SBIR Phase II
Contract No. FA9550-16-C-0010

SMART Bandage for Monitoring Wound Perfusion

April 18, 2018

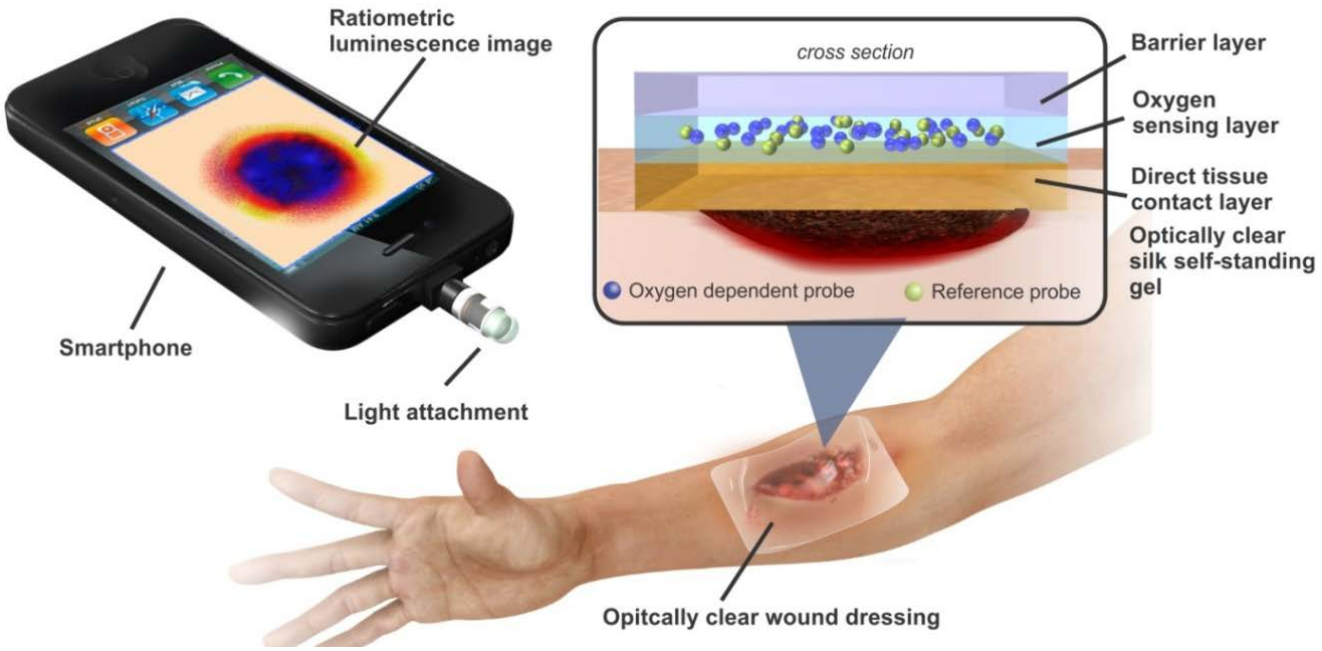
Triton Systems, Inc.

Oxygen Sensing Wound Dressing

- Continuous oxygen supply is critical for wound healing.
  - Additional energy source for repairing process
  - Promotes proliferation of fibroblasts, collagen synthesis, and angiogenesis
  - Resistance to infection – polymorphonuclear leukocytes activities
  - 5 – 20 mmHg pO_2 for chronic wound tissue, 30 – 50 mmHg for control tissue
  - Proliferation of fibroblasts: pO_2 > 15 mmHg
- Oxygen is delivered by capillary beds and through skin.
- Polarographic oxygen sensor – a planar or a needle electrode
  - Consumes oxygen
  - Point measurements
- Oxygen sensing wound dressing to monitor tissue perfusion
  - A transparent wound dressing
  - Provides real-time maps of tissue oxygenation across entire wounds, surgical beds, or burn sites
  - Eliminates the need for dressing removal for perfusion monitoring

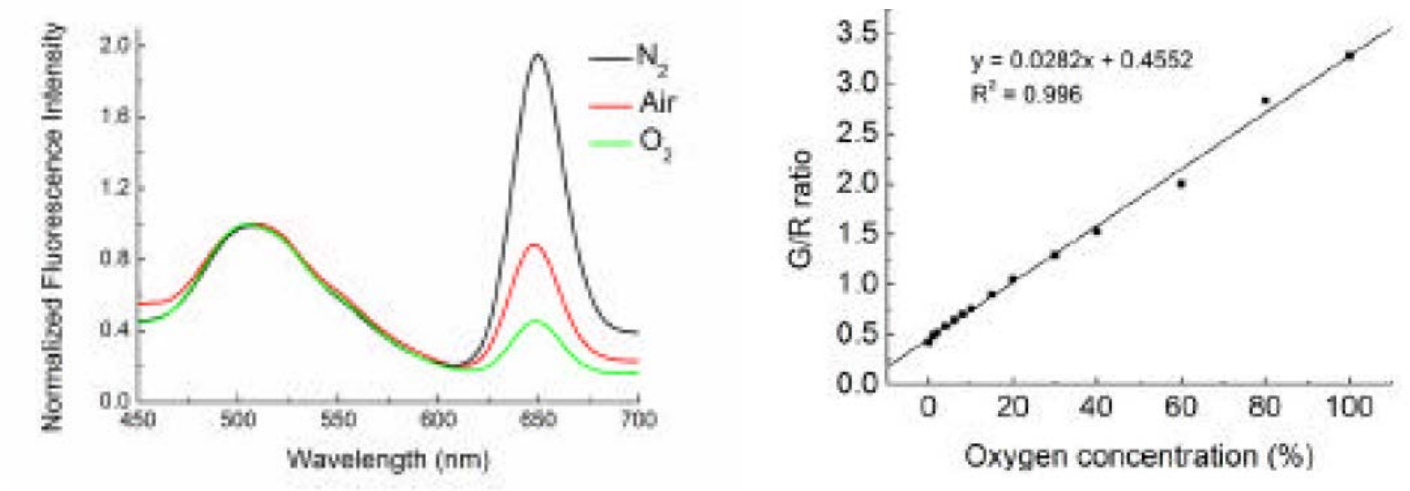
Our Approach

- A transparent wound dressing to detect tissue oxygenation
  - A semi-permeable barrier layer, an oxygen sensing layer, and a direct tissue contact layer
  - The oxygen sensing layer contains an oxygen sensing dye (red fluorescence) and a reference dye (green fluorescence).
- A smart phone app to monitor real-time tissue oxygenation
  - Ratiometric luminescence imaging analysis: G/R ratio $\propto pO_2$



Ratiometric Luminescence Imaging (RLI)

- Oxygen sensing dye – red channel
  - Excitation: 409 nm
  - Emission: 650 nm
- Reference dye – green channel
  - Excitation: 409 nm
  - Emission: 510 nm



Wang XD, Meier RJ, Link M, Wolfbeis OS. 2010. Photographing oxygen distribution. *Angew Chem Int Ed Engl* **49**:4907–4909

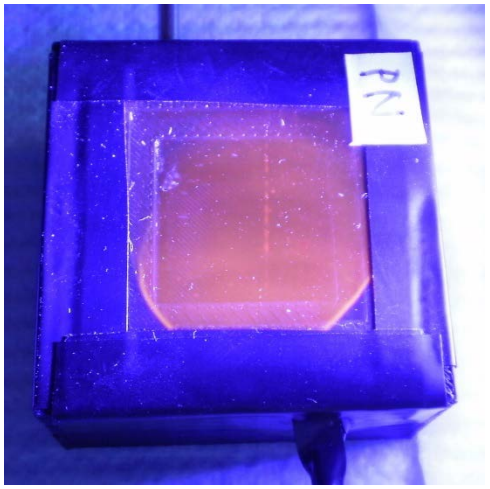
Advantages of RLI

- Inexpensive sensor (RGB)
- 2-D mapping of oxygen perfusion level of wound sites
- Repetitive and non-invasive sensing
- Insensitive to reflective excitation light
- Independent of light intensity and drifts of light intensity and photodetector

- Disadvantages
  - Differential photobleaching of reference and oxygen sensing dyes
  - Background color

- Luminescence lifetime imaging
  - Decay time of luminescent triplet emitters
  - Requires more sophisticated imaging system

Transparent Oxygen Sensing Wound Dressing



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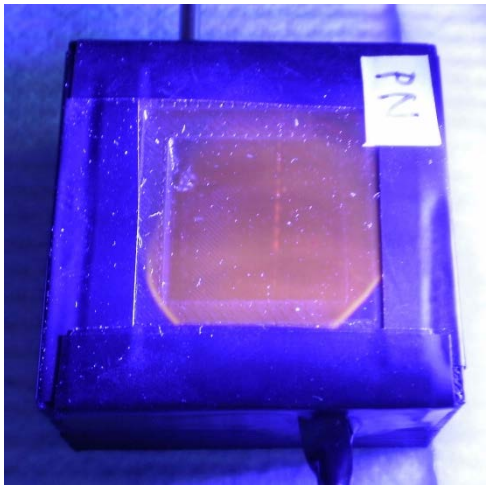

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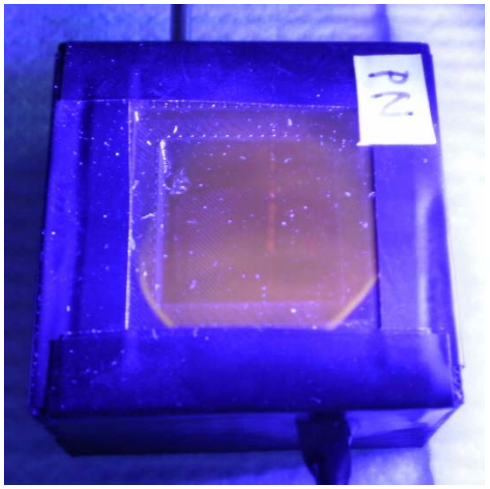

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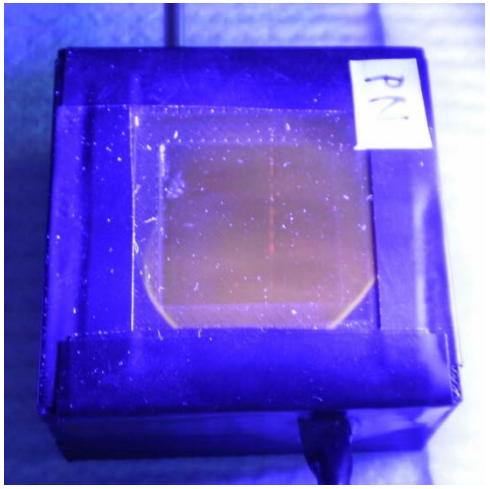

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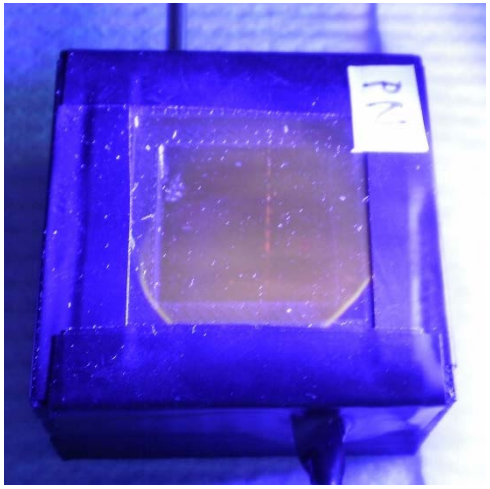

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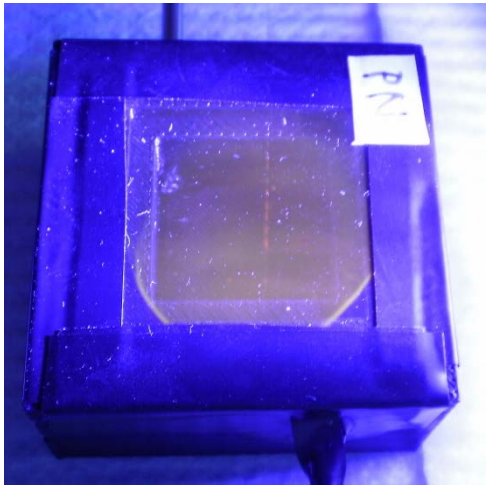

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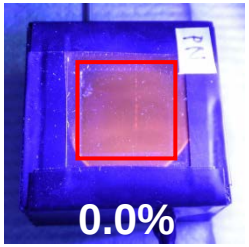
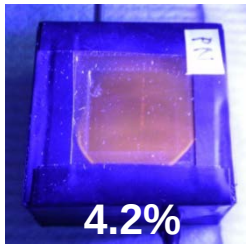
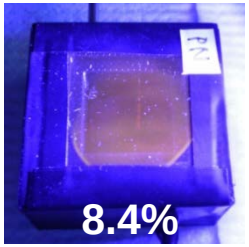
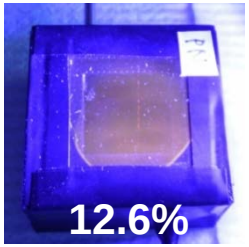
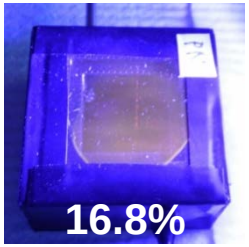
Correlation between G/R and Oxygen Content

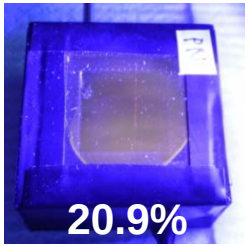


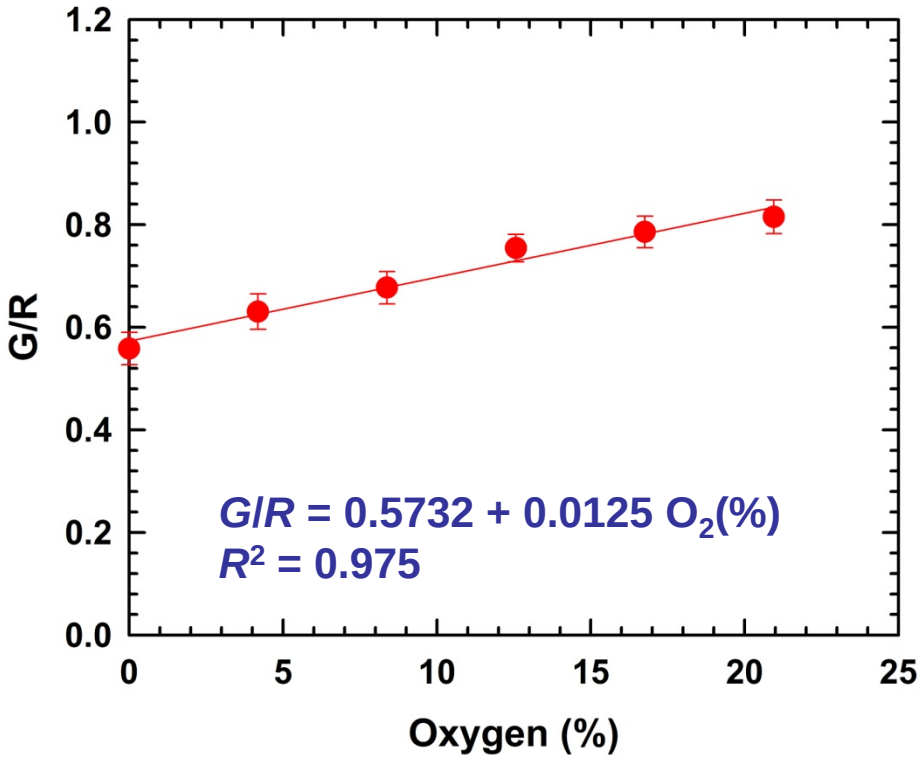






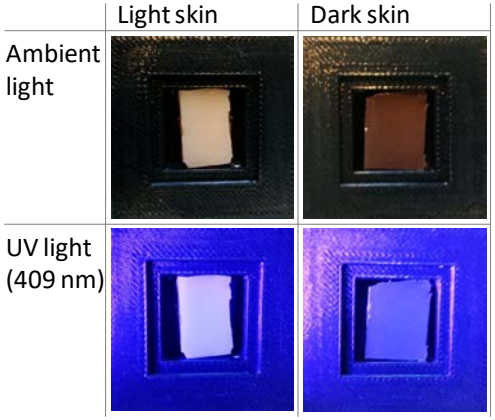


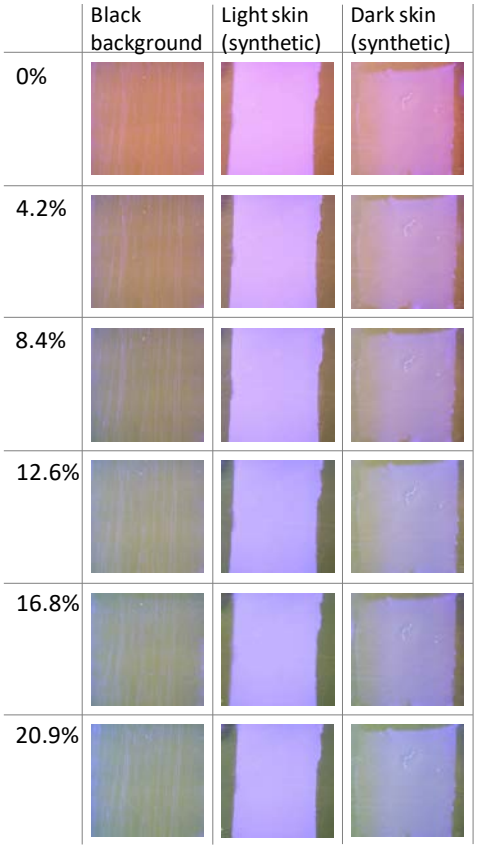


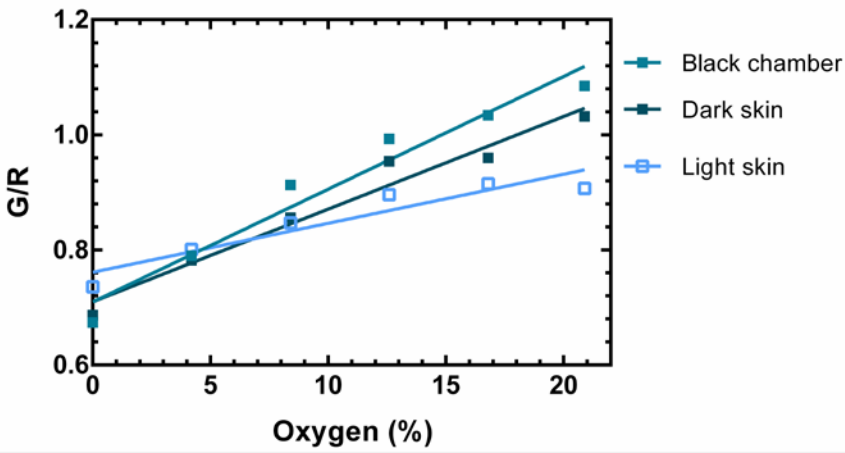


Effects of Background Color on Calibration

- Two different colored skin models as a background color
- Both light and dark skin models decreased the slope of the calibration curve.
  - Light skin background significantly affected the calibration which may be due to the fluorescence of the light skin interfering with the fluorescence signal of the bandage

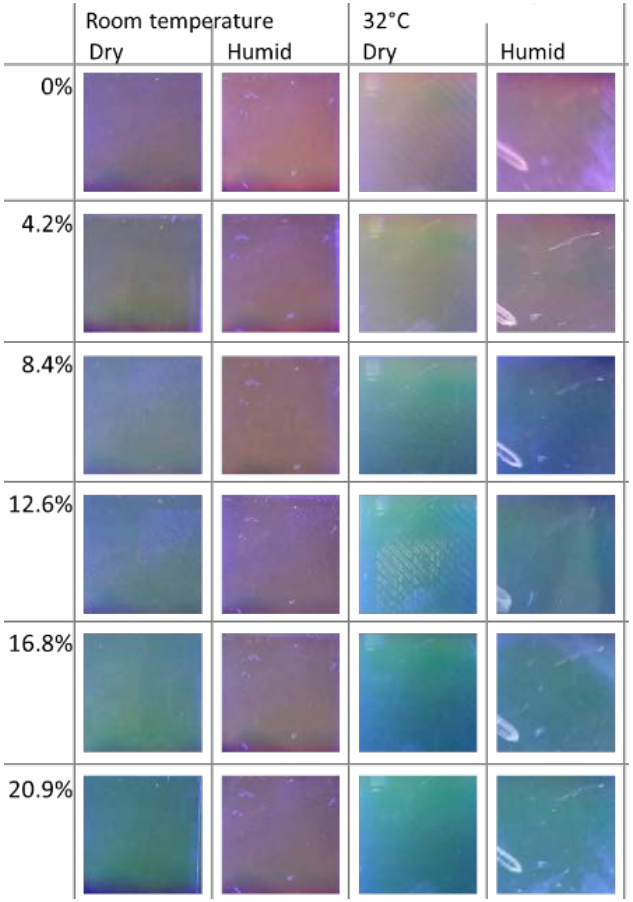


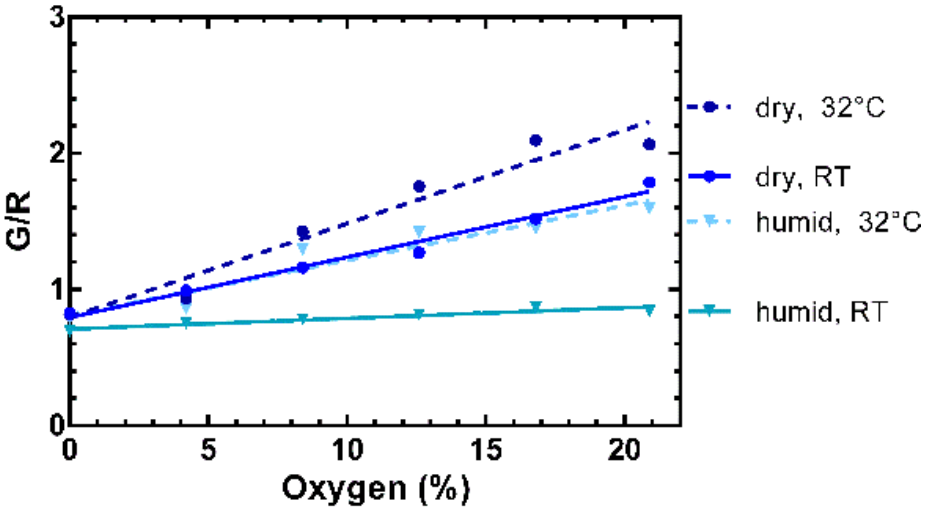




Effects of Humidity and Temperature

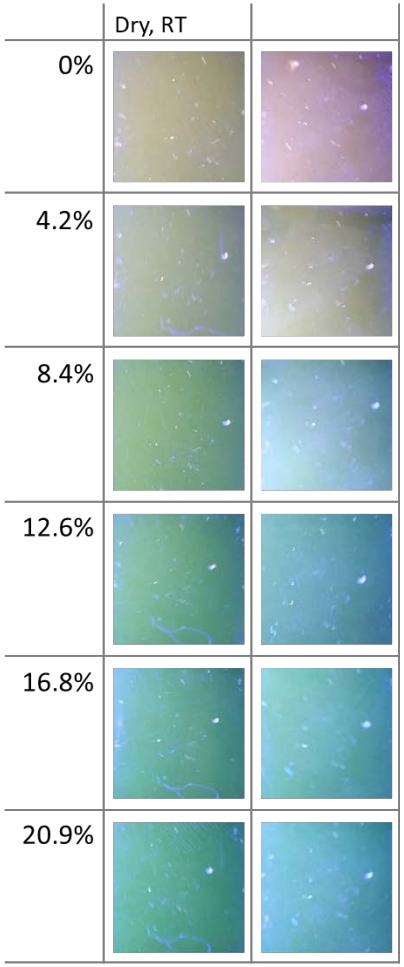
- Humidity – decreased slope
- Elevated temperature (32°C) – increased slope
- Combination (32°C, humid) – comparable to dry, room temperature

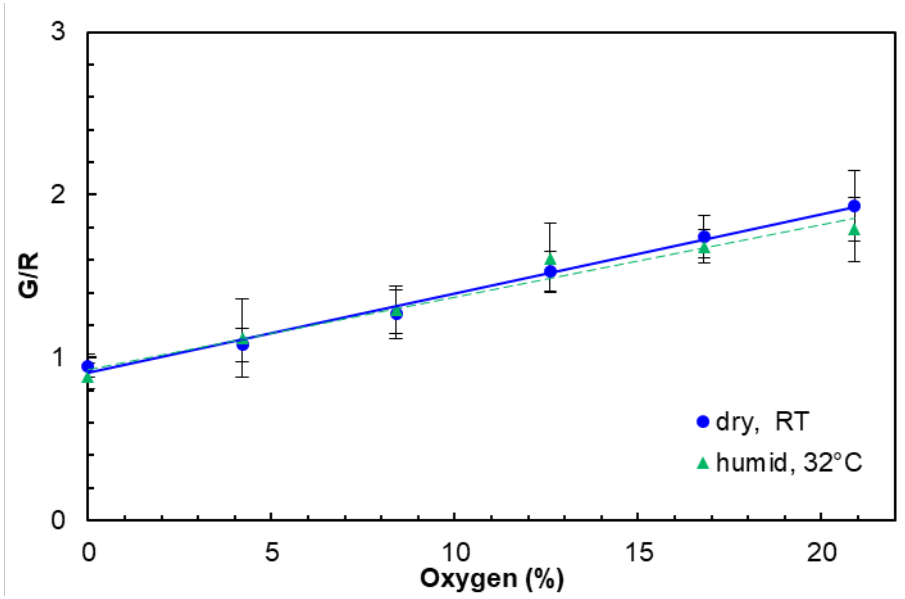




Combined Effects of Humidity and Temperature

- Calibration of bandage under dry, RT conditions to accurately quantify oxygen levels using the bandage under in vivo conditions (humid, 32°C)
  - Demonstrated repeatability (n=6 independent samples)

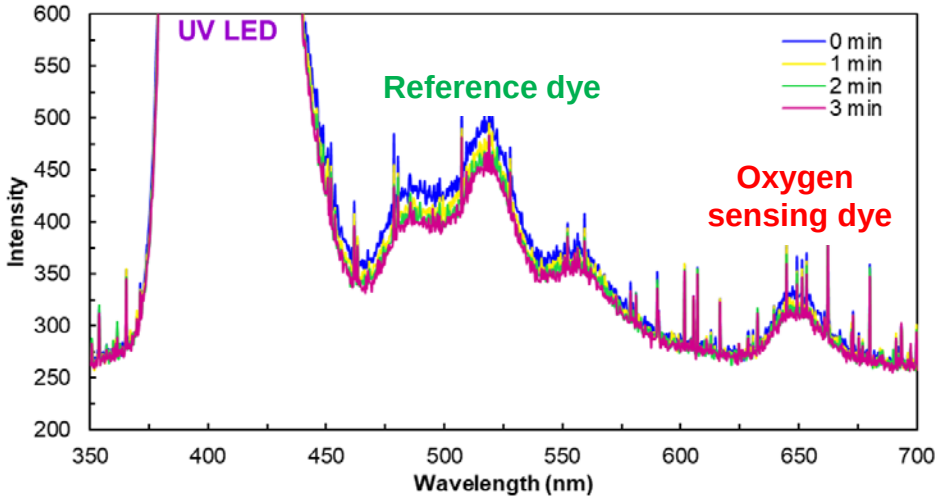


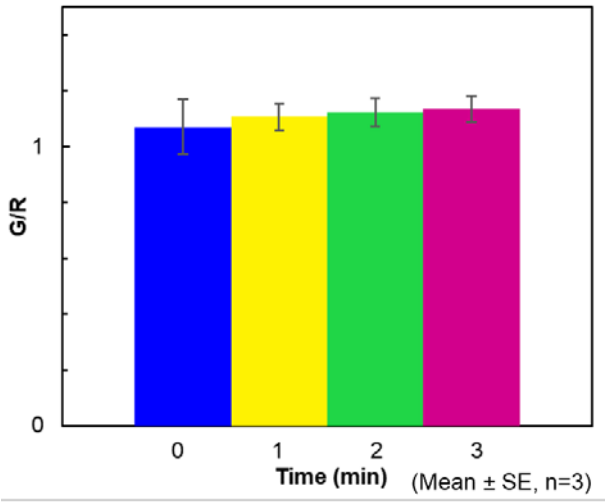


(Mean ± SD, n=6)

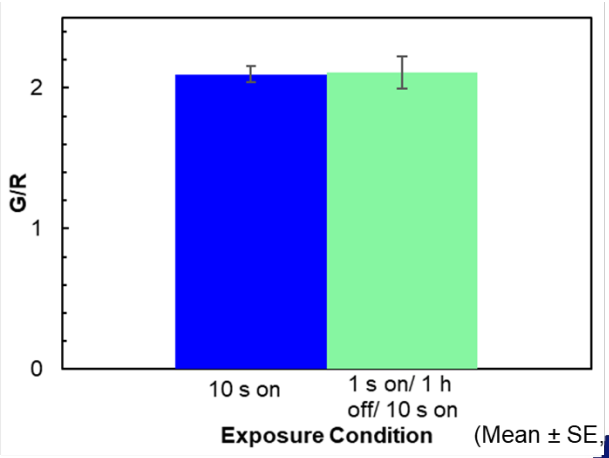
Photostability of the Bandage

- Exposure to continuous purple UV LED light (409 nm)

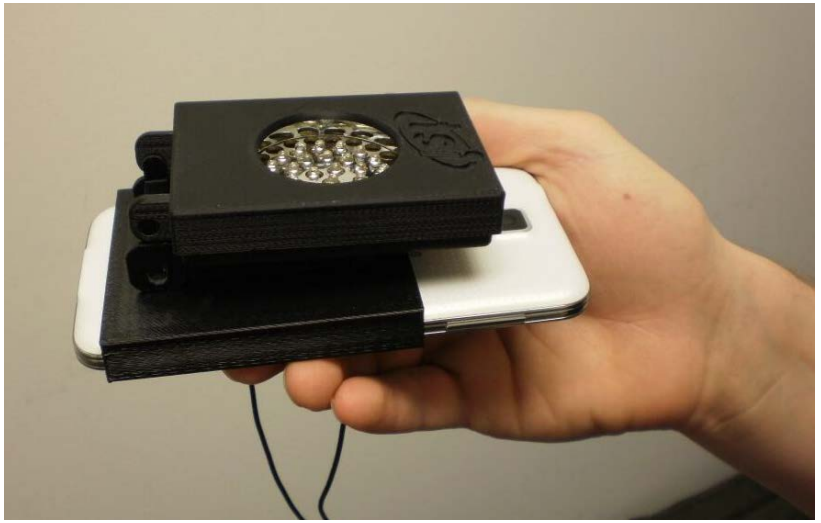


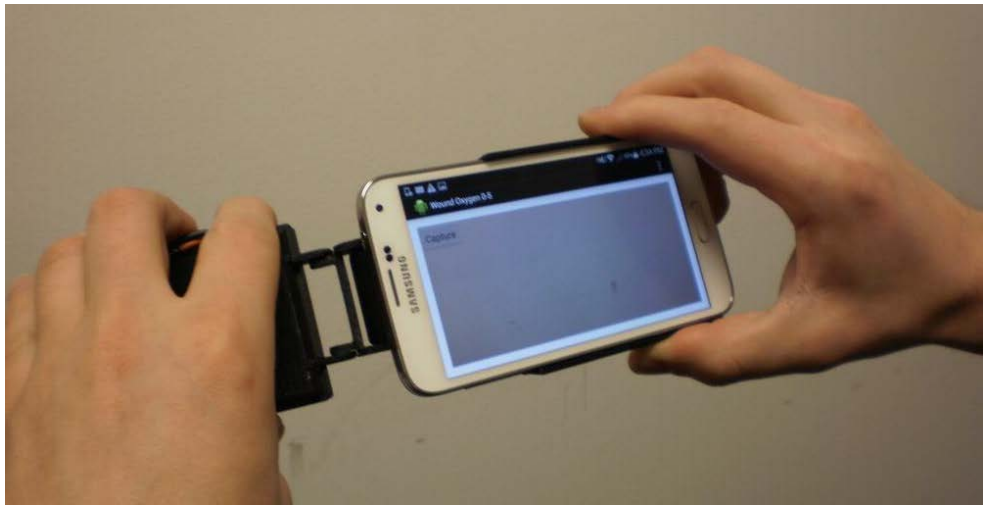


- Exposure to intermittent illumination
  - Dye signals fully recover and G/R value is restored after 1 h of no UV exposure



Purple LED Light Attachment to Smartphone

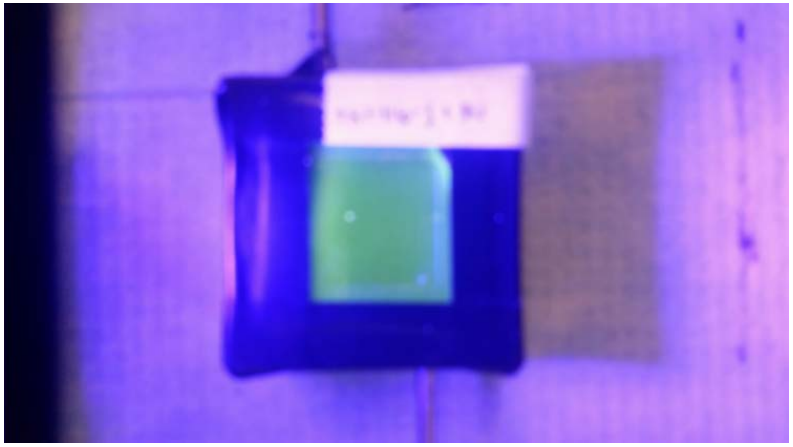




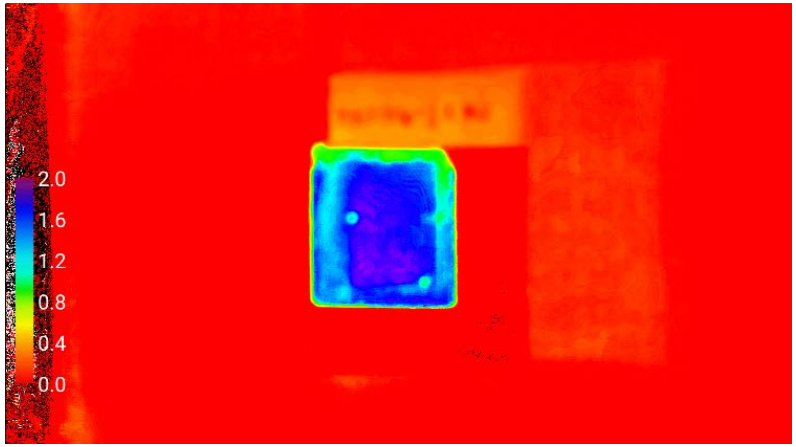
Smartphone App for RLI

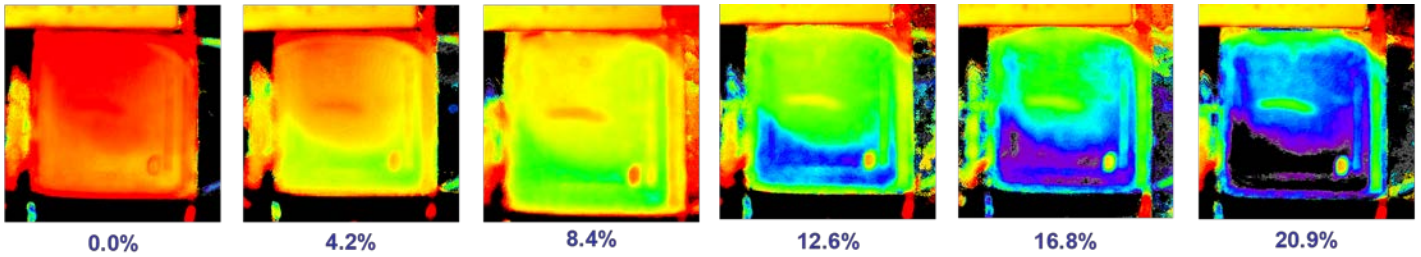
- Functions of the app
  - Synchronize the flash of the UV LED light array
  - Capture images of the illuminated bandage
  - Retrieve an image and calculate G/R
  - Display a processed G/R spectrum image with quantified oxygen levels

Raw



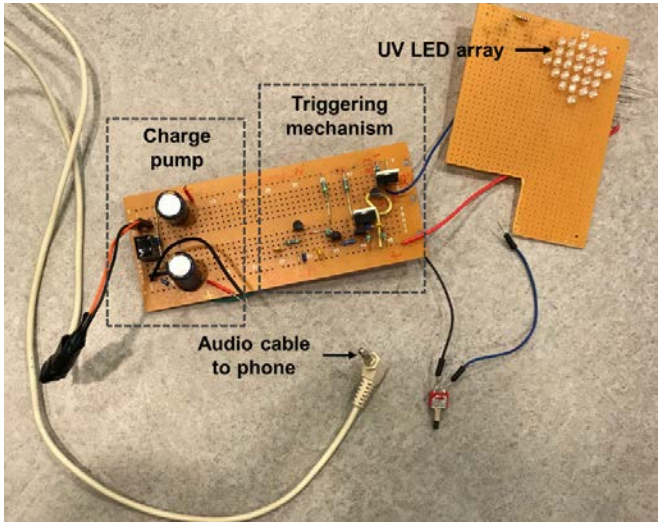
Processed





Next Steps

- Synchronization of UV flash
  - Skin tissue has strong autofluorescence that can interfere with the phosphorescence from the wound bandage
  - Use a trigger-delay mechanism to temporally gate out the short-lived tissue autofluorescence from the longer-lived signal from the bandage
- Stability studies
- Tissue perfusion imaging in a small animal hypoxia model
- Tissue perfusion imaging and wound healing in a large animal wound model



Breadboard prototype of the charge pump and triggering mechanism electronics