Characterization of Subcutaneous Oxygen Microsensors In Healthy Volunteers: In Vivo Evidence of a Tool for Future Management of CLI Patients

Peter A. Schneider, MD
Honolulu, Hawaii

Stephen Kanick PhD, Peter A Schneider MD, Natalie Wisniewski, Kerstin Rebrin, MD
Disclosure

Peter A. Schneider, MD

Potential conflicts of interest to report:

Consulting: Silk Road, Surmodics, Profusa, CSI, Cardinal, Terumo

Chief Medical Officer: Intact Vascular, Cagent, Vesper

Scientific Advisory Board: Abbott, Medtronic, Boston Scientific
We make most decisions in CLI management based upon clinical experience. What if we had a tool to objectively evaluate perfusion?

Pre-operative triage

- Perfusion at tissue level?
- Degree of microvascular impairment?

Intra-operative monitoring during EVT

- How many tibials?
- Add BTA angioplasty?
- How to know when finished?
- How beneficial is indirect revascularization?

Post-operative monitoring

- Who needs a re-intervention?
- How to monitor after marginal improvement from EVT?
- Can we monitor remotely?
Lumee™ Oxygen Platform is designed to measure oxygen and may provide immediate feedback on the quality of revascularization along the entire course of the patient’s recovery.
How does Lumeetm Oxygen work?

- Soft biocompatible hydrogel sensor injected into subcutaneous space
- Excitation light from surface reader reaches hydrogel in tissue.
- Fluorescence chemistry on hydrogel responds based on analyte concentration. Reader collects emissions and data sent to cloud.
## Comparison of hemodynamic and perfusion monitoring approaches

<table>
<thead>
<tr>
<th></th>
<th>Ankle Brachial Index (ABI)</th>
<th>Toe Brachial Index (TBI)</th>
<th>Skin Perfusion Pressure (SPP)</th>
<th>Transcutaneous oximetry (tcpO₂)</th>
<th>Lumee™ Oxygen</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td><img src="image3.png" alt="Image" /></td>
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<tr>
<td><strong>Advantages</strong></td>
<td>Inexpensive and easy to perform</td>
<td>Inexpensive and easy to perform</td>
<td>Insensitive to arterial calcification</td>
<td>Direct assessment of oxygen extraction from microvessels</td>
<td>Easy to use method provides continuous real time data at locations of interest.</td>
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<tr>
<td></td>
<td>Inexpensive and easy to perform</td>
<td>Insensitive to tibial arterial calcification</td>
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<td><strong>Why isn’t it more broadly used?</strong></td>
<td>Incompressible arteries associated with diabetes</td>
<td>Requires intact toes and not representative of all foot wounds, digital vessel calcification</td>
<td>Movement from subject or pressure tubing equipment can introduce artifacts.</td>
<td>Sensitive to temperature and motion. Not applicable to plantar side of foot. Functions by heating tissue. Tempermental.</td>
<td>Still in investigations</td>
</tr>
</tbody>
</table>
Healthy volunteer study performed to compare tissue oxygen measured by Lumee™ Oxygen and tcpO₂ during pressure cuff-occlusions.

Comparative analysis showed that Lumee™ Oxygen sensors detected decreases in oxygen during circulatory interruption and time traces were highly correlated with tcpO₂.

Results indicate that Lumee™ Oxygen measures changes in tissue oxygen in human in vivo.
Healthy volunteer study protocol

Study Design

• Study enrolled healthy volunteers under an IRB-approved protocol (Quorum IRB Review File #30672/1, Protocol #TP0004).

• Enrolled 7 subjects, each had Lumee™ Oxygen sensor subcutaneously injected in forearm

• Subjects sampled during 10 visits after sensor implant (range 6-105 days)

Methods

• Pressure cuff used to temporarily induce circulatory interruption in upper arm

• Each vascular occlusion test included:
  • 15 min warm up
  • 5 min baseline
  • 2 min pressure cuff
  • 10 min recovery
  • Repeated twice per visit

• Tissue oxygen measured by:
  • Lumee™ Oxygen
  • Transcutaneous Oximetry (i.e tcpO₂)

Analysis

• Sampled 109 occlusions in total, of which 95 were deemed artifact-free

• Algorithm aligned start times of occlusions across devices

• Exploratory comparative analysis characterizes accuracy, variability, and long-term stability of Lumee™ Oxygen
What clinically-relevant questions does this study address?

**Question**

- Does Lumee™ Oxygen monitor tissue oxygen in vivo?
- Are there observed differences between Lumee™ Oxygen and tcpO_2?  

**Analysis**

- Performance analysis compares Lumee™ Oxygen to a reference method
- Analysis compares dynamics between devices
Lumee™ Oxygen and tcpO₂ both show responsivity to vascular occlusion tests

Representative single occlusion response of simultaneously measured Lumee™ Oxygen (A) and two tcpO₂ channels (B).

Plotted time traces depict the following phases during the vascular occlusion test(s):

(I) **Baseline**
(II) **Occlusion**
(III) **Recovery**
Lumee™ Oxygen detected changes in oxygen *in vivo* confirmed by tcpO$_2$

- Lumee™ Oxygen and tcpO$_2$ sensed a statistically significant decrease in oxygen during occlusion (n=95, p<0.001 for each device, one-sample t-test)

- Decreases were not different between the two devices (n=95, p=0.315, one-way ANOVA)
Lumee™ Oxygen response proportional to tcpO\textsubscript{2}

- Correlation between oxygen dynamics measured by Lumee™ and tcpO\textsubscript{2} during vascular occlusion tests was assessed by Pearson product moment correlation coefficient.

- Majority of traces were either highly correlated (with 61% having $r>0.9$) or correlated (with 83% having $r>0.8$).
Lumee™ Oxygen detected faster rates of oxygen change

Rates during occlusion and recovery faster by Lumee™ Oxygen than tcpO₂. (p<0.001, Wilcoxon signed-rank test)

Lumee™ Oxygen detected reactive hyperemia

Oxygen overshoot observed in 38% of Lumee™ Oxygen traces, compared with 4% for tcpO₂

Lumee™ Oxygen provided enhanced sensitivity to vasomotion

Lumee™ Oxygen detected larger fluctuations than tcpO₂ (p<0.001, Wilcoxon signed-rank test)
Summary / Conclusions

• Healthy volunteer study performed to compare tissue oxygen measured by Lumee™ Oxygen and TcPO2 during pressure cuff-occlusions

• Comparative analysis of tissue oxygen time traces showed that Lumee™ Oxygen sensors detected decreases in oxygen and were highly correlated with tcpO₂.

• Lumee™ Oxygen showed some differences in responsivity compared to tcpO₂, with larger background fluctuations at baseline, faster rates of change during provocations, and reactive hyperemia response in a subset of measurements.

• Results indicate that Lumee™ Oxygen measures changes in tissue oxygen in human subjects that were confirmed by a commercially available tissue oximetry device.
Clinical development of Lumee™ Oxygen Platform

Ongoing clinical investigations
• Oxygen monitoring near ischemic areas (OMNIA). Sites: Graz, Munster, Vienna.

Other Presentations (at LINC 2019)
• M.Montero-Baker- Intra-sensor analysis of subcutaneous oxygen microsensors reveal heterogeneous reperfusion response during revascularization procedures for CLI patients. Thur 24th at 14:00-14:05 in Room 6.
• M.Brodmann- Characterizing the relationship between oxygen measured by subcutaneous microsensors during revascularization procedures and wound healing in CLI patients. Thurs 24th at 16:43-16:49 in Room 1

Related Publications
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CLINICAL RESEARCH TEAM

Clinical /Medical Affairs

Profusa
San Francisco, USA
- Kerstin Rebrin, M.D., Ph.D.
- Ulrike Kamecke, M.S.
- Wayne Menzie
- Melanie Schipfer, Ph.D.
- Sayanti Banerjee, Ph.D.
- Stephen C Kanick, Ph.D.

Medical Advisory Committee

- Peter Schneider, M.D. (Kaiser)
- Miguel Montero-Baker M.D. (Baylor)
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