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Title: Development and Evaluation of 3D-printed Cardiovascular Phantoms for Interventional Planning and Training

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Author Questionnaire

1. **Microscopy**: Does your protocol require the use of a dissecting or stereomicroscope for performing a complex dissection, microinjection technique, or something similar? **No**

2. **Software:** Does the part of your protocol being filmed include step-by-step descriptions of software usage? **Yes, all done**

3. **Interview statements:** Considering the COVID-19-imposed mask-wearing and social distancing recommendations, which interview statement filming option is the most appropriate for your group? **Please select one**.

   ☒ Interview Statements are read by JoVE's voiceover talent.

4. **Filming location:** Will the filming need to take place in multiple locations? **No, walking distance within same building**

Current Protocol Length

Number of Steps: 28
Number of Shots: 47

Introduction

1. Introductory Interview Statements

1.1. The presented method allows for the creation of patient-specific anatomical cardiovascular models for in-vitro testing, teaching and planning of procedures.

1.1.1. *3.6.2.*

1.2. This method offers a standardized approach to creating 3D-printable individualized anatomical models based on radiological datasets that can be easily included in flow loops or training setups. While this modeling approach is focused on the cardiovascular system, it can be transferred to other anatomical structures.

1.2.1. *3.1.2.*

1.3. The quality of the radiological dataset has a big influence on the difficulties encountered during modeling. For the first models, use a dataset with minimal movement artifacts and a high spatial resolution.

1.3.1. *2.2.1.*

Protocol

2. 3D-model creation

2.1. To begin, define a range of Hounsfield unit values **[1]** by opening the **Thresholding** tool **[2]**, resulting in a combined mask of the contrast-enhanced blood volume and bone structures **[3]**.

2.1.1. WIDE: Establishing shot of talent at the computer.

2.1.2. Added shot: Close: Shot of the screen and talent working in the segmentation software

2.1.3. SCREEN: Step.2.1.2.mkv. 0:04 – 0:25.

2.2. Remove all bone parts that are undesirable in the final 3D-model by using the **Split Mask** tool, which enables the marking and separation of multiple areas and overall slices, based on Hounsfield values and location **[1]**.

2.2.1. SCREEN: Step 2.2.1.mkv. 0:15 – 1:01. *Video Editor: Speed up the clip as the bone parts are marked.*

2.3. Following this separation, ensure that a mask containing the contrast-enhanced blood volume remains. This can be done by scrolling through the coronal and axial planes and matching the created mask with the underlying dataset. From this mask, calculate a rendered 3D polygon surface-model **[1]**.

2.3.1. SCREEN: Step 2.3.1.mkv. 0:00 – 0:35.

2.4. Click the **Local Smoothing** tool to adjust the surface of the segmented model manually and locally. Focus on removing rough polygon shapes, single peaks, and rough edges created by previous trimming operations **[1]**.

2.4.1. SCREEN: Step 2.4.1 with_timeskip.mkv. 0:06 – 0:40, then 1:10 – 1:15. *Video Editor: Speed up as the surface is smoothed.*

2.5. To allow the later connection of the model to a flow loop, include tubular parts with defined diameters adjusted to the available hose connectors and tube diameters **[1]**.

2.5.1. SCREEN: Step 2.6.1 .mkv. 0:01 – 0:06.

2.6. To place a datum plane parallel to the opening cross-section of the vessels, select the tool **Create datum plane** and use the preset **3-point plane**. Next, click on three equally spaced points on the vessels cross-section to create the plane. Input an offset of 10 millimeters in the command window and confirm the operation **[1]**.

2.6.1. SCREEN: Step 2.6.1 .mkv. 0:07 – 0:30.

2.7. Select the **Draw Sketch** tool from the menu and choose the previously created datum plane as the location of the sketch. In the sketch, place a circle roughly on the

centerline of the vessel and set the radius constraint to match the outer diameter of the hose connector **[1-TXT]**.

2.7.1. SCREEN: Step 2.7.1.mkv. 0:04 – 1:04. **TEXT: 24 mm for aortic inlet; 8-10 mm for subclavian, carotid, and renal vessels; 16-20 mm for the distal opening of the vessel**

2.8. From the created sketch, use the **Extrude** tool to create a cylinder with a length of 10 millimeters. Orient the extrusion to move away from the vessel opening, to create a distance between the cylinder and the vessel cross-section of 10 millimeters **[1]**.

2.8.1. SCREEN: Step 2.8.1.mkv. 0:01 – 0:46.

2.9. Then, use the **Loft** tool to create a connection between the vessel ending and the geometrically defined cylinder. Ensure a smooth transition between the two cross-sections, thereby avoiding turbulence and low flow areas in the final 3D flow model **[1]**.

2.9.1. SCREEN: Step 2.9.1_with_timeskip.mkv. 0:10 – 0:48, then 1:00 – 1:03.

2.10. Finally, use the **Hollow** tool to make a hollow blood space. In the command window, input the required wall thickness and set the direction of the hollowing process to "move outward". Confirm the selection to execute the hollowing process **[1]**.

2.10.1. SCREEN: Step 2.10.1.mkv. 0:05 – 0:40.

3. 3D-printing and flow loop setup

3.1. After uploading the printing file from the slicing software to the 3D-printer **[1]**, ensure that the amount of printing material and support material in the printer's cartridges is sufficient for the 3D-model and start the print **[3][4]**.

3.1.1. SCREEN: Step 3.1.1.mkv. 0:05 – 0:16.

~~3.1.2. WIDE: Talent starting the print on computer and moving to printer to start~~

3.1.3. Added shot: CLOSE: Talent starting model print on computer

3.1.4. Added shot: CLOSE: Talent starting model print on printer

3.2. Following the printing process, remove the support material from the finished model **[1]**. First, remove the support material manually by gently squeezing the model **[5]**, Place the model on sink **[3]** and then immerse it in water or a respective solvent after removing the cover **[4]**. Dry the model in an incubator set to 40 degrees Celsius overnight **[7]**. NOTE: Please take note of the shot sequence in VO narration, its non-sequential

3.2.1. WIDE: Talent removing model from printer NOTE: Shot 3.2.2 is the close up shot for 3.2.1

~~3.2.2. CLOSE: Talent removing model from printer~~

3.2.3. CLOSE: Talent placing build platform with model on edge of sink

3.2.4. CLOSE: Talent removing cover from model and submerging in water NOTE: Shot 3.2.6 is the alternative shot for 3.2.4 with different time points filmed, beginning and final model without support material

3.2.5. Talent squeezing the model to remove support material.

3.2.6. ~~Talent immersing the model in water.~~

3.2.7. WIDE: Talent putting the model in an incubator. NOTE: Shot 3.2.8 is the close up shot for 3.2.7

~~3.2.8. Talent putting thein an incubator~~

3.3. On the next day, embed the model in 1% agar. Use a plastic box with at least 2-centimeter side margins around the model **[1]** and drill holes into the walls to allow the tubes to be connected from the vessels to the pump and the reservoir **[2]**.

3.3.1. Box for embedding.

3.3.2. Holes in the walls of the box.

3.4. Add agar to water and bring it to a boil **[1]**. After stirring the mixture, let it cool for 5 minutes and pour it into the box to create a bed of at least 2-centimeter height **[2]**.

3.4.1. Boiling agar NOTE: Different time points filmed

3.4.2. Talent pouring cooled agar in the box.

3.5. While the agar bed sets, connect the model to a non-compliant PVC tube using commercial hose connectors at every opening **[1]**. Use zip ties to fix the connection between the hose connectors and the 3D-model and ensure that there is no fluid leakage **[2]**.

3.5.1. PVC tube. NOTE: Multiple shots for different sides of the model

3.5.2. Talent fixing the connectors with zip ties. NOTE: Multiple shots for different sides of the model

3.6. Guide the PVC tubes through the drilled holes into the box **[1]**, then place the model on top of the set agar bed **[2]**. To prevent agar leaking from these holes, use heat proof modeling clay to seal it **[3]**.

3.6.1. Talent guiding the PVC tube through the holes.

3.6.2. Talent placing the model on the agar bed.

3.6.3. Talent sealing the holes with clay.

3.7. Next, fill the box with agar and cover the model by adding a 2-centimeter layer on top **[1]**. Allow the agar to fully cool and set for an hour at room temperature **[2]**. *Videographer: This step is important!*

3.7.1. Talent covering the model with agar. NOTE: Different time points filmed

3.7.2. Set agar. NOTE: Different time points filmed

3.8. Agitate the ventricle using a piston pump with a stroke volume of 120 to 150 milliliters **[1]**.

3.8.1. WIDE: Talent agitating the ventricle. NOTE: 3.8.2 is the close up shot for 3.8.1

~~3.8.2. CLOSE: Talent agitating the ventricle.~~

4. Clinical imaging

4.1. For CT imaging, place the entire flow loop within the CT scanner with the drive unit standing close by **[1]**. Connect the contrast agent pump directly to the reservoir of the flow loop so the flooding of the model with contrast agent can be simulated during scanning. This is especially useful for visualizing vascular pathologies **[2]**.

4.1.1. Talent placing the flow loop in the scanner.

4.1.2. WIDE: Talent connecting contrast agent to the pump NOTE: 4.1.3 is the close up shot for 4.1.2

~~4.1.3. CLOSE: Talent connecting contrast agent to the pump.~~

4.2. Perform CT as a dynamic scan over the whole model to visualize contrast agent inflow. Inject 100 milliliters of 1 to 10 diluted iodinated contrast agent into the model's reservoir at a speed of 4 milliliters per second **[1-TXT]**. Start the scan using bolus triggering in the leading tube, with a 100 Hounsfield unit threshold and a 4-second delay **[2]**. *Videographer: This step is important!*

4.2.1. Talent starting the CT scan. **TEXT: 100 kVp tube voltage, 400 mA tube current, 1.2 mm Collimation**

4.2.2. Talent starting the scan.

4.3. To perform sonography, put a small amount of ultrasonic gel on top of the agar block to reduce artifacts **[1]**. Start the pump and use the ultrasonic head to locate the anatomical structure of interest **[2]**.

4.3.1. Talent putting gel on agar block.

4.3.2. Talent starting the pump.

4.4. Use 2D-echo mode to evaluate leaflet movement, as well as the opening and closing behavior of the valve **[1]**. Use color Doppler to evaluate blood flow across the valve and spectral Doppler to quantify the flow velocity following the heart valve **[2]**.

4.4.1. LAB MEDIA: 4.4.1.wmv. 00.00.00-00.00.04

4.4.2. LAB MEDIA: 4.4.2.wmv. 00.00.00-00.00.03

4.5. Insert an access port into the PVC tube directly below the 3D-model to allow for an easier access of the anatomy with a cardiac catheter or guidewire **[1]**. After starting the flow loop, check for leakage at the port entrance point. If necessary, use a two-component adhesive to seal the opening **[2]**. *Videographer: This step is important!*

4.5.1. Talent inserting the access port into the PVC tube.

4.5.2. Talent checking for leakage at the port entrance.

4.6. Place the 3D model on the patient table underneath the C-arms of the X-ray machine **[1]**. Use X-ray imaging to guide the catheter and guidewires through the anatomic structure **[2]**. ~~For balloon dilation or stentgraft placement, use continuous X-ray mode to visualize the expansion of the device **[3]**.~~ NOTE: 4.6.3 was not filmed, hence corresponding VO is not required

4.6.1. Talent placing the model on table. NOTE: Combined with 4.6.2

4.6.2. Talent guiding the catheter and guidewires through the structure. NOTE: Multiple shots

~~4.6.3. Talent visualizing the expansion of the device.~~ NOTE: 4.6.3 was not filmed

4.7. For 4D-MRI, use a 1.5 Tesla scanner and ensure that the acquisition protocol consists of a non-contrast-enhanced MRA and the 4D-Flow sequence **[1]**. Acquire an isotropic dataset with 25 phases and a slice thickness of 1.2 millimeters **[2-TXT]**. Set the velocity encoding at 100 centimeters per second **[3]**.

4.7.1. MRI setup.

4.7.2. Talent acquiring an isotropic dataset. **TEXT: TE 2.300, TR 38.800, FA 7 °, matrix size 298 x 298**

4.7.3. Talent setting the velocity.

4.8. Perform the 4D-Flow image analysis with a commercially available software. First, import the 4D-MRI dataset by selecting it from the flash drive. Then, perform semi-automated offset correction and correction of aliasing to improve image quality **[1]**.

4.8.1. SCREEN: Step 4.8.1.mkv.

4.9. The centerline of the vessel will be automatically traced, and the software extracts the 3D volume **[1]**.

4.9.1. SCREEN: Step 4.9.1.mkv. 0:01 – 0:20.

4.10. Finally, perform quantitative analysis of flow parameters by clicking on the individual tabs in the analysis window. Flow visualization, pathline visualization, and flow vector can be visualized without further input. For quantification of pressure and wall shear stress in the respective tab, place two planes by clicking on the **Add Plane** button **[1]**.

4.10.1. SCREEN: Step 4.10.1.mkv. 0:14 – 1:10.

4.11. Move the planes to the ROI by dragging them along the centerline, so that one plane is placed at the beginning of the ROI and one at the end. The pressure drop across the ROI and wall shear stress will be visualized and quantified in the diagram next to the 3D-model **[1]**.

4.11.1. SCREEN: Step 4.11.1.mkv.

Results

5. Results: Clinical imaging of the 3D-printed model

5.1. The presented 3D-printed models offer a wide range of possibilities in CT-imaging. The printed material can be easily distinguished from the surrounding agar and possible metallic implants. Therefore, the use of a contrast agent is normally not required, except for generating dynamic imaging sequences **[1]**.

5.1.1. LAB MEDIA: Figure 3 A.

5.2. When using ultrasonic imaging, it is possible to distinguish between the model's wall, the surrounding agar **[1]**, and thin dynamic objects like heart valve leaflets **[2]**. The agar layer on top of the model provides realistic haptic feedback during the scanning process **[3]**.

5.2.1. LAB MEDIA: Figure 3 B.

5.2.2. LAB MEDIA: Figure 3 B. *Video Editor: Emphasize where 2 is pointing.*

5.2.3. LAB MEDIA: Figure 3 B.

5.3. Flow analysis within the flow loop offers a wide range of possible applications in pre-interventional imaging. 4D-MRI sequence enables visualization of fluid flow, turbulences, and wall shear stress within the 3D-printed model, making it possible to analyze flow patterns following artificial heart valves **[1]**.

5.3.1. LAB MEDIA: Figure 3 C.

Conclusion

6. Conclusion Interview Statements

6.1. This workflow can be transferred to different interventional medical procedures for training or planning purposes.

6.1.1. *4.6.1*

6.2. The technique allows for a closer in-vitro examination of the flow behavior in large cardiovascular vessels and offers great potential for individualized therapy planning.

6.2.1. *4.6.2 - 4.6.3*