Radiometric quantification of intramuscular pH to diagnose acute compartment syndrome (ACS)

Will Bacon, Mark Austin, Kelsey Murphy, & Alex Goodman

Client: Dr. Christopher Doro Advisor: Professor Jeremy Rogers



Diagnosing Compartment Syndrome

- Diagnostic issues and challenges of acute compartment syndrome (ACS)
- Current understanding of ACS
- Requirements for ACS technology
 - Continuous biochemical monitoring
 - Ability to reach fascial compartments of varying depths
 - High grade of accuracy
- Comparison of various probe configurations
 - Hydrogel-Dye Microenvironment
 - Reflective pH-reactive adhesive
 - Microdialysis Spectrometer
- Proposed design for diagnosis

Current diagnosis of Compartment Syndrome

Clinical Examination 5 P's OF CIRCULATORY CHECKS

- P Pain
- Paresthesia
- P Paralysis
- Pulse
- Pallor



Intracompartmental Pressure Reading



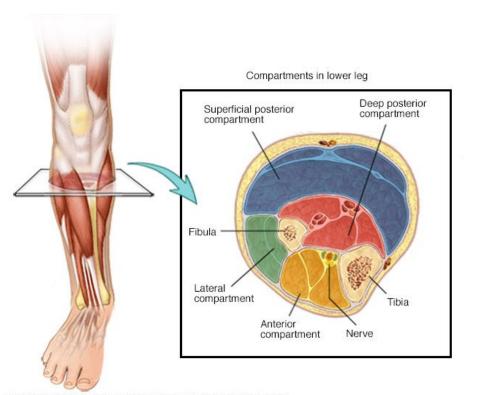
35%

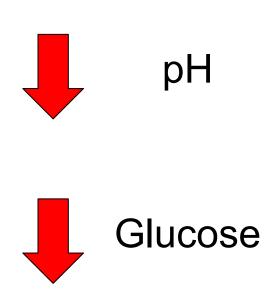
False-positive diagnosis



(Doro etl. al)

Acute Compartment Syndrome

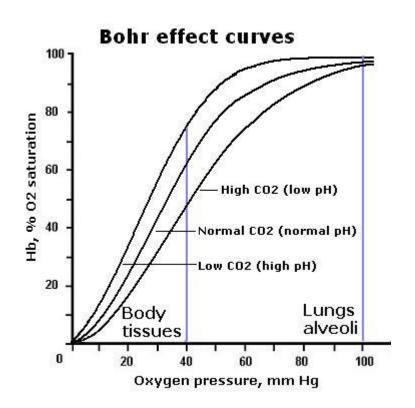




@ MAYO FOUNDATION FOR MEDICAL EDUCATION AND RESEARCH, ALL RIGHTS RESERVED.

pH as a Biomarker

- Lack of O₂ leads to lactic acid byproduct
- The Bohr Effect
 - $\circ \quad \mathbf{I}\%0_2 = \mathbf{I}pH$
- Reactive with a variety of dyes
- Normal pH ~ 7.35
 - Measurement of relative change to this standard



Requirements for ACS Technology

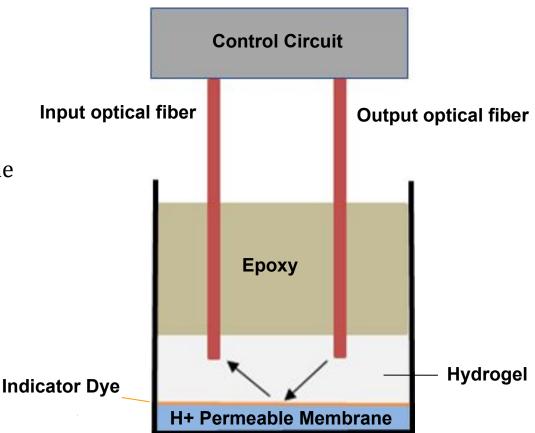
- Continuous biochemical marker monitoring
 - 1 sample/10 minutes
- Depth below skin
 - 1-5 cm
- Standard of care
 - 16 gauge needle max
- Easy to use
- Cheap and disposable



Hydrogel-dye Microenvironment

Configuration

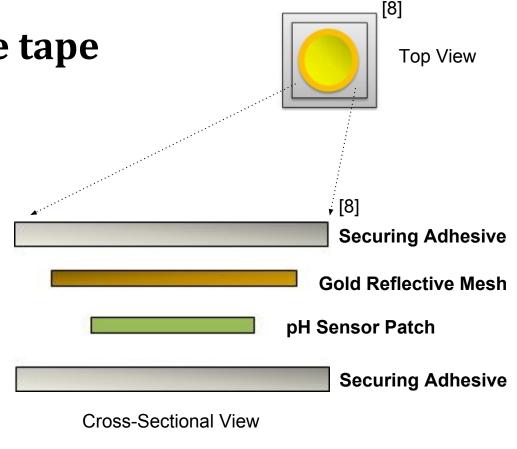
- pH indicator dye is immobilized on a hydrogel.
- Selectively permeable membrane adhered between indicator dye and hydrogel.
- Optical fibers held in place with epoxy glue.
- Intensity of light reflected off indicator dye correlates to pH.



Reflective pH-reactive tape

Configuration

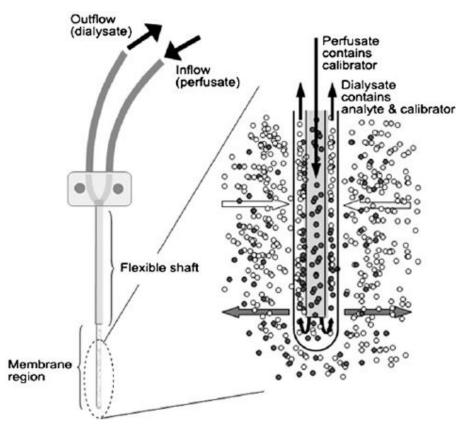
- Composed of four layers
 - Two securing adhesive layers
 - One Gold Mesh layer
 - One pH indicator dye layer
- Tape adhered to commercially available transmissive pH probe.
- Transmissivity of light emitted from probe is measured and correlated to pH.



Microdialysis Chamber

Configuration

- Microdialysis probe continuously perfused via inlet tube.
- Semipermeable membrane allows analyte to diffuse into probe.
- Dialysate containing analyte sent to analysis chamber via outlet tube.
- Spectrometry performed on outlet tube to determine pH



Depiction of Microdialysis process [10]

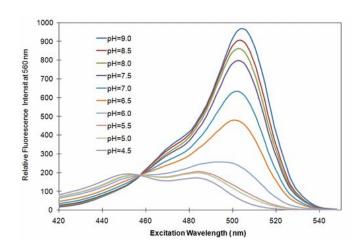
Design Matrix

Criteria (Weight)	Hydrogel Microenvironment		Reflective pH Tape		Microdialysis chamber	
Accuracy and precision (35)	5	35	4	28	3	21
Biocompatibility (25)	4	20	4	20	5	25
Invasiveness (15)	3	9	3	9	3	9
Ease of Reuse(10)	2	6	4	8	4	8
Measurement Continuity (10)	5	10	5	10	3	6
Cost (5)	3	3	4	4	3	3
Total	83/100		79/100		72/100	

Future Work: Phase 1 (Fall Semester)

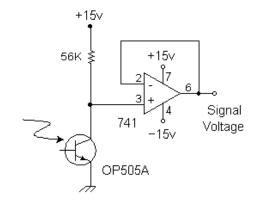
Chemistry

- pH indicator
 - o BCECF
- Immobilization/encapsulation



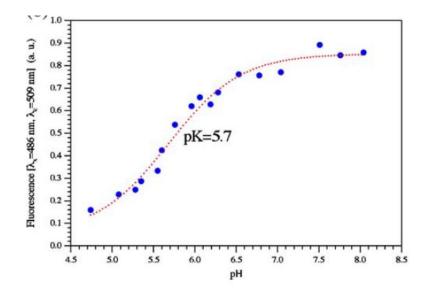
<u>Instrumentation</u>

- Dichromatic excitation
- Optimizing optical feedback
- Developing analytical circuit
 - Correlate response, pH



Future Work: Phase 2 (Spring Semester)

- Integrating 'cuvette', instrumentation
- Testing
 - Stability of connection
 - Signal collection
 - Calibration against other probes



References and Acknowledgements

- [1] Anon, (2018). [image] Available at: https://i.pinimg.com/originals/4a/5b/1f/4a5b1f49b7979b859a5757399369e764.jpg [Accessed 5 Oct. 2018].
- [2] Anon, (2018). [image] Available at: https://emedicine.medscape.com/article/307668-workup [Accessed 5 Oct. 2018].
- [3] Anon, (2018). [image] Available at: https://www.mayoclinic.org/diseases-conditions/chronic-exertional-compartment-syndrome/symptoms-causes/syc-20350830 [Accessed 5 Oct. 2018].
- [4] "BCECF", Genecopoeia.com, 2018. [Online]. Available: http://www.genecopoeia.com/product/bcecf/. [Accessed: 02- Oct- 2018].
- [5] R. Bizzarri, M. Serresi, S. Luin and F. Beltram, "Green fluorescent protein based pH indicators for in vivo use: A review", Analytical and Bioanalytical Chemistry, vol. 393, pp. 1107 1122, 2009.
- [6] N. Boens, W. Qin, N. Basaric, A. Orte, E. M. Talavera, and J. M. Alvarez-Pez, "Photophysics of the Fluorescent pH Indicator BCECF," The Journal of Physical Chemistry A, vol. 110, pp. 9334–9343, Jun. 2006.
- [7] "Bohr Effect Explained: Why Oxygen Is Released in Tissues," Causes of Cystic Fibrosis: Low O2 in Body and Ion Pumps. [Online]. Available: https://www.normalbreathing.com/CO2-bohr-effect.php. [Accessed: 03-Oct-2018].
- [8] Derendorf, H. (2007). A microdialysis probe of concentric design. [image] Available at: https://www.researchgate.net/publication/6369883_AAPS-FDA_Workshop_White_Paper_Microdialysis_Principles_Application_and_Regulatory_Perspectives.
- [9] https://openi.nlm.nih.gov/detailedresult.php?img=PMC3505898_CRIM.ORTHOPEDICS2011-678525.002&req=4. (2018). [image].
- [10] Ocean Optics. Introduction to pH and optical pH sensing. (2018).
- [11] A. Whitney, R. V. O'Toole, E. Hui, M. F. Sciadini, A. N. Pollak, T. T. Manson, W. A. Eglseder, R. C. Andersen, C. Lebrun, C. Doro, and J. W. Nascone, "Do one-time intracompartmental pressure measurements have a high false-positive rate in diagnosing compartment syndrome?," *Journal of Trauma and Acute Care Surgery*, vol. 76, no. 2, pp. 479–483, 2014.