Comparing near infrared spectroscopy and transcutaneous oxygen measurement in hard-to-heal wounds: a pilot study

Objective: Oxygen plays an integral role in all phases of the wound healing process and tissue oxygenation is a key determinant of wound healing. A comprehensive evaluation of patients with hard-to-heal wounds must include measurement of oxygenation in and around the area of skin breakdown. The current gold standard, transcutaneous oxygen measurement (TCOM), has numerous drawbacks and as a result has fallen into disuse.
Method: This study compared measurement of tissue oxygenation of near infrared spectroscopy (NIRS) with TCOM in patients with acute and hard-to-heal wounds. The Shapiro-Wilk test was used to evaluate the normality of the data. The level of agreement between NIRS and TCOM was determined using Bland-Altman analysis. The relationship between TCOM and NIRS was examined using Pearson correlation.
Results: A total of 24 observations were obtained from 10 patients using TCOM and NIRS. The weighted mean partial pressure of oxygen (pO_2) in the study population was 39.54mmHg (8.96 standard deviation). Bland–Altman analysis showed that mean difference was positive (18.75), suggesting an overestimation of oxygen measurements using TCOM compared with NIRS. The oxygen levels measured by TCOM and NIRS showed a strong correlation (r=0.74).
Conclusion: The wound and hyperbaric community would benefit from a simplified procedure for measuring tissue oxygenation. These findings suggest a strong trend toward correlation between NIRS and TCOM. A further study in a larger population is recommended. NIRS offers several advantages over TCOM. Clinicians have immediate point-of-care visualisation of tissue oxygenation using a handheld device. The procedure takes minutes to perform and is less operator-dependent than TCOM. Finally, NIRS allows measurement of oxygenation in the wound bed, while TCOM does not.
Declaration of interest: The authors have no conflicts of interest.

advancements in wound care • hard-to-heal wounds • near infrared spectroscopy • oximetry • peripheral vascular insufficiency

Hard-to-heal wounds can take weeks to months to heal, resulting in pain and diminished quality of life (QoL). In addition, open wounds can lead to complications, such as infection, amputation, sepsis and death.[1–3] An estimated 8.2 million people in the US have hard-to-heal wounds, at a cost exceeding $28 billion dollars annually.[3,4] A number of factors impede wound healing: moderate-to-heavy bacterial load, low tissue oxygen tension, elevated inflammatory proteases, diminished growth factors, the presence of nonviable tissue and host factors, such as age and comorbid conditions.[5,6]

Tissue oxygenation is a key determinant of wound healing.[7,8] Oxygen is involved in numerous biological processes including cell proliferation, angiogenesis and protein synthesis.[8] In patients with Wagner 3 and 4 diabetic foot ulcers (DFUs), hyperbaric oxygen therapy (HBOT) has been shown to promote healing.[9] Similarly, in Wagner 1 and 2 DFUs, topical oxygen treatment has been shown to be efficacious.[10] Wound oxygenation measurement is part of the standard evaluation of a patient with a hard-to-heal wound. The gold standard in assessing oxygenation, transcutaneous oxygen measurement (TCOM), measures the partial pressure of oxygen on the skin surface using heated electrodes.[10–15] Several studies have demonstrated the value of TCOM.[10,11,13] It can predict the likelihood of wound healing in patients with and without diabetes. In addition, it is used to decide on the level of amputation and determine the best candidates for HBOT.[14,16] However, TCOM has several drawbacks: the procedure is labour and time-intensive, room temperature must be kept between 68°F and 72°F, probes cannot be applied directly to the wound bed or over bony prominences, and the disposable electrodes are expensive.[16,17] As a result, the search for a simpler alternative continues.

Near infrared spectroscopy (NIRS) is a novel method for measuring tissue oxygen saturation (StO_2). Oxygenated and deoxygenated haemoglobin molecules differentially absorb light in the near infrared portion of the electromagnetic spectrum (700–2500nm).[16–18] At these wavelengths, they are the main absorbers of light or chromophores (melanin is also a chromophore in the near infrared spectrum but to a lesser extent than haemoglobin).[19,20] The NIRS device studied uses six wavelengths to measure the absorbance of oxygenated and deoxygenated haemoglobin. Comparing the relative ratios of oxygenated and deoxygenated

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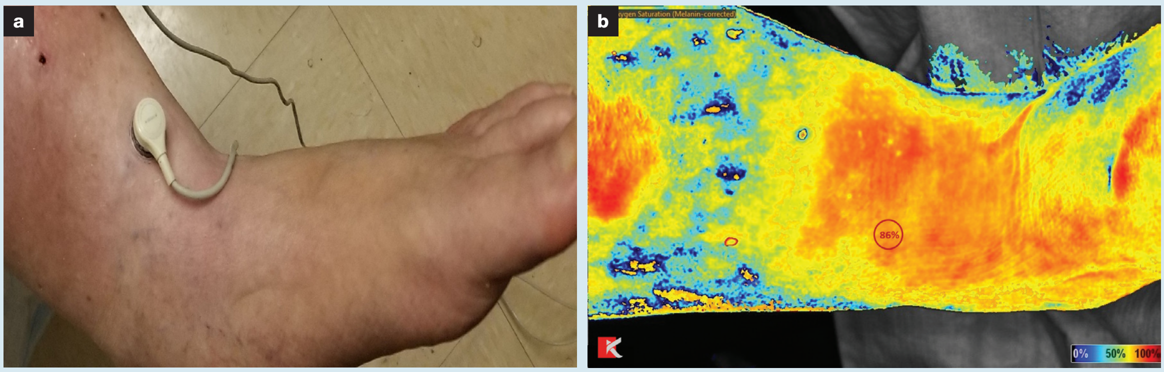
Fig 1. A 67-year-old male withproximal wounds on the left leg, of one month's duration. Transcutaneous oxygen measurement (TCOM) (**a**); near infrared spectroscopy image in the same location as the lead placement for the TCOM electrode shows adequate oxygenation in the area of the TCOM lead (**b**)



haemoglobin allows the calculation of tissue oxygen saturation. In contrast to TCOM, which measures free oxygen that diffuses to the surface of the skin, NIRS measures the oxygen bound to haemoglobin.[21,22] Finally, NIRS measures oxygenation saturation in all the vascular beds in the area of interest.

There are several advantages of NIRS over traditional TCOM. It is noninvasive and does not require skin contact or injectable dyes.[23,24] The handheld system permits rapid point-of-care assessment of tissue oxygenation. It can visualise any area of the skin or wound including the wound bed. It is reproducible and not highly operator-dependent. NIRS can distinguish between venous and arterial occlusion in an ischaemic flap and detect vascular occlusion with high sensitivity and specificity.[25]

Methods

This study compared a NIRS device (Snapshot$_{NIR}$, Kent Imaging, Canada) with a TCOM device (Perimed, US) in patients with hard-to-heal wounds. Patients with acute and hard-to-heal wounds from a single outpatient wound and research centre took part in the study. The inclusion criteria were patients >18 years of age with a hard-to-heal wound of at least four weeks' duration. Patients receiving investigational drug or device treatment within 30 days of the study visit were excluded. All patients signed an Institutional Review Board-approved informed consent form and agreed to have deidentified image assessments released for research. In parallel, eligible patients suspected for vascular insufficiency were also assessed using the NIRS device. The measurements were collected by taking a NIRS image in the same location as the lead placement for the TCOM electrode (Fig 1).

Wound care followed a standard procedure for all patients: the dressings were removed and the wounds were cleansed with normal saline. A single measurement was taken with the TCOM and NIRS devices with the patients supine. Only lower extremities were evaluated. The order of the devices was alternated between evaluations. Care was taken to obtain the NIRS image in the same location as the TCOM lead. Melanin correction was used for patients with Fitzpatrick 3 skin colour or higher (the older version of the device could not correct for individuals with pigmented skin). The NIRS images were captured when the two lasers converged on the centre of the wound or skin indicating that the camera was the appropriate distance away. The room temperature was kept at 70°F with 25% humidity during all testing. All the subjects were evaluated on a single day under the same conditions.

In two patients, assessments were obtained from both the right and left leg and in one patient, both proximal and distal regions were measured (the authors wanted to see if using different parts of the same extremity or different extremities had any noticeable effect).

Statistical analysis

In order to compare the NIRS with TCOM, StO_2 was converted to partial pressure of oxygen (pO_2) using the standard Severinghaus oxygen dissociation curve.[26] The Shapiro–Wilk test was used to evaluate the normality of the data as it is more sensitive for smaller samples (W=0.97). Bland–Altman analysis was used to assess the level of agreement between NIRS and TCOM. The mean difference between measurements (TCOM−NIRS) was defined as bias and standard deviation (SD) was used to calculate 95% confidence limits of agreement (LOA, bias±1.96SD). The correlations between TCOM and NIRS were examined using Pearson correlation. The following values were used to interpret correlation: r<0.20=very weak; 0.20–−0.39=weak, 0.40–0.59=moderate; 0.60–0.79=strong, and 0.80–1.0=very strong; p-value was 0.95.

Results

A total of 10 patients took part in the study (60% male, mean age 58 years, range: 35–83 years) with a total of 24 observations (12 NIRS and 12 TCOM assessments).

A normal ankle/brachial index (ABI) was observed in three patients, two patients had mild–moderate vascular insufficiency (ABI: 0.71 and 0.88) and five patients had non-compressible vessels. Of the 10 patients, two had diabetes, and two patients had both venous insufficiency and mild oedema (Table 1). These patients were included to look at the effect of skin changes on TCOM and NIRS measurements. All wounds studied had been present for >4 weeks.

Study results are summarised in Table 2 and demonstrate a correlation between TCOM and NIRS. Briefly, the weighted mean pO_2 in the study population was 39.54mmHg (SD: 8.96). The data follow a normal distribution (W=0.97, p=0.95). The oxygen levels measured by TCOM and NIRS showed a strong correlation (r=0.74) but with an expected systematic bias. Bland–Altman analysis showed that mean difference was positive (18.75, Fig 2), suggesting an overestimation of oxygen measurements using TCOM compared with NIRS.

Table 1. Baseline characteristics (n=10)

Age, year	
Median	56
Range	35–83
Gender, n (%)	
Female	4 (40%)
Male	6 (60%)
Ethnicity, n (%)	
African American	2 (20%)
Hispanic or Latino	0 (0%)
Caucasian	8 (80%)
Comorbidities, n (%)	
Diabetes	2 (20%)

Discussion

The noninvasive optical technology, NIRS, lends itself to a number of clinical indications throughout medicine including the detection of breast tumours,[27] evaluation of plaque formation in arterial disease,[28] muscular function,[29] and a variety of neurologic conditions.[30,31]

Measuring tissue oxygenation is fundamental to evaluating a patient with a hard-to-heal wound.[3] Advanced wound and hyperbaric centres have relied on TCOM as a non-invasive vascular assessment. However, the drawbacks of TCOM have led to the search for an alternative technology to assess oxygenation. In the clinical setting, NIRS offers several advantages over TCOM. Clinicians have immediate real-time visualisation of tissue oxygen saturation, avoiding a delay in implementing a treatment regimen. The ease of use allows clinicians to frequently reassess tissue viability, such as in the case of a compromised flap undergoing HBOT.[32] The straightforward nature of the procedure improves interoperability reliability.[23]

The study demonstrated that the NIRS compares as expected with TCOM in assessing tissue oxygenation in a typical wound clinic population. The two methods of measurement correlate well in this small group of patients. The findings are similar to a study done using an earlier version of the NIRS device used in this study without melanin correction. This investigation also had a small sample size, but provides further evidence that NIRS technology could be used as an alternative to the more cumbersome TCOM device.[33]

The observations fall outside the upper limit of agreement on the Bland–Altman plot; however, this is expected based on the method of comparison. The conversion of StO_2 to pO_2 relies on the oxygen dissociation curve that can be influenced by temperature, pH and pCO_2. TCOM measures oxygen at the surface of the skin under a heated electrode. Heating the skin is necessary to increase oxygen diffusion to the electrode and ensure a reliable reading. However, the increased temperature also shifts the oxygen dissociation curve to the left. Therefore, TCOM may overestimate the pO_2 value. In contrast, NIRS does not warm the skin. As a result, a lower pO_2 value is expected when converting saturation to pO_2 using the 37°C degree dissociation curve. In short, NIRS and TCOM do not measure the vascular beds under equivalent conditions. Despite the difference in conditions, the study demonstrates a correlation between modalities. Larger clinical studies in the wound care population are planned to adjust for bias between the measurements and establish the equivalence of NIRS and TCOM.

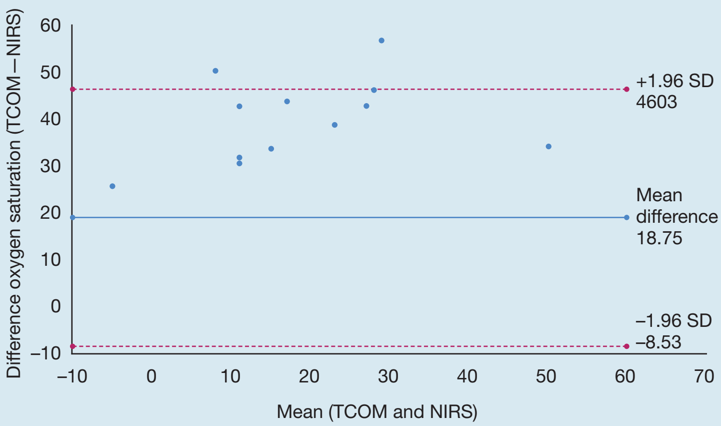
There are other devices that measure oxygenation not included in this study. Spatial frequency domain frequency (SFDF) commercialised by Modulim (Irvine, US) also measures tissue oxygen saturation. However,

Table 2. Partial pressure of oxygen

KENT converted (mmHg)[1]	TCOM (mmHg)	Mean pO_2 (TCOM+NIRS)
9	59	34
42	71	56.5
37	48	42.5
25	36	30.5
46	54	50
29	56	42.5
35	52	43.5
26	41	33.5
28	23	25.5
26	37	31.5
27	50	38.5
32	60	46

[1]Converted to partial pressure of oxygen (pO_2) using the using the standard Severinghaus oxygen dissociation curve; TCOM—transcutaneous oxygen measurement; NIRS—near infrared spectroscopy

Fig 2. Bland–Altman plot



TCOM—transcutaneous oxygen measurement; NIRS—near infrared spectroscopy; SD—standard deviation

SFDF devices on the market, at the time of writing, are restricted to the plantar surface of the foot whereas NIRS can visualise tissue oxygenation anywhere on the body. Hyperspectral imaging (Hypermed, Memphis, TN) measures tissue oxygen saturation, using NIRS, by evaluating the ratio of oxygenated to deoxygenated haemoglobin. It also compared favourably to TCOM in two head-to-head studies of NIRS and TCOM; one to detect peripheral arterial disease and a second to evaluate amputation stumps.[34,35]

Limitations

This study was designed to inform a larger planned comparative clinical trial. The small sample size is one of the limitations of this study. In addition, all the TCOM and NIRS measurements were performed by clinicians with extensive experience on both devices. This limited the ability to examine inter-rater reliability. Future trial design will include clinicians with varying levels of expertise with the devices. Finally, half of the patients had non-compressible vessels preventing measurement of ABI. The trial did not include toe/brachial index (TBI) measurements. Although ABI and TBI measure perfusion rather than oxygenation, the information could have added to the knowledge gleaned from the trial.

Conclusion

This trial suggests that NIRS is comparable with the standard practice of transcutaneous oximetry in evaluating tissue oxygenation. The authors suggest expanding the comparison to a larger population of patients seen in the wound and hyperbaric centre. **JWC**

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Reflective questions

- What is near infrared spectroscopy (NIRS)?
- How does NIRS compare with transcutaneous oxygen measurement (TCOM) in measuring tissue oxygenation?
- What are the advantages of NIRS over TCOM?

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