



Acute Compartment Syndrome Quantification Device

BME Design 301

05/02/2018

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Abstract

Acute Compartment Syndrome (ACS) is characterized by an increase in pressure within a muscle cavity that results from experiencing local trauma. An increase of internal pressure can lead to a reduction in blood flow to the area, a decrease in local oxygen, and can result in ischemia. Traditional methods of measuring ACS include direct pressure measurement, which has shown to result in a 35% misdiagnosis rate. The goal of this project is to develop a device to safely and accurately quantify ACS. The preliminary design is a device that can measure the metabolic factor of pH *in vivo* through the use of fiber optic technology. This device will use a comparison of two different wavelengths of light reflected through a pH-sensitive dye to identify the amount of hydrogen ions in solution. The dye should be responsive in the pH range of 5 to 7 and be capable of being immobilized onto a hydrogen-permeable glass surface. A fabrication protocol was developed to provide a repeatable procedure for immobilization. Successful validation for the use of optical fiber technology in this application was done through measuring reflected light rays and use of a commercial spectrometer. Future work entails immobilization of the chlorophenol red dye on the glass surface. Once the device is developed, a pH test for sensitivity will be executed to determine the success of this device. The final step in making the device effective is to determine a well defined pH range for ACS through live animal studies.

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Introduction

Acute Compartment Syndrome (ACS) is a condition of elevated pressure within a muscle cavity. It is the result of a prior local trauma which leads to increased swelling and decreased internal blood flow to a muscle cavity [1]. This increase in pressure can lead to a halt of blood flow in or out of the cavity. As a result, the muscle's oxygen supply is depleted, which can lead to muscle ischemia. The primary concern with ACS is the lack of oxygen supplied to the muscle and the potential of long-term muscle damage or death.

The current quantification strategy for Acute Compartment Syndrome is evaluating the blood pressure in the muscle cavity. The issue with this method is that there is not a specific change in pressure that has been proven to accurately quantify a compartment [2][3]. There are some medical conditions that lead to a change in cavity pressure within the wide range currently used, without displaying any other symptoms of being a compartment. This overlap contributes to the 35% misdiagnosis rate observed [4]. Once diagnosed, the treatment path for ACS is an emergency fasciotomy to reduce pressure and restore blood flow to the dying muscle. This is an extremely invasive surgery and ideally avoided, if possible [5]. If ACS were to be better diagnosed, these unnecessary emergency fasciotomies could be avoided. Due to the severity of the treatment option and the high misdiagnosis rate, a device to better quantify Acute Compartment Syndrome is desired. This device would reduce the misdiagnosis rate and decrease time to diagnose, preventing any unnecessary muscle death and prevent unnecessary surgical intervention.

Background

Due to the drastic changes in the environment of a compartment, there are many factors that could be considered to diagnose Acute Compartment Syndrome more effectively. A lack of oxygen in a muscle cavity leads to a reduction in oxidative phosphorylation. As a direct result, local metabolic factors such as pH and glucose have been proven to decrease [4]. Under the advisement of trauma surgeon Dr. Doro, the metabolic factors of glucose and pH were the suggested initial considerations for this project. Glucose was the factor measured by the previous group working on this project. It has been shown to decrease significantly in an induced compartment in dogs, leading to the assumption that it would be a valid biomarker to measure for this device [6]. The previous group had difficulties with calibrating a device that measures glucose, but provided evidence for the theory of using glucose as a marker for Compartment Syndrome [7]. This calibration difficulty was what led to the eventual failure of the glucose quantification device. pH is the other suggested metabolic factor to measure. It has also been shown to decrease significantly within a developing acute compartment and is, therefore, another suggested marker [4]. In order to progress with these potential markers, research into the quantification and calibration of such a device must be conducted.

The final device, as requested by Dr. Doro, must be able to quantify a developing or preexisting compartment quickly and safely. He intends it to be used in a trauma environment,

meaning it must be easy and quick to calibrate (within 5 minutes), simple to sanitize, and easy to transport. The device must be able to fit into a 16 gauge needle. As seen in Appendix A, accuracy of the biomarker chosen should be within a 5% error range.

There is one existing device that can be used to diagnose ACS. Oxygen content in solution can be measured by a competing device called the OxyLite™ probe, developed by Oxford Optronix (Figure 1). The probe uses a fluorescence-based optode sensor that is able to measure dissolved oxygen *in vivo*. OxyLite™ uses a platinum-based fluorophore bound to the sensor tip which allows for accurate readings within ± 0.7 mmHg. The platinum used in the sensor tip makes the price of sensors too expensive for clinical applications.



Figure 1: The OxyLite™ uses fiber optics in conjunction with a platinum-based fluorophore to obtain dissolved oxygen measurements *in vivo*.

[8] O. Optronix, *Tissue pO2 and in vitro dissolved oxygen monitors*. 2017.

Preliminary Designs

Glucose Probe

A probe that is designed to measure the metabolite glucose would be based on a continuous glucose monitor (Figure 2). A continuous glucose monitor is made up of three main components: a transmitter, sensor, and monitor [9]. A perforated 16 gauge needle (1.02mm in diameter) would house a thin wire coated with glucose oxidase, which would then be inserted in a muscle compartment. Once in the compartment, the glucose in the surrounding tissue and fluid would react with glucose oxidase to form hydroxide. The volume of blood needed to generate an accurate measurement is about 1 μ L, with at least a thirty second reaction time [9]. The generated electrical potential between hydroxide and the wire would be transmitted to a sensor outside of the muscle compartment and then displayed on a monitor [9].

A reading of two muscle compartments is necessary to diagnose ACS via a glucose measurement. For example, a measurement in one knee is taken and compared to one from the other knee and a substantial difference between glucose levels would indicate ACS.



Figure 2: A continuous glucose monitor would be based off a blood glucose meter [10].

Ion-Selective Field Effect Transistor (ISFET) Probe

A hydrogen ISFET probe measurement is based on the control of the current flowing between two semiconductor electrodes. These two electrodes, the so-called drain and source electrodes, are placed in a silicon chip together with a third electrode, called a gate, between them. The gate is in direct contact with the solution to be measured. The gate electrode consists of a chemical layer that is sensitive to hydrogen ions. Materials like silicon oxide (SiO₂), silicon nitride (Si₃N₄) and aluminium oxide are used in the pH sensing layer. Hydrogen ions will reside at the surface of the chemical layer in proportion to the pH. The positive charge of the hydrogen ions produces an electric field that influences the current between the source and drain. When the pH value changes, the current through the transistor will change accordingly. To maintain the drain–a control current at a constant value is applied via the reference electrode. The change in the control voltage is a measure of the pH value of the sample. A disadvantage of an ISFET probe is that the calibration has a known drifting problem, thereby requiring frequent calibrations between uses [11].



Figure 3: A hydrogen ISFET probe manufactured by DeltaTrak [12].

pH Microsensor

pH microsensors are miniaturized pH sensors designed for measuring in small volumes and with high spatial resolution. Sensors manufactured by PreSens designs have tips that are 1.5 mm in diameter and larger. These sensors are based on a 14 mm silica fiber which enables integration into various small scale environments. These sensors do not require reference

electrodes and there is no leakage of electrolytes, a clear advantage over common electrodes [13]. The PreSens sensors are able to measure pH values between 5.5 to 8.5 and have a response time of less than 2 minutes. The main disadvantages with this sensor is that the diameter of the microsensors is far too large to fit inside a 16 gauge needle and it does not have FDA approval.



Figure 4: A pH microsensor designed by PreSens [13].

pH Polymer Probe

The pH polymer probe uses a silicone-based polymer containing an immobilized dye that responds to changes in pH [14]. A sample is injected into a sample well where it comes in contact with the polymer. The hydrogen ions in solution permeate the polymer and react with the dye, thereby causing a structural change in the dye. When the dye is struck with certain wavelengths, the dye in the polymer fluoresces. The rays of light reflect off the surface of the polymer at different angles which are then measured via spectrophotometry to obtain a reading of pH. The pH polymer probe requires that the pH measurement of the muscle compartment takes place outside of the patient's muscle compartment.

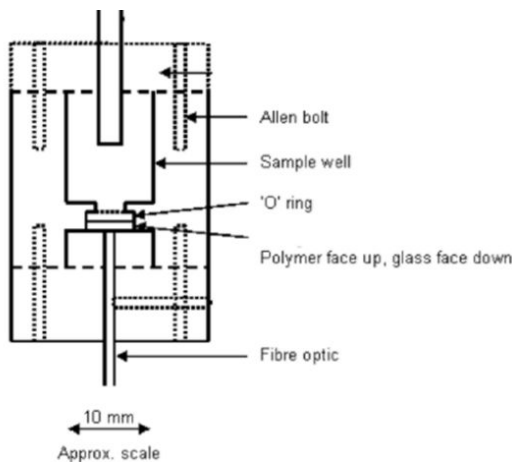


Figure 5: A pH polymer probe would measure pH of a blood sample outside of the muscle compartment [14].

pH Optic Fiber Probe

The pH optic fiber probe would utilize two beams of light of differing wavelengths to measure the pH of a muscle compartment [15]. The probe would contain a silicone-based polymer that allows hydrogen ions to permeate through. A fluorescent dye immobilized in a hydrogel would react in the presence of hydrogen ions. Beams of light guided via optical fibers would strike the surface of the hydrogel and reflect at angles that differ from those observed when the dye is not fluorescent. Each wavelength of light would have a different reflection

response. The difference in reflection would indicate the pH of the solution. The light beams would be transmitted back to a photodiode by another optical fiber and be analyzed with spectrophotometry. The pH optical fiber probe would be able to take continuous measurements inside the muscle compartment.

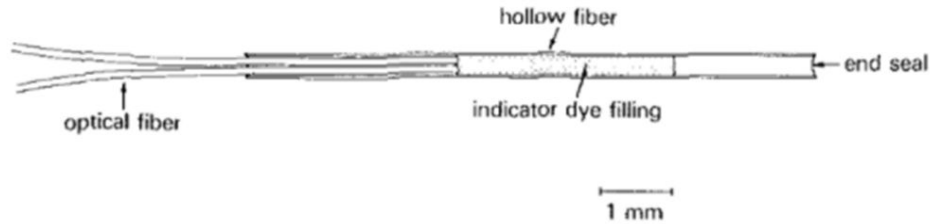


Figure 6: A pH optical fiber probe would measure pH inside the muscle compartment in vivo [15].

Preliminary Design Evaluation

Criteria (weight)	Glucose Probe		pH Polymer System		pH ISFET Probe		pH Microsensor		pH Optic Fiber Probe	
	3/5	15	3/5	15	2/5	10	5/5	25	5/5	25
Size (25)	3/5	15	3/5	15	2/5	10	5/5	25	5/5	25
Safety (20)	5/5	20	5/5	20	4/5	15	4/5	15	5/5	20
Accuracy/Reliability (15)	3/5	9	5/5	15	4/5	12	5/5	15	5/5	15
Ease of Use (15)	1/5	3	3/5	9	5/5	15	5/5	15	5/5	15
Ease of Fabrication (10)	2/5	4	4/5	8	2/5	4	2/5	4	4/5	8
Sterility (10)	5/5	10	5/5	10	5/5	10	3/5	6	3/5	6
Cost (5)	5/5	5	3/5	3	2/5	2	1/5	1	3/5	3
Efficacy (0)	N/A		N/A		N/A		N/A		N/A	
Total	68		80		68		81		92	

Table 1: Design Matrix Evaluating the Preliminary Designs. Design criteria are listed in the left-most column decreasing in weight from top to bottom. The remaining columns are filled with each preliminary design and corresponding score for each category.

Size

The most important constraint for this project is the size requirement. As the probe must fit inside a 16 gauge needle, the probe tip must be very small in order to even get a reading from the suspected compartment. Fiber optics are very small and come in a variety of sizes, making it the design that best fits the size requirement. The pH microsensors also did well in this category because the probe tip is quite small. Although it does not currently fit the size requirement of the 16-gauge needle, there is potential for further scaling down of the microsensors to more accurately fit the requirement. The other designs do not currently fit the size requirement specified in the product design specifications and will not be feasible to scale down (Appendix A).

Safety

Each of the preliminary designs will need to be inserted into a muscle compartment in order to evaluate if there is a compartment present after injury. The device must not cause any adverse side effects such as tissue damage while recording metabolite concentration. Here, the pH fiber optic probe was rated the highest because, as the main component transmits light through a pH indicator hydrogel, there is minimal chance of harm to the body. The body will not be in any contact with any chemicals preventing adverse biological reactions *in vivo*. The glucose probe and the pH polymer system tied with the fiber optic probe in this category because the glucose system that will need to be altered has already been FDA approved and is regularly used by diabetics. The pH polymer system is also very safe because a sample can be removed by a normal needle used in hospital settings, then analyzed. The pH ISFET probe can measure pH effectively but there is a concern that heat from the current could negatively affect a patient. The pH microsensors use a similar technology, so the generation of heat would also be a concern with this design.

Accuracy/Reliability

Because the measurement of a metabolite is necessary in order to more accurately diagnose Compartment Syndrome, the device created must also be able to provide an accurate diagnosis and avoid misdiagnosis. This category also takes into account the accuracy of the metabolite used in the diagnosis of Compartment Syndrome. Due to this, the glucose probe scored to lowest. Glucose is a metabolite that varies dramatically throughout the day. This reason for this variability has to do with the time of day, when the patient ate, and any shock resulting from trauma. For these reasons, the pH probes scored higher because the pH in the body remains between a 7.35-7.45 [16]. Even if there was a decreased pH due to shock, a compartment would express a pH dramatically below this range. The pH polymer system, the pH microsensors, and the pH optic fiber probe all scored the highest in this category. This is because the error range for the pH polymer system and the pH microsensors were within +/- .03 and +/- .05 of a pH,

respectively [13][14]. The pH fiber optic probe has been shown to measure pH very accurately, with a standard deviation of .01 pH units [15]. Even when kept in buffer solution at a pH of around 6.84, the calibration of the probe drifted less than .02 units [15]. For the purposes of this project, this deviation would not be of consequence.

Ease of Use

For this category, the main criteria was to determine if the device could be easily calibrated by the user (i.e. nurses and doctors). Here, the glucose probe scored the lowest. This was primarily due to the fact that a previous team attempted to calibrate a glucose probe. This proved to be extremely difficult and not realistic for use in a trauma environment. In addition, our client has also run into complications with calibrating glucose probes. This leads to the assumption that nurses and doctors may also struggle with calibration, especially in a stressful, hospital setting. The pH polymer system received the second lowest score because while calibration may be easier, the requirement of removing the sample from the body before analysis will prove to be more difficult than taking a reading inside the body. Calibrating a pH probe with a buffer solution is a well-known, simple method of calibration. For these reasons, the other pH probes all received the highest score due to this ease of calibration, and the fact that a reading can be taken from inside the body.

Ease of Fabrication

This category took into consideration the feasibility for the team to be able to manufacture these preliminary designs. The pH polymer system and the pH optic fiber probe received the same score. This is because both devices have the most parts that are able to be purchased, with minimal fabrication. Both fabrication protocol would mainly entail assembling parts together. The glucose probe, pH ISFET probe, and pH microsensor all received lower scores. The previous group had issues with the fabrication of a working glucose probe prototype which factored into the score. For the other two pH probes, a lower score was awarded due to the necessity of scaling down existing technology in order to fit the size specifications. Fabrication of a probe with this decrease in size will be difficult when working on such a small scale.

Sterility

Sterility is another important factor because the device will be in contact with the fluids of the human body. Cross-contamination should never occur. However, because all these systems have the ability to be sterilized, the weight of this category was smaller than many other categories. Here the glucose probe received the highest score because a new needle would be used every time a sample was needed. The pH polymer system was also tied in this category because the actual system would not be in contact with the human body, but only the sample of fluid contained in a well. The pH ISFET probe also tied in this category because the system would be able to be sterilized by autoclaving. The pH microsensor received a lower score

because while the needles can be replaced, it is more costly to replace these needles, compared to the alternatives. The pH fiber optic probe also received a lower score as well because it cannot be autoclaved due to the potential for the plastic optic fibers to melt. Alternatives to this would be using gas or alcohol to sterilize the device, which would not be as ideal as autoclaving.

Cost

Cost was given a low weight due to the budget limit specified in the PDS (Appendix A). Current glucose monitors that are on the market are relatively inexpensive, giving the glucose probe the highest score in this category. The pH polymer system and the pH fiber optic probe followed with the second highest scores. The pH polymer system is expensive but because nearly all parts will be able to be reused, it appears to be a one time expense. This expense mainly comes from the price of a spectrophotometer that may need to be purchased. Similarly the fiber optic pH probe has more expensive reusable parts, with other pieces, such as the optical fibers that are relatively cheap. The pH ISFET probe and the pH microsensor received the lowest scores because there are many parts of the entire system that, while reusable, pose a considerable cost.

Efficacy

There is currently not enough information or data to make a solid conclusion on this aspect of the matrix.

Proposed Final Design

As seen in Table 1 above, the fiber optic probe was the design that scored the highest, receiving a score of 92 out of 100. This is primarily due to the fact that this design scored the highest in the top four categories within the design matrix. As seen in Figure 7, the proposed design is a probe that consists of 2-3 fibers. One or two fibers will transmit two different wavelengths of light through a glass disk containing pH indicator on the surface [14]. When being used, the hydrogen ions in a potential compartment will react with the pH indicator by diffusing through a semipermeable glass disk at the probe tip in order to establish an equilibrium of hydrogen ions based on the theory of diffusion [17]. The reacted pH indicator will contain both “acidic” ions and “basic” ions [17]. These ions reflect different wavelengths of light. By exposing the indicator to different wavelengths of light, a ratio of the “acidic” and “basic” ions can be determined by measuring the wavelength of light that is transmitted back to a spectrophotometer or photodiode by a different optic fiber. This ratio of ions can then be used to calculate the pH [17].

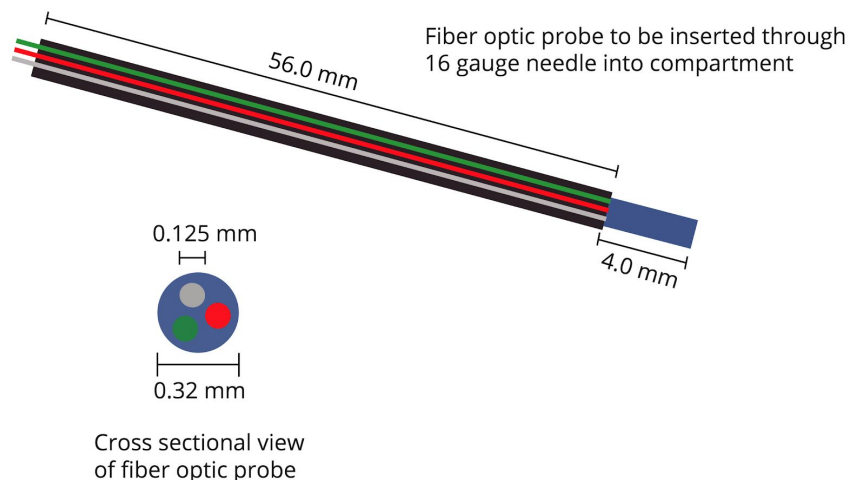


Figure 7: Image of the proposed final design. There are three optic fibers pictured. Two fibers (red and green) transmit light to the glass disk at the probe tip, while one optic fiber (grey) will transmit light back to a photodiode or spectrophotometer.

Dye Selection and Fabrication

pH Dye Selection

As mentioned in the PDS (Appendix A), the fiber optic pH sensor should be able to measure the pH value from 5 to 7. Therefore, the indicator to be used within the pH measuring system should be within the appropriate range and be sensitive to small changes in the pH within this range. Based on the pH indicator Table 2, azolitmin, bromocresol purple, bromothymol blue, chlorophenol red and phenol red could be potential options [18]. Besides the consideration of the pH range, the pH indicator should have no adverse biological reaction and avoid any irritations to tissues or cells. The pH indicator, furthermore, must have stable chemical and physical properties to prevent dissociation and diffusion that may cause insufficient color reflection and inaccurate pH measurement. After evaluating the pH dye options compared to these considerations, chlorophenol red was deemed the best option (Table 2).

Azolitmin	red	4.5	8.3	blue
Bromocresol purple	yellow	5.2	6.8	purple
Bromothymol blue (second transition)	yellow	6.0	7.6	blue
Phenol red	yellow	6.4	8.0	red
Chlorophenol Red	yellow	4.8	6.7	purple

Table 2: A table containing the pH ranges for potential pH indicators to be used.

pH Dye Immobilization

	Physical	Chemical
Disadvantages	Not effective Leaching problems	Difficulty of fabrication Time consuming
Advantages	Simple and versatile	Excellent immobilization of the pH-sensitive dye No leaching issues

Table 3: Pros and cons of physical and chemical immobilization methods.

When looking at different means for applying the chlorophenol red to the probe, there were two main strategies. Table 3 above compares these two options of physical encapsulation and chemical immobilization. The optimal choice of the immobilization technology should avoid any leaching and still be cheap and easy to use. As leaching is of great concern in this application, chemical linking was deemed the safest and most valid immobilization technique. A fabrication protocol was adapted from literature for immobilizing the chlorophenol red onto the thin glass disks [19]. A materials list and protocol are found in Table 4.

Materials	Chlorophenol Red Immobilization Protocol
Anhydrous ethanol	<ol style="list-style-type: none"> 1. Combine 60 ml of TEOS, 60 ml anhydrous ethanol, and 4 ml deionized distilled water in a 250ml beaker at room temperature. 2. Then add 84 mg chlorophenol red and stir for 60 min. at 60°C. 3. Drop a single glass disk into the solution and let soak for 3 min. 4. Slowly remove the glass disk with tweezers using caution to not disturb the thin film. 5. Let dry for 3-5 days. 6. Soak in deionized water to remove any unattached fragments prior to use.
Chlorophenol red	
Deionized distilled water	
Glass discs	
Dialysis tubing	
Tetraethyl orthosilicate (TEOS)	

Table 4: list of materials needed for chlorophenol red immobilization listed on the left and protocol listed on the right.

Final Design Validation

A professional Ocean Optics spectrometer was used to validate the theory of using optical fibers to transmit wavelengths of light accurately. As seen in Figure 8, solutions of varying colors falling within the chlorophenol red range were created. These solutions were

analyzed with the use of the spectrometer and a graph of the wavelengths reflected vs their intensity was developed (Figure 9). As expected, the colors reflected wavelengths of light corresponding to their visual color, validating the use of fiber optics when measuring wavelengths of visible light.



Figure 8: Image of color of waters used in spectrometer testing.

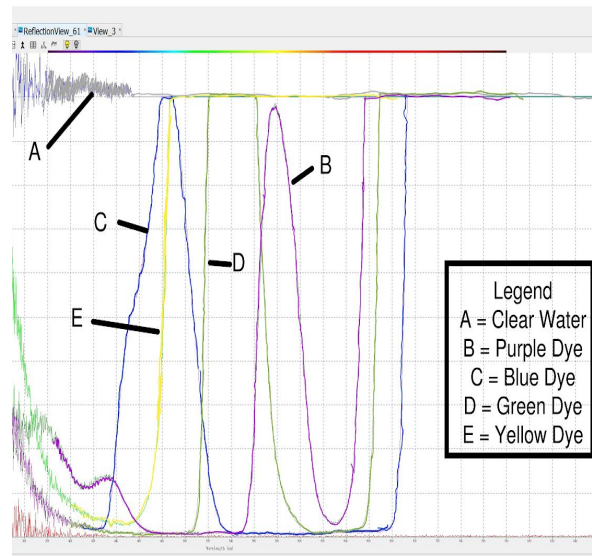


Figure 9: Graph of wavelengths reflected vs. percent reflected (intensity) of varying colored solutions.

When calculating the percent error of the spectrometer, the theoretical values of the wavelengths corresponding to each color were used. It is important to note that the percent error of the clear water and the purple water were not calculated. The percent error of the clear water was not calculated because clear water reflects all wavelengths of light, as seen in Figure 9. In addition, the percent error of the purple dye would be flawed. This is because violet light corresponds to a certain range of wavelengths, but purple does not. Purple is considered a cross between blue and red wavelengths. Because it is up to the manufacturer of the dye to choose which wavelengths of blue and red to use when creating the purple dye, the percent error of the wavelengths would not be accurate. However, in Figure 9 it is possible to see that two different wavelength ranges exist in the purple dye, both of which correspond to the blue and red wavelengths of the visible spectrum. The percent error calculated corresponds to the midpoint

wavelength where one hundred percent reflectance was seen, in comparison to the midpoint of the accepted range of values (Table 5).

Color of wavelength	Percent Error
Blue	3.19%
Yellow	6.96%
Green	0%

Table 5: A table of the percent error of colors tested using the spectrometer.

Although these values are close to our five percent accuracy range, the midpoint values are slightly lower than the accepted theoretical values when calculating the values for percent error. While this did not lead to a dramatic change in accuracy and the theoretical ranges of the spectrum vary, this means that the range that is needed for the design is highly dependent on the pH indicator dye. Ultimately the calibration of the final probe using the pH indicator will be of the utmost importance in the future.

After the design validation was complete, a schematic of the necessary hardware to be implemented into the probe was created (Figure 10). This block diagram breaks down all the components that will need to be used in order to incorporate the technology of the spectrometer into the software and hardware of the designed pH probe.

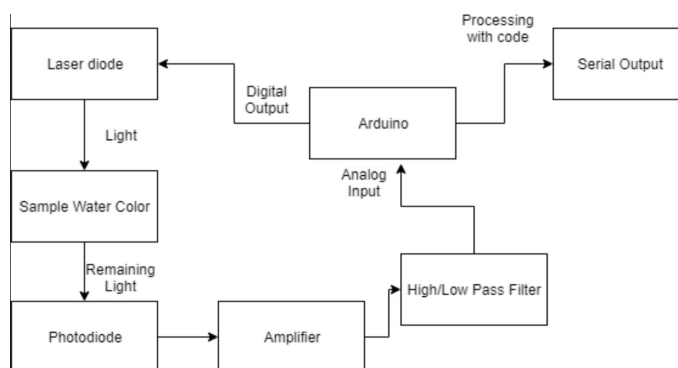


Figure 10: Block diagram of circuitry for probe wavelength to pH conversion.

Future Work

Future work entails immobilization of the chlorophenol red dye on a glass surface that is permeable to hydrogen ions. After the device is developed, a calibration and sensitivity test for pH values should be executed to determine the success of the probe.

The design validation shows the theory of the functionality of fiber optics incorporated in the final design can be an excellent method to determine the wavelength of a specific colored solution. The next step is to recreate the probe. Unlike the professional spectrometer used in design validation, the probe that uses the fiber optics for both transmission and collection of reflected lights needs to output a voltage value associated with a corresponding wavelength. The specific ratio between the detected wavelength and pH value can be found and therefore a system with an Arduino microcontroller can evaluate and display the pH value.

The clinical and biomedical goal of the probe is to determine a pH range for ACS through live animal studies.

Conclusion

The goal of this project is to design a functioning in-body pH sensor with quantifiable feedback as a means to reduce the misdiagnosis rate of Acute Compartment Syndrome. As determined by the design matrix (Table 1), the fiber optic pH probe was chosen as the best design due to its size, accuracy, ease of use, and safety. The pH indicator of chlorophenol red was selected as the indicator dye and the immobilization protocol for it was developed. The final step completed thus far has been the validation of the optic fiber theory via spectrometer testing of colored solution from the chlorophenol red range. Future steps mainly involve the building and testing of the actual probe. The accuracy and precision of the device will be quantified and further improvements will be conducted using *in vitro* testing. Should the prototype of this design be successful, this device will be able to help more accurately diagnose Acute Compartment Syndrome.

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Appendix A

Product Design Specifications

Function:

The goal of this project is to develop a device to more accurately quantify and detect Acute Compartment Syndrome (ACS). This medical complication often impacts trauma patients and is extremely hard to detect, with a current false positive diagnosis rate of 35% []. The decision whether or not to treat a patient for ACS is highly dependent on clinical diagnosis which becomes an issue in cases where the patient is unresponsive or in extreme pain. The current means to quantify ACS involves measuring the intracompartmental (IC) pressure and comparing it to the current accepted value of delta 30. There are a few logistical reasons why this method is not ideal, the most prominent being the fact that different muscles can maintain extremely different deltas prior to damage. Location and prior strenuous experiences on the muscle are just two potential reasons for these delta variations.

As a result of these diagnostic conflicts, a means to definitively quantify ACS is desired. A key factor in ACS is the decrease of oxygen to the compartment which leads to the ceasing of cellular respiration. As a result, many biochemical markers typically seen in an *in vivo* environment are reduced. Two key markers, glucose and pH, have both been seen to decrease in induced ACS in dog trials. These, along with other metabolic biochemical markers, are suspected to be effective measurable variables.

The focus of this project is the development of a device that accurately quantifies ACS via a metabolic biomarker while taking into account patient safety.

Client requirements:

- Probe must accurately detect positive ACS
- Must enter the body in an 16 gauge needle or smaller
- Probe must be a length between 4-6 cm
- Must measure the pH of a compartment within a range of 5-7 pH units

Design requirements:

1. Physical and Operational Characteristics
 - a. *Performance Requirements:* The probe of the measuring device should be able to accurately (within 5%) and consistently measure a specific metabolite inside a muscle compartment *in vivo*. The output of the device should display the measurement of that metabolite that is easily readable by the user. The time needed to calibrate the device should be less than 5 minutes. The device will be used whenever ACS is suspected to be present in a patient.
 - b. *Safety:* The probe that measures the metabolite would be a hollow needle. The needle needs to comply with FDA standards. The circuit should be insulated well to prevent electrical shock to both the patient and user.

- c. *Accuracy and Reliability:* This device need to be specific enough to determine the concentration of the biomarker within a hundreth. For particular biomarkers, a change by even a tenth can be damaging to the body. As such, this device would need to accurately measure a biomarker, and be extremely reliable so a patient does not get misdiagnosed.
- d. *Life in Service:* The primary portion of the device is likely going to be one-time use. As it is a needle-based product it will not remain in the body for more than a minute and penetrate about 4-6 cm into the body. The circuitry and interface for the device will be developed for multiple uses, ideally it would function for multiple years. It should be mobile from one examination room to the next.
- e. *Shelf Life:* The circuitry for the device will should not have a shelf life. Any chemicals used in the device, if unopened, should have a shelf life of multiple years.
- f. *Operating Environment:* The device should be able to detect the accurate value in all situations. The device should normally be used in a hospital setting for the diagnosis of ACS.
- g. *Ergonomics:* The device should be easy and quick to use in a trauma setting. It must be able to be set up, used, and diagnose ACS in a timely manner in order for the medical specialist to begin treatment.
- h. *Size:* The device must be able to fit into a 16 gauge needle.
- i. *Weight:* Given the size requirement for the device, the probe must be very light in order to be able to fit through a 16 gauge needle, and the corresponding circuit must be able to held in the user's hand.
- j. *Materials:* Any materials that have the potential to elicit an adverse reaction in the body should not be used for this project.
- k. *Aesthetics, Appearance, and Finish:* The device must have a smooth finish in order to prevent excessive tissue damage, promote ease of use, and reduce patient discomfort.

2. Production Characteristics

- a. *Quantity:* There is no specific production requirements at this point. A long-term requirement would be the ability to mass produce the exposable portions of the device. At this moment, a functional prototype is what is necessary for the client, so quantity of the product is not a concern.
- b. *Target Product Cost:* In order to get a working prototype, the target product cost in not a concern at the moment. Later, cost of production will need to be investigated and from there the assessment of the product cost can be made.

3. Miscellaneous

- a. *Standards and Specifications:* As a device that would be used in a clinical setting, IRB approval would be needed if testing ever needed to be done on humans. In addition, FDA approval would be necessary if this product were ever to be used commercially.
- b. *Customer:* The client would like for the device to be as precise as possible, with a small enough probe that can fit through a sixteen gauge needle. In settings where this device may need to be used, the patient will often be unresponsive to any questions and this

probe will need to be small enough as not to cause any alarm and small enough where surgery is not required to perform this test.

- c. *Patient-Related Concerns:* The most important concern to address is accuracy. With the current false positive rate of 35% this device should be able to more accurately diagnose Compartment Syndrome, in order to avoid any needless fasciotomies, a procedure that ultimately would cause unnecessary needs for a patient should they be falsely diagnosed with Compartment Syndrome.
- d. *Competition:* There are currently no existing probes that are capable of diagnosing Compartment Syndrome in a human. However, there are many other probes that can detect pH and glucose that can be adapted for this need.

Appendix B

Working Principle of Probe Design

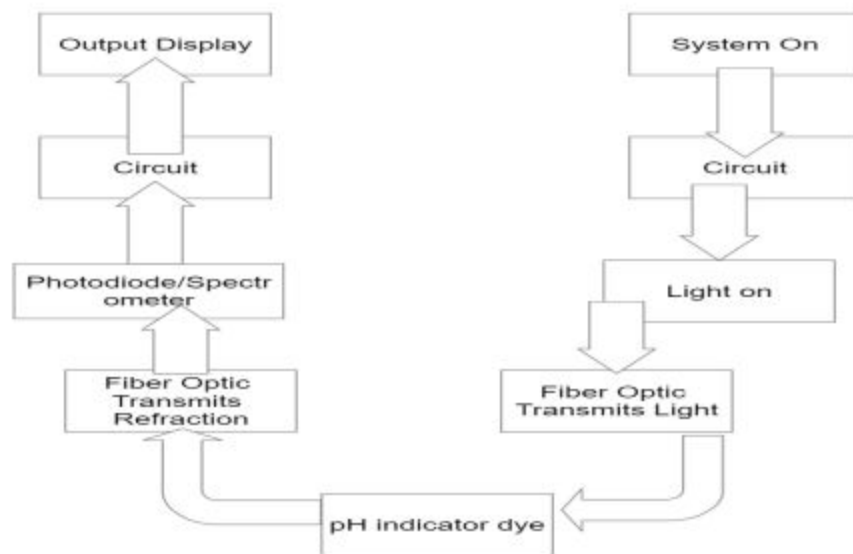


Figure B1: Block diagram of the working principle (the blocks on the right would focus more on fabrication; the blocks on the left would focus more on code programming).

Appendix C

Fabrication Protocol: Immobilizing Chlorophenol Red

Materials	Chlorophenol Red Immobilization Protocol
Anhydrous ethanol	<ol style="list-style-type: none">1. Combine 60 ml of TEOS, 60 ml anhydrous ethanol, and 4 ml deionized distilled water in a 250ml beaker at room temperature.2. Then add 84 mg chlorophenol red and stir for 60 min. at 60°C.3. Drop a single glass disk into the solution and let soak for 3 min.4. Slowly remove the glass disk with tweezers using caution to not disturb the thin film.5. Let dry for 3-5 days.6. Soak in deionized water to remove any unattached fragments prior to use.
Chlorophenol red	
Tetraethyl orthosilicate (TEOS)	
Deionized distilled water	
Glass discs	
Dialysis tubing	

Table C1: list of materials needed for chlorophenol red immobilization listed on the left and protocol listed on the right.

Appendix D

SolidWorks Drawings of pH Probe

Models of the pH probe were made using SolidWorks. Figure 1 is an isometric view of the device, depicting green, red, and return optical fibers that run through the probe. Figure 2 is a top view of the device. Drawings of the design were also made using SolidWorks. Figure 3 is a top view of the device which depicts the overall length of the probe as 60 mm. 56 mm of the probe houses 3 fiber optic cables while the remaining 4 mm contains a glass disc with immobilized dye. Figure 4 displays a side view of the probe. The overall diameter is 0.32 mm and the diameter for each optical fiber is 0.13 mm.

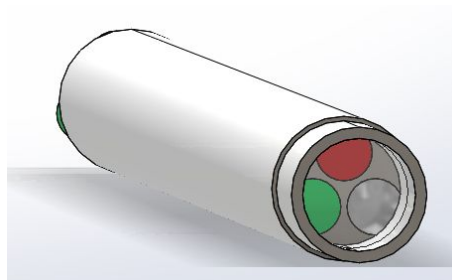


Figure D1: An isometric view of the probe created in SolidWorks. Green, red, and return optical fibers run throughout the probe.

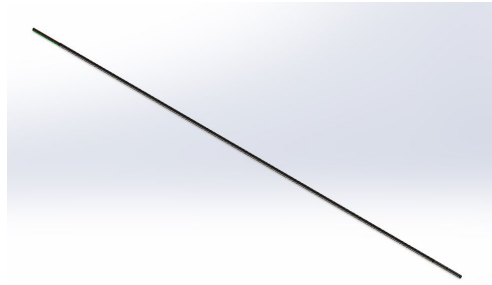


Figure D2: A top view of the model probe. The length of the probe is 60 mm.

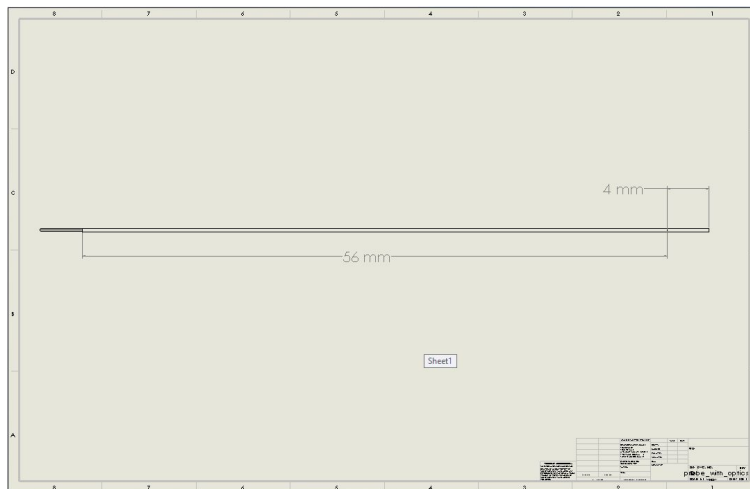


Figure D3: A top view of the probe is shown. The 56 mm of the probe contains 3 fiber optic cables while the remaining 4 mm contains a glass disc with immobilized dye.

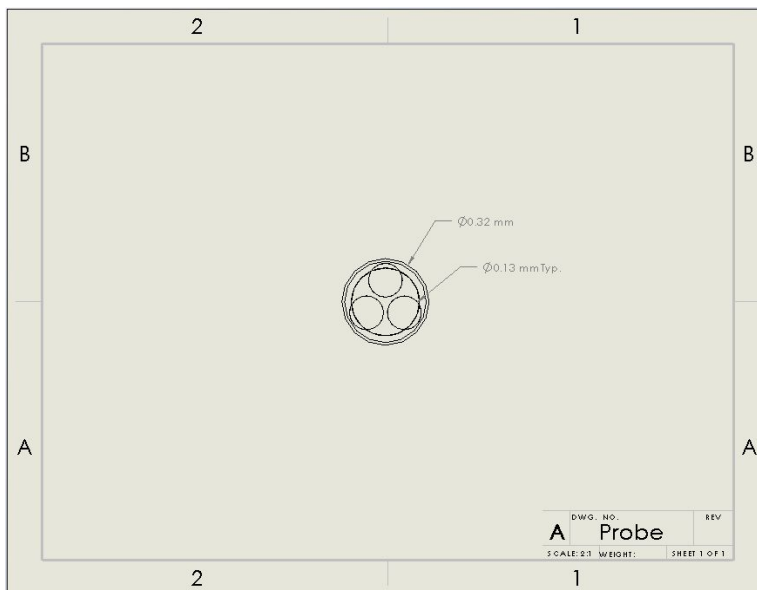


Figure D4: A side view of the probe. The overall diameter is 0.32 mm and the diameter for each optical fiber is 0.13 mm.

Appendix E

Percent Error Calculations

Blue:

Midpoint of experimental wavelength range: ~ 485 nm

Midpoint of theoretical wavelength range: ~ 470 nm

$$\text{Percent Error: } \left| \frac{470-485}{470} \right| \times 100 = 3.19\%$$

Yellow:

Midpoint of experimental wavelength range: ~615 nm

Midpoint of experimental wavelength range: ~575 nm

$$\text{Percent Error: } \left| \frac{575-615}{575} \right| \times 100 = 6.96\%$$

Green:

Midpoint of experimental wavelength: ~540 nm

Midpoint of experimental wavelength: ~540 nm

$$\text{Percent Error: } \left| \frac{540-540}{540} \right| \times 100 = 0\%$$

Purple:

The percent error for purple was not calculated due to the fact that it is a composite of two different colors at ratios dependent on the choice of the manufacturer. Due to this variability, calculating the percent error was not feasible.