Improving Diagnostic Technology of Acute Compartment Syndrome by Quantifying Intramuscular Glucose

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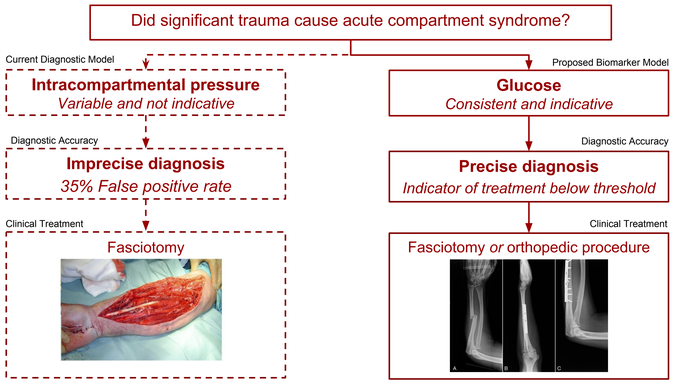
Abstract

Acute compartment syndrome (ACS) is a condition in which the pressure of the muscle compartment increases significantly due to a traumatic injury. The consequence is a decrease in the pressure gradient of blood flow which causes arterial blood to bypass the injured muscle. This trauma leads to cell anoxia, muscle ischemia and muscle death. Diagnosing ACS is problematic as current methods rely on subjective assessments, such as clinical examinations, and uninformative intracompartmental pressure readings. These assessments often return false-positive diagnoses. It has been shown that alternative biochemical markers, specifically glucose, lead to a more indicative quantification of this trauma. While current technology exists to detect glucose in canine models, these are unfit for humans. Our goal is to translate these tools to a clinical setting with a diagnostic glucose probe to analyze the glucose concentration in muscle and increase the specificity of the diagnosis.

Critical Emergency Room Question



Intracompartmental pressure readings are too variable between patients for precise ACS diagnosis. A definitive measure is critical so patients avoid unnecessary and invasive surgeries.[1,2]

Intramuscular Glucose Detection

- Glucose shown to decrease in canines with ACS[3]
- Sub threshold is a clear indicator of muscle ischemia
- Translating results to emergency room requires:
  1. **Rapid device calibration**
  2. **Bioelectrochemical sensor**
  3. **Deep tissue penetration (2-8 cm)**

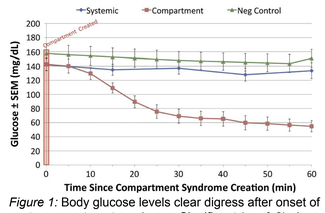


Figure 1: Body glucose levels clear digress after onset of acute compartment syndrome. Significant (p = 0.2) glucose deviation was detected after 15 minutes and remained stable at 60 (mg/dL).Suggests ACS detection must be done immediately upon E.R. arrival[3] ,

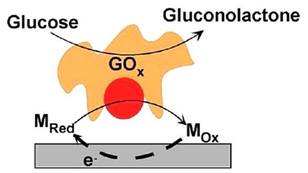


Figure 2: The tip of an ACS glucose probe is chemically active and reacting with glucose *in vivo*. A redox reaction between glucose, glucose oxidase (GO_x) metal mediator(M_{red}/M_{Ox}) and electrode are shown above. Electron (e^-) transfer drives current through circuit. More importantly, the reaction is oxygen independent and occurs regardless of compartmental conditions[4].

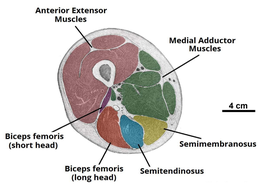


Figure 3: ACS probe will enter physical environments such as the anterior muscle compartments of the thigh, shown above. Sensor must reach compartments 3 - 8 centimeters below skin and remain *in vivo* for multiple hours. Scale bars assume a male thigh with a diameter of 15 centimeters[5] .

Fabrication Scheme

Electrode Engineering → **Signal Processing** → **Delivery Model**

Electrode Engineering

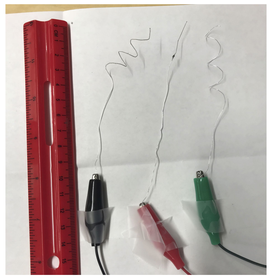


Figure 4: Three electrodes shown connected to the wires leading to the circuit. From left to right; reference, working, and counter electrode. The working electrode has been extended using silver epoxy.

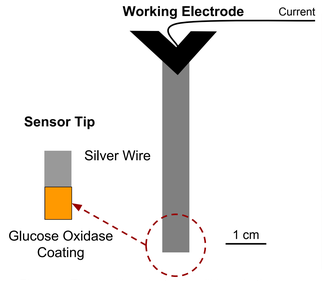


Figure 5: The working electrode will invade the body and react with intramuscular to create a current. The signal will follow the wire into a circuit where a current will be converted to a glucose concentration. Width not to scale.

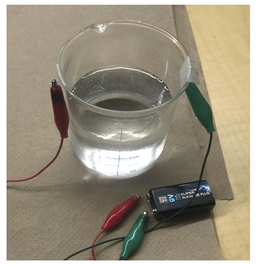


Figure 6: Chloriding the silver wire in a 1.23 M potassium chloride solution. The reference electrode, shown in green, is connected to the cathode of the 9V battery.

Signal Processing

- Three electrode potentiostat utilized for chemical to electrical transduction.
  1. Maintains constant + 300 mV (vs. Ag/AgCl reference) at working electrode
  2. Converts current produced from redox reaction at working electrode into a voltage
- Arduino Uno and Arduino IDE were utilized for data analysis.

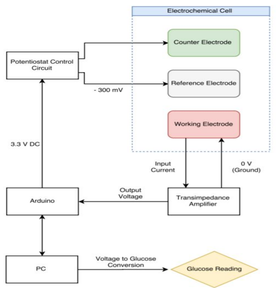


Figure 7: Block diagram of circuit. This block diagram outlines how the Arduino, circuit, electrodes, and PC interact with one another to ultimately take the input voltage from the Arduino and turn it into a glucose reading. Arduino IDE is used to make the voltage to glucose conversion.

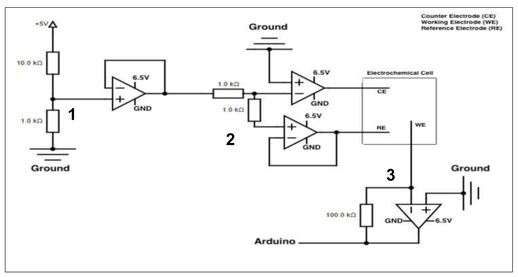


Figure 8: Three-electrode potentiostat circuit diagram. This circuit diagram depicts the overall configuration of the Arduino controlled potentiostat that was used for testing. There are three main components of this circuit – the voltage divider (1), the control circuit (2), and the transimpedance amplifier (3). The LM324 quad op-amp was the only op-amp used, and it was supplied with +6.5 V and 0.0 V using a DC power supply.

Delivery Model

- Synthetic model to observe electrode delivery and invasiveness
- Stylet guided entry system leads electrodes through various depths
- Sponge mimics depth of body, meat represents the compartment
- Electrode was not connected to circuit and model shown to subjective observation
- Successfully penetrates 8 centimeters

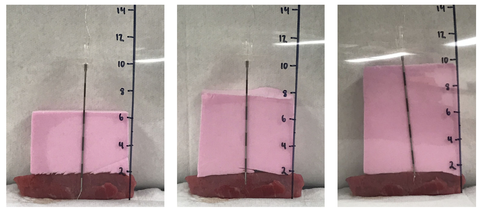


Figure 9: Three cross sections shown of electrode invasiveness at 4, 6, 8 centimeters. Models are shown to verify that an electrode can be successfully inserted in a highly invasive way. Insertion ranges vary to accommodate multiple depths ACS can occur within a muscle.

Testing and Results

- Initial Probe Testing: Nine PBS/Glucose solutions
  - 0, 25, 50, 60, 70, 100, 300, 500, and 1,000 mg/dL glucose concentrations
  - Concentrations of solutions were measured with the Contour Next ONE Glucose Meter

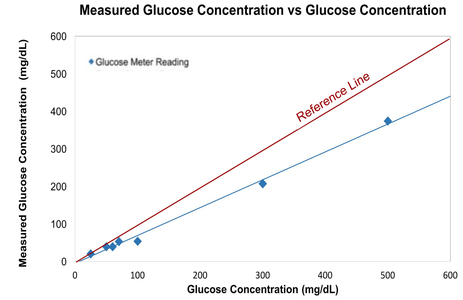


Figure 10: Graphical representation of collected testing data. Shown in red, a reference line outlines a perfect correlation between experimental and predicted values. Shown in blue, a store-bought Contour NEXT One Blood glucose meter provides a second quantitative source.

Discussion

Electrodes
- Reverse engineered a commercially available working electrode
- Further development required to obtain a custom built glucose monitor
- Unknown chemistry of the working electrode lead to difficulties with the interaction between the reference, counter and working electrodes
- Consumer market glucose sensor is most sensitive in higher ranges and less accurate within our range of interest

3-Electrode Potentiostat
- Designed and built a potentiostat control circuit and transimpedance amplifier
- Verified expected voltage differences between electrodes and after each stage of the potentiostat

Stylet Insertion Needle
- Incorporated a readily available stylet system to effectively penetrate into any compartment
- The stylet housed glucose sensor from muscle environment

Future Work

- Demonstrate feasibility on liquid and muscle models
- Remake electrodes from scratch by coating platinum wire with a more specialized monitor that can accurately read 50 dL/mg to 200 dL/mg
- Shrink electrode system into one insertion device
- Calibrate prior to use
- Translate design to be usable in hospital, trauma settings, and active military fields for on-site ACS diagnosis

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