Group #11

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BMEG 350 | Final Project Subretinal Transplants for Functional Vision Loss

Aly Khan Nuruddin

Albin Soni

Pierce Alikusumah

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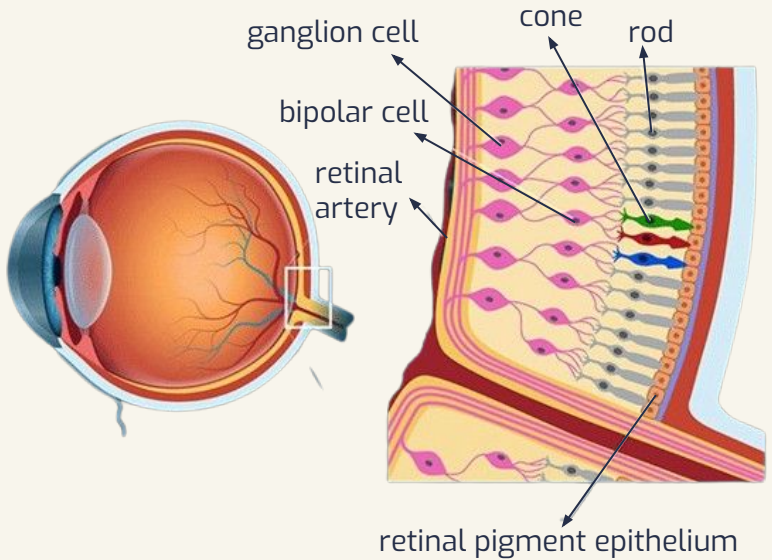
Section 01:
Problem Overview

Anatomy & Physiology of the Retina

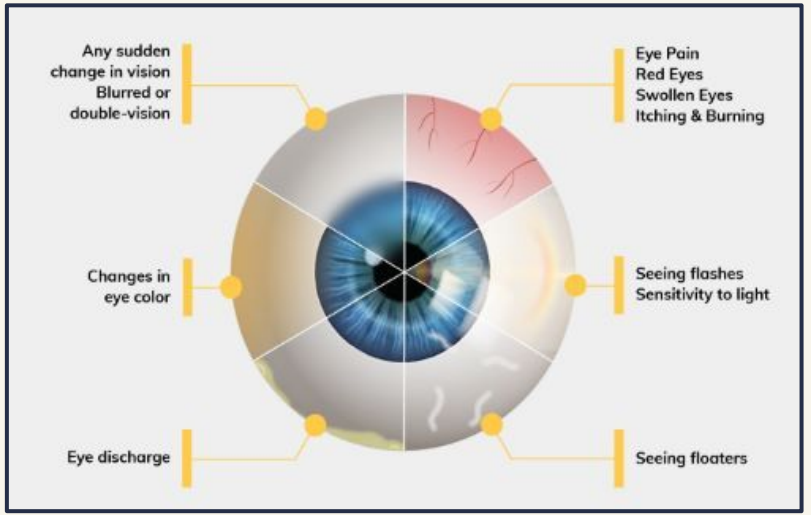
- **Retina:** Thin Layer of Photosensitive Tissue which is Located in the Back of the Eye (l)
- **Function:** Converts Light Energy to Signals that are Transmitted via the Optic Nerve to the Brain for Processing into 3D Images
- **Structure:** Neural Layer Consists of Fovea while Peripheral Layer Consists of Macula
  - *Photoreceptor Cells*
    - *Rod Cells*
    - *Cone Cells*
    - *Retinal Ganglion Cells*
  - *Glial Cells*



https://www.allaboutvision.com/resources/retina.htm

Retinal Diseases

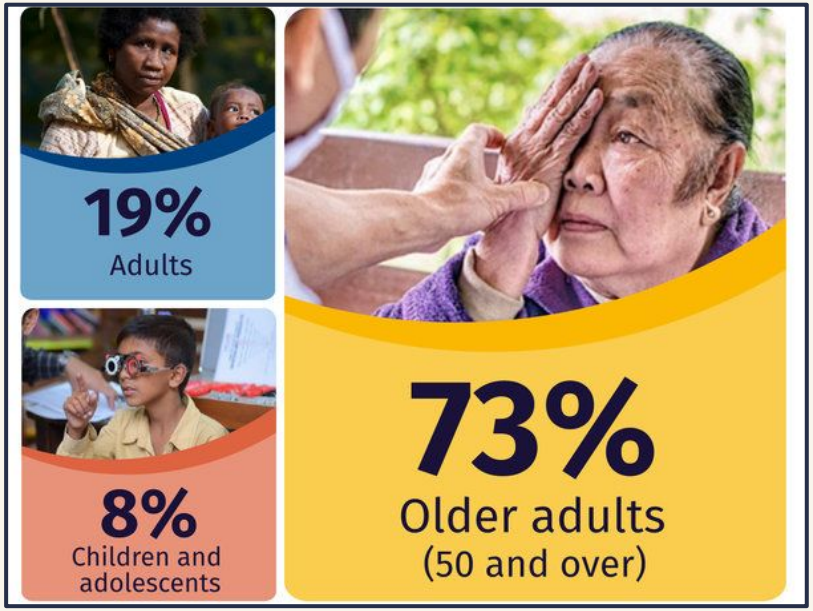
- Results from any Injuries or Irregularities in the Retinal Tissue with First Symptoms Being Changes in the Central Vision (2)
  - Removes Ability of Eyes to Convert Photons to Electrical Signals
    - Absence of Rods and Cones
  - Interrupts Eye-Brain Communication
    - Optic Nerve Death
- Most Common Retinal Diseases Include:
  - Retinal Tear
  - Retinal Detachment
  - Epiretinal Membrane



https://calgaryoptometry.com/common-eye-diseases-disorders-issues/

Vision Loss

- Debilitating Condition that Involves Partial or Complete Loss of Sight in the Eyes (3)
  - *Normal Vision:* No Irregularities in Ability to Perceive Colors, Contrasts and Details: 20/20 Visual Acuity
  - *Partial Vision:* Limited Sightedness with Blurriness: 20/70 > Visual Acuity
  - *Low Vision:* Severe Impairment or Blindness: 20/200 Visual Acuity



https://www.iapb.org/learn/vision-atlas/inequality-in-vision-loss/age/

Disease Incidence & Prevalence

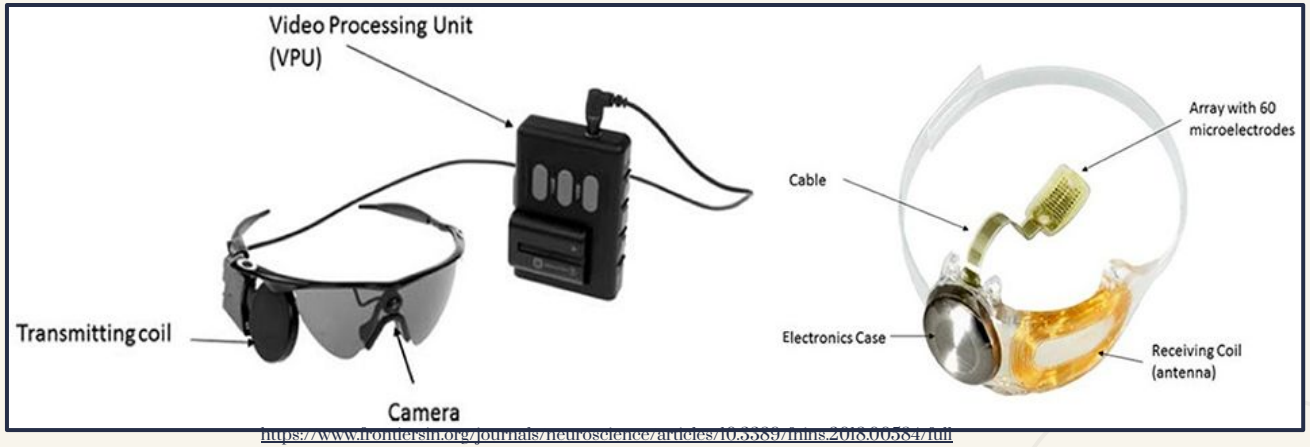
- Factors Affecting Incidence Rates (4):
  - Age
  - Sex
  - Location
  - Lifestyle
  - Income
  - Education

Section 02:
Research Landscape

Modern State-of-the-Art Interventions

Solution #1: Bionic Eye (5)

- An Electrical Visual Prosthesis Implanted into the Eye To Replace Natural Retinal Layer
- Attempts To Mimic Signals, from Rods and Cones, through a Camera to Simulate Vision

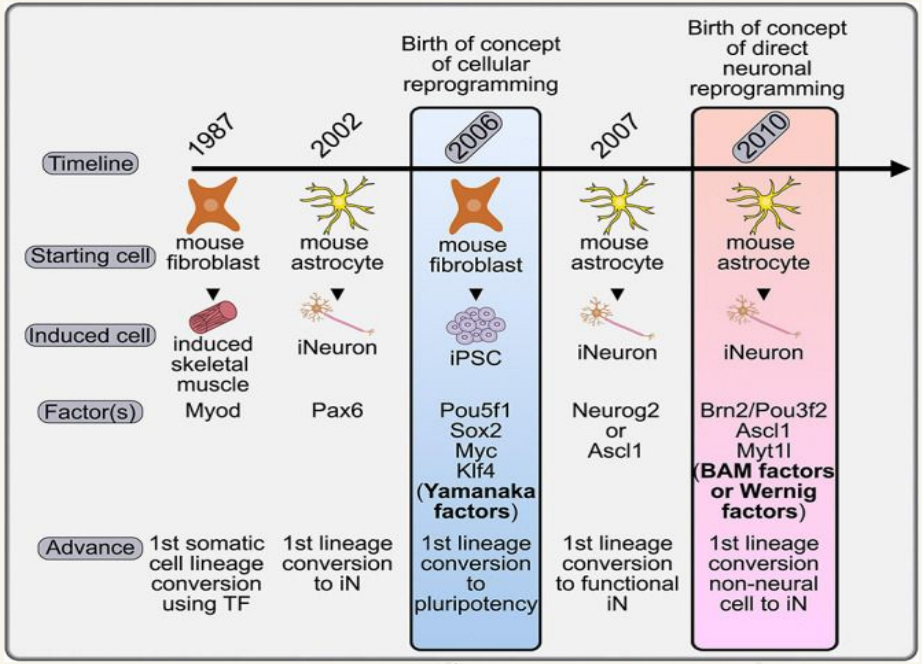


https://www.frontiersin.org/journals/neuroscience/articles/10.3389/fnins.2018.00584/full

Modern State-of-the-Art Interventions

Solution #2: Sub-Retinal Layer Induced Glial Transformation (6)

- Regeneration of the Retina via Glial Cell Stimulation by Inducing Changes in its Structure to Adequately Mimic the Properties of Cone Cells
- Non-Invasive Technique that Requires no Transplantation in the Eye Socket



https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8287587/#:~:text=Direct%20neuronal%20reprogramming%20is%20an%20innovative%20new%20technology,neurons%20%28iNs%29%20without%20passing%20through%20a%20pluripotent%20state.

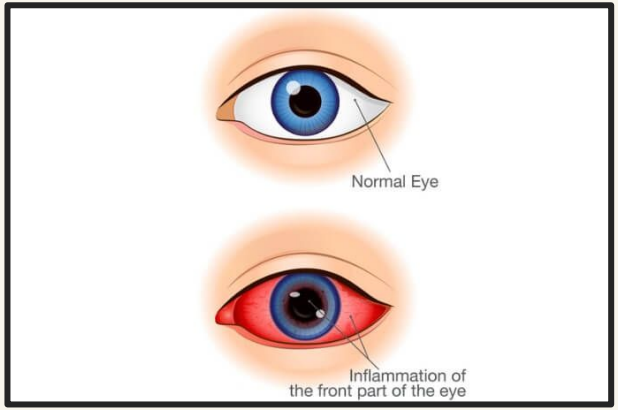
Limitations

- Bionic Eye (5) 
  - Expensive(~$115,000 - $150,000 USD)
  - Bulky with Multiple Components
    - Requires Lifestyle Changes
  - Invasive
- Subretinal Layer Induced Glial Transformation (6) 
  - Limited to Cells Available within Patient

Section 03:
Design Requirements

Duration of Lasting Side Effects

- Many Solutions Cause Lasting Side Effects (7)
  - Inflammation, Swelling, Redness
- Severity of Unintended Side Effects Vary
  - Most Severe Symptoms Last up to 6 Weeks



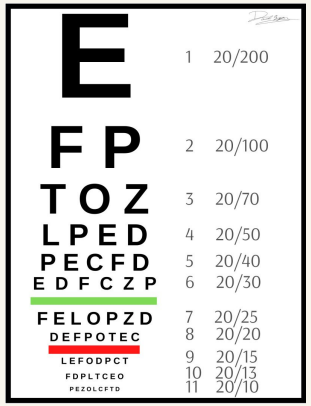
https://www.allaboutvision.com/resources/retina.htm

Requirement #1.

The solution must not cause any unintended side-effects for more than 6 weeks

Restoration Ability

- Patients Expect Vision to be Restored to a Certain Extent Post-Recovery (8)
  - Solutions Must Achieve This
- Snellen Chart is an Industry Standard Method to Quantify Visual Acuity (9)
  - Presented in the Format of “X/Y”
- Research Shows that 83% of Patients who Underwent Treatment for Retinal Issues had an Acuity of 20/40 Post-Recovery (10)



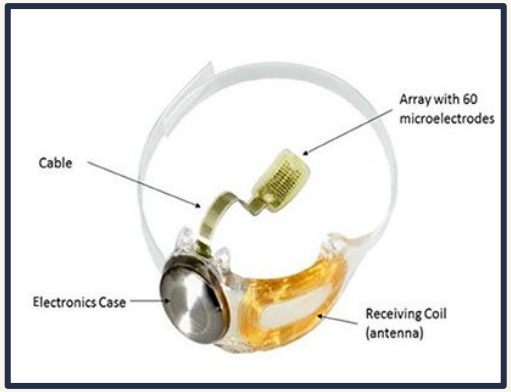
https://www.ncbi.nlm.nih.gov/books/NBK564307/figure/article-35714.image.f1/

Requirement #2.

The solution must at least restore partial vision with 20/40 acuity or better

Cost

- Cost is Critical to Ensuring Accessibility of Possible Solutions to Various Demographics (5, 6)
  - UN Sustainable Development Goal #3
- Current Solutions are Diverse in Price (11)
  - Argus II Retinal Implant: $115,000 - $150,000 USD
  - Cochlear Implants: $50,000 - $100,000
  - Neurostimulators: $25,000 - $50,000 USD



https://www.frontiersin.org/journals/neuroscience/articles/10.3389/fnins.2018.00584/full

Requirement #3.

The solution must cumulatively cost less than $100,000 USD

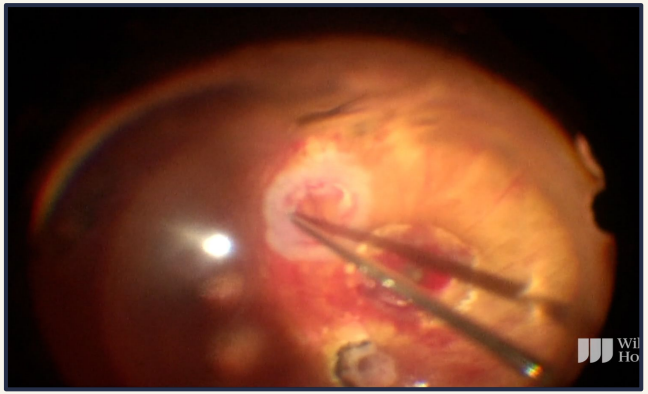
Section 04:
Proposed Solution

Cultured Subretinal Transplant to Restore Vision

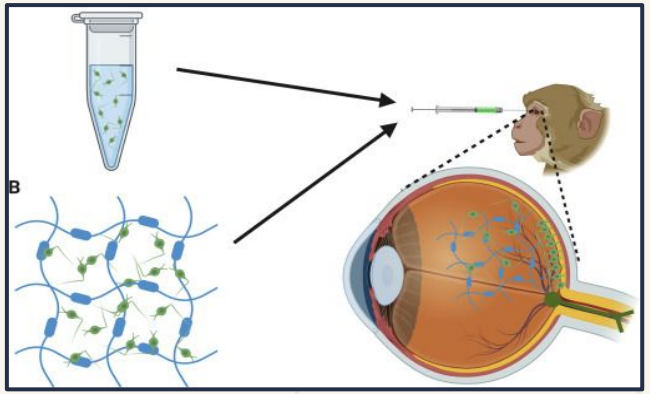
https://facellitate.com/introduction-to-cell-culture-and-its-applications/

Cultured Subretinal Transplant to Restore Vision

- Stem Cells are Collected from Patients (6)
- Cells are Differentiated into Retinal Cells
- Surgical Transplant of Cultured Retinal Cells into Patient
- Natural Formation of Synapses through Healing
  - Leads to Restoration of Vision



https://eyetube.net/series/inside-the-wills-or/autologous-retinal-transplant-for-a-full-thickness-macular-hole



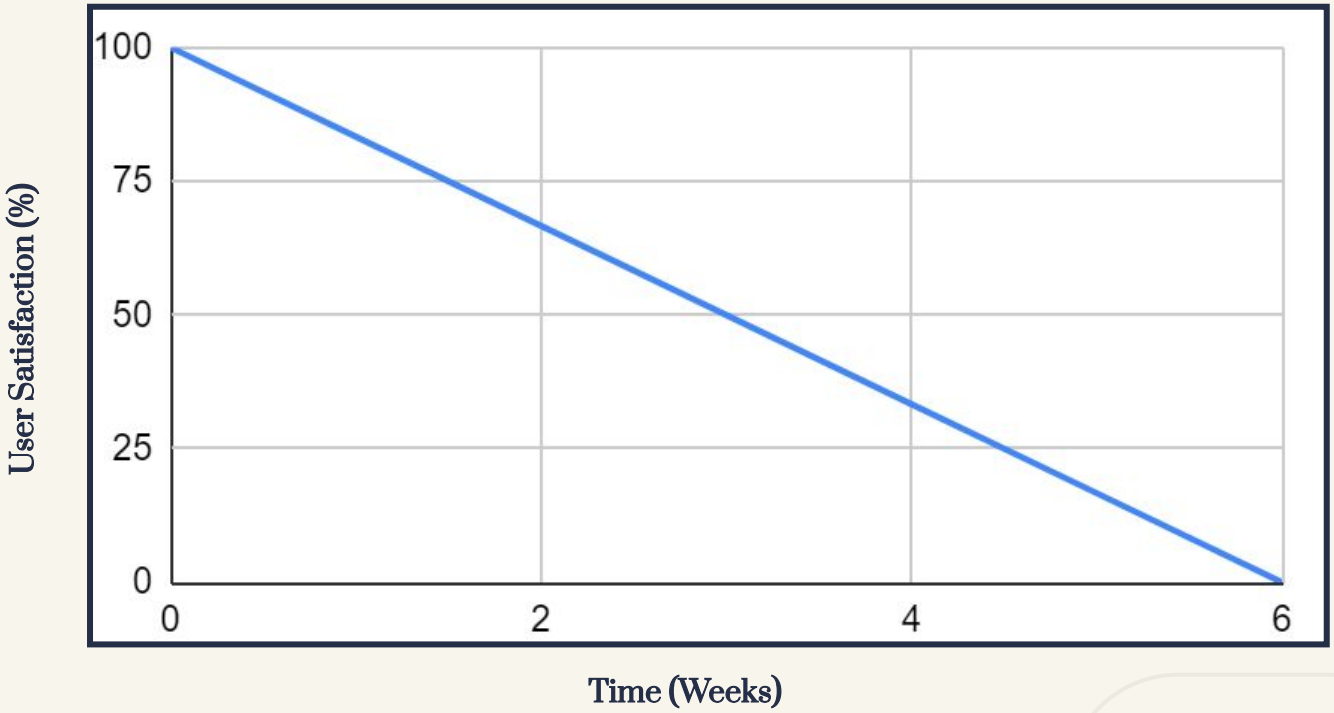
https://www.sciencedirect.com/topics/medicine-and-dentistry/retinal-transplantation

Advantages of the Solution

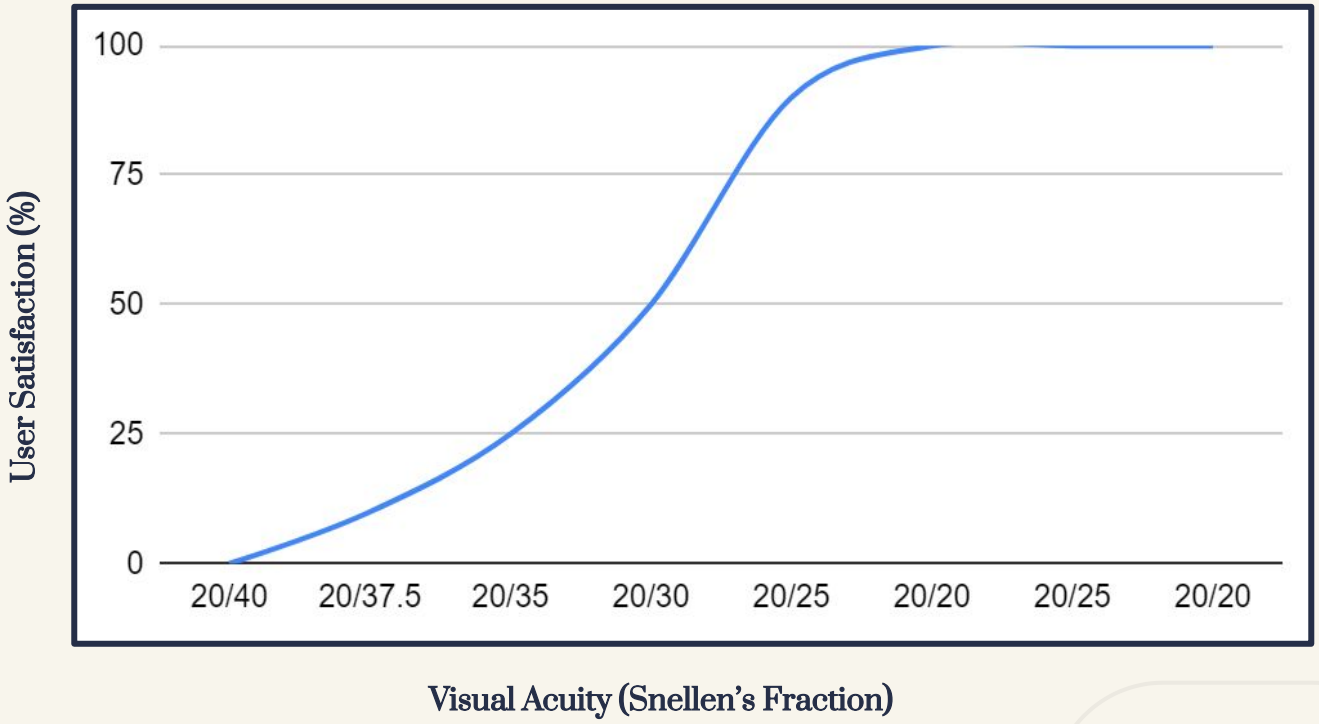
- Autologous Cells would Bypass the Need for Immunosuppression
- Allogeneic Stem Cells would Allow for the Upscale of the Solution
- Procedure could be done with Minimally Invasive Techniques
- Costs around $2000 - $4000 USD (11)
    - So far the Cheapest Solution

Section 05:
Validation Strategies

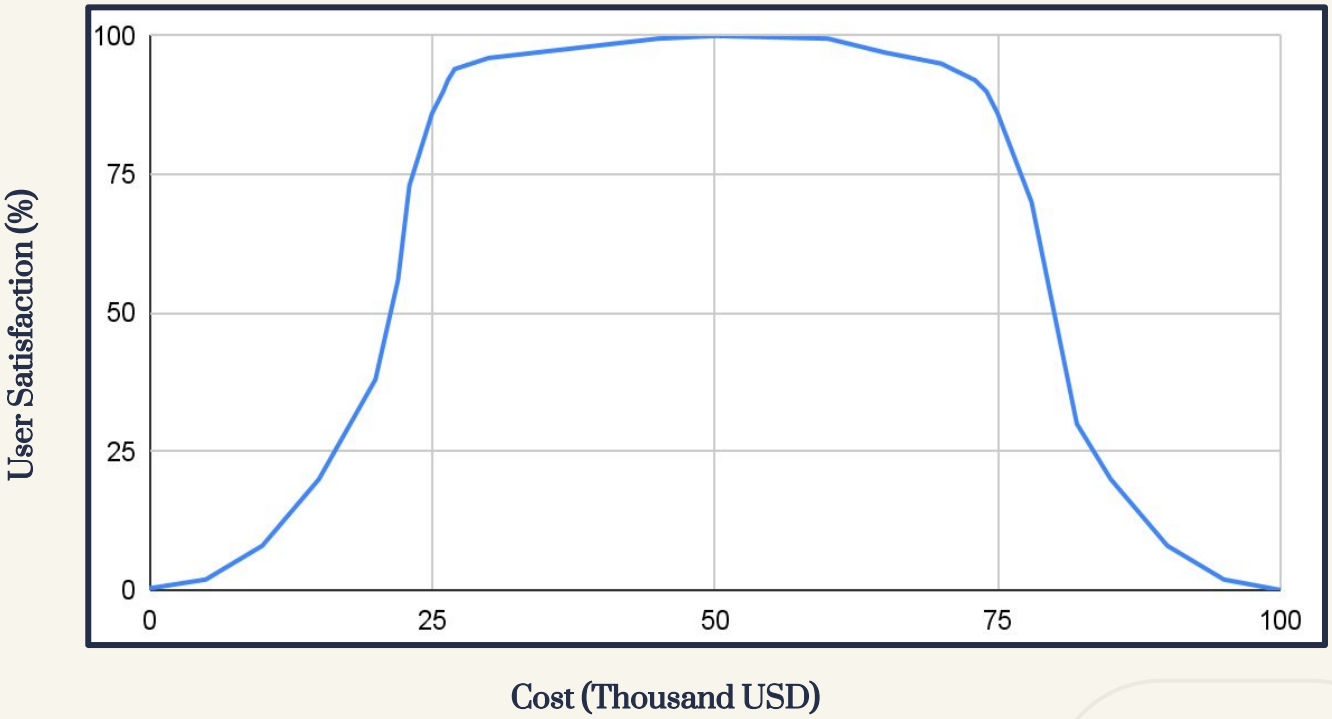
Duration of Lasting Side Effects



Restoration Ability



Cost


User Satisfaction (%)
100
75
50
25
0
0
25
50
75
100
Cost (Thousand USD)

Section 06:
Limitations

Shortfalls of the Technical Design

- Requires an Interdisciplinary Team of Experts (12)
  - Engineers, Physicians, and Lab Workers
- Autologous Stem Cell Therapy has Difficulty with Scale Up because of the Individual Requirements
  - Cells are Harvested from the Patients Themselves
- Allogeneic Stem Cells Elicit an Immune Response
- Currently, Cannot be used as an Emergency Treatment
  - Culture of Cells Takes Time to Grow

Section 07:
Future Work

Potential Areas for Improvement

- Invest in Scaling Up the Cell Manufacturing Process
  - Optimize Bioreactors: Increase Batch Size
  - Reduce Cost and Increase Accessibility

- Pivot from Autologous to Allogeneic Cell Therapy
  - Technique to Bypass the Immune System
  - Generate Universal Donor Cell

- Improve the Restoration Capabilities of Solution
  - Beyond Retinal Injury Treatment
  - Improve Healing Efficiency

Conclusion

Vision Loss is a debilitating retinal disease that can potentially be addressed by the promising, minimally-invasive bioengineering solution of **Cultured Retinal Implants** although questions about its viability and efficacy need to be adequately addressed before effective implementation within clinical settings.

Section 08:
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Thank You!