Design, Fabricate, and Test an *in vitro* System to Investigate Therapeutic Hypothermia in Porcine Eyes

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B.S., University of Illinois at Chicago, 2016

THESIS
Submitted as partial fulfillment of the requirements for the degree of Master of Science in Bioengineering in the Graduate College of the University of Illinois at Chicago, 2017

Chicago, Illinois

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Acknowledgements

Dr. Hetling was my first positive experience with being a student at UIC. I was a transfer student and had missed orientation so I couldn't get in touch with anyone who could sign off on my classes. Dr. Hetling responded immediately and took care of me. It's been a pleasure to learn from him during my undergraduate career in some of my favorite classes. However, the lessons I've learned through him throughout this graduate experience are invaluable. My belief in the timeline of merging with cyborgs has been extended but not extinguished.

I'd like to thank my wife for her continued support of me pursuing my dreams. Through the entirety of my academic career and despite its many twists and turns, she quizzed me, pushed me, and I couldn't have gotten here without her.

I'd also like to thank Dr. Kotche for her unique and engaging approach to my education. From working together on WIESP, to MADLab, the BEST program, and teaching my first and last BioE classes, she has always been a positive influence on the people around her.

I would like to thank Dr. Esmailbeigi for enabling me to pursue my true neuroengineer dreams. To paraphrase, who know Brain-Computer Interfaces could be so hard? I learned a ton about the fringes of the fields that got me interested in bioengineering in the first place.

My family has also been incredibly supportive of me and have always had my back. Thanks to my Mom and Dad, and brothers Max and Jack for always being there for me.

I also need to thank Michael Sunshine for his mentorship. I learned so much about research and science under him as well as the rest of the Moritz lab and the CSNE team for welcoming me and teaching me so much.

Thanks to the very kind and patient people at Butcher and Larder, for almost a whole year I got to say to people, "Yeah, I just have to go see my eye guy and then I'll be available." You guys rock.

SJD

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List of Abbreviations

TBI	Traumatic brain injury
PTSD	Post-traumatic stress disorder
TECs	Thermoelectric coolers
HPC	Hypothermic preconditioning
CAD	Computer-Aided Design
DAQ	Data Acquisition Device
RTD	Resistance Temperature Detector
IOP	Interocular Pressure

Summary

Traumatic eye injuries are 4th in volume behind traumatic brain injury (TBI), post-traumatic stress disorder (PTSD), and hearing loss for serious injuries among active duty personnel. An injury to the eye is a precursor for a long-term visual disability including blindness or loss of visual acuity and is often caused by ischemia to the retinal cells responsible for vision. Therapeutic hypothermia has been shown to have a neuroprotective effect. If the eye can be cooled, it may be possible to mitigate this damage. The eye can be treated by local hypothermia, avoiding the risks and slow implementation associated with systemic hypothermia. The main goal of this project was to reduce the temperature of the posterior pole of the eye and proximal optic nerve by contacting the anterior surface of the eye.

In this thesis, a compact solid-state eye cooler is proposed to address the significant need for a portable, field-deployable, robust means of achieving and maintaining therapeutic cooling of eye tissues following traumatic injury. In clinical use, the objective is to develop a device that will be applied as soon as possible after injury, during transport from the field, and while the patient is awaiting definitive therapy in the hospital.

The data shows that placing the anterior of the eye in contact with the ECR system described in this study cools the anterior of the eye an average of 14.99°C, the equator an average of 12.20°C, and the posterior of the eye an average of 6.59°C. Posterior tissue cooling of 6.59°C exceeds the design specification of the device, indicating that therapeutic effects can be reached with the current system.

1. Introduction

1.1 Significance

Traumatic eye injuries are 4th in volume behind traumatic brain injury (TBI), post-traumatic stress disorder (PTSD), and hearing loss for serious injuries among active duty personnel. Open-globe injuries accounted for 55%, eyelid injuries 33%, orbital fractures 13%, corneal and conjunctival foreign bodies 11%, and traumatic optic neuropathy and optic nerve avulsion 3% of eye injuries during Operation Iraqi Freedom in 2003-05. An injury to the eye is a precursor for a long-term visual disability including blindness or loss of visual acuity. Therapeutic hypothermia has been shown to have a neuroprotective effect. If the eye can be cooled, it may be possible to mitigate this damage.

1.2 Problem Statement

The only methods for cooling the eye and surrounding tissue currently in use are application of an ice pack or irrigation with cold saline. Neither of these is ideal for use in the field during combat scenarios. The development and validation of a device which is secured to the soldier's face as well as being intuitive, self-regulated, and amenable to field use will greatly enhance the opportunity to save vision in traumatic injury to the eye or optic nerve. The purpose of this device was a potential application as a field deployable eye cooling device.

1.3 Specific Aims

The main goal of this project was to reduce the temperature of the posterior pole of the eye and proximal optic nerve by contacting the anterior surface of the eye. The following Aims were pursued to develop this device:

1. Design and fabricate a bench-test scleral contact eye cooler. The design should contact the sclera of the eye as accessible *in vivo* and with the view of the cornea unobstructed during cooling.
2. Design and fabricate a thermal sensor array that will allow measurement of the ocular tissue temperatures at up to eight locations simultaneously. The temperature of each sensor should be sampled at a minimum frequency of 1 Hz, and the data digitized and transferred to a computer for real-time monitoring and off-line analysis.
3. Develop a protocol for implanting thermal sensors into an enucleated porcine eye at clinically relevant locations.
4. Design and fabricate an in vitro test environment that replicates the in vivo thermal environment of the eye.
5. Determine experimentally if it is possible for the described system to achieve cooling to 30 degrees Celsius in the posterior of the eye by placing a cooling ring on the anterior sclera.

1.4 Summary of Results

It has been shown that cooling the posterior of the eye is possible by contacting the anterior scleral tissue with a cooling ring integrated with thermoelectric coolers (TECs). This demonstrates the feasibility of an eye cooling system that only requires electricity and doesn't necessitate the inclusion of liquid systems and complex pumps. However, the addition of an airflow system was necessary to remove heat from the local environment of the eye and minimize heat recirculation. This system can be used as a research tool to show the effects of cooling the anterior surface of the eye as well as providing data for detailed thermal models of the eye. With additional design modifications, it may be possible to adapt this approach to field situations.

1.5 Eye Anatomy

The functional neural tissue of the eye responsible for vision is located in the retina at the posterior of the eye. However, due to the surrounding bone and musculature, this tissue is difficult to access on a living patient. *In vivo*, only certain portions of the eye are accessible for contact by a therapeutic device: the cornea and a portion of the sclera. A diagram of the relevant anatomy can be seen in Figure 1. However, due to the importance of viewing pupillary response after a traumatic event, any device applied to the eye must leave the cornea visible to medical technicians. This leaves the anterior sclera adjacent to the cornea and under the eyelids as the best area for contact with a therapeutic device.

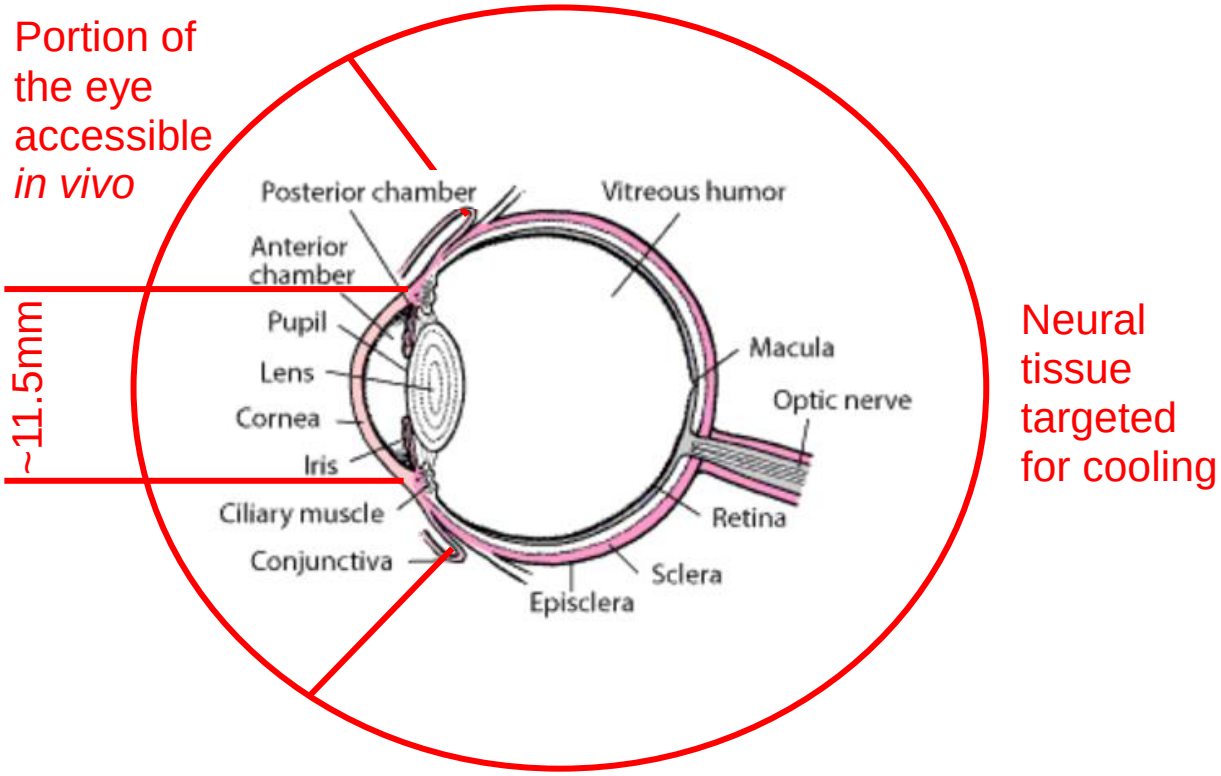

Figure 1. A cross-sectional view of the eye with relevant anatomy highlighted.

For an *in vivo* subject, the body provides a variety of natural heat sources (e.g. blood to the eye and surrounding tissues, eye musculature and adipose tissue). This means that any device

designed to cool the eye tissue must overcome the natural heat in the environment generated by the body.

1.6 Medical Rationale

Ischemia is a restriction of blood supply to tissues. It is typically caused by a narrowing or blockage of the artery supplying that tissue. If the tissue doesn't receive the adequate amount of blood, this can lead to cell death.

The eye cooler proposed here is motivated by the successful use of systemic hypothermia to minimize damage in several clinical research scenarios. A 1°C drop in body temperature decreases cerebral metabolic rate by about 6%–7%. Hypothermia reduces oxygen demand, preserves energy stores, and prevents lactate production and the development of acidosis by decreasing metabolic rate and stimulating neural glucose utilization. [1] This in turn reduces neural cell death during periods of low oxygen supply as experienced during ischemia. Therapeutic hypothermia (32–34°C) is strongly recommended by the 2010 American Heart Association guidelines for use in patients after out of hospital cardiac arrest. [2, 3] Additionally, after traumatic brain injury, decreasing body temperature (35–35.5°C) can reduce intracranial hypertension while maintaining sufficient cerebral perfusion pressure without cardiac dysfunction or oxygen debt. [4]

There is substantial evidence for benefit of localized hypothermia, specifically in the eye, in pre-clinical studies. In a rat model where ischemia was simulated by ligating the optic nerve with a suture, the rats treated with an icepack on the eye showed similar levels of healthy nuclei in the inner nuclear layer of the retina as a rat without ischemia. They concluded that, cooling the eye protects the retina from tissue damage in temporary retinal ischemia in the rat. [5] It has also been suggested that aberrant angiogenesis and exacerbated gliosis are factors implicated in the

increased thickness of the inner layers of the retina as result of hypoxia-ischemia, whereas treatment with hypothermia is able to prevent those alterations. [6] Hypothermic preconditioning (HPC), where a rat is exposed to either global or local hypothermia 24 hours before ischemia is induced, has also been shown to have a neuroprotective effect. Three days after ischemia, a significant decrease of glutamate uptake and glutamine synthetase activity was observed in ischemic retinas, whereas local HPC significantly prevented the effect of ischemia on these parameters. [7]

A vitrectomy is a surgical procedure done to remove all or some portion of the vitreous humor of the eye. When the humor is removed, this can damage the retinal cells in the posterior of the eye. Retinal cell health is often measured by it's a- and b-wave amplitudes which are portions of the neural response as measured by an electroretinogram. When vitrectomies were performed on rabbit models, the vitreous cavities were continuously irrigated at three different temperatures (8, 22, and 38°C). Seven days after the procedure, the recovery rate of a-wave amplitudes was significantly lower in the 38°C group than in the 8°C group, and that of b-wave amplitudes was significantly lower in the 38°C group than in either the 8°C or 22°C group. [8]

There are numerous disadvantages of systemic hypothermia (e.g., arrhythmias, rewarming abnormalities, increased infection risk). [9] Localized hypothermia avoids these undesirable effects while achieving the desired effect on target tissue. Uniquely, in the case of the eye, the target tissue is readily accessible, with no or minimal effect upon the other organs.

No commercial device exists to achieve targeted, regulated cooling of the eye, rendering ice packs or other bulky and non-regulated methods (e.g. chilled saline irrigation) the only current options. Invasive cooling via anterior chamber or vitreous catheters is impractical and hazardous in a field situation. In order to have the greatest chance at mitigating injury, the

device will need to be applied as soon as possible after injury, requiring it to be practical for application in austere environments.

Currently, there are two issued U.S. patents for targeted eye cooling. [10, 11] Both devices circulate cooled fluid through a unit that conforms to the shape of the eye, requiring substantial external instrumentation (reservoirs, heaters, pumps). One of these devices is shown in Figure 2. Because of the bulky and fragile external instrumentation, fluid-based systems are impractical for field use.

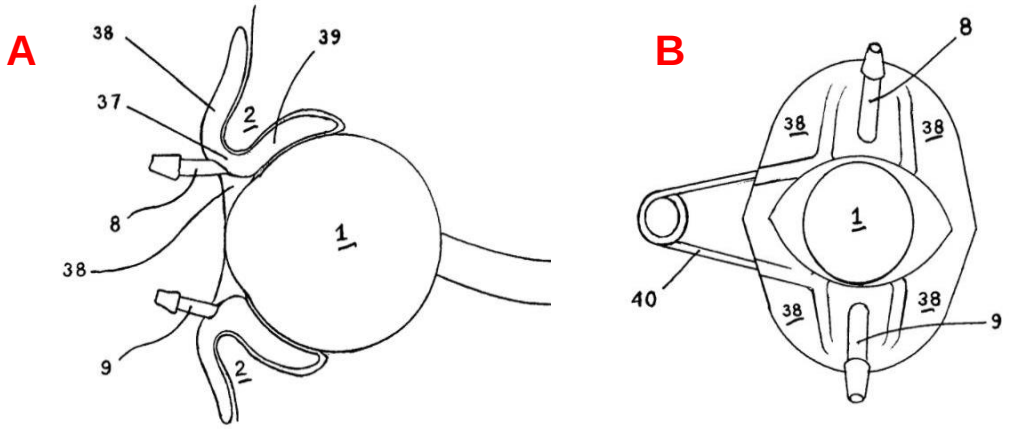

Figure 2. A patented design for cooling the eye with circulating liquid. A) A display of the side view of the thermal-regulating plural layer lid speculum where the part of the device is tucked under the eyelids with thermal-regulating shell-like posterior extension over the eye. Its anterior portion (38) cools the eyelids while its posterior portion (39) hooks under the lid to serve as a lid speculum (37) as well as a thermal-regulating apparatus for both the lid and the eye. B) Representation of the frontal view of the thermal-regulating lid speculum with underlying posterior shell extension and an inserting clamp attached. The frontal view of the thermal-regulating lid speculum with its anterior portion (38) visible and its posterior portion (39) functioning as a shell extension hidden from view and an inserting clamp (40) attached. [10]

1.7 Thesis Goals

In this thesis, a compact solid-state eye cooler is proposed to address the significant need for a portable, field-deployable, robust means of achieving and maintaining therapeutic cooling of eye

tissues following traumatic injury. In clinical use, the objective is to develop a device that will be applied as soon as possible after injury, during transport from the field, and while the patient is awaiting definitive therapy in the hospital. The rationale is well supported by the above-cited clinical studies of efficacy of hypothermia in stroke, and post-cardiac arrest. The eye can be treated by local hypothermia, avoiding the risks and slow implementation associated with systemic hypothermia.

2. Specific Aim 1) Design and fabricate a bench-test scleral contact eye cooler. The design should contact the sclera of the eye as accessible *in vivo* and with the view of the cornea unobstructed during cooling.

2.1 Design Requirements

The eye cooling ring (ECR) is the primary functional component of the entire system. The goal of the ECR is to cool the portion of the sclera that is accessible *in vivo*. The ECR forms a heat conduit between the eye tissue and heat pumps, described below. While the temperature of the ECR necessary to cool the eye tissue was unknown, it was assumed that an ECR temperature of 0°C would be the lowest acceptable temperature to avoid damage to the tissues in immediate contact with the ECR.

The ECR design was also constrained by multiple physiological requirements. First, the sclera must come in contact with the eye cooler and the eye cooler cannot damage the surrounding tissue (e.g. abrasion, puncture, contusion). Secondly, the view of the cornea must remain unobstructed to not impede neurological assessment of pupil diameter. For the bench-top system developed here, the presence of the eyelids was ignored.

2.2 Methods

2.2.1 Heat pump criteria

In order to design the ECR interface between the eye and heat pumps, the heat pumps had to first be identified. Peltier cells, also known as thermoelectric coolers (TECs), were chosen as the heat pumps due to their alignment with the goals of the system. TECs are advantageous when compared to liquid cooling due to their compact size, enabling the system to be portable.

A portable system is required for the field deployable application. Another advantage of the TECs is the ability to control the temperature gradient by modulating the amount of current through the cells. This will allow the system to be precisely regulated.

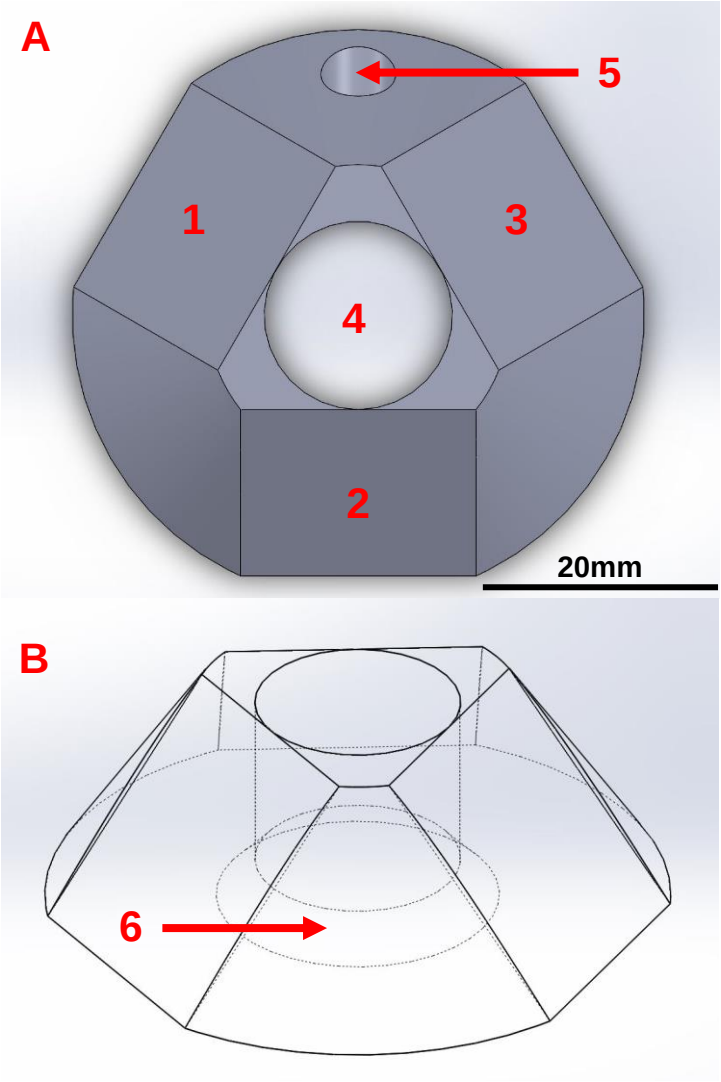

Figure 3. CAD renderings of the aluminum portion of the ECR. A) A top-down view of the ECR. (1-3) are the mounting locations for the TECs. The width of the TEC mounting area is 20mm. The diameter of the corneal viewing port (4) is 16mm to facilitate observation of corneal changes. A hole for the ECR support rod, which connects the ECR to the positioning apparatus, is also marked (5). B) The transparent oblique view of the aluminum portion of the ECR. The scleral contact ring (6) is the only portion of the ECR that comes in immediate contact with the eye.

To ensure that the ECR achieved the maximum rate of heat flow with minimal device size, multiple compact TECs must be able to fit around a porcine eye. The porcine cornea has a diameter of 16mm and cannot be obstructed by one of the TECs. As shown in Figure 3, three TECs with a width of 20mm can be positioned equidistant around the eye while minimizing the

distance between the TECs and the portion of the ECR in immediate contact with the eye, the scleral contact ring.

TECs create their thermal gradient using the thermoelectric effect. Thermoelectricity was first described by the Seebeck-Peltier Effect, which shows that when a circuit composed of two dissimilar metals is exposed to different temperatures at the junction, it will generate electricity. Inversely, William Thomson later discovered that heat is absorbed or produced through an electric current runs through a circuit composed of a single material that has a temperature difference along its length. Additionally, he showed that the heat difference is proportional to the electric current and the temperature gradient. When current passes through the TEC, heat flows from one side to the other. This occurs because the electrons in the material are being driven from the hotter side to the colder side.

While staying within the size constraints, a TEC with the largest rate of heat energy movement was chosen in order to maximize the rate of heat flow from the eye. The TECs used in this system were potted TE-31-1.4-1.15 from TE Technology Inc. (Traverse City, MI). They were chosen because they measure 20mm by 20mm and have a high maximum power rating for their size, meaning that the rate of heat transfer will be high. The specifications for the TECs shown in Figure 4 can be seen in Table I.

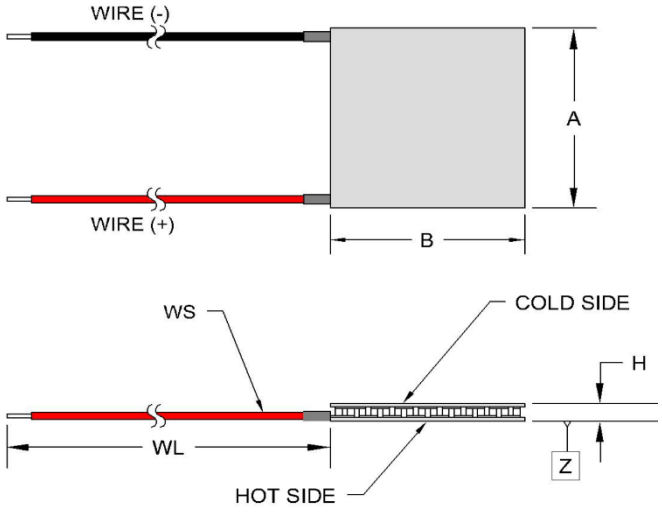

Figure 4. The TECs used in the ECR. The widths (A, B) are 20mm, the height (H) is 3.6mm, the wire size (WS) is 0.34mm2, and the wire length (WL) is 120mm.

Vmax (V)	3.8
Imax (A)	7.9
Qmax (W)	18.6
DTmax (°C)	69

Table I. The specifications for the TECs used in the system. Given values are for a hot side temperature of 27°C, which matched the environment during the experiments. Vmax, Imax, and Qmax are the maximum voltage, current, and power ratings for each TEC, respectively. DTmax is the maximum temperature differential the TEC is able to provide.

The TECs were powered by a Precision Variable DC Power Supply Digital made by YescomUSA (City of Industry, CA), the specifications of which are described in Table II. The circuit diagram for the TECs wired in parallel is shown in Figure 5.

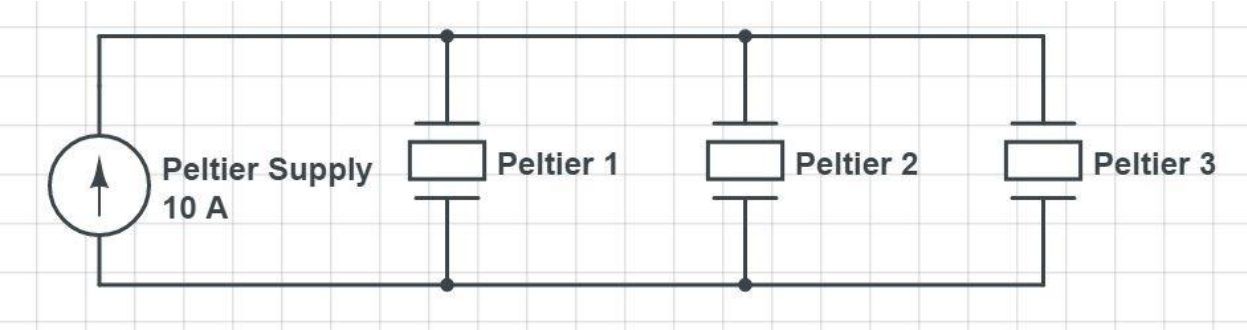

Figure 5. Circuit diagram of the power supply to the TECs. They are placed in parallel so each TEC receives the same amount of current. At ten amps, the heat sinks were unable to effectively transfer the heat to the air circulated through them, and so this was established as the upper current limit for the system.

Output voltage	DC 0-30V Continuous adjustable
Output current	DC 0-10A Continuous adjustable
Display resolution	Voltage: 0.1V, Current: 0.1A
Display precision	±1% ±1digit
Voltage stabilization	0.05% +1mV
Current stabilization	0.1% +10mA

Table II. The specifications for the power supply used to power the TECs of the system.

2.2.2 ECR assembly

Once the TECs were selected, the ECR could then be designed. The ECR was designed to minimize the thermal impedance between the TECs and the ring that comes in contact with the sclera. This was accomplished with a design that kept the TECs as close to the eye as possible

while maximizing the cross-sectional area between the TECs and the target. Additionally, the design ensured that there were no “pinch points” that would impede heat flow between the TEC and the scleral ring. A computer-aided design (CAD) representation of the ECR is shown in Figure 3.

The TECs were attached to the eye cooler with a thermally conductive epoxy (50-3100) from Epoxies (Cranston, RI) to maximize heat transfer. This epoxy has a thermal conductivity of 2.16 watts per meter-Kelvin.

The ECR was machined from aluminum to facilitate efficient thermal transfer from the TECs to the eye. While other metals such as copper have greater thermal conductivity as shown in Table III, aluminum is advantageous because it oxidizes slowly, is easier to machine, and is lighter which makes it more viable for deployment in the field.

Material	**Thermal Conductivity (W/m-K)**
Stainless Steel	<20
Titanium	22.3
Iron	80.2
Aluminum	237
Copper	402

Table III. Thermal conductivity of materials considered for the ECR. [13]

Once the maximum temperature difference for the TEC is reached (DTmax), the TEC cannot further cool the eye cooler ring. To facilitate the transfer of heat to the environment, heat sinks were added to the hot side of each of the TECs. This increases the surface area of the hot side, allowing more efficient conduction of heat to the environment. The heat sinks used in this

system were 1.000" wide extruded aluminum heatsinks acquired from HeatsinkUSA (Greenville, MI) and the specifications are detailed in Table IV.

Alloy	6063-T6
Width	1.000”
Fin Height	0.366”
Base Height	0.098”
Thermal Resistance (°C/W/3”)	~14.00

Table IV. The specifications for the heatsinks used in the system. Thermal resistance is expressed as temperature rise per unit rate of heat dissipation for a three-inch portion of the heat sink. The heatsinks were designed in imperial units and the TECs in metric, so the 1” (24mm) heatsinks extend beyond the edges of the 20mm TECs.

Initial testing showed heat recirculation between the heat sinks and the exposed faces of the ECR. At first, the ECR contact ring was cool to the touch, but then it plateaued and began warming. It was determined that the heat in the air coming from the heat sinks was being reabsorbed by the ECR. To mitigate this, insulating foam (Great Stuff Insulating Foam Sealant) made by Dow Building Solutions (Midland, MI) was added to the exposed portions of the ECR that were not contacted by the TECs or the eye. The ECR before and after insulation was added can be seen in Figure 6. Additionally, a ⅛” thick sheet of neoprene was attached with silicone sealant to the top and bottom surfaces of the ECR. These steps ensured that heat only entered the ECR system though the scleral contact ring.

Finally, an airflow system was implemented to increase the flow of air over the heat sinks to remove heat from the immediate environment of the eye. As a final step, tubes attached to a vacuum (Vacmaster VH105) made by Vacmaster (Greenville, SC), were positioned over each heat sink, adding convective heat transfer to move heat from the fins of the sinks. The warm air was then pumped twenty feet away from the experimental setup to avoid creating a closed system.

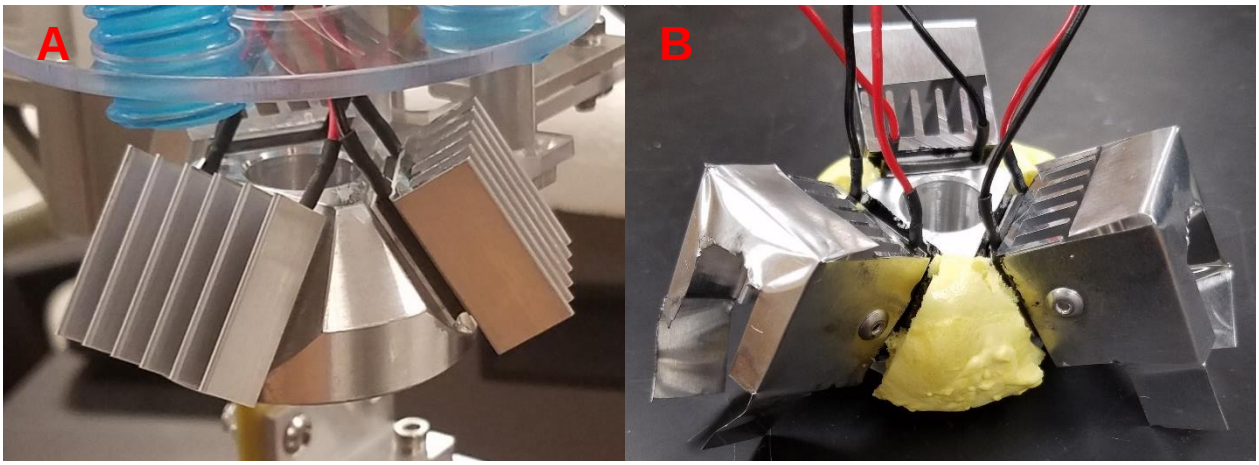

Figure 6. The ECR before and after the addition of insulation. A) The ECR prior to insulation. The exposed portion between the two TECs was absorbing heat from the room air, which was in turn being warmed by the heat sinks, resulting in heat circulation within the system instead of the desired heat removal. B) After insulating foam was added to the exposed portions.

2.2.3 ECR temperature

To monitor the temperature of the ECR portion in contact with the sclera, a thermistor was attached to the ECR with thermal epoxy near the scleral ring portion and then covered with the neoprene and sealed with silicon sealant. The position of this thermistor can be seen in Figure 7. How this thermistor measures temperature change is described more fully in Aim 2.

Figure 7. A view of the inferior side of the ECR. The black liquid is the thermally conductive epoxy. This ensured that heat was efficiently transmitted to the ECR thermistor (shown in the red circle). This portion was later insulated with neoprene.

2.3 Results

The primary focus of Aim 1 was to design a cooling system that would contact the anterior sclera while maintaining the ability to visually assess the cornea. The scleral ring has a surface area of 259.45 mm^2, which will allow it to cool a large portion of the sclera that will be accessible on a living patient. A CAD mockup of the final design can be seen in Figure 8.The main design goal was to reach 0°C at the scleral contact ring of the ECR. To test this, the ECR was suspended in air at room temperature (22°C), the vacuum was turned on, and then one minute into data acquisition, the power supply to the TECs was turned to different ampere settings.

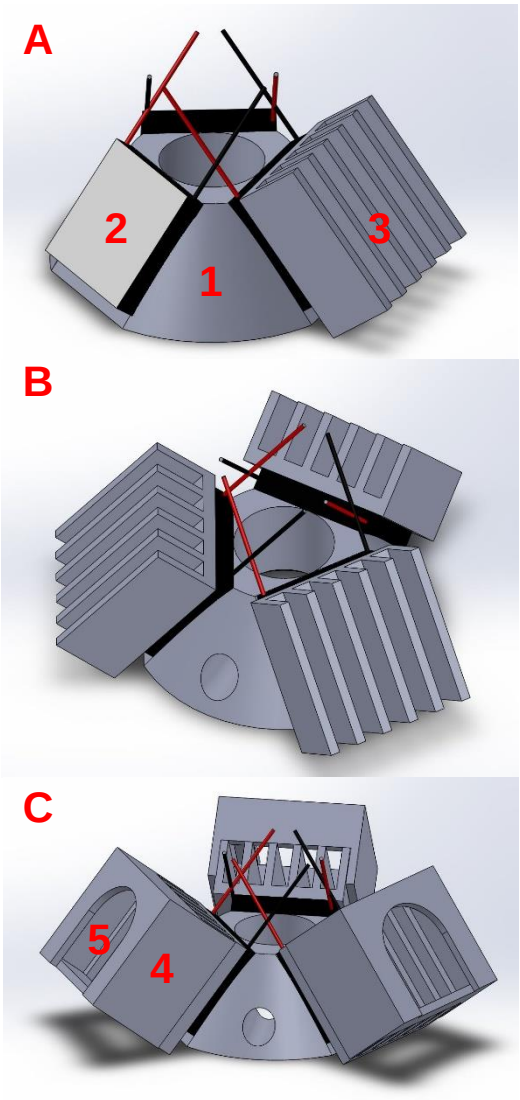

Figure 8. CAD renderings of the ECR assembly. A) The aluminum portion of the ECR (1), an attached TEC (2), and one of the heatsinks (3). Bonding between the ECR, TECs, and heat sinks was accomplished with thermally conductive epoxy.
B) A rendering with all of the heatsinks attached.
C) A rendering with the airflow guides (4) and vacuum attachment points (5) attached to the system. The airflow guides ensure that the air is being drawn along the heatsink fins and the vacuum attachment points affix the vacuum tubes during the experiment.

As shown in Figure 9, when turned to the maximum power setting, the ECR was able to reach temperatures of just above 0°C. The system also demonstrated that the amount of cooling could be regulated by the adjusting the current flow to the TECs.

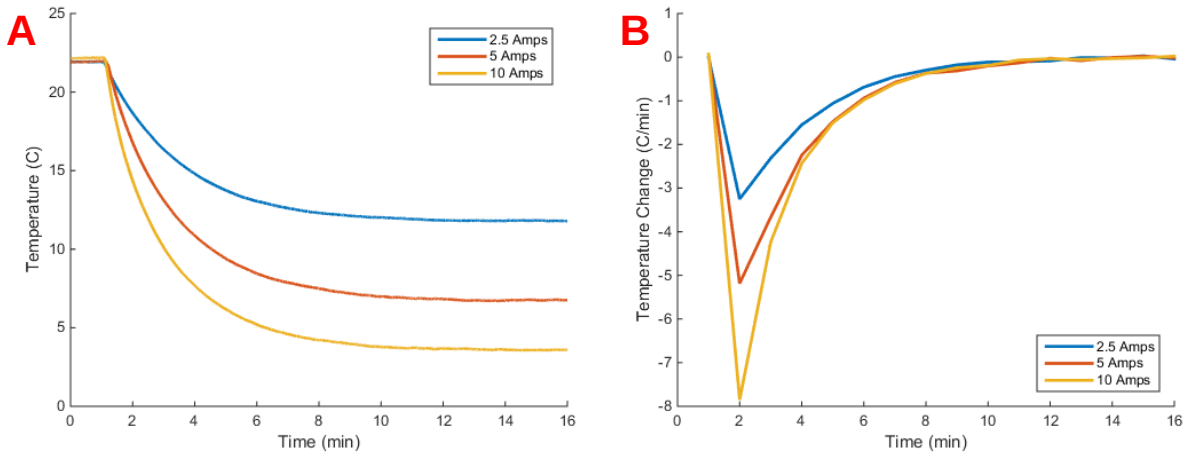

Figure 9. A) The temperature of the ECR vs. time for three TEC currents. The ECR reaches steady state after approximately 10 minutes. B) The rate of temperature change of the ECR. The rate of change is most dramatic in the first minute after the ECR is powered. The system is considered to be as steady-state when the temperature changes are less than 0.1°C/min.

2.4 Discussion

Designing an ECR to contact the sclera, support the attachment of multiple TECs, and maintain visual analysis of the cornea was shown to be possible. Additionally, the scleral contact ring of the ECR was able to reach the target temperature. It was assumed that this temperature on the anterior portion of the sclera would translate to therapeutic temperatures at the posterior tissue of the eye.

3. Specific Aim 2) Design and fabricate a thermal sensor array that will allow measurement of the ocular tissue temperatures at up to eight locations simultaneously. The temperature of each sensor should be sampled at a minimum frequency of 1 Hz, and the data digitized and transferred to a computer for real-time monitoring and off-line analysis.

3.1 Design Requirements

3.1.1 Measurement locations

To monitor temperature changes throughout the eye, locations for thermal measurement needed to be determined. Eight locations were initially chosen to observe the temperature change as shown in Figure 10. However, for this proof of concept work, three locations were used: anterior (near the cornea), posterior (near the optic nerve), and the equator (equidistant between the anterior and posterior locations). These locations provide an overall view of thermal change across the eye, especially for the retina and optic nerve, which are the main targets for therapeutic cooling. These locations are also valuable for validating a thermal model of the eye.

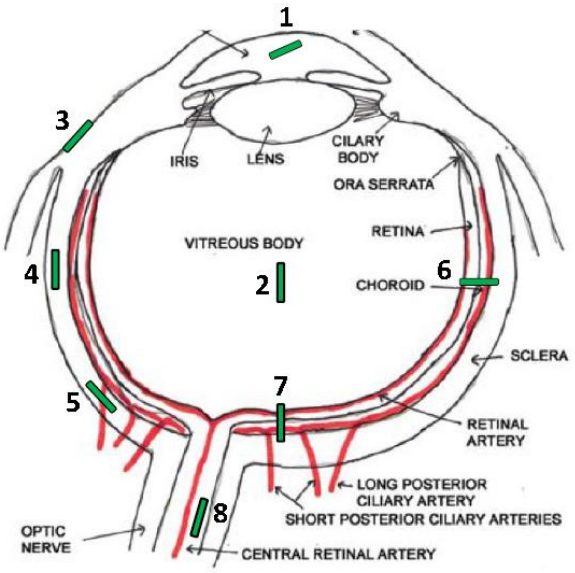

Figure 10. Temperature sensors (thermistors) can be surgically implanted at the eight locations indicated (green bars represent sensors and are approximately to scale), as follows: 1) anterior chamber, 2) vitreous, 3-5) within scleral flaps at three locations, with position 3 under the scleral ring of the eye cooler, 6-7) trans-scleral insertion to sample retinal temperature, 8) within optic nerve stump.

3.1.2 Transducer requirements

The type of thermal transducer needed to be able to represent the temperature of the eye tissue without being affected by the adjacent environment (e.g. the vitreous humor, the oil bath). Scleral thickness for porcine eyes is 1.12 ± 0.23mm near the corneal scleral limbus, 0.86 ± 0.18mm near the equator and optic nerve head [12]. Therefore, the transducer must have a diameter less than 0.8mm.

The thermal transducers needed to be durable enough to be exposed to temperatures between 0°C and 37°C and take five seconds or less to respond to a 10°C change in temperature. The transducers must have leads long enough to span the two-foot distance between the oil bath and the circuit board while being flexible enough to be maneuvered around the ECR positioning system and edges of the oil bath.

3.1.3 Data acquisition requirements

A circuit was required for capturing the information coming from each thermal transducer and converting it into a voltage that could be passed to a data acquisition device (DAQ) and digitized for off-line analysis. As described in section 3.2.2, the circuit was designed to convert a 1°C change into a 200mV difference measured by the DAQ. The chosen DAQ would therefore need to be able to detect changes on the mV scale to be able to accurately capture the voltage changes from the circuit. To capture a 0.2V per degree change over 37°C, the DAQ will need to have an input range of 7.4V. To detect temperature change, the DAQ also needs a resolution of at least 1 bit per 20mV (equivalent to ≤20mV/bit). Temperature changes in the eye were assumed to occur rather slowly, so the DAQ needed to be able to capture data at a sampling rate of at least 1Hz.

3.2 Methods

3.2.1 Temperature Probe

The thermistors chosen for this study were NTC MA100s, made by Amphenol Advanced Sensors (Wallingford, CT) as seen in Figure 11. Thermistors are passive electrical resistors that change their impedance as a function of temperature. These thermistors are 5mm long and have a diameter of 0.762mm which is sufficiently small enough to fit within the scleral wall. The native leads were not long enough or thick enough to interface with the circuit on the breadboard, so additional wire was soldered onto the thermistor leads to compensate. Additional relevant specifications of these probes can be seen in Table V.

Figure 11. Example of the thermistors used in this study, with a U.S. quarter dollar coin for scale. Thermistor dimensions are provided in the text.

Resistance in Ohms @ 25°C	10k
Resistance Tolerance	±0.1°C
Operating Temperature	0°C - 50°C
Thermal Response Time in Still Water (63% Response)	2.0 seconds

Table V. The specifications of the thermistors used for monitoring the temperature change in the porcine eye.

Another thermistor that was considered for this study was the Micro-Betachip (MCD) thermistor made by TE Connectivity (Schaffhausen, Switzerland). These thermistors are smaller than the ones ultimately used, with a diameter of 0.5mm and a length of 3.3mm. However, they were twice the price of the MA100s and the MA100s were already working well in the preliminary tests, and so the MA100s were used for this entire proof-of-concept study.

3.2.2 Signal conditioning

Resistances of the thermistors needed to be converted into degrees for analysis. To accomplish this, the circuit shown in Figure 12 was built. This circuit accomplishes four main tasks: 1) Converts change in thermistor resistance to a change in voltage, 2) Linearizes the relationship between temperature and voltage, 3) Sets desired sensitivity (200mV/°C), and 4) Sets voltage endpoints (0V at 37°C and 7.4V at 0°C). Each operation is discussed below.

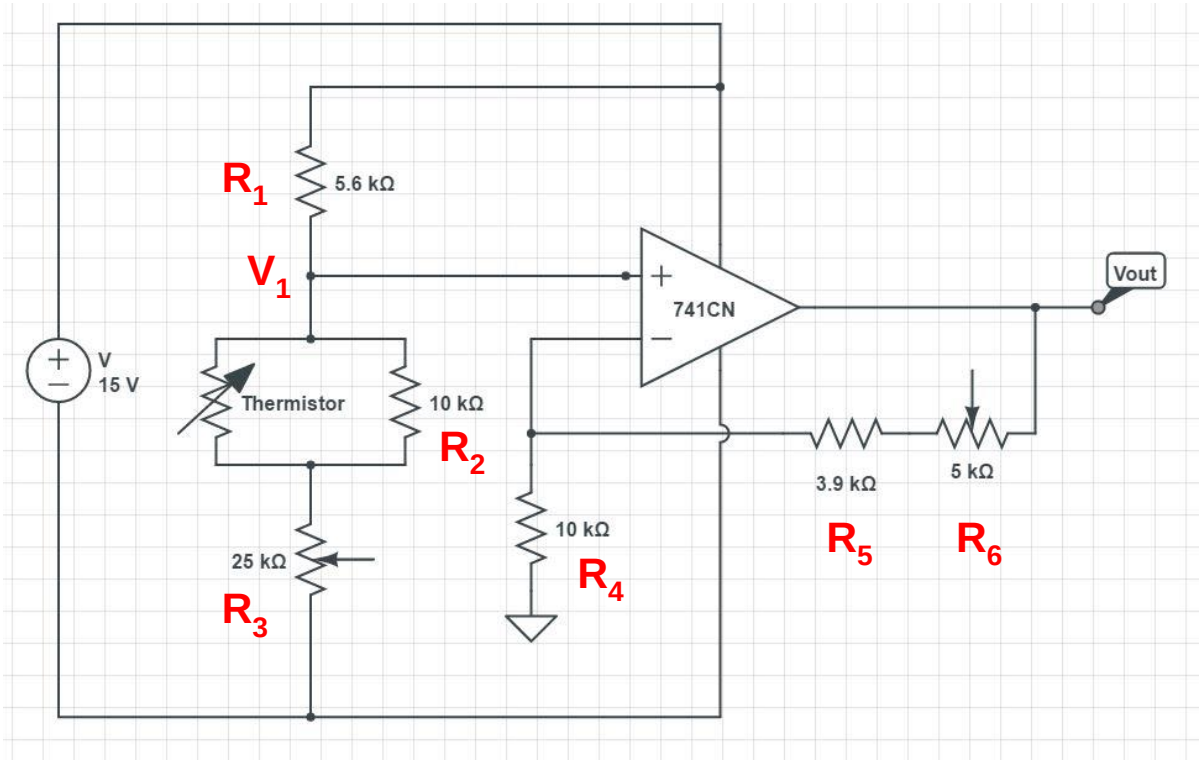

Figure 12. Circuit diagram for converting thermistor temperature to voltage. The 25kΩ potentiometer (R3) adjusts the DC offset. The 5kΩ potentiometer (R6) adjusts the gain of the channel to match 200mV/°C. This diagram was generated with the online software made by CircuitLab Inc. (Sunnyvale, CA).

The thermistors in this study have a resistance of approximately 12.5kΩ at room temperature (22°C). With a 10kΩ resistor (R_2) in parallel with the thermistor, this gives this portion of the circuit an equivalent resistance of ~5.6kΩ at room temperature as shown in Equation 1.

$$\frac{1}{12{,}500} + \frac{1}{10{,}000} = 0.0001769;\ 0.1769^{-1} = 5{,}652 \qquad \text{(EQ 1)}$$

Next, a voltage divider is created by putting a resistor (R_1) of similar value in series with the thermistor portion and connecting the middle of those resistors to one of the inputs of the operational amplifier. A 25kΩ resistor (R_3) placed in series with the thermistor portion adjusts the DC offset and was used to zero the voltage output of each channel at the target temperature of 37°C. The voltage into the noninverting input of the operational amplifier was calculated using Equation 2.

$$V_1 = \frac{\left(\frac{R_T R_2}{R_T + R_2}\right) + R_3}{R_1 + \left(\frac{R_T R_2}{R_T + R_2}\right) + R_3} * V \qquad \text{(EQ 2)}$$

This circuit is designed to translate a 1°C change into a 200mV change. As part of the feedback resistance used for the gain, a potentiometer was incorporated for fine-tuning. As shown in Equation 3, a gain of 1.56 was required to bring the unamplified voltage from 128mV/°C to the 200mV goal.

$$\frac{V_o}{V_i} = \frac{(R_5 + R_6) + R_4}{R_4};\ \frac{200}{128} = \frac{(5.6k) + 10k}{10k} = 1.56 \qquad \text{(EQ 3)}$$

To compensate for the variability between individual thermistors, the 5kΩ potentiometer (R_6) was placed in series with the 3.9kΩ resistor (R_5) to create the feedback resistance. With

operational amplifiers, the feedback resistors need to be placed in voltage divider with a gain resistor and connected to the other input of the amplifier. The gain resistor used here was a 10kΩ resistor (R_4). This made it possible to adjust the gain from 1.39 to 1.89. The resistance of thermistors decreases as temperature increases, so the circuit was constructed to output 7.4V at 0°C and 0V at 37°C once the potentiometers were properly adjusted.

3.2.3 Calibration

There were slight differences between thermistor responses over the same temperatures. For each distinct temperature measurement channel, the circuit shown in Figure 12 was built and tuned to negate these differences. Calibration was done by placing the thermistors in 37°C water and then adjusting the DC offset potentiometer until the voltage from each channel was at 0V. With the circuit providing a gain of 0.2V/°C, when the thermistors were at body temperature (37°C), there should be 7.4V difference from freezing (0°C). Then, the thermistors were transferred to an ice water bath and the gain potentiometer was adjusted until each channel was at 7.4V. The temperature of the baths was measured by a Fluke 52-2 digital thermometer made by Fluke (Everett, WA). This thermometer has an accuracy of ± 0.05% (of the temperature being measured) + 0.3°C.

3.2.4 Data Acquisition

Voltages from each channel were captured by a Dataq DI-2108 data acquisition system, made by DataQ (Akron, OH) and then analyzed in MATLAB. The data was sampled at a rate of 100Hz at a 16-bit resolution. A 16-bit resolution on signals between -10V and +10V means that are 3276 bits per degree and the DAQ can detect voltage changes of 0.3mV. This resolution exceeds the requirements. The signals were not filtered.

3.3 Results

The four channels shown in Figure 13 have a mean voltage of -0.033 V and a standard deviation of 0.116 V for the first 30 seconds of the test while they are submerged in the warm oil. At 32 seconds, they were removed from the oil and submerged in the ice bath. After reaching steady state (~7 seconds), the channels had a mean voltage of 7.411 V with a standard deviation of 0.037 V. Converted to degrees, the system has a standard deviation of 1.16°C when at 37°C and a standard deviation of 0.37°C when at ~0°C.

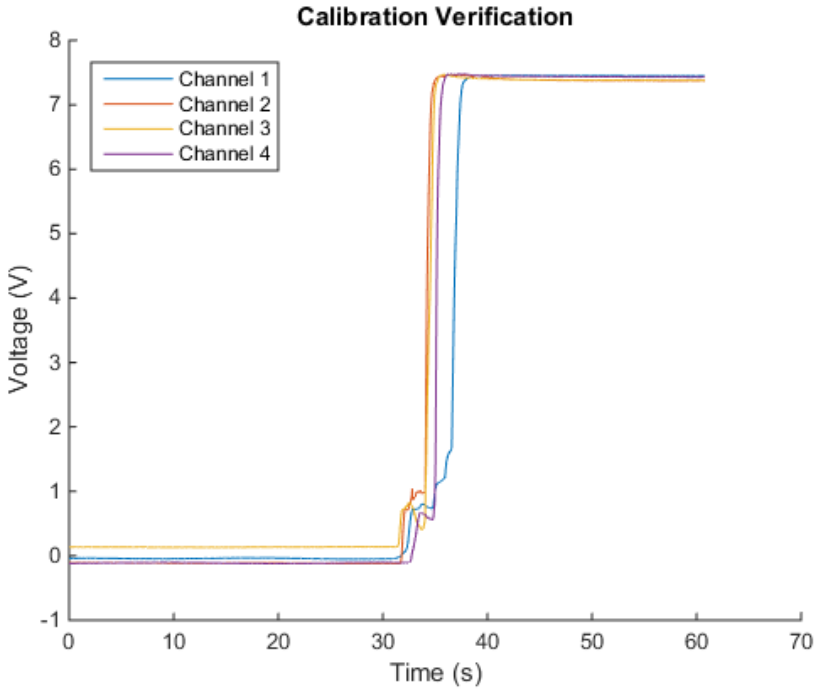

Figure 13. The thermistors were initially submerged in a water bath at 37°C for approximately one minute before data acquisition began at t=0 in the plot. At t=30 seconds, the thermistors were placed in an ice bath at approximately 0oC. The deflections in the curves occurring at t=30-35 seconds is due to movement of the thermistors from one bath to the other through room air.

In order to test the linearity of the system, six thermistors were taped to the temperature probe of the Fluke thermometer and placed in warm water. Ice was gradually added and the temperature of the Fluke was recorded to determine accuracy over the entire range of temperatures that the eye would be exposed to. This test was repeated two days later to ensure confidence in the results and this is shown in Figure 14. The first trial had a R^2 value of 0.9886 and the second had a R^2 value of 0.9982. This demonstrates the high linearity of the system.

The overall slope on the first calibration day was 177mV/°C and it was 180mV/°C on the second day. The y-intercept for the first calibration day was 7.5V and for the second day it was 7.6V.

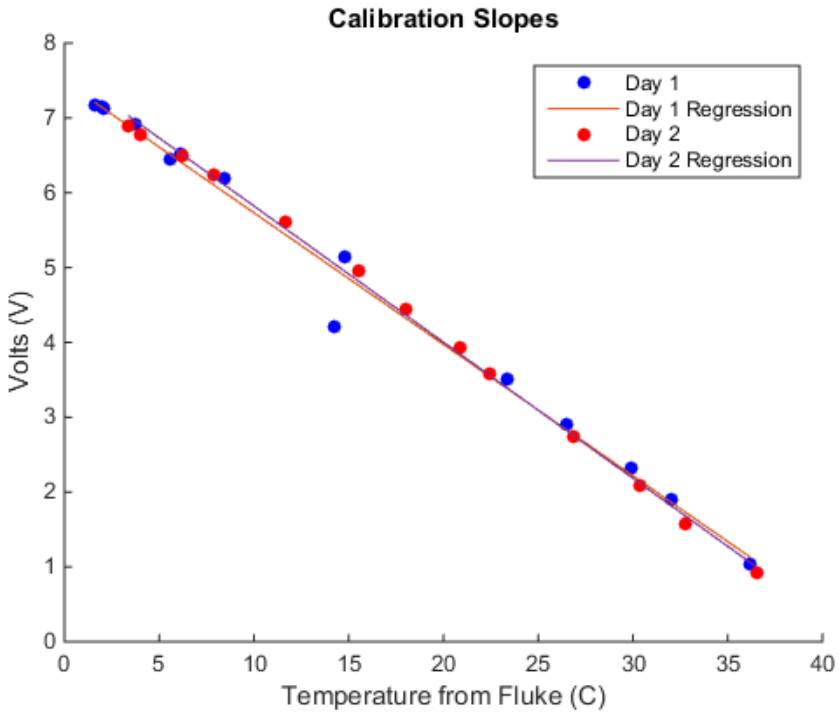

Figure 14. The channels displayed very similar behavior between days, demonstrating high consistency.

3.4 Discussion

There are a variety of thermal transducers which each have unique strengths and weaknesses. Infrared sensors can indirectly read the temperature of surfaces but were determined to not be accurate enough for this application. Thermocouples are inexpensive, but too bulky to be implanted in the scleral wall. Resistance temperature detectors (RTDs) are more accurate than thermocouples, but are still too large to be implanted in the scleral wall and are fragile. Therefore, thermistors were determined to be the proper thermal transducer for this study.

The thermistors used in this study are small enough to be amenable to all implant locations shown in Figure 10. They also have a response time short enough to measure the temperature changes present in this study. The circuit could be tuned to compensate for the manufacturing variability between thermistors and is stable enough to not require calibration between experiments. Additionally, it could digitize eight channels of temperature data, making off-line analysis possible.

The thermistors used in the calibration analysis don't align better with the 200mV/°C because of issues with the calibration. The temperature baths were not completely at the 0°C and 37°C targets, which meant that the thermistors were calibrated slightly off of the true values. For the thermistors used in the eye trials, the thermistors were tuned to the true temperature of the baths.

High precision temperature measurement is difficult. Even quality commercial digital thermometers such as the Fluke used during calibration of the described system have a precision of ±1 degree centigrade. The tolerance of the digital thermometer makes tuning the thermistors challenging because the possibility exists that they are being calibrated to a full degree centigrade from the true temperature of the environment. With the temperature measurement system exhibiting a standard deviation between 0.37°C and 1.16°C, the system is accurate enough to capture the overall temperature changes required to evaluate the concept. Greater precision can be attained in the future by using thermistors with tighter tolerances, and with more careful tuning and calibration of the system.

4. Specific Aim 3) Develop a protocol for implanting thermal sensors into an enucleated porcine eye at clinically relevant locations

4.1 Requirements

The first portion of developing the instrumented eye preparation procedure is establishing the surgical protocol. This involves taking the eye as received from the butcher and securing the implanted thermistors in the eye at the predetermined locations. After the eye is implanted with the thermistors, it must be positioned properly in a warm oil bath and then have the ECR brought in contact with the anterior portion of the eye.

The thermistors must be implanted while minimizing tissue disruption, avoiding leaking vitreous, and maintaining the interocular pressure (IOP). They also should not interfere with the eye support ring, and not obstruct the pupil or the ECR contact area. The protocol also needs to result in stable and repeatable insertion of the thermistors at the required locations.

4.2 Methods

The porcine eyes are sourced from a local butcher (Butcher and Larder, Chicago, IL). They are removed from the skull by the butcher, using a ham knife, leaving most of the adipose tissue surrounding the eye intact. After extraction, the eyes were transported to UIC (~30 minutes) and placed individually in plastic bags filled with tap water and frozen to preserve the tissue until needed. Upon thawing by running the eyes in the bag under warm tap water, the excess adipose tissue needs to be removed and discarded without damaging the sclera or the optic nerve. This was accomplished using toothed forceps and dissection scissors. The difference can be seen in Figure 15.

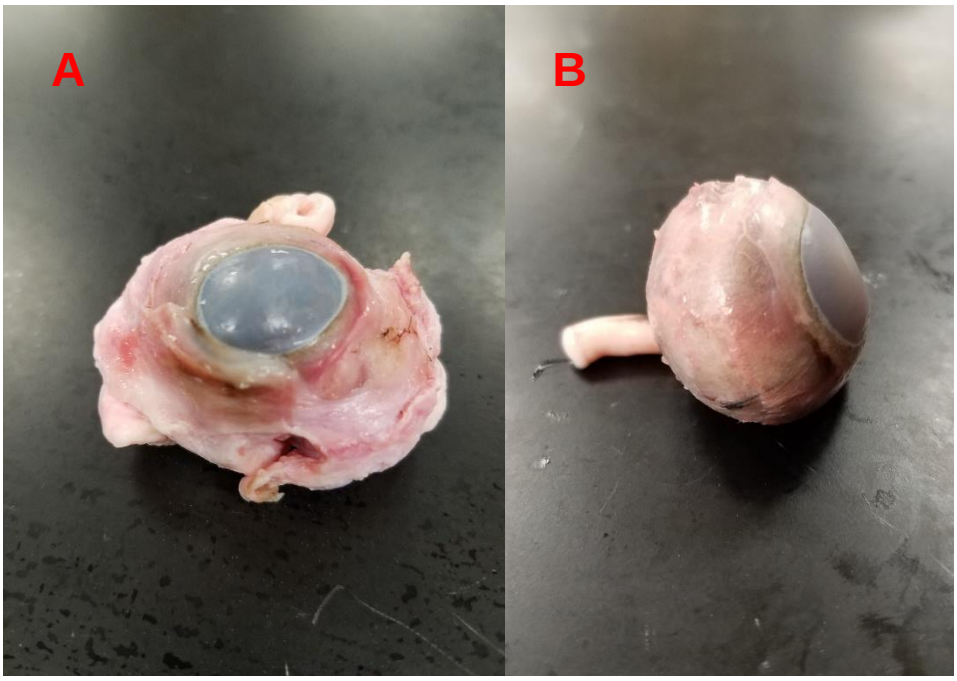

Figure 15. A) A porcine eye with surrounding tissue intact. B) The eye with the excess tissue removed and ready for thermistor implantation.

4.2.1 Surgical preparation

Thermistor implantation is challenging without means to hold the eye stable. To address this, an eye holding ring was designed and fabricated from aluminum as seen in Figure 16. Then a support was built to provide a steady attachment point for the eye holding ring and minimize movement of the eye during the implantation surgery. The eye was glued to the holding ring with 2-3 drops of cyanoacrylate. The incisions for the thermistor implantation could then be made with greater control.

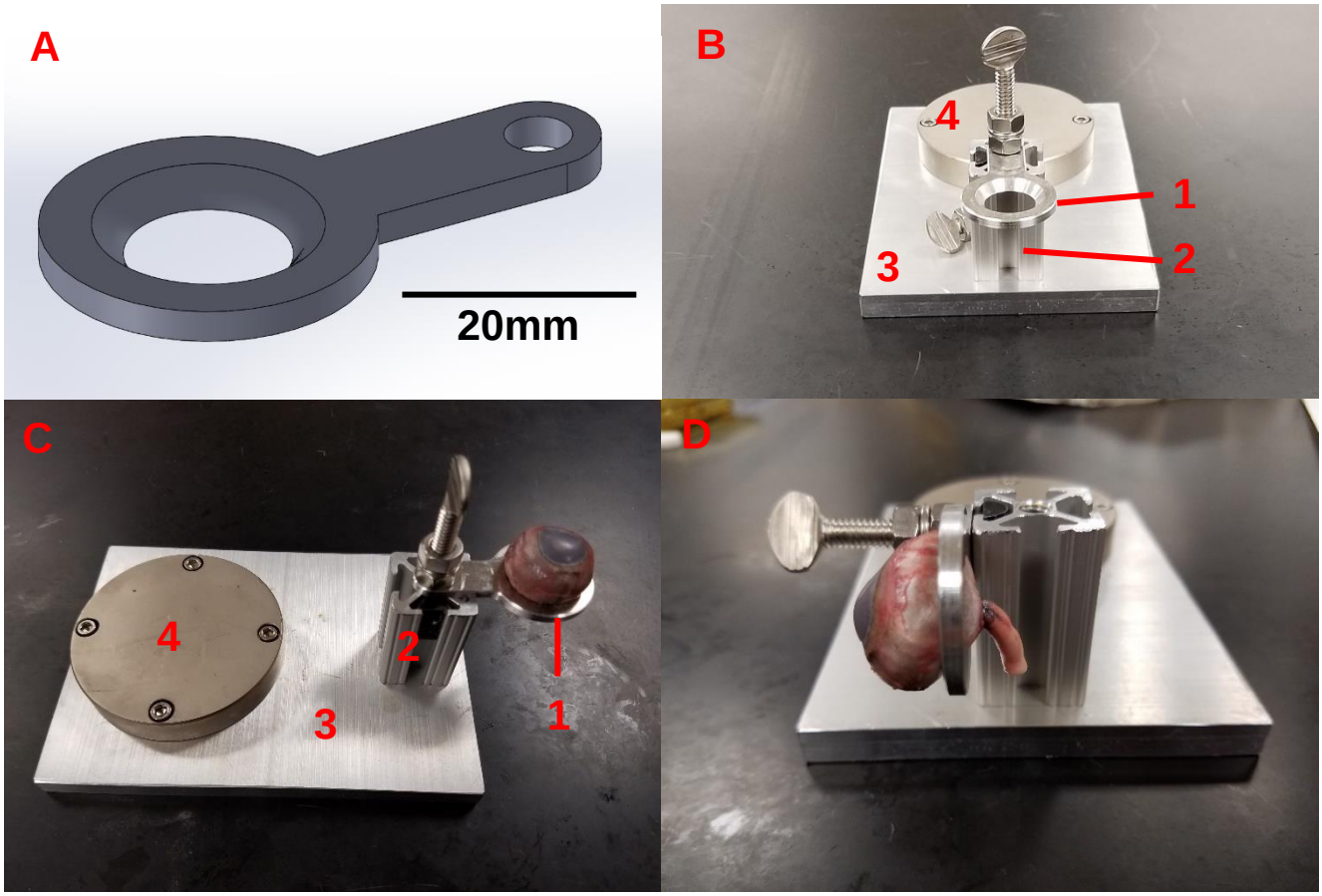

Figure 16. The surgical eye manipulator. Eyes were glued to the holding ring by placing four drops of glue equidistant on the holding ring surface in contact with the eye and then placing the eye in the holding ring. The glue used was super glue (cyanoacrylate) made by Pacer Technology (Rancho Cucamonga, CA). The eye could then could be positioned in the transverse and sagittal plane to aid thermistor implantation. Post procedure, the eye was removed from the holding ring and the holding ring was placed in an acetone bath overnight to remove residual glue. A) A CAD representation of the eye holding ring. The anterior diameter of the portion of the ring that contacts the eye is 22mm and the posterior diameter is 16mm. The screw hole is 6.5mm in diameter to facilitate the use of a #10-24 screw. B) A frontal view of the surgical eye holder. It consists of the eye holding ring (1), the post for connecting the eye holding ring to the base (2), the base of the holder (3), and a weight for ease of use (4). C) A side view of the surgical eye holder with an eye ready for thermistor implantation. D) Another frontal view of the surgical eye holder but with the eye secured in the vertical plane. This was useful for implanting thermistors on the equator of the eye.

4.2.2 Thermistor placement

An instrumented eye with eight thermistors as shown in Figure 10 was determined to be excessive for this proof of concept study. While a method of implanting all eight thermistors was determined, the overall response of the eye could be adequately determined with three

thermistors. The first thermistor was placed anteriorly, as close to the cornea as possible. This measured the temperature of the tissue directly in contact with the ECR to determine if it was possible to bring the posterior of the eye to therapeutic temperatures while not reducing the anterior tissue to lower than 2°C. Another thermistor was embedded along the equator of the eye, providing information about the middle tissues. A diagram of this method of thermistor placement and how it interacts with the overall system is shown in Figure 17.

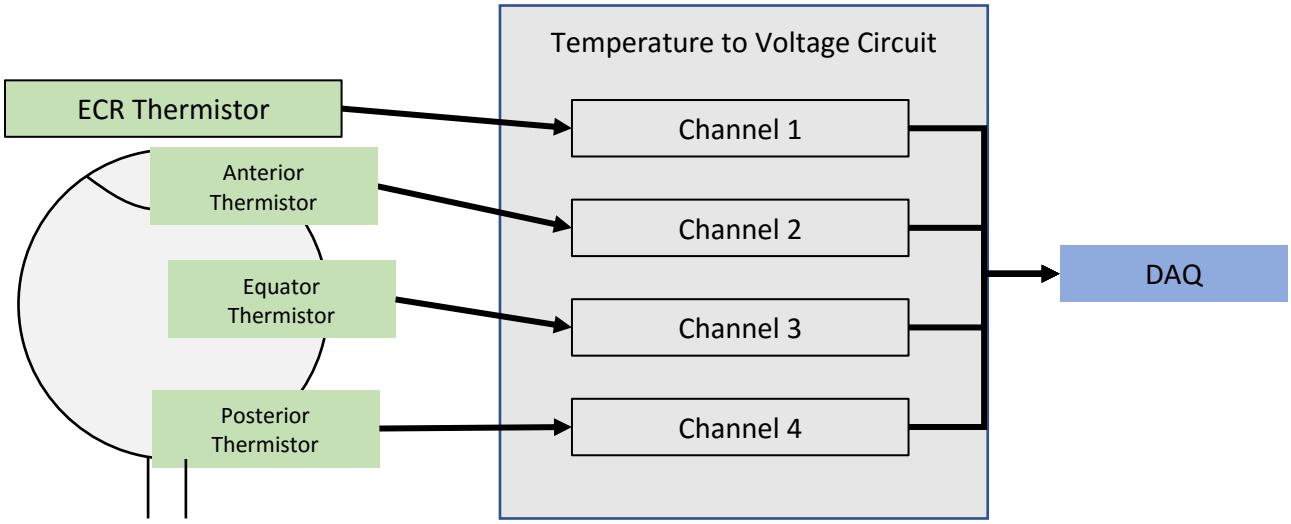

Figure 17. The ECR thermistors and the thermistors implanted in the eye each connect to a single channel on the circuit. These channels are then connected to a DAQ to capture and store the data. The three representative channels are shown.

A thermistor implant location tool as shown in Figure 18 was designed and built to determine exactly where the equator thermistor should be placed. For the proof of concept work presented here, this level of precision was deemed unnecessary but will be useful in future work.

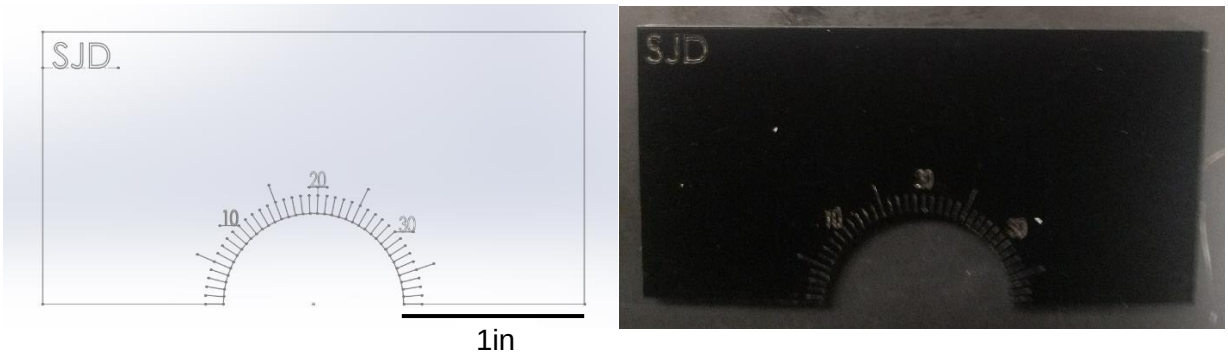

Figure 18. The thermistor implant location tool. A) CAD rendering of the thermistor implant location tool designed to assist with precise placement of the thermistors on the equator of the eye. B) The tool on a workstation.

The last thermistor was placed within the sclera near the optic nerve, determining if it was possible to reach the posterior pole of the eye with therapeutic cooling. These locations are diagramed in Figure 19.

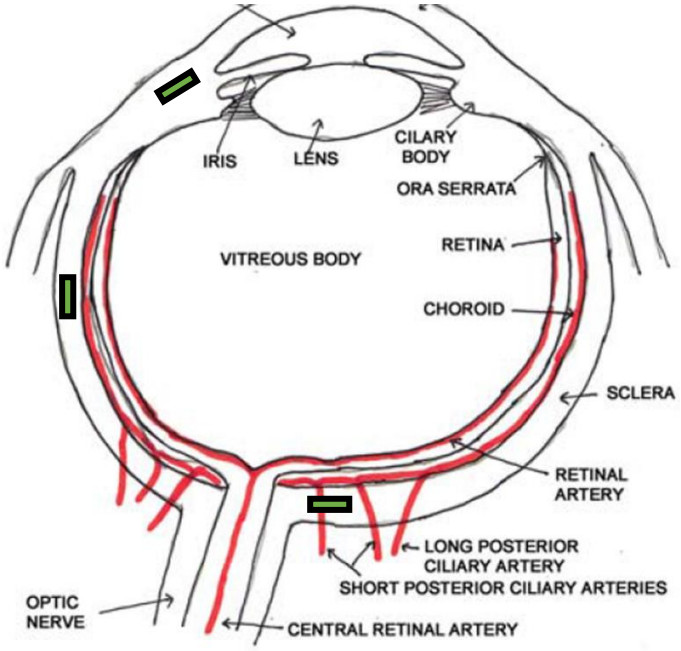

Figure 19. The target locations for the thermistors. One is placed anteriorly, directly under the scleral ring of the ECR to measure the temperature change of the tissue in contact with the ECR. A second thermistor was located within the sclera near the equator of the eye (half way from the corneal pole to the posterior pole along the outside of the eye). A third thermistor was also located within the sclera near the posterior pole of the eye, just temporal to the optic nerve origin. The equator and posterior thermistors are monitoring tissues that are thermally closer to the oil bath than the target retinal tissue, and probably underestimate the amount of cooling experienced by the retina. Figure adapted from [14].

The thermistors were implanted within the sclera by first creating a pocket within the sclera using a spear point scalpel (1.25 lightning blade micro spearpoint) made by Surgical Specialties (Wheeling, IL). Once the pocket was approximately 5mm deep, the thermistor was inserted into

the pocket and secured with a 4.0 nylon suture. The suture ensured that the thermistor stayed in the pocket as well as surrounding the lead end of the thermistor with scleral tissue, minimizing the impact of the warm oil on the temperature reading. This placement from an example trial is shown in Figure 20.

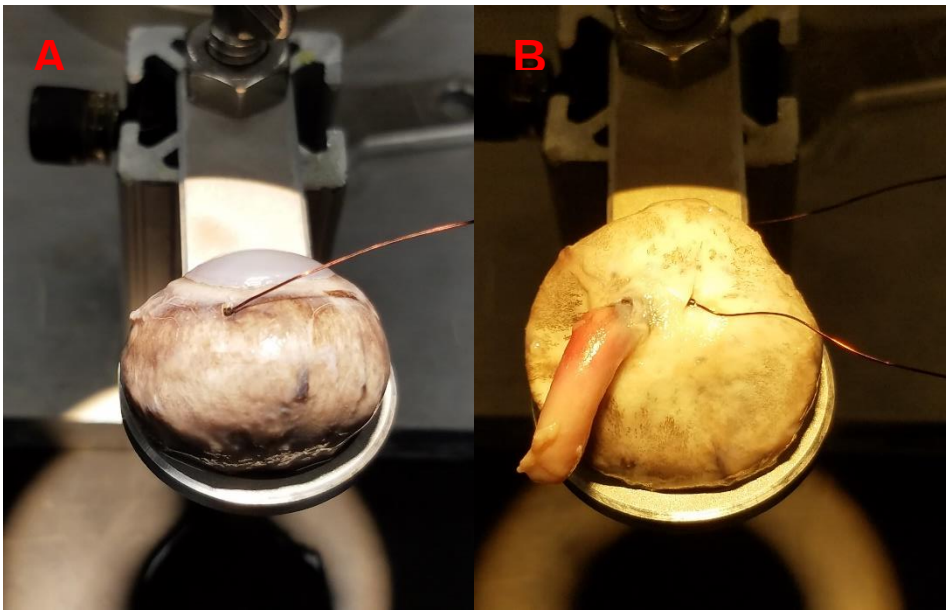

Figure 20. A) An eye with the anterior thermistor implanted before being secured with a suture. B) The posterior thermistor implanted before being secured with a suture.

If an accidental puncture occurred, the site was closed with the same glue (cyanoacrylate, Pacer Technology, Rancho Cucamonga, CA) used to affix the eye to the eye holding ring in surgical preparation. The IOP was restored by injecting saline into the vitreous humor using a syringe with a 26 gauge needle.

4.2.3 Location Verification

To precisely measure where each of the thermistors in the eye were implanted, an eye holder for use in a MRI machine was built as shown in Figure 21. The MRI holder is designed to allow an eye holding ring with the same dimensions used in the experiment (but made of MRI compatible acrylic) to be removed from the eye translator described in Aim 4 and placed directly into a tube built for a small-scale research MRI machine.

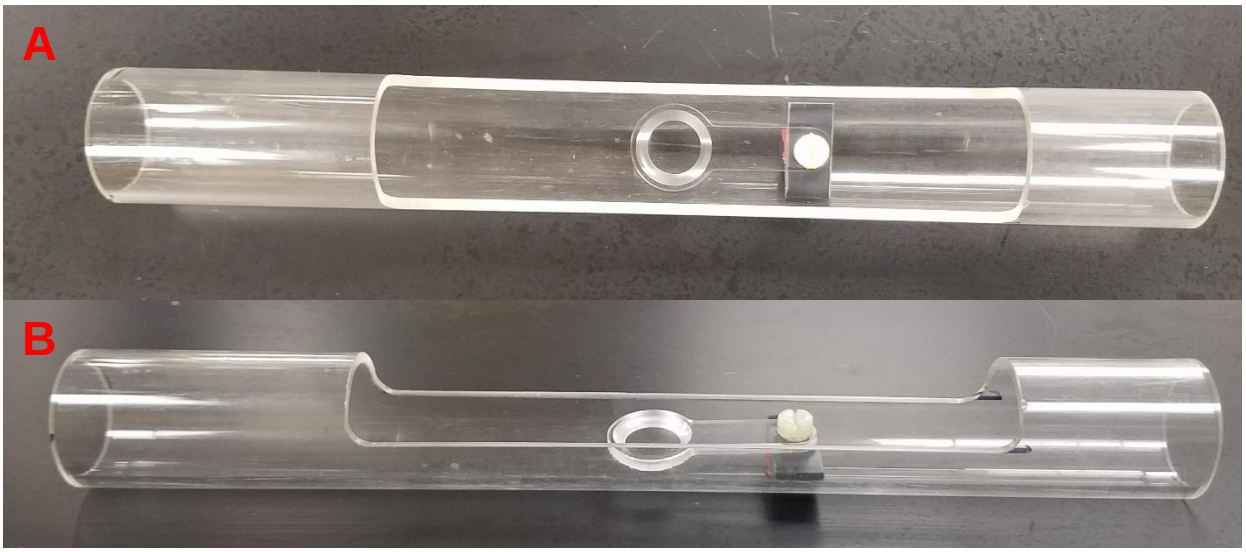

Figure 21. The device built for placing the instrumented eye into an MRI machine for precise imaging of thermistor location. A) A top-down view of the MRI holder. B) An oblique view of the MRI holder.

4.3 Results

While over 25 eyes were implanted to determine the proper surgical and experimental protocols, the results from five eyes are presented in this study. While the thermistor implant location tool was not used in this study, the implant position was estimated to have a variance between trials of less than 3mm. The thermistors were salvaged by snipping the suture with surgical scissors and carefully removing the thermistor from the scleral pocket. Occasionally, the thermistor would fail due to erosion of the insulation on the lead or a physical break between the thermistor body and the lead. For one trial, another thermistor was implanted in the vitreous humor but this was determined to be unnecessary to meet the proof of concept goal of the study.

4.4 Discussion

More than twenty eyes were successfully implanted with three or more thermistors using a simple surgical protocol. One challenge was the repeatability of thermistor location. Due to inconsistencies in the sourcing of the porcine eyes, some eyes were procured without retaining anatomical landmarks such as eyelids. This made it difficult to ensure that the thermistors were

placed in the same relative position across trials. However, the distance of the thermistor from gross landmarks (e.g. the optic nerve and the edge of the cornea) remained relatively precise and repeatable across experiments. The depth of thermistor placement within the sclera across experiments was also variable, but due to the diameter of the thermistor and thickness of the sclera, this concern was determined to be minimal.

Although the thermistor implant location tool was not used in this study, it may be useful in future studies to assist the precision of thermistor implantation and repeatability across experiments. This will be especially important for MRI studies which will require consistent placement.

Another concern was the control of the IOP. Upon puncture and leaking of the vitreous humor, the eye was injected with saline until it had approximately the same IOP as it did upon thawing as judged by feel. However, this method was imprecise and could be controlled for in a more regulated manner in future studies.

While MRI verification of thermistor position was ultimately not performed in this study, it will be of great use to future studies hoping to model heat flow of the eye.

5. Specific Aim 4: Design and fabricate an *in vitro* test environment that replicates the *in vivo* thermal environment of the eye

5.1 Design Requirements

As previously discussed, the eye *in vivo* is surrounded by tissue at approximately 37°C. To accurately test if the ECR can cool the posterior of the eye, a similar environment must be designed for *in vitro* testing. The test environment needed to leave the anterior portion of the eye exposed to air in order to mimic the environment *in situ*.

Next, a positioning system is needed to accurately and consistently bring the ECR into contact with the eye while not interfering with the leads to the thermistors or TECs on the ECR. This system needed to accept the eye holding ring used during the surgical implantation procedure.

5.2 Methods

5.2.1 Design of eye "environment"

The isolated eye lacks the normal orbital fat, critical for temperature regulation of the eye. To simulate the adipose tissue that surrounds the eye *in situ*, the eyes were lowered into a bath of heated vegetable oil, maintained at 37°C. Canola oil has similar thermal conductivity as adipose tissue (0.19 W/m-K vs. 0.20 W/m-K, respectively [15]) and has been used previously to create phantoms to study tissue heating. By placing the eye in the oil when it is heated to 37°C, this will mimic the thermal environment of the body. [16, 17]

5.2.2 Design of the eye translator

A system was designed to precisely lower the eye into the oil as well as bring the eye cooler directly down on top of the eye. Additionally, this system was built with sockets for the TEC power supplies and thermistors to aid in cable management. The eye cooler was attached to the translating tower with acrylic posts to mitigate thermal transfer from the eye cooler. The eye holder portion of the translating tower was designed to allow the holding rings to be transferred from the surgical station to the holder portion while ensuring precise alignment with the eye cooler. The mount between the ECR and the eye translator system was built out of acrylic to thermally isolate the ECR from the translator apparatus.

5.3 Results

The oil bath (PolyScience, Niles, Illinois) took approximately twenty minutes to warm up from room temperature to the target 37°C, but once at that temperature, it stayed consistent and there was no temperature gradient present throughout the bath. This was determined by heating the oil to 37°C and then placing the lead of the Fluke thermometer into the oil bath at 27 different locations. The bath was divided into 9 separate sections in the horizontal plane (an evenly spaced 3x3 grid) and tested at the center of each section. These same sections were tested at three separate depths of the bath. This sufficiently modeled the thermal environment present *in situ*.

The translator system was built incorporating two separate linear translators (Rack and Pinion Stage 55021, Edmund Optics) able to keep the ECR aligned above the eye and bring them into contact while keeping the eye partially submerged in the oil. As shown in Figure 22, the translator has two portions, one for controlling the height of the eye and the other for the ECR.

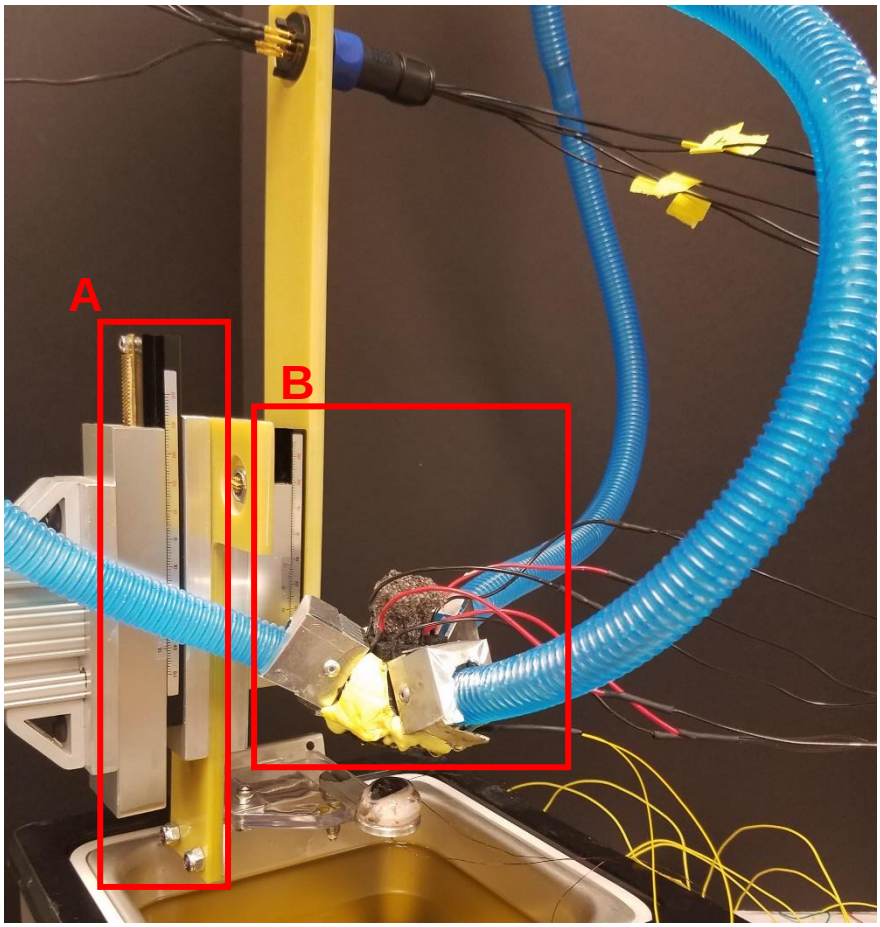

Figure 22. The translator system for lowering the eye into the oil bath and placing the ECR onto the eye. A) The portion responsible for adjusting the height of the eye. This translator affects the position of the eye and ECR together, without affecting their relative positions. B) The portion responsible for adjusting the height of the ECR. When this translator moves, it moves the ECR relative to the eye.

When it was visually determined that the oil contained too many impurities to be sufficient for testing, the bath was emptied and wiped down with paper towels then refilled with fresh canola oil. After removing the eye from the eye holding ring, the eye was disposed of and the eye holding ring was soaked in acetone overnight to remove residual glue.

5.4 Discussion

The oil bath is capable of maintaining a consistent and stable temperature throughout, mimicking the thermal environment of the eye. The translator system can successfully lower the eye into the oil and can bring the ECR into direct contact with the eye.

A limitation of the eye environment was its fixed and relatively unmoving nature. A DC motor could potentially be used to rotate a propeller in the oil bath to circulate the oil and ensure a more uniform temperature and to mimic the thermal stability of extraocular tissues provided by blood circulation. However, during one trial another thermistor was added to the bath near the eye and showed the temperature of the oil had an average temperature of 36.52°C with a standard deviation of 0.25°C so this concern was minimal.

Once challenge was standardizing the depth of the eye in the oil. In all trials, the equator thermistor of the eye was beneath the oil while the anterior thermistor was above it. However, a more controlled protocol could be explored to ensure that the depth of the equator thermistor or distance from the oil to the anterior thermistor doesn't affect the temperature readings.

Another challenge was ensuring ECR contact with the eye. The insulation surrounding the ECR made it difficult to determine if the ECR was in full contact with the eye. For future studies, a contact sensor or some other method of determining corneal contact may be incorporated.

6. Specific Aim 5) Determine experimentally if it is possible for the described system to achieve cooling to 30 degrees Celsius in the posterior of the eye by placing a cooling ring on the anterior sclera

6.1 Requirements

The main goal of this study was to determine whether it would be possible to reduce the temperature of the posterior eye tissue to a therapeutic level with the described system.

As mentioned previously, enucleated porcine eyes were implanted with three intrascleral thermistors. One was adjacent to the cornea, another next to the optic nerve, and the last along the equator of the eye. The eye was suspended in 37°C vegetable oil to simulate the adipose tissue that surrounds the eye *in situ*. A cooling ring was then lowered onto the anterior portion of the eye.

6.2 Methods

6.2.1 Time to Equilibrium

During the first few minutes of the initial trials, the temperatures across the eye were rising despite contact with the ECR. This was determined to be because the eye had not come to equilibrium at the temperature of the bath and was being warmed by the bath after being instrumented at room temperature.

6.2.2 Temperature vs. Time Following ECR Application

Once the ECR contacted the eye, the vacuum was turned on and data acquisition began. One minute into the procedure, the power supply to the TECs was turned to 10 amps. At this level of

current, the heat sinks begin noticeably warming, indicating that their ability to remove heat from the warm side of the TECs is ending.

6.2.3 Rate of Temperature Change

The rate of temperature change is also important to understand how quickly the eye can be cooled and when it has reached a steady state.

6.3 Results

A typical trial is shown in Figure 23. All trials have shown that the anterior portion of the eye exhibits the greatest cooling, followed by the equator and finally the posterior.

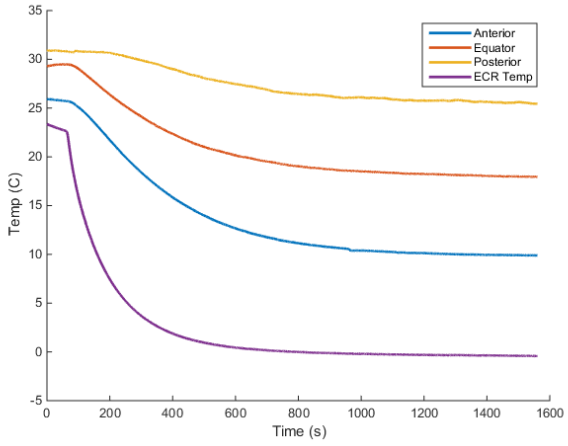

Figure 23. The temperature response of a typical cooling trial. The ECR quickly reaches 0°C while the anterior tissue that is in touch with the ECR also cools significantly. As expected, the posterior portion doesn't cool as much as the anterior or equator, but does exhibit significant cooling.

6.3.1 Time to Equilibrium

For experiments after the first, the eye was placed in the bath for twenty minutes before being contacted with the ECR. This 20 minute period was determined by how long it took for the temperature measured by the probes to stop changing once placed in the bath. This can be seen in Figure 24.

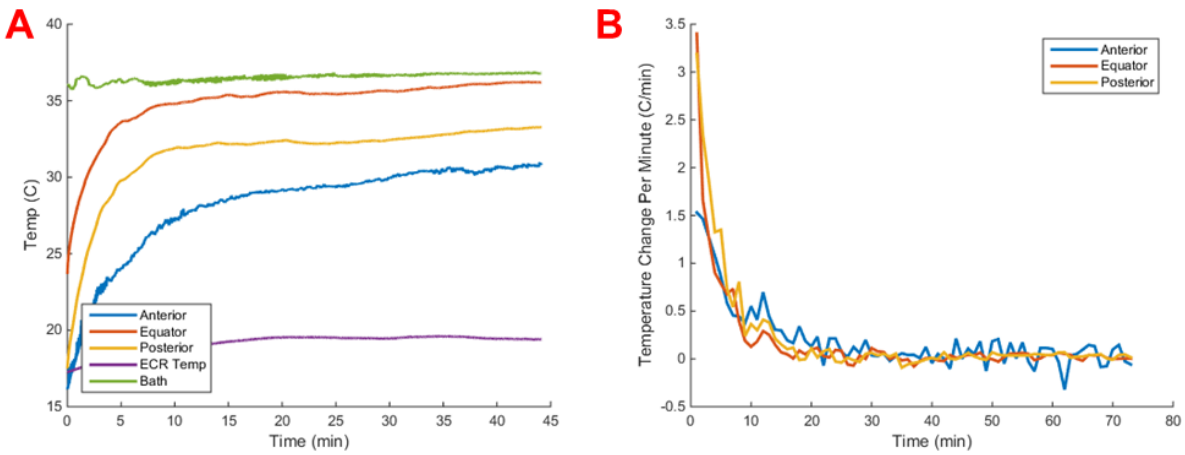

Figure 24. The instrumented eye was placed in the oil bath without being contacted by the ECR. A) A temperature over time plot of the instrumented eye coming to equilibrium. Due to the anterior portion of the eye not being submerged in the oil, it was not expected to reach 37°C. However, it is curious that there is a temperature difference between the equator and posterior.B) After 25 minutes in the oil bath, all tissues of the eye are at a thermal equilibrium, indicating that the ECR can be applied and powered.

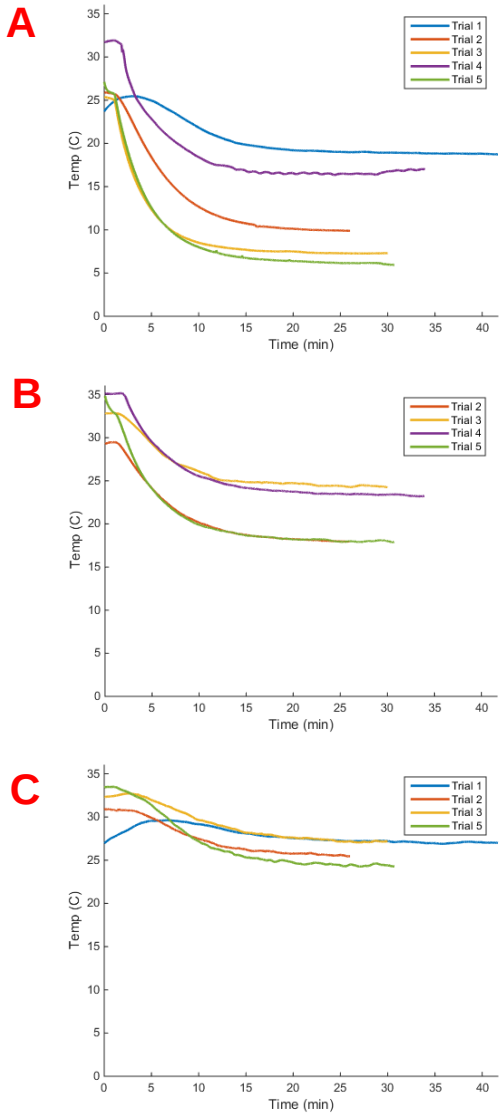

Figure 25. The temperature responses for the different tissues across all the trials presented in this study.
A) Temperature response of the anterior thermistor. Across all trials, the mean temperature decrease of the anterior probe was 14.98°C with a standard deviation of 6.11°C. B) Temperature response of the equator thermistor. Across all trials, the mean temperature decrease of the equator probe was 12.20°C with a standard deviation of 3.48°C. C) Temperature response of the posterior thermistor. Across all trials, the mean temperature decrease of the posterior probe was 4.93°C with a standard deviation of 3.77°C. Without counting the first trial, this changes to a mean decrease of 6.59°C with a standard deviation of 2.22°C. In one trial, the posterior probe broke during use so that data was not included.

6.3.2 Temperature vs. Time Following ECR Application

The rate and extent of cooling was analyzed for all locations across all trials and is shown in Figure 25. As mentioned previously, the eye used in the first trial wasn't submerged in the oil bath for twenty minutes prior to data acquisition which causes the initial rise in temperature at the early stages of the experiment. This behavior is not present in any of the other trials.

6.3.3 Rate of Temperature Change

To assess when each location in the eye comes to thermal equilibrium, the temperature change for each minute was calculated and plotted on the same time axis as the experiment occurred as shown in Figure 26. Once the temperature change reached zero, that portion of the eye was assumed to be at thermal equilibrium.

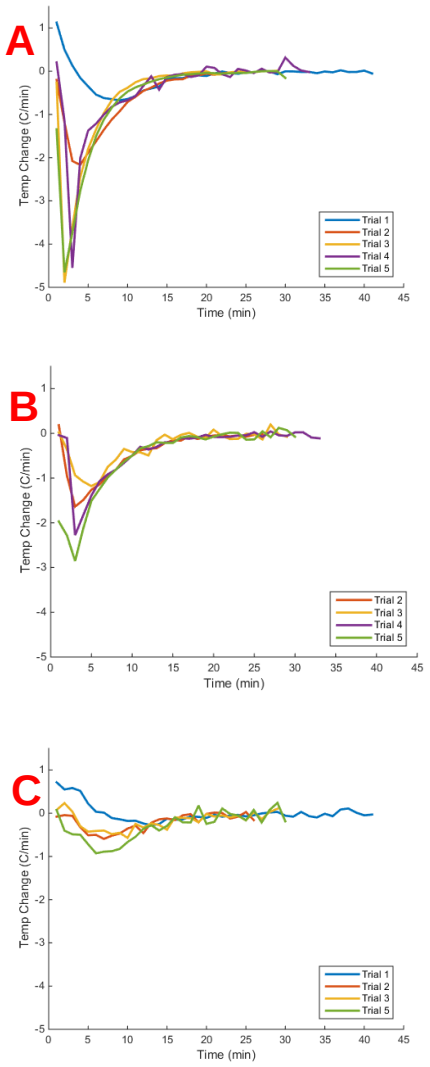

Figure 26. After 25 minutes in contact with the ECR, all tissues of the eye are at a thermal equilibrium, indicating that the maximum possible cooling with the current system has been reached.
A) The anterior tissues showed the greatest initial rate of cooling, with most eyes dropping over 4°C per minute at one point.
B) The equator tissues also showed a steep initial rate of cooling, with most eyes reaching their maximum rate within 4 minutes.
C) The posterior tissues exhibited the slowest rate of cooling but mimicked the other tissues in reaching thermal equilibrium after 25 minutes.

6.4 Discussion

The data presented shows that placing the anterior of the eye in contact with the ECR system described in this study cools the anterior of the eye an average of 14.99°C, the equator an average of 12.20°C, and the posterior of the eye an average of 6.59°C. Posterior tissue cooling of 6.59°C exceeds the design specification of the device, indicating that therapeutic effects could be reached with lower power output. However, some freezing of the tissue directly in contact with the cooler was observed. This may damage the anterior tissue and requires further investigation.

A more physiologically accurate model would be to perfuse the ocular vasculature and circulate body temperature saline through the eye. This may warm the anterior tissue, but may also assist with cooling the posterior tissue by cycling cooled “blood” back to the posterior of the eye.

One of the trials didn’t have a thermistor implanted in the equator due to tissue degradation caused by issues with thawing the tissue. During one trial, the leads to the posterior thermistor broke rendering that data unusable.

7. Future Work

Removing heated air from the heat sinks was the limiting factor in how cold the ECR could get. To improve the performance of the eye cooling device, the heat needs to be dissipated from the TECs in a more efficient manner. Liquid cooling is more efficient for dissipating heat than passing air over heat sinks. However, liquid cooling requires a water pump, water-to-air heat exchanger, and a reservoir which takes up additional space. In the spirit of this device being field-deployable, liquid cooling was not considered for the application.

Treating this system purely as a research tool for modeling temperature flow through the eye, a probe immersed in liquid nitrogen could be placed against the anterior portion of the eye, making the tissue dramatically cooler than is possible with a TEC based system.