

A Novel Pressure Regulating Brain Imaging Implant For Ultra-Large Field-of-View MicroscopicImaging in NHPs

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Problem Definition & Need

Problem Definition

Several problems challenge mesoscopic imaging in the brain: 1) Difficulty with positioning high-NA objectives near the brain; 2) Creating a flat imaging window against the surface of the brain; 3) Adjusting the imaging window to changes in swelling and pressure in the brain, such as those that may occur due to hydration changes and other physiological factors; 4) Preventing growth of dura and biofilms that cloud the imaging window; 5) Follow-on MRI imaging of the animal post-implantation.

Need Statement

Need a thin, strong, radiolucent, and pressure regulating implant for ultra-large field-of-view microscopic imaging in primates.

Design Inputs

Functional Requirement

Maintain a flat, clear, imaging window against the surface of the brain.

Constraints

- Radiolucent
- Thin enough to allow for an objective with a working distance of 2mm to image the brain.
- Allow for water immersion objective.
- Capable of holding attachments & bearing weight (at least 5 lbs).
- Imaging window must be at least 20 mm in diameter.
- Coverslip must move parallel to chamber to allow for manual control of the imaging window.
- Must be durable, last at least six months and be usable on awake monkeys.
- Must be hermetically sealed to prevent infection.

Silicone Design

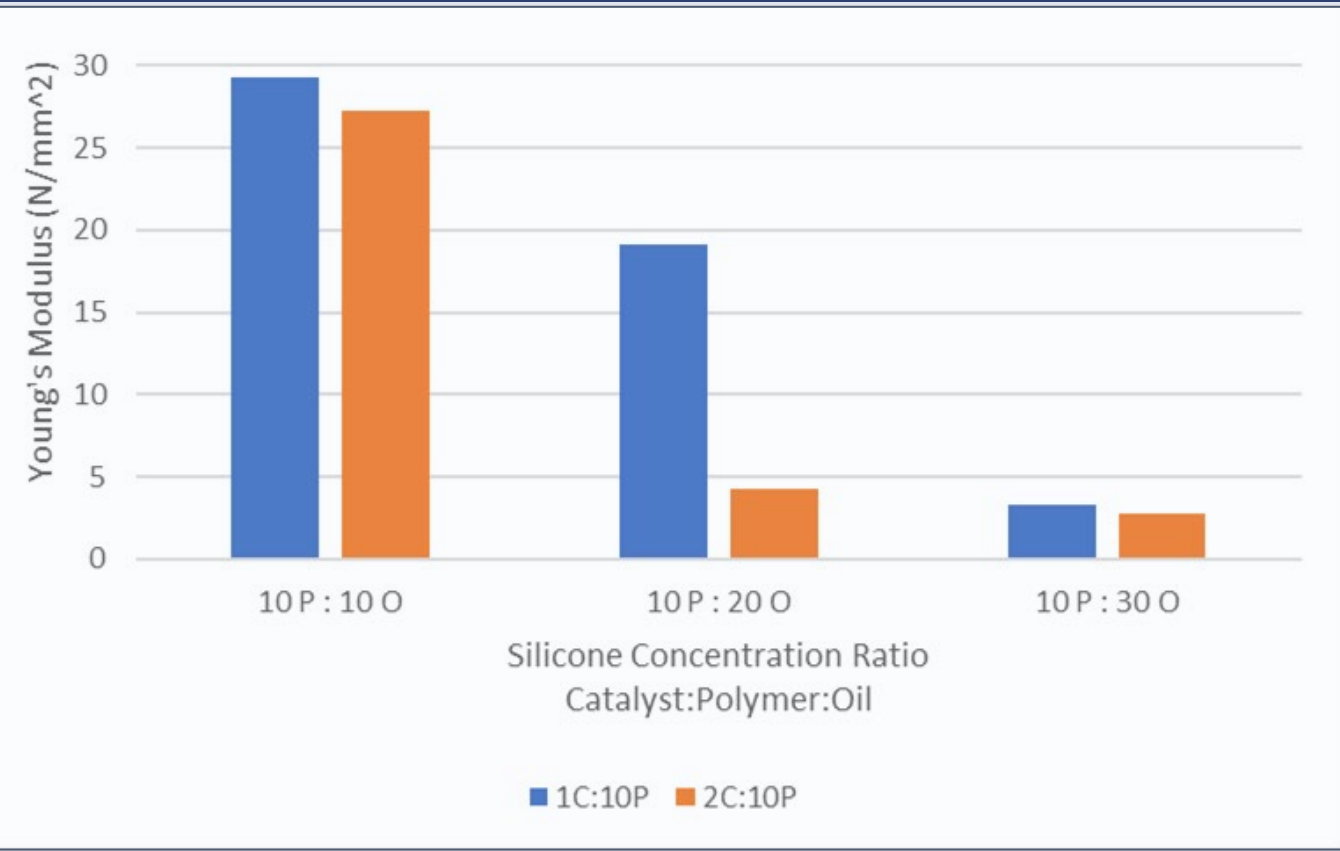


Figure 1: Various concentrations of platinum cured silicone with oil.

The mechanical properties of platinum cure silicone can be modified based on the concentrations of silicone oil, catalyst, and a hydrid vinyl-functional siloxane polymer mix. We chose a concentration ratio of 2c:10p:30o because it had the smallest Young's modulus. The Young's modulus of mammalian brains is only .5 - 1.0 kPa. Therefore we need a very low young's modulus to match and apply appropriate pressure¹.

Prototype Development

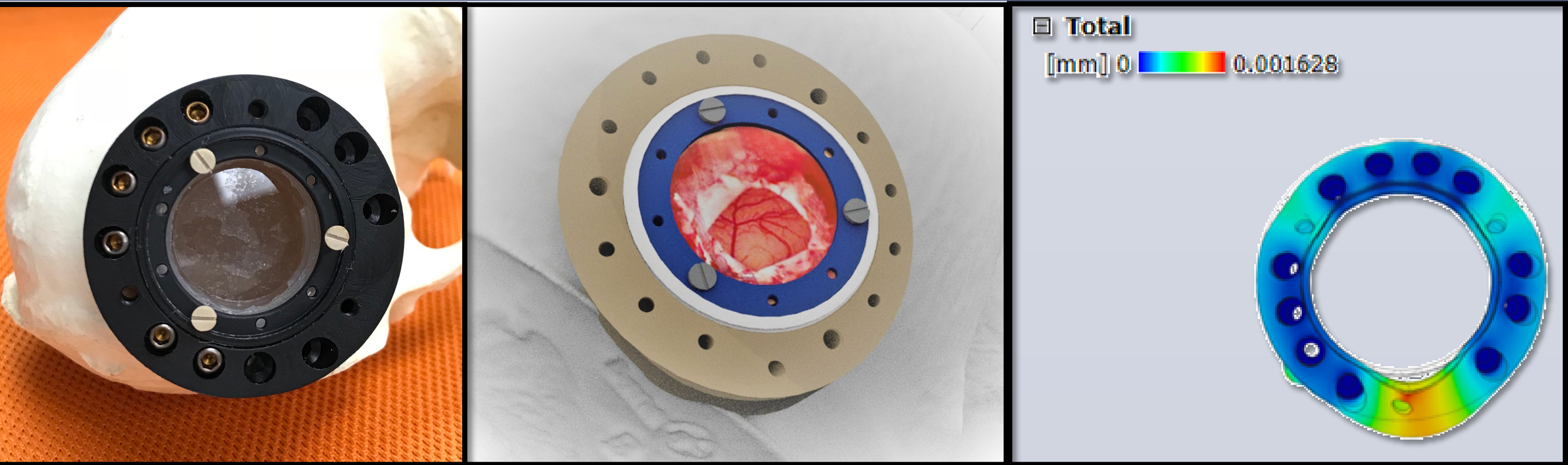


Figure 2: Comparison of early machined prototype with phantom brain (left) to advanced CAD model (middle) and results of a simulated static stress test on CAD model(right)

- A prototype implant was machined by Xometry using a 5-axis machine. A phantom brain, made of a silicone mixture, was added to mimic the mechanical properties of the brain.
- A simulation of five pounds of static stress placed on the implant was performed using Autodesk Fusion 360. Results indicate the maximum displacement caused by this amount of force would be .001628 mm.

Engineering Design Solution

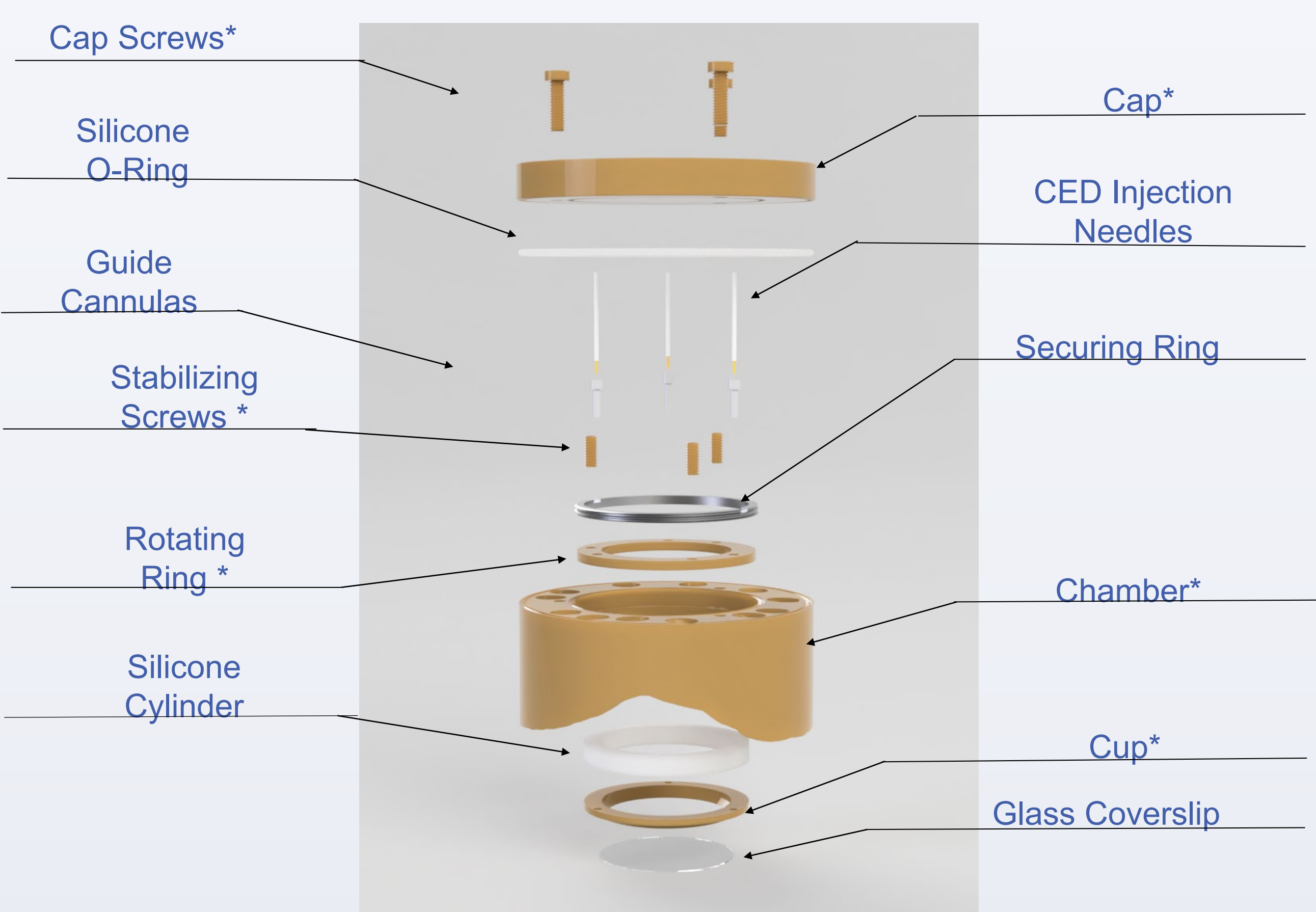


Figure 3: Exploded view of annotated imaging implant prototype. *Indicates part is made of PEEK plastic, chosen for its radiolucent properties, strength, and ability to be sterilized.

Component Listing with Description

Cap & Cap Screws- Removable cap for imaging and cleaning.

Silicone O-Ring - Approximately .4 mm thick, prevents bacterial movement between chamber and cap. There are two O-rings, one on the outer and one on the inner diameter of the chamber. The cap and chamber have indents to accommodate the rings and squeeze them when the cap is completely secured.

Thin Securing Ring - Secures rotating ring against the bottom shelf of the chamber and prevents it from moving up.

Stabilizing Screws – Pushes against cup and prevents the imaging cup from moving closer to the chamber. Threaded into the bottom securing ring and penetrates silicone.

Guide Cannulas - Cannulas are threaded into the rotating ring at 3 different locations and sealed with silicone glue. These cannulas allow for 18G CED needles to penetrate the cylinder.

CED Injection Needles – Convection enhanced delivery needles. Designed for cortical injections but can also be used to deliver drugs or imaging contrast agents into the soft tissue.

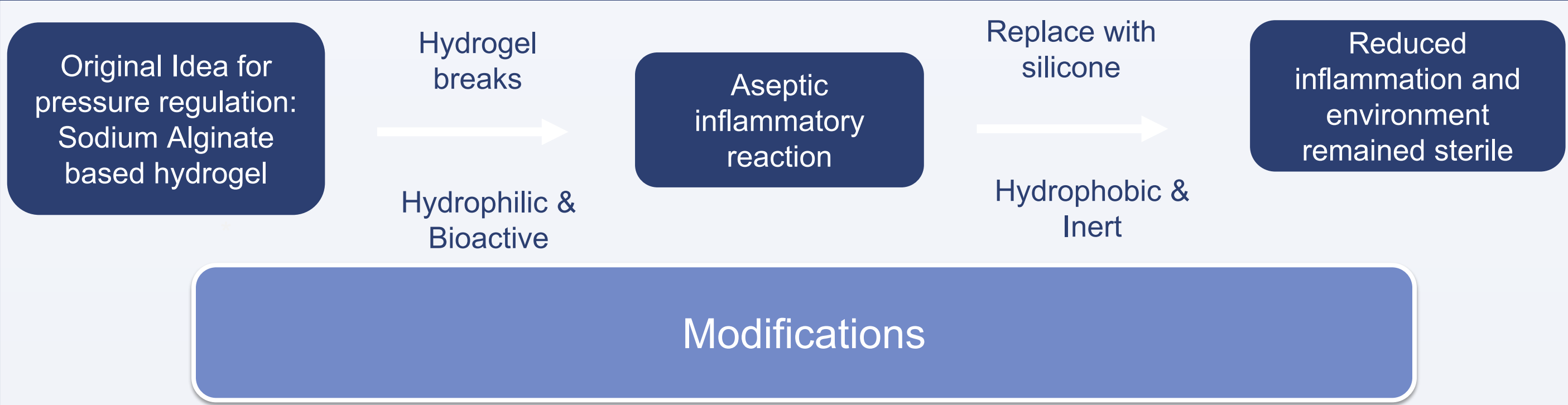
Rotating ring – Multiple threaded holes for the height adjusting screws and can rotate to adjust the positions of the screws. Sits between shelf in chamber and thin securing ring.

Chamber - Has holes for bone screws that are perpendicular to the surface of the bone to increase the strength of the bond between the chamber and bone². It also includes three threaded holes on the top to allow for attachments and to secure the cap.

Silicone – Chosen for its ease in manufacturing, control of mechanical properties, and ability to be sterilized. Serves as a spring to adjust for pressure changes caused by the variations in swelling in the brain. Although not indicated in the drawing, the silicone connects to the lip of the imaging cup and rotating ring to create a sealed environment.

Imaging Cup & Glass Cover Slip – The glass is glued to the cup. Together they create a bowl that can hold liquid for a water immersion objective.

Failures & Modifications



- Added two O-rings to gasket.
- Used Metabond along with screws to secure implant, resulted in errors with screw length & positioning
- Switched from silicone to TechBond glue, issues with hermetically sealed bonds persist

Results

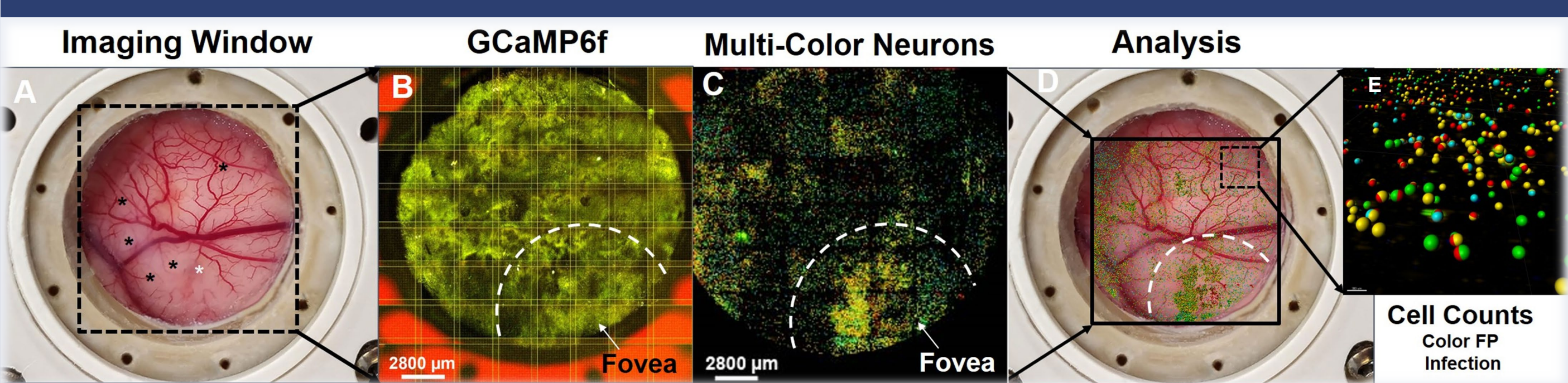


Figure 5: (A) 2cm imaging window (stars indicate previous probe sites). White star indicates the LGN CED injection site. (B) Stitched 2P image (49 tiled 2800 µm stacks) of GCaMP6f infected cells.(C) Multicolor scan of multiple fluorescent protein cells. (D) Positions of individual best of multi-color FP cells. E) Hyperspectral brainbow analysis. We were able to successfully transfect the cortical area beneath the implant with five multi-color fluorescent proteins and GCaMP6. The implant allowed for impressive imaging using our 2-photon scope and after analysis revealed successful transfection of the virus injected. The results indicate that the implant was successful in its ability to keep enough dural and pial regrowth at bay to allow for the imaging previously discussed.

Future Work: OBServe Implant



Figure 6: Left: Photorealistic rendering of the proposed OBServe implant with the silicone mount. Right: Exploded view of the OBServe implant and mount.

References

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