Modalities to Determine the Adequacy of Pedal Revascularization in CLTI

A Look at Evolving Technologies

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‘Connecting the Dots’ in Pedal Perfusion

- Mechanical or biologic intervention
  - Improved blood flow
  - Improved tissue perfusion
  - Improved wound healing

Beyond “Straight-Line Pulsatile Flow in the Associated Angiosome”: An Evolution in Clinical Thought

- Angiographically assessed blood flow ≠ tissue perfusion and may not correlate with or predict wound healing post-intervention (surgical, mechanical or biologic)
- Macro-circulation v. microcirculation pathology remains an issue
- Evolving methods surrogates of tissue level perfusion are evolving, but require validation:
  - Laser Doppler methods (MOXY, Pedra™, Modular™ Imaging, Laser Associated Scientists FlowNet™)
  - BOLD-MR tissue oxygenation

Challenge of Assessing Adequacy of Revascularization in CLI

What’s Wrong with the ABI in CLI?

- Does not tell the entire story in the CLI patient:
  - Lower accuracy in intrinsic pedal artery disease
  - Lower accuracy in multilevel disease (almost all CLI patients)
  - Not everyone performs toe pressures/waveforms

Analysis of IN.PACT DEEP trial on the association between changes in perfusion from pre- to postrevascularization and clinical outcomes in critical limb ischemia
Unadjusted Kaplan-Meier curves among ankle (Panel A) and toe (Panel B) pressure groups for MALE. The log-rank test revealed a statistically significant difference between MALE only among the toe (Panel B), not the ankle (Panel A), pressure groups. MALE=major adverse limb events.

Hammad et al, Cathet Cardiovasc Interven 2017

What are Evolving Surrogates of Tissue Perfusion That May Translate into Improved Wound Healing

- Angiographic wound blush
- Methylene Blue angiography
- Pedal BOLD-MR
- Laser Doppler methods (MOXY™, Pedra™, Modular Imaging™)

The Basic Principles: Pedal BOLD Assessment

Kos, et al., Invest Radiol 2009; 44: 741-747

Pedal BOLD MR in PAD – A Case Study (Baseline vs. 30d Follow-up)

<table>
<thead>
<tr>
<th></th>
<th>Overshoot</th>
<th>Reserve</th>
<th>Dynamic range</th>
<th>Time to peak</th>
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<tbody>
<tr>
<td>Baseline 01-002</td>
<td>3.07%</td>
<td>4.43%</td>
<td>7.50%</td>
<td>215</td>
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<tr>
<td>30 days</td>
<td>10.51%</td>
<td>4.29%</td>
<td>14.80%</td>
<td>110</td>
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<tr>
<td>TP=33</td>
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<td>TP=40</td>
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Baseline & 30d PEDAL BOLD
Ox-Imager CS™
(by Modulated Imaging)

- Based on Spatial Frequency Domain Imaging (SFDI)
- Sub-surface imaging 10x deeper than visual inspection
- Real-time wide-field assessments
- Only system to measure multiple tissue components:
  - Tissue Oxygen Saturation (StO2)
  - Blood volume (HbO2, HbR)
  - Compromised circulation

Automatic correction for melanin, body curvature and patient motion

Vascular Assessment

<table>
<thead>
<tr>
<th></th>
<th>Visual (no Ultrasound)</th>
<th>Angiogram (61 mins)</th>
<th>Waveform (20 mins)</th>
<th>ABI (20 mins)</th>
<th>Ox-Imager StO2 (7 mins)</th>
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</thead>
<tbody>
<tr>
<td>Right</td>
<td>Normal</td>
<td>Highvess</td>
<td>1.14</td>
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<td></td>
</tr>
<tr>
<td>Left</td>
<td>Occluded artery</td>
<td>Rhoaphic</td>
<td>0.72</td>
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<td>30%</td>
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Pedra’s Real-Time Tissue Perfusion Monitor

The sensor that is attached to the patient’s skin houses a laser light source. This emits a highly coherent laser light, which is scattered by the moving red blood cells in tissue up to a 7.5mm depth. A detector on the sensor picks up the laser speckle pattern generated from constructive/destructive interference of scattered light. The level of scattering and blurring of the speckle pattern yields a signal as to the amount of perfusion in the underlying tissue.

Pedra Technologies™

Blood Perfusion Index (“BPI”) Tracks Ballooning In Real Time

Red circles show BPI dips with ballooning.
12 human case studies in UK

Emerging Technologies to Assess Pedal Perfusion:

- Non-invasive diagnostics, beyond toe pressures to assess pedal perfusion, are essential to the care of CLI patients
- Ox-Imager CS™ and Pedra™ are evolving non-invasive tissue perfusion technologies that hold the potential to guide clinical treatment in the CLI population and assessment of pedal perfusion
- All these new technologies await clinical validation prior to market introduction
The End