CONTINUOUS MONITORING OF MICROVASCULAR FUNCTION AND PERFUSION IN EARLY SEPSIS WITH NON-INVASIVE OPTICAL SPECTROSCOPY

INTRODUCTION
Sepsis Burden & Intervention
- Estimated 25% mortality in developed countries
- 20% increase in mortality since 1980
- 60% of patients suffer lasting disability
- 80% of cases occur in inpatient and high-risk populations
- Global need for accessible technology to aid early sepsis identification
- Non-invasive, bedside, real-time & continuous monitoring

Peripheral microvascular dysfunction (MVD)
- High-amplitude, low-frequency oscillations in the cerebral circulation reflecting impaired arterial vasodilation
- Occurs early in sepsis, preceding tissue injury and shock

Cerebral MVD
- Unknown but suggested as a contributing cause to the high incidence of acute and long-term cognitive dysfunction in sepsis

OBJECTIVES
- Investigate non-invasive optical spectroscopy techniques capable of monitoring microvascular health continuously at the bedside
  - Near-infrared spectroscopy (NIRS)
  - Diffuse correlation spectroscopy (DCS)
  - Continuous wavelet transforms (CWT)

Aim: Continuously monitor peripheral and cerebral microvascular health in a rat fecal peritonitis model using a hybrid NIRS/DCS system
1. Demonstrate a non-invasive bedside approach for peripheral MVD detection
2. Assess cerebral microvascular function in early sepsis
3. Assess perfusion changes in the brain and skeletal muscle in early sepsis

RESULTS
Vasomotion
- HbT Oscillations
- S02 Oscillations
- O2B Oscillations

Perfusion Changes
- MAP after 6 hours:
  - Control: 89.5 ± 6.9 mmHg
  - Septic: Crashed below 65 mmHg in 9/10 rats after 5.4 ± 0.6 hours
- Lactate after 6 hours:
  - Control: 0.49 ± 0.23 mmol/L
  - Septic: 1.35 ± 0.53 mmol/L

CONCLUSION
- Peripheral MVD can be detected non-invasively at the bedside with optical spectroscopy
- Significant cerebral vasodilation observed in HbT signal
- Decreased arterial blood pressure
- Significant early drop in skeletal muscle perfusion
- While the brain is partly protected, the skeletal muscle is an early diagnostic target in sepsis

LIMITATIONS
- Animal model simplifies clinical heterogeneity of sepsis
- Disruption to central autoregulation caused by anesthetics (sodium pentobarbital)

Future Work:
- Investigate sex differences
- Investigate changes in oxygen metabolism

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INTRODUCTION

Sepsis Burden & Intervention

• Improved timely medical intervention → 53% decrease in sepsis mortality rate since 1990 [1]
• Still accounts for 20% of deaths worldwide [1]
  • 85% of cases occur in vulnerable and low-resource populations [1]
• Global need for accessible technology to aid with early sepsis identification
  • Non-invasive, bedside, frugal, real-time & continuous monitoring

Peripheral microvascular dysfunction (MVD)

• High-amplitude, low-frequency hemoglobin oscillations in the skeletal muscle reflecting impaired arteriolar vasomotion [2,3]
  • Occurs early in sepsis, preceding tissue injury and shock [2]

Cerebral MVD

• Unknown but suspected as a contributing cause to the high incidence of acute and long-term cognitive dysfunction in sepsis [4]
OBJECTIVES

Investigate non-invasive optical spectroscopy techniques capable of monitoring microvascular health continuously at the bedside.

- **Near-infrared spectroscopy (NIRS)**
  - Tissue hemoglobin content (HbT) & oxygen saturation (StO2)

- **Diffuse correlation spectroscopy (DCS)**
  - Relative blood flow (rBF) with respect to baseline

- **Continuous Wavelet Transform (CWT)**
  - Dynamic decomposition of signal into frequency bands to isolate microvascular oscillations: 0.0095 - 0.16 Hz [3]

**AIM:** Continuously monitor peripheral and cerebral microvascular health in a rat fecal peritonitis model using a hybrid NIRS/DCS system

1. Demonstrate a non-invasive bedside approach for peripheral MVD detection
2. Assess cerebral microvascular function in early sepsis
3. Assess perfusion changes in the brain and skeletal muscle in early sepsis
METHOD

Sprague-Dawley rats (7-9 weeks old) – n=14 (7 male; 7 female)

- Control group (n = 4): intraperitoneal injection of saline (0.3 mL/100g)
- Experimental group (n = 10): intraperitoneal injection of fecal slurry (0.3 mL/100g) to induce sepsis
- Optical probes secured on the scalp and hind limb to acquire NIRS/DCS measurements for 6 hours post injection
  - HbT, StO2, and rBF quantified on MATLAB using fitting algorithms [5,6]
- Compare vasomotion power (0.02-0.05 Hz) and perfusion changes
  - Baseline: first 5 mins of acquisition 0.5 h post injection
  - Time frame 1: 0.5-2 h post injection
  - Time frame 2: 2-4 h post injection
  - Time frame 3: 4-6 h post injection

Fig 2. Observed peripheral vasomotion in HbT signal of a septic rat
RESULTS

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**Vasomotion**

**MAP after 6 hours:**
- **Control:** 89.5 ± 6.9 mmHg
- **Septic:** Crashed below 65 mmHg in 9/10 rats after 5.1 ± 0.6 hours

**Lactate after 6 hours:**
- **Control:** 0.49 ± 0.23 mmol/L
- **Septic:** 1.35 ± 0.53 mmol/L
CONCLUSION

• Peripheral MVD can be detected non-invasively at the bedside with optical spectroscopy
• Significant cerebral vasomotion observed in HbT signal
  • Precedes altered brain inflammation [2]
• Significant early drop in skeletal muscle perfusion
• While the brain is partly protected, the skeletal muscle is an early diagnostic target in sepsis

Limitations:

• Animal model simplifies clinical heterogeneity of sepsis
• Disruptions to cerebral autoregulation caused by anesthetic (sodium pentobarbital)

Future Work:

• Investigate sex differences
• Investigate changes in oxygen metabolism
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