DEPARTMENT OF
Biomedical Engineering
UNIVERSITY OF WISCONSIN–MADISON

Compartment Syndrome

BME400 Preliminary Report

October 9th, 2019

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Abstract

Acute compartment syndrome (ACS) is a complex and difficult-to-diagnose condition in which trauma causes increased pressure in a muscle compartment, which can subsequently lead to muscle ischemia and death. Current methods of ACS diagnosis are often inaccurate, with pressure-based diagnosis reaching a rate of 35% false-positive in one study. False-positive ACS diagnosis results in unnecessary fasciotomies, which are incredibly invasive and expensive procedures that often leave the patient with permanently impaired peripheral limb function. More recent methods of ACS diagnosis continue to suffer from inaccuracy and a lack of supporting literature, indicating the necessity of a new, more effective method to reduce misdiagnosis of ACS. The previous team that worked on this project fronted a solution involving Ion-Sensitive-Field-Effect-Transistor (ISFET) pH sensors to detect acidic intramuscular environments indicating muscle ischemia, which we will be miniaturizing and implementing in a 16-gauge needle for eventual use in humans after testing in animals. Furthermore, we are in the process of designing and testing a user interface to display the pH on a screen and record pH input values for a physician to use for ACS diagnosis in a clinical setting.

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Introduction

Acute compartment syndrome (ACS) is a difficult-to-diagnose and complex condition caused by an increase in muscle compartment pressure resulting in insufficient blood flow to the muscle tissue, causing muscle ischemia and possible tissue death [1]. ACS is remarkably

uncommon, with an annual incidence of approximately 7.3 per 100,000 men and 0.7 per 100,000 women [2]. Because of this, there is limited information available from literature, and no gold standard for clinical diagnosis [3]. Furthermore, current methods of ACS diagnosis are flawed, with false-positive rates for direct pressure-based diagnosis reaching up to 35% [4]. The treatment for ACS is usually a fasciotomy of the affected muscle compartment, which can involve complications such as uncontrolled bleeding and infection [3]. Even if initially successful, subsequent operations are needed to remove dead muscle tissue and prevent sepsis, sometimes requiring limb amputation [3]. Fasciotomy survivors suffer from diminished range of motion, pain, and emotional trauma, making false-positive fasciotomies a serious issue when the patient endures all of this due to a misdiagnosis, especially after dealing with the high cost of fasciotomy operations as well [3]. Seeing that ACS misdiagnosis is a fixable problem in modern medicine, our client, Dr. Christopher Doro, submitted this project to the BME department in an effort to minimize false-positives and reduce the number of ACS patients that suffer as a result.

Current methods of ACS diagnosis involve first testing compartment pressure directly using a catheter-enclosed pressure monitor [5]; however, this is often error prone and can result in misdiagnosis. More recent advancements have resulted in the formation of companies such as Odin Technologies and their near-infrared spectroscopy (NIRS)-based Valkyrie, which estimates blood oxygenation and is completely non-invasive [6]. However, NIRS has yet to demonstrate great accuracy in diagnosing ACS, and given that the technology has been in existence for several decades, it may not be the best solution [3]. Another alternative developed by NASA looked into the possibility of using ultrasound to estimate compartmental pressure, but this also has yet to be proven effective [7].

Given the issues with current methods of ACS diagnosis, and the ineffectiveness of other existing alternative methods, the previous team selected to work on this project decided to use pH as a biomarker threshold for diagnosis [8]. They tested an Ion-Sensitive Field Effect Transistor (ISFET) for pH measurement and saw that it was appropriate for this application. However, the ISFET sensor casing is too large to be inserted in a 16 gauge needle, the largest possible for insertion in human patients [3]. Our team aims to take this previous work and advance it to the point of laboratory animal testing and possible clinical environment testing. Our goal is to design and test a device for clinical use capable interfacing with an ISFET probe and measuring the pH within a muscle compartment, and displaying and recording the pH so a physician can use it as a reliable indicator of whether compartment syndrome is actually occurring. Furthermore, we plan to miniaturize the previous team's ISFET concept to facilitate insertion into a 16 gauge needle; though this size is not required for animal testing, it will allow us to more easily reach the point of possible human testing later on.

Background

Acute Compartment Syndrome

ACS is a limb- and life-threatening condition in which a bone fracture or some other kind of blockage prevents blood from leaving a muscle compartment (see figure 1) [5]. This inability for blood to leave causes an increase in intracompartmental pressure which, upon exceeding arterial pressure, prevents blood from entering the compartment. The lack of fresh blood causes a buildup of tissue metabolites such as CO_2 that can cause tissue death and necrosis, both of which are able to damage the patient's whole body or at least prevent the muscles in the compartment from ever healing [5]. Because of these serious consequences, if a compartment may have ACS but test results are inconclusive, the default decision is that 6 hours after injury or symptom

onset, a fasciotomy (see figure 2) is performed to reduce intracompartmental pressure and allow blood flow to return to normal [5].

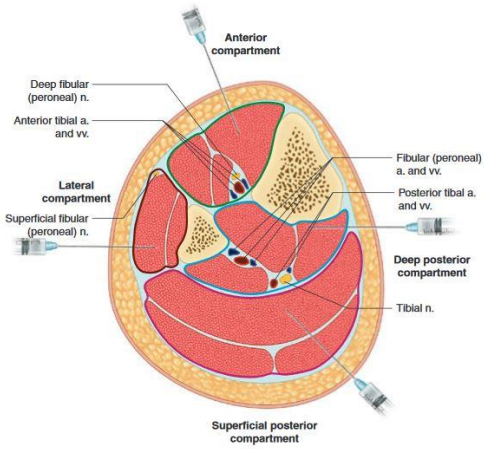

Figure 1: Muscle compartments in the lower left leg [5].

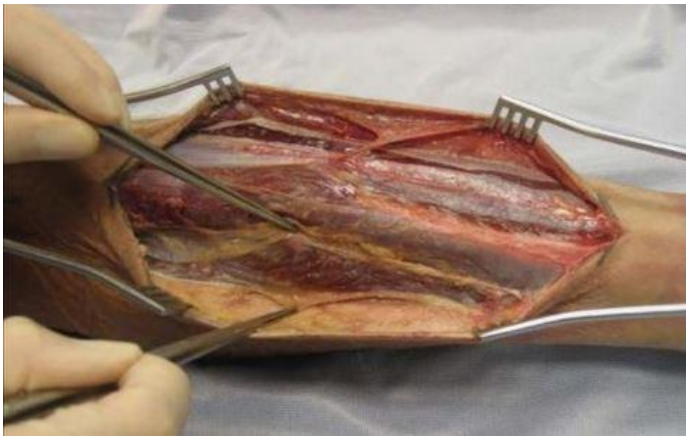

Figure 2: Fasciotomy [3].

Conventional methods of diagnosing ACS include measuring intracompartmental pressure for the increase that is associated with blood outflow blockage. However, this method is highly unreliable and results in a very large percentage of false positive diagnoses (35%) [4]. Another more accurate diagnostic method is to detect the partial pressure of oxygen in the blood of the compartment to detect the decrease associated with ACS. This method, while very reliable, is also far more expensive than pressure measurements [3, 9]. Recent research has indicated that pH is also a reliable method of diagnosing ACS and can be implemented in a more cost-effective manner than partial pressure of oxygen diagnostic methods [10]. Because of this, the work of previous semesters was focused on selecting a suitable pH probe for use in humans. Legal restrictions require that the largest needle that can be inserted into a human patient is a 16 gauge needle, with tip inner diameter of 1.422 mm [3]. It is this restriction, in addition to the accuracy and precision of the pH probes, which inspired the groups of previous semesters to use a ion-sensitive field-effect transistor (ISFET) probes for pH measurement [8].

ISFET pH Probes

ISFET probes are a special type of field-effect transistor (FET) which has a selectively permeable membrane that allows only H^+ ions across it [11]. This, as you may know from biology/physiology courses, will eventually reach an equilibrium potential at which the concentration gradient caused by the lower [H^+] on the FET side of the membrane (causing H^+ to enter the FET) is balanced by an electrical gradient produced by the solution's attempt to reach a concentration equilibrium (the influx of positive charge from H^+ entry repels other positively charged H^+ ions, opposing the concentration gradient) [12]. The equilibrium potential serves as the gate voltage for the FET which regulates the current flowing from Drain to Source (see figure 3). The reference electrode is used to determine the equilibrium potential of the solution as a whole, not just of H^+, for comparison with the gate potential [11]. In this way, the ISFET accounts for any effect non-H^+ ions have on the gate potential, increasing the accuracy of the pH reading [11].

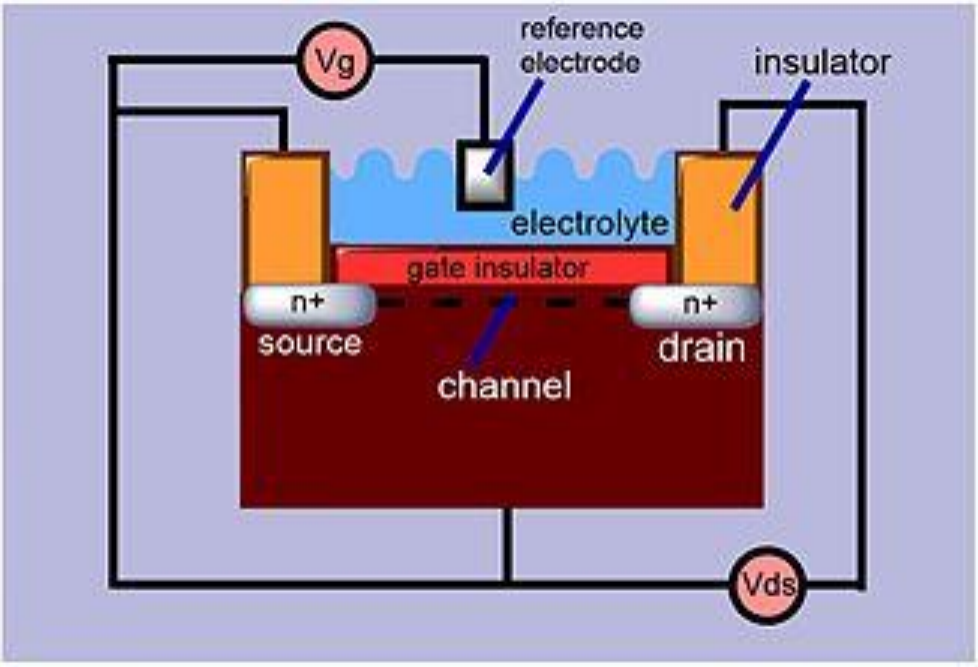

Figure 3: Diagram showing the structure of an ISFET pH probe [13].

Preliminary Designs

Design 1: Touchscreen Interface

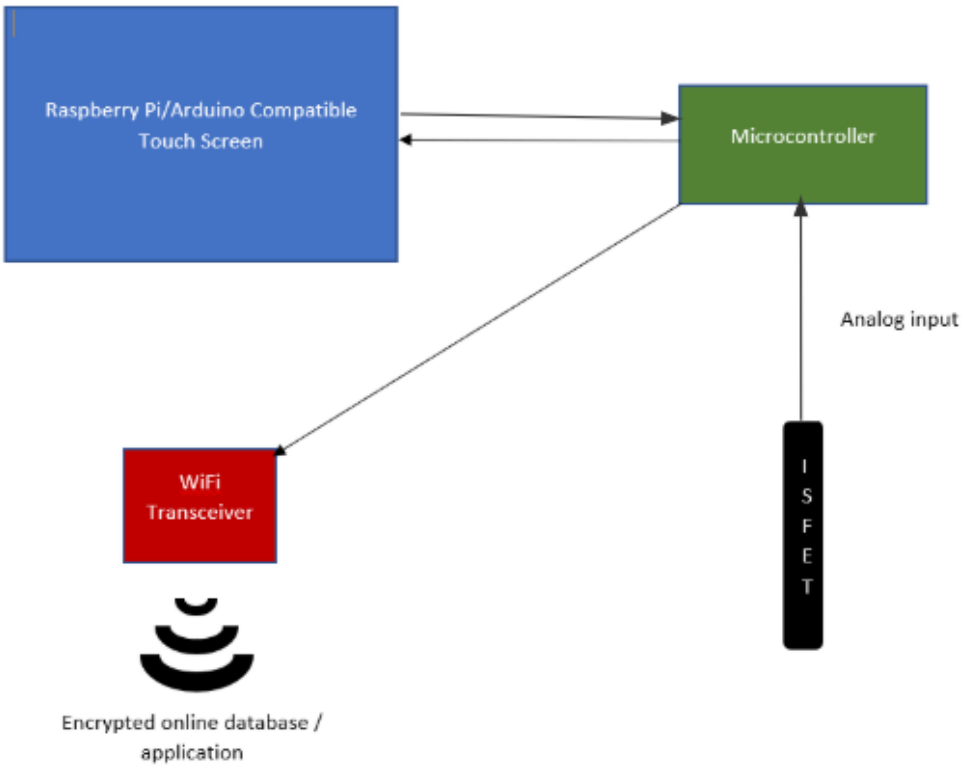

Figure 4: The first proposed design with a microcontroller which interfaces with the user through a touch screen display, and is capable of sending data over a Wi-Fi transceiver.

The first design is the "TouchScreen" Design, and uses a touch screen to interact with the user. A microcontroller determines the pH from the ISFET sensor and displays the signal on the touch screen user interface. The user can also set up a Wi-Fi connection which can upload the data to a cloud-based location, so it is viewable from multiple devices in real time. This would allow the user to monitor multiple cases simultaneously, and can determine the status of a case

from any location. This design emphasizes the value of a clinician having access to the data at all times, so a closer eye can be kept on a patient.

Design 2: LCD-screen Display

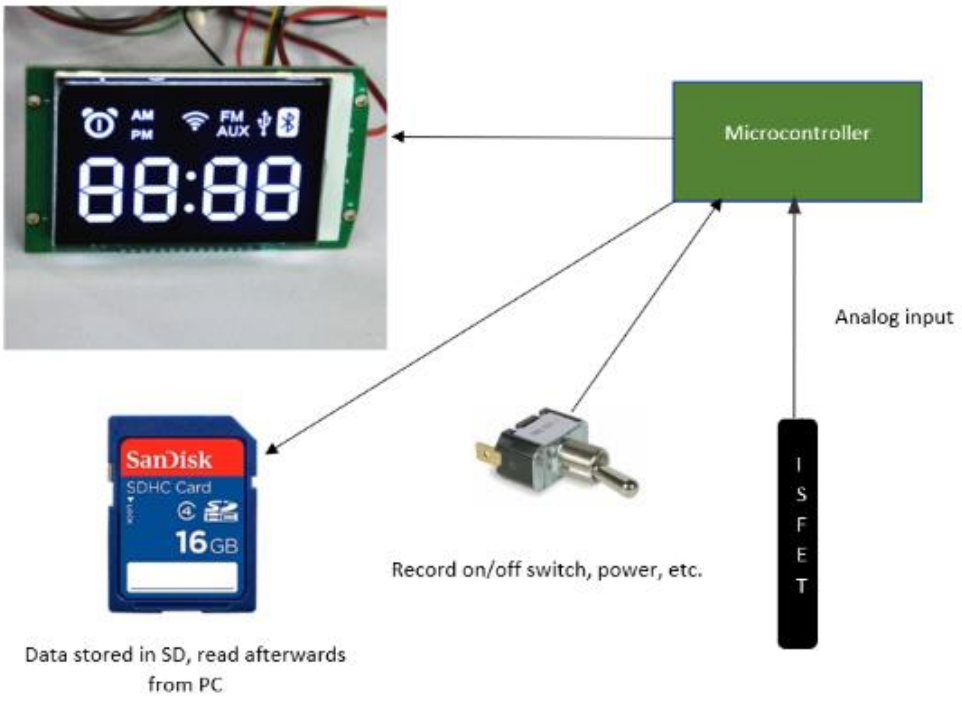

Figure 5: The layout of the LCD design which involves a microcontroller connected to the ISFET sensor, SD card Hub, LCD display, and power switch

The second proposed design uses a microcontroller to receive and interpret the signal from the ISFET sensor and displays the data in real time on an LCD display while saving the data simultaneously to an SD card, which can be reviewed later for clinical evidence. The entire circuit is controlled by a power on/off switch. The SD card will create folders to hold the data of each case and will be capable of recording data for at least 48 contiguous hours. The LCD design aims to stress reliability and resilience by having simpler components, which can withstand more

extraneous conditions while being less prone to failure. The drawback to this design is having a lack of accessibility to this information from multiple locations.

Design 3: Phone/Computer Interface

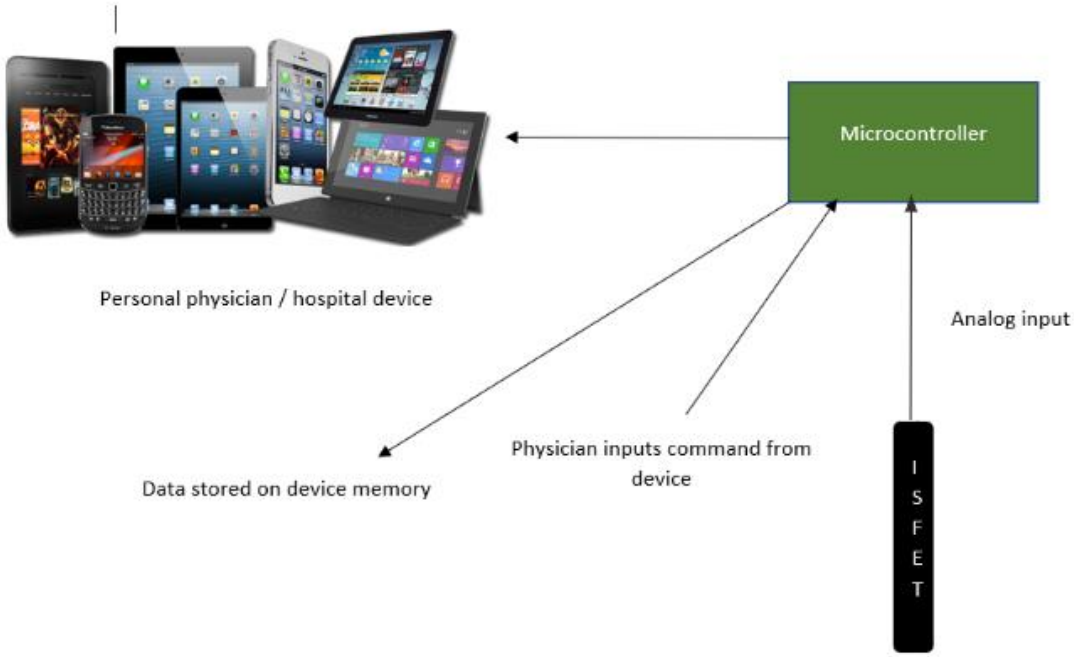

Figure 6: The third interface design that interfaces the user through the microcontroller with phone/computer.

The third interface design requires an application installed in the phone or computer that can either be personal physicians' or hospital devices. The physicians can use the application to start, view, save, and edit the pH recordings up to 48 hours. Once the ISFET is inserted into the muscle compartment, the physicians can input their command to start recording. The analog input from the ISFET sensor will be sent to the microcontroller which will display the digital output on the devices. The pH recordings of the muscle compartment will be stored in the device memory thus giving an easy access for the physicians. This design aims to make it easier for

physicians to obtain and view the data as needed. However, there is a concern about the patients' medical information security as these devices have the potential to be hacked.

Preliminary Design Evaluation

Criteria	Touch	LCD	Phone/Computer
Reliability (25)	20	25	20
Safety (25)	20	25	15
Resilience (20)	13	20	15
Portability (15)	15	8	12
Ease of Use (10)	6	9	7
Cost (5)	3	5	4
Total (100)	77	92	73

Figure 7: The design matrix for our three preliminary designs with ratings for each category.

The second design was our leading design and led every category except for portability. The LCD display is more reliable because it does not depend on wireless connectivity for operation, which reduces risk of data loss. The LCD is safer because it would have less user interaction, and it would require less sterilizing of the display. The Touch and Phone/Computer designs would get blood and other fluids on them from being used during procedures; furthermore, the Phone/Computer design would be carried with the doctor out of the hospital requiring extra precautions. Resilience is referring to the designs ability to withstand normal operating stress, which includes wear/tear and dropping. The LCD has much simpler components, and the display has reduced risk of breaking compared to a touch screen. Portability, which was dominated by the touch screen followed by the phone/ computer, refers to

how accessible this data is from multiple locations. The touch screen would use Wi-Fi to upload this data and have it be accessible from any location while simultaneously displaying in real-time next to the patient. The Phone/Computer design uses bluetooth to send the data to an associated electronic device, so this can be moved throughout the operating room, but is still limited to within the necessary range of the bluetooth transceiver. The LCD data is displayed in real time by a wired connection to the arduino and can only be transferred by SD card, which gives it the lowest score in this category. The LCD is the easiest design to use because it requires minimal interaction from the user after being powered on. The Touch Screen and Phone/Computer would require the user to setup the proper connections prior to use. Finally, The LCD has the cheapest components, so it received a perfect score in the cost category.

Proposed Final Design

The LCD interface design was chosen as the proposed final design due to its reliability, safety, resilience, ease of use, and low cost. This design has less complicated components which includes switches for record, and on and off, an LCD screen, an SD card, microcontroller, and the ISFET sensor. The sensor will record the pH readings in the muscle and send the analog input to the microcontroller and display the numbers on the LCD screen. At the same time, the pH values will be recorded in the SD card for up to 48 hours of recording. This interface design is simple and easy to use for clinicians, providing the important information at all times.

The prototype will also focus on miniaturizing the previous prototype to match the requirement of being no larger than a 16 gauge needle. The previous sensor was 3 mm in diameter, but the inside diameter of a 16 gauge needle is 1.422 mm. To accomplish this, we are working with the Wisconsin Center for NanoScale technology and discussing with existing

manufacturers of ISFET sensors. Figure 8 below is a microscopic image of the ISFET sensor used in the previous prototype without its housing.

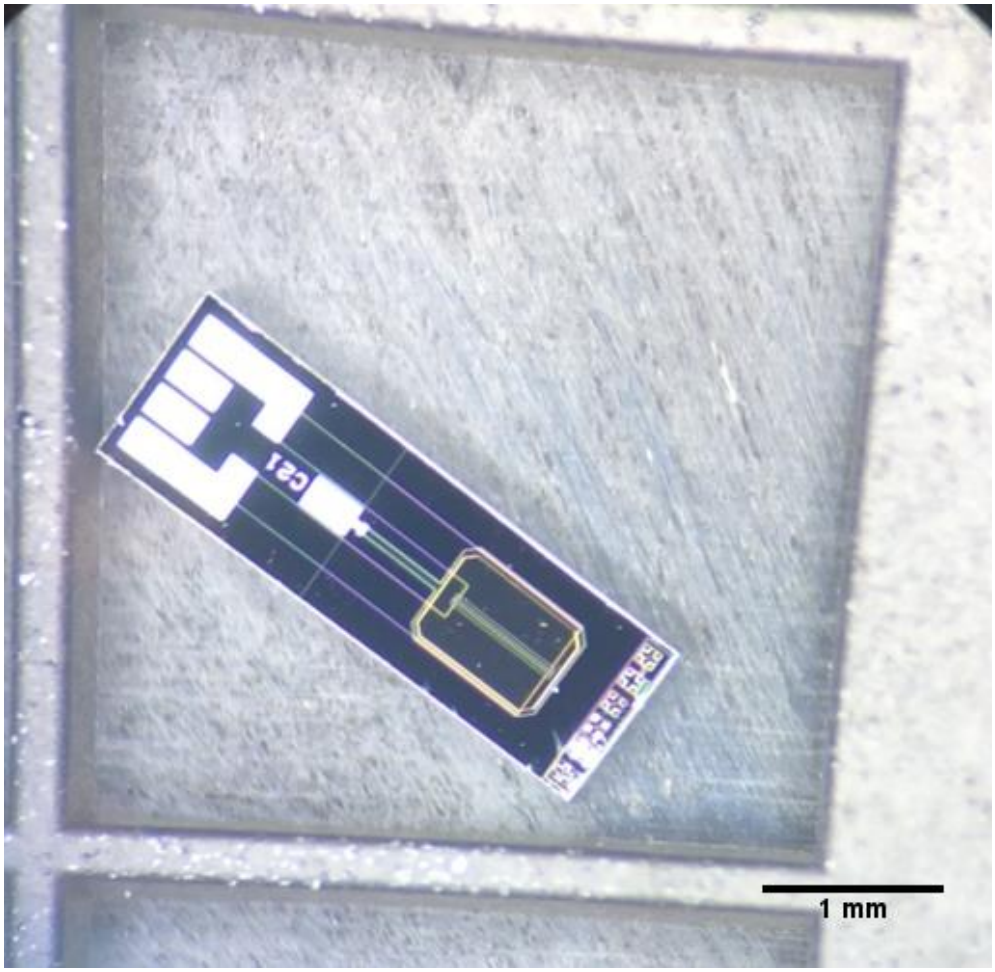

Figure 8: The micro ISFET produced by Sentron. This sensor is approximately 1mm in width and ~3mm in length. [14]

Winsense is a manufacturer from Thailand that makes a slightly bigger sensor that is 1.4 mm in width and 3.5 mm in length. [15] This would only provide .022 mm of additional room inside the needle. Future research will be focused on creating an ISFET/reference configuration that will fit inside the 16 gauge needle.

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Appendix

Product Design Specification

pH Probes to Diagnose Compartment Syndrome

Date: 26 September 2019
Team Members: Jonah Mudge, Lucas Ratajczyk, Hunter Huth, Nur Saidin
Advisor: Dr. Amit Nimunkar
Client: Dr. Christopher Doro

Function:

The pH probe interface must reliably display the pH level read by an ISFET sensor, and record it on a screen that is easily usable by a surgeon. It must be capable of recording pH data for a clinically relevant time period, while ensuring that no data or timestamps are lost. The device must also feature buttons (on a touch screen or otherwise) that are simple and reliable for a surgeon to interact with quickly, especially in high-stress situations in an OR. Along with probe interface is the ISFET probe casing, which must be able to fit into a 16 gauge needle while allowing accurate pH readings.

Problem Statement:

Compartment syndrome is a difficult-to-diagnose condition that occurs when tissue pressure in a muscle compartment rises enough to cause ischemia and possible muscle death. False-positive diagnosis of compartment syndrome can lead to expensive, invasive surgeries, and unnecessary surgeries. Our goal is to design and test a device for clinical use capable interfacing with an ISFET probe and measuring the pH within a muscle compartment, and using the pH as a reliable indicator of whether compartment syndrome is actually occurring.

Client requirements:

- Create a device capable of measuring intramuscular pH *in vivo*
- The device must be able to record at least 48 hours of pH measurements
- The device should be minimally invasive

Design requirements:

1. Physical and Operational Characteristics

a. Performance requirements:

- The probe should accurately measure the pH that relates to compartment syndrome that is within the range of 5 to 7.
- The probe must continuously record the pH inside the compartment up to 48 hours.

b. Safety:

- The electronics should not cause electrical shock to the user or patient.
- The device should not cause any infection to the muscle compartment.
- The device should not dissociate or fragment during compartmental insertion.
- The device must not release toxic materials into the patient.
- The device must be sanitizable to prevent transfer of infectious material.

c. Accuracy and Reliability:

- The device must be able to acquire the signal from the ISFET probe without noise
- pH read from the probe must be accurate within a range of 5 - 7
- Accuracy must be within 0.1 to ensure accurate readings and diagnosis

d. Life in Service:

- The probe must maintain its structure and function over many daily uses.
- The probe is disposable for a single use but the electronics of the pH sensor should last at least 5 years.
- The electronic systems must be resilient for repeated use without breakdown.

e. Operating Environment:

- The probe must survive insertion into a muscle compartment without shattering
- The probe casing must not degrade or otherwise allow any leakage into the muscle compartment during insertion and monitoring
- The main analyzer/probe interface must be able to survive falls in the case of an accidental drop
- The main analyzer/probe interface must be able to weather small spills of bodily fluids or chemicals that might occur during an OR situation

f. Ergonomics:

- The handheld probe interface should be shaped in a form that is easy to hold and does not pose any risks of injury from dropping

g. Size:

- The probe must fit through the hole of a 16 gauge needle
- The handheld portion of the device must not exceed a prism of the size 8”x8”x3”

h. Weight:

- The probe must not exceed 2 ounces in weight
- The handheld portion of the device must not weigh more than 16 ounces

i. Materials:

- Semiconductor for the probe
- Metal for the wiring to and within the handheld device
- Hard plastic for the housing of the handheld portion of the device

j. Aesthetics, Appearance, and Finish:

- Skin safe coating and material for use inside the body (muscle compartment)
- The device should be intuitive and simple to understand and operate
- The coating of the handheld portion of the device should have a rough texture to allow for better grip in time-sensitive situations

2. Production Characteristics

a. Quantity: 1 (prototype)

b. The budget is dependent upon grants received by the client with minimum immediately available funds exceeding $1,000

3. Miscellaneous

a. Standards and Specifications:

- The size of the needle is limited to a 16-Gauge needle to align with standards for use in trauma patients.

b. Customer:

- Customers (practicing trauma doctors) would desire a pH sensor that is placed inside a 16-gauge needle, which can read the real-time pH inside the muscle compartment of a patient who is at risk for compartment syndrome.

c. Patient-related concerns:

- The device must have a detachable and replaceable needle/sensor. The display and electronics casing should be sterilizable with an alcohol.
- Material of the device doesn't cause an inflammatory response, which could further increase pressure in the limb.

d. Competition:

- The Valkyrie by Odin Technologies uses Near-infrared spectroscopy to estimate the blood oxygenation. This device has a benefit of being completely non-invasive, but this technology has been around for decades without success in accurately diagnosing compartment syndrome.
- Patent (US7381186B2) by NASA is a system which uses the reflections of ultrasonic waves emitted into the compartment to estimate compartmental pressure.