Acoustic Sorting for Cell Injection Therapies

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Problem Overview

Corneal edema is characterized by a blue "cobblestoned" appearance in the eye.[1] If unregulated, canines develop painful ulcers on their ocular surfaces and progressively lose vision, resulting in blindness, and about **90M dogs** are at risk of developing this.[2] Corneal transplants are the leading surgical intervention for human cases.[3] However, early successes were unable to be scaled up due to an inability to maintain the cell viability of the donor endothelial layer, as well as a lack of canine donor supply.[4]

Cellular injection therapy has been growing as an alternative to corneal transplants due to higher immune compatibility[5] and its ability to serve many canine patients (Fig. 1).

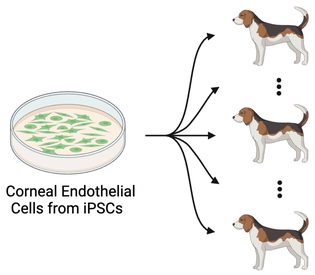

Fig. 1. Corneal endothelial cells derived from iPSCs can treat multiple patients

Background

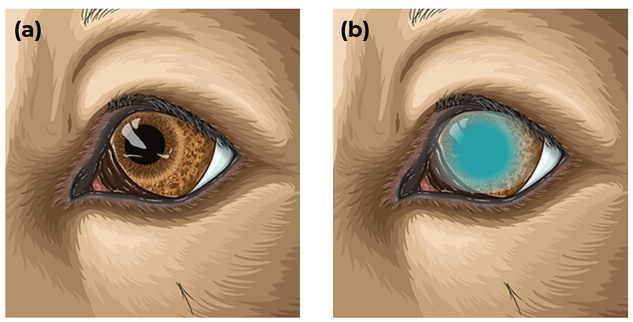

Fig. 2. (a) Normal Cornea (b) Corneal Edema

Corneal edema (Fig. 2b) is a condition where fluid overaccumulates in the middle layer of the cornea due to a damaged endothelial layer.[5] **Induced pluripotent stem cells (iPSCs)** can differentiate into non-target cell types, and the cells can experience stressful conditions during transportation. Both result in nonviable cells in the injected sample (Fig. 3).

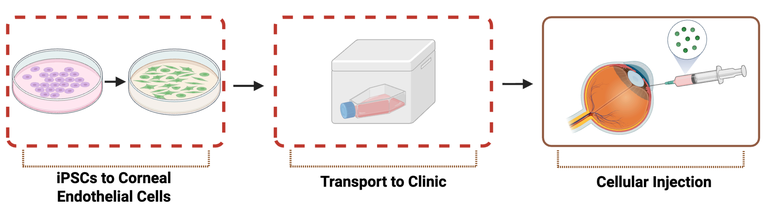

Fig. 3. Cellular Injection Workflow. Red borders indicate pain points.

Clinical Need

Veterinary technicians need a method of maximizing preoperative cell viability in order to ensure successful monolayer formation after endothelial cell injections in canines with corneal edema.

Our Solution: Sort-A-Cell

Sort-A-Cell separates live and dead cells from an iPSC-derived sample. Specializing in **adherent** cells, Sort-A-Cell can be used to purify cell samples at the **point of care**. The mechanism uses **acoustic waves** to sort cells by their **viability** before the live corneal endothelial cells are used in cellular injection therapy.

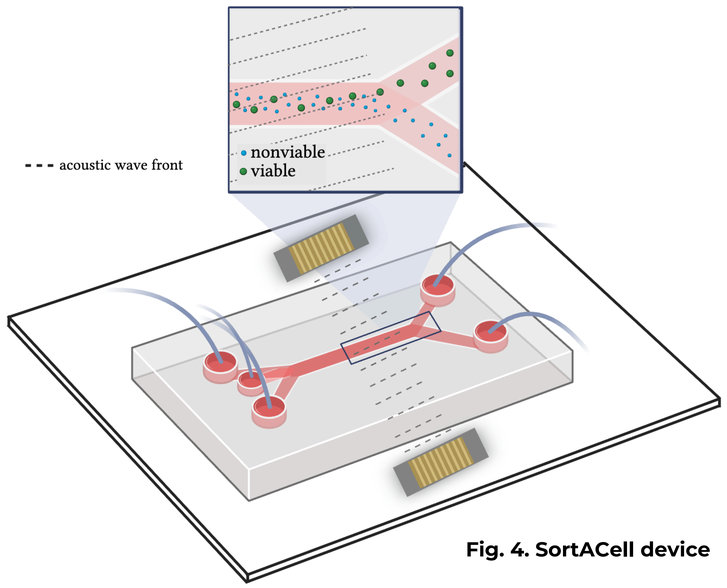

Fig. 4. SortACell device

- Suitable for lab use and is applicable for sorting all cell types, including future stem cell injection therapy procedures.
- Label-free sorting mechanism allows futher processing of cells
- Significantly cheaper than flow cytometry
- Portable machine with an automated workflow that requires few steps and minimal training

User Needs

Maximize Preoperative Cell Viability

Stable Monolayer Formation

Minimize Cell Clumping

Maintain Sterility of Cell Processing

Testing Results

Preliminary experiments show **live cells** have a size of **8.01 ± 0.14 µm** and **dead cells** have a size of **6.91 ± 0.07 µm**. The data imaging was processed through Fiji v 1.54s.

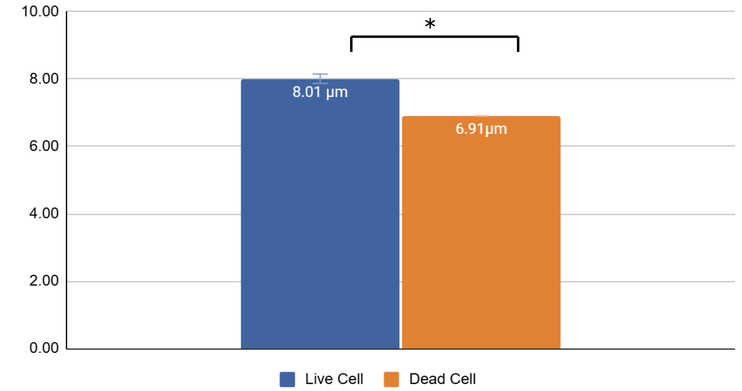

Fig. 5 Radius difference between live and dead cells. *p < 0.001

Acoustic Mechanism

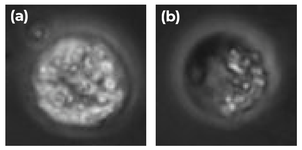

Fig. 6. (a) Live cell (b) Dead cell

$F_a \propto r^3$

$F_d \propto r$

Acoustic force (F_a) scales cubically with size. Although the drag force (F_d) also increases, the resulting net upward force still grows quadratically with cell size.

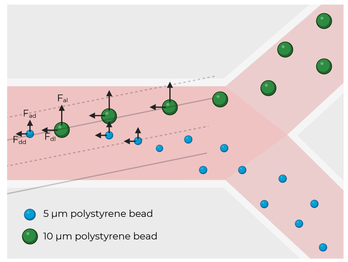

Fig. 7. Acoustic Waves Interacting with polystyrene beads

Future Work

- Conduct experimentation on density disparity between live and dead cells
- Test the separation capability of Sort-A-Cell device on 5µm and 10µm polystyrene beads
- Conduct experimentation on optimal peak-to-peak voltage and flow rate
- Finalize design of integrated fluid handling systems

Acknowledgements

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