

# Stereotactic Device for Animal MRI

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## Table of Contents

<b>Table of Contents.....</b>	<b>2</b>
<b>Abstract.....</b>	<b>3</b>
<b>Background Information.....</b>	<b>3</b>
<b>Problem Statement.....</b>	<b>4</b>
<b>Motivation.....</b>	<b>4</b>
<b>Client Requirements &amp; Design Specifications.....</b>	<b>5</b>
<b>Preliminary Research.....</b>	<b>7</b>
<i>Heating Concerns.....</i>	<i>7</i>
<i>Materials and 3D Printing.....</i>	<i>7</i>
<b>Existing Devices.....</b>	<b>8</b>
<b>Prototype Restraining Design .....</b>	<b>10</b>
<b>Heating Design Solutions.....</b>	<b>11</b>
<i>Air Chamber.....</i>	<i>12</i>
<i>Fluid Piping.....</i>	<i>13</i>
<i>Air Piping.....</i>	<i>14</i>
<i>Piping Design.....</i>	<i>15</i>
<b>Design Evaluation.....</b>	<b>15</b>
<b>Future Work.....</b>	<b>18</b>
<b>References.....</b>	<b>20</b>
<b>Appendix A: Product Design Specifications.....</b>	<b>21</b>

## **Abstract**

During magnetic resonance imaging (MRI), it is important that the tissue being imaged is kept immobile and properly aligned with the axis of the machine. For brain imaging of rodents, specifically rats and mice, a stereotactic device is beneficial for minimizing head movement of the anesthetized animals during the imaging process. In addition, metabolic rates of animals decrease when under anesthesia, which can cause the animal's body temperature to drop low enough to induce hypothermia or death. Thus, a heat source to regulate body temperature becomes necessary when imaging over an extended time period. To address both of these concerns, three design alternatives have been considered, each a stereotactic device containing a heating component. Ultimately, by comparing the advantages and disadvantages of each, our team chose one design to pursue. Throughout the rest of the semester, this design will be developed and tested, hopefully resulting with a final prototype.

## **Background Information**

Magnetic Resonance Imaging (MRI) is a versatile technique that generates detailed images of soft tissues in the body. MRIs are used to diagnose many conditions as well as to support research. In an attempt to gain a deeper knowledge of the function of the brain, many researchers have begun using MRI technology to image various regions of the brain. Due to the restrictions and costliness of human subject testing, much imaging research is done on animals, specifically rodents. Because the quality of an MRI image relies on the subject remaining motionless, certain conditions must be imposed on scanned rodents. Animal subjects must be both restrained and anesthetized, tasks which require specialized lab equipment. Stereotactic restraints function by aligning the animal, specifically its head, into an exactly calibrated position that allows for coordinate

mapping of the image. Both anesthetic and restraint are required to obtain useful images from animal subjects.

### **Problem Statement**

Dr. Ian Rowland of the Radiology Department at UW-Hospital does research involving MRI of rats and mice. He needs a stereotactic device to minimize head movement of the animals while they are positioned within a 4.7 Tesla MRI scanner. In addition, the device will need to incorporate a heating element to allow for a longer scanning duration without danger to the subject. This will allow a higher resolution scan of the animal's brain and will provide more useful information for research. Dr. Rowland uses specifically sized MR coils to gain a higher resolution scan of the target areas. Although existing stereotactic devices exist, they are poorly compatible with his MR coils. The entirety of our restraining device needs to fit within these MR coils. Also, available stereotactic devices are also not very compatible with the client's anesthetic methods, as most restraints obstruct the animal's mouth. The mask can currently be firmly affixed to the animal with tape; however, this is a very inconvenient design. Anesthetic delivery cannot be obstructed by our restraining system. Finally, the design must be carefully constructed so that it does not interfere with the magnetic imaging process.

### **Motivation**

Animal safety becomes a concern without a proper heating device. Potential hypothermia or death of an animal becomes an issue concerning ethics and improper treatment of lab animals during research. As far as research is concerned, convenience and quality will be greatly increased with a well-constructed device. With an accurate

head restraint, the clarity of images will increase. In addition, a consistent heating apparatus that will maintain proper body temperature of the animal will allow researchers to image over extended time periods with minimal concern for animal safety.

Dr. Rowland does neuroscience research using high-resolution small animal MRI. Neuroscience research involving small animal MRI could involve furthering knowledge of neuroanatomy, demyelinating diseases such as multiple sclerosis, and diagnostic capabilities of MRI in the treatment of stroke in humans [1]. These are merely a few examples of neuroscience research involving small animals, and there is incredible potential for the use of MRI in improving healthcare. Ultimately, we hope our device can aid MRI research, a field actively pursuing new treatments of diseases, new diagnoses, and a better understanding of physiology.

### **Client Requirements & Design Specifications**

There are many requirements that needed to be followed when creating this device to ensure that it can be functional for our client. First, the device cannot interfere with the MRI images that are being created. This means that there cannot be any type of metal or ferrous material in the device because these types of materials disrupt the image by interfering with the magnetic field of the scan. The magnetic field created by our client's device is 4.7 T. This is strong enough to rapidly accelerate magnetic objects and cause significant damage to the animal and the machine, making material selection crucial to the design. The magnetic field should not be able to deform our prototype in any way to ensure the safety and integrity of the lab.

Second, the restraint must be made so that it aligns the animal's brain centrally along the axis of the MRI machine. By aligning the subject's brain in this way, it allows

our client to gain the best possible image from the scan. From existing work done by our client, we know that a rat's brain is located 6 mm forward and 6 mm up from the rodent's ear canal. To accomplish proper alignment, our restraint will need to be recessed below the upper edge of the cradle.

A major component of our design is the incorporation of a heating element. The lowered metabolic rates the subjects experience while anesthetized can be harmful if prolonged. The client wants the animal's body temperature to remain near its conscious value of 37°C, within  $\pm 5^\circ$ . This converts to a range of about 90-107°F. As explained above, the current heating method is inadequate, and the design of a new system would allow for prolonged imaging and higher resolution scans. This system will need to be carefully regulated, as overheating can also significantly harm the animal by causing burns.

The client needs a device that fits in his specific MRI coils. Our design will be placed within a half-cylinder cradle that will in turn be inserted into the specialized MRI coils. To be functional in the rat MRI coil, the device needs to fit within a circular cross-sectional area with a diameter of 63 millimeters. The mouse restraint has similar size constraints, but with a diameter of 36 millimeters.

Any movement throughout the course of a scan can blur the image and greatly reduce the image's clarity. Thus, our restraint must be able to inhibit the animal from moving while imaged. Since our client is specifically imaging the brain, properly securing the head is vital in our design. However, the restraint needs to be made so that it is not too tight on the animal that could cause it any harm. Therefore, our device

must have very fine adjustability so that the technician can find the appropriate force to exert on the animal.

During the imaging process, the client uses an anesthetic mask to supply the animal with isoflurane. Our device must not obstruct the anesthetic mask from completely covering the animal's mouth and nose to ensure the animal stays anesthetized through the entire imaging process. This can be difficult because the standard method of securing the subject involves hooking the rodent's teeth into a sliding device that is gently pulled by the technician to elongate the snout and restrain the animal. Our design must be able to achieve the same restraining capability without obstructing the oral anesthetic.

## **Preliminary Research**

### *Heating Concerns*

As stated previously, animals under anesthesia over extended periods of time need some sort of heat source to maintain proper body temperature. Currently, Dr. Rowland utilizes a device that blows hot air on the animal, but he feels this is inadequate. He explained that if the animal is moist, the device could actually cool the animal rather than heat it, and he feels a good solution would be to design a heating component in the base of the device that uses circulating air or water. The heating component cannot have any hot spots for the safety of the animal. Thus, circulation and heat distribution will be key factors in determining a possible design.

### *Materials and 3D Printing*

The 4.7 Tesla MRI scanner used in Dr. Rowland's lab generates a substantial magnetic field, impacting which materials can be used in the device. To take these

concerns into account, our design alternatives consider either constructing the device with a 3D printer or primarily using plastic for construction. The concept of 3D printing may be new to many, and thus it shall be explained briefly.

The Digital Media Center in the Biotechnology building on campus has a 3D printer that has been used to construct objects used in MRI scanners in the past. This printer is a Zcorp Z406, and it constructs models out of a plaster made with gypsum powder and infiltrated with cyanoacrylate. It works by slowly constructing layer upon layer of plaster, using one bin to feed gypsum powder into another where the product is built. The Zcorp model is accurate to .003" and can construct a model up to a volume of 8"x10"x8" [2]. At the suggestion of our client, our team has decided 3D printing could provide an easy way to accurately construct most of the device, and it is likely to be used for our final design.



**Figure 1: Zcorp Z406 3D printer [2].**

### **Existing Devices**

Many stereotactic devices are on the market for use with animal imaging. The industry standard employed by stereotactic devices to keep rats and mice still is by securing the ears and teeth. Therefore, most devices include two screws that go into the ears and a tooth hook. The ear screws are gently inserted into the ear canals and can have



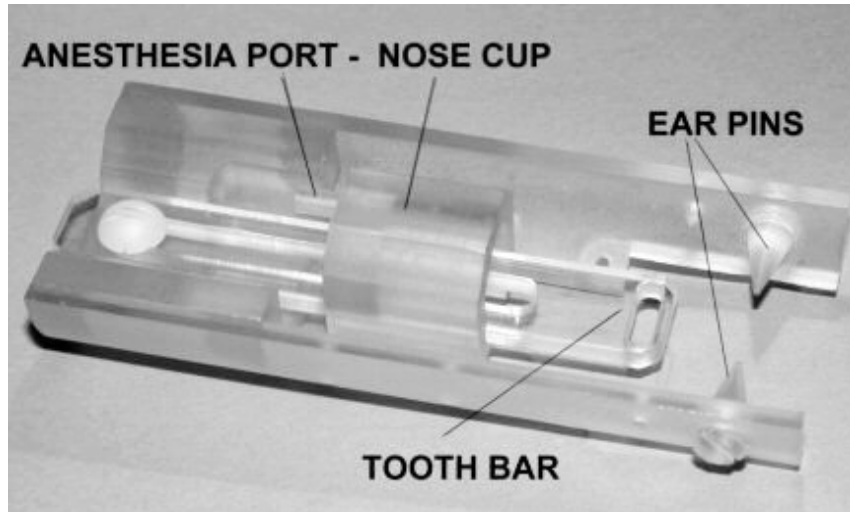
variable depth depending on how tight it needs to be on the animal. The tooth bar is connected to the front teeth of the animal and then pulled forward which puts enough force on the animal that it is fixed in that position.

One company that makes them is David KOPF instruments. They make two models, Model 324: MRI Head Holder for Rat, and Model 325: MRI Head Holder for Mouse (See Figure 2). Both of these models are made with a non-metallic engineering thermal-plastic material called Delrin. The rat holder can accommodate a rat's head of 210-250 grams and can fit a MRI tube with a diameter of 35.5 millimeters. The mouse holder is made to fit a MRI tube of 26.67 millimeters. It also includes three sets of ear bars of .220, .250, and .280 in length [3].



**Figure 2: MRI head holders for rat and mouse respectively from KOPF Instruments[3].**

There is also a stereotactic device that is used at the Enzyme Research Facility on campus. It is very similar to the picture seen below. It has the same industry standards with the ear screws and tooth bar. This one is different than the KOPF holders in that it also has the anesthesia port and mask built into it. When the animals teeth are connect to the hook, the tube for anesthesia is run into their mouth and then a nose cup is slid over so that the mouth and nose is covered. .



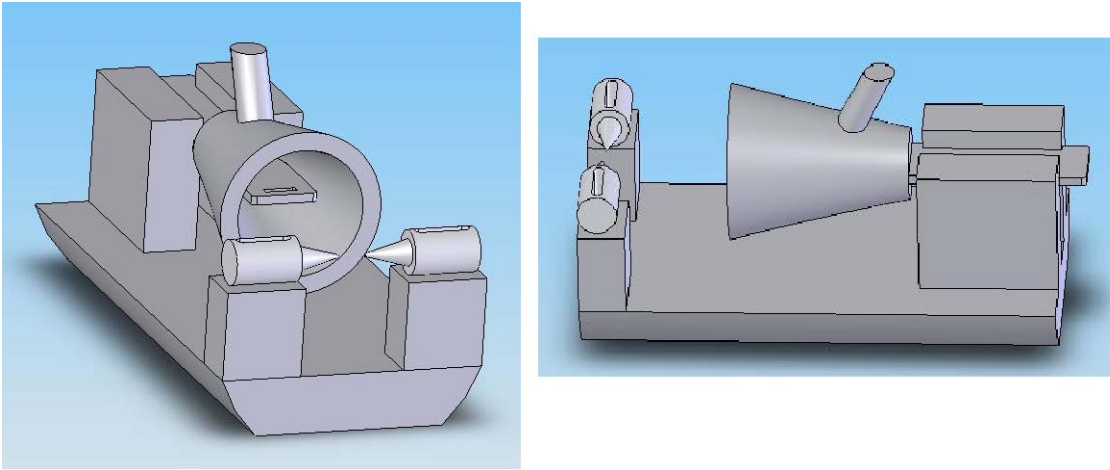
**Figure 3: Stereotaxic device similar to the one the Enzyme Research Facility uses [4].**

The reason these devices are not viable options for our client is that they don't easily fit the specific MRI coils of the client. Another way the above devices are inadequate is that they lack an incorporated heating element, which is required by our client.

### **Prototype Restraining Design**

Our restraining device will use the same industry standard for fixing the animal. There will be screws that go into the ear canals; however, the tooth hook will be slightly different. It is similar to the Enzyme Research Facilities device in that it incorporates the anesthesia mask with the tooth hook. The anesthesia mask can slide along the bar of the tooth hook. This way when the rat's teeth are on the hook the anesthesia mask will also go over their mouth and nose. This will make it easier for the technician to put the animal in the restrain and create less hassle getting the anesthesia mask on. We are currently investigating the option of using 3D printing technology to manufacture this

design. This process would create the device out of a gypsum-polymer plastic that is MRI compatible.



**Figures 4 and 5: Designs of our restraining device made on SolidWorks.**

The design will also be made so that that the restraint fits inside the trays that the client puts inside the MRI coils. This will ensure that the restraint is small enough to fit in the client’s coils. It also needs to be recessed below the top of the tray so that the animal’s brain is centrally aligned down the axis of the MRI coils.

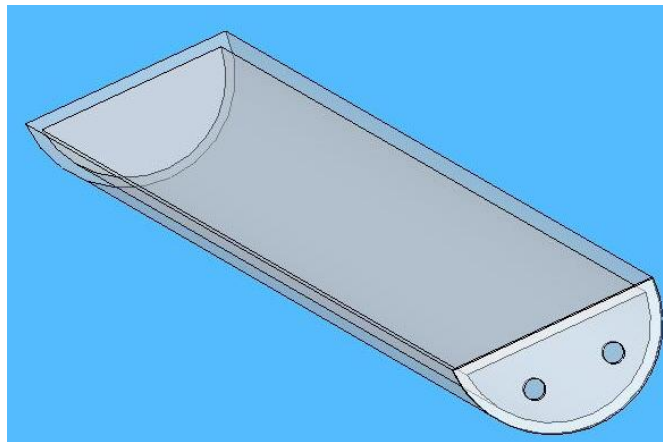
### **Heating Design Solutions**

Our three options all included the same restraint design. Given the limited amount of space inside the MRI tube, the existing type of restraint with some modification works best for our application. The variance in our designs comes in heating the anesthetized animal. Two heating mediums were considered as well as two structural designs. In all of the designs, the animal’s temperature will be monitored through a rectal temperature probe that is interfaced with an SA Instruments, Inc. Model 1025 Small Animal Monitoring and Gating System.

### *Air Chamber*

The air chamber would modify the client's existing tray for the animal to contain an air compartment underneath. Plexiglas® would be used to create a platform over the air cavity. One of the end pieces of the trough would be drilled with two holes providing an input for the hot air and an output for recirculation. The heated air would be provided by the client's current hot air blowing system. Because of the discrepancy in size between the blower and the inlet, an adapter piece would be needed to step down the size of the supply air.

The air chamber would be inexpensive to make because it does not involve many new parts. Plexiglas®, plastic tubing, and the adapter piece would be the only purchases. However, since cost is of little concern, the shortfalls of this design take precedence. Because the chamber would be nearly one meter long, a volume of 3.22 liters is created. This volume will be hard to heat evenly because the inlet and outlet are next to each other. Adapting the current hot air gun to be used with small diameter tubing (.25 inch) will also prove difficult because it may cause too much pressure in the tube. This could cause the bed to crack or failure of seals. The use of hot air itself is undesirable because it has a low thermal conductivity (.024 W/(m·K)) [5].



**Figure 6: The air chamber design.**

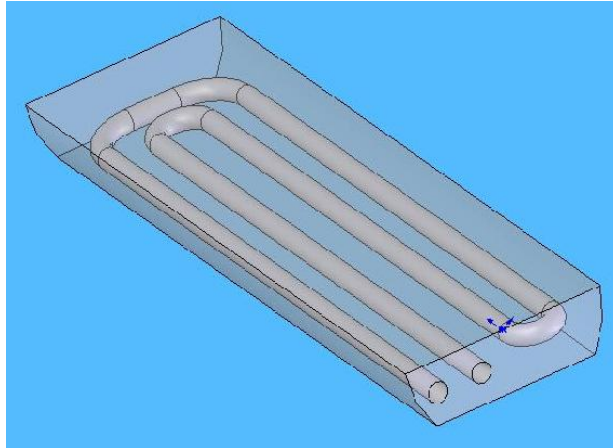
### *Fluid Piping*

The next option involves pumping heated water through a bed of 3-D printed material. The printed material is made from gypsum powder that is bonded together layer by layer. After the entire object is made, it is coated with cyanoacrylate, commonly known as Superglue™. This coating hardens by polymerizing using water. Thus, using it with a design that moves water through the material would be desirable. The hot water would enter the inside port and exit the outside port as shown in Figure 7. This water would be supplied by a heating system consisting of three main parts: a water heater, water pump, and reservoir. These components are also used in other environments, such as landscaping and home aquariums, and we hope to modify these existing solutions to fit our specific design requirements.

This design has several important advantages over the other designs. The bed itself requires no machining because it is made entirely using the 3-D printer. Accessory parts to implement this design are inexpensive as well. The pump, heater, and tank can all be found for under \$200. Water is an especially desirable medium to conduct heat because it has a higher thermal conductivity ( $0.6 \text{ W}/(\text{m}\cdot\text{K})$ ) [5].

Piping water through a printed bed also has significant concerns. While all the other parts to this heating element are inexpensive, the bed itself costs  $\$8/\text{in}^3$  for materials and  $\$20/\text{hr}$  for labor. While this is not a major concern for our client, if the project were to be duplicated elsewhere, this cost could become significant. The major concern with using water, however, is if a failure in the system occurred. If a fitting on the bed were to fail, for example, water could leak into the MR tube and cause damage to the machine.

Therefore, to prevent this, a kill switch will need to be implemented to detect a failure that could damage any of the other systems. Upon such detection, the pump would then be stopped to prevent any more water from flowing.



**Figure 7: The water and air piping designs.**

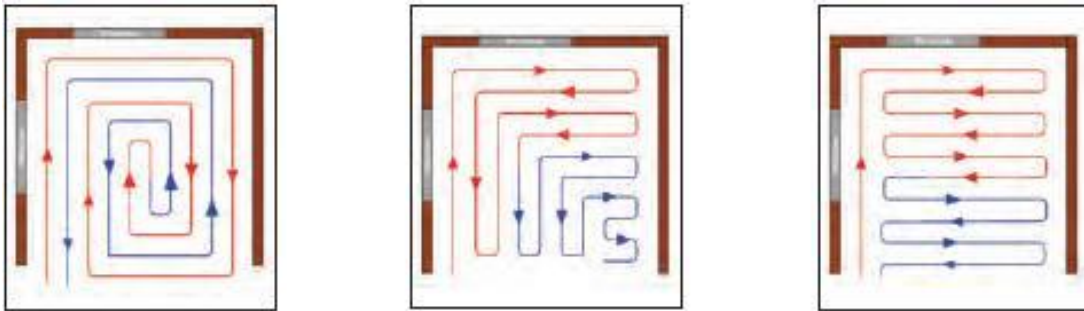
### *Air Piping*

The final design solution is a combination of the first two. It implements the use of the 3-D printed bed, but uses hot air in place of water. The hot air would still be supplied by the client's heat gun.

This option provides greater security to the MR system because there is no possibility of a water leak. Printing the bed also allows an easy construction because no machining is needed. However, since hot air is being used, some of the concerns from the air chamber still exist. Moving the air from the heat gun to the bed will prove difficult, but more importantly, air's poor thermal conductivity would increase the start up and reaction times.

## *Piping Design*

To decide piping layout for use in the water and air piping designs, in-floor heating systems provided an appropriate model. After considering three patterns outlined by Infloor Heating Systems, a design modeled after their Counterflow Spiral was adopted. It provided an even distribution of heat by placing cold pipes next to hot pipes and also allowed the inlets and outlets to be conveniently placed next to each other.



**Figure 8: From left to right: Counterflow Spiral, Double Serpentine, and Single Serpentine piping layouts [6].**

## **Design Evaluation**

With these three designs in mind, we created a design matrix (Table 1) that would allow us to evaluate the ability of each design to meet the needs of the client. In our matrix, we had 5 criteria on which we assessed our designs. These criteria were Cost, Heat Transfer-Efficiency, Heat Consistency-Quality of Circulation, Durability and Ease of Manufacturing. We assigned a relative weight to each criterion, then rated the designs' performance on a scale of 1-10. These rating were multiplied by the weight and summed to produce the design's total score.

	<b>Heat Consistency (.3)</b>	<b>Heat Transfer (.25)</b>	<b>Durability (.2)</b>	<b>Ease of Manufacturing (.2)</b>	<b>Cost (.05)</b>	<b>Total</b>
<b>Air Chamber</b>	4	6	8	6	8	<b>5.9</b>
<b>Fluid Piping</b>	9	8	7	8	5	<u><b>7.75</b></u>
<b>Air Piping</b>	7	5	8	6	6	<b>6.55</b>

**Table 1: Design Matrix**

The most important criterion in our matrix was heat consistency. It is critical for the safety of the animal that our platform has a very uniform heat distribution with as few hot spots as possible. We deemed this would be achievable by the design that was best able to circulate the heating medium through the platform. We gave the fluid piping design the highest score because a fluid is able to flow very regularly and consistently through a pipe system. The air chamber received the lowest rating because it does not possess any internal channels. Without any structure to direct the air flow, there is no way to direct the dispersal of heat through the platform, and would yield the least uniform heat distribution on the platform.

The ability of the heating medium to transfer heat to the mouse was our next highest weighted criterion. The fluid piping design again had the highest rating because water has a much higher thermal conductivity and specific heat capacity than air. Thermal conductivity is directly proportional to the rate at which a substance can transfer heat energy to another material, and specific heat capacity is a measure of the amount of heat energy required to raise the temperature of a substance by a certain quantity [5]. Thus, by water having a higher thermal conductivity than air, it is able to transfer heat to the platform more quickly than water. Also, water contains significantly more energy in



the form of heat than air of the same temperature, and thus could disperse more heat to the platform than air if heated to the same temperature. The air piping received the lowest rating because there is a much smaller volume of air than the chamber design, and it also has to heat much more material than the chamber.

Durability is another significant consideration for our design. Although the device will be used in a controlled laboratory environment, the unit should be able to withstand frequent use. All of these designs involve a circulating heating medium. Sustained circulation can eventually degrade materials if they are not durable enough. This was an especially great concern for the fluid piping design. However, after talking with Mr. Alan Wolf, a senior consultant in the Biotechnology Media Center where the 3D printing is done, we were assured that the 3D printing material would be able to endure sustained fluid flow. Nevertheless, moving fluid still has more potential to damage materials than moving air at a similar velocity, and we gave the fluid piping a slightly lower rating than the designs using air.

The ease of manufacturing is important to the design process in two ways. First, a design that is easier to manufacture can generally be manufactured more quickly, which would allow our team more time to run testing. Also, easily manufactured designs can often be done with a higher quality than very complex construction. The use of 3D printing technology allows our team to create a fairly intricate design that only requires knowledge of a 3D drafting program, such as SolidWorks. Also considered in this rating is the ability for our team to assemble the heating and pumping components. For the air designs, we would adapt the existing hot air blower to fit our needs. When searching of methods to heat and pump water, our team was able to find options that are inexpensive

and simple. With the simplicity of 3D printing and the high availability of necessary components, there was very little variance between ratings. The fluid piping held only a slight advantage because we felt modifying the existing heating system would actually be more difficult than our proposed fluid heating and pumping design.

Cost was considered in our design matrix, however to a small extent as it is not a large concern to our client. Although the cost of 3D printing is rather high, the cost of accessory components to all of our design is very minimal, thus the overall costs are all relatively low. These additional components would include a pump, a heating device, a reservoir, and connective tubing from the reservoir to the heating platform. The air chamber would be very simple and inexpensive, so it achieved the highest ranking, and the fluid piping received the lowest rating due to the cost of printing and other necessary apparatus.

After totaling the scores of all the criteria for each design, the fluid piping design emerged as the prototype that would best meet our client's requirements. Thus, this is the design that our team will pursue to create a heating element for our stereotactic device.

### **Future Work**

In the upcoming weeks, we will be doing further research into the specific layout of our heating system. We need to ensure that the startup time from when the researcher turns our unit on to the time it is warm enough to heat the animal is minimal, and we also want to ensure that the heat lost as the water is pumped from our heating tank to the platform is also kept to a minimum. We will be running tests with the 3D printed samples to examine how heat is transferred through the material. For example, if we have a pipe of a certain diameter and thickness, we want to know how much heat the water loses

travelling through a known length of pipe and what the temperature on the outside of the pipe is. This will help us determine the most uniform and efficient piping design for our platform.

Our team also needs to determine what temperature the platform needs to be to heat the animal to an internal body temperature of 37°C. Once we have established this temperature, we will need to determine how hot the water must be to heat the platform to this required temperature. Ideally, we will be able to integrate our system with the SA Instruments, Inc. Model 1025 Small Animal Monitoring and Gating System currently used by the lab to monitor the animal's temperature. This would allow for a fully automated heating system that adjusts to the mouse's body temperature.

We will be constructing our prototype in phases after the necessary testing has been done to justify specific dimensions for our components. We are currently investigating the methods by which we will build our stereotactic device, whether via 3D printing or milling in the machine shop. Components such as the heater and pump we hope to have ordered within the next few days to provide us with the necessary source of hot water to run our future testing. Current options include modifying a CPU water-cooling unit consisting of a pump and reservoir and inserting a heater, or using an aquarium with a small landscaping pump and heater. There are many accurate and inexpensive aquarium heaters available on the market which would function well as our heating device. As time allows, we hope to deliver the completed prototype to the lab with enough time for them to evaluate our design and for us to make the necessary modifications to deliver a functional product.

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## APPENDIX A

### *Product Design Specifications*

#### **Stereotactic device compatible with a 4.7 tesla magnetic resonance imaging system**

##### Team Members

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##### **Problem Statement**

This project requires the design and fabrication of a stereotactic device used to minimize the movement of the heads of anesthetized animals whilst positioned within a 4.7 T magnetic resonance (MR) imaging scanner.\* The magnetic field within the scanner is approximately 100,000 times greater than the Earth's magnetic field and therefore significantly restricts the choice of materials that may be used. Consequently, the entire system should be constructed of MR-compatible materials that are non-magnetic and non-conductive, to avoid artifacts and distortion of the MR images. The device should fit into a range of MR coils used specifically for imaging mice or rats and should also be able to support the positioning of additional MR coils so that images may be obtained from different anatomical regions. Further refinements might include the incorporation of a warming unit, using circulating water or air, within the base of the device. The unit construction may involve the use of 3D printing techniques. In addition, the stereotactic device should also be compatible with a dedicated uCT/PET system so that images may be more easily merged between the three different imaging modalities. In addition to the design and fabrication processes, this project would provide the opportunity to gain some experience with the use of both a 4.7 Tesla dedicated animal MRI and a uCT/PET systems.

##### **Client Requirements:**

- The unit cannot interfere with the imaging device (MRI compatible)
- The unit has to be able to fit within the rat and mouse specific coils
- Anesthetic mask must be able to reach the animal's mouth
- Animal's head should be stable and centrally aligned within the MRI
- The unit should be able to heat the mouse at a constant temperature, as programmed by the imaging technician.

##### **Design requirements**

- Two units will be needed, one for the mouse coil and one for the rat coil.
- The unit must be able to deliver an anesthetic to the animal using a mask.
- The design must include a restraining device and a heating element.
- The rodent's brain must be located in the center of the coil while in the restraint.
- The rodent must be kept at a temperature within 5° of 37°C
- All motors and pumps must be kept at least 3m from the restraining unit.

## **Physical and Operational Requirements**

- a. *Performance Requirements* – The device should be able to be easily adjusted to fit the subjects. Specifically, the ear pegs should be able to firmly fit to the mouse’s head, and the tooth bar should adjust to provide firm restraint. Also, the mouse’s mouth must be accessible for the anesthetic mask. Although a standard rat weighs approximately 300g, our platform must be able to support a large rat that may weigh up to 500g.
- b. *Safety* – The unit cannot harm the animal in any way, including over/underheating or excessive pressure on the skull.
- c. *Accuracy and Reliability* – The mouse’s brain must be located directly in the center of the coil. The heating unit must be able to automatically hold a constant temperature programmed by the technician.
- d. *Life in Service* – The unit should be able to withstand frequent use in a controlled, clinical environment for a long duration.
- e. *Shelf Life* – The unit should not degrade while in storage.
- f. *Operating Environment* – The unit should be able to withstand a strong magnetic field, up to 4.7 T, without deforming. Animal waste should not be able to affect the performance of the unit. The heating unit should not cause damage to the restraining device.
- g. *Ergonomics* - The device should be able to firmly restrain the animal without causing any harm. The device should be easily adjusted by the imaging technicians.
- h. *Size* – The unit must be able to fit within the specific diameters of the rat and mouse coils. The rat coil is 63 mm in diameter, the mouse is 36 mm in diameter, each has a depth equal to its radius. All motors and pumps must be kept at least 3m from the restraining device. The restraint must center the rat’s brain in the center of the MRI. A rat’s brain is located 6 mm forward and 6 mm up from its ears.
- i. *Weight* - The weight should be as minimal as possible.
- j. *Materials* – All materials inside the MRI must be MR compatible. These materials are non-metallic such as plastic or silicon based products, or non-ferromagnetic. Non MR compatible materials must be kept 3m from the restraining unit.
- k. *Aesthetics* – The heating unit must be easy to read, preferably with numerous small visual indicators for the technicians to monitor.

## **Product Characteristics**

- a. *Quantity* – 2 units are needed. A similar design can be used for each, but they must be able to fit the different sized subjects (rat and mouse) and their respective imaging coils.
- b. *Target Product Cost* – Budget will be adequate for the manufacturing of these units.

## Miscellaneous

- a. *Standards and Specifications* – The client will ensure his IACUC protocol allows for the use of our device.
- b. *Customer* – The customer would prefer a unit with visual indicators for the heating system.
- c. *Patient-related concerns* – The product will need to be sterilized in between each use by scrubbing with antiseptic and a tissue. *Competition* – There are numerous other similar stereotactic devices for small rodents. Examples are the KOPF Model 324 MRI Head Holder and the Harvard Apparatus 51624 Mouse Adaptor. However, no current models have an integrated heating element as well. This model is also specifically designed to fit the coils mentioned above.