MRI Liver Phantom for Transarterial Chemoembolization Simulation

Final Design Report
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Abstract

Liver cancer in various forms is a major cause of mortality and current treatment methods are highly ineffective. Transarterial chemoembolization (TACE) is a chemotherapy delivery technique which improves the localization of treatment. Currently, TACE is guided through X-ray imaging but would benefit from utilizing real time 3D MRI. The purpose of this project was to create an MRI phantom of the liver and abdomen which would allow interventionalists to practice TACE catheterizations. The phantom that was created accurately depicts the eight Couinaud segments of the liver as well as key abdominal arteries. Initial tests indicate that the vasculature can withstand the maximum flow of the pump (3 L/min). Additionally, both the phantom vasculature and enclosure are water tight. Finally, the phantom produced minimal artifact allowing for accurate MR imaging. In the future, tube diameter adjustments along with the addition of pulsatile flow will enhance the flow characteristics of the phantom. Additional testing with interventional radiologists will be performed.

Table of Contents

Problem Statement

The goal of this project is to develop and construct an MRI compatible liver phantom which represents the arterial vasculature of both the human liver and abdomen. This phantom will be utilized by interventional radiologists to simulate cancer treatments and practice catheterization procedures under the guidance of magnetic resonance imaging. The dual imaging suite at the University of Wisconsin Hospital is an excellent location for interventionalists to conduct MRI guided procedures due to the proximity of the X-ray machine, which they are familiar with. Training radiologists on the use of MRI as an effective imaging modality has the potential to increase the localization and effectiveness of transarterial chemoembolization procedures.

Background Information

Liver Cancer/Current Treatment

Primary liver cancer and hepatic metastases of the liver represent a significant medical problem throughout the world. The liver is the most common site of metastatic tumor deposits in the body and hepatic metastases represent a major cause of mortality in patients with other malignant tumors [1]. Specifically, hepatic metastases are common in the case of both colorectal and breast cancer. In 20-30% of colorectal cancer cases, the liver is the only site of

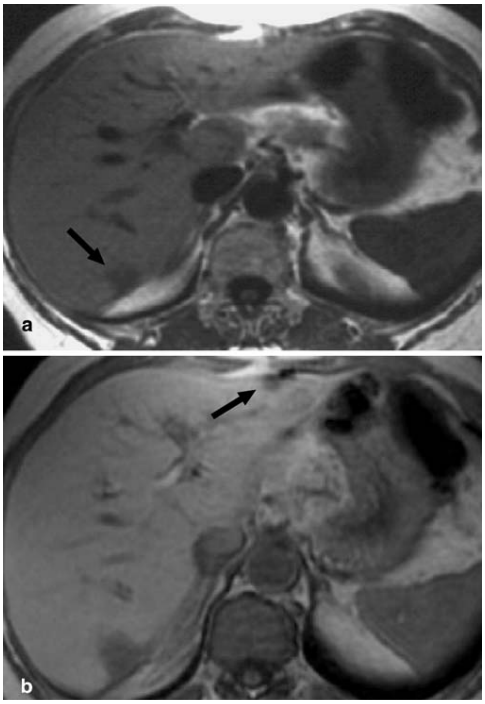

Figure 1 – Liver metastases found in liver segment VII (above) and III (below) using MR imaging [4]

metastases. Hepatic involvement in almost all forms of cancer is often indicative of a life threatening illness [2]. Depending on the primary site of cancer, 30-70% of patients who die from cancer have liver metastases present in their autopsy [3]. In addition to metastases, primary liver tumors in the form of hepatocellular carcinoma continue to be a major cause of death, especially in Asia [5]. For this reason, effective identification and treatment methods are necessary to improve a patient's chance of survival when diagnosed with either primary liver cancer or hepatic metastases.

Unfortunately, current treatment methods for liver cancer in its various forms are highly ineffective. The most promising hope for a cure is surgical resection. Five years after surgical resection of colorectal metastases, 40% of patients are alive, and 30% are disease free. However, in the case of colorectal liver metastases only 20% of all lesions are surgically operable leaving an enormous portion of patients to rely on systemic chemotherapy and radiation treatments [6]. While promising breakthroughs have been made in the localization of these treatments, systemic treatments continue to be extremely ineffective. For example, the response rate to the most commonly used chemotherapy agent (5-fluorouracil) in the treatment of hepatic metastases worldwide is only 20%. Survival rates for patients with unresected cancer vary based on the origin of the study; however, the following figures give a good indication of the ineffectiveness of systemic treatment: "1-year survival for solitary or limited liver metastases varies from 38 to 83%, whereas 3-year survival for solitary or limited metastases extends from 0 to 33%, and the figures for multiple and diffuse metastases fall between 0 and 4% [6]." Localized treatments take on many forms, including transarterial chemoembolization, radiofrequency ablation, cryogenic ablation. In the case of liver cancer treatment, transarterial chemoembolization has proven significantly more effective than systemic approaches.

TACE (Transarterial Chemoembolization)

Transarterial chemoembolization is a localized administration of both chemotherapeutic drugs and embolizing agents. While the cytotoxic drugs kill cells in the area of the cancerous tumor, the embolizing agents cause peripheral arterial occlusion restraining the drug to the affected area. Restraining the drug at the location of the tumor effectively increases contact time, prior to the drug's removal by the liver [7]. Chemoembolization procedures are carried out in an effort to effectively reduce the size of tumors prior to surgical intervention. In addition, TACE has been shown to effectively reduce the size of unresectable metastases in 50% of cases to allow other ablative procedures such as radiofrequency ablation or cryogenic ablation to be carried out [2]. Transarterial chemoembolization is especially effective in highly vascularized regions where tumors promote angiogenesis [8]. The dual blood supply of the liver increases the effectiveness of transarterial chemoembolization while improving its overall safety to the patient. Blood is supplied to the liver via two major sources, the portal vein and the hepatic artery. The hepatic artery provides 25% of blood flow to the liver; however, 95% of all primary and metastatic tumors derive blood from this source. The portal vein provides the remaining 75% of blood to the liver. Because the peripheral arterial occlusion only decreases at most 25% of the blood flow to the liver, healthy tissue is able to survive on a constant supply of venous blood. Within the liver, the hepatic artery branches into eight separate Couinaud segments, and therefore

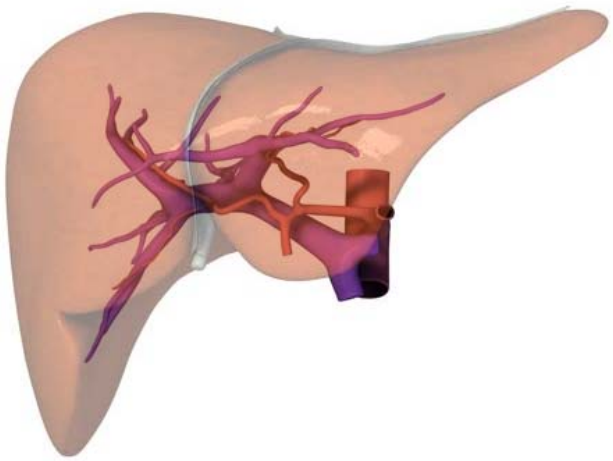

Figure 2 - Representation of the liver vasculature highlights the hepatic arterial system in red and the portal venous system in purple [9]

catheterization procedures can effectively target individual segments [10]. Localized hypoxia created by the embolization in the area of the tumor increases the effectiveness of the cytotoxic drugs. Current administration of chemotherapy and embolizing agent is carried out through a catheterization of the femoral artery to the location of the target area. This procedure is currently guided almost exclusively through X-ray digital subtraction angiography, yet advancements in MR technology make magnetic resonance imaging a more versatile guidance technique [5].

X-ray DSA/MRI Techniques

Through the use of X-ray digital subtraction angiography, real time high resolution imaging is possible. This technique, however, falls short of magnetic resonance imaging in many situations. The localization of tumors relies entirely on the uptake of contrast agent to highly vascularized regions, thus tumors are often not visible [5]. Using simple 2D MRI scans, it was determined that the placement of catheters near their target tumors was incorrect in 40% of X-ray guided cases [11]. For this reason, current TACE procedures most often utilize a pre-operative CT or MRI scan prior to catheter placement under X-ray guidance. Bi-plane views are available in X-ray DSA however, interventionalists would benefit greatly from three dimensional images. In addition to its reduced ability to target tumors effectively, X-ray delivers high doses of radiation, which can have a negative effect on patients whose immune systems are weakened by consistent chemotherapy treatments [5].

Magnetic resonance imaging does not emit radiation and therefore has no effect on the compromised immune system of patients. This has the possibility to reduce both hepatic failure and side effects such as pain, nausea and vomiting. Magnetic resonance imaging benefits from a very high degree of soft tissue contrast, thus tumors are much more easily visualized in MRI

studies. The greatest benefit of MRI over X-ray DSA is that recent advances in MR technology allow three dimensional, real-time imaging. Now, through the use 3D real-time MRI, interventionalists have the ability to actively guide the catheter to the location of the tumor, while visualizing tumor location at the same time. A multitude of undersampling techniques make real-time imaging both spatially accurate and temporally feasible [5]. This effectively eliminates the need for two separate procedures, a pre-operative CT/MRI scan for tumor localization and an X-ray DSA for catheter tracking. While MRI is undoubtedly a superior imaging technique for transarterial chemoembolization procedures, most interventionalists are accustomed to using X-ray as a catheter guiding tool and have not utilized the benefits of MRI for this application. Significant training is necessary before these interventionalists to become comfortable using MRI and a phantom suitable for such applications will prove beneficial. The phantom currently used in the Medical Physics Department at the University of Wisconsin is inadequate and does not address these needs.

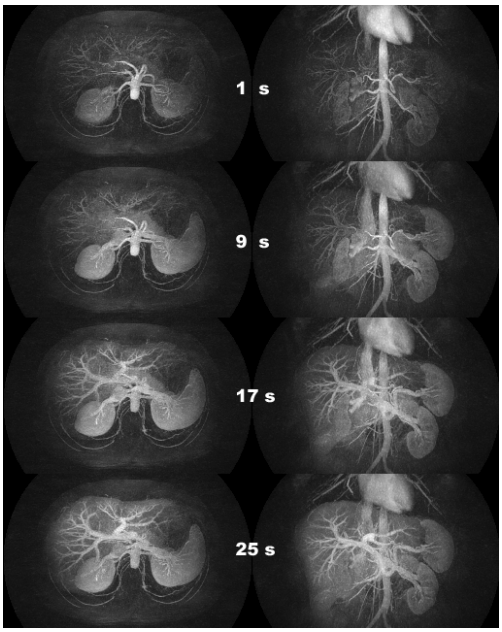

Figure 3 - 3D real time image of abdomen using time resolved VIPR rendering. Annotation shows time after scan initiation. [5]

Current Phantom

The abdominal phantom being used in the University of Wisconsin Medical Physics Department possesses a number of shortcomings that make it ineffective for aforementioned uses. Most importantly, the phantom does not contain liver vasculature past the hepatic arteries,

leaving out the detail of the eight Couinaud segments. Representation of the liver vasculature is required for practicing targeted catheterization procedures. In addition, this phantom is filled with an opaque gel which makes visualizing the vasculature outside of the MR scanner very difficult. The top of the phantom has been removed to allow this gel to be added or removed leaving it exposed to the bore of the MR scanner. In the event of a vascular leak, this could cause significant damage to the scanner. Additionally, the placement of fluid line connectors in a position directly perpendicular to the phantom walls causes an increased likelihood of them breaking during transport. This could cause a substantial fluid leak. Given the shortcomings of the current device, a series of requirements were determined which would address the needs of both interventionalists and members of the medical physics group.

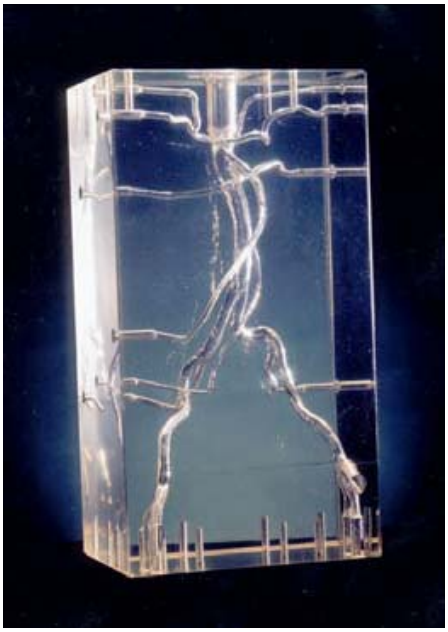

Figure 4 - Current abdominal phantom used by the Medical Physics Department of the University of Wisconsin is commercially available from Shelly Medical Imaging Technologies. [12]

Design Requirements

Following discussion with interventionalists and partners in the Medical Physics Department, Dr. Wally Block outlined a series of initial requirements that were built upon throughout the semester. The first and most critical of this project's requirements is that the phantom should include all eight Couinaud segments of the liver as well as key abdominal vessels. The vessels that should be included are the following: abdominal aorta, both femoral arteries (left and right), both renal arteries (left and right), superior mesenteric artery, the entire

celiac trunk (hepatic artery, left gastric artery, splenic artery), and the eight Couinaud segments of the liver. Inside the phantom, the vessels listed above should lie three inches off the side of the phantom, with the exception of their entrance/exit points. This ensures that signal arising from the edges of the phantom does not interfere with signal coming from the vasculature.

Dr. Block made it clear that a high level of detail and precision were not necessary when creating the vasculature. The primary concern was that all regions of the phantom are accessible through the use of a guide-wire catheter. The researchers must be able to visualize the movement of the catheter using the MRI scans, and use these images to make the correct catheter movements to arrive at a particular location within the phantom. The important fact is that the phantom is being used to test the ability of the researchers to make the correct movements using MRI visualization, *not* for the researchers to arrive at the correct portion of the liver based on their memory recall and knowledge of the liver.

To address a shortcoming of the current phantom, vessel exit points on the right and left sides of the phantom should be designed such that they are not easily breakable. As mentioned, the current phantom uses connectors that are attached perpendicular to the enclosure walls. This orientation creates a lot of torque on the connectors when setting up the phantom in the bore of the MR machine. Outside of the phantom, a catheterization port should be included in one of the femoral arteries to allow interventionalists to practice catheterization procedures in the same manner they would on a patient.

Adequate flow must be achievable in all vessels of the phantom to allow contrast agent delivered via a catheter to fill and vacate all vessels within ten seconds. The flow should be generated in the vasculature network through the use of the flow pump currently used in the client's lab. The current pump provides a maximum flow rate of 3L/minute. Thus, the new

phantom should tolerate this flow level with ease, and provide the ability to tolerate higher flow rates. The pump that is currently used is a peristaltic Masterflex pump (model number: HV-77521-40) equipped with a Masterflex pump head (model number: HV-77250-62).

Because of restrictions within the MRI scan room, the phantom must be attached to the flow pump which will remain outside of the scan room. Therefore, supply and return lines will need to run from the phantom to the scanner control room, where the pump and other ferrous metallic objects can safely reside. Fluid lines running from the phantom should be joined together through the use of manifolds, minimizing the number of fluid lines running back to the pump in the control room. Additionally, all supply/return lines should enter and exit the bore of the scanner on the same side. Each line running out of the scan room should be compatible with the current phantom / pump setup. This will require purchasing specific quick disconnect parts so the lines can quickly be plugged into the current pump network.

Once created, the phantom vasculature must be surrounded by a water tight enclosure. This will allow the user to fill the phantom with different substances to alter its imaging characteristics. Also, the phantom should be easily transported from the MRI scan room to labs and offices in the Medical Physics Department via a four wheeled cart.

Finally all materials used to construct the phantom must be MRI compatible (non-ferrous). All ferrous components utilized, specifically the pump, must be located outside of the scan room in the MRI control room. Given this set of requirements, a number of design options were considered before coming to a consensus on the components to be used in the final design.

Vasculature Network Design Research / Methods

One of the initial tasks in completing this project was designing the layout of the liver vasculature and surrounding abdominal vasculature of the phantom. Research of the vasculature layout began by analyzing the current phantom, which included the key abdominal vessels that were required for the phantom being developed. A scaled image of the current phantom was used to identify key anatomical points and dimensions of the abdominal aorta as shown in figure 5. These measurements were used when creating the aortic branches in the new phantom.

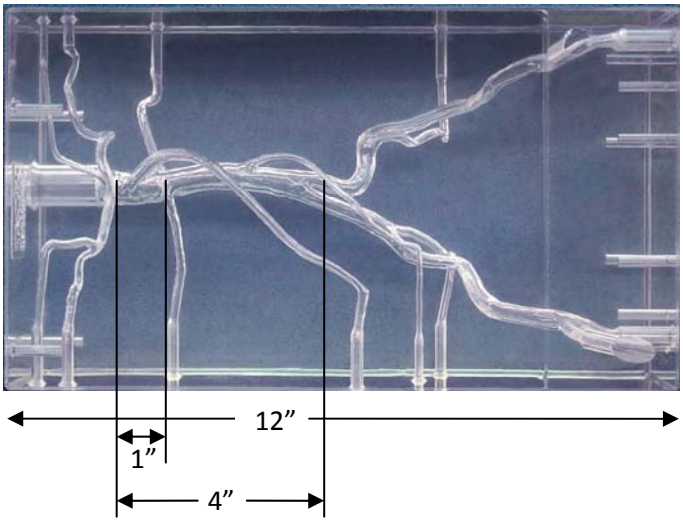

Figure 5 - Image showing current phantom with actual measurements. This image was used to determine distance between celiac trunk, renal arteries, and femoral artery split.

The next aspect of vasculature research involved determining branch regions for arterial vessels leading to each of the eight Couinaud segments of the liver. After consulting with Dr. Mark Rice, Section Chief of Liver Transplantation at the University of Florida, as well as Dr. Wally Block, the consensus was that liver arterial vasculature is extremely variable and impossible to mimic perfectly. Using liver arterial vasculature details from Mevis Medical Solutions [13], a computer model was produced which

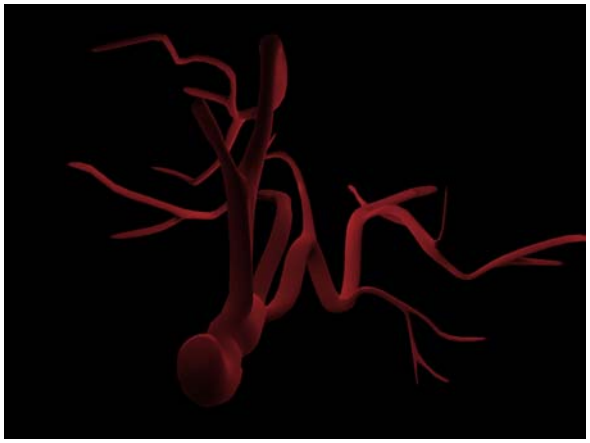

Figure 6 – The liver arterial vasculature model that was created using Autodesk Maya 3D Max. The vasculature in the new phantom was based off of this model.

provided a basis for recreation of the liver arterial vasculature. The model was created using the modeling program Autodesk Maya 3D Max.

With abdominal vessel measurements, and an accepted model of the liver arterial vasculature, the last step in vasculature research was to determine approximate dimensions of the vasculature of the liver, and thus the dimensions of the phantom enclosure. This was done by combining knowledge from the current phantom with actual abdominal MRI scans provided by Dr. Block. The result of combining these resources was the 8"x8" measurement shown in figure 6. Combing this information with the requirement that key vessels be located three inches from all sides of the phantom enclosure, the size was determined to be 14"x14". The last dimension (the height) was determined using the height of the current phantom combined with anatomical information. The abdominal aorta runs just beneath the liver, and the femoral arteries are near the anterior surface of the legs. Thus, the anterior posterior dimension of the current phantom (which includes the abdominal aorta and both femoral arteries) was determined to be sufficient for the purpose of the new phantom. This dimension on the current phantom is 6.75 inches. This dimension was increased to eight inches to further minimize artifact from the edges of the phantom. Thus, the final dimensions of the phantom enclosure were set at 14"x14"x8". After determining specific phantom dimensions, a number of construction techniques were researched and considered for vascular recreation.

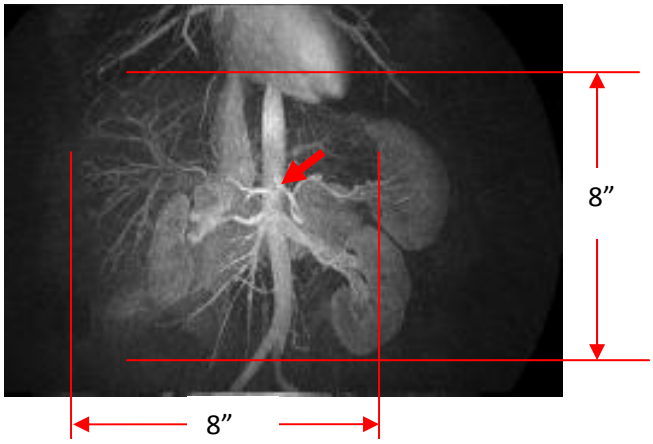

Figure 7 - Abdominal MR image used to determine phantom enclosure size. Using the known distance from the femoral split to the celiac trunk (≈4"), the labeled dimensions could be calculated.

Materials/Construction Methods

Three different approaches to creating the vascular network were examined in the initial design stages. One approach that was considered was to create a wax mold of the vasculature. Once created, this mold could be coated in silicone and melted away to yield the complete vascular network. The benefit of this method is that it would yield one continuous structure. Thus, it would not be as prone to leaks as the other methods which require junctions to be made between discontinuous components. Furthermore, the vasculature network would be completely customizable which would allow obscure branches and turns in the vasculature to be created. The downside of this method is that the wax mold would be extremely difficult to construct. Current team member Justin Schmidt has experience creating vessels from wax molds. From experience, it was noted that the method is only practical for small scale vessels. Even for small vessels, the wax mold easily breaks, and takes a long time to construct. Constructing an entire abdominal network, even in separate pieces, would likely take a long time and be very challenging. As mentioned, this level of precision and detail are not required, therefore this method presents unnecessary hurdles which can be avoided by choosing alternative methods.

The next approach investigated was the creation of a 3D model using the 3D printing services at the Digital Media Center of the University of Wisconsin. This method is somewhat similar to that of the wax method in that the 3D model would be coated with a material (such as silicone), and then removed to leave a hollow, continuous vasculature. The printer is capable of printing a variety of file types including our Maya vasculature model, or even an actual MRI image. When this idea was discussed with Dr. Alan Wolf, who runs the 3D printing lab, it was made clear that removing the 3D model after coating it with silicone would not be practical.

Additionally, the cost for this method is extremely high ($8 per cubic inch plus $20/hour labor). Thus, this method was eliminated from consideration.

The final vascular recreation tactic researched was the use of Tygon® tubing in conjunction with various forms of vascular junctions. This is the method that Dr. Block initially suggested that we look at. The initial drawback of using this method was that using standard barbed connectors at every junction would be extremely limiting. The connectors would make it impossible to create locations of the vasculature where multiple branches come together such as the celiac trunk. This would drastically limit the paths that the vasculature would be able to take. This problem could resolved by eliminating the use of connectors in areas with multiple branches, and by directly joining pieces of Tygon® tubing using adhesive. This method allows flexibility in where branch points are located, and also allows the vasculature to quickly be constructed. Thus, this method was incorporated into our final design.

Final Design

After considering a number of methods for vascular creation it was decided to utilize Tygon 2001® tubing in the final design. Based on previous research, complex branches were created by drilling/cutting holes in one of the vessels, and inserting the end of the other vessel into the hole without blocking any flow. These junctions were tacked in place with a hot plastic melt then layered in silicone caulk to ensure a water tight seal.

Figure 8 - Image shows Tygon® tubing vascular network suspended within the acrylic enclosure

This method allowed for variability in the branch angles and the option to branch off any size tube desired. Simple junctions were created using barbed wye connectors. The tubing used for the vasculature ranged from an inner diameter of 1/8" to 5/8" which was dependant on the vessel created.

The created vasculature was suspended within an acrylic enclosure which serves the purpose to both maintain the vasculature orientation and also to hold a gel material that will be used to mimic the MR imaging characteristics of the abdominal tissue. The enclosure was made from 3/8" width acrylic sheeting and measures 14.75" x 14.75" x 8.75" creating the proper inside dimensions. The five sides of the enclosure (excluding the top) were adhered together using acrylic cement which causes the fusion of the pieces into one solid piece of acrylic. Silicone caulk was used to line the inside of all the joints ensuring that the enclosure is water tight. Holes were drilled in the side of the box for the different connectors that were used to make the transition from the vasculature inside of the enclosure to the return tubing outside of the enclosure. A variety of barbed connectors and pipe fittings were used to transition from the vasculature within the enclosure to the return tubing outside. These connectors were appropriately glued into the pre-drilled holes using a quick setting epoxy. For transition points on the left and right sides of the enclosure, elbow pipe fittings were used to reduce the torsion on the connectors which previously resulted in them breaking off.

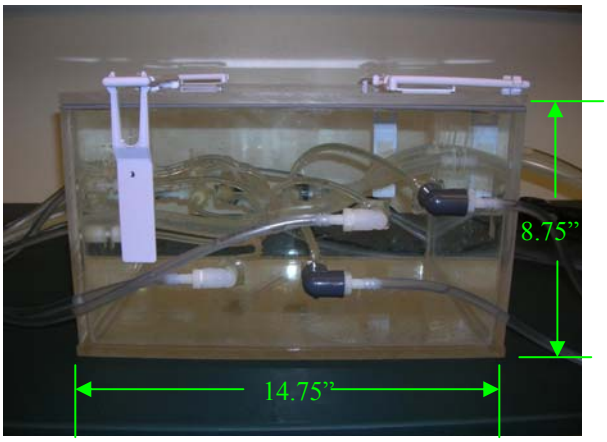

Figure 9 - Side view of the phantom with labeled dimensions. Also visible are elbow brackets for vascular junctions exiting the side of the enclosure, and the latches use to hold down the removable top.

A removable cover was made from 3/8" acrylic and measured 14.75" x 14.75" to fit exactly over the top of the sides. The top sides of the enclosure were lined with a waterproof seal that is used for weather proofing doors. This seal measured 3/8" wide and came with an adhesive backing to adhere to the top sides of the enclosure. To ensure a water tight seal between the top sides of the enclosure and the cover, the waterproof stripping was carefully cut to cover the entire area where the cover would rest. Four plastic latches were used to firmly hold the cover down against the weather stripping. The latches were adhered to the sides of the enclosure and the cover using a 3M adhesive that came with the latches. Pressure was applied to the cover while attaching the latches to ensure a water tight seal between the cover and the weather stripping.

Each of the vessels that attached to a connector on the inside of the enclosure required a return tube that provided flow to a pump reservoir which contained the water that was cycled through the system. Vinyl tubing was used to connect the vasculature to two fluid manifolds outside of the phantom enclosure. These manifolds reduced the number of tubes required to return fluid to the pump located in the control room. Half of the vessels are connected to one manifold and the other half are connected to the other. Each manifold consists of seven inflows and one outflow that returns fluid back to reservoir mentioned above. The singular outflows from each manifold are fitted with quick disconnect couplings with shut off capabilities for interfacing with the current pump setup. This water from these returns is eventually cycled back through the system via the flow pump.

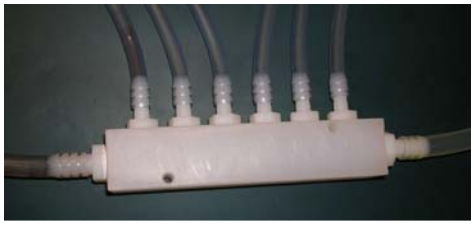

Figure 10 - Manifold used to collect fluid from tubing within the enclosure and return fluid to the pump reservoir

A catheter insertion point was also incorporated into the external tubing system to allow physicians and other researchers to insert a catheter and guide-wire into the vasculature via the right femoral artery. The femoral artery is where the majority of TACE procedures are initiated and provides a realistic situation for those using the phantom. Catheters are used in TACE procedures, but can also be used by researchers to inject contrast agent and saline into the phantom for imaging purposes. The junction between the catheter port and the tubing was made air-tight so that outside air was not introduced to the system causing artifact during the scans.

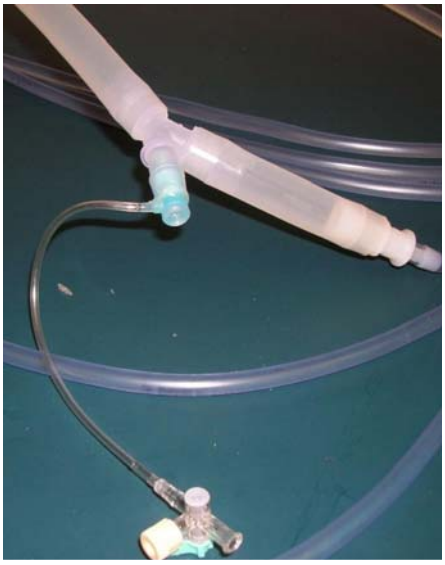

Figure 11 - Catheter port located on right femoral artery allowing entrance point for catheter

Finally, providing flow to the entire system is the peristaltic Masterflex® pump (model number: HV-77521-40) equipped with a Masterflex® pump head (model number: HV-77250-62) seen in figure 12. The pump is fitted with a serial interface that allows programmable flow control to be implemented later in the project. The pump currently provides constant flow through the system at variable flow rates and the highest flow that the pump is able to achieve is 3 L/min. This constant flow can be adjusted via a knob on the front of the pump.

Figure 12 - Masterflex® analog control peristaltic pump used to provide flow to the phantom

Following the completion of phantom construction, the device was transported to the University of Wisconsin Hospital for a variety of tests under the guidance of Dr. Ethan Brodsky.

Testing

Integrity Testing

Before testing could begin on the MRI machine, a number of integrity tests had to be preformed to ensure that the device would be safe within the scan room. Namely, the vasculature, the hose system, and most importantly the enclosure, had to be tested for leaks to prevent water from coming into contact with the scanner.

The first of these safety tests was to test the viability of the enclosure. This was the most important test that was performed because in the event of a rupture within our vasculature, the water would be contained within the box and out of the scanner. For this test, the enclosure was filled to the top with tap water, closed, and placed on a dry table. The outside of the box was dried using hand towels and the box was left overnight for a period of 24 hours. After 24 hours, the outside of the enclosure was inspected for moisture visually and in a tactile manner. Special attention was given to areas where the tubes were leaving the enclosure. Since no leaks were found, the enclosure was deemed leak proof for the purposes of our initial testing within the scanner. Since 24 hours is a relatively short span of time if the enclosure were to be permanently filled, another long term test will be performed in the future after the initial testing procedure.

Next, the hoses were tested for integrity. The viability of the hoses is important to ensure that they don't break off of the enclosure when connected correctly or incorrectly to the pump. To perform this test the enclosure was emptied and the pump was connected to the aorta of our box via the quick disconnects. The inferior and superior manifolds were connected to return

lines via the quick disconnect coupling, and the lines placed into the pump reservoir. With the feedback loop complete, the reservoir was filled with water and the pump was turned on in the forward position (water pushed into the aorta). The reservoir was continually refilled while water flowed into the closed system. After approximately six minutes the system was completely filled with water and the air bubbles were removed. At this point the speed of the pump was slowly increased for five minutes until the maximum flow was reached (3 L/min). While water was running through the system at maximum rate, junctures outside of the box were inspected for leaks. These junctures included the quick disconnects and the entrances and exits to and from the box. Since leaks were not found the pump was run at 3 L/min for a period of five minutes and the junctures were inspected a second time.

Satisfied with the integrity of the hoses when run in the correct manner, a battery of tests that simulated misuse was performed. First, the pump was run backwards (water pushed into the left and right femoral arteries) for a period of two minutes. Then each of the hoses was systematically kinked one-by-one to increase the pressure within the system. This test was vital in that it simulates a person stepping onto a hose or kinking a hose during a testing procedure (which is entirely possible due to the long length of the return lines). Although no hoses erupted from the enclosure, a considerable amount of backpressure was achieved and noted by the vigorous shaking of the pump.

Finally, the vasculature was checked for leaks. Although this test was unimportant to the safety of the scanner (due to the leak proof enclosure), a leak proof vasculature is necessary for production of clear MRI scans. For example, if gadolinium, a commonly used contrast agent, was administered through a leaky vasculature, it could leak permanently into the enclosure.

This would result in unproductive MRI images because the surrounding tissue would be emphasized in addition to the vasculature.

To perform this test we first filled the bottom of the box with around two inches of water. Next a two lumen catheter was inserted in the catheter junction. The tip of the catheter was navigated intravenously through the vasculature to the start of the aorta (the entrance into the vasculature). A syringe of red food coloring was connected to the lumen of the catheter. With the flow at 3 L/m a small amount of food coloring was administered into the aorta. The dye quickly (approximately 3.06 seconds) colored every hose within the vasculature and flushed out of the vasculature after a short period of time (approximately 5.62 seconds). This test was repeated five times and after each time the outside of the vasculature and the water underneath the vasculature was visually checked for coloration. This test also indicated that flow is present in all portions of the vasculature.

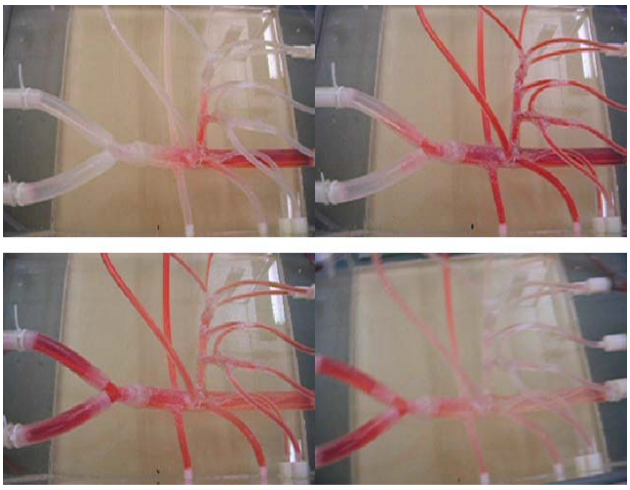

Figure 13 – Time-lapse image of red food coloring moving through the vasculature

MR Imaging Studies

With the physical testing complete MRI testing was initiated. The device, pump, and return lines were easily transported up to the 1.5T XMR/MR4 scanner in the UW-Hospital radiology

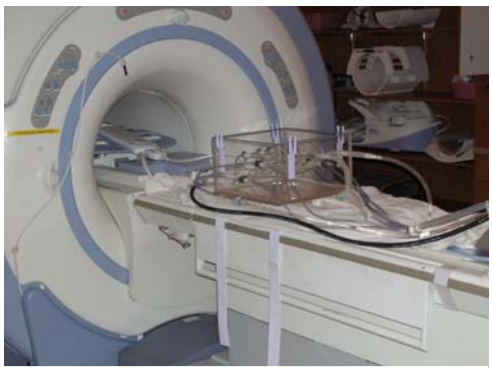

Figure 14 – Phantom setup in the MRI scan room without the body coil

department. The device was placed on the MRI table and strapped into a body coil for imaging purposes. The return lines were run into the control room where a sink was present. The entire setup of the device took about ten minutes. The vasculature was then filled with water but for these preliminary tests the enclosure was unfilled. It should be noted that these scans were preformed with tap water flowing through the vasculature. Although tap water was used for the scans, our client ensured us that the quality of the scans would improve if a blood mimicking solution was used.

The first scans were 3D optical surface scans that ensured that the spatial features of vasculature would correctly appear in the MRI images. The specific scan parameters were Degree Field Of View (DFOV)= 50.9 cm, Echo Time (TE)=2.2 ms, Repetition Time (TR)=20 ms, using a FAST_GEMS pulse sequence with the body coil. One view of the resulting 3D image is shown in figure 15. The images were imported into Adobe Photoshop and labeled to check spatial consistency with the phantom. There are two versions of this scan, one with the return lines cropped and one with them present.

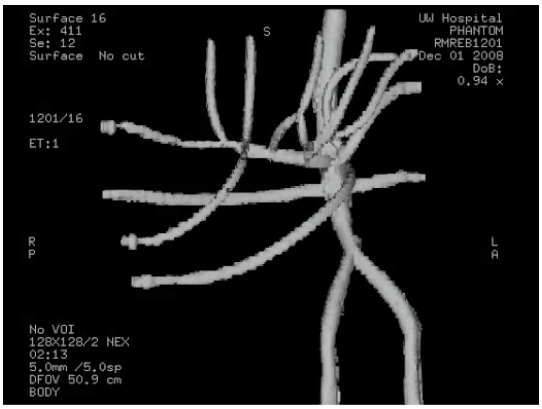

Figure 15 – 3D surface reconstruction of the phantom vasculature without return lines

The next scan that was performed highlighted the flow by utilizing a Vastly Undersampled Isotropic Projection Reconstruction (VIPR) pulse sequence. The images produced by this scan indicate that flow is present through the vasculature and is able to be imaged by the MRI.

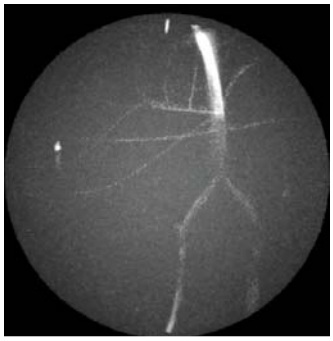

Figure 16 – VIPR flow dependent MR image

Next, a two-lumen catheter was introduced into the phantom. A syringe filled with gadolinium contrast (diluted 10:1 using saline solution) was placed at the end and used to fill the catheter. The contrast-filled catheter was then imaged to ensure that a catheter would show up on the MR scans. This is important because, ultimately, the MRI scans will be the only tool utilized by the radiologists to direct the catheter while mimicking the TACE procedure. Although a simple two lumen catheter was used during these scans, a more expensive catheter with MR active tracking capability will be used during the actual procedure. This will provide the physician with the exact point of the catheter tip throughout the procedure.

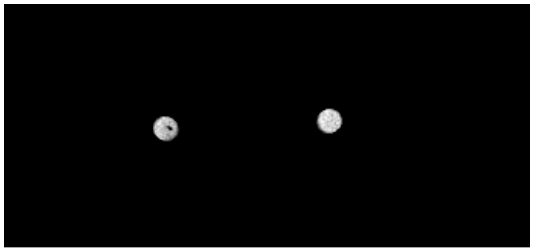

Figure 17 – Axial slice through femoral arteries with catheter (black dot) seen in the right (left on the image) femoral artery.

With the catheter in place, a final test was run to test the flow of contrast (10:1 gadolinium) through the vasculature. Unlike the prior scans, this scan was run in real time. A series of images were recorded while the contrast flowed through the vasculature. This test was performed much like the prior dye test. With the catheter already in place from the previous scan, the scan was started and the contrast was administered to the phantom. When recording images in real-time, the flow of contrast through the vasculature can easily be identified.

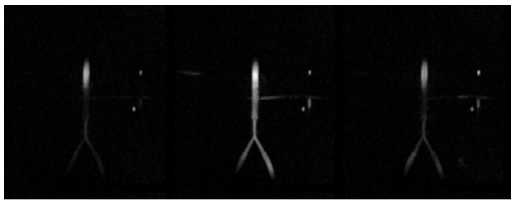

Figure 18 – Time-lapse image of contrast flowing through a slice of the phantom containing the aorta and femoral arteries.

Future Work

Even with the success of the first iteration prototype, there are plenty of enhancements that can be made to the prototype. The first of these is the addition of pulsatile flow capability. A LabJack® DAQ unit has been purchased, and can be used to interface to the client's current

pump via a DB9 serial connection. With this interface, the flow rate of the pump can be controlled from a computer allowing multiple different flow patterns to be used with the phantom. Furthermore, the possibility of upgrading to a similar, more powerful pump needs to be investigated. The current pump's flow rate is 3L/minute. However, the physiological value for flow at the aorta is 5L/minute [14]. Thus, the addition of a stronger pump may be advantageous in mimicking the flow characteristics of the human heart. This will be important for the researchers performing the TACE procedure due to the physical implications of guiding a catheter through an active flow vascular network. The pulsatile flow and the increased flow rate may cause additional difficulty of guiding the catheter to a target location. Difficulties such as these are important to include in the phantom so that the researchers will know what to expect when moving to human subjects.

Another enhancement to consider is the addition of a substance to the inside of the phantom enclosure that mimics imaging characteristics of surrounding abdominal tissue. This material will likely be made out a gelatin. Specifically, the material would mimic the T1 and T2 relaxation times of the surrounding tissue for imaging purposes. Additionally, the tap water within the vasculature will be replaced with a blood mimicking substance. The result will be a phantom that mimics not only the vasculature network, but also the surrounding tissue which will make the contrast between vasculature and background decrease. Thus, this would function as another realistic hurdle that the interventionalists would have to overcome while navigating a catheter through the vasculature.

The last possible physical enhancement is the use of cyclohexanone to increase the strength of the Tygon to Tygon bonds in the vasculature. Cyclohexanone acts as a solvent which

fuses the Tygon® tubes together to create a bond that is as strong as the Tygon® tubes themselves [15]. This would ensure long term durability of the phantom's vasculature.

In addition to prototype enhancements, two types of additional testing can be performed during the upcoming semester. The first is a quantitative flow test using advanced MR imaging techniques. The client has made it known that this is possible, and would likely be beneficial since an emerging area of research is flow quantization using MRI. Although flow was verified using the red dye test, quantifying the flow will identify areas which made need some fine tuning.

Finally, the TACE procedure should be performed on the phantom. The procedure will be the ultimate test of the accuracy of the phantom given that the researchers are able to access all portions of the phantom via catheterization and that they can visualize the movement of the catheter via the MRI scans. With feedback from the interventionalists performing this procedure, final adjustments can be made to the phantom.

Conclusion

The success of the first iteration prototype has been witnessed in discussion with Dr. Block as well as through performed testing procedures. With the primary goals for the semester completed the door has been opened for considerable improvements as we move to the future. Primary focus will be on implementing the necessary prototype improvements, while continuing to consider ways to test the devices validity. From there the focus will shift to writing and running tests which address project's motivation - an improved catheterization guidance technique using magnetic resonance imaging.

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Appendix A:

Expense Breakdown

Component	Part Number	Vendor	Quantity	Cost/unit	Cost
Tygon tubing (7/8 in. I.D)	9449K48	McMaster	2 ft	$6.13	$12.26
Tygon tubing (3/4 in. I.D)	9449K47	McMaster	4 ft	$5.18	$20.72
Tygon tubing (1/2 in. I.D)	9449K46	McMaster	3 ft	$2.29	$6.87
Tygon tubing (7/16 in. I.D)	9449K45	McMaster	3 ft	$2.04	$6.12
Tygon tubing (3/8 in. I.D)	9449K44	McMaster	5 ft	$1.85	$9.25
Tygon tubing (5/16 in. I.D)	9449K43	McMaster	3 ft	$1.65	$4.95
Tygon tubing (1/4 in. I.D)	9449K42	McMaster	8 ft	$1.49	$11.92
Tygon tubing (3/16 in. I.D)	9449K41	McMaster	3 ft	$0.96	$2.88
1/2" wye connector	53415K242	McMaster	1 (10 pack)	$8.95	$8.95
3/16" wye connector	53055K154	McMaster	2	$2.38	$4.76
Weld-on #3 acrylic cement	7528A13	McMaster	1	$12.77	$12.77
Clear cast acrylic (2ft by 2 ft by 3/8 in)	N/A	Delvie's Plastics	2	$30.00	$60.00
1/4" to 1/8" straight barbed connector	53415K118	McMaster	1 (10 pack)	$7.63	$7.63
1/8" female pipe to tube adapter	5116K301	McMaster	1 (10 pack)	$5.34	$5.34
3/16" to 1/4" straight barbed connector	53055K131	McMaster	2	$1.43	$2.86
1/8" female pipe 90° elbow (push to connect)	5111K385	McMaster	10	$4.11	$41.10
1/8" male pipe to tube adapter	5372K111	McMaster	3 (10 pack)	$6.22	$18.66
1/4" female pipe 90° elbow (push to connect)	5111K386	McMaster	5	$6.01	$30.05
1/4" male pipe to tube adapter	5372K112	McMaster	3 (10 pack)	$3.86	$11.58
1/8" wye connector	2808K127	McMaster	1 (5 pack)	$5.26	$5.26
1/2" to 1/4" straight barbed connector	2974K267	McMaster	1 (10 pack)	$4.74	$4.74
3/8" male pipe to tube adapter	5372K118	McMaster	1 (10 pack)	$4.07	$4.07
Fluid manifold	5364K232	McMaster	1	$33.00	$33.00
Fluid manifold	5364K231	McMaster	1	$30.38	$30.38
1/4" female pipe 90° elbow	4596K121	McMaster	9	$2.61	$23.49
1/8" male/female pipe 90° elbow	45505K125	McMaster	4	$19.59	$78.36
1/2" to 3/8" straight barbed connector	5047K27	McMaster	2	$1.63	$3.26
3/8" wye connector	53415K241	McMaster	1 (5 pack)	$8.55	$8.55
5/8" to 3/8" straight barbed connector	2974K273	McMaster	1 (10 pack)	$5.00	$5.00
3/8" to 1/4" straight barbed connector	5121K271	McMaster	1 (10 pack)	$3.22	$3.22
3/8" to 3/8" straight barbed connector	5121K171	McMaster	1 (10 pack)	$3.14	$3.14
Tube Clamps	9579K62	McMaster	2 (20 pack)	$6.49	$12.98
Tube Clamps	9579K64	McMaster	1 (20 pack)	$6.49	$6.49
3/8" quick disconect w/ shut off (male)	51545K53	McMaster	2	$9.95	$19.90
3/8" quick disconect w/ shut off (female)	51545K33	McMaster	2	$13.03	$26.06

Labjack U3 HV	N/A	LabJack	1	$114.00	$114.00
LJTick Proto Boards	N/A	LabJack	2	$10.00	$20.00
Vinyl Tubing (1/4 in I.D.)	N/A	True Value	34 ft	$0.39	$13.26
Vinyl Tubing (3/8 in I.D.)	N/A	True Value	10 ft	$0.45	$4.50
Vinyl Tubing (1/2 in I.D.)	N/A	True Value	4 ft	$0.49	$1.96
Vinyl Tubing (5/8" I.D.)	N/A	True Value	2 ft	$0.59	$1.18
Safety1st Latches	N/A	True Value	4	$2.49	$7.47
Weather Stripping	N/A	True Value	1	$4.89	$4.89
Silicone Sealent	N/A	True Value	2	$2.89	$5.78
Hot Glue Sticks	N/A	True Value	1 (10 pack)	$2.19	$2.19
Epoxy	N/A	True Value	4	$2.99	$11.96
				TOTAL	**$733.76**
				Total (w/ returns)	**$662.61**

Appendix B:

Product Design Specification
Transarterial Chemoembolization Simulator (liver phantom)

Client:	Dr. Wally Block Ph.D.
Advisor:	Dr. Bill Murphy Ph.D.
Team Members:	Ryan Carroll (BWIG)
	Ben Engel (Team Leader)
	Eric Printz (Communications)
	Justin Schmidt (BSAC)

Project Background:
Liver cancer treatment can often involve higher, more targeted doses of chemotherapy if delivered directly to the liver. Professor Block's lab is integrating capabilities to guide cancer treatment to the liver using magnetic resonance imaging. Current x-ray treatments significantly over treat the patient's liver because radiologists and other clinicians cannot visualize the tumor. The lab is in need of a simulator (phantom) that will simulate the arterial vessels of the abdominal and liver so they can simulate treatments and train interventional radiologists on using the new MRI guidance techniques. The project will include adding flow capabilities using a flow pump to simulate pulsatile flow. Flexibility exists in how realistic the vascular network has to be. In addition opportunities exist to work with scientists and interventional radiologists after the semester is complete.

Terminology:

Superior	Towards the head with respect to the transverse plane
Inferior	Towards the feet with respect to the transverse plane
Right	Towards the right side of the body with respect to the sagittal plane
Left	Towards the left side of the body with respect to the transverse plane
Anterior	Towards the top half of the body with respect to the coronal plane
Posterior	Towards the bottom half of the body with respect to the coronal plane

Project Scope

Phase I (Fall Semester)

- Development of a rough/working model of the liver vasculature with specific surrounding vasculature
- Development of a proper enclosure for this model with dimensions and materials appropriate for MRI compatibility
- Single speed flow through use of current programmable flow pump provided by the lab
- Safety and reliability testing to ensure device is ready for use in scan room
- Usability testing with interventional radiologists to receive feedback on potential improvements and efficacy of design

Phase II (Spring Semester)

- Improvements on vasculature network detail
- Possible 3D modeling and mold formation
- Integration of pulsatile flow through provided programmable flow pump
- Possibility of upgrading to a pump with greater capabilities upon proof of concept

Product Requirements:

- Phantom will require a port for catheter entrance located in the femoral artery (the site of the majority of catheterization procedures)
- Phantom will require 2-3 inches of space between the vasculature model and sides of phantom enclosure to minimize MRI artifact
- This is especially true on the superior end of the phantom
- Size of enclosure: 14”x14”x8”
- Vasculature:
    - The phantom should include the following vessels:
        - Abdominal aorta
        - Left gastric artery
        - Left/Right Hepatic Arteries – leading to liver vasculature detailed below
        - Splenic artery
        - Left/Right renal arteries
        - Superior Mesenteric Artery (SMA)
        - Both Femoral Arteries
    - Liver vasculature should be detailed to the level of the eight arteries entering each of the eight Couinaud segments of the liver
    - Only arterial vessels need to be included as treatments are not generally delivered through venous vasculature
    - Liver detail
        - The exact reconstruction of the vasculature is not important because liver vasculature is extremely variable
        - The main requirement here is that the interventionalist simply has something to practice guiding a catheter through based on MRI images
- The bottom side of the phantom should conform to the shape of the MR coil that it will be sitting in to minimize any potential damage to the coil from a heavy phantom.
    - This can be implemented through the use of a layer of foam separating the phantom and the MR coil
- The final weight of the product should such that it is capable of being moved by a single researcher (less than 80 pounds)
- Entrance/exit points to the phantom
    - Entrance
        - Aorta
    - Exit
        - 8 Couinaud segments
        - R/L femoral artery
        - Superior mesenteric artery
        - R/L renal artery

        - Left gastric artery
        - Splenic artery

Design Materials

- The surrounding box will be made using acrylic sheeting
- Tube fittings outside of the box should be easily/quickly disconnected and reconnected for movement of phantom
- Tygon tubing will be used for the vasculature phase 1 prototype of the phantom
- Silicone based epoxy will be used to join the Tygon tubing
- Flow pump – a pump currently in use in the lab will be used for phase 1
    - Pump Details:
        - Masterflex L/S Analog Control peristaltic pump drive, model **HV-77521-40**
        - L/S High Performance Pump head, model **HV-77250-62**
        - Website reference: http://www.masterflex.com/catalog/product_view.asp?sku

Budget

This project is funded by a grant (NCI1 RO1-CA116380) that our client has obtained for the project