Imaging techniques to determine tissue perfusion in critical limb ischemia

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Disclosure

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I have the following potential conflicts of interest to report:

- [x] Consulting
- [ ] Employment in industry
- [ ] Stockholder of a healthcare company
- [ ] Owner of a healthcare company
- [ ] Other(s)

- [ ] I do not have any potential conflict of interest
Tissue perfusion in CLI

- Diagnosis and follow-up of critical threshold of tissue perfusion
- When does tissue perfusion decrease to a certain threshold which is critical for tissue loss?
- Currently available hemodynamic parameters are not made for this
- Revascularization is the key element to restore adequate tissue perfusion in CLI
- But how to determine if this was successfully achieved?
- Angiogram alone is not reliable
Tissue perfusion in CLI

- Ideal test for foot perfusion:
  - inexpensive
  - readily available
  - reproducible
  - improve the clinician’s ability to predict outcomes
  - provide perfusion data specific to the area of the foot with a wound

- Improving the ability to evaluate foot perfusion would benefit patients with CLI by
  - assisting with the etiology of a non-healing wound
  - identifying patients with poor perfusion in the angiosome of interest who might benefit from revascularization
  - identifying patients with seemingly adequate perfusion who may not require revascularization
  - selecting a target vessel for revascularization
  - providing insight when revascularization is sufficient
  - facilitating surveillance for patency

Tissue perfusion in CLI

- Current modalities of foot perfusion have limitations
  - Arterial non-compressibility makes the ankle–brachial index (ABI) non-meaningful in many patients with CLI
  - Transcutaneous oximetry has a high coefficient of variation
  - Intra-procedural measures of foot perfusion are attractive to the interventionalist to direct the target and extent of revascularization

... but there are limitations!

✓ ‘Angiographic blush’ have been reported to correlate with wound healing but is somewhat subjective and dependent on technique
✓ Two-dimensional (2D) angiographic perfusion imaging is an intra-procedural method that attempts to provide objective angiographic data of perfusion but is also technique-dependent and is yet to be validated
✓ ............
Tissue perfusion in CLI_Imaging techniques

Transcutaneous oximetry (TcPO2)

measures oxygen diffusion from the capillary beds to the epidermal layer of the skin
Sensor-containing electrode placed on the skin, warms the surrounding skin leading to local hyperthermia, measures the partial pressure of oxygen in the underlying tissue

Benefit
- Can be predictive of wound healing
- Identify individuals with nonhealing ischemic wounds who may benefit from hyperbaric oxygen therapy (HBOT)
- Noninvasive, bedside tool with no radiation exposure

Limitation
- Mechanism of action (skin perfusion): barriers to diffusion can lead to falsely low TcPO2 values
Tissue perfusion in CLI Imaging techniques

**Laser Doppler flowmetry and imaging**

Limitations due to their mode of action, no broader use

**Skin perfusion pressure (SPP)**

SPP obtained with laser Doppler is noninvasive and time-efficient  
Measure hemodynamics at a wound edge

Some data on the ability of SPP to predict wound healing that suggest it is superior to ABI and TcPO

Two-dimensional angiographic perfusion. Right: Color map of the foot generated from a standard catheter-based angiogram. Left: Time density curve representing the time to peak contrast density in the foot. The average time to peak contrast density for this patient was 4.0 seconds.
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Two-dimensional angiographic perfusion imaging

Available evidence/3 studies

- Majority of patients increase in perfusion was observed after revascularization
- ABI correlated well to time-to-peak and peak density ratios
- Improvement in 2D angiographic perfusion parameters was observed following revascularization

Benefit

- Practical, as it can be incorporated into a standard angiogram
- ‘Angiosome specific’, providing information of regional foot perfusion
- Theoretically could guide revascularization decisions in real time

Limitation

- No evidence on longitudinal outcomes associated with 2D perfusion parameters
- Modality not standardized
  - Technique would need to be the same across operators and institutions so that the data generated would be generalizable to patient care.

Miguel Montero-Baker et al; Vascular Medicine 2020, Vol. 25(3) 235–245
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**Indocyanine green angiography**

- Water-soluble contrast agent quickly bound to plasma proteins
- Visualization of local-regional blood flow by a charge-coupled camera to detect the fluorescence emitted after excitation by a laser light source of a specific wavelength

To obtain the objective fluorescence intensity curves to assess foot perfusion in the patient with CLI, a single area of the foot is analyzed and there must be virtually no movement of either the foot or camera once recording begins. However, looking in this single view may limit subjective visualization of regional perfusion variations in the entire foot.
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**Indocyanine green angiography**

**Available evidence/3 studies**

- Ingress (the increase in fluorescence intensity from baseline) and Ingress rate (the increase in intensity over the time to maximum intensity) have shown some correlation with ABI and toe pressure\(^1\)
- Able to detect severe ischemia, based on the Wound-Ischemia-foot-Infection (WIfI) classification, with reasonable accuracy\(^2\)
- Parameter of time to half-maximal intensity to detect response to revascularization\(^3\)

**Benefit**

- appear to show promise for providing incremental information

**Limitation**

- Need for intravenous access
- Contraindication in previously documented iodinated contrast allergies
- Specialized equipment
- Inability to assess perfusion deeper than 5 mm

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Oxygen Microsensors

- Injectable oxygen microsensors to directly monitor oxygen in the subcutaneous tissue in vivo.

Soft biocompatible hydrogel sensor injected into subcutaneous space.

Fluorescence chemistry on hydrogel responds based on analyte concentration.

Reader collects emissions and data sent to cloud.
Tissue perfusion in CLI_Imaging techniques

Oxygen Microsensors

Available evidence/3 studies

- Healthy volunteer study provided validation of the ability of oxygen microsensors to reliably detect changes in tissue oxygen confirmed by TcPO2, with data over 3 months after sensor injection
- FIH/10 CLI: patients average tissue oxygen in the affected foot increased after EVR
- Post-market Registry study (OMNIA): Increases in oxygen levels assessed during endovascular revascularization procedures were associated with wound healing 3 months following the procedure

Benefit

- Sensitivity to both arterial insufficiency and microvascular impairment (eg diabetics)
- Treatment planning and long-term monitoring
- Prediction of wound healing

Limitation

- Limited data available

Tissue perfusion in CLI_Imaging techniques

Single photon emission computed tomography (SPECT)

Assessment of skeletal muscle microvascular perfusion
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Impact in CLI patients

Proper diagnosis
Identification of differences related to sex and ethnicity
Reduction of major amputation
Identification of procedural failures or incomplete revascularization
Potential for telemedicine to reduce disparities in CLI
Potential cost savings in the care of patients with CLI