DREXEL UNIVERSITY
School of
Biomedical Engineering,
Science and Health Systems

Diffuse Near Infrared Spectroscopy Prediction of Healing in Diabetic Foot Ulcers: A Human Study and Cost Analysis

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Abstract

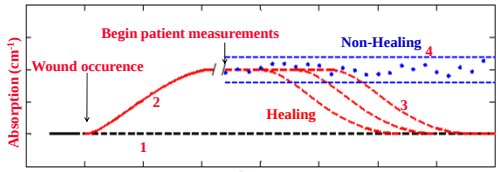
With diabetes rates on the rise in the United States, diabetic foot ulcers have become increasingly prevalent, resulting in nearly 75,000 annual cases at a cost of $5 billion. A key component to this cost is due to expensive wound therapies which can exceed $1,800 per week. Wound size reduction method is unreliable with a positive predictive value of less than 60%. Diffuse Near-Infrared Spectroscopy (DNIRS) uses 70-MHz modulated light in the diagnostic window (650-900nm) non-invasively to quantify levels of oxy- and deoxy-hemoglobin in the wound bed, which when measured over time, can show a trend towards or away from healing based on the changes in oxy-hemoglobin concentration from week to week. In this study, DNIRS was used to monitor 46 human diabetic foot ulcers longitudinally over the course of 20 weekly or bi-weekly measurement sessions. In just four weeks, the DNIRS system has a 91% positive predictive value (sensitivity of 0.9 and specificity of 0.86; p<0.002). These data indicate that it could be possible to objectively predict healing in 4 weeks using DNIRS and make decisions to cease or continue expensive treatments based on physiological conditions and health of the underlying tissue, not solely on the estimated size of the wound. Discontinuing ineffective treatments after 4 weeks could have potentially saved over $12,600 per patient, based on the treatment regimen of patients in this study

Objective

The goal is to give clinicians a means to:

- **Assess the efficacy of treatment modalities used in chronic and diabetic wounds in patients.**
- **Reduce the time and improve accuracy in predicting healing to allow faster changes in treatment regimen if necessary**

Hypothesized wound healing model



1. Dashed black line represents normal (non-wound) tissue
2. Solid red line the result of the animal study
3. Dashed red line the hypothesized curve for healing wounds. The amount of time required for the healing curve to converge with the baseline is not known.
4. Blue markers represent measurements on non-healing wounds

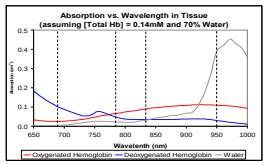
Research Hypothesis

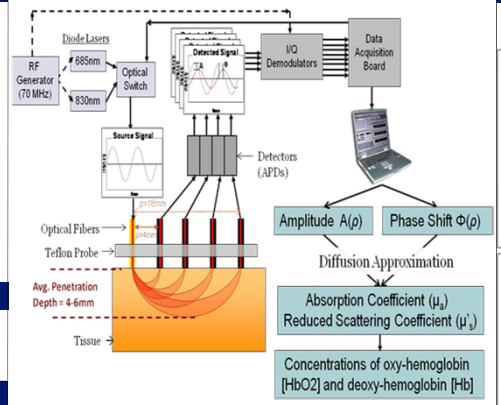
It is hypothesized that decreases in oxygenated and total hemoglobin concentrations over time will be predictive of healing in diabetic foot ulcers.

Frequency-Domain Near Infrared Spectroscopy

Diffuse near infrared (NIR) spectroscopy provides quantitative information about tissue beneath the wound surface

- **Optical Absorption Coefficient (μ_a) at NIR wavelengths is determined mainly by deoxygenated and oxygenated hemoglobin**
- **Optical Reduced Scattering Coefficient (μ_s') gives information about tissue structure (organization, composition)**





Oxyhemoglobin concentration ([HbO_2]) and deoxyhemoglobin concentration ([Hb]) are calculated from measured values of μ_a by minimizing the difference between the left and right sides of the following equation:

$$\varepsilon^{\lambda}_{Hb}[Hb] + \varepsilon^{\lambda}_{HBO2}[HbO_2] + \mu^{\lambda}_{a,H2O}(\%\ H_2O) = \mu^{\lambda}_{a,measured}$$

where:

$\varepsilon^{\lambda}_{Hb}$ and $\varepsilon^{\lambda}_{HBO2}$ are the molar extinction coefficients of deoxy- and oxyhemoglobin,

$\mu^{\lambda}_{a,H2O}$ is the absorption coefficient of pure water at each wavelength (λ),

(% H_2O) is held constant at 70%.

Overview of human study

Patient selection

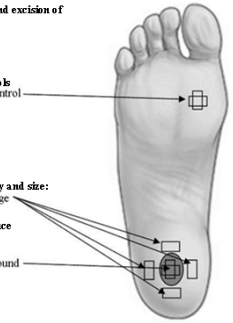
- 46 subjects with diabetic foot ulcers were recruited from Drexel University Wound Healing Center
- 30 to 65 years of age with diabetes mellitus
- Wounds <1 cm^2 were studied.
- Ankle-Brachial Index > 0.75.
- Patients had debridement of necrotic tissue and excision of
- acute osteomyelitic bone prior to enrollment.

Standard wound care

- Weekly or biweekly debridement
- Treatment with moist wound healing protocols
- Offloading when appropriate
- Universal precautions were followed
- Active wound healing modalities were used
- in patients when indicated.

Optical measurements

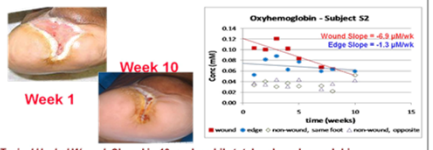
- Weekly or bi-weekly basis
- Different locations based on wound geometry and size:
  1. Directly on the wound
  2. On intact skin at the edge of the wound
  3. On non-wound control tissue at a distance of at least 2 cm from the wound



Results of Human Study

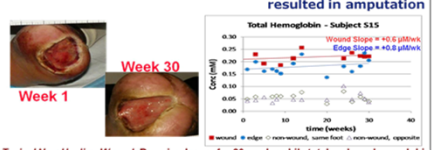
The rate of change in hemoglobin concentration over time was quantified by fitting a linear trend line to the plots of [Total Hb], [Oxy-Hb], and [Deoxy-Hb]

Healed Wounds: 7 out of 16 wounds healed



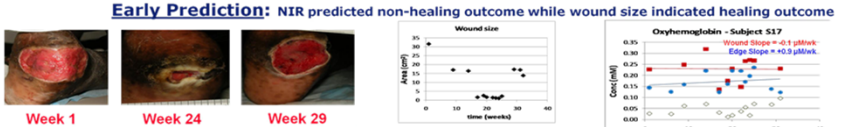
Typical Healed Wound: **Closed in 10 weeks while total and oxy-hemoglobin concentrations in wound decreased and converged with control.**

Non-Healing Wounds: 9 wounds remained unhealed or resulted in amputation



Typical Non-Healing Wound: **Remained open for 30 weeks while total and oxy-hemoglobin concentrations did not converge with control.**

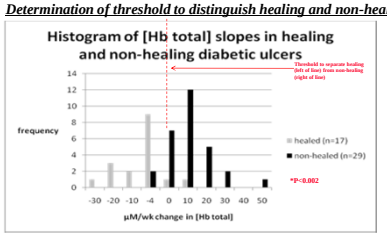
Early Prediction: NIR predicted non-healing outcome while wound size indicated healing outcome



- **Wound size decreased sharply through week 18, but did not close and required OR debridement after week 25.**
- **NIR total and oxy-hemoglobin measurements in wound did not converge with non-wound measurements.**

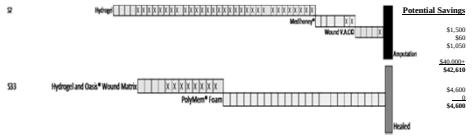
Summarized Results

Determination of threshold to distinguish healing and non-healing ulcers



Typical Healing and Non-Healing treatment charts

(x's represent treatments beyond 4 weeks which did not heal the wound)



Predictive Power of DNIRS using total hemoglobin compared to wound size

	Optical Data				Size Data	
	Full study timeframe		First 4-5 weeks only		First 4 weeks only	
	Healing	Non-Healing	Healing	Non-Healing	Healing	Non-Healing
Predicted Healing	15	2	9	2	13	8
Predicted Non-Healing	2	27	1	12	4	21

DNIRS Predictive Power

(using [Hb total] slope over first 4-5 weeks)

Sensitivity: 90%

Specificity: 86%

Wound Size Predictive Power [gold standard]

(using 40% reduction over 4 weeks)

Sensitivity: 76%

Specificity: 72%

Average Potential Savings

(based on 30 patients with treatment data available)

$12,600 / patient

Total Potential Savings

(based on 30 patients with treatment data available)

$370,000+

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