Head Holder for MR-Guided Drug Delivery

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1. Abstract

Parkinson's disease is an incurable degenerative brain disorder largely affecting the elderly population that decreases the dopamine levels in the brain. The use of Convection-Enhanced Drug Delivery (CED) to overcome the blood brain barrier by direct infusion via catheter to the brain is being researched as a method of restoring dopamine in the brain tissue. Currently, real-time magnetic resonance imaging (MRI) is being used in conjunction with the CED procedure in order to effectively monitor the infusion. High quality images require the use of the additional carotid coils (similar to a large pair of headphones). Since the desired antenna array rests against the testing subject's ears and temples (beagles and rhesus monkeys), other head holders for similar drug delivery experiments cannot be used due to the ear bars, which are commonly used to restrict the movement of the animal's head in the x-, y- and z-directions. The procedure requires that the animal be removed from the head holder and returned to the same position later in the procedure. It is important that the head holder restricts the translational movement of the head to 1 mm or less, be entirely MRI-compatible, and compatible with the current experimental setup.

A redesigned head holder device has been fabricated out of high-density polyethylene (HDPE) with modified ear bars that can be positioned under the carotid coils and adjusted on a sliding track. The ear bars are made from one piece of solid brass, designed with a thicker base that slides on the HDPE headrest and is secured using a thumbscrew through the long axis of the ear bar. These ear bars were designed to slide into a complementary grooved track built into the headrest to prevent rotational and lateral movement. This design meets the most challenging client requirements of restricting the translational movement error margin to 1mm and allowing for reproducible positioning due to its similar structure to current head holders. The device has been tested for tolerances to translational movement in the x-, y-, and z-directions by using still photography, force-sensing resistor to measure the force causing the skull's displacement, and ImageJ (NIH). The images were used to measure the distance to a reference point, which was then compared to a baseline distance. The reproducibility of the device was tested by taking a baseline picture, removing the model skull, and then replacing and photographing the skull once again. The displacement of the skull in each image was measured using the baseline image. There was no significant difference between the means of the displacements of the control group and the final prototype (p=0.314). This design enables real-time CED testing within the MRI machine, which is integral to Parkinson's disease research.

2. Introduction

2.1. Parkinson's Disease

Parkinson's disease (PD) is a chronic and degenerative brain disease. Often affecting men and women over the age of 50 years, PD is one of the most common central nervous system disorders of the elderly. It is estimated that 500,000 Americans are currently affected with PD and 50,000 more people are diagnosed each year. These numbers are expected to increase with the aging population [1].

Symptoms include tremors as well as difficulty with movement and coordination, which are a result of destruction of dopamine producing neurons. The lack of dopamine (neurotransmitter) causes improper cell messaging, which manifests in the loss of muscle function. Continual nerve destruction and subsequent reduction in dopamine levels results in progressive worsening of symptoms. The exact cause of the destruction is unknown. In addition, there are no blood or laboratory tests for a conclusive diagnosis, which makes the disease difficult to diagnose accurately [2].

Currently, there is no cure for Parkinson's disease. Treatment, usually medication based, focuses on reducing the symptoms and slowing disease progression [2]. The effectiveness of many systemic pharmaceutical treatments are further limited by lack of ability to cross the blood-brain barrier to reach the damaged neurons [3].

2.2. Convection Enhanced Drug Delivery (CED)

Parkinson's research has focused on techniques that allow more localized delivery of dopamine-restoring medications. Convection enhanced drug delivery (CED) is especially useful in overcoming the blood-brain barrier and reducing systemic toxicity [4]. A sketch of CED can be seen in Figure 1. The main components of CED are a catheter placed directly into the brain target and a continuous infusion of fluid. Using stereotaxic equipment and corresponding imaging methods, a surgeon directs the needle to a specific location in the brain with high accuracy. Once the needle is inserted, a continuous flow of infusate creates a pressure gradient, which forces the agents through the extracellular spaces via bulk flow. Theoretically, a homogenous distribution will be obtained [3]. CED also has applications to treat brain tumors [4].

Currently, CED is only used experimentally. Current difficulties include hardware malfunction, uneven volume distribution, and infusate reflux along the outside of the catheter. Therefore, further research and method refinement is needed for success in clinical translation [3].

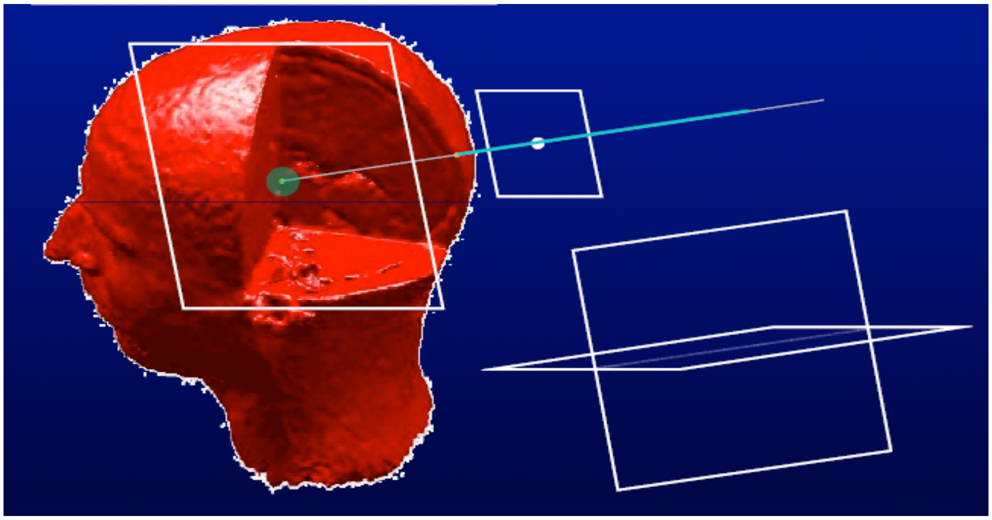
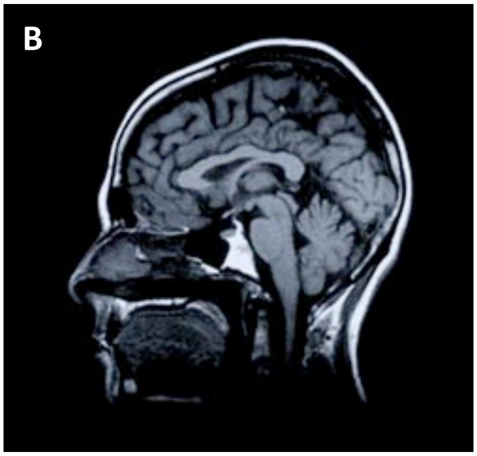


Figure 1: Sketch of CED. Brodsky EK, Block WF, Alexander AL, Emborg ME, Ross CD, and Sillay KA. "Intraoperative Device Targeting Using Real-Time MRI." *IEEE Biomedical Sciences and Engineering Conference (BSEC)*, 2011. https://www.ornl.gov/bsec_conferences/2011/presentations/Brodsky.pdf

2.3. Magnetic Resonance Imaging (MRI)

To monitor the progress of CED, researchers have turned to magnetic resonance imaging (MRI). A MRI marker is mixed with the medications in the infusate. Throughout the infusion procedure, the MRI is used to verify the position of the catheter and to track the volume distribution of the infusate. Dr. Wally Block, our client, is working on creating software that combines CED with real time magnetic resonance imaging (MRI). The software is then used to monitor needle alignment and insertion as well as drug delivery [5].

MRI is a non-invasive imaging procedure that is commonly used in a clinical setting. A standard MRI scanner and image can be seen in Figure 2. MRI uses high magnetic fields and basic spin physicals to create high contrast images of soft tissue [6].



B. Example of MRI image. Cedars-Sinai. "MRI Brain." 2011. http://www.cedars-sinai.edu/Medical-Professionals/Imaging-Center/Neuroradiology/MRI-Brain.aspx

Figure 2: A. Example of MRI scanner. http://www.usedct-scannersandmri.com/ge-ct-mri.html

During an MRI scan, the subject lies on the table of the MRI scanner and is slid into the bore of the MRI to the middle of the magnetic field with accuracy of 1 millimeter. Underneath the plastic encasing, there are large superconducting magnets that create large magnetic fields that range from 0.5 to 3 Tesla (5,000 to 30,000 Gauss). In comparison, earth's magnetic field is approximately 0.5 Gauss [6]. When the patient is subjected to these high magnetic fields, the spins of the protons in the tissues align with the magnetic field [6].

Another component, the radiofrequency (RF) source, creates pulses of RF frequency. If the frequency of the RF pulse matches the angular frequency of the proton, the proton gains a photon of energy, which causes a change in the alignment of the proton's spin. Energy is released as the proton realigns with the main magnetic field and is recorded by the RF detector. Different types of tissues give different responses. Tissues that contain more water typically appear white in the images [9].

Additional non-superconducting magnets are used to create a gradient in the strength of the main magnetic field. Therefore, spatial distribution can be determined by using only a select frequency range of RF pulses. High resolution results from repeating the scanning process over small slices. The raw data is then subject to complex digital processing to create the final images [10].

2.4. Current Research Methods

The client currently uses Rhesus monkeys and Beagles as test subjects for convection-enhanced drug delivery experiments, which require the use of a head holder to immobilize the head of the testing subject. An MRI interventions port is placed toward to the back of the skull and used to help guide the insertion of the catheter into the brain (Figure 3B). The client also uses a MRI antenna array to increase the signal to noise ratio of the MRI images (Figure 3A).

Figure 3: A. Photo of carotid coils. B. Photo of MRI Interventions port. Photos courtesy of Kevin Beene**.**

2.5.Current Head Holders

The head holder that our client currently uses is shown in Figure 4. It is designed so that the animal lies in a supine position (on its back). Bars are placed in the ears, at the top of the palate and at the zygomatic arches (below the eyes). This effectively prevents translational and rotational motion of the head. This head holder, however, is incompatible with the carotid coils. Therefore, our client requested a different head holder that is compatible with the carotid coils.

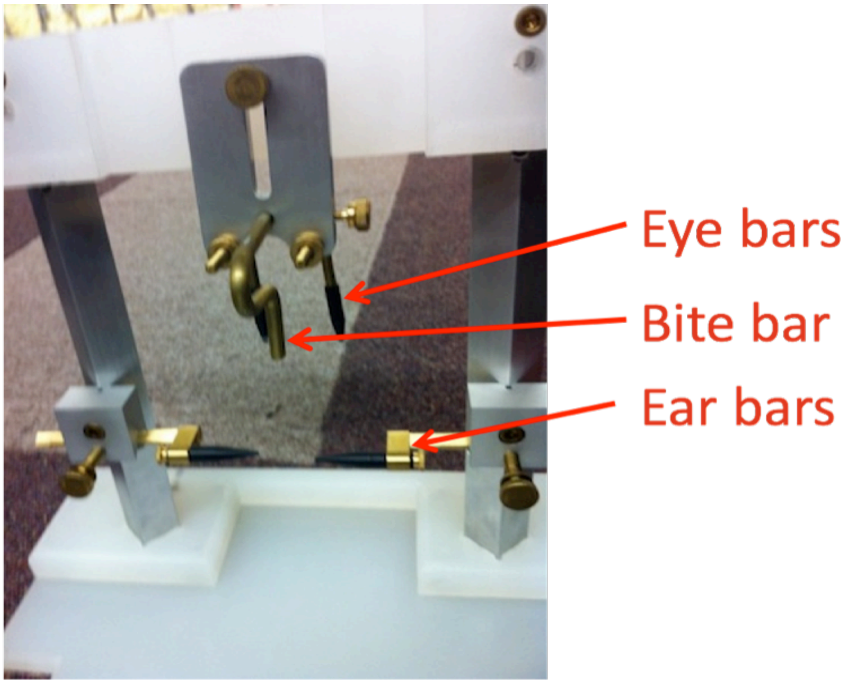


Figure 4: Photo of current head holder. Photo courtesy of Hope Marshall**.**

2.6. Animal Treatment Regulations

In order to engage in animal research, the investigator must submit an animal protocol. The protocol is a contract between the university and the investigator that describes the reason for the research, a detailed description of the research and euthanasia, and contains information about the species and number of animals. Pain management, monitoring procedures and endpoints are documented within the protocol to ensure that the least amount of stress is inflicted upon the animals. The Institutional Animal Care and Use Committee (IACUC) must approve all experimental protocols that involve the use of animals. The Graduate School ACUC oversees the Wisconsin National Primate Center [13].

Although the new head holder device was not used on live animals in the duration of this semester, the device was designed with the animal in mind. Therefore, immobilization methods cause minimal pain or stress to the animal.

3. Problem Statement

The client is working to create software that is able to display real-time imaging of convection-enhanced drug delivery using an MRI machine. High quality images require the use of the additional coils. Since the desired antenna array rests against the testing subject's ears and temples, the current head holder used for similar drug delivery experiments cannot be used due to the ear bars. Thus, the client requires a head holder device that does not interfere with the contact that the MRI antenna array needs to make with the head of the testing subject.

4. Design Specifications

Since the head holder will be used for convection-enhanced drug delivery experiments, it is imperative that the head holder restricts the translational movement of the head to 1 millimeter or less. The device must be MRI-compatible, meaning it cannot contain ferrous materials and it must fit within the MRI bore, which has a height and width of 34 centimeters and 60 centimeters, respectively. The head holder device must also be compatible with the experimental setup used by our client. Specifically, it must account for the use of the MRI antenna array (carotid coils), the MRI Interventions port, and the breathing tube. The device should also allow for accurate repeatable positioning each time that the animal is removed and repositioned within the head holder. Lastly, given that the client works with both Rhesus monkeys and beagles, the device should allow for certain adjustments to be made depending on which testing subject is used so that the same degree of accuracy can be achieved despite the differing anatomies.

5. Designs

5.1. Design Alternative 1: Eye Bar Design

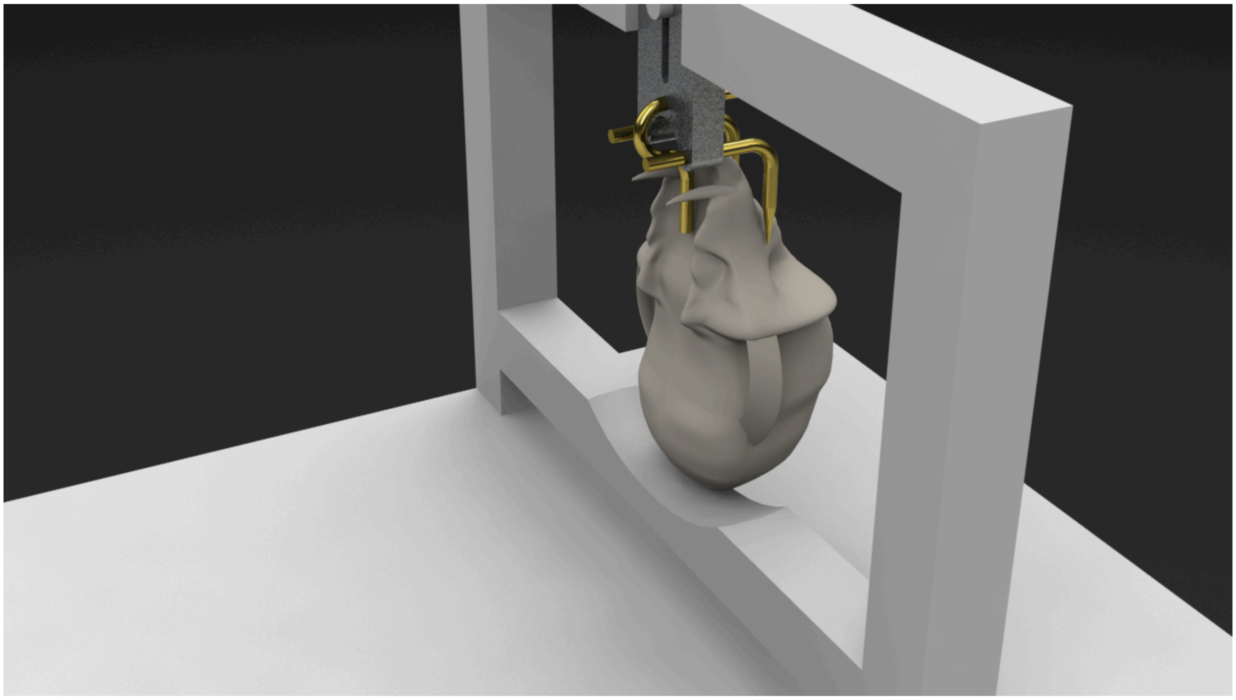


Figure 5: SolidWorks drawing of eye bar design. Sketch produced by Gabriel Bautista.

The Eye Bar design is based on current stereotaxic devices and uses current palate and eye bars, shown in Figure 5. These bars are made of brass and are held by a nylon plate in order to be MRI compatible. The bars push down on the zygomatic arches as well as up into the hard palette, limiting translational movement of the head. The plate, as well as the bars can be adjusted using set screws, which allow for a variety of head sizes to be used with this device.

In order to replace the ear bars traditionally used in stereotaxic devices, the frame of this device is designed to cradle the head of the animal. A foam-like material will be placed on the headrest, which will conform around the back of the skull of the animal and hold it in place. This along with the pressure from the eye bars restricts skull movement in the y-axis.

The major disadvantage of the Eye Bar design is the difficulty of manufacturing the device. Although the device uses parts from current stereotaxic devices (eye and palate bars), a new frame will have to be built in order to hold these parts. The frame must be built out of aluminum in order to be small enough and still maintain the physical properties required. Compared to HDPE, aluminum is harder to work with which increases manufacturing time and difficulty.

5.2.Design Alternative 2: Band/Track Design

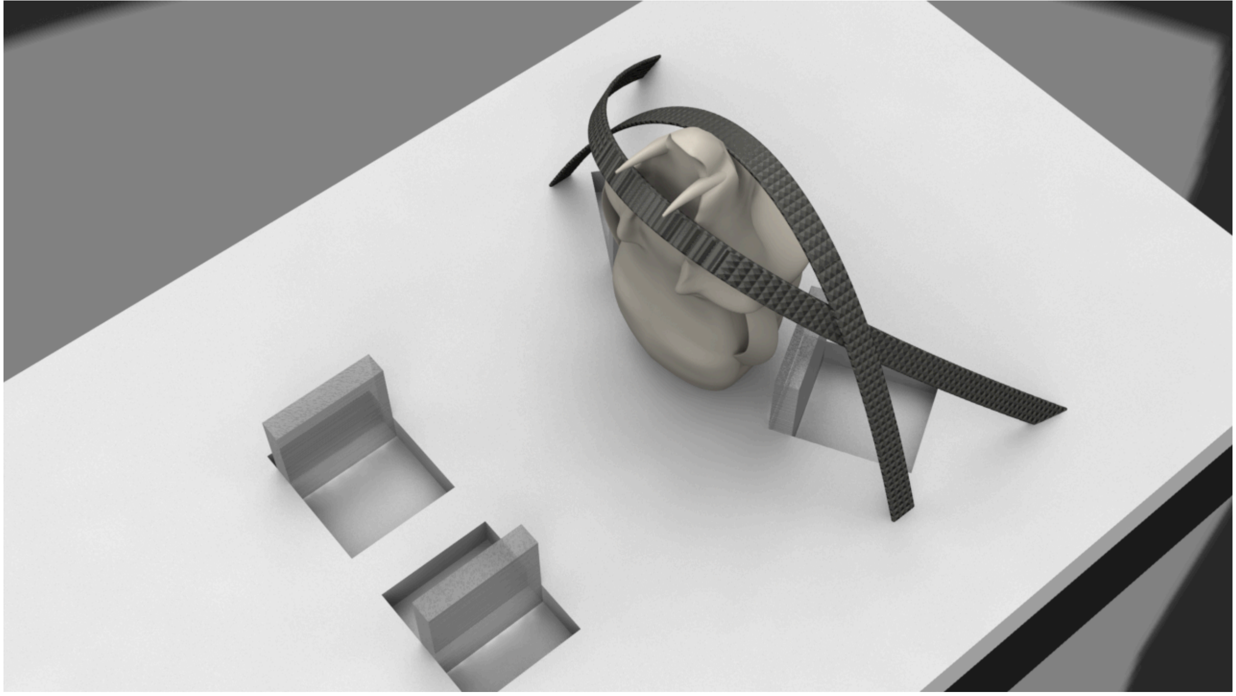


Figure 6: SolidWorks drawing of Band/Track design. Sketch produced by Gabriel Bautista.

The Band/Track design, as seen in Figure 6, includes four high-density polyethylene (HDPE) blocks that slide back and forth along tracks built into the backboard supporting the Rhesus monkey or Beagle. Two blocks immobilize the head on the plane of the board by pushing against the head diagonally, shown in Figure 6, and the remaining two blocks push against the animal's neck at the jaw. The sliding mechanism for the blocks is a T-slot mechanism with thumb screw to secure the position.

In addition, the Band/Track design includes two adjustable crisscrossing elastic straps anchored to the backboard using plastic alligator clips (not shown) on either side of the head, as seen in Figure 6. These straps have been designed to immobilize the head in the y-direction represented by the plane perpendicular to the backboard. One strap will press against the animal's forehead while the other will press against the first molars behind the canines.

The Band/Track design will be easy to sterilize in between uses, as it is composed primarily of HDPE plastic. The straps will be made of silicone rubber, a strong yet easy to sterilize material.

One advantage of the Band/Track design is that it is highly adjustable and versatile. Since silicone rubber is an elastic polymer that would mold to the face shape of either animal, the Band/Track design would be effective in immobilizing the head of either the Rhesus monkey or the Beagle. In addition, the sliding mechanism built into in the backboard for the tracks would make the block placement adjustable to a fraction of a centimeter. The adjustability of the block placement in conjunction with the versatility of the bands holds the design to the 1 mm translational movement error standard specified by the client. The Band/Track design would be low cost, as well.

With respect to ergonomics, the Band/Track design would be advantageous since the HDPE blocks would slide easily and would be tightened into place using a simple screw mechanism. The bands would be easily adjusted, by clamping down the alligator clip, as well, which would make the head immobilization process relatively quick and straightforward for the surgeon.

The major disadvantage of the Band/Track design would be the durability of the silicone rubber bands. As the silicone rubber bands would be used multiple times, the tensile forces applied to the bands in conjunction with the sharp contact points against the animal's teeth as well as the points of contact with the alligator clips, would wear out the bands. A solution would be fabricating multiple silicone bands for the client so they could switch out the bands as they start to wear.

5.3. Design Alternative 3: Fork Support Design

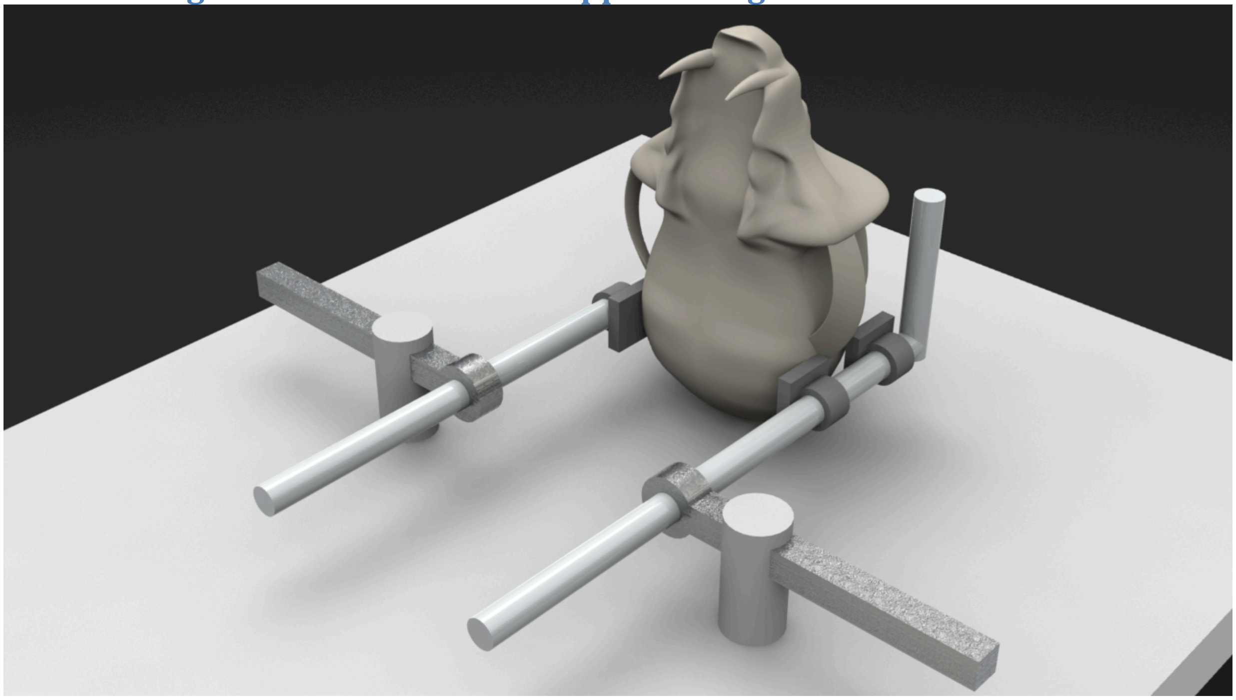


Figure 7: SolidWorks drawing of fork support design. Sketch produced by Gabriel Bautista.

The fork support design is composed of two L-shaped bars that anchor near the neck. The bars slide along the long axis of the board and toward or away from the head to accommodate varying anatomies. The L-shaped bars are also designed to rotate medially and laterally with respect to the top of the head. These are used to cradle the base of the head without blocking the MRI Interventions port. In addition, two sliding blocks on each side support the head near the ears. The carotid coils will be placed over the blocks near the ears.

All components will be made of HDPE. Therefore, the device will be low cost and easy to sterilize between uses. In addition, the device will be durable enough to withstand multiple uses. All moving parts will be secured using screw-lock mechanisms similar to the current head holder. This allows the bars to be adjusted to many positions along the long and short axes of the board. This also allows the bars to assume a large degree of rotational position to better cup the head. A thumb-screw mechanism can be used to make quick adjustments.

One disadvantage of the fork support design is it lacks direct stabilization in direction coming out of the board (the y-direction). The L-shaped bars only indirectly provide stabilization in the y-direction. Therefore, it is unclear if the desired accuracy of less than 1 millimeter of immobilization will be easily achieved with this design. Another disadvantage of the fork support design is the difficulty in fabrication of the parts. However, the team could consult machinists in the student shop or use three-dimensional printing for custom parts in order to fabricate this design alternative effectively.

6. Initial Design Matrix

Table 1: Design matrix used to compare three designs with weighted categories.

	Weight	Band/Track Design	Fork Support	Eye Bar Design
Cost	10%	10	8	8
Ease of Construction	15%	12	12	6
Ease of Use/Ergonomics	20%	20	16	16
Durability	25%	15	20	25
Margin of Error	30%	30	12	24
TOTAL	100%	87	68	79

The design matrix (Table 1) used to assess the three design alternatives was divided into the five categories of cost, ease of construction, ease of use, durability, and margin of error. Each of the designs was assigned a score of one to five, with five being the highest, for each category. Since each category has a unique weight based on their relative importance, the scores from each category were multiplied by their respective factors. The final scores for each design were reached by adding the scores of each individual category.

In the design matrix, cost was considered the least important category and given the smallest weight. Since the current head holder cost about $2,000 to manufacture, the team is confident that all of the design alternatives will be constructed at a mere fraction of the cost of the original head holder. The Band/Track design received the highest score in this category because the group believed that using the two straps to replace mechanical parts would make the Band/Track design the least expensive alternative.

In the ease of construction category, the Band/Track design and the Fork Support design scored identically. The Band/Track design will lead to a more complicated fabrication process due to the tracks that need to be built into the board. While the Fork Support design appears to be simpler than the Band/Track design, special care will have to be paid to the construction of the posts of this design to ensure that they remain stable and rigid. The Eye Bar design received the lowest ranking in the ease of construction category since it is based on the current head holder, which used brass for the eye bars and palate bar. Using brass as the raw material for the eye bars and palate bar of this design will lead to a more difficult manufacturing process. In the ease of use category, the Band/Track design received the maximum score due to the simplicity of the two straps versus other mechanical parts.

However, the Band/Track design alternative earned the lowest score in the durability category since the bands will likely need to be replaced due to normal wear over time. The Eye Bar design ranked the highest in this category due to the inherent strength and rigidity of the brass parts.

The last category, margin of error, was deemed the most important, and thus given the highest weight, due to the requirement that the device restrict translational movement of the head to 1mm or less. The Band/Track design received the maximum score in this category because the two straps in combination with the four tracks will ensure immobilization of the head in all directions. On the other hand, the Fork Support received the lowest score in this category due to its lack of explicit y-axis immobilization.

After summing the scores for each of the designs, the Band/Track design had the highest score, followed by the Eye Bar design with the second highest score, and then the Fork Support design with the lowest score of the three alternatives. The band/track design was chosen as our final design.

7. Design Change

During initial MRI observation, it was discovered that there is an additional requirement for the design is reproducibility of position; the device must allow the subject to be removed and then placed back in the head holder at the same position. The band/track design, the previous final design, does not allow a high degree of repositioning but the eye bar design does. In addition, a collaborator required that we include ear bars to ensure minimal translational motion of the head. Therefore, a new design, as seen below in Figure 8, was created from the eye bar design to include a track with minimal ear bars. This design still allows room for the carotid coils to be positioned on top of the ear bars and between the vertical supports. An additional change to the original eyebar design includes trapezoid-shaped supports at the base to add stability to the vertical components and prevent motion or damage due to torque.

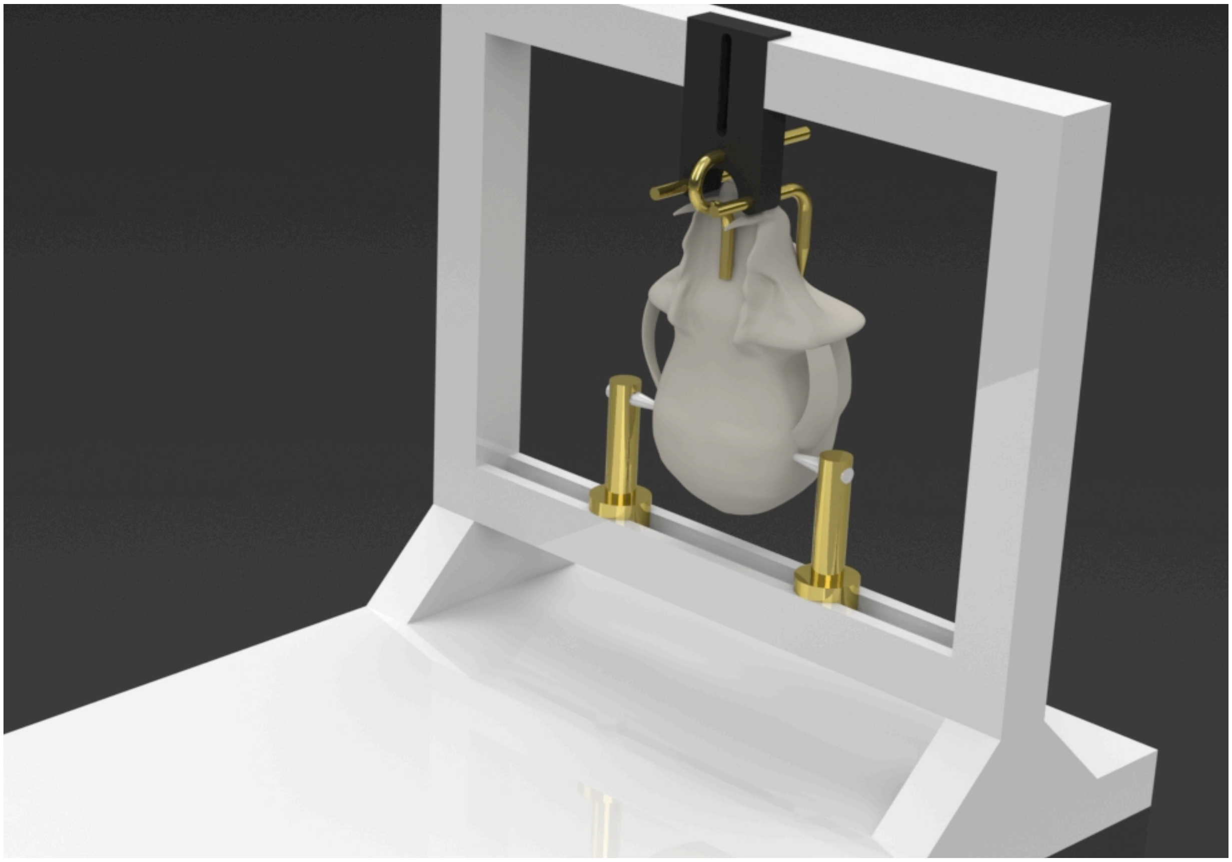


Figure 8: SolidWorks sketch of final design in accordance with new design criteria. Sketch produced by Gabriel Bautista.

8. Design Construction

8.1. Frame

Four 2.54 cm x 2.54 cm x 30.5 cm rectangular cubes of HDPE were cut and modified in length to 25.4 cm, 27.9 cm, 27.9 cm and 30.5 cm, representing the headrest and sliding track, the sides, and the top components of the frame, respectively. Next, a central notch 3.8 cm wide was milled into the top component of the frame so that the plastic supporting the palate and eye-bars would slide into the frame securely, shown in Figure 8. A central hole was drilled and threaded (1/4-20) in order to adjust the plastic plate supporting the palate and eye-bars and allow for adjustment. Two trapezoidal supports were cut using the band-saw and finished with the mill, shown in Figure 8. Notches 2.54 cm x 2.54 cm x 1.27 cm in depth were cut into the trapezoidal supports and flats on each side of the supports were milled 3.8 cm up the diagonal slopes from the corners of the trapezoid to secure them to the board with a screw in the vertical direction. A notch 1.27 cm in depth and 2.54 cm tall was milled out of each of the components of the side frame so the side frame supports would slide into trapezoidal supports to eliminate rotational motion of the tall plastic frame, shown in Figure 8. For the bottom frame component, a 1.27 cm wide notch, 1.27 cm in depth was milled out throughout the length of the component in order to form a sliding track on which the adjustable ear-bars would sit. A slot 0.64 cm wide was then milled out throughout the length of the notch so that the thumbscrew would fit and secure the ear-bars into place, shown in Figure 8. The board and all frame components were center-drilled, predrilled and counter-sinked before using brass woodscrews (#10) to secure the parts of the frame and wedge supports together and to screw the frame into the board.

8.2. Ear Bars

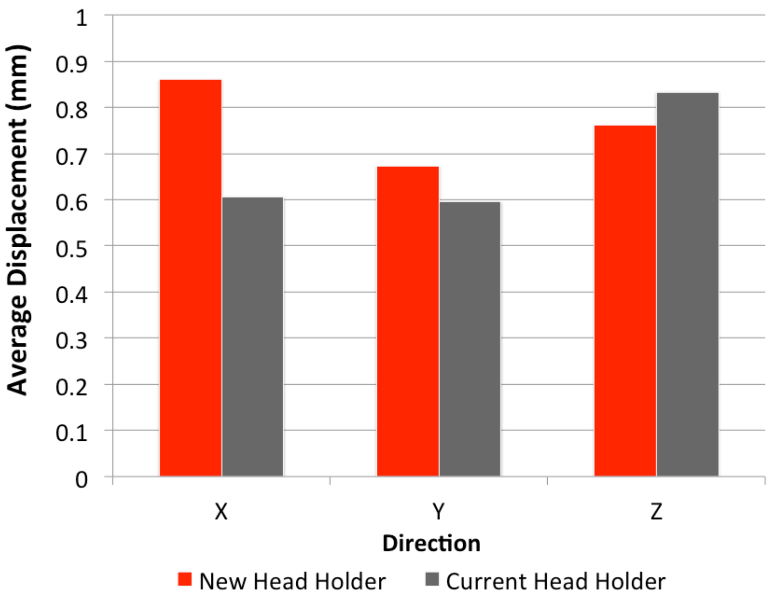
In order to create the ear-bars, the drop saw was used to cut two 7.6 cm sections out of a 2.54 cm diameter brass rod. The lathe was then used to turn the diameter down to 1.27 cm for 5.1 cm in length of the brass rod, shown in Figure 8. The lathe was also used to drill and thread (1/4-20) a hole starting at the bottom face of the ear bar and extending 1.91 cm along the long axis. When assembled, the thumb screw will fit into this hole. Next, the mill was used to face 0.64 cm off of the side measuring 2.54 cm in diameter with a height of 0.8 cm to create the sliding component, shown in Figure 8. Both sides of the brass rod were faced in order to guarantee that the ear-bars slide flush with the HDPE slot. A hole 0.64 cm in diameter was then drilled through the top of each brass part and threaded (1/4-20). The ear-bar components that stick into the monkey's ears were created by turning down a nylon screw, shown in Figure 8.

9. Testing & Results

9.1.Force-Displacement Test

In order to assess the new head holder's ability to restrict translational movement to 1 mm or less, baseline photographs of the model skull being held in both the new prototype and old head holder were taken from the front, side, and top views. For each view, translational forces were applied in the x-, y-, or z-directions, depending on the two-dimensional plane of each view. A voltage divider with a force-sensing resistor (FSR) was calibrated using a mass set and used to quantitatively measure the amount of forced being applied (average force of 28.25 ± 1.91 N). While the force was being applied, a second photograph was taken of the device with the skull. ImageJ (NIH) was used to analyze each photograph by measuring the displacement of the head according to fixed reference points on the skull and head holder device. There was on average 7.30 ± 4.44 pixels/mm for each individual image, allowing for displacement measurements to an accuracy of fractions of a millimeter. The six separate trials for each translational direction were averaged for both devices and this average displacement was graphed, as shown in Figure 9.

Figure 9: Force-Displacement Test



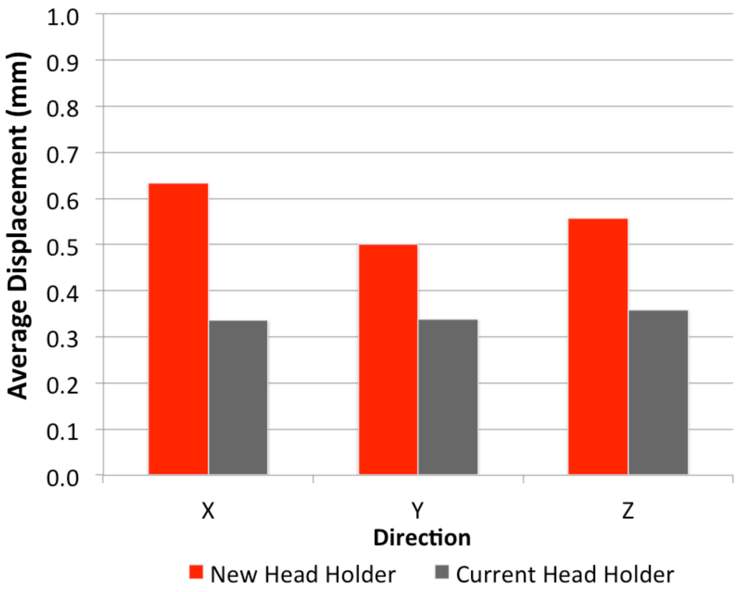
The average displacement in the x-, y- and z-directions for the new head holder was found to be 0.86 mm, 0.672 mm and 0.762 mm, respectively, all of which are below the requirement of 1 mm. These displacements differed by no more than ±0.25 mm from the current head holder's displacement measurements under the same conditions. Statistical analysis of the displacement measurements showed no significant difference between the means of the displacements of the current head holder and the final prototype (p = 0.314), meaning the effectiveness of the new head holder in restricting translational movement matched that of the current head holder.

9.2.Reproducibility Test

One of the main client requirements for the head holder was that the device needed to allow the animal to be removed and then replaced in the head holder in the same position (± 1 mm).

In order to test for this desired reproducibility, baseline photographs of the model skull being held in both the new prototype and old head holder were taken from the front, side, and top views. Then, the skull was removed from the device and repositioned back in the device as accurately as possible. Still photographs were then taken again from each of the three views, and ImageJ was used to assess the position of the model skull relative to fixed points. There was an average of 7.43 ± 0.29 pixels/mm for each individual image. This process was repeated for three trials and the displacements of the skull were averaged for each translational direction and then graphed, as shown in Figure 10.

Figure 10: **Reproducibility Test**



The average displacement in the x-, y- and z-directions for the new head holder was found to be 0.633 mm, 0.50 mm and 0.557 mm, respectively, all of which are below the requirement of 1 mm. These displacements differed by no more than ±0.30 mm from the current head holder's displacement measurements. Statistical analysis of the displacement measurements showed significant difference between the means of the displacements of the current head holder and the final prototype ($p = 0.002$). While this result is unexpected, the overall results of the experiment still showed that the new head holder allowed for very specific repositioning of the animal's head.

9.3.MRI Compatibility Test

In addition to testing the device for translational movement and reproducibility, the head holder was tested in the experimental setup in the MRI machine and with the carotid coils. As shown in Figure 11, the carotid coils were placed around a cube phantom, which rests on the headrest of the frame, to simulate how the head holder would actually be used with an animal model.

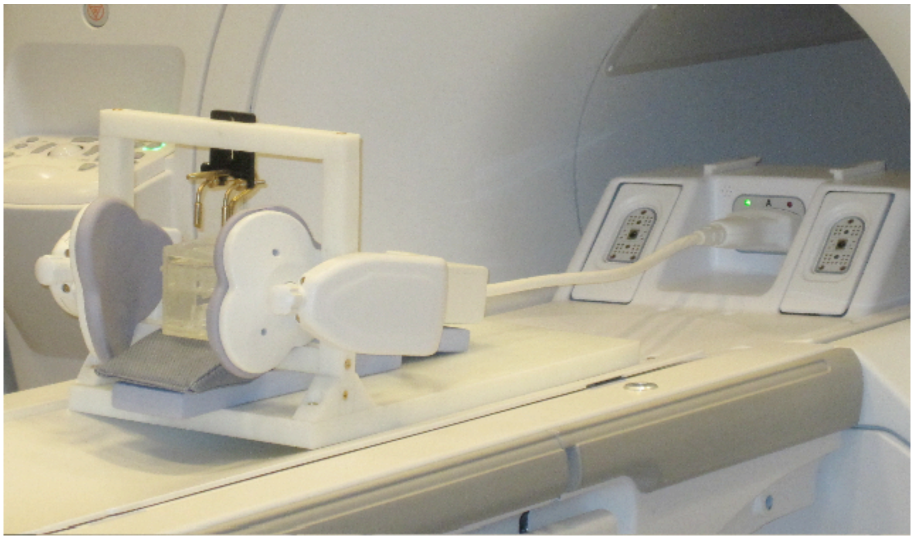


Figure 11: MRI Testing setup with carotid coils and cube phantom. Photo courtesy of Kevin Beene.

After confirming that the head holder is compatible with the experimental setup, the head holder was used with a cylindrical phantom to test for any interference with the MR image. Figure 12 shows the MR images from this phantom test. Image A shows the scan of the sphinx head holder, one of the current head holders, with the cylindrical phantom at 25 ms echo time while image B shows the new head holder at 25 ms echo time. Though the sphinx design has little to no disturbance to the image, the brass ear bars of the new head holder cause large areas of interference in the MR image. However, the MR image using the new head holder at 5.1 ms echo time (image C), which the most commonly used echo time for the CED procedure, shows much less interference due to the ear bars. In order to reduce the disturbance, the ear bars should be made out of HDPE instead of brass.

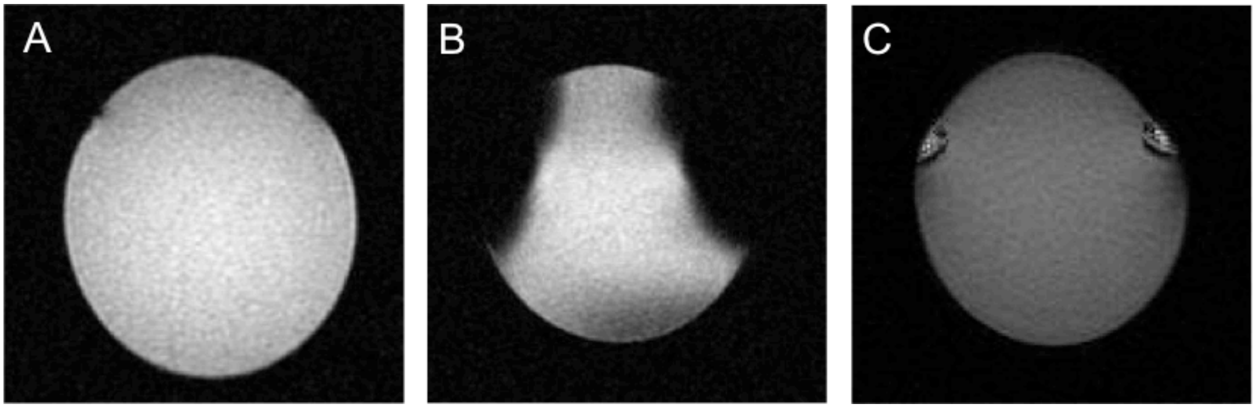


Figure 12: MRI Scans. A. Scan of sphinx design with 25 ms echo time. B. Scan of new design with 25 ms echo time. C. Scan on new design with 5.1 ms echo time. Photos courtesy of Wally Block.

9.4. Testing Error

The main source of experimental error is testing on rhesus monkey skull. This model fails to account for the additional motion due to compression of skin and muscle tissue. Using the skull to collect data for both the new design and the sphinx design was done to provide a direct comparison between the devices.

Another source of error is associated with the photography method chosen to measure displacement. The distance from the camera inevitably varies slightly between photographs. However, this variable was controlled by reporting the pixels per millimeter as well as the standard deviation.

Variability in the loading of the FSR for force measurements could also be another source of error. In order for the circuit to output the same voltage for two equal forces, these forces must be placed in the exact same spot. If the FSR had loads placed on it in different spots, the readings would vary significantly and the wrong force would be measured.

10. Cost Analysis

Table 2: Itemized Expense Report

ITEM	COST/ITEM	QUANTITY	AMOUNT
12” x 24” x 1” High Density Polyethylene Sheet	$35.35	2	$70.70
3/8-16” Nylon Bolts	$2.45	2	$4.90
½” x 1 5/8” Brass Brackets	$2.97	2	$5.94
¾”-#10 Brass Screws	$0.35	4	$1.40
1.5”-#10 Brass Screws	$0.50	12	$6.00
2”-#10 Brass Screws	$0.43	2	$0.86
12” of 1” OD Brass Rod	$43.00	1	$43.00
¼-20 1½” Nylon Screws	$0.27	10	$2.72
Transportation Fee	$15.00	1	$15.00
		TOTAL	$150.52

The original budget was $1,000. Our total expenses were significantly less at $150 as seen in Table 2. Budget had little effect upon the design process and materials selection. The low total cost is advantageous for the client and will allow funding for design changes in the future.

11. Timeline Evaluation

A timeline of the design process over the course of the semester is shown in Table 3 below. The dates correspond to the Fridays that end the weeks for the progress reports. The highlighted boxes are the projected schedule that was created at the beginning of the semester. The "X's" represent events that occurred during that week.

Table 3: Semester Schedule

Task	Jan	Feb				March					April				May
	27	3	10	17	24	2	9	16	23	30	6	13	20	27	4
Project R&D															
Background Research	▨ X	▨ X	▨ X	▨ X	▨ X										
Design Brainstorm			▨ X	▨ X	▨ X	▨ X									
Final Design Selection						▨ X	▨ X	▨ X							
Manufacturing								▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	X	
Testing										▨	▨	▨ X	▨ X	▨ X	▨ X
Deliverables															
Progress Reports	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X
PDS		X	▨ X	▨ X	▨ X		X								X
Midsemester Presentation					X	▨ X	▨ X								
Midsemester Paper						▨ X	▨ X	▨							
Final Poster													▨ X	▨ X	▨ X
Final Paper														▨ X	▨ X
Meetings															
Team	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X
Advisor	▨ X	▨ X	▨	▨ X	▨ X	▨ X	▨	▨	▨	▨	▨	▨ X	▨ X	▨ X	▨ X
Client		▨ X				X	▨ X							X	▨
Website															
Updates	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X	▨ X

There were no significant deviations from the proposed schedule throughout the course of the semester. Manufacturing took longer than expected but this is largely to the need for precise machining on mating surfaces. This was also delayed due to choice to make the ear bars in the shop as opposed to rapid prototyping.

12. Future Work

Testing the prototype in the MRI with a phantom revealed some problems with image interference even at low echo times. To remedy this problem, the brass ear bar holder's will need to be redesigned using a non-metallic material such as the HDPE used in other parts of the device. Image quality can also be improved by reducing the distance between the carotid coils and the skull of the subject. This can be achieved by replacing the vertical supports that hold the pallet and eye bars with diagonal supports, shown in Figure 13. The redesigned setup allows the coils to rest directly on the skull of the subject, which will provide the best image resolution possible. Potential design modifications also include widening of the board and the addition of clips that fit into the MRI table for stabilization purposes. Lastly, MRI tests with phantoms and real test subjects will be conducted. These tests will be used to assess if the overall quality of the image acquired using this design is on par with the client requirements.

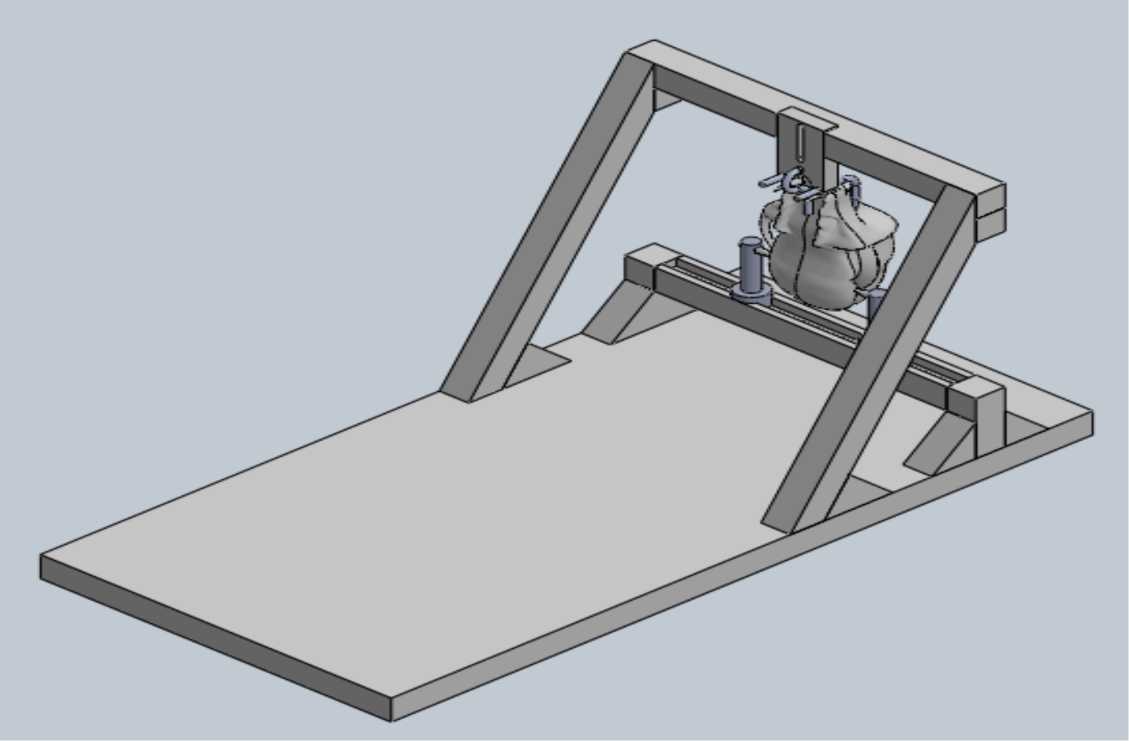


Figure 13: Modified design with modified ear bars and diagonal supports, which allow more room for the carotid coils. This design is to be built in the future. Sketch produced by Gabriel Bautista.

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- Nikki Goecks (Collaborator)
- Ethan Brodsky (Collaborator)
- Chris Ross (Collaborator)

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15. Appendix

15.1. Product Design Specifications

Head Holder for MR-Guided Drug Delivery Testing (head_holder)
Product Design Specifications

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May 9, 2012

Function: Convection enhanced drug delivery (CED) monitored through real time MRI requires immobilization of the subject's head. Our client, Professor Wally Block, requests a head holder device that is compatible with his experimental setup for in vivo studies on beagles and rhesus monkeys. The head holder must not include ferrous materials or parts that will conflict with the MRI antenna array. Due to the high degree of accuracy required, the device must restrict translational movement to less than 1 mm.

Client Requirements:
Our client wants a head holder that:

- Is compatible with MRI and experimental setup
- Restricts translation motion to less than 1 mm
- Allows reproducible positioning
- Works with beagles and rhesus monkeys

Design Requirements:

1. **Physical and Operational characteristics**

   a. Performance requirements: The device should be reusable, easily sanitized, compatible with MRI, and prevent unnecessary damage to tissue.

   b. Safety: Device cannot harm animal, including inhibiting breathing or swallowing.

   c. Accuracy and Reliability: Immobilization should prevent translational movement from exceeding 1 mm. Animal must be able to be removed from the head holder completely and then returned to the same position.

   d. Life of Service: Device must be reusable and last 5 years.

   e. Shelf Life: Device should be stored at room temperature and atmospheric pressure.

   f. Operating Environment: Device will be exposed to high magnetic fields at room temperature.

   g. Ergonomics: Device must be easily used by one person including maneuvering and placement. Device must also conform to both species of subjects.

   h. Size: Device must fit within the MRI bore (60 cm across) with other experimental instruments (brain port and ear coils) for real time MRI infusions and animal monitoring.

   i. Weight: Maximum weight of device should be no more than 9 kg.

   j. Materials: Device should contain materials that are compatible with MRI. It should not contain ferrous materials. Materials must be easily sanitized. Materials must also be sufficiently rigid to withstand forces necessary for immobilization.

k. Aesthetics, Appearance, and Finish: Finish should be conducive for gripping and have no ill effects on animals.

2. **Production Characteristics**

   a. Quantity: One functional device is needed.

   b. Target Product Cost: Total production cost should be less than $1,000.

3. **Miscellaneous**

   a. Standards and Specifications: IRB/IACUC approval is needed to test on live animals.

   b. Customer: Client is environmentally conscious and would prefer a reusable or semi-reusable device. A reusable device is also the most practical. Functionality, however, is main priority to the client.

   c. Patient-related concerns: Device cannot be harmful to animal and therefore must immobilize head without harming the animal. Device will be sterilized between uses.

   d. Competition: All other head holder devices are not compatible with experimental setup (ie use ear bars) or MRI. Current devices (although incompatible) cost approximately $2,000. A cheaper device is requested by the client.