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Word Count: 4518
Number of Figures: 6
Number of Tables: 1
Number of Equations: 0
Number of Supplements: 3
Number of References: 10

Advisor Approval: _____*John F. Angle*___________ Date:___03-May-2024____
John Angle, M.D.

Development of Hepatic Vasculature Models for Preoperative Planning

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Abstract

Hepatic arterial embolization is a procedure widely used in the treatment of liver tumors that involves the navigation of a catheter through the minute vasculature. However, this procedure presents challenges due to individual variations in the complex vascular anatomy and difficulty visualizing the 3D branching of the vessels through 2D X-ray imaging during the surgery. Thus, clinicians have recognized the need for enhanced training and preparation methods to address these concerns. Indeed, over 1⁄4 of surgical residents polled indicated that they lack the confidence to perform on patients independently from overseeing physicians.[1] It is essential for practicing surgeons and residents to gain experience and confidence in utilizing surgical tools and imaging methods. To address these concerns, physicians and researchers have turned to the creation of 3D-printed anatomical models that can be used to teach and practice surgical strategies. This method allows for patient-specific and rapidly-prototyped models. The challenge that remains is the recreation of the small, hollow, and tortuous geometry of the vessels. Here, we present the development and application of three manufacturing methods of hepatic vasculature models for use as preoperative planning tools: hollow 3D printing, casting of a solid model in silicone, and 3D printing of a negative-space model. Utilizing 3D printing in combination with additional manufacturing methods, we were able to address some limitations of 3D printing alone. From this work, we determined that the 3D printed negative space model was the most ideal method of those tested for the creation of a preoperative planning tool for hepatic arterial embolization.

Keywords: Interventional radiology, preoperative planning, 3D printing, hepatic arterial embolization

Introduction

Hepatic arterial embolization is a minimally invasive procedure that is performed to treat inoperable hepatic (liver) tumors. It is associated with increased lifespan, shrinking of tumor size and density, and reduction of symptoms. However, inadequate skills can lead to treatment-induced liver failure or blockages of the main hepatic artery, posing severe health risks for the patient.[2] Additionally, difficulties performing the procedure can lead to reduced efficiency in the operating room and increased exposure to radiation as the patient is continually imaged. Thus, physicians must be adequately trained to handle this surgery and its challenges to provide improved patient outcomes. Currently, the first time that many medical residents perform this procedure is on a patient in the operating room. However, when polled, over a quarter of surgical residents in the U.S. reported that they did not feel confident performing surgeries on their own.[1] This limitation in medical training is due to the fact that throughout the history of medical teaching and learning, it has been a challenge to find viable, realistic organ models on which to practice. Traditionally, human cadavers have been an integral part of the medical teaching curriculum, as these provide the student and physician with a tactile experience. These have been used to visualize human anatomy, study the feel of tissues, and practice procedures.[3] Nonetheless, cadavers pose several unique challenges, including the degradation of tissue and scarcity of supply.[4] As a result, the use of cadaveric models has decreased in recent decades in favor of newer modeling techniques.[5]

As an alternative to cadavers, multiple forms of organ models have been developed, with varying degrees of realism. One recent area of study is the creation of virtual reality (VR) models. Using this technology, medical students and surgeons are able to immerse themselves in a virtual operation and repeatedly practice the steps of a surgical procedure. Some VR models can be toggled to allow the user to "strip away" anatomical layers of the body like the parenchyma, enhancing the ability to visualize the internal structure of the organs with more detail. While this method has been shown to improve surgical outcomes and increase the efficiency of procedures, these models is not necessarily true to life since the user is unable to physically feel how they are interacting with the organs and tissue in the body.[6]

The diffusion of 3D printing into the medical field and interventional radiology has spread rapidly since the first 3D printer was patented in 1986, and the creation of anatomical and surgical organ models has benefited greatly from this technology. Specifically, the ability to generate 3D models from patient scans has created new opportunities for individualized medicine. 3D printing, or additive manufacturing, has allowed physicians to create models for preoperative planning and produce customized products to match a specific patient's anatomy.[7] From medical imaging data, physicians can 3D print accurate models of a patient's organs, bones, or blood vessels. 3D printing technology has advanced significantly, and various materials are now available for different applications. Each material has unique properties, such as flexible and tensile behaviors, that make it suitable for specific use cases. For instance, plastics (e.g. PLA, ABS) offer ease of use whereas resins (e.g. SLA, DLP) provide high resolution for prints.[8]

Currently, the use of 3D printing for preoperative planning and medical teaching has spread to a variety of clinical fields, including cardiology, interventional radiology, and neurosurgery. Up to this point, two main trajectories of 3D printing have been explored: 1) hollow modeling of relatively large structures or vessels and 2) solid modeling of smaller-scaled anatomical structures and vasculature. For the first example, modeling of the heart and aorta has been completed; however, the models lack fine details and do not include vessels smaller than the aorta.[9] For the second, a solid model of the hepatic vasculature tree and tumor was printed and cast in clear silicone, resulting in a more realistic anatomical visualization. While these examples and similar models using these same techniques have been used for preoperative planning purposes, both methods have clear limitations to their use and realism. Namely, the printing of small-scale features is a major area of difficulty within medical 3D printing, which is of utmost importance to the printing of vasculature models. Studies have found that "dimensional errors are most variable when small features are printed," and that features between 0-10 mm had the highest error and variance when compared to the original medical images.[10] While the human aorta may be on the order of magnitude of centimeters, the smaller arteries and capillaries are roughly one thousand times smaller. Thus, it is necessary to determine the best methods to combine the two modeling techniques for printing a small-scale, hollow vasculature model that is highly accurate.

Our main objective is to create a highly detailed and precise 3D model of the hepatic vascular system with the ability for a catheter to be navigated through the network. This will not only enhance visual accuracy but also introduce a level of interaction that mimics real-world procedures. The methods of anatomical model creation being explored are hollow 3D printing, casting of a solid model in silicone, and 3D printing of a negative-space model. These models represent a significant advancement in the field, with future iteration upon this work providing medical professionals with a powerful tool for education, training, and preoperative planning.

Results

Hollow, 3D Printed Model

A hollow, 3D printed model was created by manually selecting the area around the vessel lumen in a CT scan and 3D printing in elastic resin (Figure 1A). Elastic resin was chosen because it gives the user a mechanical feel most similar to human vasculature. Because the elastic resin is clear, the catheter was able to be visualized in the vessels. However, after printing, the resin filled the middle of the hollow vasculature and thus was unable to be fully catheterized. This issue occurred as a result of the inherent 3D printing process, as internal support structures were unable to be printed inside the vessel to support the lumen as there would be no way to remove them after printing. Furthermore, this model was overly simplified due to the difficulty of manually adjusting the digital model to create a hollow vasculature model. Despite the challenges with the anatomical resolution, this model was cost-effective and only required about $26 dollars of resin to produce. Overall, due to the lack of complexity and inability to fully catheterize the physical prototype, this model was deemed impractical for preoperative planning and teaching purposes.

Casted, Negative Space Model

A casted, negative space model was created by inserting a 3D printed solid model of complex vasculature into silicone, allowing it to harden, and then pulling it out to create a silicone mold of the hepatic tree (Figure 1B). Because of the multi-step process required for the creation of this model, it was the most hands-on and time-intensive method. Since the solid model of the complex vasculature was printed using standard Grey resin that has been validated to be compatible with the Formlabs © 3L 3D Printer, it printed successfully with no errors. This theoretically would have resulted in a highly accurate, negative space model following the removal of the 3D printed vascular tree from the cured silicone mold; however, the silicone mold and Grey resin were less flexible than anticipated. Overall, the act of removing the complex model resulted in damage to the silicone mold. The silicone model was ultimately cut into four parts in order to pull the model out, but small segments of the solid model remained in the mold because of its complexity. Although this anatomical model had more complexity than the hollow 3D printed model, the finer details got lost and destroyed. The silicone was also not transparent, and therefore we were unable to fully confirm that the three tumors of this model were able to be reached by the catheter. This model was fairly cost-effective, requiring about $61 worth of resin and silicone to produce. Overall, this was not the most viable model due to the inability to completely catheterize and the loss of vasculature details within the silicone mold.

3D Printed, Negative Space Model

A 3D printed, negative space model was created in computer-aided design software by creating a “case” around the complex vasculature model (Figure 1C). It was printed in two halves that fit together to create a solid block (Figure 1D). Each of the halves was successfully printed with the vasculature being completely hollow. A hole was left on the outside of the case where the main hepatic artery began, so a catheter was able to be inserted into the artery to reach each of the three tumors. Because this model was printed in clear resin, we were able to visualize the catheter in the vessels to confirm that the vasculature had successfully been printed. One of the halves of the model were printed on supports. Because the model was life-sized, the weight of the resin block caused it to partially break off the edges of the supports during printing. This caused slight bending in that half of the model, so the two halves were not perfectly flush. Another drawback of this model is that it required almost four liters of resin, meaning that it cost roughly $610 to produce and was time-consuming to print. However, this was the most successful model in that it represented highly complex vasculature, was able to be fully catheterized, and was true to scale.

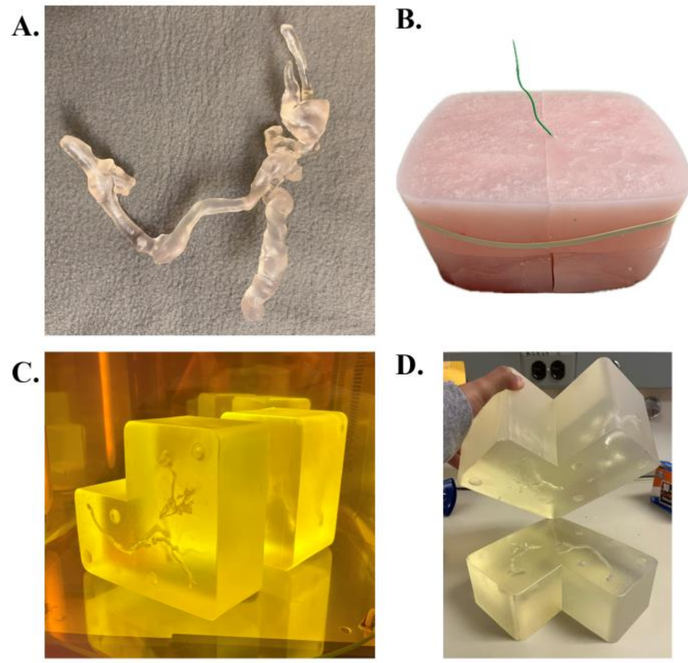

Fig. 1. Overview of the three model variations. A) Simplified, hollow 3D printed model. B) Casted negative space model. A wire (in green) was inserted into the opening of the main hepatic artery to demonstrate that the model is partially hollow after the removal of the embedded vasculature model. C) The 3D-printed, negative space model in the process of being cured. D) Demonstration of how the two halves of the 3D printed, negative space model open and fit together.

<u>Discussion</u>

Impact

Throughout the course of our project, the focus shifted. The initial plan was to design a catheterizable vasculature model using a single-step process of designing and 3D printing it hollow. However, as the project progressed and printing of the hollow model began, the focus shifted towards testing multiple manufacturing methods to determine which may be ideal for future implementation in terms of ease and the accuracy of the resulting model. Thus, the work that was accomplished through this project may help to provide physicians at UVA Health and beyond with an understanding of which methods may be viable for future development of anatomical models for use in the clinic. From this work, three different manufacturing methods were developed and assessed, and an optimal method of the three was determined by comparing printing time, cost, and accuracy (Table 1). Overall, a life-sized, detailed model of the hepatic vasculature was successfully created and was able to be catheterized. Compared to previous 3D-printed preoperative planning tools that have been developed, this model includes small-scale details of the branching arteries and arterioles that are necessary to practice arterial embolization.

Table 1.

Comparison of the 3D Printing Results for Each Model

	Model Type		
	Hollow, 3D-Printed Model	Casted, Negative Space Model	3D-Printed Negative Space Model
Time Estimate	20 h 33 m	7 h 51 m	32 h 14 m
Layers	1429	1519	992
Volume (mL)	132.02	69.24	4096.22

Even the creation of solid, non-hollow anatomical models that was completed as part of the proof of concept testing has value in the clinic and teaching space. Having a tactile and accurately scaled representation of the vasculature could allow medical students to gain a better understanding of their patient's anatomy and visualize features of the body that typically require more invasive methods to be seen. We envision that the solid models could be incorporated into a sort of training tool kit that could be used by students to supplement their education and enhance their anatomical understanding.

Limitations

One limitation that delayed the start of the project was delayed access to patient scans. Since the project involved using patient data, it was important to determine if an IRB was required. After correspondence with a Clinical Research Coordinator at UVA Health, it was determined that an IRB submission was not required. Additionally, access to patient scans was delayed because the IR team was trying to determine the best method of anonymizing patient data.

Once printing started, the team faced some technical challenges. The Elastic 50A resin is a recently developed material by Formlabs ©. It has a higher viscosity than the standard hard resins, requiring more force from the mixer arm to level out the resin in the tank. When first printing with the Elastic 50A resin, the print paused and a "Mixer Check Failure" error occurred, indicating that the mixer decoupled from the tank. From a visual check, the mixer arm was still attached to the tank, but in an attempt to fix the error, the arm was unattached and then reattached. The error remained, so it was overridden on the printer panel and the print continued without issues afterwards. This error populated each time the Elastic 50A resin was used. Because of this, someone had to constantly check on the print and manually fix the mixer arm for the print to resume. This led to delays to the prints, especially because most of the models required an overnight print with 23-32 hour print times.

Furthermore, another challenge was removing the supports from the models. Since the models consist of small, tortuous vessels and the printed supports are the same material and color as the model, it was challenging to discern what features needed to be removed. To address this, the team referenced the digital model to determine what was a support and what was part of the model.

The hollow, 3D-printed model was printed without internal supports because there was no way to remove them due to the tortuous geometry and the miniature diameters. Because of this, the model filled up with resin and did not print completely hollow.

Future Work

More efforts must be made in order to properly train future physicians and provide them with a robust educational experience. Once a viable manufacturing process has been selected or established, future work could involve assessment of the model with clinicians and students. Since the ultimate goal of the vasculature model is to be used by students, residents, and physicians to learn or plan complex surgical procedures, it is essential that their input be captured. The model could be used and catheterized by current physicians to determine if the physical and mechanical characteristics resemble those of the real human vasculature. Similarly, the preferred 3D printed negative space model should be taken and tested in the fluoroscopy suite of the Interventional Radiology Department to ensure that the chosen resin material does not block the transmission of light during X-Ray or CT imaging. Third, the 3D printed negative space manufacturing method could be tested using other resin types to determine if the complexity of the vasculature could be captured using an elastic, physiologically-relevant resin.

Materials and Methods

The CT scans were originally selected by Dr. Angle as appropriate examples of hepatic vasculature and tumors. The files were acquired from the UVA Health picture archiving and communication system (PACS) as DICOM files. The software syngo.via was used to anonymize the patient data retrieved from PACS. Patient CT scans were processed through the following procedure for all three manufacturing methods, with method-specific details being provided in the respective subsection (Figure 2). The patient scans were exported into 3D Slicer, an open-source software for 3D modeling and visualization of medical scans. 3D Slicer was utilized to complete the segmentation and adjust the 3D digital model. First, the thresholding function was used to segment, or isolate, the liver vasculature from the surrounding anatomy. This feature works by grouping the pixels by how light or dark they appear. A contrasting agent is injected into the main hepatic artery before the CT scan is acquired, so the vessels stand out against the darker surrounding tissue and are able to be segmented. Manual adjustments were made to the threshold range to achieve a balance between creating an excessively large range that resulted in unwanted anatomical features being included and creating too narrow a range that resulted in a reduction of the lumen diameters.

The segmented vasculature was rendered in 3D Slicer and additional manual adjustments were made to the model. The contrasted hepatic vasculature was similar in brightness level to the bone, so the scissor tool was used to remove the skeleton from the segmentation (Figure 3A, 3B). The smallest vessels were then removed to create a refined model that would be feasible to 3D print (Figure 3C). Once a digital model was completed, it was exported as an STL file and imported into PreForm, the 3D printing software for the Formlabs © printers. PreForm autogenerated supports, auto-oriented the model, provided options to customize print settings, and provided detailed print information such as print time, material usage, and number of layers required for the model. Following the initial automation of the model support and orientation parameters, manual adjustments were made in order to limit the printing time and the amount of support required. Resin stereolithography printers were used for the 3D prints to achieve high-resolution printing. The printed model was carefully removed from the build plate, then placed into an isopropyl alcohol bath, and washed for 30 minutes to remove excess resin. The model

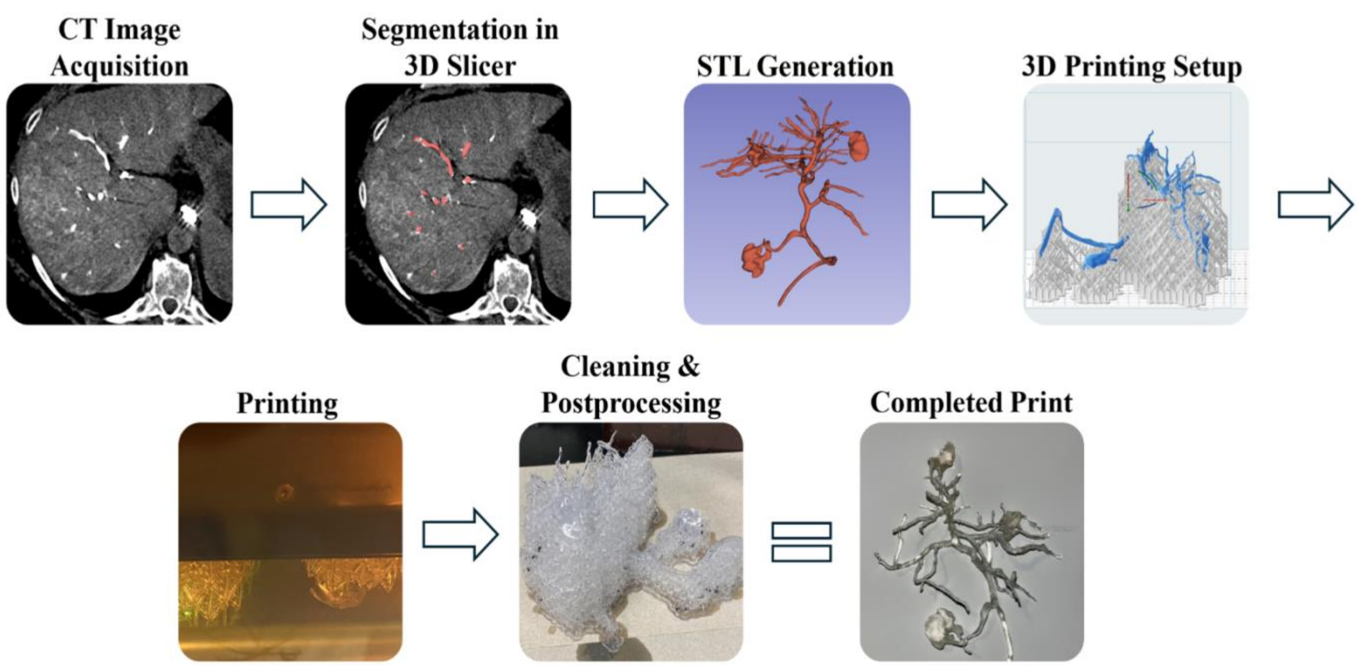

Fig. 2. Flowchart of the model production process: 1) CT scan provided by Dr. John Angle (IR Department at UVA Health). 2) Used automatic thresholding followed by manual adjustment (the vessels identified by the thresholding are highlighted in pink). 3) The segmented, thresholded model is rendered in 3D. 4) The STL file is exported to PreForm 3D printing software; supports are generated (in white) and the printing parameters are adjusted. 5) The SLA printer is prepared, including the tank, resin cartridges, and build plate. The print is allowed to run (~22 hours). 6) Post-processing steps are completed, including an isopropyl alcohol bath (10 minutes), manual removal of supports, and light-curing (20 minutes). 7) The solid model is completed.

was then placed into the curer and cured for the appropriate amount of time for each specific resin type. The supports were then manually removed from the printed model using surgical scissors, tweezers, and forceps.

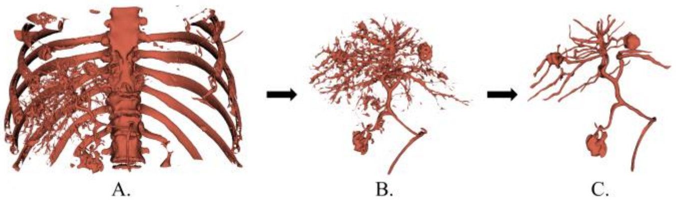

Fig. 3. Overview of the manipulation process of the automatically thresholded model in 3D Slicer. A) Upon initial thresholding, the vasculature and bones were all rendered into the model. The vasculature was excessively detailed and messy. B) The spine and ribcage were manually removed, leaving the tortuous vasculature tree and tumors behind. C) To focus on the main arteries, arterioles, and tumors, the excess branching and thresholding artifacts were manually removed from the vasculature model.

Proof of Concept Testing

To assess the capabilities of the Formlabs © 3+ printer, a tube model with decreasing diameter sizes ranging from 5 to 1 mm was developed and printed (Figure S1). This test confirmed that the resin and 3D printer were able to support hollow printing, as well as printing at a miniature scale.

Fig. 4. Our first 3D-printed prototype of the hepatic tree and single tumor.

The first prototype was a scaled-down, solid model of the hepatic tree and was completed on a Form 3+ printer (Figure 4). The Elastic 50A resin from Formlabs © was initially identified to mimic the physiological properties of vascular tissue. We intended to print the completed hollow model but had to change directions due to technical difficulties. We attempted to use the Elastic 50A resin for this print; however, the printer had unexpected technical issues. The mixer arm, which is used to spread the resin evenly in the tank, decoupled multiple times despite outside assistance and troubleshooting. Due to these issues, the Grey resin was used instead because the printer previously worked with the Grey resin and a tank was already filled with the material, which shortened the timeline for the print setup. This prototype verified that the printer had the capabilities to create complicated, tortuous geometries at a small scale.

Fig. 5. Solid vasculature model, printed in the clear, flexible Elastic 50A resin.

The second prototype was a life-size, solid model of a patient case that included three tumors (Figure 5). This was completed on a Form 3L printer, which has a larger build volume and an additional laser compared to the Form 3+ printer used previously. This model was printed with the Elastic 50A resin to test the compatibility of the resin with the 3L printer since Formlabs © indicated on their website that they had not assessed the performance of this new resin with this particular printer. This print job took about 23 hours to print.

Hollow, 3D Printed Model

The first model was a life-size, hollow model of a patient case that included one tumor. This model was significantly simplified, with less branching vasculature because of the difficulty of manually hollowing the digital model. In the digital model, each vessel was manually cleaned up slice by slice in each plane of the CT scan using the brush and hollowing functions in 3D Slicer. Once the digital model was completed, the model was printed on the Form 3L printer in Elastic 50A resin. The "Mixer Check Failure" error populated in the middle of printing, but we overrode the error and the print continued without issues afterward. This print job took about 20.5 hours. When the model was taken off of the printer, we saw that large portions of the hollow vessels were filled with the resin. We washed the holes with IPA, but wet resin remained inside. We left the model to completely dry for a few hours before curing it in the machine.

Casted, Negative Space Model

The second model involved a multi-step manufacturing process to create a negative space model by casting a 3D-printed vasculature model in liquid resin. The patient case used for this model was a hepatic vasculature tree with three tumors and the digital vasculature model was designed to be solid and include additional vessels and complexity compared to the hollow model. The Formlabs © Grey resin was selected to print the hard, solid vasculature model to be cast. To cast the vasculature model, 10A Super Elastic liquid silicone was acquired from Amazon. This is a two-part solution system that cured and solidified over the course of several hours upon combination. The silicone was chosen due to its relatively low cost, ease of use, and elastic material properties. The vasculature model was slowly lowered into the vat of liquid silicone in a plastic tub and left to cure at room temperature for two days. Once cured, the hardened silicone and embedded resin vasculature model were removed from the plastic container. The silicone model was bisected with a serrated knife to create two halves for easier removal of the printed vascular tree; however, the model was too firmly embedded (Figure S3). While the initial goal was to remove the entire vasculature model in one intact piece, the vessels were then intentionally broken in an attempt to better remove them from the silicone. Pliers and tweezers were used to remove segments of the resin model from the silicone.

3D Printed, Negative Space Model

The third model was a life-size, two-part negative space model created in Autodesk Fusion. The STL file of the complex vasculature from model two was imported into Fusion as mesh. Then, a rectangular "case" was created around the vasculature and extraneous material was removed to create a block that encased the complex vasculature body. The block was then also converted to mesh, and the body of the vasculature was cut from the block using the "Combine" function. This left a solid block with the vasculature cut out from it. This model was then cut in half at the middle of the box so that when printing, excess resin could drip out of the holes where the model was cut. Four spherical buttons were added to one of the halves and cut from the same plane on the other half. This was done so that the model could fit together easily and could be catheterized (Figure 6).

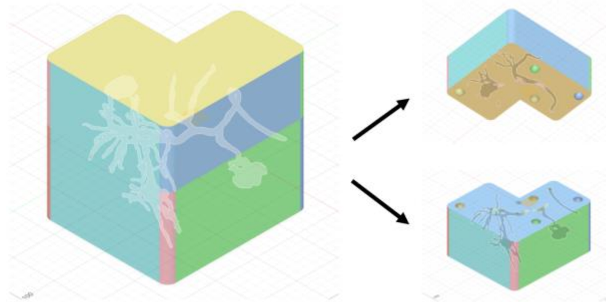

Fig. 6. Visualization of the mesh of the two-part model with complex vasculature cut out.

The two halves were set up in Preform to be printed on the Form 3L printer in clear resin. The half with the buttons cut out from it was printed directly onto the build plate, while the other half with extruded buttons was printed with supports on the build plate (Figure S2). This model was printed in clear resin because we did not have time to test the radiopacity of different resins, and we wanted to be able to visualize the catheter moving through the vessels.

End Matter

Author Contributions and Notes

K.S.T. designed the hollow, 3D-printed model. S.G.G. designed the solid vascular model for the casted model. R.T.P. designed the 3D-printed, negative space model. K.S.T., S.G.G., and R.T.P. all contributed to the 3D printing, additional manufacturing, and post-processing activities of the three models and prototypes.

The authors declare no conflict of interest.

Acknowledgments

We thank Dr. John Angle for his oversight of our project and the UVA Interventional Radiology Department for allowing us to shadow and observe them and for providing insight on the CT scans. We thank Gabrielle Fuller and Matthew Beyer for their insights about 3D printing. This project was funded by the UVA Biomedical Engineering Department.

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Supplementary Material

Fig. S1. Model of the hollow tubes created in Fusion, used to test the resolution of hollow printing.

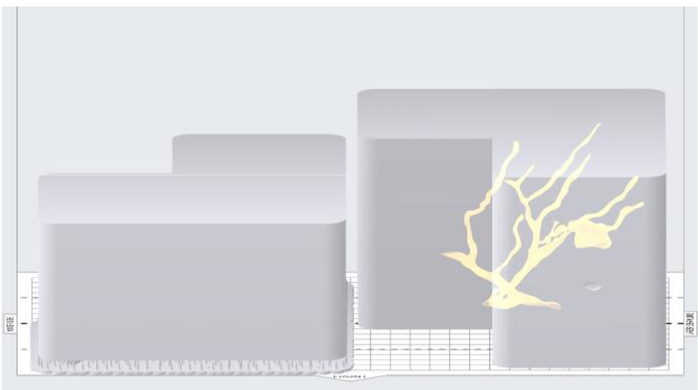

Fig. S2. Negative space model set up in Preform: top half with buttons (on the left) is set up with supports while the bottom half (on the right) is set up directly on the build plate.

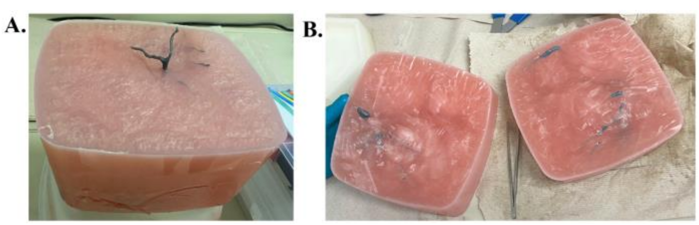

Fig. S3. A) The cured and casted, negative space model before attempted removal of the embedded vasculature tree. B) The silicone and vasculature tree after being halved to aid in the removal of the resin tree.