BMEG 350 - Problem Identification [Group #11]
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A. Abstract

The following document focuses on the medical condition of vision loss or impairment, which typically occurs due to degradation of photoreceptor cells in the retina. The report will provide an overview of the disease incidence, establish the key anatomical and physiological aspects of the retinal tissue, and outline valid biomedical approaches to tackle the problem.

B. Problem Description

The retina is a thin layer of tissue that lines the back of the eye and is responsible for converting light into electrical signals sent to the brain [1]. It works in conjugation with other prominent structures of the eye that receive and focus light (iris, cornea) [2]. Considering the importance of the retina, any injury or irregularities involving the structure can often be very serious, possibly resulting in complete vision loss. The mechanism for vision loss varies depending on the type of retinal injury. Generally, the loss of retinal tissue can either remove the ability of the eyes to convert light to an electrical signal (through the absence of cones/rods) or interrupt communication between the eye and brain (optical nerve death) [3]. Of the countless types of retinal injury; [1] retinal tear, [2] retinal detachment, and [3] epiretinal membrane are among the most common [4]. Incidence rates vary between populations, sex, location, and lifestyle, among other factors [5,6]. These conditions can be caused by various factors, but all lead to vision loss due to the damage or degradation of retinal cells. Therefore, the problem can holistically be specified as a pressing need for innovative solutions to address retinal damage, with the goal of restoring retinal function.

C. General Tissue Function

The specific tissue of interest for this anatomical and physiological challenge, as outlined above, is the retina. A critical component of the human visual system, the retina, which is located in the interior of the eye, is responsible for generating a geospatial view of the outside world by converting energy from photons into focused, multi-dimensional images [7]. Residing in the retina is a layer of specialized nerve cells called photoreceptors that detect light, while neuronal and glial cells propagate a series of electrochemical impulses for processing in the visual centers of the brain [8]. There are two primary types of light-sensing cells; rods and cones. The former yields 'scotopic' vision and is well-suited for dimly-lit environments while the latter produces 'photopic' vision that is better adapted to well-lit conditions. Moreover, rods have low acuity with highly convergent retinal pathways and are monochromatic, containing only the pigment rhodopsin. Meanwhile, cones have high acuity with less convergent retinal pathways and are trichromatic for the pigment photopsin; thus capturing different parts of the visible spectrum [9]. Another class of photoreceptors, the retinal ganglion cells play a critical role in regulating circadian rhythms, pupillary photosensitivity, and the release of melatonin [10]. Aside from the plethora of cells, the peripheral layer and macula are two other constituents of the retina. The macula is the most sensitive region of the retina and is involved in producing high-resolution vision, with an

abundance of cone photoreceptors. Meanwhile, the peripheral layer predominantly houses rod cells and is responsible for generating a wider field of view [11].

Hence, within the context of the problem, a loss of retinal cells is the most significant precursor of vision loss and can occur due to aging, excessive radiation, or physical trauma. As retinal cells do not regenerate naturally, any potential solutions must focus on increasing the healing factor of the retinal layer by transplanting cultured cells, as is common, or by converting dormant glial cells into photoreceptors, which is the more novel approach [12].

C. Current Strategies

Multiple treatments combat different conditions of the retina. For the scope of this project, we would want to focus on the healing of retinal damage that could result from vision loss. An example of a unique solution currently in clinical trials is the use of bionics. A bionic eye is being tested, according to the "Fighting Blindness Canada" webpage where an electrical visual prosthesis is implanted into the eye to replace the natural retinal layer. This electrical implant would attempt to mimic the signals captured by a camera that, normally, retinal cells would produce to simulate vision in the brain. Hence, the proposed solution would be effective regardless of the presence of a retinal layer [13].

Another solution currently being developed is the use of lab-grown eye cells. These cells are derived from stem cells extracted from the human skin, which can then be differentiated into retinal cells. A major challenge encountered in the study was whether the retinal cells could create synapses for neural connections. Subsequently, this was tested in the investigation and Dr. Gamm, the lead researcher, observed using tracers that the cultured cells formed sufficient synaptic junctions. Presently, the research group is looking to commercialize their prospective solution for the treatment of human eye disorders [14].

Glial cells under the retinal layer could also be stimulated to induce a change in their function, making it possible for them to share some properties with cone cells. Unlike the previous two approaches, this solution is non-invasive and does not require any transplantation. Through selective gene expression, Professor Cayouette and his team have identified a process for the conversion of dormant Müller cells to retinal neurons. In fish, Müller cells are known to regenerate retina although this is not the case in mammals. Nonetheless, this solution could potentially restore vision loss, least to a certain extent [15].

E. Conclusion

The following report underlined a need to address the debilitating nature of vision loss, which predominantly occurs due to retinal conditions. The anatomical components of the retina, namely the photoreceptor cells, peripheral layer and macula, play a crucial role in receiving, processing and transmitting electrochemical signals for visual perception. Currently, both invasive and non-invasive interventions are being explored, although further research needs to be conducted before these solutions could possibly be implemented within clinical settings.

F. Contributions

Name	Student Number	Contributions	Signature
Pierce Alikusumah	49101710	Current Strategies	***P.A***
Albin Soni	90290693	Problem Description	***Albin***
Aly Khan Nuruddin	89444137	General Tissue Function	***Aly Khan***

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BMEG 350 - Design Requirements/Criteria & Ethical Implications [Group #11]
March 02, 2024

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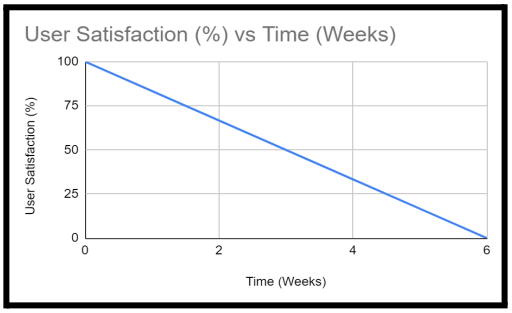
A. Design Requirements

Requirement #1: *The solution must not cause any unintended side-effects for more than 6 weeks*

Description: An autoimmune response is a condition triggered by the immune system mistakenly attacking the healthy cells instead of malignant ones. This undesirable reaction often results from medications and invasive treatments, which are commonplace in vision restoration (1). Some unintended side-effects of retinal surgery are benign such as inflammation, swelling, redness or irritation, while others including temporary blurriness, reduced nighttime vision and photosensitivity are moderate (2). However, complications can manifest in the oculus and generally relate to formation of cataracts, increased intraocular pressure, retinal infections and severe scarring.

Justification: An autoimmune response can drastically compromise the body's function, leading to poor immunity, nerve degeneration and vision loss. Currently, the failure rate for surgical treatment ranges from greater than 20% to less than 5% (3). These figures heavily depend upon the operation performed, disease profile, and overall patient health. However, given the severe consequences of potentially aggravating existing conditions, it is a must that the solution keeps unintended side-effects to a minimum. While some milder, unpleasant issues are unavoidable, it is incumbent that the design satisfactorily addresses the primary concern while facilitating a smooth recovery.

Evaluation Criteria: The solution must not cause an autoimmune response or any unintended effects for greater than 6 weeks. A key feature of many retinal complications is persisting inflammation, which can cause permanent blindness if left unaddressed (4). The swelling of the uvea in the retina, called posterior uveitis, is caused by several factors including surgery, infection, and autoimmune diseases (5,6). In severe cases, symptoms can last up to 6 weeks after initial diagnosis (7). Therefore, any solutions with undesirable complications that last beyond 6 weeks will result in no satisfaction. User satisfaction will decrease linearly as the recovery time from the side-effects increases, starting from the day the solution was administered. Hence, devices that cause side-effects to last longer than usual will be removed from consideration.



Comparison to State-of-the-Art Technologies: The lab-cultured cell transplant would have no issues with autoimmune responses due to its derivative coming from the patient's stem cells (8). Moreover, the cell reprogramming solution is minimally invasive and does not introduce any foreign bodies (9). The bionic eye may have the highest risk of causing unintended complications, however, post-operative studies exhibit an infrequent occurrence of inflammation in the implant site (10). This solution is fairly invasive in comparison, which increases its recovery period, while other designs have relatively lower recovery periods.

Requirement #2: *The solution must at least restore partial vision, with a 20/40 acuity or less*

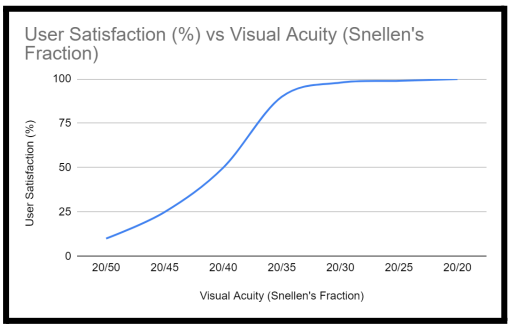
Description: Vision restoration refers to either surgical or non-surgical interventions that enhance the visual function of individuals with impaired sight (11). Normal vision is denoted by no irregularities or restrictions in the ability to perceive colors, contrasts and details, with a visual acuity of 20/20. In comparison, partial vision concerns limited, blurred sightedness

Justification: Vision loss is a debilitating condition that greatly reduces overall quality of life by exacerbating social isolation, mental stress, emotional anxiety and dependence (14). According to the WHO, around 2.2 billion people suffer from short and far sightedness worldwide, with 45 million being blind, with

with an acuity greater than 20/70. Finally, severe impairment in visualization, termed blindness, is defined with an acuity of 20/200 (12). Strategies for tackling the widespread issue range from corrective surgery, retinal prostheses and stem-cell therapeutics to visual aids, lenses and active rehabilitation (13).

almost half of the casse being preventable (15). Hence, to address this persistent problem, it is essential that the solution restores vision, preferably fully but at least partially. Since this is the most critical requirement of the device, a failure to adhere to this criterion would essentially render the solution as useless.

Evaluation Criteria: Proposed solutions should restore visual acuity, defined by the Snellen Chart, at a degree comparable to existing treatments, at least 20/40 post-recovery (16,17). A rating of 20/40 indicates that the subject can see an object at 20 feet, while the control with normal vision can view the object at 40 feet (18). Given the limited visual acuity information available online for the selected technologies, retinal detachment treatments have been used instead to provide some context. Research shows that 83% of patients who underwent retinal detachment surgery had an acuity of 20/40 post-recovery (16,17). Solutions that have a visual acuity of 20/50 would result in no user satisfaction. Satisfaction would be maximum when visual acuity reaches perfect, 20/20 vision. Enforcing this criterion ensures that the chosen solution would be capable of repairing the retina, and restoring vision to a satisfactory amount.



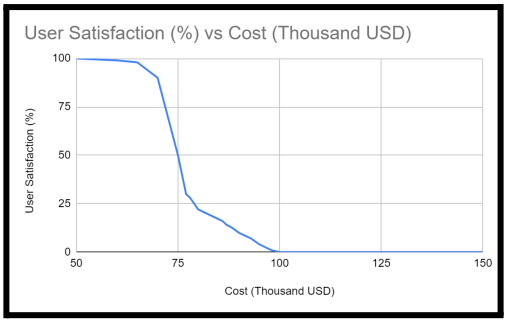
Comparison to State-of-the-Art Technologies: The lab-cultured cell transplant restores lost vision through the addition of cones from cultured cells tested on mice (19). Meanwhile, the reprogramming cell solution takes into account how many cells are converted into cones, which is responsible for the bulk of high-acuity vision (9,20). Finally, the bionic eye solution simulates signals that mimic the photoreceptors in the retina for the brain to render vision. Patients with the Argus II implants have shown better visual acuity due to adjustments in electrical stimulation, resulting in sufficient restoration of lost vision (10). Hence, the bionic eye has the highest improvement, followed by the cell transplant and reprogramming solutions.

Requirement #3: *The solution must cumulatively cost less than $100,000 USD*

Description: The costs associated with each solution varies with the technology, and are fundamentally dependent upon the type of intervention it addresses. Typically, surgical procedures incur a higher cost due to expenses for the operating space, surgeon expertise, specialized tools, anesthesia and postoperative care. Similarly, sophisticated medical devices and aids would also be costly due to research and development investments. Non-surgical interventions are comparatively cheaper with costs for regulatory compliance, clinical trials and customization. Other factors such as insurance, location and privatization also influence costs for treating retinal injuries, which range from $6000 to $150000 USD.

Justification: Cost-effectiveness is critical for the device to be accessible to patients from different demographics. An equal, equitable access to healthcare is a fundamental tenet of the UN Sustainable Development Goals and contributes towards reducing social disparity. Due to the diverse nature of the solutions, it is difficult to identify a precise price range for affordable treatments. The Argus II retinal implant, costs about $115,000 to $150,000 USD (21). Meanwhile, cochlear implants and neurostimulators cost $50,000 to $100,000 and $25,000 to $50,000 USD (22,23). Thus, the upper limit for the aforementioned implants is averaged to set the threshold for the requirement, which equates to $100,000 USD.

Evaluation Criteria: In order to achieve an acceptable balance between working capital for solution development and patient accessibility, proposed solutions costing $75,000 USD will receive a user satisfaction score of 50%. User satisfaction would be at its lowest as the cost approaches $100,000 USD, the maximum permissible value based on existing technologies (22,23). Meanwhile, maximum satisfaction would be observed as the price reaches $50,000 USD, a value decided on as it is half the maximum threshold. This makes sense conceptually as users would feel most satisfied with a lower-cost product, while higher costs would act as a barrier, discouraging individuals with limited finances to seek treatment. However, users also care about product quality. Having maximum satisfaction occur at a cost of $50,000 USD instead of $0 USD ensures an acceptable compromise for pricing and quality. Users would become increasingly dissatisfied as price increases, hence the use of an s-curve.



Comparison to State-of-the-Art Technologies: The associated pricing ranges for the lab-cultured transplant, cell reprogramming, and bionic implant technologies are between $2,000 and $4,000, $4,000 and $10,500 and $115,000 and $150,000 USD, respectively (21,24). The cost of the bionic implant exceeds the threshold of 100,000 USD, thereby failing this requirement. To be noted, the cost for cell reprogramming was estimated from a similar minimally invasive procedure for refractive surgery, LASIK (25). Comparatively, lab-cultured transplants cost more due to the amount of time and care required to culture the cells.

Table #1: *Plausibility and Satisfaction for the State-of-the-Art Technologies*

	Requirement #1		**Requirement #2**		**Requirement #3**	
Bionic Eye (Argus II)	PASS	30%	PASS	100%	FAIL	0%
Lab-Cultured Cell Transplant	PASS	80%	PASS	78%	PASS	100%
Cell Reprogramming	PASS	80%	PASS	60%	PASS	100%

D. Other Requirements

Requirement #4: *The solution must be feasible for patients with varying retinal conditions*
Requirement #5: *The solution must comply with existing quality assurance and safety standards*
Requirement #6: *The solution must be biocompatible to minimize postoperative complications*

E. Ethical Implications

The proposed solutions would restore vision, which is a vital component for the intended functioning of the human body. As not all treatments are covered by insurance, the sale and development of eye-medical devices are heavily regulated by the government to ensure patient safety (26). In Canada, medium to high-risk devices that come into contact with the eye for more than 30 days are categorized as ‘Class III’ (27,28). In conclusion, it is imperative that chosen solutions follow regulations set out by the government when it comes to the development, maintenance, and sale of these technologies to promote patient welfare.

F. Contributions

Name	Student Number	Contributions	Signature
Pierce Alikusumah	49101710	Comparison of State-of-the-Art Technologies	***Pierce***
Albin Soni	90290693	Evaluation Criteria, Ethical Implications, References	***Albin***
Aly Khan Nuruddin	89444137	Discussion, Justification, Proofreading	***Aly Khan***

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