

The Product Design Specification (PDS)

High Throughput Quantitative Ex Vivo Murine Brain MRI Capsule

Client: Dr. JP Yu, Radiology

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Section Number: 303

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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. Functionality and Usability

The primary update to this PDS is the emphasis on producing a usable product by the end of the project deadline. This relates to the quality of the scans, the elimination of leaking and bubbles, and ensuring the product can be reusable. Formerly, the emphasis was increasing the number of brains that can be scanned per scan.

2. Orientation of murine brains

The brain's midline must be parallel with the center axis of the MRI bore cylinder, and all brains must remain oriented in the same plane, perpendicular to the axis. This orientation must be maintained through the scans. At the moment, the client loads the brains into 3 mL and 5 mL syringes (for mice and rats, respectively) 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 properly, they can twist or turn within the syringe and the midlines can become misaligned during transport from the lab to the MR-scanner. This does not necessarily decrease the quality of the scan; however, it does significantly increase the post processing time to realign the brains for comparison. This background explains why the orientation must be kept consistent.

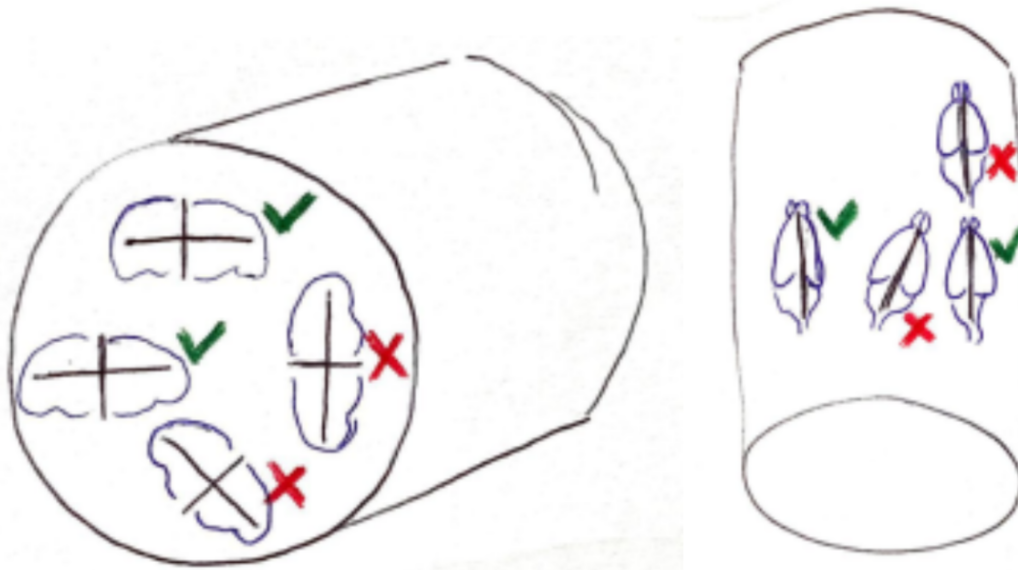


Figure 1. Brain's midline is parallel with the center axis of the MRI bore cylinder. *Figure 2. All the brains in the same cross-sectional plane.*

3. Packing efficiency

Attempt to scan more than 3 rat brains and more than 6 mice brains at a time. These numbers are based on increasing the amount that the lab is currently able to scan 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 a large amount of time is spent during post processing to adjust and fix any problems with the scan. In addition, it takes 75 minutes just to load and unload 12 brains from their syringes.

Other Requirements

4. Have a complimentary scientific procedure to make the process standardized and reproducible. Because the clients are doing scientific research, they are interested in having reproducible results that any scientist could verify. Their current method does not fulfill this requirement.
5. MRI compatible: Material must not obscure image. (See design requirements for more details).[informal interview with MRI technician]
6. Reusable: The clients would like to reuse the device after removing and/or discarding brains.
7. 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]
8. 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 produces a poor quality 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 1-3 hours to load and unload 12 brains 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
- Provide 2-4 usable units at the end of the semester

Design requirements

1. Physical and Operational Characteristics

a. Performance requirements:

Within a timeline of 18 months, the lab has been able to scan ~163 mice brains and ~63 rat brains. The product must be able to perform this many scans in this timeframe. It can be reusable or a product that can be mass produced, so long as the client can themselves replace the product when it stops functioning and perform this many scans per year.

The following standards should be maintained or improved upon. Current method of loading results in approximately 2 mL fluorinert loss per brain loaded, 12 brains loaded per hour, 12 brains unloaded in 15 minutes, and the loss of another 1 mL of fluorinert, in addition to the destruction/loss of a 3 mL and 5 mL syringe for mice and rats, respectively, when unloading each brain. With the lab's current loading method, they are able to scan up to 6 mice brains or up to 3 rat brains at a time. Each scan costs \$500 and takes about 20 hours.

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 snugly 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. Must also be able to be both sealed and reopened once, but preferably can be reused at least 50 times (approximately sealed and opened once per month).

e. 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, waterproof, and should not move within the scanner.

f. Ergonomics:

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.

g. 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.

h. Weight (redundant):

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

i. 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 consequently decrease imaging accuracy. A non-biodegradable, waterproof material that is compatible with Fluorinert is preferred.

j. 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 2-4 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 4-8 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.