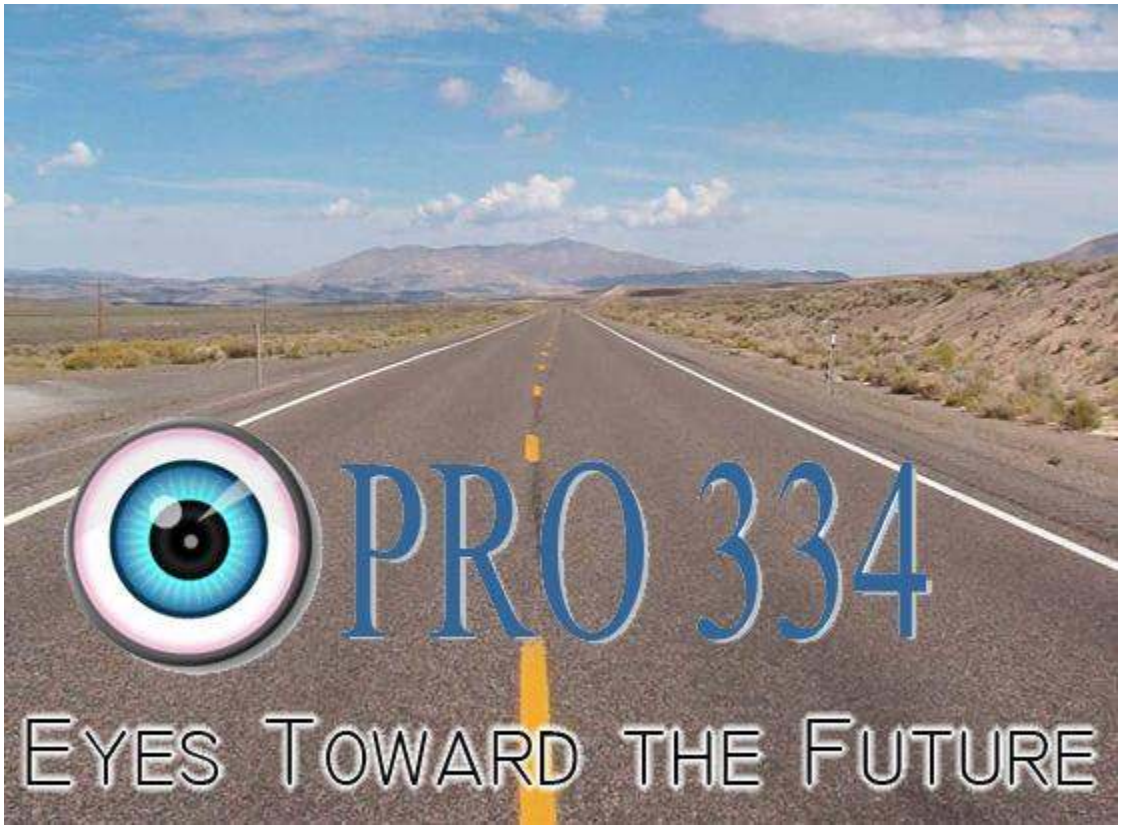
PLANNING FOR HUMAN

IMPLANTATION OF A

CORTICAL VISUAL PROSTHESIS



Fall 2009 IPRO 334 Final Report
The Interprofessional Projects Program

Illinois Institute of Technology

Chicago, Illinois

Executive Summary

We are providing a consultation to the sponsor, the IIT Visual Prosthesis Team, on how to proceed with preparation for human implantation of their intracortical visual prosthesis, which will be accomplished by researching different aspects and requirements for said implantation with an emphasis on subject perspective and selection. The device itself consists of electrode modules implanted in the visual cortex of individuals with blindness. By inducing a current in the modules, the volunteer would potentially perceive phosphenes, or light perceptions similar to camera flash afterimages, which could possibly form functional vision. The sponsor's study would be focused on developing an assistive device for individuals with complete blindness.

The previous semester of this IPRO had researched a large number of topics related to the technical aspects of the device, the medical risks, the psychological impact, as well as the impact in ethical and political terms, as well as the effect on media. Though ambitious, the lack of focus and solid conclusion in their report was to their detriment. Their wealth of information, though over-reaching, will provide a starting point for future semesters.

Many ethical issues may arise during our research. We must be careful not to succumb to any professors' or sponsors' biased opinions, or the bias in the opinions of other people. We must be sure to cite all sources which we use. We will need to receive appropriate certification before assisting in focus groups. We will maintain the confidentiality of the data acquired during our research. Finally, we will be sure to not do anything illegal during the course of our research.

The cost of our IPRO project only includes expenses listed on the budget. All costs relating to the actual device are covered by the sponsor.

The solution to our problem will be to create a comprehensive, as well as scientifically and morally justified, framework for the selection of potential volunteers. This solution will be implemented as an impartial consultation with the sponsors. Also, a report will be created analyzing the current progress of the sponsor's intracortical visual prosthetic device and what further action is required on behalf of the sponsor to begin human implantation trial(s). This report will include details on the sponsor's conformation to US Food and Drug Administration (FDA) guidelines and further requirements to fulfill prior to implantation. The report will also include recommendations for volunteer education and care both before and after the procedure, an analysis of practical uses of the device, an assessment of the planned experiments for the volunteer, and an analysis of possible ethical dilemmas related to human implantation of the sponsor's device.

Purpose and Objectives

We, EYEpro 334, are committed to making a positive step towards the assessment of the implantation of an intracortical visual prosthesis in a human. The purpose of the IPRO is to research the current state of the device so that we can make suggestions and pose questions to the sponsor regarding the human implantation step. With the fresh perspectives and multiple disciplines of the IPRO team, the sponsor should benefit from the varied suggestions and be aware of issues discerned from outside observers.

The device consists of a camera to capture data from the surroundings. From there the information is interpreted by an external processor which will then signal the stimulation modules implanted in the visual cortex via magnetic induction. The modules each consist of 16 electrodes attached to a controller chip. All power is supplied through magnetic induction from the external device. This device is aimed at providing low resolution visual perception to persons with blindness. For the initial study, the volunteer would not be expected to receive complete usable vision. This study is meant to examine the functionality of the device in a human brain.

The figure shown above is an artist's rendition of the device supplied by the sponsor. Shown is the mounted camera device, which transfers the data to the implanted modules. The module is shown to scale with a penny and the electrodes to scale with a single strand of hair. The electrodes then stimulate the visual cortex to induce phosphenes.

Our objective is to research the issues that volunteers should feel concerned about from a medical, technical, and ethical perspective by:

- Creating a comprehensive, as well as scientifically and morally justified, framework for the selection of potential volunteers.
- Creating a report analyzing the current progress of the sponsor's intracortical visual prosthetic device and what further action is required on behalf of the sponsor to begin human implantation trials. This report will include details on the sponsor's conformation to FDA guidelines and further requirements to fulfill prior to implantation.

The sponsor for the IPRO is the Intracortical Visual Prosthesis Team at IIT. The team is comprised of the members from the University of Chicago, Huntington Medical Research Institutes in Pasadena, CA, EIC Laboratories in Norwood, MA, and Micro Probe Inc in Frederick Maryland. The sponsor is requesting consultation on how to proceed with preparation for human implantation which will be accomplished by researching different aspects and requirements for implantation and patient selection.

There are several issues that the sponsor has encountered. The problems being addressed in our IPRO are such:

- The sponsor is having difficulty applying animal models to human volunteers.
- What are the ethical considerations in selecting volunteers?
- There could be special considerations for our target volunteer pool (individuals with blindness).
- It is difficult to know whether a given plan of informed consent is good enough to actually inform the patient.
- There is no current outline for selecting volunteers.
- It is uncertain whether or not the device is actually ready for human implantation.
- It is unknown if there will be an issue with brain plasticity in volunteers who have been blind for an extended period of time.

Through our research, we have also found problems that similar devices have experienced. Those pertaining to the sponsor's device are listed below:

- There is a problem of brain shrinkage due to electrodes.
- There are various problems with chronic implants.
- Dealing with heat dissipation can be a problem for some implants.
- Alternative materials for in vitro electrodes (ex. titanium nitride, platinum, etc.) are better than others for certain applications.
- There is an issue with the external use of power and its level of dissipation to last the device for a longer period of time.

Organization and Approach

The team began the semester by developing their objectives through team building and brainstorming sessions. As a result of these beginning sessions, the team split into two sub-teams according to the goals created: Team A and Team 1. Team A was meant to deal with questions surrounding volunteer selection, while Team 1 was to focus on regulatory hurdles and analyzing the sponsor's work along with similar devices. As such, the research methods were different for each team. In retrospect, the forming of two teams created a rift in the overall team. It was hard to bring the two teams together to create a cohesive final report, and one team often found itself ignorant of the other team's progress.

Within each sub-team, a leader, a recorder and a spokesperson were chosen. The whole team also appointed a leader that would be responsible for managing the time of the IPRO and keeping track of deliverables. An iGroups moderator for the team was also appointed to manage the iGroups files, discussion, and calendar tasks.

Team A began the semester by dividing further into three groups. Each group was responsible for a different aspect of volunteer selection, though they were encouraged to share relevant information between each group. The three groups were physiological, psychological, and ethical. Each group came up with questions that they would attempt to answer through their research. They focused on one question in particular and then moved on to the next one. To aid in this process, reports were required for each question researched and due dates were set. If needed, follow up research was also assigned. It was thought that in this way, the research would stay focused. In addition, every other week, the questions of each group were re-evaluated to make sure that they still fit into the overall goal of making a framework for subject selection. A revisions manager was appointed to keep a detailed log of the changes made to the questions or objectives of the team and the reasons they were changed. For the most part, research was done using Galvin Library and other online searches to find relevant articles and studies that could help answer the questions posed by the team. However, focus groups being conducted by the sponsor concurrent to this IPRO were also useful in inspiring questions to answer.

Team 1 approached the problem by first developing their knowledge of the sponsor's research to understand the progress of the sponsor in the development of the device, and also to gain insight into the sponsor's prospects and concerns regarding the device. This initial research involved finding and analyzing the sponsor's publications to gain a fundamental understanding of operation of the device and of the progress the sponsor has made towards conducting a study in a human volunteer. In addition to researching the sponsor's device, Team 1 also researched publications by other groups which were working on devices similar to the sponsor's device. This research was conducted to survey other visual prostheses and gain an understanding of the different approaches being currently researched to improve vision in those with blindness.

Both teams conducted interviews – facilitated by Professor Troyk – of experts who could offer further insight into understanding the ethical, legal, and medical aspects of visual

prosthetic implantation studies. Leo Towle Ph.D. was interviewed on the neurological and medical consequences of the device. Dr. Towle was able to answer questions with respect to the medical procedure of the device implantation, as well as other questions with regard to the day to day living of the participant. Lawyer Don Weber was interviewed on the legal obligations the sponsor has to the volunteers and understanding of informed consent. Mike Davis, Ph.D., was also interviewed on the ethical implications and concerns regarding human implantation. Dr. Davis provoked thoughtful discussions about the ethical implications of a study involving human volunteers. The use of these experts offered the team insight into the problem from a medical, legal and ethical perspective.

The team used internet databases through the Galvin Library, including PubMed, EBSCOhost, Academic Search Premier, ISI Web of Science, and Google Scholar, to comprise the bulk of their research. US patents were also examined online. It was decided to use this method of researching because it was easy to obtain articles and studies quickly through the internet with the help of Galvin Library. Information obtained in this form was used in class discussions and lead to further debates in less than straightforward issues, such as ethics, that were still necessary for providing useful suggestion to our sponsor.

Analysis and Findings

At the end of the semester, we were able to provide suggestions and concerns to the sponsor in the form of a report, which is attached in the appendix. The major points of each suggestion are listed here.

The IPRO team suggests that risk analysis be performed on the current state of the device. This needs to be done before the selection of the volunteers in order to form a formalized list of risks associated with the device.

A formal code of ethic for the sponsor's team needs to be developed. This code is important because it will help guide the team through their research, as well as provide assurance to the public.

The IPRO team recommends that the sponsor compensates volunteers on an individual basis. The compensations are suggested to be based on a questionnaire format developed to assess how much each individual participant is entitled to.

Regarding the volunteers right to withdraw, after considering contrasting opinions, the IPRO team came to the conclusion that the right to withdraw should be left to the volunteer.

Informed consent is a crucial part of any study dealing with volunteers. The IPRO team has proposed a system to ensure that the volunteer is properly educated in order to give

informed consent. In situations where the volunteer speaks a different language, has difficulty understanding English, or prefers to read Braille, special considerations need to be taken into account. Two pre-operative tests were also proposed in order to serve as a preliminary screening process, as well as a baseline for comparing any changes that have occurred during the sponsor's research.

Literature suggests that the visual cortex is recruited for other functions in individuals whose onset of blindness occurs before age 5. This might have unexpected ramifications for the sponsor's research. Hence, the IPRO team does not recommend selecting such individuals at first. They may be selected later on in the study when more data needs to be collected from a larger pool of volunteers.

The report, which includes these suggestions and a bibliography of our sources, was supplied to our sponsor on December 4, 2009.

Conclusions and Recommendations

After a semester of researching literature related to the device and assessing the current state of the device, it is the conclusion of the IPRO 334 team that the sponsor is not ready for a human implantation study at this time.

There are definitely more issues left unresolved through the IPRO team's research that need to be addressed before the sponsor can consider human implantation. In our report, the IPRO team has tried to provide suggestions that would contribute to the furtherance of the sponsor’s study.

The IPRO 334 team recommends that future IPROs address the unanswered questions described in the report compiled this semester. The framework for subject selection must be further developed, supplementing it with new suggestions. Also, future members may want to further investigate the risks associated with this specific device. This IPRO has discovered the risks associated with similar devices, but there may be additional risks specific to this device which have not been discovered or researched yet. As for team organization, in order to avoid forming two polarized teams, the next IPRO should create either overlapping sub-teams or have a team leader outside of any sub-teams to solely assign tasks and overlook their progress.

Appendix

There were no expenses for this team.

Team Members, Roles, and Authorship

David Bern – iGroups Moderator

Authored:

- "Language Barrier" Section of Sponsor's Report
- Midterm and Final Presentation
- Poster
- Project Plan
- Final Report

Content Edited:

- "Pre-operation and Post-Operation Protocol" Section of Sponsor's Report
- "Failure Mode Effect Analysis" Section of Sponsor's Report
- "Volunteer Education" Section of Sponsor's Report
- "Brain Plasticity" Section of the Sponsor's Report

Shanyl Chen – Spokesperson (Team 1)

Authored:

- "Test for Functionality" Section of Sponsor's Report
- Midterm and Final Presentation
- Project Plan
- Final Report

Mary DeRoo – Sub-team Leader (Team A)

Authored:

- "Volunteer Understanding" Section of Sponsor's Report
- "Preoperative Tests" Section of Sponsor's Report
- "Pre-existing Medical Conditions" Section of Sponsor's Report
- Midterm and Final Presentation
- Brochure
- Poster
- Project Plan
- Final Report

Content Edited:

- "Informing Volunteer of Other Options" Section of Sponsor's Report
- "Voluntary Withdrawal" Section of Sponsor's Report
- "Determining Autonomy" Section of Sponsor's Report
- "Brain Plasticity" Section of the Sponsor's Report
- "Conclusion" of Sponsor's Report

David Gorski – Team Leader

Authored:

- "Voluntary Withdrawal" Section of Sponsor's Report
- "Determining Autonomy" Section of the Sponsor's Report
- Midterm and Final Presentation
- Brochure
- Project Plan
- Final Report

Thomas Kelley – Treasurer

Authored:

- "Pre-Operational and Post-Operational Protocol" Section of Sponsor's Report
- Midterm Presentation
- Project Plan
- IPRO 334 Logo
- Final Report

Content Edited:

- Lead editor of Final Report and Sponsor's Report

Alexander Leasenby – Spokesperson (Team A)

Authored:

- "Brain Plasticity" Section of Sponsor's Report
- "Inform Volunteer of Other Options" Section of Sponsor's Report
- "Pre-existing Medical Conditions" Section of Sponsor's Report
- Midterm and final presentation
- Poster
- Brochure
- Project Plan
- Final Report

Content Edited:

- “Background” Section of Sponsor’s Report
- “Voluntary Withdrawal” Section of Sponsor’s Report
- “Preoperative Tests” Section of Sponsor’s Report
- “Volunteer Understanding” Section of Sponsor’s Report
- “Language Barrier” Section of Sponsor’s Report

Zhi Li – Minute Taker (Team A)

Authored:

- “Background” Section of Sponsor’s Report
- “Code of Ethics” Section of Sponsor’s Report
- “Compensation” Section of Sponsor’s Report
- “VoluntaryWithdrawal” Section of Sponsor’s Report
- “Conclusion” Section of Sponsor’s Report
- Midterm and Final Presentation
- Project Plan
- Final Report

Maham Subhani – Minute Taker (Team 1)

Authored:

- “Failure Mode Effect Analysis” Section of Sponsor’s Report
- “Conclusion” Section of Sponsor’s Report
- Midterm and Final Presentation
- Poster
- Brochure
- Project Plan
- Final Report

Aanchal Taneja – Sub-team Leader (Team 1)

Authored:

- “Testing Matrix” Section of Sponsor’s Report (Removed from Report)
- “Conclusion” Section of Sponsor’s Report
- Midterm and Final Presentation
- Poster
- Brochure
- Project Plan
- Final Report

*Hannah Pyrkh** – Minute Taker (Team A)

Authored:

- Midterm Presentation
- Project Plan

*Hannah Pyrkh was a member of this IPRO until October 26, 2009 when she withdrew from the class due to illness.

Final Report for the Sponsor

I. Background

The IPRO 334 team is comprised of nine students from different disciplines and cultural backgrounds. The role of this team was to help the sponsor identify and suggest areas or issues that need to be addressed to begin the human implantation of an intracortical visual prosthesis. The IPRO team understands that the device is intended for research purposes and is not at a stage where it can be considered as a treatment for blindness.

The IPRO team approached its task from two different, but equally important, directions. To do this, they split into two sub-teams, which were tasked with analyzing the needs of this project from a potential volunteer's perspective and a researcher's perspective respectively.

Our objectives were:

1) To assemble a framework for the selection of potential volunteers.
2) To assess the current state of the device and provide a useful suggestion based on our findings.

3) To assimilate the work of both sub-teams into a comprehensive report

II. Technical Concerns

1. Creating a pre-operation and post-operation protocol

Based on the team's research, the IPRO team recommends that the following are included in the pre-operational protocol for surgical implantation of the device.

1. Conduct an allergen test on all volunteers for all materials that compose the device and the insertion tool.
2. All volunteers must be medically cleared for surgery by an internist, or a specialist such as a cardiologist.
3. To determine the effectiveness of the device, prior to implantation, the visual performance of each volunteer is to be documented, including a validated low vision quality of life questionnaire to asses the overall benefits of the prosthesis when used in the home and other settings outside of the clinic.

Based on the team's research, the IPRO team recommends that the following are included in the post-operational protocol for surgical implantation of the device.

1. Maintain a watch of all volunteers until a primary safety endpoint is reached to capture surgical complications and potential long-term adverse events. The endpoint is to be determined by the sponsor's surgical team based on cumulative

and persistent rates of a group of adverse event rates obtained from the medical literature for similar invasive surgical procedures.

2. After implantation, the effectiveness of the device should be determined by creating an assessment of the volunteer's phosphene "visual field" map when stimulating individual or pairs of stimulus array electrodes. To accommodate for a prosthesis relying on an external mounted camera for visual input, it is advisable to generate a phosphene map while simultaneously monitoring the subject's camera and head position to account for movements during stimulation of individual electrodes.
3. In accordance with the recommendations of the most closely related FDA document on the subject, they advise in their 2009 Investigational Device Exemption Guidance for Retinal Prostheses to plan to follow volunteers for three years or longer, but to be prepared to address the possibility of post-approval studies that may continue 5-10 years after implantation (FDA 16).
4. Volunteers' visual performance should be evaluated at intervals of at most three months for the first year and at intervals of at most six months thereafter.

2. Tests for functionality

Before this device is implanted into a volunteer, it needs to pass through a series of tests for functionality. Functional testing is done to test the long-term functionality of a device in vitro. For the device, certain parameters need to be tested to ensure that it not only works, but also does not cause harm to the volunteer.

The electrodes in the array need to be tested individually to ensure their functionality. These tests include determining the range of stimulation that the device can provide. Within this, the optimal safe stimulation range for electrodes in the human brain needs to be determined. Characteristic behavior of the stimulation also needs to be found and tested: such as the charge of the pulses, the resistance of the electrodes, etc.

Other functional tests for the stimulator array include: tests for DC resistance, dielectric strength and AC impedance, which are important to ensure that the device complies with electrical connection and conduction specifications; tests to ensure that the array is still functional after being submerged in saline solution for a period of time as well as the ability of the stimulator array to function after being implanted using the high speed insertion tool. This is by no means an exhaustive list of all the functional tests that need to be performed on the device. This list is just to direct the sponsor in the right direction towards the course they should be heading in terms of their thinking for performing functional tests on this device.

Since this is an electrical device, it will generate heat while it is in use. The question has been raised as to how is this heat dissipated, and the sponsor has replied that, in theory, because of the small amounts of power employed as well as the body's homeostatic ability (especially in the case of the brain), the body will be able to take care of all heat dissipation on its own without any help.

There has been no evidence of any study on how much heat the device emits while in use, as well as to how effective the body, the brain in particular, is at dissipating this heat. It is recommended that actual tests be performed on the device and the brain's

ability to dissipate heat also be gauged so as to not place the volunteers into any unnecessary risk.

The members of IPRO 334 suggest that functional testing needs to be performed on the stimulator array of the device, as has not yet been done on the current prototype. The thinking of the sponsor, while conducting the functional tests, should be along the lines of the examples mentioned above. In addition, studies should be done into the brain's compensation with the heat generated by this device while it is working.

3. Failure Mode Effect Analysis

The U.S. Department of Health and Human Services describes the importance of performing a risk analysis. Failure Mode and Effect Analysis (FMEA) is a method used to determine the quality of the engineering of a product. It helps identify and counter weak points of the engineering of a device and is used in the early conception phase. It ensures that the device or product is easy to use as well as valuable and not harmful. The FMEA analyzes potential failure modes of a device. The failure modes are classified based on severity or by determination of the effect they will have. Failure modes are any errors or defects in the device which can potentially and actually affect the volunteer. Therefore, the procedures of FMEA should be employed to further analyze the risks associated with the specific prosthetic device.

A description and analysis of all the increased risks to which the volunteers will be exposed to needs to be included in a report or plan. The report should also include how these risks will be minimized. The IDE (Investigational Device Exemption) application

should describe the method used to conduct this risk analysis. The application should also include sufficient detail to support the method that was chosen to analyze the risks.

To fulfill the risk analysis requirement, it is recommended that a Failure Mode and Risk Analysis summary on the electronic components and circuitry be performed. The Failure Mode and Risk Analysis summary should identify and assess the risks due to any potential electronic hazards/failures, the potential severity of these risks, and how to eliminate or reduce them.

The possible risks and failure modes discussed by the team are further discussed below. There were a variety of factors relating to the device that needed to be considered to determine if they would or could cause any potential harm. The temperature of the device is an issue of concern. There is no current evidence of how much heat the device emits. It is also currently unknown how well the body and the brain will dissipate heat. Therefore, it is something that needs to be further investigated to determine how the body will react to the heat. It is also important in determining which materials are the best choices to be used.

The diameter of the electrodes is also a technical concern. It was discovered that the thicker the diameter of the electrodes, the more likely they are to stay in place and work properly. But, the thicker the electrode, the greater threat to the volunteer. The small electrodes also have the risk of breaking more easily than the larger, thicker ones. Therefore, the diameter is something that needs to be looked into further in order to assure that there is a balance between ensuring that the volunteer is under no threat but the electrodes are also working at optimal levels. The thickness of the electrodes can also

potentially affect the brain. The IPRO Team also believes that the sponsor should be confident in the ability of the electrodes to function without breaking so that the risk of damage due to breakage of electrodes can be minimized or eliminated.

Aside from the potential damage posed by an electrode, the brain may also experience trauma or swelling due to damage incurred during normal activities, such as playing sports or accidents such as falls. It is currently unknown whether the device will be affected by brain trauma or the brain shaking back and forth. It could potentially cause the device to break or even damage the brain, because the device is anchored onto the brain. The sponsor needs to further look at how the device and the brain will be mutually affected by accidents or trauma. Similarly, the arterial blood pressure in the brain could also have an effect on the device. Things such as sneezing affect the body internally and also cause the brain to shake suddenly, which again can damage the device.

This FMEA needs to be performed in order to understand the potential hazard posed by these risks, as well as to find other potential risks. It is important to analyze the risks in order that they can be fully understood and can be minimized. It is the responsibility of the sponsor to evaluate the hazards and find these risks so that it can be ensured that the volunteer is at minimal risk. The risk analysis should be done in a formalized manner in the early stage of the device so that improvements and adjustments can be made to the device if needed due the potential presence of the risks presented in this report as well as other risks that have not been found yet. Additionally, it would be hard to appear legitimate to potential volunteers if the risks of the device have not been formally analyzed.

III. Ethical Concerns

1. Code of Ethics

To the IPRO team's knowledge, the sponsors do not currently hold a common code of ethics. This is undesirable, because in the event of a crisis, this may create a conflict of interest amongst the members. The World Medical Association (WMA) Declaration of Helsinki is the obvious first choice, as it is a standard code of ethics that many scientific journals require researchers to adhere to (Chwang 378), and its most recent revision in 2008 makes it clear that it is intended to be a set of "ethical principles for medical research involving human subjects"(59th WMA General Assembly). However, it does not explicitly account for research involving brain surgery or implants. The IPRO 334 team feels that, by expanding on the principles laid out in the Declaration, a better set of guidelines may be provided for the sponsor.

Article 16 of the Declaration states that "The responsibility for the protection of research subjects must always rest with the physician or other health care professional and never the research subjects, even after they have given consent."(59th WMA General Assembly). The statement is vague, because 'protection' is not well-defined. It is necessary for the sponsor to consider the risks involved in the study, and to set a common ethical bar that would more clearly define when the volunteer may be exposed to reasonable and manageable risk, and when the volunteer's decisions must be overridden by the researchers' concern for their well-being. This requires knowledge of the risks posed by the device itself upon implantation. The studies with animal models to date

were not done with the completed device, therefore the IPRO team recommends that the sponsor first design and conduct a series of long-term safety and functional tests using a complete device with animal models before recruiting human volunteers for implantation.

Article 19 of the Declaration states that “every clinical trial must be registered in a publicly accessible database before recruitment of the first subject.”(59th WMA General Assembly). This does not apply to the sponsor's study, as clinical trials generally refer to drug trials conducted on large groups of people, whereas the sponsor's research involves a device implanted in a few selected individuals. Subjects, or participants in the study, must be chosen without data from clinical trials to support the choice. As such, the selection of volunteers should be based on available data from animal models as well as other relevant studies. It goes without saying that the data obtained from the study still needs to be registered in a publicly accessible database for the benefit of future research done with similar devices.

Article 24 of the Declaration states that “Special attention should be given to the specific information needs of individual potential subjects as well as to the methods used to deliver the information.”(59th WMA General Assembly). The sponsor is working with blind participants, which means that information would most conveniently be conveyed orally. Braille was considered as one channel of communication, and should be made available to volunteers who prefer that channel, but the IPRO team feels that verbal communication encourages persons with blindness who may not be fluent in reading Braille to participate in the study as well. The article also states that “If the consent cannot be expressed in writing, the non-written consent must be formally documented

and witnessed." The IPRO team recommends that the sponsor document the consent by making a video recording of the process as well as a written transcript.

2. Compensation

There is no doubt that compensation for the volunteers is necessary, but one of the issues that arises is the question of how much the volunteers should be given as monetary compensation. It is intended to offset the costs of participating in the research, not be the reason a volunteer chooses to participate. With volunteers potentially coming from diverse backgrounds, it is recommended that the sponsor compensate each participant differently, as appropriate. A highly-paid worker in some other company may be sacrificing a significant amount of pay to participate in the research, which justifies paying him more than, for example, an unemployed person. A questionnaire may be developed to help determine the rates for each volunteer. Volunteers must also be made to understand that there will be differences in compensation.

Some studies opt to pay their volunteers immediately whenever they attend the scheduled testing sessions. Others choose to pay them on completion of the study. The IPRO team feels that payment upon completion would help encourage the participants to continue with the study. However, because the volunteer has the right to withdraw at any time, they should be able to receive compensation upon withdrawal. Credit for payment should, therefore, be accumulated over time as the volunteer participates in the study. Thus, volunteers are compensated for as much time and effort as they have put in to aid the research.

3. Voluntary Withdrawal

According to the Declaration of Helsinki, "The subject should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal." (Helsinki) What does this mean for the sponsor? It is a general consensus among researchers and volunteers that there is a right to withdraw at any time if they wish to. The principle of respect for persons, outlined in the Belmont report, requires that an autonomous person's decision to withdraw from a study be respected, even after consent has been given. Although some people debate the absoluteness of this right (Chwang, 370-378), the IPRO team believes that in the case of this research, the volunteer's right to withdraw should be protected for a few key reasons. First, it is the IPRO team's opinion that, ethically, a volunteer cannot be held in a study against their will. In the unlikely event that that there is a misunderstanding about the study, and the volunteer does not agree with the way that the study is going, then they should not be forced to continue. The team feels that at the point that a volunteer is forced to carry on with a study that they no longer wish to participate in, the researchers are not looking at the participants as volunteers but as lab animals. The IPRO team recommends that it is in the best interests of the sponsor to comply with this social expectation. Second, the volunteer is not expected to suffer undue harm from withdrawing during the study, which would justify the consideration of having the volunteer to waive his or her right to withdraw. The cost of the research may be high enough to consider Chwang's argument for allowing the waiver of a volunteer's right to withdraw, but the IPRO team thinks it is still more important at this time to avoid scandal

that would detract from public opinion of the research and the sponsor. The IIT Research Team should make it possible for volunteers to withdraw at any time.

Should the situation arise that a volunteer no longer wishes to participate in the study, there are a few responsibilities that the team needs to follow through with before letting the volunteer go. The first of which is to make sure that the volunteer know what risks they are incurring by ending the study prematurely. Another thing that the team needs to do is to retain all external components of the device. This will render the inter cortical modules useless and dormant, which takes away any risk of malfunction that could damage the brain if left untreated. In spite of this precaution, if the volunteer withdraws without informing the team, it could be difficult to take the external devices from them. One way to avoid the continued use of experimental external equipment is to not allow them to take these devices home with them. This was decided to be an unreasonable precaution, as continuous use of the device is needed for the volunteer to train his/her brain in its use. If the external components are left in the possession of the volunteer, however, then the team needs to program some safeguards that will keep the volunteer from using the device after withdrawing without telling anyone. An example of these safeguards would be programming a time delay that causes the device to stop transmitting if it is not reactivated. Another way to stop the device from working would be to use a battery that needs to be charged by the research team.

IV. Informed Consent

1. Informing volunteers of alternatives

This project is unique in that it stimulates the visual cortex directly to produce visual perception; however there are many other visual prostheses in development. In some situations, the other devices may be less risky or more beneficial, whether from less invasiveness of surgery, in the case of all non-brain implants, or an increased resolution potentially available from other devices. Some options do not require surgery at all, such as sensory substitution (Meijer). Participation in this study also runs the risk of exclusion from future studies. Though other studies may exist for visual prostheses, many are still in experimental and research stages as well and therefore not necessarily within the grasp of the volunteer. Therefore, it is the opinion of the IPRO 334 team that the volunteer must be appropriately informed of these options before the IIT team can ethically pursue their involvement. Informing potential volunteers of other options is brought up in the Belmont Report and the Declaration of Helsinki (two standards for research-study ethics) supporting the opinion that this should be included in the informed consent education process.

Due to the required brain surgery, the sponsor's device requires the most invasive surgery when compared to other prostheses, as the skull must be cut into and the brain exposed. There is therefore potential for a bacterial infection of the brain, called meningitis, which can cause inflammation and has a high mortality rate (Richard V Goering). However, the sponsor's device has the advantage of requiring the least possible amount of the visual pathway to be intact, as only the visual cortex needs to be functional. Implants stimulating the optic nerve are less invasive, requiring only eye surgery which carries much lower risk – especially for those with already damaged eyes and vision (J. Delbeke). However, this implant will not be functional if the volunteer has

a damaged optic nerve or visual cortex. Retinal implants carry a similar risk (Yanai et. all), however they do not function in the case that the retina is completely non-functioning, as well as the previous criteria. Retinal implants also carry the advantage of a pixel-like input, leading to easy mapping of the visual field. Least invasive is a sensory substitution device, which uses another sense to replace a missing one. The most common sensory substitution for individuals with blindness is replacing sight with sound or tactile sensation. A product known as the vOICe, uses a covert camera connected to a notebook PC to assist with obstacle avoidance and environmental mapping. Similarly, there are tactile systems, such as the Forehead Retina System, which detect objects and obstacles and translate this to vibration via a worn device (Meijer). Another benefit to this option over surgical alternatives is that these are both commonly available.

Additionally there is a risk of informing the person too much. It is the suggestion of the IPRO group that basic information is given on the options, giving the individual freedom to research the subjects more if interested, or to ask questions about them. The suggestion of a chart-style organization listing the benefits, risks, and applicability was made by the IPRO 334 group; however, without vision the potential volunteers would be unable to use the information in this format. A chart may still make the information easily organized for researchers and any sighted family members supporting the potential volunteers at information sessions.

2. Volunteer Understanding

Before a volunteer can be selected to undergo a potentially dangerous and experimental procedure, they must be properly informed of the risks, potential benefits,

effects on their lives, alternative options, etc. However, giving the volunteer a stack of information is one thing, but making them understand the material is quite another. The Belmont Report breaks down informed consent into three elements; information, comprehension, and voluntariness. It mentions that the ability of the volunteer to comprehend the information is largely dependent upon the organization of the information given (Commission for Protection). Thus, researchers should take great pains in designing a structure in which to inform the volunteer that will adequately prepare them to make a difficult decision.

The structure of the informed consent should include sessions in which a knowledgeable person informs the volunteer, a reference of the information for the volunteer to take away with them, and a way for the researchers to determine whether everything was understood.

1. **Information Sessions.** The information sessions must be conducted multiple times. It has been established that repetition increases the retention of information in many psychological studies. It is proposed that there should be at least three information sessions. The first should be with potential volunteers, detailing the procedure, risks, and possible benefits of the device and information that is relevant to their immediate decision to continue with this study. A second session should be conducted with the selected volunteer that references everything in the informed consent document. After this session, the reference material should be sent home with the volunteer and the oral exam should follow in a separate session. Finally, a third session should be conducted to clarify any questions identified by the volunteer or any misunderstandings as discovered from the oral

exam. These sessions should provide the repetition needed for retention of information and understanding. Also, during each of these sessions, the researchers must question the volunteer about the amount of information being given. In a 1980 study by Cassileth, Zupkis, Sutton-Smith, and March, 200 cancer volunteers were given the same amount of information to constitute their informed consent. When tested on the information, the volunteers that had earlier stated that the information received was "just right" scored notably better than those who had stated it was "too much" or "not enough" (Silva and Sorrell 2). Since the sponsor's study is anticipated to have a single participant, it would be possible to tailor the information given to their needs. By giving the volunteer an amount of information that is "just right" for them, the understanding of the volunteer should be greater. In situations that the volunteer perceives the information as "too much", additional sessions can be scheduled to augment their understanding in smaller doses.

2. **Reference.** The participant should be given the appropriate information in an organized and portable form. This can be given according to the volunteer's preference; in Braille or audio format. Either way, the information must be organized and specific topics should be easy to reference. This would involve labeled tabs in the Braille format and separate audio tracks in the audio format. It is important for the participant to have a reference to take home so that they can share the information with others that they feel are vital to their decision making process. Also, according to a study by Morrow, Gootnick, and Schmale, cancer volunteers who were able to go home before signing an informed consent form

received significantly higher scores when tested on their understanding of the information. In addition, volunteers able to take the form home also generally had a better understanding, though this was not found to be statistically significant (Silva and Sorrell 2). Thus, the volunteer should be able to go home and digest the information before the oral exam.

3. **Oral Exam.** The Belmont Report (Commission for Protection) mentions the inclusion of some sort of test to assess the understanding of the volunteer before they consent to a study. This should be done in the form of an oral exam, so that the time can be easily followed with a question and answer session where the volunteer can put forth questions that came up as they thought about the procedure and device. Also, by requiring the volunteer to respond to questions during the exam, they will be participating in a form of active learning. However, it should be stressed to the volunteer that a "passing score" is not required to continue on with the study. The exam is merely to be used as a tool to assess the volunteer's understanding and decide what information should be expanded on in the follow-up information session. Also, in order to reduce stress that may unintentionally result from the exam, it should be conducted more as an informal interview and referred to as such.
4. **Involving Friends and Family.** The IPRO 334 team also suggests the inclusion of the friends and family of the volunteer in the education process. If the people involved in the eventual decision of the volunteer to participate have knowledge of the device and understand the risks and benefits, they will be more capable of having active conversations to promote the volunteer's understanding. The IPRO

334 team realized through the course of the semester that describing the vision expected by the sponsor's device to sighted individuals is difficult. When told that the implants will help the blind, people tend to assume that it will be complete vision. When explained further, there was still confusion over what amount of vision the volunteer will be able to perceive. The IPRO 334 team suggests some sort of visual representation of what type of vision is expected for the participant. Although no one is sure exactly what they will see, an approximation could still make the expectations better understood. One member of the IPRO 334 team, David Bern, wrote an application in python that takes an input from a webcam and creates a picture that represents this approximation. It can be adjusted to show extremely low resolution of the camera input. It is felt that this could be a useful learning tool for sighted individuals to understand the expected results.

It is a concern of the team that volunteers may feign understanding of the risks and benefits of the procedure or unintentionally mask their true expectations. For instance, they may say that they do not have unrealistic expectations for the device without realizing that they actually do. It is the suggestion of the IPRO 334 team that a family member be present during the oral exam. It is believed that this would create a more comfortable environment for the volunteer and elicit a more honest and realistic response from the volunteer. Unfortunately, the disadvantage of having the family member or friend there is that they may urge the volunteer towards a decision with which they are uncomfortable. However, the IPRO team believes that the benefits of family or friend involvement outweigh the risks.

3. Finding a way to determine autonomy

Autonomy of the volunteers is a crucial element to the study. If the sponsors are not sure that the volunteers are able to make their own rational decisions, then it cannot be know if they really want to be a part of the study. However, there is also the risk of underestimating the volunteers based on preconceived notions about their situation. With this study, there should be respect of all volunteers' autonomy until it is proven that the volunteers are unable to make their own rational decisions. It is not the job of the researchers to protect the volunteers. However, it is the responsibility of the researchers to inform the volunteers.

As was discussed in the *Volunteer Understanding* section of this report, the information sessions can be tailored to the individual volunteers. This is important because every volunteer will have different circumstances and there may be information that will be pertinent to one volunteer that may not be as important to another volunteer. One of the key pieces of information that should be given to the volunteers is the risks that are specific to their situation. For instance, if the volunteer is the sole supporter of their family, they need to be informed that this may cause them to be unable to work for a while.

There is also the point at which the researchers have to realize that some of the volunteers can not make their own reasonable decisions. This is a sensitive issue because even though a volunteer may not be autonomous, they may still want to participate. It will be beneficial to include a psychological evaluation into the volunteer selection process and thus screen out those who are not autonomous.

V. Volunteer Selection

1. Pre-operative tests

Past experiments involving visual prostheses have conducted preoperative tests and demonstrated their use in selecting potential volunteers to receive the prostheses. In an experiment conducted by (Yanai, et al) involving a retinal prosthesis, an electrically evoked potential was recorded by passing current from a Burien-Allen corneal electrode to an ipsilateral retroauricular electrode and it was recorded whether or not the volunteer saw light from said current. A darkness adjusted bright flash test was also performed to determine whether or not volunteers could perceive light and at what level. Intraocular stimulation of the retina was performed during surgery by placing an electrode array on the internal limiting lamina in the macular region and stimulated for testing. While many of these tests are very retina specific, conducting preoperative tests on volunteers would be a useful aid in selection. For instance, determining the level of usable light perception in a potential volunteer could help to influence a decision about their participation by the sponsor and the volunteer themselves. While there are fewer tests that can be safely done directly with the visual cortex preoperatively, as most would involve brain surgery, transcranial magnetic stimulation is a noninvasive test that could provide insight in the selection process.

1. **Bright Flash Tests.** Dark adjusted bright flash tests were used by (Yanai, et al) to determine the level of light perceived by a participant with blindness. The participant waited in a dark room for some time before bright flashes were produced. Some participants who had previously been diagnosed as having no

light perception were still able to perceive the bright flashes.

By performing the bright flash test on potential candidates, it can be determined the level of light perception that they have, despite previous diagnoses which may be inaccurate. The device is highly experimental and the possibility of the volunteer losing their pre-existing light perception is a possibility. The bright flash test would help the participant to recognize the potential loss of this perception and help them to make an informed decision about whether to participate in the study.

A secondary benefit to this preoperative test would be the information it would provide for the continued study of the device. By doing this test before and after the operation, the effect of the visual prosthesis system on light perception could be gathered. Though conclusive results about this effect could not be obtained through just one study, by repeating this as the sponsors conduct more human studies, more information could be gathered that would prove useful in future volunteer selections.

2. Transcranial Magnetic Stimulation. Transcranial magnetic stimulation (TMS) is a noninvasive way to produce phosphenes or scotomas in humans. By producing a high current pulse in a coil of wire placed somewhere in close approximation to the brain, though outside of the skull and surrounding epithelium, a magnetic field is created. This magnetic field induces an electric field that in turn causes current to flow in the brain, creating the previously

mentioned perceptions, phosphenes and scotomas, when the coil is positioned above the visual cortex (Hallet 147).

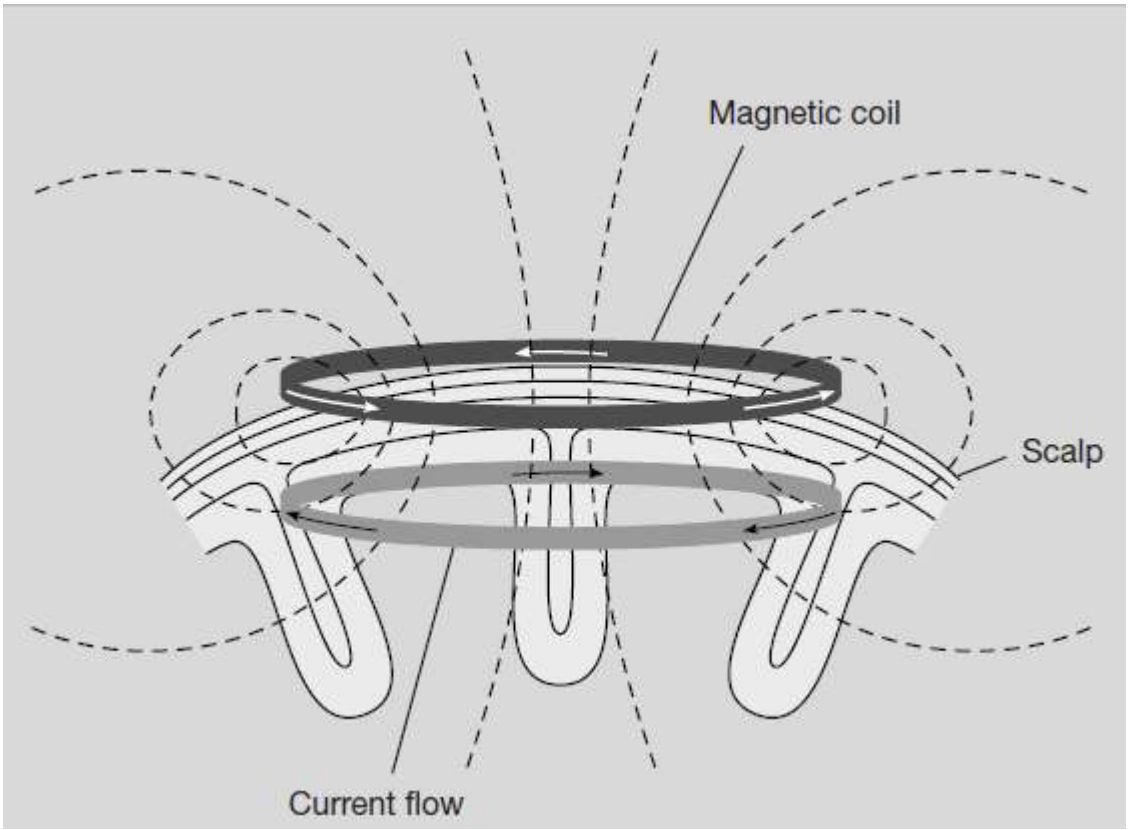


Figure 1: *Describes the mechanism behind TMS. The dotted lines represent the magnetic field produced by the current flowing in the coil above the scalp (Hallet 147).*

A detailed protocol for the use of TMS to produce phosphenes and determine the location of the stimulation in the brain can be found in a study by (Fernandez, et al), cited in the bibliography. The protocol used was able to produce phosphenes in a portion of blind participants. The participants with some vision or late onset blindness were more likely to see phosphenes. This protocol should be considered by the sponsor, as a systematic approach must be taken

when conducting tests to aid in selecting a candidate. The study also suggests the use of TMS to "…map the function of the remaining visual cortex in blind subjects devoted to vision and hence, aid in the determination of their suitability for the implantation of visual neuroprosthetic devices." It is the position of the IPRO 334 team to agree with this suggestion, as the production of phosphenes is the goal of the implant and this would help to assess the ability of a potential volunteer to produce them.

Also discussed, was the use of functional magnetic resonance imaging (fMRI). The idea was that the volunteer could visualize seeing a light. If the visual cortex is intact, the same location in the brain should light up in the fMRI as the part that interprets actual vision. It was decided by the IPRO team that this was not a reliable test, as fMRI does not have time resolution and asking the volunteer to envision a light is not reliable (Hallet 147).

In addition, as mentioned in the "Brain Plasticity" section of this report, the visual cortex can be recruited by other senses if the person was blinded before the age of five. It is possible that if the sponsor's prosthesis was implanted into such an individual, the stimulation from the electrodes could interfere with the senses to which the visual cortex has been reassigned. TMS could be used to determine the possibility of this interference in a potential volunteer who was blinded at a young age by testing if other functions are impaired while using TMS.

2. Brain Plasticity

An aspect of neuropsychology that needs to be taken into consideration for this project is the concept of brain plasticity, a term used to describe the ability of the brain to adapt to stimuli. This happens at various levels, but the general trend is that the brain's ability to adapt seems to wane with age. This is why before age three babies are able to go from learning basics of body mechanics to learning a language, while high school adolescents can struggle through several years of language and never attain fluency. On some levels, such as that of creating new habits, the actual change in brain structure is minimal; simply new connections being made between existing neurons. However, brain plasticity is concerned with much larger scale changes in the brain as well. A system known as cross modal reassignment is a form of neuroplasticity in which one type of sensory input replaces another. Using this, the human mind is able to recover, sometimes completely, from brain injury or disease, cognitive dysfunction, or sensory disability (Practical Memory Institute). The proposed mechanism of this is the reassignment of sections of the brain to either replace the missing or damaged sections (Hetherington) (Sabel), or employing unused sections of the brain to compensate for lost senses or function. The latter has been verified to occur in some individuals with blindness; in whom the unused visual cortex shows up active in functional imaging tests while they were listening to various pitches, when processing speech, when reading Braille and when processing tactile spatial information (Roder) (Gougoux) (Cohen) (Sathian).

The level of recruitment is not constant throughout individuals with blindness, however, and it seems to depend heavily on the age at which the person first became blind. In one study (Wittenberg), the volunteers were split into three groups: individuals who had been blind before age 5, those with blindness in which the onset was after the age of 5, and a control group of sighted volunteers. The individuals were then subjected to repetitive transcranial magnetic stimulation (rTMS) was used to stimulate the primary somatosensory cortex (S1- the area of the brain most responsible for processing tactile data) and test its connection to the early visual cortex (V1 and nearby areas). RTMS is the use of a fluctuating magnetic field, created by a powerful electromagnet, at different frequencies and intensities to activate or deactivate cortical areas noninvasively. While the S1 area was being activated by rTMS, the brain was monitored by positron emission tomography, or PET, which produces a three dimensional picture of the body's functional process via the gamma rays emitted by a biologically-active tracer introduced into the body. The areas with a greater positive difference of emissions showed more blood flow, and thus increased activity. In this study, individuals with earlier onset blindness consistently showed the most blood flow to their early visual cortex, showing significant activation. The group of individuals with later onset blindness showed less activation, and in a different pattern, and the sighted control group showed minimal activation. This showed data consistent with the general rule that plasticity decreases with age. Or in summary, those who were blinded earlier were better able to adapt to being able to use their visual cortex for tactile processing.

But the real question is whether or not this could be influenced by the implantation of an intracortical device. A similar study (Cohen) tested the functionality of

the visual cortex in individuals with early- onset blindness (again defined as onset prior to the age of 5). In this case groups of individuals with early-onset blindness were asked to read strings of Braille letters with and without rTMS being used to disrupt their visual cortex function. The group had additional errors in identifying the letters. They also had several significant qualitative observations: reporting negative sensations (such as "missing dots" or "dots feeling faded"), positive sensations (such as "phantom dots" or "extra dots"), and confusing sensations (such as the "dots don't make sense") (Roder).

This could be a significant problem in this study, as the intracortical device is supposed to stimulate this area to produce phosphenes. Instead the device runs a risk of causing tactile and auditory sensations in the individual which could be unpleasant and detrimental to attempts to read Braille and to assess their surroundings using auditory and tactile senses. It is the opinion of the IPRO 334 team that the implanted device would most likely cause similar sensations to transcranial magnetic stimulation.

In light of this research, it is the opinion of the IPRO 334 team that individuals with congenital blindness and blindness with onset before the age of 5 would not make ideal candidates. These individuals do not necessarily have to be excluded completely, but should be informed of the risk of possible interference as part of the education process leading to informed consent. As discussed in the preoperative test section, transcranial magnetic stimulation could be a good preoperative test to assess this phenomenon in each individual. Testing the device in these individuals could prove or disprove the problem, and deactivation of the device could stop any odd sensations. However, it may be in the interest of the researcher to look into excluding these

individuals for the first test, because it is to be done on such a small group of (1-2) volunteers.

In contrast to the articles mentioned above, a study conducted by Sadato et al measured the brain activity of individuals with blindness while reading Braille versus sighted individuals during similar tactile reading activities. In the study, the visual cortex was found to be the most active section of the brain for individuals with blindness, while it was completely inactive in the sighted volunteers. The major difference in this study was that there was no discrimination between persons with early onset or late onset blindness. The ages of onset were cited for the study 4.3+/- 5.5 years. While the age of onset of several of these individuals likely falls into the younger than 5 years old category, at least one did not. Therefore, there is some chance that the unwanted tactile senses could occur in these individuals. This could possibly be determined using transcranial magnetic stimulation as a preoperative test, as referenced in the preoperative test section of the report.

3. Language Barriers

Consideration must be given to a volunteer's language usage both in oral and written communications by use of the Braille writing system. As noted in "A Model for Intracortical Visual Prosthesis Research" by Troyk et al., when attempting to simulate a visual Braille system, volunteers in the Dobelle study were unable to match speeds attained during standard tactile Braille usage (Troyk 1006; Dobelle 111). A prosthetic which simulates a visual Braille representation would function by stimulating the visual cortex, while the visual cortex may also be required to read that same image. Sadato et al.

found that when performing tactile tasks, the visual cortex of a blind person is activated whereas the visual cortex is deactivated in a normal person when performing the same tactile tasks (526). Thus, the visual cortex is perhaps recruited to process tactile information when reading Braille similar to how it is activated when reading in a sighted person. Melzer et al. found that the visual cortex was the most active part of the brain during the reading of Braille (186).

This presents possible problems when considering volunteers for implantation studies. If the volunteer already knows Braille, the new stimulation in the visual cortex may disrupt their processing; similar to how TMS disrupts their reading of Braille (Hallet 147). The effects of such disruption are unknown, possibly directly simulating the sensation of reading Braille or degrading the person's current tactile ability to read it, as mentioned in the brain plasticity section of the report.

Different tasks performed by the visual prosthetic device would require different resolutions. Attaining a maximum resolution from the device is not necessarily the best option (Troyk 1008). Perception requires more details than bitmapped stimulations provide, and tapping in to other streams of event information signaling may allow for lower resolution images to be perceived better than at a higher resolution without the additional information (Merabet S132).

Minimum resolutions for different tasks must also be found, which may vary by language. For instance, the C-Sight device was created by a team of Chinese scientists to test the feasibility of a visual reading system by attempting to process Chinese characters into a phosphene map (Xinyu 20). This requires a higher resolution in some instances, as

Chinese characters can contain many strokes. The English alphabet is significantly simpler in comparison (Xinyu 27). The Chinese characters are, however, logograms and so even if the character is not completely distinguishable, some of the meaning is perhaps retained (e.g. the character for rest is made up of the characters for tree and man, thus a man resting on a tree. If the character is not completely distinguishable as unique, some of the meaning is perhaps still retained in the information that is discernable). Since Chinese characters often represent more than a single letter as the English alphabet does, then perhaps with sufficient resolution the ability to read from the phosphene map will be comparable to regular Braille reading. The minimum resolution for 100% accuracy for reading Chinese characters was found to be 12x12 (Xinyu 27). The accuracy of identification of Chinese characters steeply fell when the resolution was reduced from 12x12: accuracy of 50% was attained at a 10x10 resolution and 10% accuracy was attained at a 8x8 resolution.

2. Complications with Pre-existing Medical Conditions

Research was done to identify possible complications during brain surgery resulting from pre-existing medical conditions. Though information could be found on the general risks of any such procedure, specific information regarding medical conditions that could be relevant to the sponsor's study were not found. Conditions (such as diabetes) were researched due to their connection to blindness (in this case diabetic retinopathy, a leading cause of blindness in the US). An inconclusive study was found that related diabetes to an increased likelihood of surgical site infection (SSI). However, the evidence was not strong enough to support the exclusion of potential volunteers with

diabetes (Mangram, et al). Similarly, basic information was found on requirements and conditions for brain surgery, such as the requirement that patients should not smoke before or after brain surgery. However, this is information that is commonly known by medical professionals, so the surgical team should already be well aware of it. As a result, it was decided by team discussion that medical professionals involved in the actual procedure should be determining any exclusion criteria regarding pre-existing medical conditions because of their training and experience.

VI. Conclusion

After a semester of researching literature related to the device and assessing the current state of the device, it is the conclusion of the IPRO 334 team that the sponsor is not ready for a human implantation study at this time.

The IPRO team suggests that risk analysis be performed on the current state of the device. This needs to be done before the selection of the volunteers in order to form a formalized list of risks associated with the device.

A formal code of ethic for the sponsor's team needs to be developed. The code is important since it would help guide the team through their research, as well as provide assurance to the public.

The IPRO team recommends that the sponsor compensates volunteers on an individual basis. The compensations are suggested to be based on a questionnaire format developed to assess how much each individual is entitled to.

Regarding the volunteers right to withdraw, after considering contrasting opinions, the IPRO team came to the conclusion that the right to withdraw should be left to the volunteer.

Informed consent is a crucial part of any study dealing with volunteers. The IPRO team has proposed a system to ensure that the volunteer is properly educated in order to give informed consent. In situations where the volunteer has a language besides English as their primary language, has difficulty understanding English or prefers to read Braille, special considerations need to be taken into account. Two pre-operative tests were also proposed in order to serve as a preliminary screening process, as well as a baseline for comparing any changes that have occurred during the sponsor's research.

Literature suggests that the visual cortex is recruited in individuals whose onset of blindness occurs before age 5. This might have unexpected ramifications for the sponsor's research. Hence, the IPRO team does not recommend selecting such individuals at first. They may be selected later on in the study when more data has been collected.

There are definitely more issues left unresolved through the IPRO team's research that need to be addressed before the sponsor can consider human implantation. In this report, the IPRO team has tried to provide suggestions that would contribute to the furtherance of the sponsors study.

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VIII. Appendix

```
# Python code which interprets a webcam and outputs a theorized image
# of what a person using the sponsor's device would possibly see.
# Copyright (C) 2009 David Bern
from VideoCapture import Device
import ImageDraw, sys, pygame, time
from pygame.locals import *
from PIL import ImageEnhance, ImageFilter, Image, ImageOps
res = (1280,800)
pygame.init()
cam = Device(devnum=0)
cam.setResolution(640,480)
screen = pygame.display.set_mode(res, pygame.FULLSCREEN)
pygame.display.set_caption('Webcam')
pygame.font.init()
font = pygame.font.SysFont("Courier",11)
def disp(phrase,loc):
    s = font.render(phrase, True, (200,200,200))
    sh = font.render(phrase, True, (50,50,50))
    screen.blit(sh, (loc[0]+1,loc[1]+1))
    screen.blit(s, loc)
brightness = 1.0
contrast = 1.0
shots = 0
resolution = 30
blackwhite, gray, color = range(3)
display_color = color
while 1:
    camshot = cam.getImage()
    camshot = ImageEnhance.Brightness(camshot).enhance(brightness)
    camshot = ImageEnhance.Contrast(camshot).enhance(contrast)
    for event in pygame.event.get():
        if event.type == pygame.QUIT: sys.exit()
    keyinput = pygame.key.get_pressed()
    if keyinput[K_1]: brightness -= .1
    if keyinput[K_2]: brightness += .1
    if keyinput[K_3]: contrast -= .1
    if keyinput[K_4]: contrast += .1
    if keyinput[K_r]: resolution -= 1
    if keyinput[K_t]: resolution += 1
    if keyinput[K_b]: display_color = blackwhite
    if keyinput[K_g]: display_color = gray
    if keyinput[K_c]: display_color = color
    if keyinput[K_p]:
        contrast = 1.0
```

```
    brightness = 1.0
    resolution = 30
if keyinput[K_q]: cam.displayCapturePinProperties()
if keyinput[K_w]: cam.displayCaptureFilterProperties()
if keyinput[K_s]:
    filename = str(time.time()) + ".jpg"
    cam.saveSnapshot(filename, quality=80, timestamp=0)
    shots += 1
camshot = camshot.resize((resolution,resolution), Image.ANTIALIAS)
if display_color == blackwhite:
    camshot = camshot.filter(ImageFilter.CONTOUR)
    camshot = ImageOps.invert(camshot)
    camshot = camshot.convert("1")
elif display_color == gray:
    camshot = camshot.convert("L")
camshot = camshot.resize(res)
camshot = pygame.image.frombuffer(camshot.convert("RGB").tostring(), res, "RGB")
screen.blit(camshot, (0,0))
disp("S:" + str(shots), (10,4))
disp("B:" + str(brightness), (10,16))
disp("C:" + str(contrast), (10,28))
disp("Res: %dx%d" % (resolution, resolution), (10,40))
pygame.display.flip()
```