruments vary by instrument, and the wavelengths and measurement algorithms utilized by Antera 3D® are not disclosed. Hemoglobin concentration is recorded as hemoglobin average level (hereafter, Hb score) and has arbitrary measurement units. Skin hemoglobin measurement by Antera 3D® has been reported to correlate with similar MSI instruments and has been used in the aesthetic field.[8]

Subjects

Thirteen patients (mean age, 78.4 ± 15.4 years; 9 males and 4 females) with a history of lower extremity ulceration and who were examined at Tottori University Hospital between 1 October 2021 and 31 October 2021 were included in the study. The patient demographics, clinical symptoms, comorbidities, and blood flow assessment laboratory data were collected from the electronic medical records. Of the 13 patients, peripheral arterial disease (PAD) was found in 9, diabetes mellitus in 11, and 7 received hemodialysis. Lower extremity ulcers were present in 8 patients at the time of examination. Lower Extremity Threatened Limb (Wound, Ischemia, foot Infection [WIfI]) Classification System[7] of the 8 patients with lower extremity ulcers was: stage 1 in 3 cases, stage 2 in 0 cases, stage 3 in 4 cases, and stage 4 in 1 case (Table 1).

Measurements

Two measurements were obtained: Hb score measured by Antera 3D®, and TcPO2 measured by a transcutaneous blood gas monitor.

Measurement of Hb score

Hb score was measured by Antera 3D®. Measurements were taken according to the attached instruction for use (IFU). Measurements were obtained after the patient had been resting supine or on their side for around 5 minutes out of direct sunlight in an air-conditioned examination room set to a temperature of 22.3–25.1 degrees Celsius and humidity of 61%. All measurements were performed by the same clinician. Each measurement site was wiped clean with an alcohol swab to remove skin oils before imaging. The scanner was placed on the skin, over each of two measurement sites:

Table 1. Baseline characteristics

	n = 13
Age (mean ± SD; years)	78.4 ± 15.4
Sex (male/female)	9/4
Peripheral arterial disease (%)	9 (69)
Diabetes mellitus (%)	11 (85)
Hemodialysis (%)	7 (54)
Ulcer (%)	8 (62)
Clinical stage for WIfI classification system	
Stage 1 (%)	3 (23)
Stage 2 (%)	0 (0)
Stage 3 (%)	4 (30)
Stage 4 (%)	1 (8)
WIfI classification: Wound	
Grade 0 (%)	0 (0)
Grade 1 (%)	3 (23)
Grade 2 (%)	5 (38)
Grade 3 (%)	0 (0)
WIfI classification: Ischemia	
Grade 0 (%)	0 (0)
Grade 1 (%)	5 (38)
Grade 2 (%)	3 (23)
Grade 3 (%)	0 (0)
WIfI classification: foot Infection	
Grade 0 (%)	7 (54)
Grade 1 (%)	0 (0)
Grade 2 (%)	1 (8)
Grade 3 (%)	0 (0)

SD, standard deviation; WIfI classification, Wound Ischemia foot Infection classification.

on the dorsum of the foot, 1–3 cm proximal to the bases of the first and second toes; and at the medial aspect of the lower leg, 3–5 cm distal to the medial tibial condyle, avoiding superficial veins, bony prominences, and any skin rash. The measurement sites were selected with reference to previous reports to minimize the effect on the TcPO2 value.[9] Antera 3D® scans the skin and acquires images. The time required for capture of one image was less than one second. The obtained images were then processed using the proprietary Antera 3D® software (Figs. 2a and b). The measurement site was marked as a circle with a diameter of 10 mm, and the Hb score in the range was recorded (Fig. 2c).

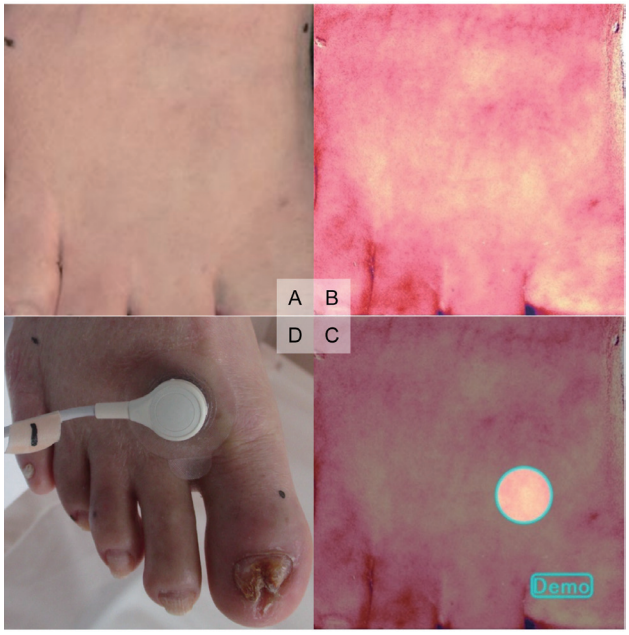

Fig. 2. Images of the measurement process. (**A**) Initial image taken with Antera 3D® that includes the pre-determined measurement point. (**B**) Image created in the supplied Antera 3D® software showing the concentration and scatter of hemoglobin. (**C**) The hemoglobin average level in the measurement point (10 mm diameter) marked in the Antera 3D® software is recorded. (**D**) Setup for TcPO2 measurement performed at the pre-determined point. TcPO2, transcutaneous partial pressure of oxygen.

Measurement of TcPO2

TcPO2 was measured immediately after measurement of Hb score. A TCM400 transcutaneous blood gas monitor was used to measure TcPO2 according to the attached IFU. A mounting ring was attached to the same measurement sites used for the Hb score measurements, contact fluid was added to the ring, and electrodes were attached to the ring (Fig. 2d). The electrodes were heated to 44°C. The TcPO2 (mmHg) was recorded at 20–30 minutes after the electrode was attached, when the value became almost constant.

Analysis

Differences in Hb score and TcPO2 were analyzed by t-test for each measurement site and for the presence of PAD. Scatter plots comparing the TcPO2 and Hb score were created and correlation between the values was analyzed using Pearson's correlation coefficient. The absolute value of the correlation coefficient (r) was defined as poor (0–0.2), weak (0.2–0.4), moderate (0.4–0.7), or strong (0.7–1.0). The 95% confidence interval (CI) was also computed. Values of $P < 0.05$ were considered to indicate statistically significant difference. All statistical analyses were performed using EZR, a

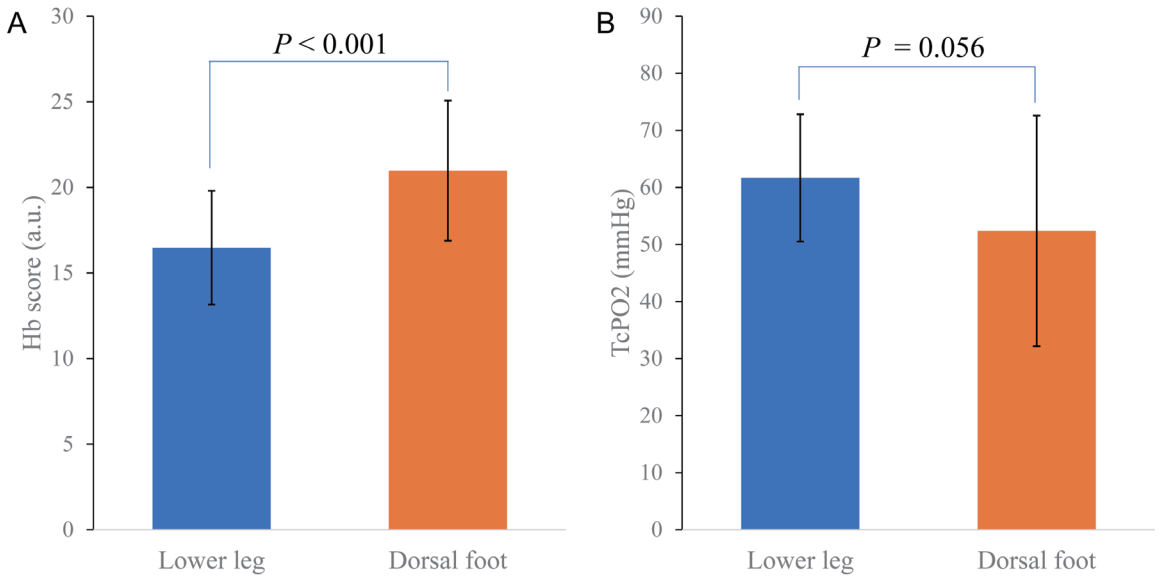

Fig. 3. Hb score and TcPO2 in the dorsal foot and lower leg. (**A**) Hb score is higher in the dorsal foot than in the lower leg ($P < 0.001$). (**B**) TcPO2 is lower in the dorsal foot than in the lower leg ($P = 0.056$). a.u., arbitrary unit; Hb score, hemoglobin average level; TcPO2, transcutaneous partial pressure of oxygen. Error bars indicate standard deviation.

statistical software that extends the functionality of R and R Commander, which is distributed free of charge on the website of Saitama Medical Center, Jichi Medical University.[10]

RESULTS

As 2/13 subjects (both male) had a history of unilateral major amputation, testing was performed on 24 limbs. TcPO2 and Hb score measurements were obtained successfully in all 24 limbs. The mean ± SD Hb score was 21.0 ± 4.1 a.u. in the dorsal foot and 16.5 ± 3.3 a.u. in the lower leg, with significantly higher in the dorsal foot ($P < 0.001$) (Fig. 3a). The mean ± SD TcPO2 was 52.4 ± 20.2 mmHg in the dorsal foot and 61.7 ± 11.1 mmHg in the lower leg, with lower in the dorsal foot ($P = 0.056$) (Fig. 3b). The mean ± SD Hb score in the dorsal foot was 22.3 ± 4.0 a.u. in patients with PAD and 18.3 ± 3.0 a.u. in those without PAD, and it was significantly higher in those with PAD ($P = 0.023$) (Fig. 4a). The mean ± SD TcPO2 in the dorsal foot was 46.9 ± 20.1 mmHg in patients with PAD and 63.4 ± 16.5 mmHg in those without PAD, and it was significantly lower in those with PAD ($P = 0.046$) (Fig. 4b). In the lower leg, there was no significant difference in Hb score or TcPO2 between patients with and without PAD (Fig. 4). A significant negative correlation was found between TcPO2 and Hb score in the dorsal foot ($r = –0.68$; 95% CI –0.85 to –0.38, $P < 0.001$) (Fig. 5a), but there was no significant correlation in the lower leg ($r = –0.18$; 95% CI –0.55 to –0.24, $P = 0.39$) (Fig. 5b).

DISCUSSION

To explore the potential of Antera 3D® as a new option for quick testing of lower extremity blood flow in clinical practice, this study examined the relationship between TcPO2 and Hb score measured by Antera 3D®. This study is the first investigation of Antera 3D® in the wound healing field.

In the dorsal foot, higher Hb score and lower TcPO2 were observed in comparison to the lower leg and in the presence of PAD. A moderate negative correlation ($r = –0.68$) was observed between TcPO2 and Hb score in the dorsal foot. We think that these are caused by compensatory vasodilation due to occlusion or stenosis of the central arteries. It has previously been reported that patients with atherosclerosis and ischemic limbs have increased blood flow in the skin of the feet.[11–13] It is also known that ischemic limbs are characterized by dependent rubor, which is dark red when the limb is lowered below the heart and changes to pallor on elevation. These conditions are thought to be due to compensatory dilation of peripheral vessels caused by stenosis of central arteries.[14] The high Hb score in the dorsal foot with low TcPO2 may reflect increased cutaneous blood flow due to compensatory dilation of peripheral vessels. In the ischemic limb, lower TcPO2 values suggest a greater degree of stenosis or occlusion of the central artery and a higher degree

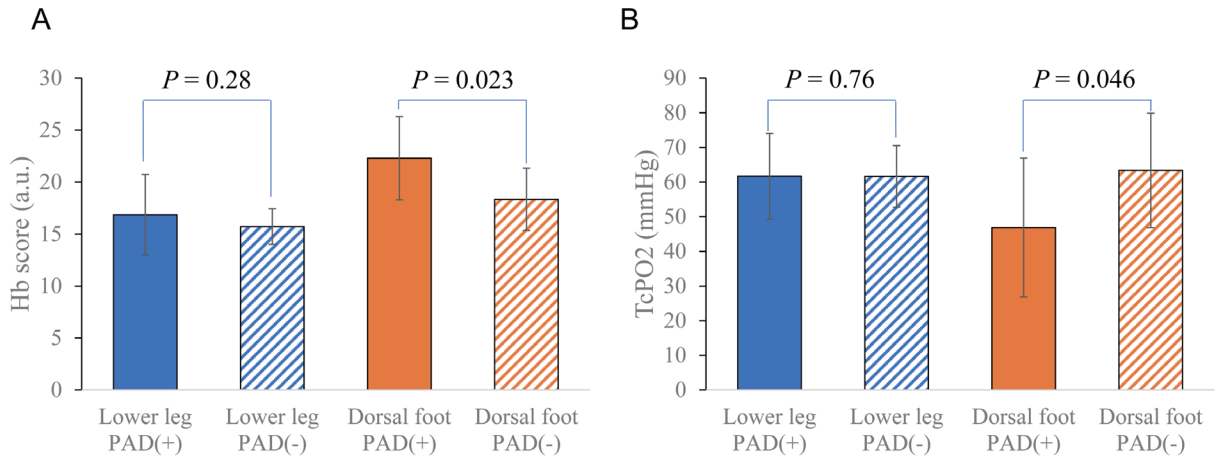

Fig. 4. Hb score and TcPO2 with and without PAD. (**A**) Patients with PAD have higher Hb score in the dorsal foot ($P = 0.023$), and no significant difference in the lower leg ($P = 0.28$). (**B**) Patients with PAD have lower TcPO2 in the dorsal foot ($P = 0.046$), and no significant difference in the lower leg ($P = 0.76$). a.u., arbitrary unit; Hb score, hemoglobin average level; PAD, peripheral arterial disease; TcPO2, transcutaneous partial pressure of oxygen. Error bars indicate standard deviation.

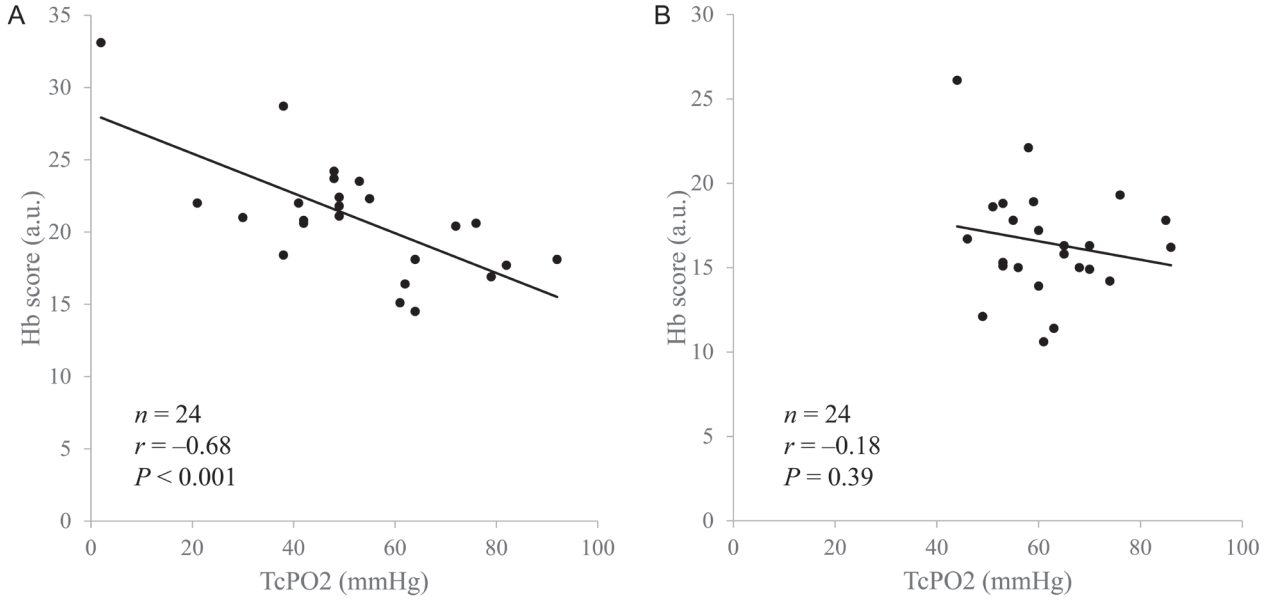

Fig. 5. Correlation between TcPO2 and Hb score at the two measurement points. (**A**) TcPO2 vs. Hb score in the dorsal foot ($n = 24$, $r = -0.68$; 95% CI –0.85 to –0.38, $P < 0.001$); and (**B**) TcPO2 vs. Hb score in the lower leg ($n = 24$, $r = -0.18$; 95% CI –0.55 to –0.24, $P = 0.39$). a.u., arbitrary unit; CI, confidence interval; Hb score, hemoglobin average level; TcPO2, transcutaneous partial pressure of oxygen.

of compensatory dilation of the peripheral vessels. This may have caused the high Hb score observed in the present study. We consider that these reasons account for the higher Hb score and lower TcPO2 observed in the dorsal foot compared with the lower leg and in the presence of PAD, and also explain the negative correlation between TcPO2 and Hb score in the dorsal foot.

In this study, the position of the patient during both examinations was supine or on their side, because not all patients were able to maintain a sitting position. It is expected that the Hb score would be higher in cases of low TcPO2 when the examination is performed in a sitting position or with the trunk higher than the lower extremities.

A similar negative correlation between TcPO2 and skin hemoglobin concentration has been reported using other spectral imaging technology. Lin et al. used a different spectral imaging technology to predict wound

prognosis at 1 year in 50 patients with diabetic foot ulcers.[15] The unhealed group with PAD complications had higher resting hemoglobin levels and lower oxygen saturation compared with the healed group. This is consistent with the present finding of a negative correlation between TcPO2 and Hb score. Therefore, we think that Hb score measured by Antera 3D® have a relationship with cutaneous blood flow in the dorsal foot.

The present study found no significant correlation between TcPO2 and Hb score in the lower leg. Similarly, the difference between Hb score and TcPO2 with and without PAD in the lower leg was not significant. This may be because skin blood flow is better maintained in the lower leg than in the dorsal foot (Fig. 3b), or because of the difficulty in unifying measurement conditions around the knee due to bone protrusion, joint contracture, and skin laxity.

The advantages of Antera 3D® are that it is a painless and quick procedure. It also enables quantitative measurement of skin parameters such as skin wrinkles, melanin concentration, and hemoglobin concentration, and the device itself is convenient and easily transported.[16] In this study, Antera 3D® could be used in all patients, and there were no cases in which examination was limited by pain or other factors. In addition, it has a shorter testing time than is required for measurement of TcPO2. Antera 3D® has the disadvantage that the 5.6 × 5.6 cm flat camera surface must be in contact with the skin surface during imaging. Therefore, it is difficult to measure the heel or the tip of the toe because of the lack of coverage.

This study has limitations, first its small sample size. Second, it did not include healthy subjects or acute cases, and is biased toward patients with chronic ulcers and relatively stable symptoms. Third, there is a lack of detail regarding the measurement principle of Antera 3D®. The manufacturer states that it uses MSI with seven wavelengths of visible LEDs, but the specific wavelengths and the method used to calculate the hemoglobin average level are not disclosed. Future studies are needed to examine larger sample sizes, including healthy subjects and severely ill patients. In addition, the effects of comorbidities, measurement site, and body position are issues to be addressed.

In conclusion, we conducted a study comparing Antera 3D® and TcPO2 on 13 patients with pre-existing lower extremity ulcers. The results suggest that Hb score measured by Antera 3D® may be related to skin blood flow. Comparative study with other blood flow tests on larger sample sizes is needed to evaluate the relationship with skin blood flow in detail.

The authors declare no conflict of interest.

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