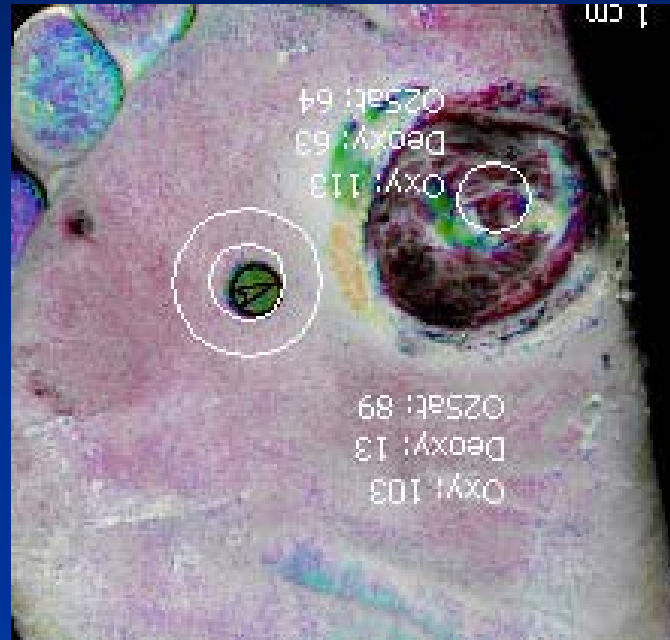
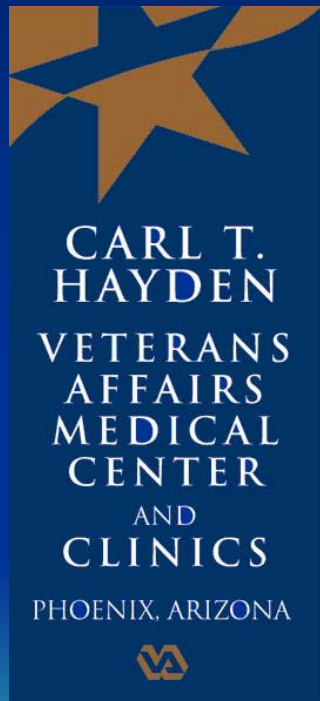


Hyperspectral Imaging Technology: Role in Microcirculatory Function Assessment, Wound Care & Limb Salvage

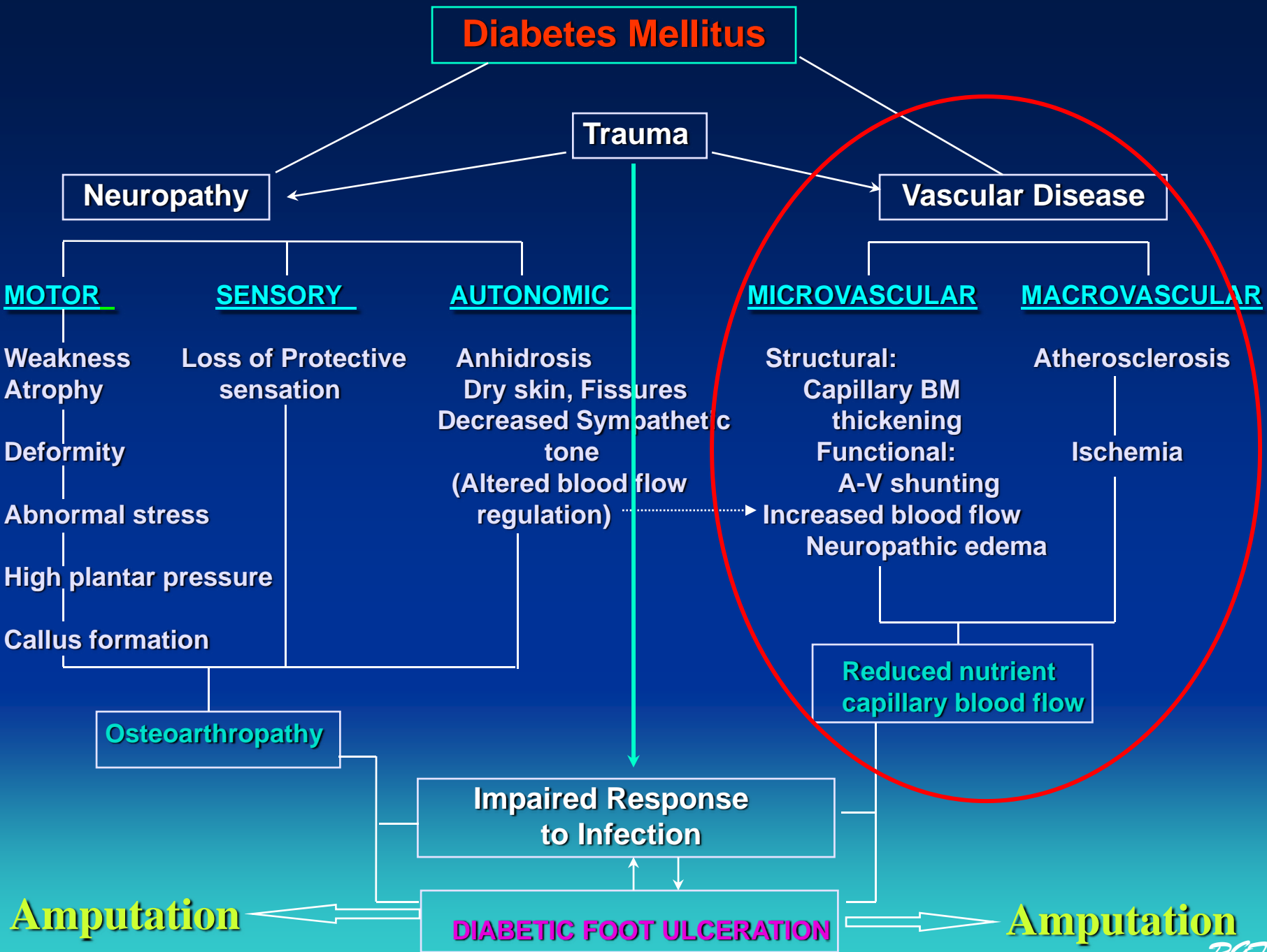


Robert G. Frykberg, DPM, MPH, FAPWCA
Chief, Podiatry Section
Carl T. Hayden VA Medical Center
Phoenix, AZ USA

DISCLOSURES

Consultant, Speakers Bureau, Research Support or SAB:

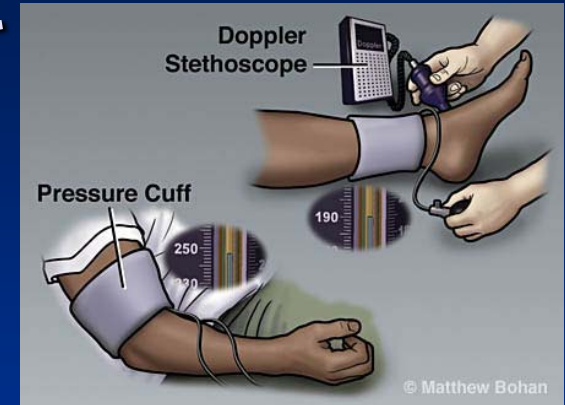
- **Hypermed**
- VasaMed
- Regeneration
- Oculus
- Sanuwave
- KCI
- Wound Solutions
- Pfizer
- Organogenesis
- Silverleaf



Diagnostic Vascular Assessment

Non-invasive arterial studies:

- ABI measurements
- Toe pressures
- Pulse-volume recordings
- Segmental pressure measurements
- Color Duplex Ultrasound
- Laser Doppler flux / imaging
- TcPO₂ – transcutaneous oxygen tensions
- Skin Perfusion Pressure (Laser Doppler)
- **Hyperspectral Imaging (OxyVu®)**



Invasive / Pre-revascularization Studies

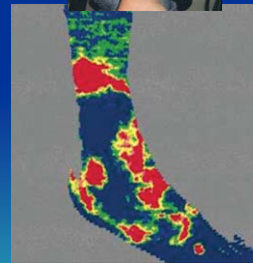
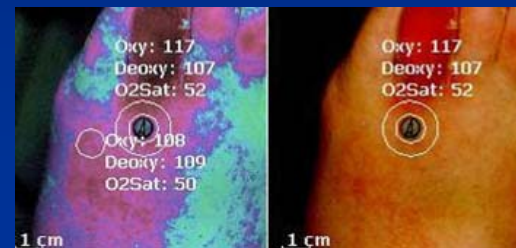
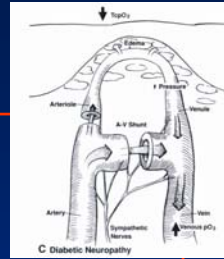
- Arteriography –
 - Digital subtraction
 - MRA
 - CTA



Evaluating the Microcirculation

Nutritive capillaries, A-V shunts

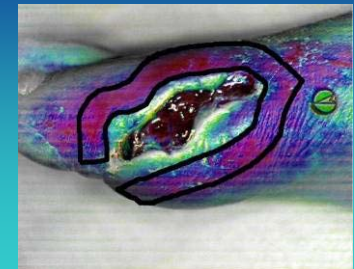
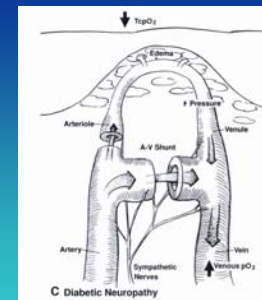
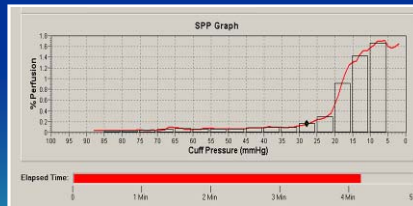
- Metabolic: Oxygenation/ Hypoxia
 - Transcutaneous Oxygen tension (TcPO₂)
 - Transcutaneous Carbon dioxide tension (TcPCO₂)
 - Oxygen saturation (SO₂) – pulse oximetry
 - Spectroscopy
 - Near infrared Spectroscopy (NIRS)
 - **Hyperspectral Imaging (HSI)**
- Perfusion/ Flow
 - Photoplethysmography
 - Laser Doppler Imaging/ Laser Doppler Flowmetry (LDF)
 - Iontophoresis: Ach/ Na Nitroprusside (endo-dep / independent)
 - Capillaroscopy
 - Skin Perfusion Pressure



Mathieu, Mani: LE Wounds 2007
Abularrage et al: JVS 2005
Cobb, Claremont: LE Wounds 2002

Novel Objective Microcirculatory Modalities: Can they do more than predict amputation levels?

- Prediction of ulcer healing –
 - Kalani 1999; Khaodhjar 2007; Yamada 2008; Bailey 2008; Nouvong 2008
- Identify early microvascular dysfunction in DM - Williams et al JVS 2006
- Post revascularization assessment – Arora JVS 2002
- Identify those with non- reconstructable CLI best served by earlier amputation – Ubbink et al. JVS 1999
- BUT ALSO – extremely useful for determining amputation levels / predicting healing where amputation becomes necessary
 - Pecoraro 1991
 - Adera 1995
 - Yamada 2008
 - Frykberg 2008, Nouvong 2008 (Posters)



Hyperspectral Imaging



- **Spectroscopy**
 - the study of the interaction between radiation and matter as a function of wavelength (λ).
 - any measurement of a quantity as function of either wavelength or frequency.
- **Spectrometry** is the spectroscopic technique used to assess the concentration or amount of a given species. In those cases, the instrument that performs such measurements is a spectrometer or spectrograph.
- **Spectroscopy/spectrometry** is often used in physical and analytical chemistry for the identification of substances through the spectrum emitted from or absorbed by them.

Hyperspectral Technology Established During Past 20 Years

- Major aerospace and military applications
- Originally used in satellite surveillance
- Imaging technology generates a “gradient map” of the region of interest



Tank

Hyperspectral Imaging

- Hyperspectral imaging is the extension of light spectroscopy, where multiple images of the same scene are taken to identify specific signature spectra of materials from the multidimensional dataset.
- In medical hyperspectral imaging, the device uses an external illumination source and a camera to image oxyhemoglobin and deoxyhemoglobin
- Provides valuable microcirculatory information on oxygen delivery and oxygen extraction.

OxyVu™ Hyperspectral Imaging

- Tissues have optical signatures from chromophores that reflect their chemical characteristics
- Two major chromophores of relevance
 - Oxyhemoglobin (OxyHb)
 - Deoxyhemoglobin (DeoxyHb)
- Oxyhemoglobin (OxyHb) and Deoxyhemoglobin (DeoxyHb) are extracted from each pixel
- HSI efficiently collects this data from over 1 million points (pixels)



OxyVu™ Microvascular Assessment



Measuring Tissue Perfusion

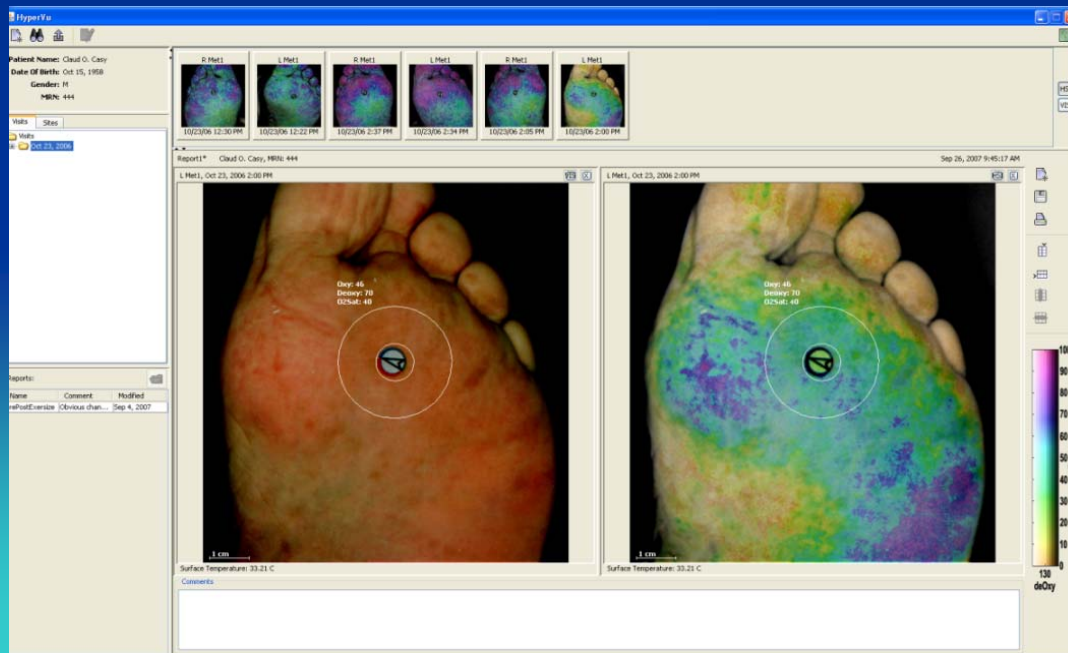
- Quantifies oxy and deoxy-hemoglobin at capillary level
- Visually depicts tissue viability
- Determines microvascular health for diagnosis and healing prediction

Advantages

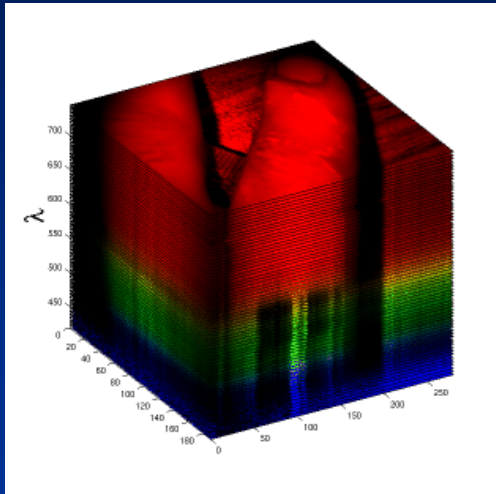
- Both visual and quantitative
- Non-contact, user friendly, rapid test

Medical Hyperspectral Imaging

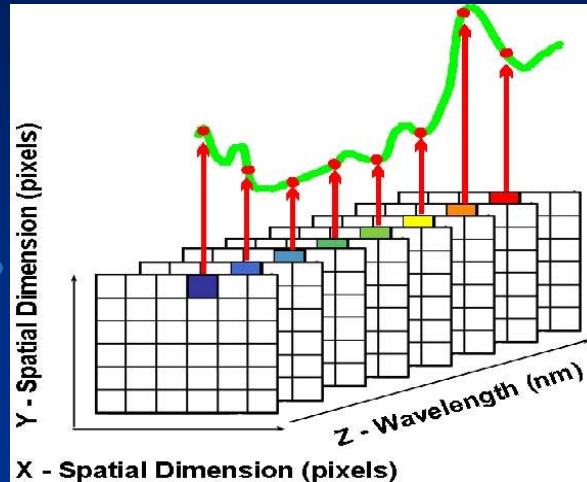
- Captures images at 15 different wavelengths
- Visible wavelengths – hemoglobin specific
- 1 million pixels of individual data
 - Oxyhemoglobin and deoxyhgb extracted from each pixel
- Data yields hyperspectral image
 - (diffuse reflectance spectroscopy)



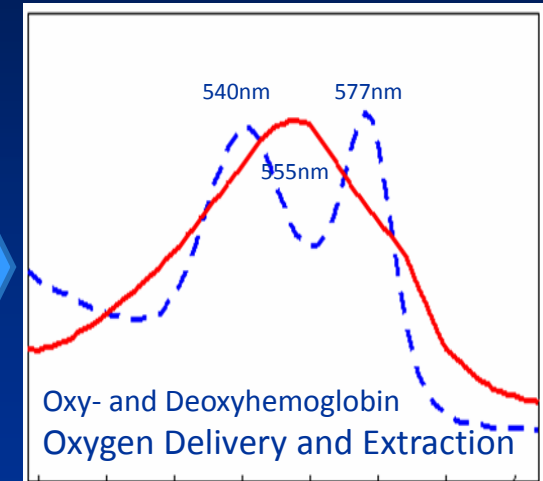
OxyVu™ Image Capture Process



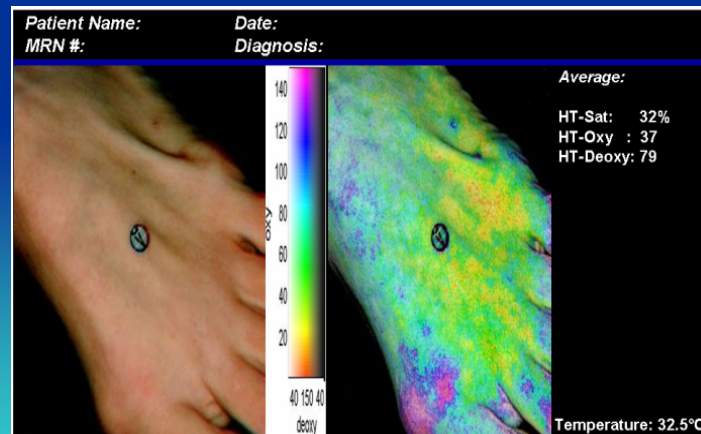
*Optics Acquire
Hyper Cube*



Spectra Isolated



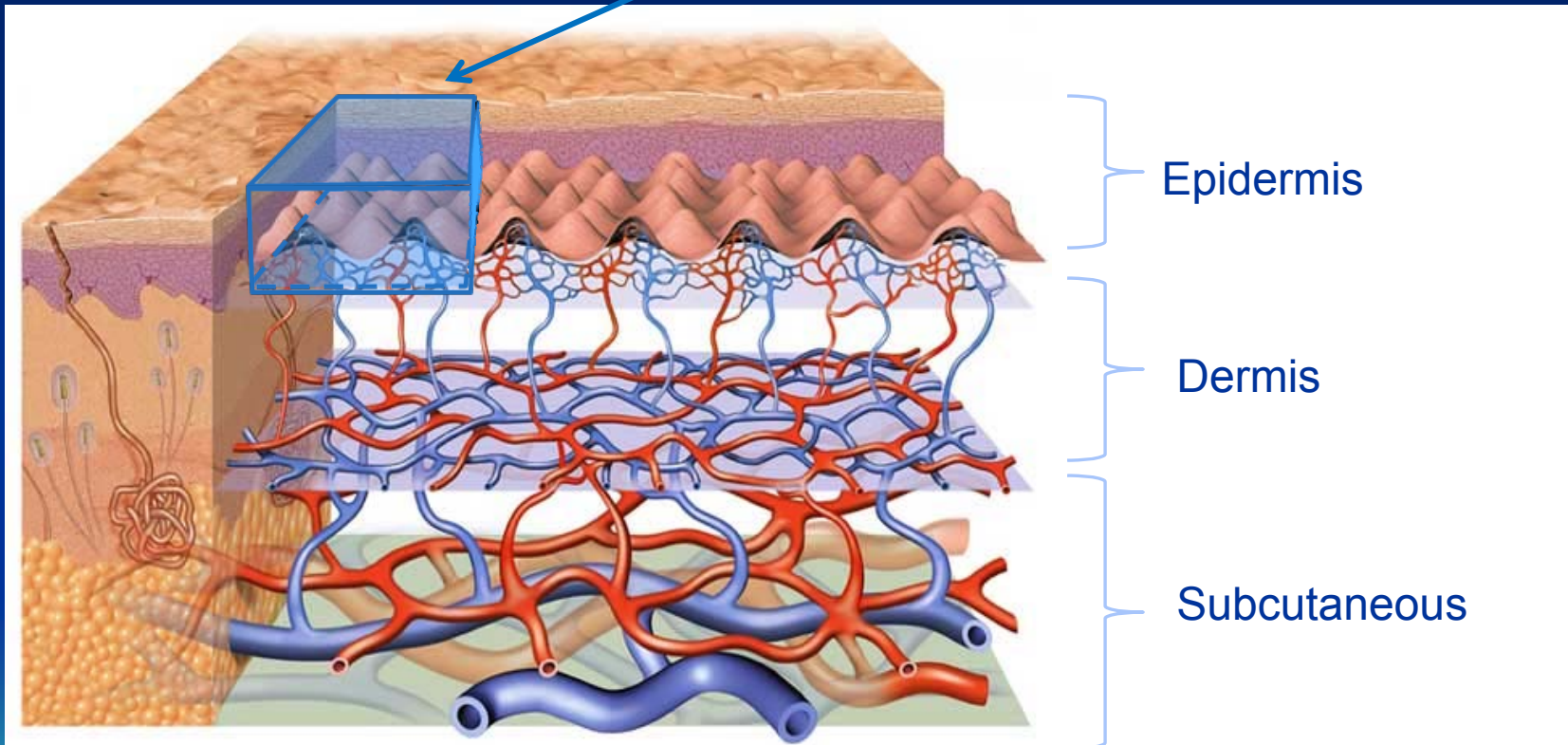
*Proprietary Algorithm
Processes and Displays Data*



Friendly User Interface

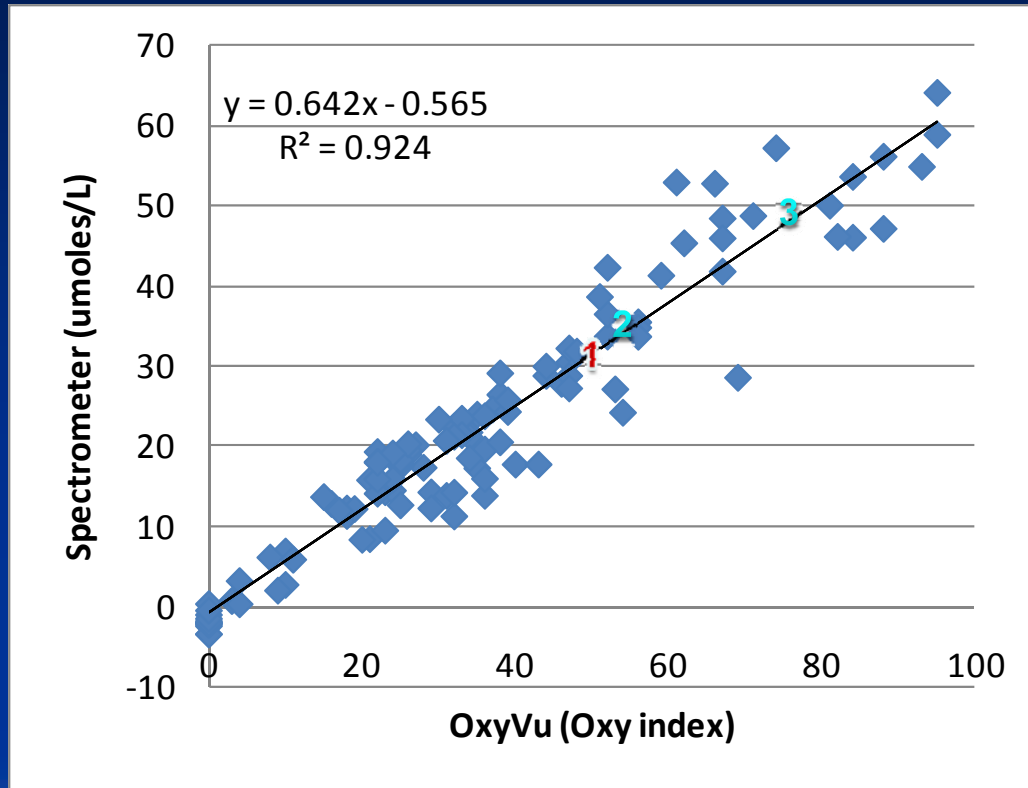
OxyVu™ Assesses Tissue Viability of the Superficial Dermis

One Pixel on CCD
Measurement 1-2mm Deep X 90 microns



HSI Measures the functional capacity of tissue to process oxygen

OxyVu™ Correlates to Spectrometer

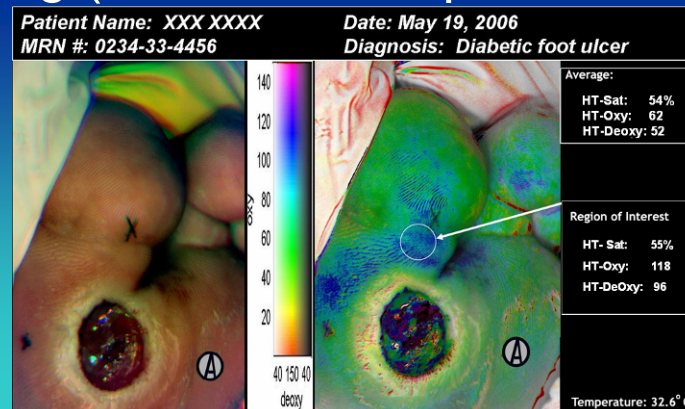


➤ The OxyVu™ Oxy index linearly correlates with spectrometer oxyhemoglobin concentration measurements ($R^2 = 0.92$)

1. OxyVu Oxy index 50 ~ 32 $\mu\text{mols/L}$ in Oxyhemoglobin
2. OxyVu Oxy index 55 ~ 35 $\mu\text{mols/L}$ in Oxyhemoglobin
3. OxyVu Oxy index 75 ~ 48 $\mu\text{mols/L}$ in Oxyhemoglobin

Clinical Evidence - Published

- Lancet (Greenman, 2005)
 - HSI can identify microvascular abnormalities;
 - HSI values show decreased oxygenation in skin when comparing non-diabetics, to diabetics, to diabetics w neuropathy; and
 - Decreased oxygenation in skin correlates when oxygenation levels in deep muscle as measured with Pi/PCr MRI.
- Diabetes Care (Khaodhiar, 2007)
 - HSI can identify microvascular abnormalities and
 - HSI can predict ulcer healing (Sens=93%, Spec=86%, 10 subjects, 21 ulcers)



Current Evidence

Clinical Publication	Data Provided
Lancet	Established OxyVu relevance to stage of disease
Diabetes Care	Pilot showing feasibility of ulcer healing
NIH2a	Pivotal study demonstrating OxyVu healing prediction (n=65)
NIH2b	Pilot demonstrates OxyVu can be an early predictor of ulceration
Frykberg Case Series	Clinical use of OxyVu in amputation planning
Sidawy, Johnson	Demonstration of improved viability post revascularization

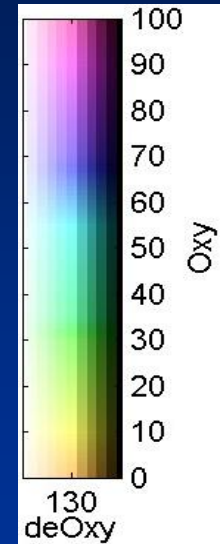
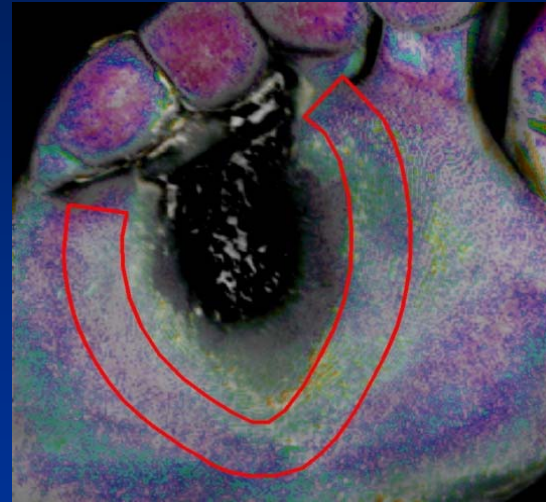
NIH IIa: Predicting Healing Potential of DFUs

Study Design

- Prospective, single-arm, double-blinded study of 66 patients with Type I and II with DFU
- 11 visits over 6 months
- OxyVu data from first visit used to predict healing at 6 months
 - 49 subjects having 65 ulcers completed 6 month study
 - 11 subjects failed to complete study, 6 still in follow-up
 - 48 ulcers healed; 17 ulcers not healed
- OxyVu images at first visit used to develop ulcer healing index

NIH IIa OxyVu™ Healing Prediction

10/06/06



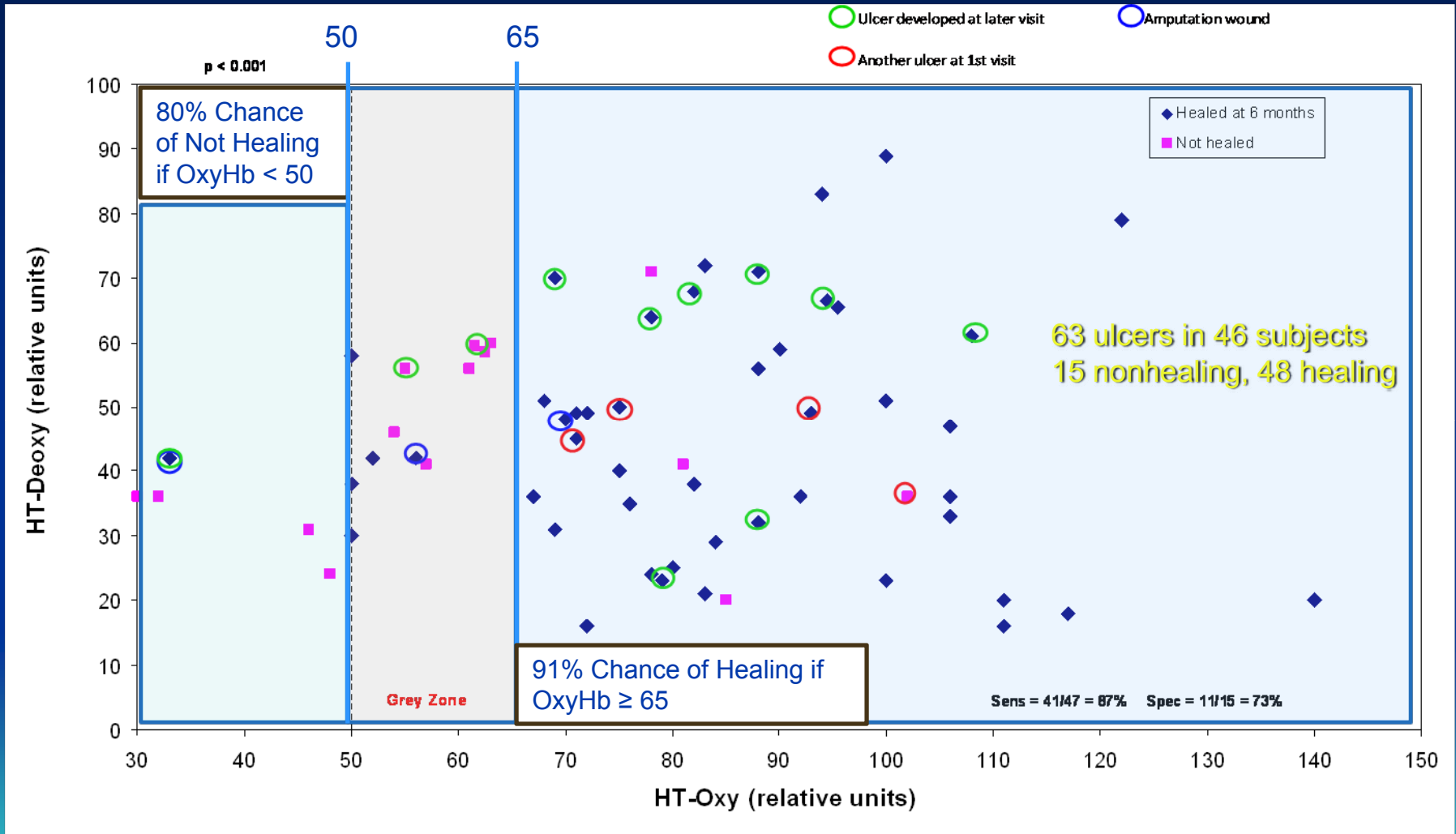
2/23/07



HT-Oxy = 75
HT-Deoxy = 34
HT-Sat = 69%

Figure 2A: Healing diabetic foot ulcer. Ulcer healed at 20 weeks.

NIH IIa: Predicting Healing Potential of DFUs

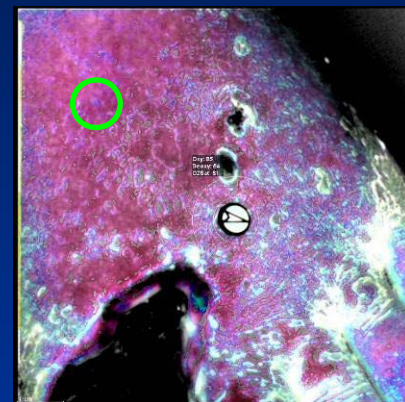


OxyVu Assessment for Amputation Level

Case Study: Saving a Foot

- Vascular Surgery advised BKA
- Initial Plan: Syme Amputation
 - Poor Doppler signals
 - TCOM: 18mmHg (Predicts 39-fold risk of failing to heal at Transmetatarsal level)
- Post OxyVu Assessment: Transmetatarsal Amputation
 - Oxy score: 85 (≥ 65 Predictive of healing)
- 4 month follow up: Patient healed with only minor wound dehiscence

Pre-Op



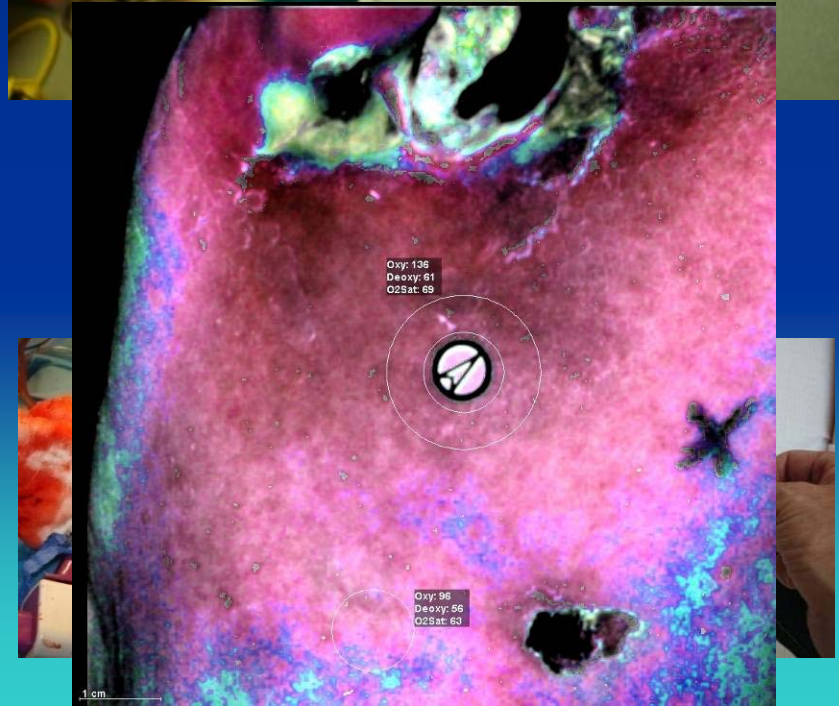
Post-Op



OxyVu Already Making a Difference

Case Study: Saving a Limb

- Initial Recommendation: BKA (non-reconstructible PAD)
 - ABI was .62 = Moderate Ischemia
 - TcPO₂ results showed 38mmHg (ankle) and 18 mmHg (TMA)
- Post OxyVu Assessment: Syme Amputation
 - Oxy score at heel: ~60
 - Oxy score at ankle: 58
- 12-week follow up: Patient healed without complications

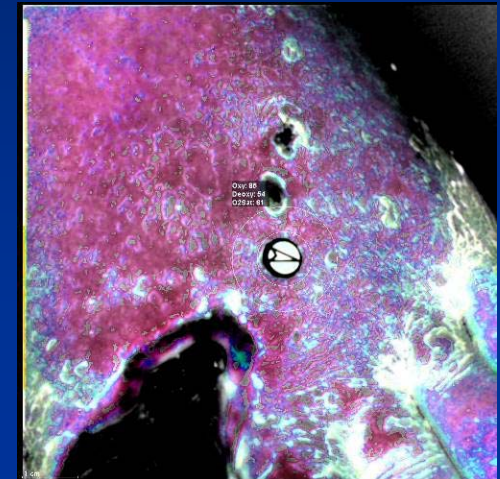


Patient Walking with New Prosthesis



Hyperspectral Imaging (HSI) Potential Uses

- Predict Ulcer Healing- Assess perfusion/tissue viability (Sensitivity ~90%, Specificity ~85%)
 - Assist in Surgical Planning
 - **Level of amputation (Current Study)**
 - Flap rotation
 - Debridement
 - Monitor progress of care
 - Early referral to vascular surgery
- Predict Development of Ulcer ($p < 0.0008$)
 - Pre-emptive care for our diabetic patients
 - Pre-op for preventive surgery
 - Screening tool

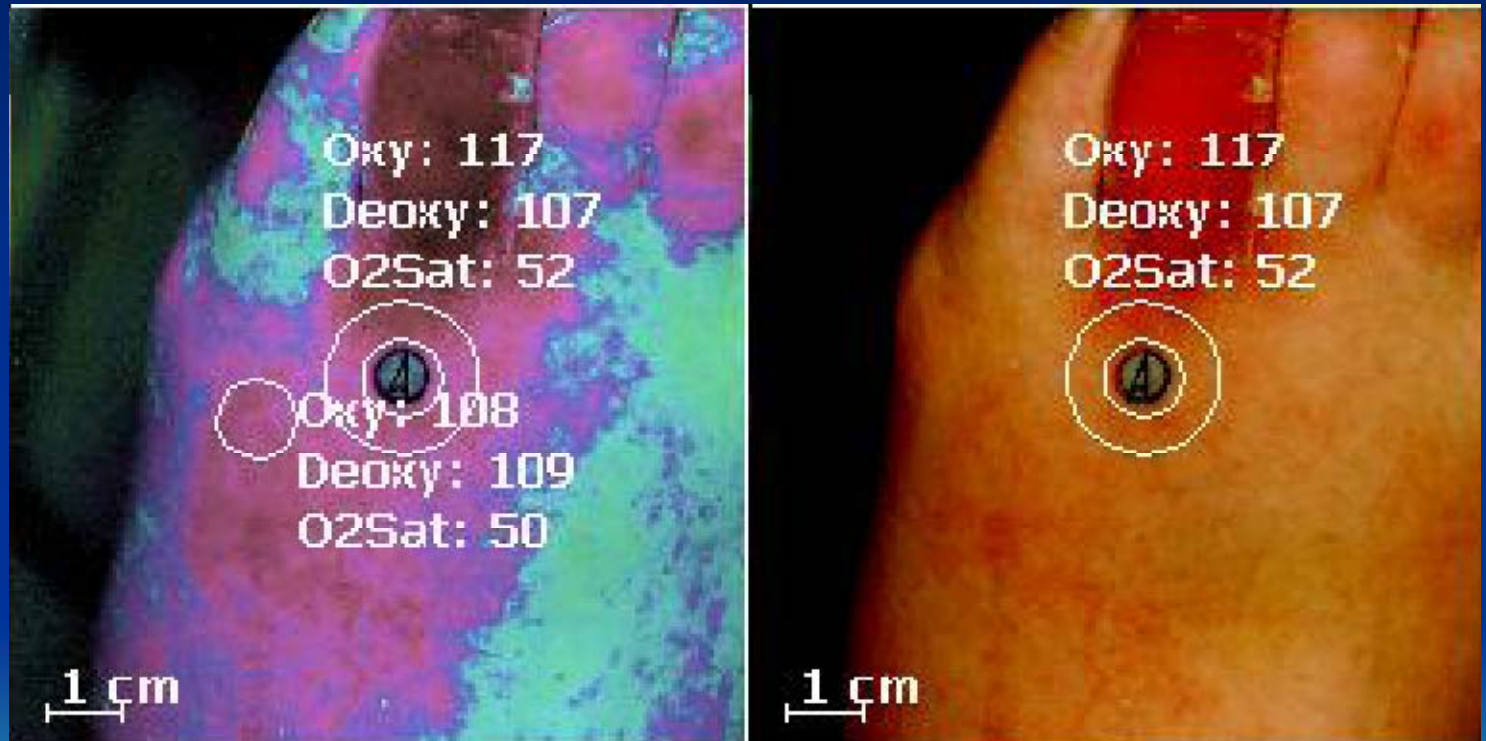


Courtesy Aksone Nouvong, DPM
Unpublished data

Summary

- Assessment of Perfusion in diabetic patients is an essential part of examination
- Both Macrovascular and Microvascular modalities are necessary
- Consider reproducibility and validity of tests in various clinical situations (edema, infection, etc)
- Benchmark data /clinical studies provide guidance, but nothing is absolute in predicting healing
- HSI is a valuable new modality for assessing local tissue metabolism/ perfusion
 - Benchmarking studies are under way

THANK YOU!



CARL T.
HAYDEN
VETERANS
AFFAIRS
MEDICAL
CENTER
AND
CLINICS
PHOENIX, ARIZONA



Robert G. Frykberg, DPM, MPH, FAPWCA
Robert.frykberg@med.va.gov