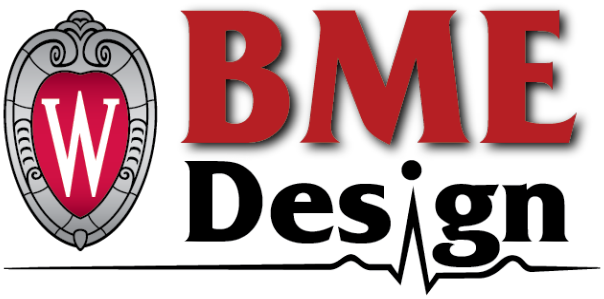

Model for Pre-Surgical Intracerebral Hemorrhage Planning

The University of Wisconsin-Madison
Department of Biomedical Engineering
BME Design 200/300

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Abstract

Intracerebral brain hemorrhaging, or ICH, is a dangerous condition that affects thousands Americans annually. Previously, doctors were only able to stabilize these patients, but with new advancements, surgeons are able to remove the clots formed from ICH. These clots have a wide range of material properties which impacts which method surgeons use to evacuate them. Currently, there is no way to determine the stiffness of clots prior to surgery. Our project aimed to design a phantom that will eventually be incorporated into a large database that surgeons can utilize to compare the MR images of their patients to MR images of the phantoms in the database, allowing them to determine the stiffness of their patients' clots. Our phantom includes a gel-gel interface that shows how different stiffnesses appear on MR scans. Other phantoms explore the stiffness of gels on MR scans, but none specifically target gel interfaces. Our more viscous clot gels appeared less stiff on the MR image than our base gels because a rigid container restricted the movement of the base gels. The clot gels were suspended in the base gels which allowed them to move more freely. The 2% alginate base gels had a stiffness of 8 Pa while the 5% alginate clot gel had a stiffness of 3- 4 Pa. Further work on this project entails changing the container to get an accurate reading of stiffness and creating a wider range of stiffnesses to develop the database.

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Introduction

Our project works with intracerebral hemorrhaging or ICH. ICH affects between 40,000 and 67,000 Americans each year with an expected 10 year survival rate of 24.1% [1]. Hypertension and old age both increase a person's risk of experiencing ICH. ICH also occurs more frequently in African Americans, Japanese people and men [2]. Until recently, doctors were only able to stabilize patients. Now multiple surgical methods have been developed that allow doctors to evacuate clots before brain damage occurs. Removal of the clot is critical since cells in the clot necrose. These cells have the potential to act as harmful biological cues in the brain [3]. For clots that are fluid or gel-like, the best method for evacuation is using a vacuum attached to a catheter to irrigate the clot. Stiffer clots require a drug based approach that dissolves the clot before it evacuated. Once the clot is less viscous, surgeons can remove it with the catheter-vacuum method used for fluid clots.

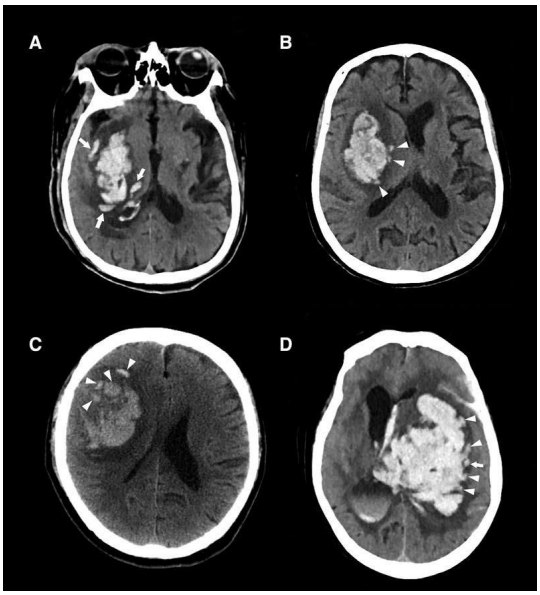

Figure 1: Heterogeneous ICH Clots [4]

ICH clots form when a blood vessel bursts, releasing blood into the brain [2]. The influx of blood results in damage to the surrounding brain cells. The arteries near the clot lack oxygen rich blood, causing the patient to experience strokes [5]. Immediate actions needs to be taken for ICH patients since blood shears white matter, resulting in brain damage. Over time, the red blood cells from the blood released in the bursting of the vessel coagulate and separate from the plasma. This separation makes individual clots very heterogeneous which complicates the decision of which method of evacuation to utilize since the best method is dependent on the stiffness of the clot. Currently, it is difficult for surgeons to asses the stiffness of clots prior to surgery. When a patient displays symptoms of ICH, it is standard for that patient to undergo diagnostic tests such as an MRI and a CT scan. These tests allow doctors to determine the location of the clot, but do not provide information about the stiffness of the clot [2]. Without knowing the characteristics of clots, it is difficult for neurosurgeons to decide on a surgical approach prior to surgery.

Our client's long-term goal is to develop a process for neurosurgeons to know the stiffnesses of clots prior to surgery which will allow them to decide on the best method to evacuate clots and increase the success of these surgeries. Professor Block, our client, aims to create a large database containing images of phantoms with known stiffnesses. Surgeons will be able to compare the images of their patients to the phantom images and deduce the stiffness of the patient's clot. Professor Block project for us was to create a phantom that will serve as a

proof of concept, showing that gels of different stiffnesses placed next to each other can be differentiated on MRI images.

A medical phantom is a device that is used to calibrate imaging devices and to develop methods to better analyze the images. Usually, phantoms mimic human tissue. Researchers are able to manipulate and analyze the phantom significantly more than they are able to manipulate the human tissues that these imaging machines are meant for due to ethical reasons. This allows imaging machinery to be tested and calibrated [6]. Our phantom has a gel-gel interface which when imaged using MRE, will show how different stiffnesses appear on MRE. The gel-gel interface is meant to mimic the interface between clots and native brain tissue such as white and gray matter.

Currently, there are no phantoms that mimic a clot-tissue gel like our design does, however other phantoms have been designed that analyze the appearances of different stiffnesses on various diagnostic images. Researchers from Switzerland designed an anatomically correct phantom that modeled white matter and gray matter. They were able to mimic the material properties of these tissues using agar gel [7]. Other phantoms have explored the idea of gel interfaces. Hydrophobic sprays and wax barriers were used to create thermostable gels-gel interfaces [8].

Background

A brain phantom is used by neurosurgeons to compare the MR scans of the phantom with a scan of their patients' brains. The phantom's purpose is to illustrate the stiffness of the patient's brain [9]. Characteristics of the patient's brain that are compared to the phantom include the rigidity, structure, clots, and fluids. It is essential for the phantom to have a precise replication of the brains components since its design helps doctors decide how they will treat the patient. For instance, when doctors begin to remove a blood clot from a patient they must decide between using a catheter or creating an incision [10]. They make a decision based on the relationship between the stiffness of the clot in the MRI with the stiffness of the clot in the phantom. Thus, it's very important for brain phantoms to represent the human brain closely.

The composition of the phantom is therefore the most important part of our design and fabrication. Our focus thus leads to the research of different biomaterials to make up our phantom. One biomaterial used in other brain phantoms, gelatin, is used due to its ease of fabrication. It is relatively simple to change gelatin's stiffness by manipulating the concentration [11]. Gelatin's linear elastic behavior makes it hard to mimic the complexity of the brains makeup [12]. Gelatin has a low activation energy barrier and thereby melts quicker and at lower temperatures than other gels [12]. However, a crosslinker can be used in order to render the resulting gel thermostable. Another commonly used biomaterial in phantom research is agarose. Agarose is thermoreversible, meaning that the gel is able to transition well from a gel to a liquid at different temperatures [13]. However, Agarose is another gel that cannot handle high

temperatures [13]. Finally, a biomaterial used for its structure, thermostability, and biomimicry is alginate. Alginate is used for phantoms due to it being structurally similar to human tissue [14]. Alginate is also unique due to its thermostability [14], meaning that the phantom is able to best tested in different environments and is durable.

The chemistry behind how the alginate gels is important to the design of our phantom. Our alginate gel will use ionic cross-linking in order to gel. Ionic cross-linking is done by combining divalent cations with a solution of alginate dissolved in pure water. This happens when the gel forms its structure when the guluronate blocks of adjacent polymer chains form bonds to one another. The reason why the divalent cations bind to the guluronate blocks is because the blocks allow for a high amount of linking with the ions[15]. This process is known as the egg-box model of cross-linking which is illustrated in figure 2. In the egg-box model of cross linking, the divalent compound forms bonds with the guluronic acid, giving the gel an egg-box structure [15]. For our specific case, we used calcium as our divalent compound. For our phantom we decided to use $CaCO_3$ as our specific cross-linker since, due to its lower stability, slows the gelation rate. In accordance to our cross-linker, we also added our buffer Glucono-δ-lactone which dissociated our divalent compound from our cross linker. This is done by our buffer decreasing the pH of the solution. The buffer also helps in that it helps slows the gelation in order to make it more gradual [15]. Finally, for the stiffnesses of our gel, we were able to come up with different percentages of alginate just by changing the concentration of the alginate we used.

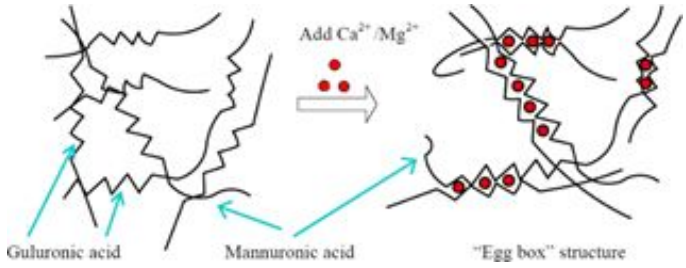

Figure 2 Egg-box model cross-linking [15]

Our client, Professor Block, proposed a project to design a brain phantom that will be inputted into a database which will used by physicians to compare the rigidity of their patient's brain scan with a scan of the phantom. Professor Block set many goals for us to meet for our design. He emphasized the importance for us to mimic the structure and rigidity of the brain. The phantom must also imitate the elasticity of white matter, gray matter, clots, and cerebrospinal fluid. Professor Block highlighted the importance of the shelf life of our phantom, as he hoped to be able to image it multiple times. The current phantoms that are utilized in his lab deteriorate quickly, so not only did he want a durable phantom, but a detailed protocol of our gel making procedure so that he was able to recreate the phantom when needed. Another important feature of the phantom is that it must handle powerful magnetic fields since it must go through MRI. Professor Block consistently emphasized that our phantom would not be used in a clinical setting, instead it was going to be used to create a database of images of clots of different rigidities.

Preliminary Designs

Designs Considered:

Design 1: "Simple Container"

Simple container is appropriately named as this is a very simple and user-friendly design. This container consists of 12 different cavities, each 20mm x 20mm x 60 mm. These can then be filled with the desired biomaterial at different concentrations to image through MRI. The overall dimensions of this container are 180mm x 140mm x 80mm, and the 12 cavities are evenly spaced between each other throughout the center of the container. The overall layout and detailed dimensions of this container can be found in figure 4. This is an extremely simple design to fabricate, as it can be 3D printed and used immediately. Biomaterials that are placed in each cavity are easily removed and cleaned out for future use or storage after imaging has taken place. This serves as a great design for proof of concept and ensuring that the biomaterial chosen is able to have its properties altered in order to mimic different stiffnesses.

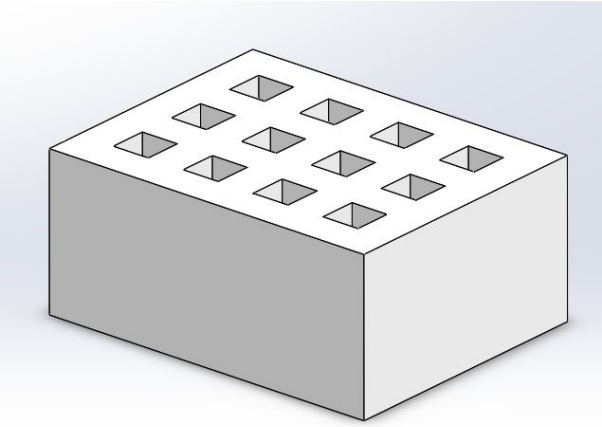

Figure 2: Isometric View of Simple Container

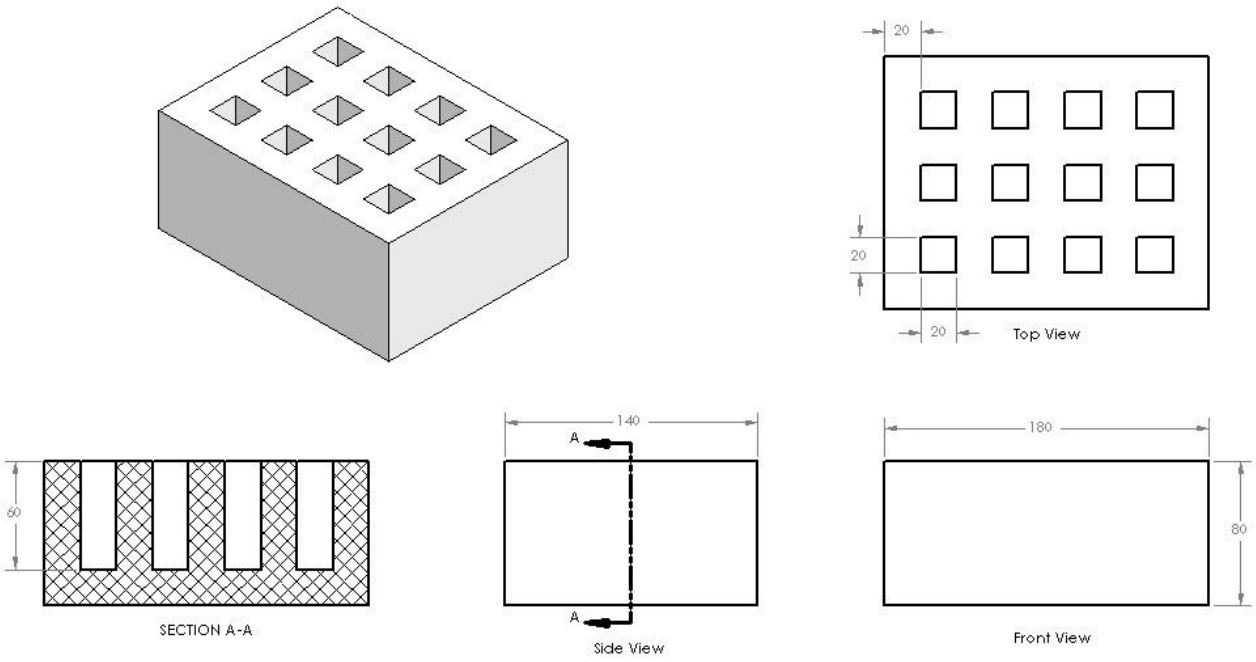

Figure 4: Detailed view of Simple Container

Design 2: Anatomical Model with CSF

This model is much closer to the anatomy of the human brain and contains compartments for white and gray matter, CSF mimicking fluid, as well as clots. In this design, there is room for four different clot stiffnesses to be inserted. These clots are surrounded by white matter, which is surrounded by gray matter, which is all surrounded by CSF. This is illustrated clearly in figure 5 and 6. This mimics the anatomy of the brain very closely, however, it doesn't have the ability to be easily emptied or cleaned because instead of containing a simple base gel, this model includes multiple different layers of gels representing the different layers of white matter, gray matter, and CSF. This model would contain two 3D printed half-spherical shells- a larger one containing the CSF, and a smaller one containing the white matter, gray matter, and blood clots. The larger plastic shell would be the outer container for the whole model, encasing the fluid and the second shell containing the gels. Between these two spherical shells there would be CSF encasing the smaller half-sphere. The gels would reside in the smaller shell, containing the gray matter, white matter, and blood clots. These clots would be embedded in one another by pouring a layer of gel and then spraying a hydrophobic spray between the layers to allow gel to gel interface, and also preventing the gels from diffusing into one another. First, a layer of gray matter gel is poured, followed by a layer of white matter, which then surrounds the blood clots of varying rigidities and stiffnesses. This would be a permanent fabrication with a much longer shelf life as opposed

to “Simple Container” whose intention is more for proof of concept than a final anatomically correct brain phantom.

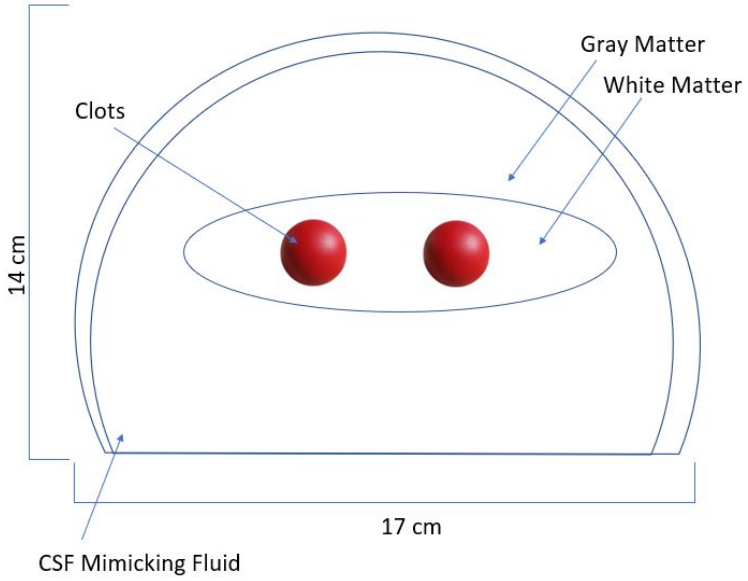

Figure 5: Side view of Anatomical Model with CSF

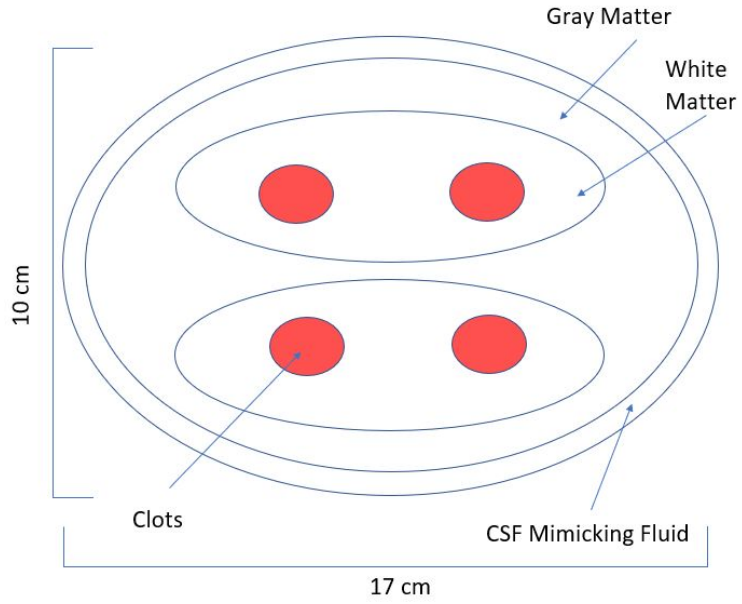

Figure 6: Top-down view of Anatomical Model with CSF

Design 3: Brain Model with 3D Case

The third and final design considered is named “Brain Model with 3D Case”. This design is very similar to the “Anatomical Model with CSF” as it replicates the anatomy of the human brain. This also has the ability to house four different densities of clots as well as white and gray matter. This design does not allow CSF to be incorporated, however, it does feature a sturdy outer shell fabricated from a 3D printed plastic that would loosely mimic the skull.

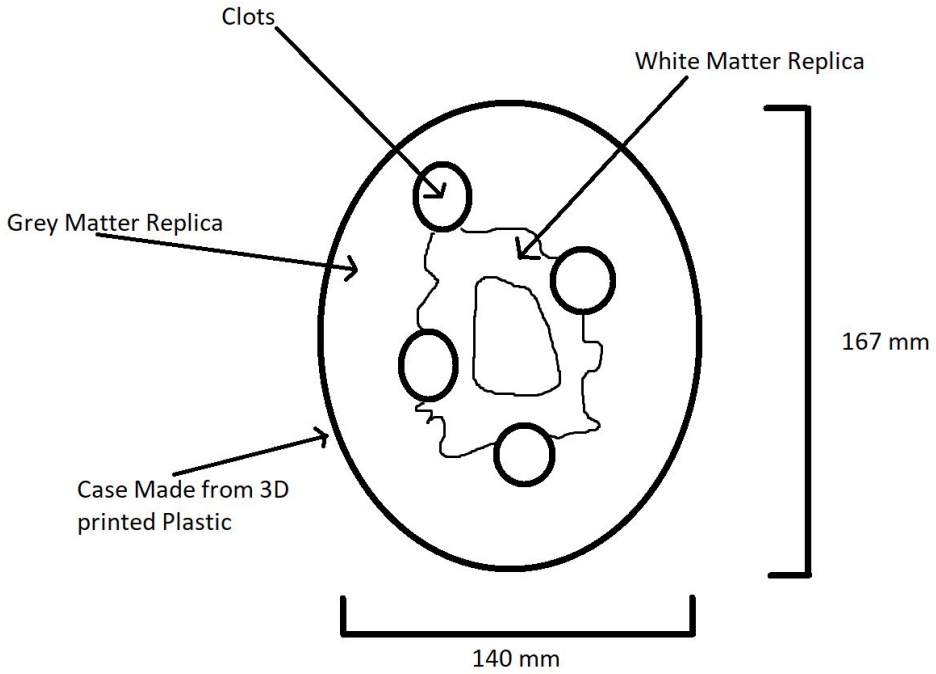

Figure 7: Detailed drawing of brain model with 3D case

Preliminary Design Evaluation

Design Matrices:

Biomaterial Design Matrix:

Criteria	Alginate		Agarose		Gelatin	
Ease of Fabrication (25)	4/5	20	4/5	20	5/5	25
Biomimicry (25)	5/5	25	4/5	20	2/5	10
Cost (15)	4/5	12	4/5	12	5/5	15
Duration (15)	2/5	6	3/5	9	1/5	3
Thermostability (10)	5/5	10	3/5	6	1/5	2
Safety (10)	4/5	8	4/5	8	5/5	10
Total (100)	81		75		65	

Figure 8: Biomaterial Design Matrix

Container Design Matrix:

Criteria	Brain Model with 3D Case		Anatomically Correct Model with CSF Fluid		Simple Container	
Compatibility with US and MRI (25)	4/5	20	5/5	25	4/5	20
Ease of Fabrication (20)	2/5	8	2/5	8	3/5	12
Accurate Stiffnesses (20)	5/5	20	4/5	16	4/5	16
Ease of Use (15)	4/5	12	2/5	6	5/5	15
Ability to Hold Multiple Clots (10)	4/5	8	4/5	8	5/5	10
Compactness (10)	5/5	10	4/5	8	4/5	8
Total (100)	78		71		81	

Figure 9: Container Design Matrix

Design Matrices Summaries:

Biomaterial Matrix Summary:

Three different biomaterials were chosen as possible options to mimic the stiffnesses of the clots and brain matter. The three biomaterials were: Alginate, Agarose, and Gelatin. The two most important characteristics of the biomaterial chosen are the "ease of fabrication" and the "biomimicry" capability. In order to be fabricated many times over at accurate stiffnesses the biomaterial needs to be easily made. Gelatin won in this category due to the extremely easy method of creation. Gelatin is a material that most people have used before, making it a very familiar material, and thus increasing its score in this category. Gelatin is also great because we are easily able to change it's stiffness just by manipulating the concentration, making it a very easy biomaterial to handle. Biomimicry is extremely important in this situation. The gel chosen needs to accurately represent the stiffnesses and consistencies of the different materials the brain is composed of. Alginate won this category due to its extreme customizability. The next tier of the design matrix has "cost" and "duration of use" at the same rating. Cost must be low due to the probability of remaking the model in the future. Gelatin won in the cost category due to its prevalence and extremely low price. Duration of use was important so that the model could be used for multiple measurements or tests before it begins to deteriorate. The final tier in the matrix had "Thermostability" and "Safety". Thermostability was chosen as a category for a similar reason as duration of use. The model has to be able to not melt or deform during tests at room temperature. Safety was considered but is not extremely important because these models will not be used in a clinical setting. Because of this, we rated each gel based on its safety in handling and fabricating. Gelatin won the "Safety" category because it is a biomaterial that is easy to handle, and is considered safe enough to ingest.

Container Design Matrix:

Three different container designs were considered for the container design matrix. The "Simple Container" design was more about testing purposes compared to the other two designs. The most important characteristic for the container design was its "Compatibility with the MRI." In order to assist in developing baseline imaging measurements, the model needs to be able to be imaged by both MRI and US with relative ease. The "Anatomically Correct Model" was by far the easiest design to image due to the lack of any material except for the mock-brain matter. "Ease of Fabrication" and "Accurate Stiffnesses" were rated as the next priorities. Similar to biomaterials, the designs need to be easily made. There exists a high probability that the design will be made more than once or redesigned and therefore needs to be easy to make. The "Simple Container" design was by far the most easy to make because it is a simple 3D-printed case with gel in slots. Again, the designs need the capacity to accurately represent the varying stiffnesses of the clots and the different components of the brain. The "Brain Model with 3D case" won this

category because the whole focus of this design was to create environments with accurate stiffnesses. “Ease of Use” was rated in its own tier of importance. The model needs to be able to easily used and measured by the different imaging softwares. The “Simple Container” design won this category due to its simple design. The final tier of the container design matrix was filled by “Multiple Clots” and “Compactness.” The design should be able to hold multiple clots in order to expedite the process during measurement. It would not be efficient to have to take different measurements for each different clot. Finally, the model must be compact in order to fit onto the MRI pillow. There is only so much space in these imaging systems and our model needs to fit.

Proposed Final Design:

The proposed final design will be the “Simple Container” filled with alginate gel. After consulting our Client and using the design matrices these two choices were obvious. The simple container design gives us an easy way to hold many different “environments” while being completely compatible with both US and MRI and easy to fabricate. The alginate was chosen for its ease of fabrication, relatively low cost, and extreme customizability. The alginate gel is capable of being manipulated into many different stiffnesses in order to simulate different kinds of clots and the differences in brain matter. Together, the proposed container design and the biomaterial give a lot of opportunity to take many measurements at the same time.

Fabrication/Development Process

Materials:

The final sample container was fabricated via 3D printing using PLA plastic. Within the container, the gels were fabricated using sodium alginate, water, calcium carbonate and glucono δ-lactone.

Methods:

The completed solidworks file was brought to the makerspace. At the makerspace the file was uploaded to the CURA 3D-printing software and converted to the appropriate file type. The inside was reduced to a simple lattice design in order to minimize weight and production time. The design holder was then printed using PLA grey material.

In order to make our Alginate gel we first dissolved alginate in water. In order to make our different concentrations of Alginate, we would only alter the amount of Alginate we dissolved in water. Then once the Alginate dissolved, we added our cross linker and buffer into the solution. For our cross linker and buffer we used Calcium Carbonate and Glucono-δ-lactone. For our cross linker we used a constant 50 mM for each concentration. We first went ahead and made our clots before we made our base gels. For our clots we used the fingertip of a latex glove. By filling the glove with Alginate and tying it tightly in a knot, we were able to keep any air out

of the clots. For our clots to fully gel we placed them in the fridge. We then followed the same procedure for our base gels only varying the amount of Alginate used to get a change in concentration. Prior to pouring of base gel solution, the clot gels were suspended in the cavity and the base gels were filled in around the clots. Finally, we placed the container in the fridge for around 20-30 minutes to allow gellation to complete.

Final Prototype:

The final prototype consisted of the 3D printed simple container that was revised based on the requests of our client. The new container contains four cavities instead of the preliminary design that contained twelve. The updated cavities are also larger than originally designed. These are each 5 cm × 5 cm × 5 cm. The overall dimensions of the container are 17 cm × 17 cm × 7 cm.

Figure 10: Sample holder containing three gel samples, two of which contain 2% base gels with 5% clots suspended, the third is a 3% gel alone.

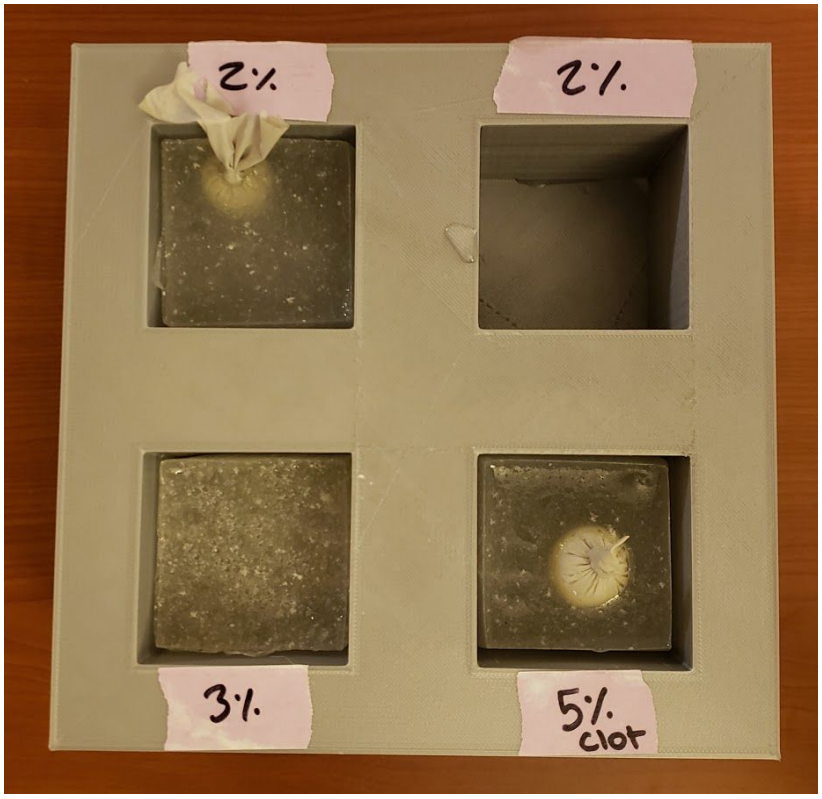

Figure 11: Top view of sample holder with gels

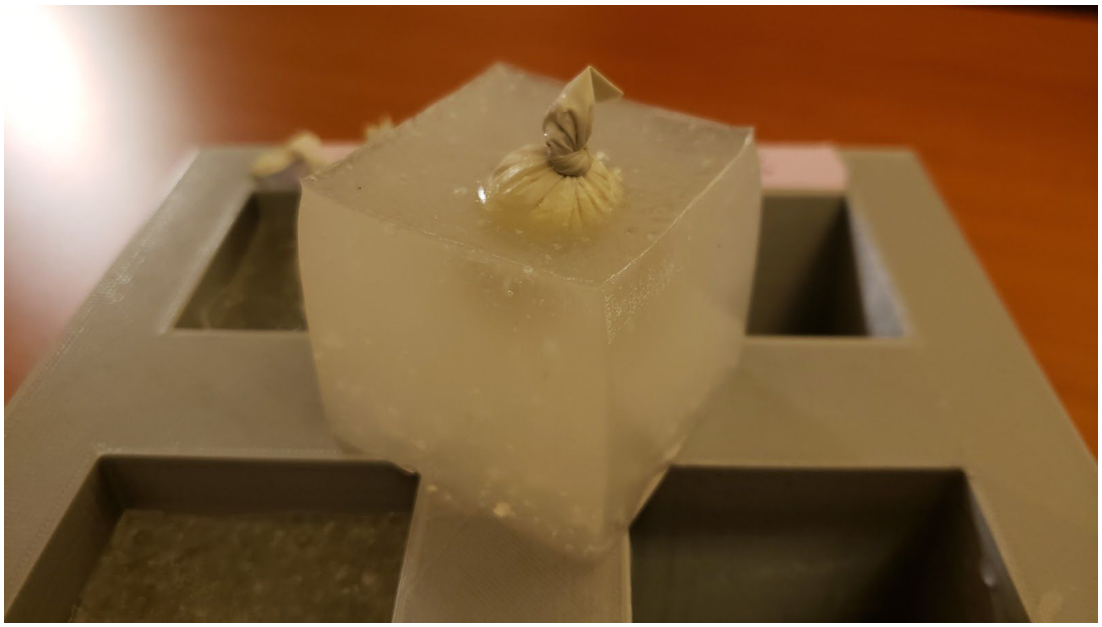

Figure 12: Detailed picture of 2% base gel with 5% gel clot suspended

Figure 13: Detailed picture of top of 3% base gel

Testing:

Testing was completed once the gels were fabricated in the sample holder. Once finished the gels were run through T1 and T2 weighted scans, perfusion-weighted imaging, as well as MRE scans. The sample holder was placed on the imaging bed of an MRI machine, and the previous tests were executed and results were collected. For the MRE tests, the sample was placed on either an MRI head pillow or a liver paddle.

Results

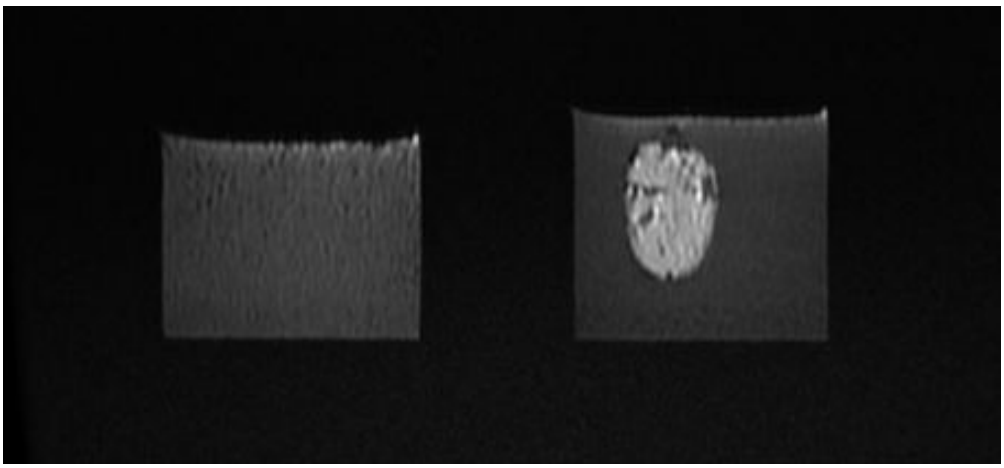

Figure 14: T1-Weighted scan result, 3% base gel seen on left and 2% base gel with 5% clot seen on right.

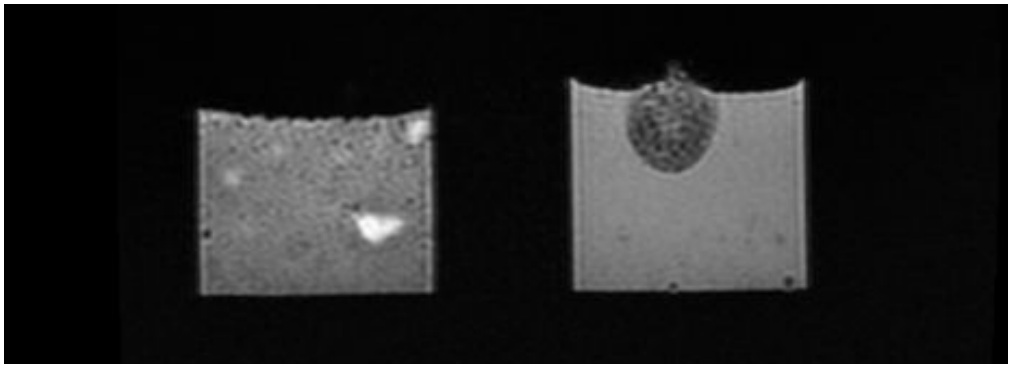

Figure 15: T2-Weighted scan result, 3% base gel seen on left and 2% base gel with 5% clot seen on right.

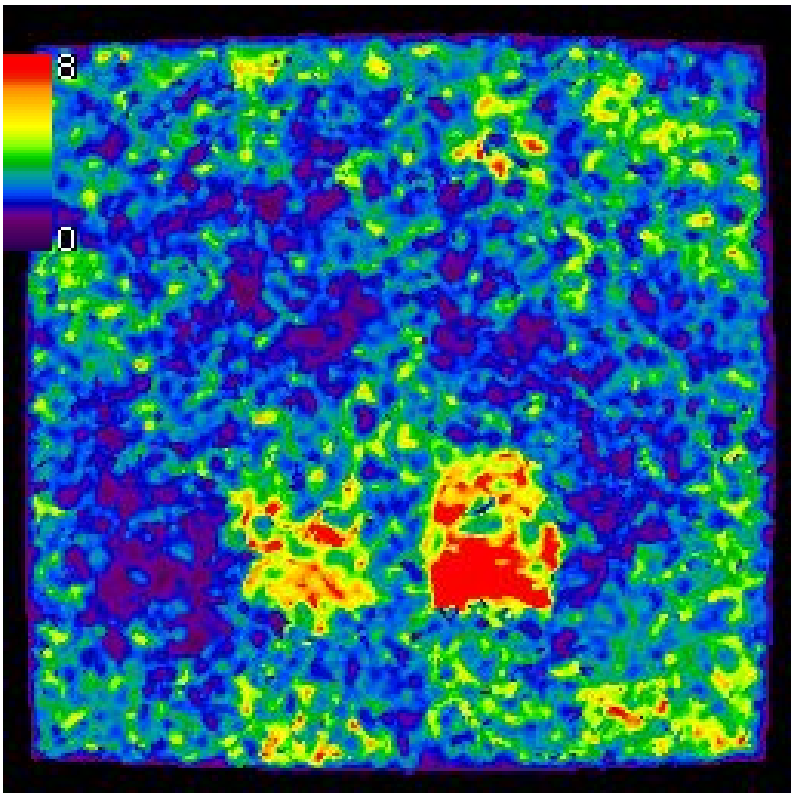

Figure 16: Perfusion MRI result, two red squares represent base gel, small blue circle on right red square is 5% clot

The MR imaging showed a clear distinction in stiffness between the base gels and the clot gels. The base gels show a stiffness of around 8 Pa. The clot gels show stiffness in the 3-4 Pa range. In the T1 image, as seen in figure 14, the clot shows a high intensity, this shows the clot is a material that exhibits T1 behavior. The base gels exhibit a high intensity in the T2 image, in figure 15, this shows that the base gels are a material that exhibits T2 behavior.

Discussion

As expected, the MR images revealed a difference in stiffness between the base gels and the clot gels. The difference in stiffness can be clearly viewed on the T1 and T2 measurements as well as the perfusion measurements. However, contrary to expectation and research conducted by Lee and Mooney, the base gels were significantly more stiff than the clot gels [8]. This result was unexpected but easily explained. MRE stiffness measurements are taken by gently sending vibrations through the material and measuring movement. Materials that move more are deemed less stiff and materials with less movement are more stiff. It was observed that the rigid, plastic walls of the sample holder restricted the ability of the base gels to respond freely to the vibrations from the MRE. Due to this restriction in movement of the base gels, the clot gels appeared to move significantly more than the base gels. Hence, on the images and the readings the clot gels were reported as less stiff than the base gels.

Keeping these results in mind, gels should no longer be imaged in the sample holder. Gels will need to be imaged submerged in water or the sample holder must change. Any material used in this design must be used in a way that does not restrict the movement of either the base gel or the clot gel.

One possible source of error in the fabrication process would be the math that led to the quantities of chemicals used. It is entirely possible that the wrong equations were used and thus the composition of the alginate gels were different than expected and caused the stiffness discrepancies observed. As discussed above, the sample holder itself was a source of error. The rigidity of the plastic sample holder prevented the base gels from moving as expected causing them to appear stiffer than the clot gels. Another possible source of error is in the weighing of the chemicals. Having the exact same amount of alginate, $CaCO_3$, and buffer is difficult and relies on having accurate measurement equipment. Differences in masses of chemicals leads to gels that are being interpreted as the same but are in actuality different. Finally, the gels were kept in refrigerators when not being imaged or made. Being exposed to the refrigerator for long periods of time could cause changes in stiffness and composition. Shortly after being removed from the refrigerator base gels were more stiff to the touch than they were after spending time at room temperature. If the gels were imaged immediately after being removed from the refrigerator the observed stiffness could be different than expected values leading to errors in imaging.

Conclusions

Intracerebral Hemorrhaging causes the formation of blood clots in the brain that can vary in stiffness. Methods of evacuation differ based on the stiffness of the clot. In order to determine stiffness the clot must be imaged in an MR. Baseline readings of materials of different stiffnesses

are needed to compare to clinical MR images for reference. Our team sought to solve this by creating a holder that can hold base alginate gels with model clot gels within them. The gels were them imaged in the MR and a clear difference in stiffness was observed. However, the sample holder restricted the movement of the base gels and thus they appeared more stiff than the clot gels. Next time, we would image the base/clot gel complex submerged in water in order to remove the movement restriction. In the future, the main goal is to make the model very-representative of the brain environment. In the short-term this involves becoming adept at controlling the stiffness of alginate. In total, alginate of six different stiffnesses will be needed in the final model. Along with this, clots need to be made mimicking different stiffnesses and consistencies. The clots are the most important aspect of this imaging model and therefore are the priority of the project. Eventually, the goal is to integrate the clots into and anatomical model of the brain. Once integrated into an accurate model of the brain, the clots will be in a prime environment for the imaging tests the Client wants to run. Beyond this, future work involves fine tuning the model. Adding more depth to our materials such as accurate T2 measurements and enhancing the biomimicry of the model are the ultimate goals. Another area to delve into the future would be looking into various other gels and procedures to make up different components of the brain. This includes mimicking various things including cerebrospinal fluid, white matter, and grey matter. An example of this was to use pig's blood as a pseudo cerebrospinal fluid. This is significant since it will give a more anatomical look to our phantom which will help make our scans more detailed.

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Appendices

Appendix A. Product Design Specification

Model for Pre-Surgical Intracerebral Hemorrhage Planning
Product Design Specifications
Date as of: December 10th, 2019

Client: Prof. Walter Block
Advisor: Dr. Kristyn Masters
Team Members:

Joe Kerwin	jekerwin@wisc.edu	Team Leader
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Function/Abstract:

Intracerebral hemorrhaging (ICH) is an extremely dangerous condition that without intervention can ultimately lead to death. Recently, new methods have been developed for evacuating clots formed as a result of ICH. However, the stiffness of the brain clots can be very different from patient to patient, which complicates the decision of what method of evacuation to utilize. Professor Walter Block presented the team with the challenge of designing a brain phantom that will eventually be used to generate a database that allows neurosurgeons to compare MRE phantom images to MRE images of ICH patients. By comparing the patient's scan to the database of phantom images, the surgeon is able to determine the stiffness of the clot prior to surgery, and decide on the best method of evacuation. Other brain phantoms have been created, but none target ICH specifically or include a gel-gel interface. Our solution is to create an alginate phantom with "clots" inside of base gels to prove materials of different stiffness can be differentiated in MRE images.

Client Requirements:

- Have a variety of stiffness of gels to create a database of known MR
- Have multiple clots within the phantom that can model varying stiffnesses of clots representing the differences in patients' clots
- Have an in depth fabrication process so that it can be replicated and improved upon for future work
- The phantom should be able to be scanned by MRI.

Design Requirements:

1. **Physical and Operational Characteristics:**
    a. *Performance Requirements:*
    The device must imitate the structure and rigidity of brain tissues to understand the rigidity of blood clots. We need a model that can be imaged in MR so that surgeons are more informed before choosing a treatment. The phantom design will allow for imaging of a large array of stiffnesses, to create a database of known stiffnesses.

    b. *Safety:*
    The device will have an outer casing that must be safe to handle. The materials that mimic the native tissue should also be safe to handle with reasonable personal equipment such as latex gloves. All the materials within the device must be safe to use with MRI.

    c. *Accuracy and Reliability:*
    Our phantom is meant to mimic the size and consistency of the human brain. The margin of error for mimicking the different brain tissues is +/- 10%.

    d. *Life in Service:*
    The phantom is meant to last for 3 months and able to withstand multiple scans. It will be stored in a refrigerator when not in use. Part of the issue with phantom work today is that the old models erode which produces unreliable results. Each scan should take 30-45 minutes, so the device must be able to be outside of a refrigerator for that amount of time.

e. *Shelf Life:*
This phantom must not deteriorate significantly over time. Alginate deterioration is characterized by cloudiness in the gel and an increased liquid character. The client wants to be able to run many tests on the phantom and it must maintain its material properties within the +/- 10% margin of error while being stored in the refrigerator.

f. *Operating Environment:*
This phantom will be exposed to extremely powerful magnetic fields and therefore can not contain any metal, as this will ruin the image that the MRI produces. The outer casing of the phantom must be compatible with Ultrasound as well.

g. *Ergonomics:*
The phantom has to be transported to various imaging machines so ideally it shouldn't weigh more than an average person can carry. A simple case such as a metal box is enough to provide sufficient protection while the phantom is not in use. The case must open to allow users to easily take the phantom out to scan it.

h. *Size:*
The average brain is 14 cm wide and 16.7 cm long. This phantom must adhere to these dimensions in order to fit inside the head coil that goes into the MRI machine.

i. *Weight:*
The average brain weighs about 3 pounds or 1300-1400 grams. The weight of this phantom can be heavier than this, as there is no cause for concern on placing the phantom on an MRI table. An average person should be able to carry the phantom so it should not exceed 10 pounds.

j. *Material:*
We need to imitate 4 different materials found in the brain. This can be achieved by varying the properties of alginate gel. The outer casing of the phantom will be 3D printed using PLA plastic.

k. *Aesthetics:*
For the scope of the project that we will be focusing on, the sample holder can be very simple, as we are just looking for a way to image different

stiffnesses of gels at one time. This way we can create a database of known stiffness values and how they are perceived in MR.

2. **Production Characteristics:**
    a. *Quantity:*
    Our client wants to model different types of clots. Our current design does this in a single phantom.

    b. *Target Product Cost:*
    Our client notified us that money was not an issue

3. **Miscellaneous:**
    a. *Standards and Specifications:*
    The phantom needs to have clots with different stiffnesses, which within 10% of the rigidities found in the human brain. The accuracy of the phantom in terms of imitating the material properties of the native tissues is more important than the design.

    b. *Customer:*
    According to Professor Block, this device is the first of its kind to be used for a brain hemorrhaging application which means there is a possibility that this design and idea will be spread past the university, but this is in the far future. They will not use our specific prototype, but they may follow our fabrication process to create a copy. Our main customers are Professor Block and his associates though. It is important that they understand our entire fabrication process and the inner workings of the phantom so they are able to use it as effectively as possible and continue to improve upon the device once the semester is over.

    c. *Patient-related concerns:*
    Since our device will not be used clinically, there aren't many patient related concerns. Each patient's clot has different material properties, so we need to mimic varying clot stiffness.

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Appendix B. Materials

Item	Description	Manufacturer	Part Number	Date	Cost	Quantity	Total
Sodium Alginate	250g of sodium alginate	Acros Organics	AC177772500	11/8/2019	$46.53	1	$46.53
3D Printed Case	Gel container made of PLA	Makerspace Lab	N/A	10/24/2019	$28.49	1	$28.49
Calcium Carbonate	Cross-linker	Dr. Master's Lab	N/A	10/31/2019	$0.00	1	$0.00
Glucono-δ-lactone	Buffer	Dr. Master's Lab	N/A	10/31/2019	$0.00	1	$0.00
						TOTAL:	$75.02