The Product Design Specification (PDS)

High Throughput Quantitative Ex Vivo Murine Brain MRI Capsule

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Function

Dr. JP Yu's lab currently takes Magnetic Resonance (MR) scans of murine brains by loading the samples into modified syringes. This method of imaging involves individually loading and processing each model separately which is inefficient and expensive.

Our team plans to streamline the process by working with the client to create MR-compatible 3-D loading capsules for murine brains which will hold the samples in the correct alignment for a scan and be able to fit more samples per scan than their current procedure permits. The capsules will be more efficient, both in terms of cost as well as research throughput. It will allow for more reproducible scientific methodology, it will be reusable, and the design will ensure the capsule is airtight and resistant to chemicals used during the process.

Client requirements

High Priority Requirements (Highlighted by client as most important)

1. **Packing efficiency**

Must be able to fit more than 3 rat brains and more than 6 mice brains per MRI scan. These numbers are based on the amount that they are currently able using their current methodology. Each MRI scan takes 24 hours and costs $500, which highlights the importance and value of this requirement. It should be noted that only once in the last 5 years was a brain rescanned due to poor quality of image, therefore all the time is spent during post processing to adjust and fix any problems with the scan.

2. **Orientation of murine brains**

Must have the brain's midline parallel with the center axis of the MRI bore cylinder, and all brains must be in the same plane (plane being perpendicular to the axis). At the moment, the client loads the brains into syringes (cylindrical) and the midlines are marked with a pen on the outside of the syringe. Then directly before scanning, 3 syringes are taped together with the midlines oriented in the same direction based on the marking on the outside of the syringe. However, because the brains do not fit the syringes, they can twist or turn within the syringe and the midlines become misaligned when transporting the brains to the MRI from the lab. This does not necessarily decrease the quality of the scan, however, it does significantly increase the post processing time. This background explains why the orientation must be kept consistent.

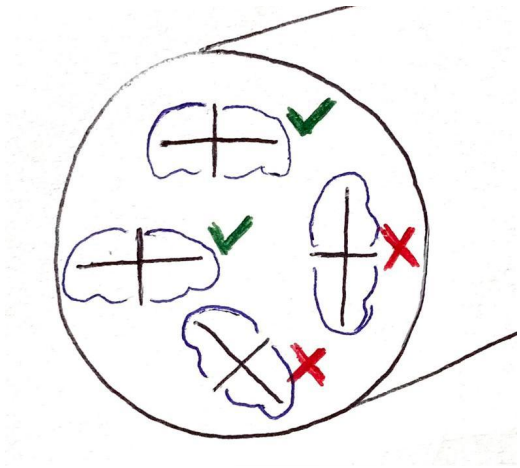

Figure 5. Brain's midline is parallel with the center axis of the MRI bore cylinder.

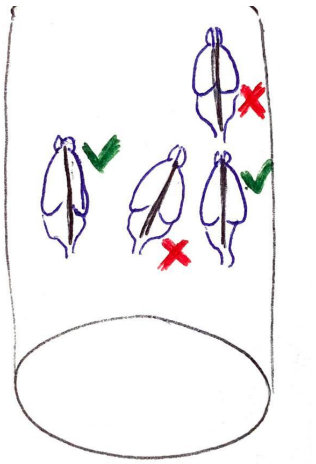

Figure 6. All the brains in the same cross-sectional plane.

Other Requirements

3. Have a complimentary scientific procedure to make the process standardized and reproducible. Because they are doing scientific research, they are interested in having reproducible results that any scientist could verify. Their current method does not fulfill this requirement.
4. MRI compatible: Material must not obscure image. (See design requirements for more details).[informal interview with MRI technician]
5. Reusable: They would like to reuse the device after removing and/or discarding brains.
6. Must not damage brains or deform brains during loading, unloading, and scanning. The lab studies the microstructure of the brain to draw implications on the impact of diseases and drugs.[3]
7. Seal in fluorinert without air. The capsule must have no air touching the brain and there must be a seal so that fluorinert does not spill. When air touches the brain, the barrier going from the magnetic properties of air to the properties of the brain causes a bad image.[informal interview with MRI technician]

Non-Essential Specifications

- Be able to retrieve fluorinert. Fluorinert is very expensive and it is currently not on the market due to supply chain issues from the pandemic. (cost consideration)
- Decrease the amount of fluorinert required for submerging brains. (cost consideration)
- Be able to retrieve the brain safely without damage (for further research). There are further tests that they sometimes want to do on the brain, which requires that they are not damaged after the MRI scan.

- Be able to resize the physical device for both mouse and rat brains. The implication was that the device can have notches or some form of physical adjustment to resize for one or the other type.
- Decrease the loading time of the brains. It takes about MMMMMM minutes to load 1 brain with the current methodology.
- Minimize vibration of the capsules and components to improve MRI scan
- Can contract or restrict the size slightly to secure the brain during the MRI
- Have points of reference to align midlines of brain with the MRI machine bore axis
- Have space for a watermark

Design requirements

1. Physical and Operational Characteristics

a. Performance requirements:

Must increase loading efficiency to higher than the current rates of 3 rat brains per MRI scan and 6 mice brains per MRI scan, which currently take long increments of time to insert and remove from individual syringes. Shall not increase scanning time to more than 20 hours. The device should also minimize air bubbles introduced to the brain samples.

b. Safety:

MRI machines and rooms cannot contain any magnetic elements or metals, which will react dangerously with the magnetic fields produced by the MR-scanner.[1] The product should not have sharp edges as the client will be loading the specimens by hand.

c. Accuracy and Reliability:

Brain samples should remain in correct alignment during the MRI scan within a margin of error of 2 degrees. Samples should fit compactly within the capsules in order to minimize shaking from mechanical vibrations caused by the MR-scanner, which could cause imaging issues. The capsules themselves should allow for simple alignment within the scanner to allow for standardization of image location. The capsules should also be easily reproducible for mass production.

d. Life in Service:

Must be in service for approximately 24 hours minimally, however, should be able to be used as a storage device for the brain samples for at least one year. Minimally must be able to be both sealed and reopened once, but preferably can be reused over the course of a year (approximately sealed and opened once per month).

e. Shelf Life:

The client did not specify a specific shelf life; we estimate that the product should have a shelf life of 1 year.

f. Operating Environment:

Strong magnetic fields will be applied to the device in the MRI machine, which require high voltage and current to power the device possibly causing high temperatures, however, the MR-scanner itself has its own cooling system to mitigate this.[2] Nonetheless, while the machine is powered the device will be exposed to high noise levels as well as vibration, and will likely be handled often. In addition, the device will be in contact with Fluorinert often. Thus, the device itself should be sturdy, and should not move within the scanner.

g. Ergonomics:

Should have the ability to sustain the force of a vacuum seal (exact force to be determined) without deformation. Brain should not be damaged during loading and unloading, and allow for simple and quick insertion and extraction, and should also protect brain samples during scanning.

h. Size:

The device(s) must fit in a cylinder bore with a diameter of 37.29mm and a length of 50.35mm. The brains must be positioned within the relatively small scanning length of the coil (50.35mm), however other parts of the device can extend outside of the coil.

i. Weight (redundant):

The device should weigh less than 15 kg when combined with brain samples as well as fluorinert.

j. Materials:

Magnetic metals should not be used since the product will involve MRI imaging. The product must not contain polar molecules that would be affected by the magnetic coil and decrease imaging accuracy. A non-biodegradable, waterproof material that is compatible with Fluorinert is preferred.

k. Aesthetics, Appearance, and Finish:

The capsule will preferably be transparent for ease of visualizing the brain positioning. Texture should be smooth to avoid damage to the brain and coil when loading and unloading.

2. Production Characteristics

a. Quantity:

The client wants 4 - 8 units of the product and the ability to reproduce the product. Since the client performs experiments on both mouse and rat brains, this quantity will double to 8-16 total.

b. Target Product Cost:

The target product cost should not exceed $30. Additional costs from test printing prototypes should not exceed $50, for a target total cost of $80. Currently, the Yu lab is using 3.5 mL and 10 mL syringes to hold each rodent brain. This is likely costing them approximately $2.00 per syringe. This does not include costs from fluorinert and imaging film, which should be reduced by our design.

3. Miscellaneous

a. Standards and Specifications:

ASTM STP1438-EB is the standard for determining whether a device or material is safe for a Magnetic Resonance environment. The most critical factor of determining whether a material is MR safe is that the material does not contain any metallic or magnetic components. [1]

b. Customer:

The customer and user is our client.

c. Patient-related concerns:

There is no patient interacting with the product, and thus this section is not applicable.

d. Competition:

No competing devices or patents were found. One study that was cited numerous times by other articles showed scans with 4 brains in one array. The brains were oriented with the top of the cerebrum toward the center axis in a radial formation.

Sources

[1] T. Woods, “MRI Safety and Compatibility of Implants and Medical Devices,” *ASTM International*, pp. 82–90, doi: 10.1520/STP11156S.

[2] “Specifications for a 4.7 Tesla/400MM Actively Shielded Magnet System,” 2001. Accessed: Dec. 15, 2022. [Online]. Available:

[3]S. Yi, B. Barnett, M. Poetzel, N. Stowe and J. Yu, "Clinical translational neuroimaging of the antioxidant effect of N ‐acetylcysteine on neural microstructure", Magnetic Resonance in Medicine, vol. 87, no. 2, pp. 820-836, 2021.