ECE 445

SENIOR DESIGN LABORATORY

PROJECT PROPOSAL

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.

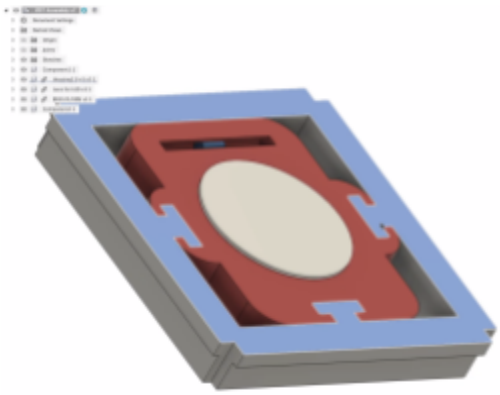


Figure 1 : Early mock-up of proposed solution

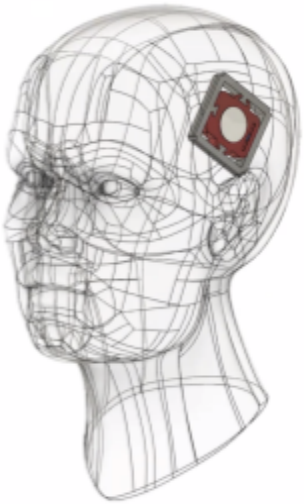


Figure 2 : Proposed solution on head model

1.4 High-Level Requirements

Requirement 1: 200J/cm^2 of 630nm wavelength hitting the 5-ALA solution

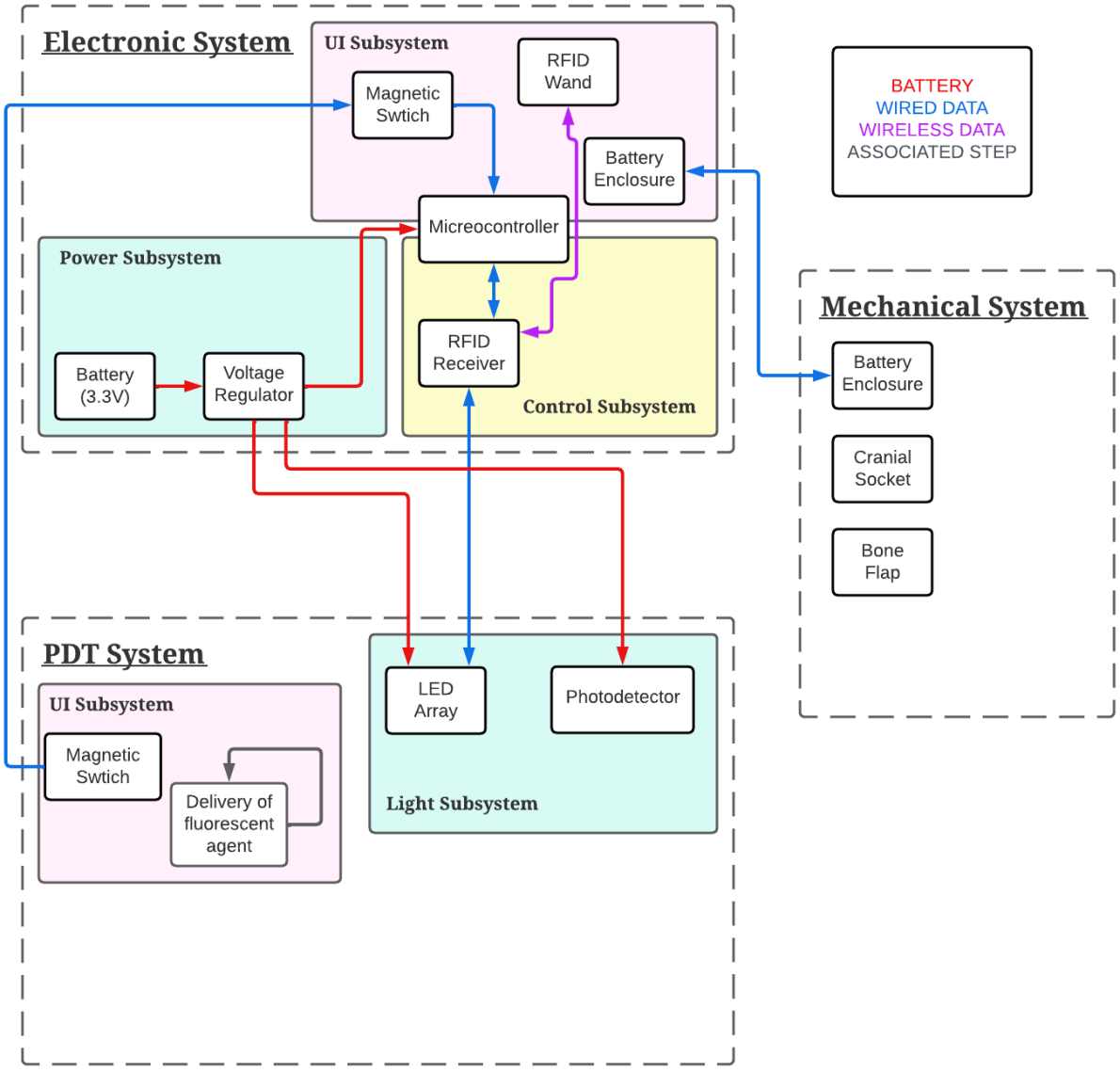
Requirement 2: temperature around the area is clinically unaffected

Requirement 3: power consumption low enough for 5 year device duration on a single battery

2 Design

2.1 Block Diagram

- Block Diagram



2.2 Subsystem Overview

Our proposed 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.

2.2.1 Electronic System

2.2.1.1 Power Subsystem

The power subsystem is relatively straightforward. It is in charge of providing power to the microcontroller, LED array, and photodetector. We are in the process of determining what battery would be appropriate to achieve our high-level goals. The power from the battery will be run through a magnetic switch initially and then through a voltage regulator into the powered components after installation and for the useful life of the device.

2.2.1.2 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.

2.2.1.3 UI Subsystem

The U, 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.

2.2.2 PDT System

2.2.2.1 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.

2.2.2.2 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.

2.2.3 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 Subsystem Requirements

2.2.1 Electronic System

2.2.1.1 Power Subsystem

- System provides up to 50mA and 3.3V for the processor.
- Depending on the PDT delivery schedule, the device can function for 5 years without battery replacement.

2.2.1.2 Control Subsystem

- Has at least three different modes of light operation.
- Able to control LED for each PDT at desired frequency and duration.
- Diode is sensed by a photodetector to ensure successful PDT operation.

2.2.1.3 UI Subsystem

- Has three different modes of operation.
- Design minimizes risk of medical complications.

2.2.2 PDT System

2.2.2.1 UI Subsystem

- 5-ALA fluorescent marker must not be toxic to patients.
- 5-ALA fluorescent marker must only damage metastatic tissues.

2.2.2.2 Light Subsystem

- Provides 25 J/cm^2 optical doses at 635 nm wavelength.
- Detectable light to ensure implant operation across multiple check-ups.

2.2.3 Mechanical System

- Final implant made of material conditioned to limit foreign body reaction.
- Seamless implantation within the cranial window with proper positioning inside the resection cavity.

2.4 Tolerance Analysis

The sizing of the battery will be a major challenge during the construction of the device. There are no restrictions on the overall weight of the device, but larger batteries may become cumbersome to the patient. On the other hand, the physical size of the battery is constrained. A potential battery that fits our size requirements has a weight of 30 grams and a capacity of 450mAh. Given a lifespan of five years and 12 photodynamic therapy (PDT) sessions per year, the LED needs to be turned on 60 times. To deliver 200 J/cm^2 during PDT, we can use a modest LED that outputs 0.1 lumens at 20mA or 200J/cm^2 in about ⅛ of a second. Although a diffuser may affect the LED output, we believe the energy delivery system is still feasible with a device-size-appropriate battery.

3 Ethics & Safety

3.1 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.

3.2 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.

4 References

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