

Evaluation of hyperspectral imaging technology in patients with peripheral vascular disease

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ABSTRACT

Background: Hyperspectral imaging technology is a novel method of using transcutaneous measurement of oxyhemoglobin (HT-Oxy) and deoxyhemoglobin (HT-Deoxy) concentrations to create a two-dimensional, color-coded “oxygen map.” The aims of this study were to compare the use of a hyperspectral imaging device with the transcutaneous oxygen measurement (TCOM), ankle-brachial index (ABI), and severity of peripheral vascular disease (PVD) and to assess their correlations.

Methods: This prospective study recruited 294 participants divided into three distinct groups composed of healthy volunteers and patients with PVD. Patients underwent measurements of lower limbs at a standardized point over the head of the first metatarsal on the plantar aspect using the hyperspectral imaging device, generating four outputs including HT-Oxy, HT-Deoxy, oxygen saturation (HT-Sat), and skin temperature, and the TCOM system, generating transcutaneous partial pressure of oxygen (TcPO₂) and carbon dioxide (TcPCO₂). Demographic data, severity of PVD, ABI, and other pertinent information were obtained from both the participants and medical records.

Results: Interoperator reliability ranged from 86% to 94% across the four hyperspectral imaging device outputs, whereas intraoperator reliability ranged from 92% to 94%. The HT-Oxy, HT-Sat, TcPCO₂, and ABI of the diseased limb correlated significantly with the severity of PVD. HT-Sat significantly correlated with TcPO₂ ($R = 0.19$), TcPCO₂ ($R = -0.26$), ABI ($R = 0.42$), and skin temperature ($R = 0.56$). HT-Deoxy also correlated with TcPCO₂ ($R = 0.27$).

Conclusions: This study demonstrates the reliability of hyperspectral imaging in comparison to TCOM, ABI, skin temperature, and severity of PVD in a series of patients. Its correlation to other established modalities and low interoperator and intraoperator variability could enable this modality to be a useful screening tool in PVD. (*J Vasc Surg* 2017;■:1-10.)

Hyperspectral transcutaneous oxygenation measurement (HTCOM) is a unique modality that creates an anatomically relevant and color-coded “oxygen map.”¹⁻⁴ This two-dimensional area for oxygenation measurement can vary in size, from an entire foot to an ulcer at the tip of the toe. The image can provide quantitative values for transcutaneous oxygenation within 15 seconds. Although this technology has been used to determine the viability of diseased tissue, especially in diabetic patients, its ability to assess the severity of peripheral vascular disease (PVD) has not been adequately studied.⁵ The HTCOM device has been used to evaluate

endothelial function in vascular patients in a recent publication by Sumpio et al, which demonstrated the ability of this technology to potentially assess and screen for the presence of PVD.⁶

The OxyVu (HyperMed Inc, Burlington, Mass) is a mobile HTCOM system that noninvasively obtains information from the subpapillary plexus by detecting the presence of chromophores that are uniquely specific to oxyhemoglobin (HT-Oxy) and deoxyhemoglobin (HT-Deoxy).⁷ Using a “target,” that is, a small sticker that measures a standard surface area of 204 mm² placed at the region of interest, the mounted camera produces light at various wavelengths that penetrates the skin to a depth of 1 to 2 mm. This process is repeated at each pixel of the digital picture with a resolution of 90 μm, producing a spectrum of colors that correlates with the density of HT-Oxy and HT-Deoxy that can then be quantified in arbitrary units (Fig 1). Oxygen saturation (HT-Sat) can be deduced from HT-Oxy and HT-Deoxy with the equation $HT-Sat = HT-Oxy / (HT-Oxy + HT-Deoxy)$.³ The OxyVu also measures skin temperature using a remote infrared temperature sensor on the imaging unit, adding a new dimension to analysis of tissue oxygenation. The OxyVu device was purchased in 2008 for approximately NZD \$50,000, and operator training took approximately half a day.

The aim of this study was to compare OxyVu with established modalities, including transcutaneous oxygen measurement (TCOM), ankle-brachial index (ABI), and

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severity of PVD, and to assess their correlations. TCOM is regarded as a useful tool for assessing the peripheral circulation in vascular surgery and can predict wound healing potential.⁸ It measures partial pressure of oxygen (TcPO₂) and carbon dioxide (TcPCO₂) on the skin surface under an electrode.⁹ HT-Sat was hypothesized to be the most sensitive marker of tissue oxygenation because it accounts for both oxyhemoglobin and deoxyhemoglobin. Intraoperator and interoperator reliability of OxyVu were also evaluated.

METHODS

The study protocol was approved by the local Northern Y ethics committee (NTY/08/08/082) and was conducted in Waikato Hospital, Hamilton, New Zealand, from December 2008 to December 2010. Informed consent was obtained from all participants.

The study was divided into three parts with distinct populations of patients in each (Fig 2). Exclusion criteria included age younger than 18 years, cellulitis or ulcers on the plantar skin overlying the first metatarsal head (region of interest in this study), lymphedema of the lower limb, severe dementia, or methicillin-resistant *Staphylococcus aureus*.

Evaluation of interoperator variability. There were 120 limbs studied in 62 patients, with 30 patients with PVD admitted for management of symptomatic arterial insufficiency and the remainder with no history of PVD. Four PVD patients had major amputations in one leg.

OxyVu readings were recorded by two trained operators within a 2-minute period. Each operator was blinded to the location of the target placed by the other operator, which was set on the plantar surface overlying the first metatarsal head. The operators placed the target sticker themselves to imitate clinical settings and to eliminate bias. Each target covered a fixed area of 204 mm² in a doughnut contour.

Evaluation of intraoperator variability. Consecutive hyperspectral readings were recorded at a fixed point over the first metatarsal head on the plantar aspect of the foot for two participants (individuals A and B, one patient with PVD and the other with no known PVD) at 2-minute intervals for 36 minutes. The numerical difference between a reading and that from 2 minutes earlier was used to calculate variation. This was equivalent to 36 comparisons ([36 minutes/2 minutes] * 2 limbs). The target sticker and camera were fixed and not moved during the assessment.

Comparing OxyVu with TCOM, ABI, and severity of PVD. The study participants were 150 patients with PVD presenting to the hospital for management of symptomatic arterial insufficiency of the lower limbs and 20 healthy volunteers. The volunteers were medical

ARTICLE HIGHLIGHTS

- **Type of Research:** Prospective nonrandomized single-center controlled trial
- **Take Home Message:** The study with 294 participants demonstrated the reliability of hyperspectral imaging to transcutaneous oximetry, ankle-brachial index, skin temperature, and severity of peripheral arterial disease with good correlation and low interoperator and intraoperator variability.
- **Recommendation:** The authors suggest that hyperspectral imaging may be useful as a screening tool in early-stage peripheral arterial disease.

students and nursing staff members in the ward who did not have a history of PVD.

Demographics of the patients, severity of PVD, hyperspectral oxygenation, TcPO₂ and TcPCO₂ (TCM3; Radiometer Medical ApS, Brønshøj, Copenhagen), and ABI were recorded using hand-held Doppler devices. The OxyVu measurement was performed before TCOM and ABI to eliminate potential errors produced from thermal hyperemia induced by TCOM.

The Rutherford classification was used to assess the severity of PVD.¹⁰ The healthy volunteers were asymptomatic and therefore scored zero. To assist with the statistical analyses, Rutherford categories 1, 2, and 3 were grouped into claudicants, and similarly Rutherford categories 4, 5, and 6 were grouped into critical limb ischemia (CLI). For the purposes of the study, this classification was called the Simplified Severity Score (SSS), whereby a scoring system of 0, 1, and 2 was applied, with 0 being volunteers (ie, asymptomatic), 1 being claudicants, and 2 being CLI patients.

Hyperspectral oxygenation, TcPO₂, and TcPCO₂ were measured in both lower limbs at a standardized point over the head of the first metatarsal on the plantar aspect. Among the group with documented arterial insufficiency, "diseased" limb referred to the symptomatic side to be treated. In the healthy volunteers, a single limb (left side) was chosen for recording of "diseased" measurements to avoid bias. Oxygenation measurements were recorded with each participant lying in a supine position in a room with a fixed ambient temperature (20°C-23°C). Measurement protocols used in the study have previously been validated.¹¹⁻¹³ TCOM measurements were obtained in a standardized fashion across all patients and recorded at 15 minutes. Participants were required to abstain from active smoking or caffeinated beverages for at least 2 hours to allow cardiovascular variables to return to baseline. Previous major amputation was an exclusion criterion in this part of the study. The correlations between OxyVu and TCOM, ABI of the diseased limb, and severity of PVD were evaluated.

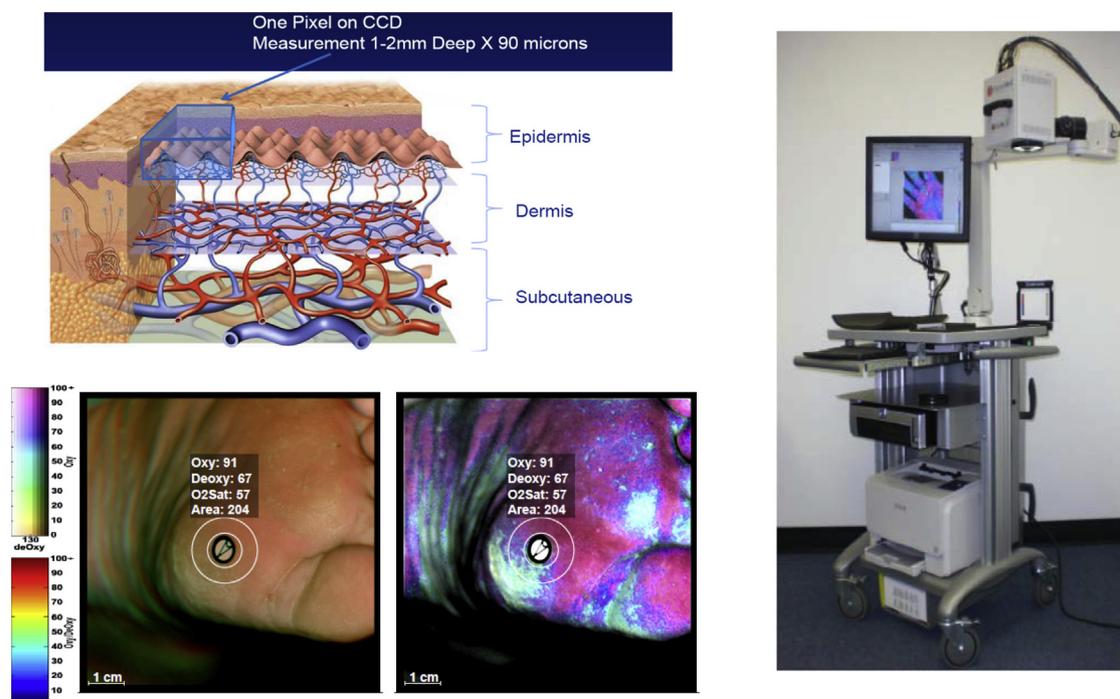


Fig 1. Diagram illustrating how the OxyVu works, the OxyVu device, and output “oxygen map.” CCD, Charge-coupled device; Deoxy, deoxyhemoglobin; O2Sat, oxygen saturation; Oxy, oxyhemoglobin. (HyperMed Inc, Burlington, Mass; <http://www.hypermed-inc.com>.)

Statistical analysis. Data were collected in Excel (Microsoft, Redmond, Wash). Statistical analyses were performed using SPSS version 22 software (IBM Corp, Armonk, NY). A type I error of 5% ($P \leq .05$, two tailed) was considered to be statistically significant.

Descriptive statistics were described in terms of the range, mean or median, and standard deviation. In comparing the means of two groups of continuous variables, parametric analysis (the Student *t*-test) was used, assuming the data followed a normal distribution. The χ^2 and Fisher exact tests were applied, depending on the size of the sample.

Pearson and Spearman correlation tests were used to determine an association between variables, depending on whether they were continuous or ordinal scale (ranked, such as the severity of PVD).

Intraclass correlation coefficients (ICCs) and the Bland-Altman test were used to assess interoperator variability.¹⁴ The within-subject coefficient of variation defined the intraoperator reliability.

RESULTS

Evaluating interoperator reliability

Fig 3 shows the correlation of the various OxyVu measurements between the two operators for 120 limbs. Overall, interoperator reliability ranged from 86% to 94%. The single-measure ICCs (95% confidence interval [CI]) of the four OxyVu measurements were as follows: HT-Oxy, 0.86 (0.80-0.90); HT-Deoxy, 0.94 (0.91-0.96);

HT-Sat, 0.86 (0.81-0.91); and skin temperature, 0.94 (0.91-0.96). The average ICCs (95% CI) were as follows: HT-Oxy, 0.92 (0.89-0.95); HT-Deoxy, 0.97 (0.95-0.98); HT-Sat, 0.93 (0.90-0.95); and skin temperature, 0.97 (0.95-0.98).

Evaluating intraoperator reliability

Fig 4 shows the mean \pm 95% CI for each of the OxyVu variables in individuals A and B. The variation during 36 minutes was small as indicated by the small 95% CI. The intraoperator reliability (coefficient of variation) was 0.92 (95% CI, 0.89-0.95) for HT-Oxy and 0.94 (95% CI, 0.92-0.96) for HT-Deoxy. The intraoperator reliability was 0.94 (95% CI, 0.92-0.96) for HT-Sat and 0.990 (95% CI, 0.986-0.993) for skin temperature.

Comparing HTCOM with TCOM, skin temperature, ABI, and severity of PVD

Basic demographic data and OxyVu readings are shown in Tables I and II, respectively. Fig 5 shows the distribution of the participants according to Rutherford classification. More than three-quarters (115/150) of the patients with PVD had CLI. Study sessions typically took 45 minutes to complete. The OxyVu measurement component was approximately a minute, with most of the time spent operating the TCOM device. A total of 340 limbs were studied in 170 participants.

Correlation between OxyVu readings and severity of PVD. Hyperspectral readings correlated with both the Rutherford classification and SSS, in particular HT-Oxy

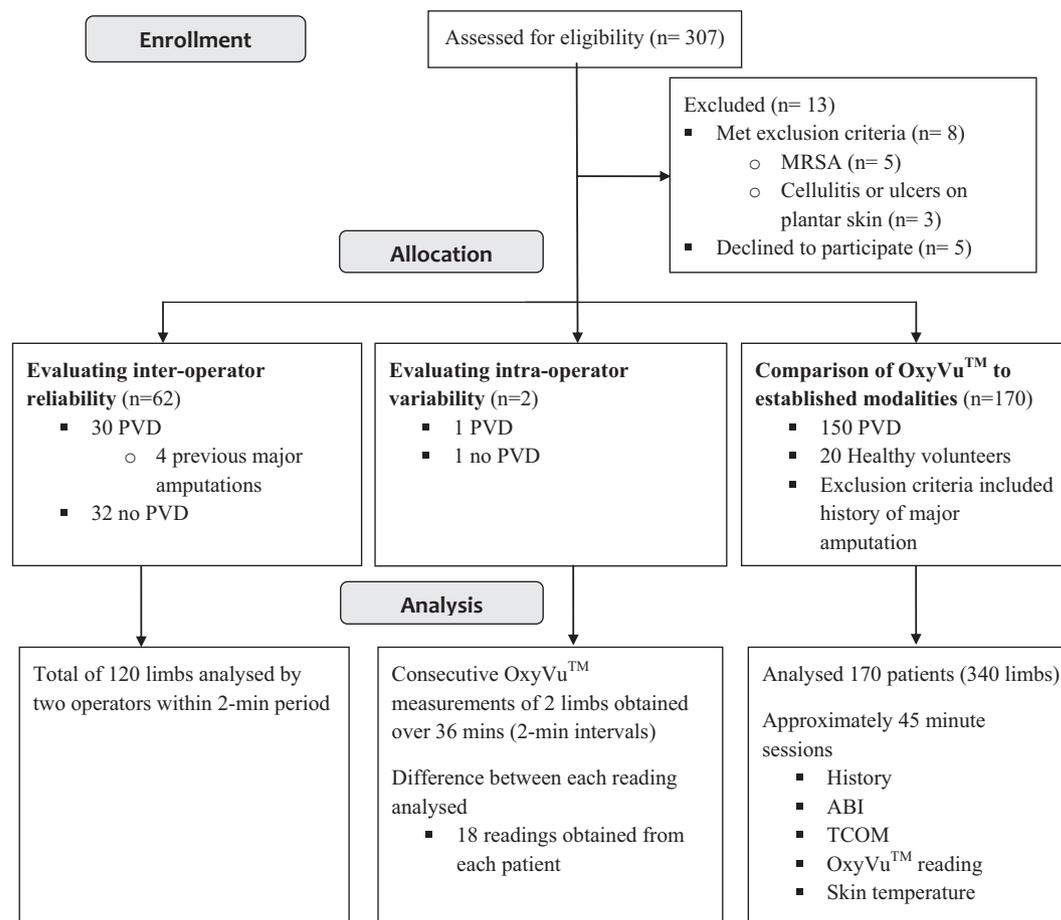


Fig 2. Diagram illustrating the enrollment, exclusion criteria, and study protocol. *ABI*, Ankle-brachial index; *MRSA*, methicillin-resistant *Staphylococcus aureus*; *PVD*, peripheral vascular disease; *TCOM*, transcutaneous oxygen measurement.

and HT-Sat (Fig 6). Table III shows that HT-Oxy and HT-Sat were influenced by the severity of PVD in both the diseased and the contralateral limbs, indicating that OxyVu was also able to detect the presence of coexisting PVD in the contralateral limb.

Correlation between hyperspectral measurements and skin temperature. The mean skin temperature of the diseased limb was lower than that of the contralateral limb (28.9°C vs 29.4°C; $P = .036$; Table II). Skin temperature was not sensitive to the severity of PVD (Table III) and did not differ between the two feet in volunteers ($P = .32$). It also correlated significantly with all three HTCOM parameters, with HT-Oxy ($R = 0.41$; $P = .0001$), HT-Deoxy ($R = -0.40$; $P = .0001$), and HT-Sat ($R = 0.56$; $P = .0001$).

Correlation between hyperspectral measurements and Doppler ABI. The ABIs of the diseased limb and the contralateral limb are described for all 170 study participants in Table IV. Those with falsely elevated ABI of more than 1.3 were excluded from analysis. Using the SSS, there was a downward trend of ABI in the diseased limb as the severity of PVD increased ($R = -0.37$;

$P = .0001$). ABI in the contralateral limb also trended with the SSS, indicating coexisting PVD ($R = -0.19$; $P = .02$). In the diseased limb, ABI correlated significantly with all the HTCOM parameters, with HT-Oxy ($R = 0.30$; $P = .0001$), HT-Deoxy ($R = -0.29$; $P = .0001$), and HT-Sat ($R = 0.42$; $P = .0001$).

Correlation between hyperspectral and TCOM measurements. Table V lists the means \pm standard deviation for TcPO₂ and TcPCO₂ in the diseased limb. These measurements were also categorized per the severity of PVD. As with HTCOM, it was expected that TcPO₂ would decrease as the severity of PVD increased and that TcPCO₂ would show the opposite trend. This pattern was more apparent for TcPCO₂. In fact, TcPCO₂ linked more strongly with the severity of PVD than TcPO₂, with Spearman rank coefficient correlation (SSS) for TcPO₂ of -0.11 ($P = .14$) vs TcPCO₂ of 0.31 ($P = .0001$).

Table VI demonstrates HT-Sat correlated with TcPO₂ and TcPCO₂. Whereas HT-Oxy did not relate to TcPO₂, there was a strong relationship between HT-Deoxy and TcPCO₂.

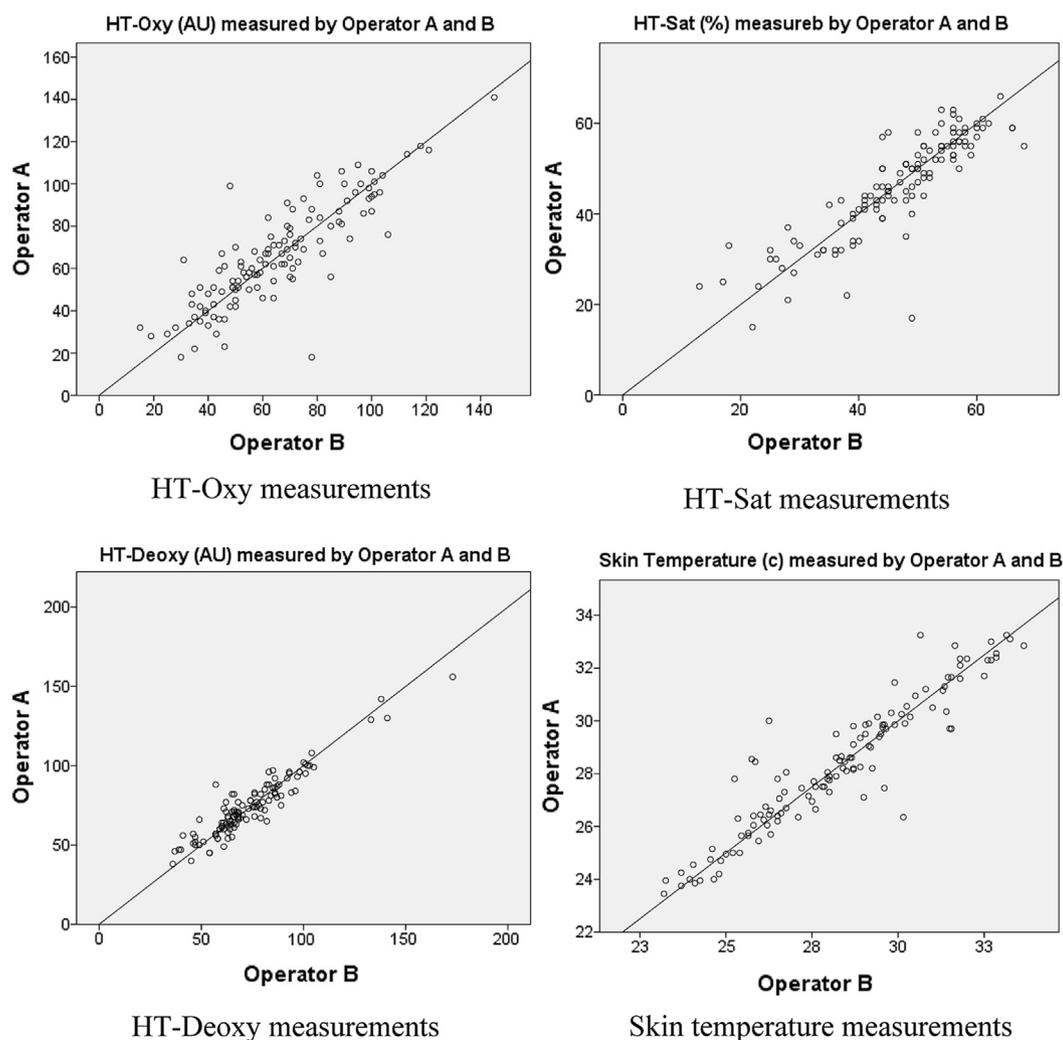


Fig 3. Scatter plots showing the correlation of the various OxyVu measurements between the two operators for the 120 limbs. AU, Arbitrary units; Deoxy, deoxyhemoglobin; HT, hyperspectral technology; Oxy, oxyhemoglobin; Sat, saturation.

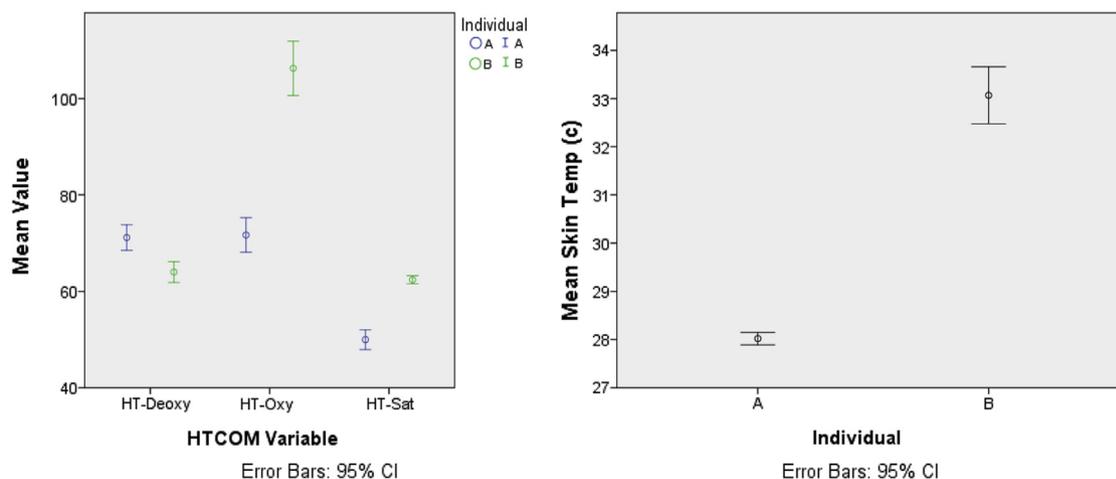
DISCUSSION

To date, this study is the largest and most extensive series validating HTCOM in patients with PVD. Various modalities were used for comparisons, including severity of PVD, skin temperature, ABI, and TCOM measurements. Hyperspectral oxygenation correlated with each one of these to some extent, indicating that the OxyVu was fulfilling the role for which it was designed, that is, quantifying oxygenation. At present, there is no established "gold standard" modality for assessing tissue oxygenation in patients with PVD, even though TCOM has been considered to be the most sensitive technique.¹⁵ Therefore, the OxyVu cannot be tested for superiority over other modalities.

As hypothesized, HT-Sat was the most sensitive of the HTCOM output because it takes into account both the concentration of oxyhemoglobin (oxygen delivery) and

deoxyhemoglobin (oxygen consumption) in a region of interest. HT-Sat was the only marker that correlated significantly with the SSS ($R = -0.29$), ABI ($R = 0.42$), skin temperature ($R = 0.56$), $TcpO_2$ ($R = 0.19$), and $TcpCO_2$ ($R = -0.26$). Other findings of interest included HT-Deoxy correlating with $TcpCO_2$ ($R = 0.27$), HT-Oxy with SSS ($R = -0.29$), skin temperature with HT-Oxy ($R = 0.41$), and skin temperature with HT-Deoxy ($R = -0.40$).

Whereas $TcpO_2$ can predict wound healing,¹⁶⁻²² this study did not show an interaction between $TcpO_2$ and HT-Oxy and between $TcpO_2$ and the severity of PVD. Fig 7 shows $TcpO_2$ values according to the severity of PVD. Mean $TcpO_2$ was higher in the claudicant group than in the control group despite that the mean $TcpO_2$ was lowest in patients with CLI, whereas the range and variance in the claudicant and CLI groups were larger



Error Bars: 95% CI
Error bar graph showing the mean \pm 95% CI of HTCOM readings in the lower limb of individuals A and B.

Error Bars: 95% CI
Error bar graph showing the mean \pm 95% CI for skin temperature in the lower limb of individuals A and B.

Fig 4. Mean \pm 95% confidence interval (CI) for each of the OxyVu variables in individuals A and B. *Deoxy*, Deoxyhemoglobin; *HT*, hyperspectral technology; *HTCOM*, hyperspectral transcutaneous oxygenation measurement; *Oxy*, oxyhemoglobin; *Sat*, saturation.

Table I. Basic demographics of participants

| | Vascular (n = 150) | Volunteers (n = 20) |
|----------------------------|--------------------|---------------------|
| Age, years, median (range) | 72 (35-91) | 36 (23-65) |
| Male | 101 (67) | 7 (35) |
| White | 128 (85) | 13 (65) |
| Active smoker | 28 (19) | 5 (25) |
| Ex-smoker (>6 months) | 85 (57) | 2 (10) |
| Diabetes on medications | 52 (35) | 0 |
| Previous angioplasty | 58 (39) | 0 |
| Previous IIB | 49 (33) | 0 |
| Previous minor amputation | 20 (13) | 0 |
| Renal disease (eGFR <60) | 22 (15) | 0 |
| ESRF on dialysis | 6 (4) | 0 |
| Hypertension | 122 (81) | 3 (15) |
| Dyslipidemia | 111 (74) | 3 (15) |
| IHD | 71 (47) | 1 (5) |
| Previous CABG | 24 (16%) | 0 |
| TIA or CVA | 40 (27) | 0 |
| COPD | 14 (9) | 0 |

CABG, Coronary artery bypass grafting; *COPD*, chronic obstructive pulmonary disease; *CVA*, cerebrovascular accident; *eGFR*, estimated glomerular filtration rate; *ESRF*, end-stage renal failure; *IHD*, ischemic heart disease; *IIB*, infrainguinal bypass; *TIA*, transient ischemic attack. Values are reported as number (%) unless otherwise indicated.

than in the control group. This finding might be explained by the reactive hyperemia that occurs in patients with PVD.

The only link yet to be explained here was why $TcpCO_2$ correlated with HT-Deoxy when HT-Deoxy did not

correlate with the severity of PVD. In addition, HT-Oxy correlated with severity but did not correlate with $TcpO_2$; this could be explained by HT-Oxy being potentially better than $TcpO_2$ for detection of PVD. HT-Deoxy and $TcpCO_2$ are two separate physiologic entities. HT-Deoxy reflects the amount of deoxyhemoglobin in the tissue, and $TcpCO_2$ quantifies the carbon dioxide concentration. An increase in the carbon dioxide level would not directly increase the deoxyhemoglobin level. Perhaps HT-Deoxy is an indicator of tissue metabolism and, indirectly, blood outflow with prolonged capillary blood transit time for diffusion. This study showed that unlike HT-Oxy and HT-Sat, HT-Deoxy was not affected by PVD. This could mean that there is no relationship between tissue metabolism and the degree of tissue ischemia. As a result of all these findings, HT-Sat remained the only consistent marker for tissue oxygenation.

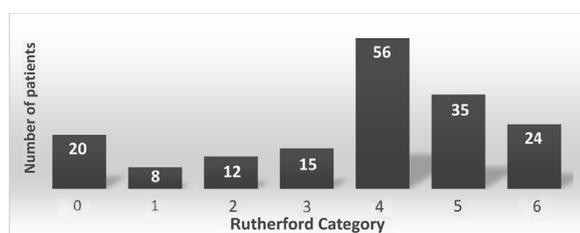
The SSS was introduced for the purposes of this study. One of the reasons for this was the relatively small number of patients in Rutherford classifications 1, 2, and 3. In addition, whereas categories of the Rutherford classification have objective assessment criteria, it remains difficult to accurately quantify these in terms of oxygen tension and perfusion status relative to a patient's clinical applicability to a particular category. The findings of this study are consistent with that observation, with tissue perfusion in patients who have a Rutherford classification of 5 and 6 appearing to be better than in those with a Rutherford classification of 4. Fifty-two patients had diabetes, and 36 (69%) of these had ulcers (Rutherford classification 5 and 6). This number was proportionately higher than for Rutherford 0, 1, 2, 3, and 4 patients

Table II. Summary of OxyVu findings in patients with peripheral vascular disease (PVD) and healthy volunteers

| | Diseased patients | | | | Volunteer patients | | | |
|--|-------------------|-----------|------|----------------|--------------------|------------|------|----------------|
| | Mean | Range | SD | <i>P</i> value | Mean | Range | SD | <i>P</i> value |
| HT-Oxy, diseased ^a | 76.4 | 11-145 | 24.4 | .31 | 100 | 49-160 | 31.3 | .19 |
| HT-Oxy, contralateral | 77.7 | 26-123 | 21.4 | | 97.1 | 56-149 | 27.8 | |
| HT-Deoxy, diseased ^a | 80.9 | 40-144 | 19.8 | <.001 | 71.2 | 49-101 | 13.2 | .43 |
| HT-Deoxy, contralateral | 74.1 | 32-124 | 16.8 | | 70.4 | 46-100 | 13.6 | |
| HT-Sat, diseased ^a | 47.8 | 11-62 | 10.6 | .007 | 56.9 | 41-68 | 8.4 | .28 |
| HT-Sat, contralateral | 50.6 | 24-66 | 8.5 | | 56.7 | 43-69 | 8.2 | |
| Temperature, °C, diseased ^a | 28.9 | 23.7-34.6 | 2.6 | .36 | 30.4 | 25.1-35.0 | 2.3 | .32 |
| Temperature, °C, contralateral | 29.4 | 23.6-35.2 | 2.8 | | 30.5 | 24.4-35.35 | 2.8 | |

Deoxy, Deoxyhemoglobin; HT, hyperspectral technology; Oxy, oxyhemoglobin; Sat, saturation; SD, standard deviation.

^aIn healthy patients, the left limb was defined as the diseased limb.

**Fig 5.** Distribution of the study population according to severity of peripheral vascular disease (PVD).

($P \leq .0001$, Fisher exact test). Patients with diabetes often have neuropathy, which impairs the sympathetic tone to the arterial vessels, causing impaired vasoconstriction and relative hyperemia from arteriovenous shunting,²³⁻²⁵ and this could be another reason for the higher oxygenation in patients classified as Rutherford 5 or 6.

Several limitations were identified in this study. Only two target points were chosen, one at the plantar aspect of the head of the first metatarsal of the diseased foot and the other on the contralateral limb. The average TcPO₂ values from two or more adjacent sites of an area are better predictors of healing potential than single site values.²⁶ One of the advantages of the OxyVu is that even when oxygenation is measured at a target point in a region of interest, the OxyVu software has the capability to quantify hyperspectral oxygenation beyond this point for an area of any size visible on the photograph by selecting the boundary on the computer touchscreen to detect potential ischemic areas. The standardized method used in this study, even though it assessed a relatively small area, eliminated systematic bias attributable to the operator.

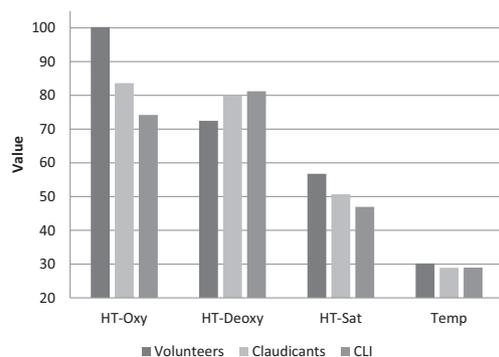
The plantar angiosome chosen at the head of the first metatarsal bone is covered by glabrous skin that is rich in arteriovenous anastomoses. This skin tissue has more oxygenation and is more reactive to changes in oxygenation than skin on other parts of the body. However, the skin in this area can be particularly thick. In some individuals, this skin can be pathologically hypertrophic,

taking the form of calluses or corns, which are common in patients with diabetic neuropathy.²⁷ OxyVu typically assesses skin 1 to 2 mm in depth, and how this might have affected the findings of the validation study is unknown.

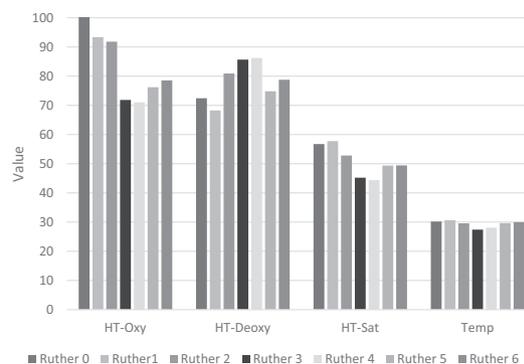
Although many of the correlation analyses were significant at $P < .05$, their clinical significance is unclear, given the relatively low correlation coefficient values. Participants with a history of lymphedema were excluded from the study. However, it is possible that some may have had clinically significant leg edema that was not identified, given the subjective nature of quantifying this on examination. A skin surface with underlying leg edema typically has less tissue oxygenation, precipitating the development of ulcers.²⁸

In addition, nearly a quarter of the healthy volunteers in the study were active smokers but with a short-term history of smoking. Although the impact of their smoking history on the measurements obtained is unknown, the ABIs recorded in this group were 0.9 to 1.2, highly suggestive of being normal. Therefore, the impact of both these factors can be assumed to not have been a large confounder in comparing oxygenation values in this study.

Whereas this pilot study did not specifically study the application of the OxyVu to wound healing, this had been explored by several other groups. Greenman et al compared 10 patients with type 1 diabetes and ulcers and monitored them for 6 months to determine healing potential.⁵ HTCOM was also compared with TCOM, laser Doppler flowmetry, and ABI. HTCOM was the only method that showed lower HT-Oxy and HT-Deoxy surrounding the ulcer. HT-Oxy at the metatarsal site of the plantar foot was lower in patients with diabetes and ulcers than in controls. A new parameter named the HT-Healing Index, generated on the basis of ulcer healing at 6 months, concluded that the OxyVu has a sensitivity and specificity of 93% and 86%, respectively, for predicting ulcer healing based on readings from the first visit. Nouvong et al conducted another study that



OxyVu™ readings in the diseased limb according to severity of peripheral vascular disease (SSS).



OxyVu™ measurements in the diseased limb according to Rutherford classification

Fig 6. OxyVu readings according to Rutherford classification and Simplified Severity Score (SSS). CLI, Critical limb ischemia; Deoxy, Deoxyhemoglobin; HT, hyperspectral technology; Oxy, oxyhemoglobin; Sat, saturation; Temp, temperature.

Table III. Spearman rank correlation coefficients and *P* values comparing OxyVu readings for the diseased limb and contralateral limbs with severity of peripheral vascular disease (PVD)

| Diseased limb | HT-Oxy | HT-Deoxy | HT-Sat | Temperature |
|---------------------------|--------|----------|--------|-------------|
| SSS | | | | |
| <i>R</i> | -0.29 | 0.08 | -0.29 | -0.11 |
| <i>P</i> value | .0001 | .29 | .0001 | .17 |
| Contralateral limb | | | | |
| SSS | | | | |
| <i>R</i> | -0.26 | -0.07 | -0.16 | -0.065 |
| <i>P</i> value | .001 | .38 | .04 | .40 |

Deoxy, Deoxyhemoglobin; *HT*, hyperspectral technology; *Oxy*, oxyhemoglobin; *Sat*, saturation; *SSS*, Simplified Severity Score.

Table IV. Descriptive summary of ankle-brachial index (ABI) in the diseased and contralateral limbs according to severity of vascular disease using the Simplified Severity Score (SSS)

| | Diseased limb | | | Contralateral limb | | |
|-------------|---------------|----------|------|--------------------|---------|------|
| | Mean | Range | SD | Mean | Range | SD |
| Volunteers | 1.03 | 0.9-1.2 | 0.10 | 1.03 | 0.9-1.2 | 0.09 |
| Claudicants | 0.74 | 0.00-1.6 | 0.35 | 0.93 | 0.4-1.6 | 0.29 |
| CLI | 0.68 | 0.00-1.9 | 0.44 | 0.93 | 0.4-1.9 | 0.33 |

CLI, Critical limb ischemia; *SD*, standard deviation.

included 73 diabetic foot ulcers in 54 patients.²⁹ Again, the study derived the HT-Healing Index, with a sensitivity, specificity, and positive predictive value of 86%, 88%, and 96%, respectively. HT-Oxy and HT-Sat at the ulcer border were lower in ulcers that did not heal in 6 months than in those that healed during this time. Taken together with the findings of this study, the OxyVu device shows promising clinical equipoise.

Table V. Transcutaneous oxygen measurement (TCOM) readings of the diseased limb according to severity of peripheral vascular disease (PVD) using the Simplified Severity Score (SSS)

| Diseased limb | TcpO ₂ | TcpCO ₂ |
|--------------------|-------------------|--------------------|
| Volunteers | | |
| Mean | 79.3 | 26.4 |
| SD | 13.9 | 12.8 |
| Claudicants | | |
| Mean | 84.2 | 28.3 |
| SD | 17.9 | 7.9 |
| CLI | | |
| Mean | 75.8 | 36.0 |
| SD | 22.8 | 14.5 |

CLI, Critical limb ischemia; *SD*, standard deviation; *TcpCO₂*, transcutaneous partial pressure of carbon dioxide; *TcpO₂*, transcutaneous partial pressure of oxygen.

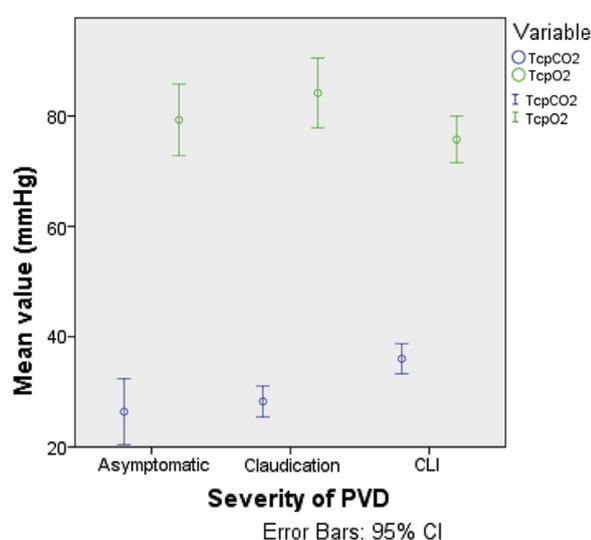
Clinical evaluation of PVD includes an assessment of tissue oxygenation to quantify severity of disease and the risk of tissue loss. However, there is no standardized tool to assess this, and therefore most clinicians use their clinical judgment at the bedside. Various modes of arteriography can be used to outline the major vessels that are patent and can identify stenotic or occlusive lesions that may contribute to tissue hypoxia but offer no indication of the adequacy of microvascular perfusion. Similarly, ABI and toe pressures have been used as surrogate markers for tissue perfusion.

Whereas TCOM has its role in clinical practice with continuous measurement of tissue oxygenation, particularly in pediatric intensive care, respiratory care, sleep medicine, and hyperbaric therapy, it is cumbersome to perform and has its limitations. Assessment of multiple sites is time-consuming, given that a single reading has a surface area of 1 cm² and may take up to 20 minutes to obtain. In addition, the intraoperator variability in

Table VI. Pearson correlation coefficients and *P* values in comparing transcutaneous oxygen measurement (TCOM) in the diseased limb with OxyVu readings

| Diseased limb | HT-Oxy | HT-Deoxy | HT-Sat |
|--------------------|--------|----------|--------|
| TcpO ₂ | | | |
| <i>R</i> | 0.02 | | 0.19 |
| <i>P</i> value | .77 | | .012 |
| TcpCO ₂ | | | |
| <i>R</i> | | 0.28 | −0.26 |
| <i>P</i> value | | .0001 | .001 |

Deoxy, Deoxyhemoglobin; *HT*, hyperspectral technology; *Oxy*, oxyhemoglobin; *Sat*, saturation; *TcpCO₂*, transcutaneous partial pressure of carbon dioxide; *TcpO₂*, transcutaneous partial pressure of oxygen.

**Fig 7.** Error bar graph showing the mean \pm 95% confidence interval (*CI*) of transcutaneous partial pressure of oxygen (*TcpO₂*) and transcutaneous partial pressure of carbon dioxide (*TcpCO₂*) in the diseased limb categorized according to severity of peripheral vascular disease (*PVD*). *CLI*, Critical limb ischemia.

TCOM has been found to be 10% for *TcpO₂* and 5% for *TcpCO₂*.^{16,26} Comparatively with the OxyVu device, the hyperspectral image can be obtained within 15 seconds and has an adjustable surface area for measurement.

With the advantages described, from a practical perspective, it may now be appropriate for further rigorous clinical evaluation of the OxyVu device for screening of arterial insufficiency, prediction of wound healing, detection of change in oxygenation after revascularization, evaluation of the potential for hyperbaric oxygen therapy, and differentiation between ischemic and neurogenic claudication.

CONCLUSIONS

Hyperspectral imaging represents a novel and validated method for measuring tissue oxygenation in patients with PVD. Our study demonstrates the reliability of the

OxyVu in comparison to TCOM, ABI, skin temperature, and severity of PVD in a large and extensive series of patients. These results confirm the ability of hyperspectral imaging in assessing the presence of PVD and potential for use as a validated early screening tool.

Melanie Hwang made significant contribution to data collection.

AUTHOR CONTRIBUTIONS

Conception and design: NC, JS, TV
 Analysis and interpretation: NC, JJ, TV
 Data collection: NC
 Writing the article: NC, JJ
 Critical revision of the article: NC, JJ, JS, TV
 Final approval of the article: NC, JJ, JS, TV
 Statistical analysis: NC, JS
 Obtained funding: NC, TV
 Overall responsibility: NC

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