ECE 445

SENIOR DESIGN LABORATORY

DESIGN DOCUMENT

Autologous Transcranial Implant for the Delivery of Photodynamic Therapy for Intracranial Brain Tumors

Shedding Light on Glioblastoma

Team No. 33

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Abstract

This document aims to provide a more in-depth explanation of our previously submitted RFA. We delve deeper into project requirements, high-level details, and ethical quandaries when starting a project of this magnitude.

Contents

1 Introduction

We aim to provide context as to the problem we are trying to solve, the solution our team landed on, as well as high-level requirements for the project overall.

1.1 Problem

Glioblastoma has a very poor prognosis of 12-15 months post-operation [1]. The current standard of treatment is surgical resection, radiation therapy, and chemotherapy [1]. One FDA-approved device on the market exists that attempts to solve a similar problem - Optune [2]. Other alternatives exist as well but they have low efficacy overall. In recent trials, photodynamic therapy (PDT) has proven effective in treating cancerous cells though currently it can only be administered mid-surgery while the brain is exposed [3].

1.2 Solution

To allow for photodynamic therapy (PDT) to be administered postoperatively, we propose developing a small transcranial implant that would provide the light source for this therapy. Our objective is to create a programmable device that can be implanted through the skull which will provide control over PDT delivery chronically, allowing patients with GBM to be photo-irradiated without re-entering the operating room after their resection is completed. Components of this transcranial implant would include the appropriate light source, a light diffuser, battery, and an on/off mechanism.

1.3 Visual Aid

In Figure 1, an early mock-up of the proposed implanted device can be seen. In Figure 2, that proposed device is positioned on a scale model head to further contextualize our goals.

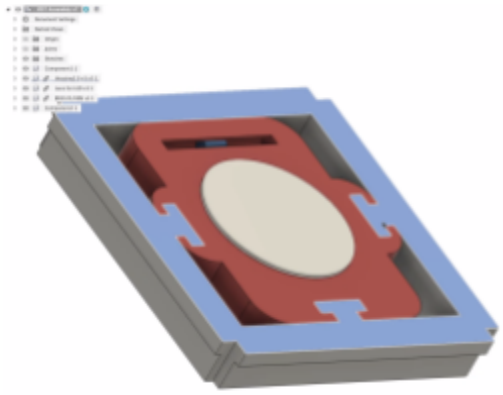


Figure 1 : Early mock-up of proposed solution

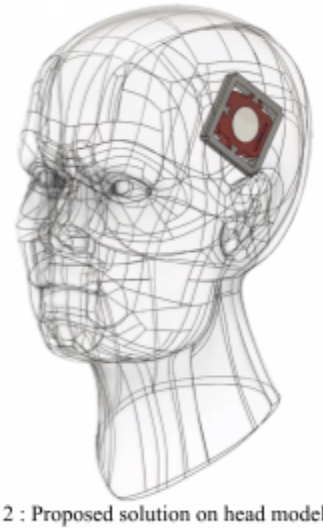


Figure 2 : Proposed solution on head model

1.4 High-Level Requirements

To be considered successful, we aim to meet the following goals:

1. The device will produce 200J/cm^2 of 635nm wavelength hitting the 5-ALA affected cells in the brain.
2. While the PDT is being administered, the temperature around the targeted area remains clinically unaffected (lower than 39º C). [5]
3. The overall power consumption of the device is low enough to last up to 5 years on a single battery charge.

2 Design

2.1 Block Diagram

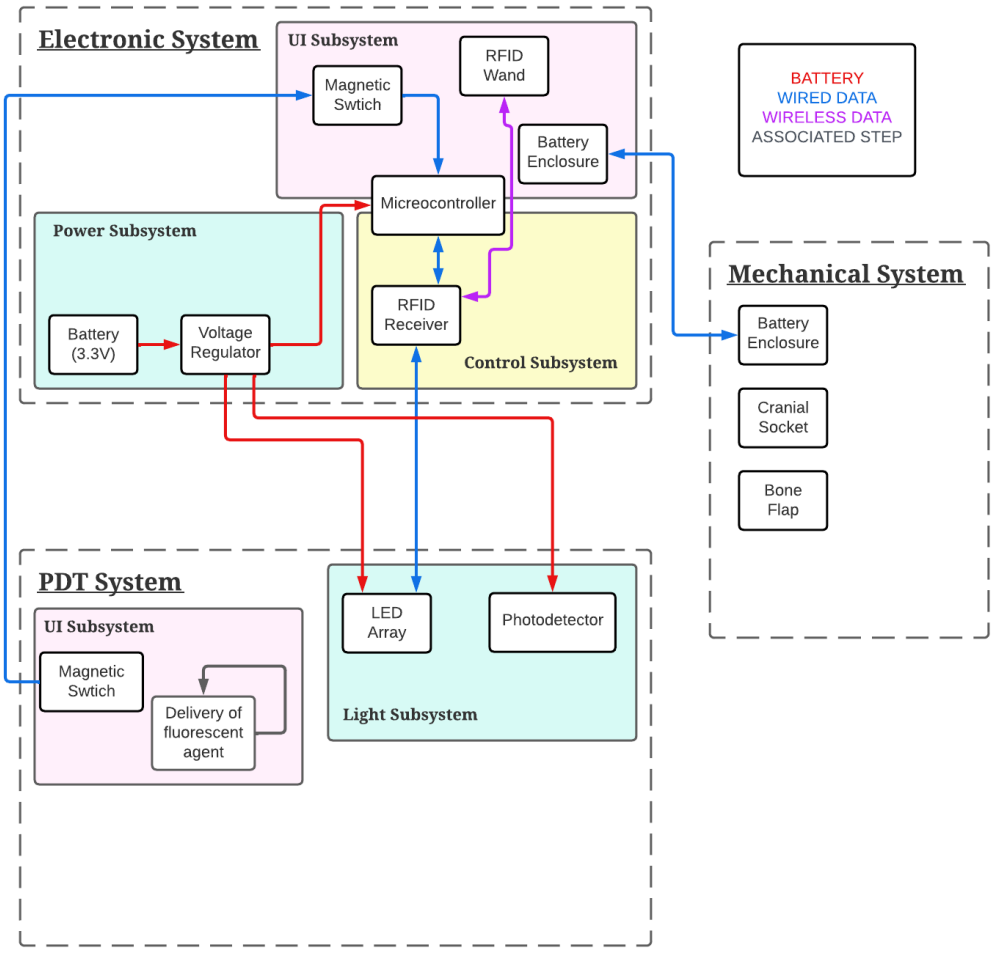


Figure 3: System level block diagram

2.2 Design

Our design will be composed of three parts, as seen in figure 3 below. The first of the three components is the socket that attaches directly to the skull. This piece has a wide flat flange that interfaces with the edges of the removed bone. Bone cement will be used to line the interface between the skull and the socket. The second component is the device housing itself. The proposed design has a circular, chamfered cutout to fit a diffusing lens that meets the specified light wavelength and intensity parameters. The housing will be screwed into the socket from the inside, allowing it to be tightly fastened to minimize the risk of movement once installed. The last and final component is the face plate. Screws will go through the face plate, through the flange, and lock themselves into the skull. This will create a tight seal while also allowing the device to be accessed down the line if necessary. Our prototype will be made out of machined aluminum but the final delivered product will have to be made out of a non-reactive material like medical-grade titanium.

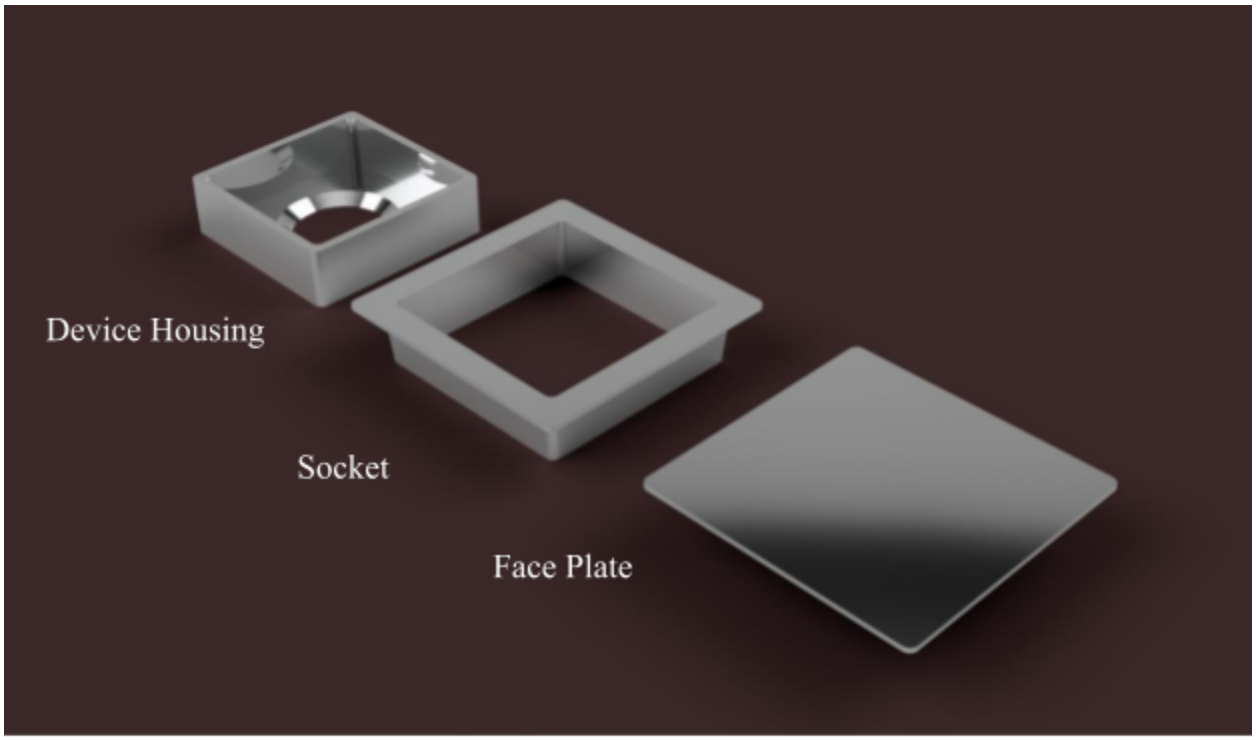


Figure 4 : Render of proposed physical design

2.3 Subsystem Overview

Our solution is broken down into three distinct systems. They consist of the electronic system, the PDT system, and the mechanical system. Each of those systems is further broken down into subsystems, discussed below.

2.3.1 Electronic System

2.3.1.1 Power Subsystem

The power subsystem is relatively straightforward. It is in charge of providing power to the microcontroller, LED array, and photodetector. The power from the battery will be run through a voltage regulator into the powered components after installation and for the useful life of the device.

2.3.1.2 Control Subsystem

The control subsystem consists of two parts; the microcontroller and the RFID receiver. The microcontroller will act as the brains of our operation. It will store the intensities, times, and intervals that the LED array will be administering the PDT. The RFID receiver will allow the doctor to prescribe an assortment of different parameters and transmit that data to the device via an RFID wand.

2.3.1.3 UI Subsystem

The UI subsystem pertaining to the electronic system contains the magnetic switch that allows the entire device to be activated after it is successfully implanted into the patient's skull. The UI subsystem also contains the RFID want, responsible for sending parameters to the implant, and the battery enclosure, built into the device itself.

2.3.2 Electronic Subsystem Verification

Requirement	**Verification**
Power Subsystem	
The battery provides 3.7V to the processor, LED array, and all other powered systems and supports at least a 50 mA draw.	Use a multimeter to test the input pins of our mcu while using all communication and switching circuits to find its current draw. Verify battery voltage and test its performance across five discharge cycles to make sure it retains its nominal value.
Depending on the PDT delivery schedule, the device can function for 5 years without battery replacement.	Battery life analysis performed in section 2.7 Tolerance Analysis.

Control Subsystem	
The system must be programmed with at least three unique treatment schemas.	Sponsors verified three sample PDT sessions. ● 1min on, 1min off, repeat 5 times ● 30sec on 30sec off, repeat 10 times ● 10sec on, 50 sec off, repeat 30 times We will know a PDT schema works when we can program the board's LED to blink according to these patterns.
The end user must be able to select the duration of the treatment as well as the frequency at which the treatment is administered.	Successful implementation will mean we can store several different PDT patterns on the mcu and choose them at will.
2.4.1.3 UI Subsystem	
The end user must be able to select the duration of the treatment as well as the frequency at which the treatment is administered.	Health care professional will be capable of selecting appropriate PDT procedure.
The implant itself must be designed to minimize any risk of postoperative complications.	This will need to be verified with medical trials.

2.3.3 PDT System

2.3.2.1 UI Subsystem

The UI subsystem pertaining to the PDT system contains the magnetic switch responsible for activating the entire device and a second important, though ancillary, step. The patient must ingest a fluorescent agent in order for the PDT to be successful. It is a crucial part of our proposed project, even though it is not a process we directly control.

2.3.2.2 Light Subsystem

The light subsystem is the “business end” of our proposed project. It contains the LED array and photodetector responsible for the administration of the PDT. The entire light subsystem is powered through the same energy source as the microcontroller. The photodetector’s goal is to ensure that the LEDs are operating appropriately. It is a failsafe in case an LED burns out or the device stops working entirely.

2.3.4 PDT Subsystem Verification

Requirement	**Verification**
UI Subsystem	
The 5-ALA fluorescent marker, which allows for the PDT to effectively target malignant cells, must not be toxic to patients.	Visual check done by a health care professional. It is safe [3].
The 5-ALA fluorescent marker must absorb into malignant cells at an exponential rate in comparison to their healthy counterparts as it's designed.	Visual check done by a health care professional. Uptake by cancer cells is magnitude higher than non cancer cells [3].
Light Subsystem	
The LED array must provide 200 J/cm^2 optical doses at 635 nm wavelength.	Photodetector implanted in test environment (gelatin) will measure 635N/m and illuminance will be measured and plotted to verify it is above 200J/cm^2
The photodetector must detect the LED array’s functionality to allow the system to operate effectively.	Photodetector verifies the light is on and will give a digital signal to mcu for us to monitor.

2.3.5 Mechanical System

Our mechanical system acts both as a higher-level system and a lower-level subsystem. It contains the socket that is attached to the skull, the battery enclosure protecting the battery within the implant itself, and the bone flap - a piece of skull removed for surgery, that the implant will directly interact with.

2.3.6 Mechanical Subsystem Verification

Requirement	**Verification**
Cranial Implant	
The final implant must be made of a material conditioned to limit foreign body reaction. This includes medical-grade titanium as well as other materials coated in an antibacterial compound.	Verification will be done by a healthcare professional. Titanium will be sanitized and administered in brain under standard cranioplasty procedure
The final implant must fit within the cranial window with proper positioning inside the resection cavity to ensure PDT administration.	Verification will be whether the device can be successfully screwed into a skull or appropriate skull proxy

2.4 Schematics

2.4.1 Electrical Schematic:

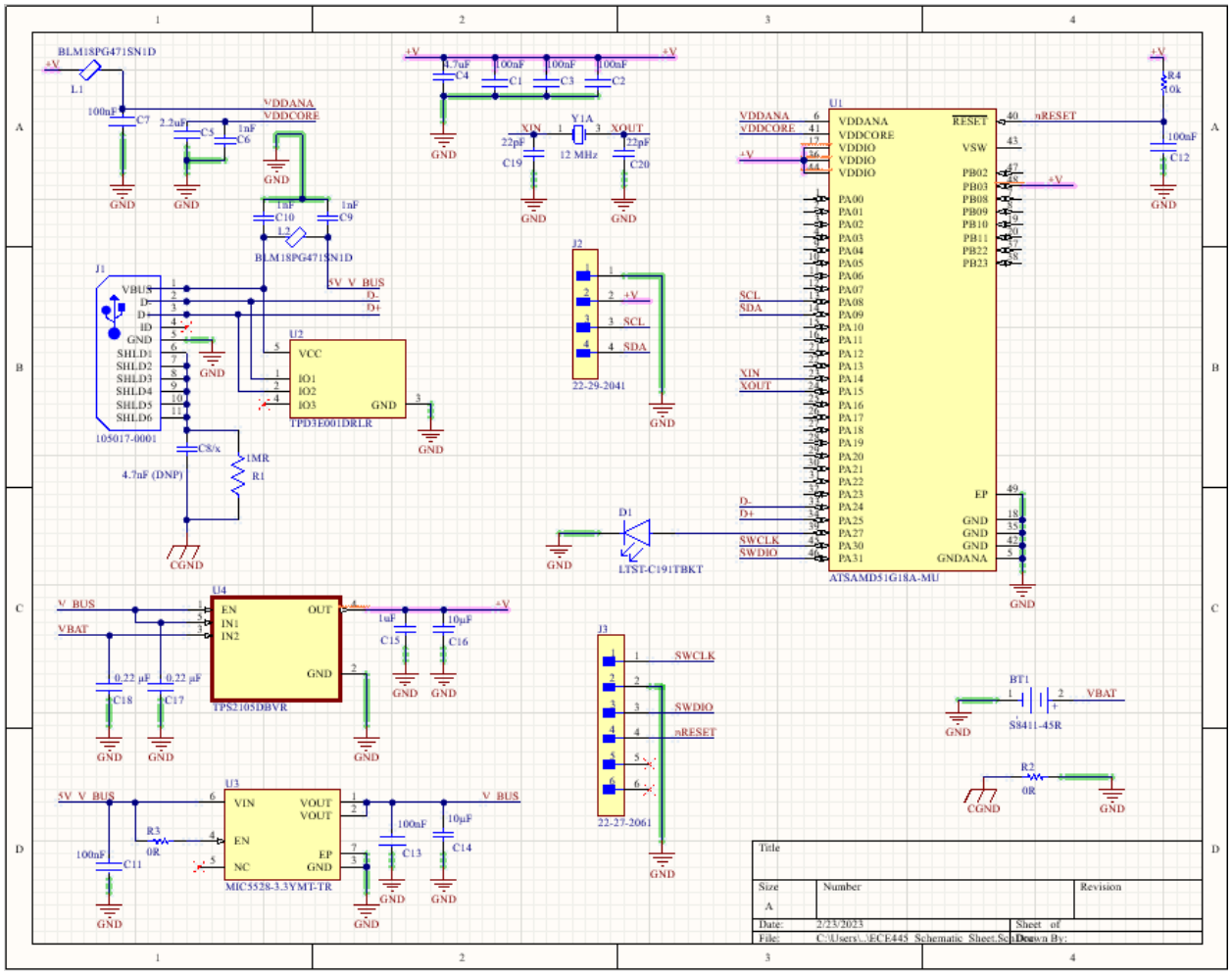


Figure 5: Main Schematic Sheet

This is the latest version of our schematic. The schematic includes different devices that were added for several reasons. Listed below are some of the main parts:

- Micro-Controller: ATSAMD51G18A-MU
- Battery Holder: S8411-45R
- Micro-USB B: 105017-0001
- Voltage Mux: TPS2105DBVR
- Voltage Regulator: MIC5528-3.3YMT-TR
- JTAG Connector: 22-27-2061
- RFID Connector: 22-29-2041
- LED: LTST-C191TBKT
- Oscillator: FQ5032B-12

2.4.1.2 Microcontroller

ATSAMD51G18A is a 48 pin microcontroller. It features a 32-bit ARM Cortex-M4 processor with Floating Point Unit, which will be capable of running all the included devices in the PCB. The microcontroller has 5 low power modes with class leading to 65uA/MHz Active power performance. This is very crucial for us since we are looking to save on power consumption when the LED is not on. It supports a variety of serial communication. However, in our case we will only be using the I2C communication.

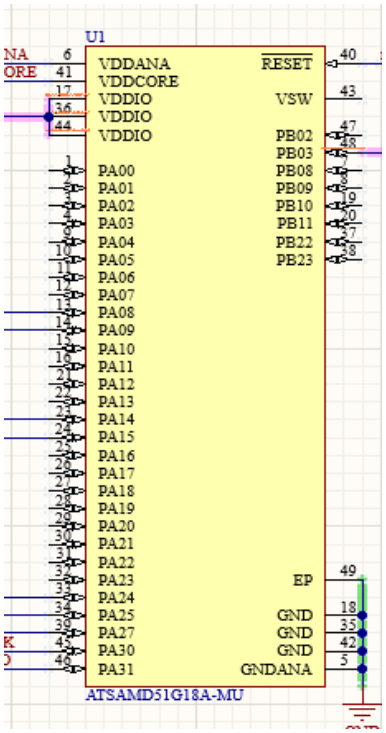


Figure 6: Micro-Controller

2.4.1.2 Battery Holder

The batter holder will hold our main source of power, which is a coin cell. The coin cell has 3.3V.

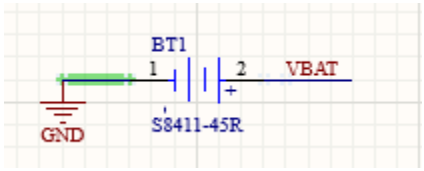


Figure 7: Battery Holder

2.4.1.3 Micro-USB B

The Micro-USB B will allow us to upload any image from our software (MPLAB) to our microcontroller. The design of the Micro-USB B was built according to medical standards. Different safety circuits were added to the USB to not risk the safety of the patient.

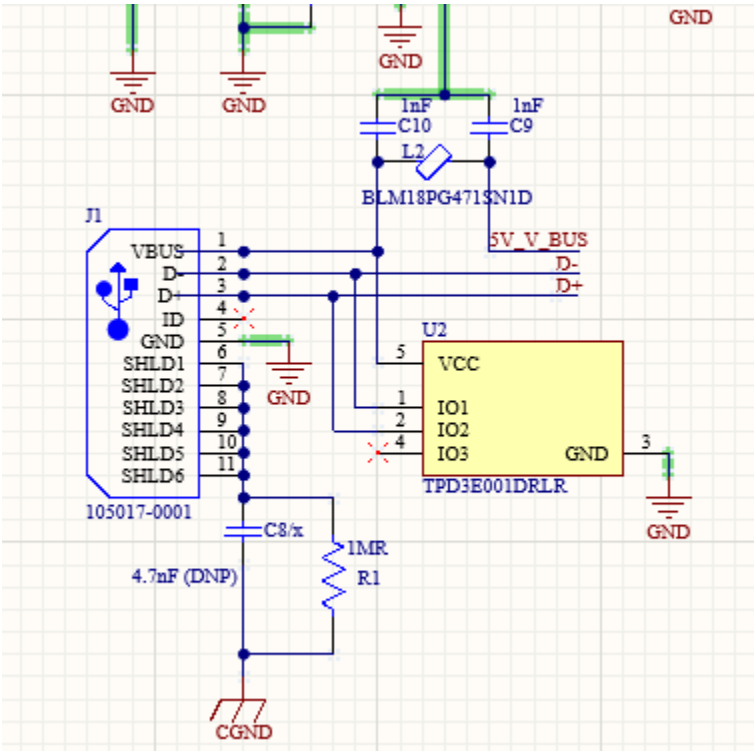


Figure 8: Micro-USB B and it's safety circuitry

2.4.1.4 IC Power Mux

This power mux will manage the two different power inputs.

- Inputs: Voltage of the battery (~3.3V) and the Voltage of the USB (5V)
- Outputs: Constant linear 3.3V

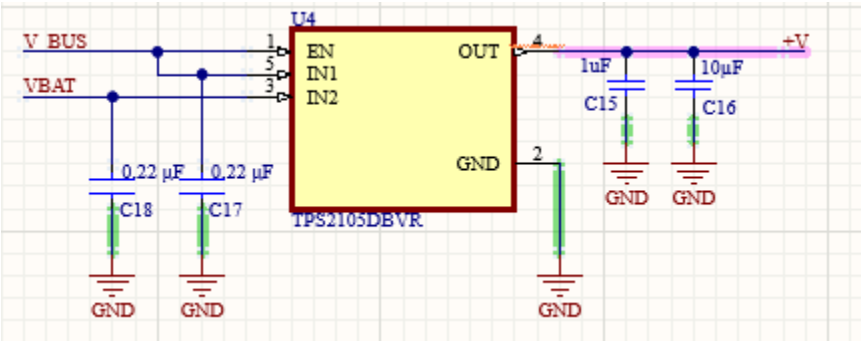


Figure 9: IC Power Mux

2.4.1.5 Voltage Regulator

The need for the voltage regulator is to drop the USB voltage from 5V to 3.3V.

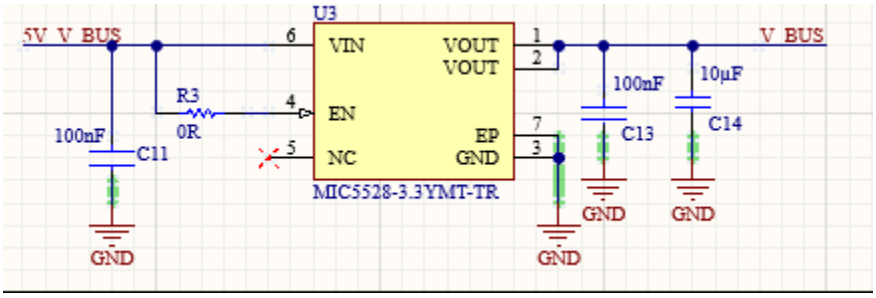


Figure 10: Voltage Regulator

2.4.1.6 JTAG connector

The JTAG connector was added to connect the processor to our JTAG debugger, which is needed for the initial run.

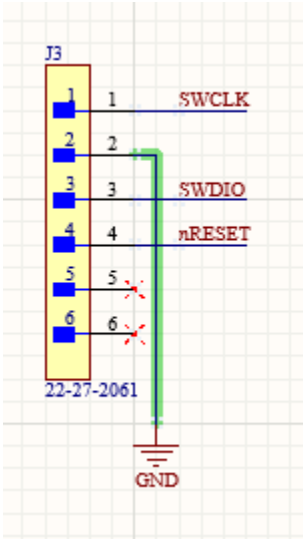


Figure 11: JTAG connector

2.4.1.7 RFID connecter

The RFID connector was added to mount the RFID on top of the PCB, and it allows it to communicate to the processor. (For now we are considering using this RFID: ANT7-T-M24SR64.)

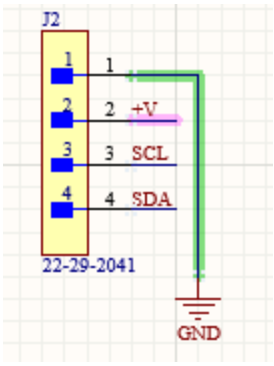


Figure 12: RFID connector

2.4.1.8 LED

The LED specification was based on choosing a LED that can deliver 635nm. For our case we chose: LSM0603412V

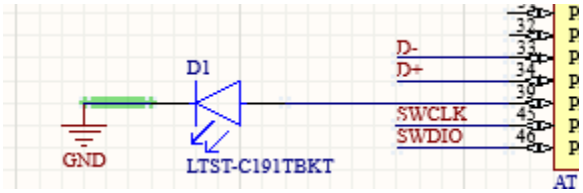


Figure 13: LED

2.4.1.9 Oscillator

The Oscillator was chosen based on the specification mentioned in the datasheet of the Micro-Controller.

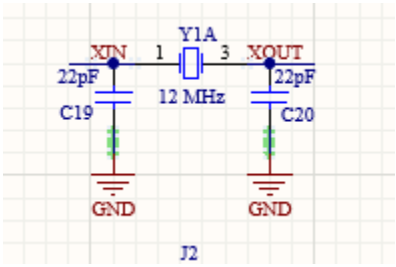
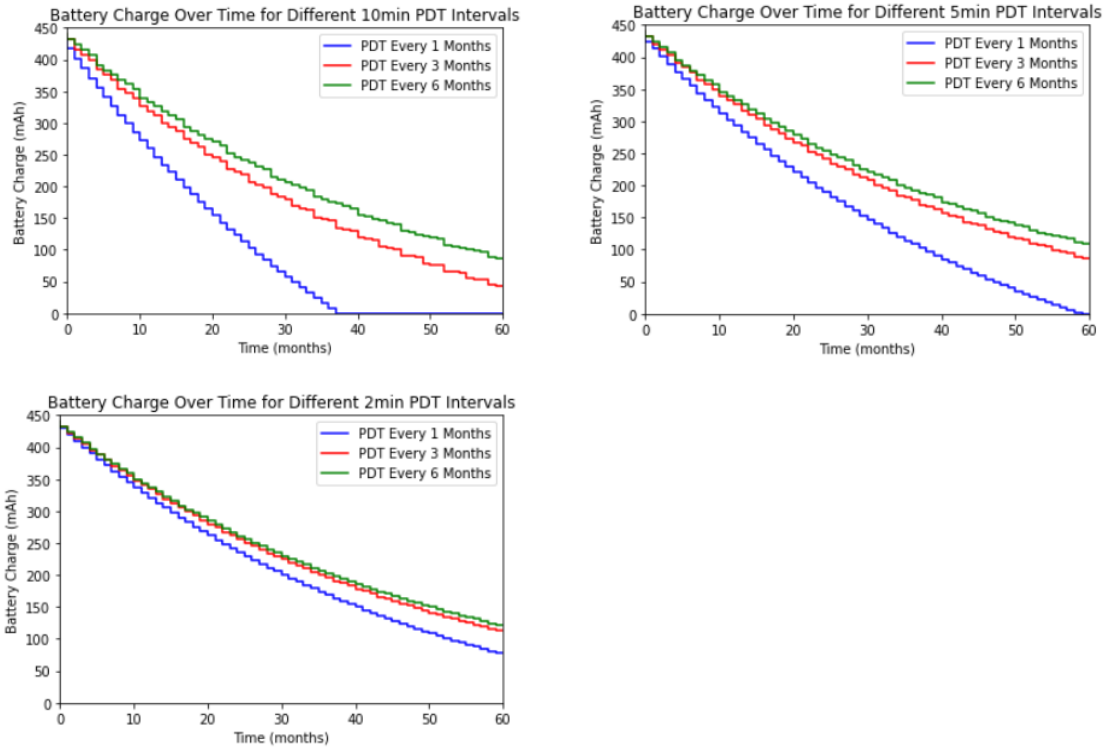


Figure 14: Oscillator

2.5 Tolerance Analysis

The sizing of the battery will be a significant engineering challenge during the construction of the device. There are no restrictions on the overall weight of the device but the physical size must be constrained to fit in the housing unit. The battery we plan to use is 11 grams and has dimensions 37x25x 5mm. Given a passive discharge rate of 2 percent per month and varied PDT session length and frequency, we believe a 450mAh to be sufficient to last five years. Below are different scenarios of the battery life assuming 45mA of active draw (20mA from the LED, 25mA from the mcu).

Figure 15: Battery Charge tolerance analysis



Further testing is required to figure out the exact active and passive draw from the battery but from this preliminary testing we think 2 minute PDT sessions of any frequency will be the most appropriate. It must be noted the intensity and length of a PDT session will vary from patient to patient and our goal is simply to provide the controls for our sponsors to implement the treatment

3 Cost & Schedule

3.1 Cost Analysis

3.1.1 Parts & Materials

Name	Manuf.	Unit Price	Quantity	Total
Battery Holder	S8411-45R	1	1.43	1.43
Capacitor	CGA3E2X7R1H104K080AA	7	0.014	0.098
Capacitor	GRM21BR61E475MA12L	1	14.01	14.01
Capacitor	GRM188R71A225KE15D	1	0.16	0.16
Capacitor	GRM188R71H102KA01D	3	0.11	0.33
Capacitor	GRM188R71H472KA01D	1	1.8	1.8
Capacitor	GRM21BR61A106KE19L	2	0.0134	0.0268
Capacitor	GRM188R61E105KA12D	1	0.0052	0.0052
Capacitor	C0805C224K5RAC	2	0.0178	0.0356
Capacitor	GRM1885C1H220JA01D	2	0.1	0.2
RFID	ANT7-T-M24SR64	1	4.92	4.92
Connector	1050170001	1	0.235	0.235
Connector	22-29-2041	1	0.29148	0.29148
Connector	22-27-2061	1	0.5988	0.5988
Resistor	BLM18PG471	2	0.1	0.2

	SN1D			
Resistor	CRCW06031M00FKEA	1	0.005	0.005
Resistor	CRCW08050000Z0EA	2	0.005	0.01
Resistor	CRCW060310K0FKEA	1	0.005	0.005
Micro-Controller	ATSAMD51G18A-MU	1	3.74	3.74
IC Power Mux	TPD3E001DRLR	1	0.52	0.52
Regulator	MIC5528-3.3YMT-TR	1	0.2413	0.2413
LED	LSM0603412V	1	$0.40	0.4
Oscillator	FQ5032B-12	1	1.16	1.16
3.7V 450mAh 502535 Lipo Battery	Amazon	3	8.99	26.97
Total				**$57.39**

3.1.2 Estimated Hours of Development

All of the members of this group are Electrical Engineering students. According to the Illini Success Report from the 2020-2021 school year, the average starting salary for an Electrical Engineering major is $80,296 per year, which equates to $38.60 per hour working 40 hours a week 52 weeks a year.

Category	Estimated Hours Jack	Estimated Hours Brian	Estimated Hours Mohamed
Circuit Design	0	0	90
Housing Design	10	0	0
Breadboard Layout	10	10	10
Soldering	10	10	10
Debugging and Testing	60	70	10
Documentation and Logistic	60	70	30
TOTAL HOURS	150	150	150

Using the hourly estimates above, we expect our labor costs for the project to be:
$38.60 (Hourly Rate) * (Total Estimated Hours) = $17,370

3.1.3 External Materials and Resources

Machine Shop

As discussed in the Physical Design portion of this document, our device will be made out of machined aluminum for our prototype. We hope to have our housing design finalized with the machine shop in the very near future to allow them the maximum amount of time to machine the parts. With that in mind, we expect the total machine shop time to be approximately **10 hours**.
Senior Design Lab Resources
We plan on taking full advantage of the soldering stations as well as the knowledge and experience of the TAs that hold office hours in the Senior Design Lab this semester.

UIUC Medical School Resources

As part of our project, we have been fortunate enough to be supported by the University of Illinois at Urbana Champaign Medical School. With that comes access to additional funding, access to a cadaver if we so choose, as well as the mentorship and understanding of professors and students at the top of their fields.

Development Resources

In order to effectively design, build, and implement the final design solution we have purchased development boards - listed in the bill of materials. One of which will be specifically designed to interact with the RFID module we plan on linking into our larger system.

3.1.4 Total Estimated Cost

After evaluating materials, labor, and development costs we have determined that the overall expenditure for our ECE445 project will be $17427.39

3.2 Schedule

Week of 2/27

Design Document, Schematic Review and Feedback, PCB Review

Week of 3/06

Order PCB, Teamwork Evaluation, Machine Shop Design Due

Week of 3/13

SPRING BREAK

Week of 3/20

PCB Arrives, Solder, Debug, Begin Techbench on PCB

Week of 3/27

Second Round PCB Order, Progress Report, Review, Debug, Continue Development

Week of 4/03

Debug, Review, Begin Preparation for Demo

Week of 4/10

Contract Fulfillment, Preparation for Demo

Week of 4/17

Mock Demo, Final Preparation for final Demo, Work on Presentation

Week of 4/24

Final Demo, Mock Presentation, Begin Finalizing Paper

Week of 5/1

Final Presentation, Final Paper and Lab Notebook Due

4 Ethics & Safety

4.1 Ethical Considerations [4]

When developing a biomedical device, there are several places where one could violate the IEEE Code of Ethics. When meeting with our project team at the University of Illinois School of Medicine, there were three points where the ethical implications were of the utmost importance.

When developing and administering a biomedical device of such delicacy as a transcranial implant, there is a concern for patient autonomy. Patients, that could otherwise be perfect candidates for PTD, and this device in particular, might not be able to make a fully informed decision due to a misunderstanding stemming from a misunderstanding of the foundational technology. Our hope is, that with the proper literature, education, and transparency, we will be able to ensure patient understanding. In doing so, we can make sure everyone that gets the implant is both a good candidate and willing to have our device implanted.

There is a serious potential for side effects after device implantation. We have to consider the possibility that that patient might want the device removed if the implant causes a drastic drop in quality of life. Other transcranial devices, such as the Responsive Neurostimulation (RNS) system have already faced a similar ethical conundrum and workshopped explantation protocols that can be adapted to our situation.

When the unfortunate circumstance of a terminal diagnosis has to be given, some patients might take it upon themselves to seek out unproven technologies, procedures, or drugs that have the potential to improve their chances. A concern of developing a device like this is that vulnerable parties might be swayed to forgo medical warnings to access a clinical trial. We hope that carefully vetting patients for an over-inflated perspective of the theoretical positives will protect both the patient's safety and the integrity of the project overall.

4.2 Safety Considerations

When administering a transcranial implant, the doctor and patient are both agreeing to put an electronic circuit and battery dangerously close to the most important organ in the body. A decision like that, as researched and studied as it can be, will always come with its share of safety concerns.

With a battery-powered system powering an incredibly strong LED array very close to the surface of the brain, there is a high potential for the device to overheat inside the skull. The temperature at which healthy brain cells begin to experience damage is between 39º and 40º C (between 102º and 104º F) [5]. Our goal is to engineer and insulate the device well enough to ensure that those temperatures are never reached. Extensive bench testing will be required to reach this goal.

Like with any medical implant, whether it is an organ transplant or a device implant, the risk of a foreign body reaction is always there. Once the prototype is proven, our goal would be to implement the final device in materials designed to limit that reaction. There are antibiotic coatings that exist as well as medical-grade resins and titanium.

5 References

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