HIGH THROUGHPUT QUANTITATIVE EX VIVO MRI OF THE MOUSE BRAIN

Joel Nitz, Anna Mercord, Ray Steinlage, Erwin Cruz, Leo DiCataldo, Allicia Moeller

Client: Dr. John-Paul Yu, Nick Stowe, and Ajay Singh Advisor: Dr. Kris Saha

Background and Motivation

- Dr. JP Yu's lab studies neurological disorders by taking MRI's of modified murine brains [2].
- Current loading and unloading method of single syringe insertion is inefficient and time consuming.
- Client wants a new standard streamlined method of loading.
- Current: 3 Rat, 6 Mice per scan. Costs $500 per scan.

Figure 1.1: Current methodology. Three rat brains in syringes taped together, then sealed [1].

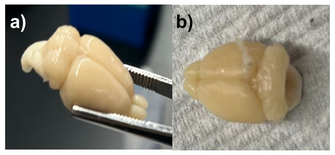


Figure 1.2: a) rat brain: avg. width: 15.0mm, avg. height: 10.5mm
b) mouse brain: avg. width: 8.6mm, avg. height: 6.7mm

Design Specifications

Design must:

- Hold greater than 3 rat brains and 6 mice brains
- Maintain brains in consistent orientation during scanning, tilting should not exceed 3 degrees
- Have complimentary scientific procedure
- Be able to fit brains and fit within coil bore (37.8 mm diameter).
- No air bubbles in contact with the brain, no leaking
- Be reusable and reproducible
- Not damage brains
- Be MRI compatible [3]
- Contain watermark

Figure 2.1: Coil inserted into MRI with 37.6mm diameter bore

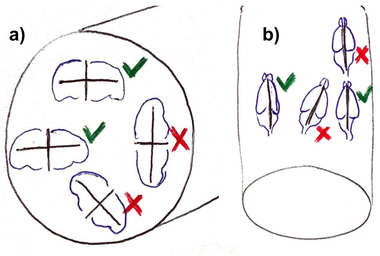


Figure 2.2:
a) **No rotating from front view.**

b) **No tilting from aerial and side view.**

Fabrication and Testing

First Prototype:

- 3D printed FormLabs Black resin - waterproof.
- O-ring caps: No leaking after being upside down for one week.
- Brains did not fit: the oval shape was not a good model of the shape of the brains.

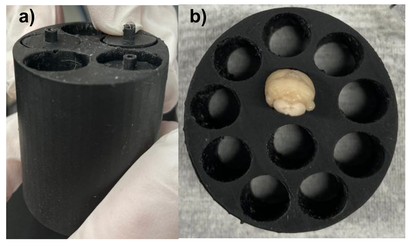


Figure 3.1: First prototypes. Oval hole, with height and width.

a) 5 brain rat cap, did not fit, seal good

b) 11 mice, did not fit

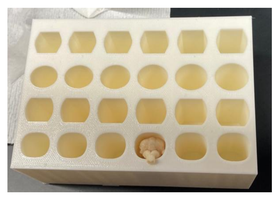


Figure 3.2: Rat brain sizing array. Chosen hole has brain in it. Dimensions height: 11.25mm, width: 15.7mm and 30° width of 15.0mm.

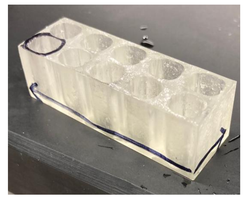


Figure 3.3: Mouse sizing array resin, chosen circled. Dimensions: height 9mm, width 7.8mm and 45° width of 7.8mm.

Size and Shape of Holes (Testing Arrays):

- Arrays of different shapes with incrementing size used to identify the best hole design.
- PLA: 1) Faster and cheaper, used for testing. 2) Dimensions were not true to size.
- PLA and FormLabs resin, resulted in incorrect cap fit and hole size.
- Chose "decanted", ovular hole
- Made all subsequent test prints in resin.

Double-Sided O-ring Seal + leak test:

- O-rings caps didn't fit. New cap array fabricated.
- Caps combined into single cap for ease of use
- Double-sided hole was tested for brain removal.
- Flourinert escapes by small release holes.
- Rubber stoppers seal release holes, prevent leaking

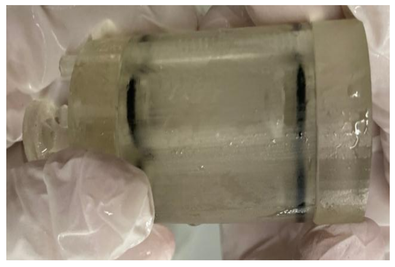


Figure 3.4: Leak testing showed that double sided capsule leaked from both sides

MRI Testing of Material:

- Final rat prototype scanned with 4 brains
- Capsule material does not show up on scan.
- 3/4 holes had air bubbles
- 2/4 rat brains tilted from aerial view.
- Brains were loaded, then hole filled with flourinert, then capped
- Some leaking from caps and rubber stoppers.
- Excess water under o-rings showed on MRI

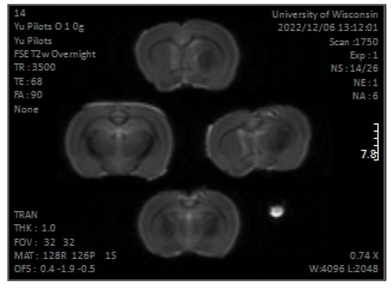


Figure 3.5: Cross-section of brains in capsule in MRI. Rightmost brain scan does not have symmetry (see figures 3.6 and 3.7)

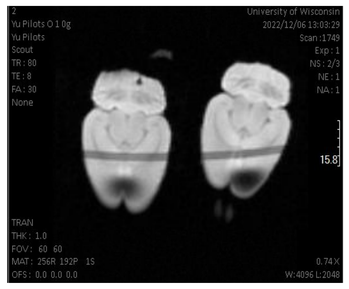


Figure 3.7: Right brain tilted approx 20°. Black marks caused by bubbles

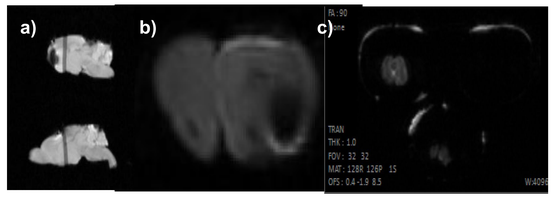


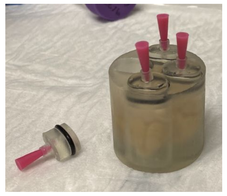
Figure 3.6: Final scans. a) brains tilted down approx 15° on side view. b) air bubbles caused black circle. c) water trapped under o-rings from water tests appear on MRI scan.

Final Prototype

Description:

- Integrated insert with back plate.
- Individual caps and stoppers
- Rat: 4 holes, Mouse: 11 holes.

Figure 4.2: Final prototype: 4 samples with watermark.



Results:

- 4 rat brains fit easily and are able to be removed.
- O-ring seal leaked slightly.
- 3 out of 4 holes had air bubbles which grew during MRI scan.
- 57% less flourinert required.
- Old mice brains fit and could be sealed without air bubbles in water.
- 2 new mice brains did not fit; no MRI scans taken.

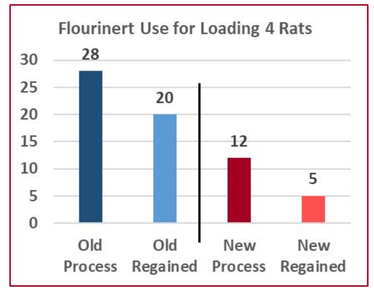


Figure 4.2: Quantities of flourinert (mL) used and recovered from loading 4 rat brains.

Future Work

- Change design to further stabilize brain orientation.
- Create a method to catch excess flourinert during loading.
- Create a more streamlined water-marker.
- Make a stopper that is more secure in the capsule.
- Re-design the mice capsule, creating wider holes to fit a larger variety of brains
- Create deeper lids to allow for variability in hole depth.

Acknowledgements

We would like to extend our sincerest gratitude to our clients, Dr. John-Paul Yu, Nick Stowe, and Ajay Singh, and our advisors Dr. Kris Saha, Dr. John Puccinelli and the BME Department.

References

- [1] K. Kania, "Small Animal MR Facility - Services & Equipment," Mallinckrodt Institute of Radiology - Washington University School of Medicine in St. Louis. https://www.mir.wustl.edu/research/core-resources/small-animal-magnetic-resonance-facility/services-equipment/ (accessed Oct. 07, 2022).
- [2] J.P. Yu, "Profile," Department of Radiology. https://radiology.wisc.edu/profile/ (accessed Oct. 07, 2022).
- [3] T. Woods, "MRI Safety and Compatibility of Implants and Medical Devices," *ASTM International*, pp. 82–90, doi: 10.1520/STP11156S.