Cannula Cell & Gene Therapy Delivery System

Malaika Alphons[1,2], Tal Dassau[1,2], Jamie Joseph[1,2], Sona Marukyan[1,3], Avani Shukla[1,4], and Emerald Tan[1,3]

[1]Department of Biomedical Engineering, [2]Department of Chemical Engineering,
[3]Department of Materials Science and Engineering, [4]Department of Mechanical Engineering
Carnegie Mellon University, Pittsburgh, PA

Objectives

Our objective is to develop a device for neurosurgeons, scrub techs, and medical technicians that can deliver cell and gene therapies to treat neurodegenerative disorders, meeting the following requirements:

1. Effectively deliver cell/gene therapies
2. Navigate to multiple parts of the brain
3. Remain secure during procedure
4. MRI compatibility
5. Biocompatibility

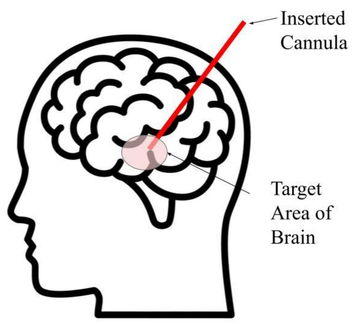

Figure 1: Diagram depicting target area of the brain for cell and gene therapy delivery [1].

Problem

- Neurodegenerative disorders like Parkinson's Disease (PD) and Alzheimer's Disease impact 55 million Americans every year [2]
  - Damage to neurons leading to loss of memory, mobility, coordination, and cognition [3]
  - 5 stages for PD as symptoms progress ending with stage 5 (bedridden, full-time caretaker, dementia) [3]
- Currently no cure and limited treatment options for only the first 4 stages [4]:
  - Medication and physical therapy
  - Deep brain stimulation
  - Surgery
- Similar devices made of different materials or for other drug therapies available

Proposed Solution

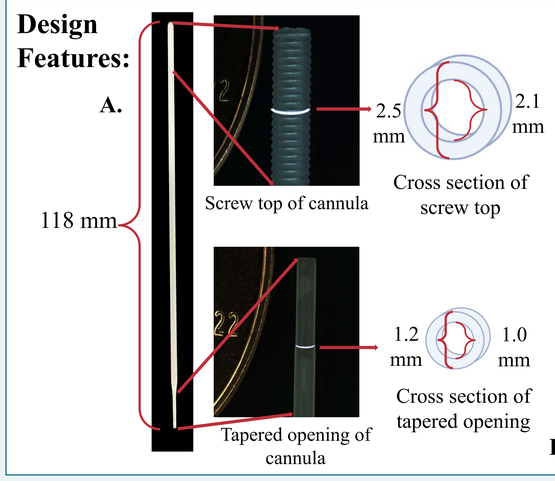

Figure 2. Design features and dimensions (A), Material considerations (B)

Testing Results

Simulation Testing:

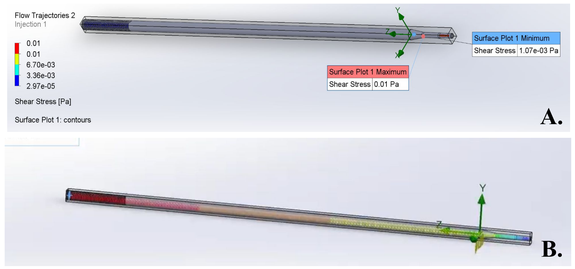

Figure 3. Results of fluid simulation through cannulas.The top images shows max shear stress is low, so cells will not be damaged in the process of delivery. The bottom image shows that pressure is greatest at the top of cannula

Brain Model:

Figure 4. 1% Agar-Based Full-size Brain Model

- Stiffness ≈ 15 kPa (comparable to brain) [5]

Puncture Testing:

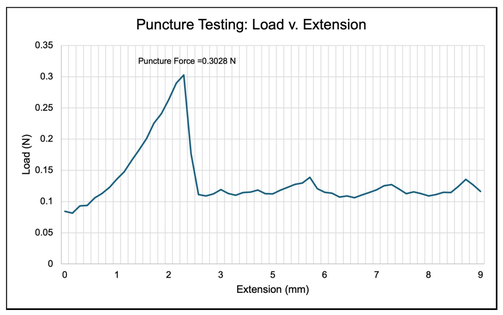

Figure 5. Puncture testing was performed using ASTM Standard F3014. Above are results for a single sample.

- 0.3 N (±0.025) is required for penetration.

Dry Testing Fluid Delivery:

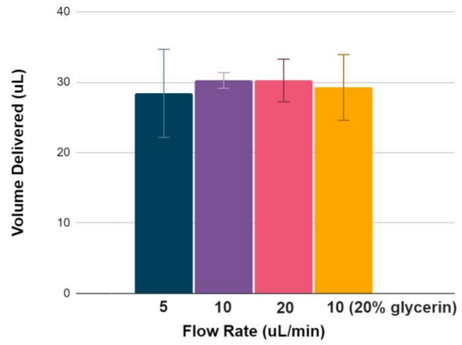

Figure 6. Graph of average volume delivered through 4 cannulas at set flow rates. All fluids are dyed water with the orange bar representing a water/glycerin mixture.

- Error bar illustrates the standard deviation.
- 10uL/min proved the most consistent delivery.

Wet Testing Fluid Delivery:

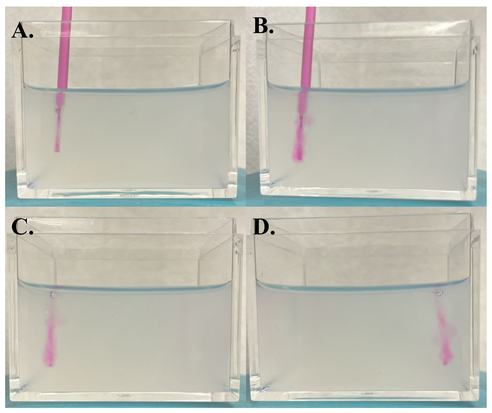

Figure 7. Images showing cannula inserted in agar-based brain model (A), spread of 30uL at flow rate of 10uL/min of dyed water delivered through cannula with cannula still inserted (B), side view 1 of spread without cannula (C), side view 2 of spread without cannula (D)

- Successful delivery due to limited spread of fluid.

Manufacturing Recommendations

- Based on previous patents with enough significant equivalent components, we recommend the 510K clearance approach
  - ClearPoint Neuro's SmartFlow Cannula is used to deliver cell and gene therapies intracranially
  - Design and material selection differences such as composed of a silica inner lumen and outer PEI and PEEK
- Utilize extrusion methods to manufacture cannula body
- For outer coating application, utilize sputtering
- Final product must undergo a sterilization process using a steam autoclave

Future Work

- Conduct further in-vivo testing
- Produce cannulas with finalized materials
- Conduct cell viability and biocompatibility testing
- Establish manufacturing process
- Begin large-scale manufacturing
- Undergo official clinical testing for patent approval

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