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TITLE: Advanced MR Flow Imaging to Better Identify and Characterize High-Risk Dural Arteriovenous Fistulas

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14. ABSTRACT

To overcome the challenges with MRI-based technique to diagnose dural arteriovenous fistulas DAVFs, which is the most dangerous vascular malformation affecting the brain and causes intracranial hemorrhage and mortality, our proposal is aimed to stratify risk of DAVF based on cortical venous drainage using advanced techniques including 7T MRI with ferumoxytol contrast agent and 3T MRI using gadolinium contrast agent. The proposed hypothesis is 7T MRI will be able to accurately identify DAVFs at high risk for causing hemorrhage compared to the "gold standard" diagnostic cerebral angiogram, and that 3T MRI using gadolinium contrast will provide comparable to 7T MRI primarily by leveraging acquisition of secondary hemodynamic characteristics of DAVFs. The study proposes to validate this hypothesis in 40 adult subjects. In this quarterly report, we present our progress with respect to the approved Statement of Work.

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1. INTRODUCTION:

In the approved SOW, we proposed that (1) the improved spatial resolution of 7T MRI combined with the alternative contrast agent ferumoxytol will enable accurate direct visualization of cortical venous drainage (CVD) demonstrated on diagnostic cerebral angiography in patients with dural arteriovenous fistulas (DAVFs), and (2) 3T MRI using gadolinium contrast will provide a similar degree of diagnostic accuracy (relative to 7T MRI) to predict CVD by leveraging acquisition of secondary hemodynamic characteristics. The project's specific aims are (1) to develop advanced 7T MRI techniques to identify DAVF at a high risk for hemorrhage as confirmed by digital subtraction angiography (DSA), and (2) to develop 3T MRI to reliably predict CVD confirmed with DSA.

2. KEYWORDS:

Dural Fistula
Cortical vein
Dural venous sinus
MRI
4D Flow

ICOSA6
3D printing
Hemodynamics
Turbulent kinetic energy

3. **ACCOMPLISHMENTS:**
   We report no significant changes in the project or its direction.

What were the major goals of the project?

Specific Aim 1: Develop advanced 7T MRI techniques to improve dural arteriovenous fistula (DAVF) diagnosis and identify DAVF at a high risk for hemorrhage as confirmed by the gold standard digital subtraction angiography (DSA)	**Timeline**	**In progress**	**Completed**
Major Task 1 Develop 3D printed in vitro models of DAVF that will be used to optimize MRI techniques in Aims 1 and 2	Months		
Subtask 1: Develop and test in vitro flow models	1 - 3		X
Subtask 2: Develop additional models as needed throughout the time period to investigate unanticipated in vivo findings.	As needed: 4 - 48	X	
Milestone #1: Submit manuscript describing in vitro flow models of DAVF	4 - 48	X	
Major Task 2 Optimize 7T and 3T acquisitions using in vitro models			
Subtask 1: Optimize imaging acquisition techniques using first in vitro models. Imaging techniques include phase contrast, pseudocontinuous arterial spin labelling, time of flight MRA, and 4D flow (3D velocity encoding across time). Compare hemodynamic variables obtained from MRI acquisitions with direct measurements and setting in the models. Perform repeated test measurements for a total of 27 acquisitions. Variables measured: (i) degree of outflow stenosis, (ii) flow velocity, (iii) venous pressure at the site of the fistula, (iv) venous pressures throughout the system, (v) volumetric flow rate of DAVF contributions, (vi) turbulent kinetic energy, (vii) cortical vein flow direction, and (viii) cortical vein pulsatility.	1 - 6		X
Milestone #2: Submit manuscript describing MRI imaging of in vitro DAVF models	6	X	
Major Task 3 Conduct initial feasibility studies to visualize large DAVF hemodynamics			
Subtask 1: Submit documents for local IRB review	1 - 3		X
Subtask 2: Submit IRB approval and necessary documents for HRPO review	3 - 6		X

Milestone #3: HRPO approval received			X
Subtask 3: Image first 3 subjects with large DAVF and review data for quality and consistency in group review sessions	6 - 9		X
Subtask 4: Address any issues discovered in Subtask 3 using computational fluid dynamics (CFD) and/or dye visualization experiments and optimize techniques Sites 1 (Dr. Amans's lab, including Mr. Valluru): Dye visualization experiments and data review Site 2 (Dr. Saloner's lab, including Dr. Kao): CFD experiments and data review	6 - 10	X X	 X
Subtask 5 – compare data obtained at 7T and 3T with DSA data Site 1 (Dr. Amans's lab, including Dr. Jiang): obtain the DSA data, perform direct comparisons and statistical analysis. Site 2 (Dr. Saloner's lab): data review	6 - 12	 X X	X
Milestone #4: submit manuscript describing proof of concept techniques in vivo	12	X	
Major Task 4 Ongoing enrollment of subjects			
Subtask 1 – scan additional 37 subjects and review data for quality and consistency in group session	12-48	X	
Subtask 2 – compare data obtained at 7T with DSA and catheter measurements	12-48	X	

What was accomplished under these goals?

Specific Aim 1 - Develop advanced 7T MRI techniques to identify DAVF at a high risk for hemorrhage.

Major Task 1: Develop 3D printed in vitro models of DAVF that will be used to optimize MRI techniques in Aims 1 and 2.

Subtask 1 (1 - 3 months): Develop and test in vitro flow models.

1) Specific objectives: To refine our 7T and 3T techniques for detection and to optimize our acceleration factors to shorten scan times, we proposed developing a series of 3D-printed flow models, each with an increasing level of complexity that simulate the complex hemodynamics within a DAVF (Fig 1). These in vitro models will serve as a reproducible test environment that allows for independent control of cerebral venous blood flow, degree of venous sinus stenosis causing resistance to typical antegrade venous outflow, arterial input function from the DAVF, as well as hydrostatic pressure in the cortical veins.

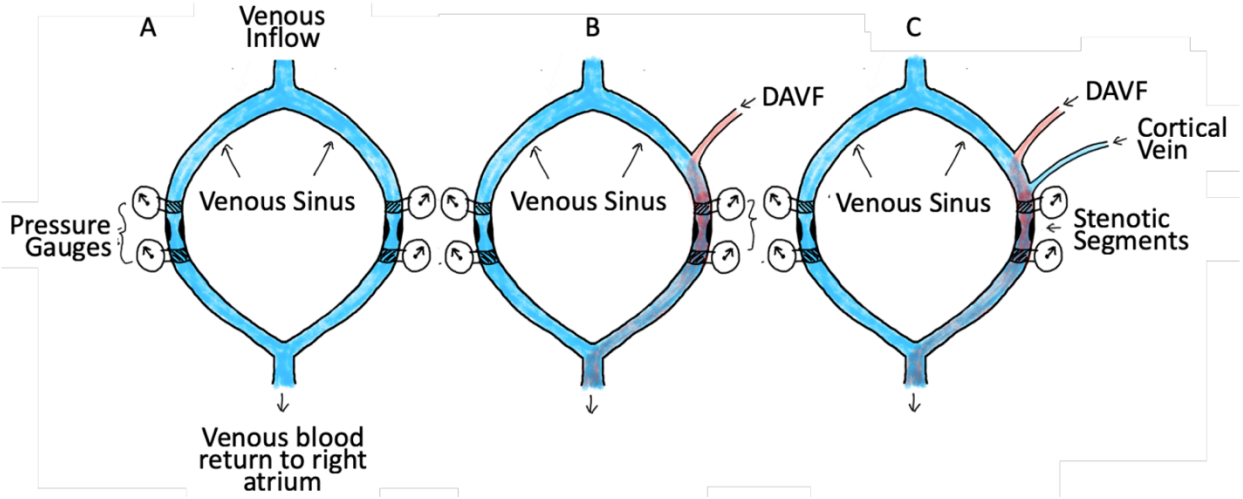


Figure 1. Schematics of 3D printed models of the dural venous sinuses with varying degrees of stenoses (labeled stenotic segments) (A), a simplified DAVF (B), and a DAVF with the potential for cortical venous drainage (C).

2) Major activities:

- We have designed an in vitro prototype that models the parallel flow circuit of the dural venous sinuses and allow for developing stenoses in each of the outflow limbs individually with preset degrees of stenosis. Both sides are designed to accommodate the stenosis segments to facilitate testing unilateral and bilateral stenosis conditions. With the help of flow regulating valves, this prototype (Fig 2) will allow us to test three distinct stenotic conditions in the lateral sinuses with stenosis segments measuring 8 mm diameter, 4 mm diameter, and 2.4 mm diameter (approximating no stenosis - 0%, moderate stenosis - 50%, and high-grade stenosis - 70%). The combination of 3 predetermined lumens in each limb yields 9 experimental geometries that will improve our ability to quantify disease in the dural venous sinuses.

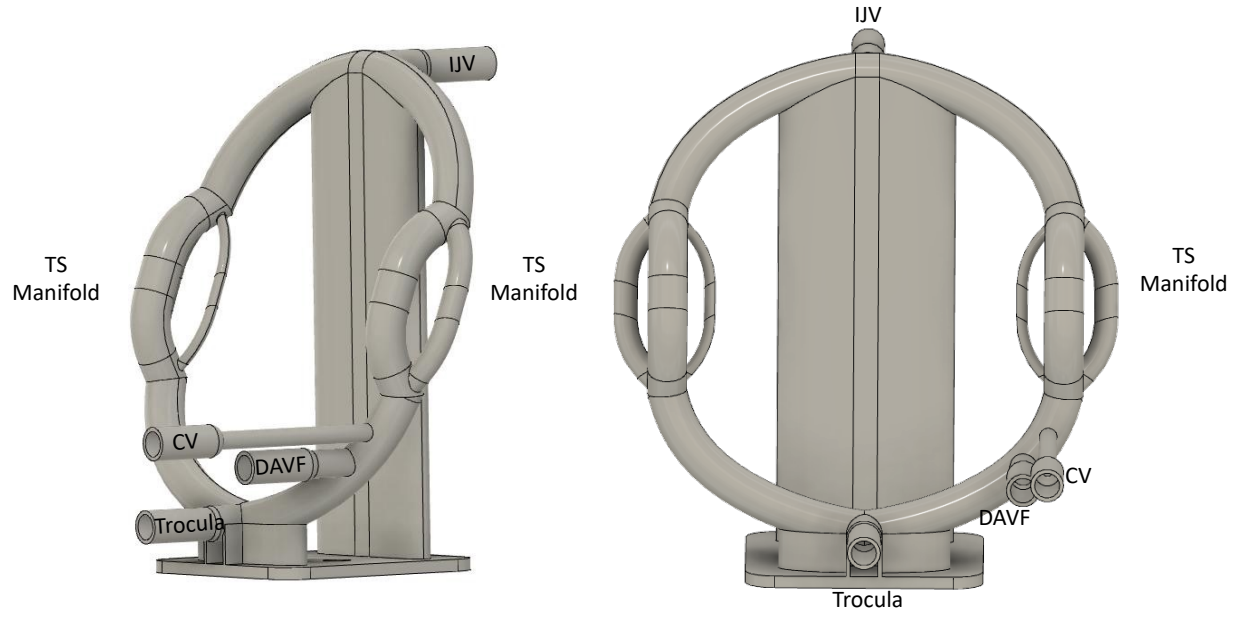


Figure 2. Parallel flow circuit of the dural venous sinuses designed using AutoDesk Fusion 360. The model shows parallel limbs to mimic predetermined degrees of transverse sinus (TS) stenoses: 8 mm (0% - no stenosis), 4 mm (50% - moderate stenosis) and 2.4 mm (70% - severe stenosis). By employing flow regulating valves across the individual stenotic segments as well as the dural arterial venous fistula (DAVF) and cortical vein (CV), this design will facilitate performing multiple test conditions (normal, low risk DAVF with no CV drainage, and high risk DAVF with CV drainage). This model incorporates a 70-degree angle for TS mimicking in vivo condition with patient lying in supine position (representing the patient lying on the patient table for MRI or neurointervention in angiosuite).

- We initially proposed 3D printing this prototype with Agilus 30A, a flexible rubber-like material which we previously used for our venous models in the lab. However, the closed-loop design of this model posed a challenge to remove supports printed with Agilus 30 and thereby 3D print it successfully. We addressed this problem by designing and building an alternative prototype with off-the-shelf tubing materials and components. We connected this prototype into a flow circuit and performed flow visualization experiments to test its feasibility (Fig. 3).
- This tubing prototype allowed us to test our design that closely simulates the pathophysiology of DAVF under varying degrees of transverse sinus stenosis (Fig. 4). We will continue performing additional dye visualization experiments with this prototype to determine the optimal flow conditions for DAVF and cortical vein. We will then proceed to the next subtask of scanning the prototype with 3T and 7T MRI using 4D Flow sequences to evaluate hemodynamics of the model.

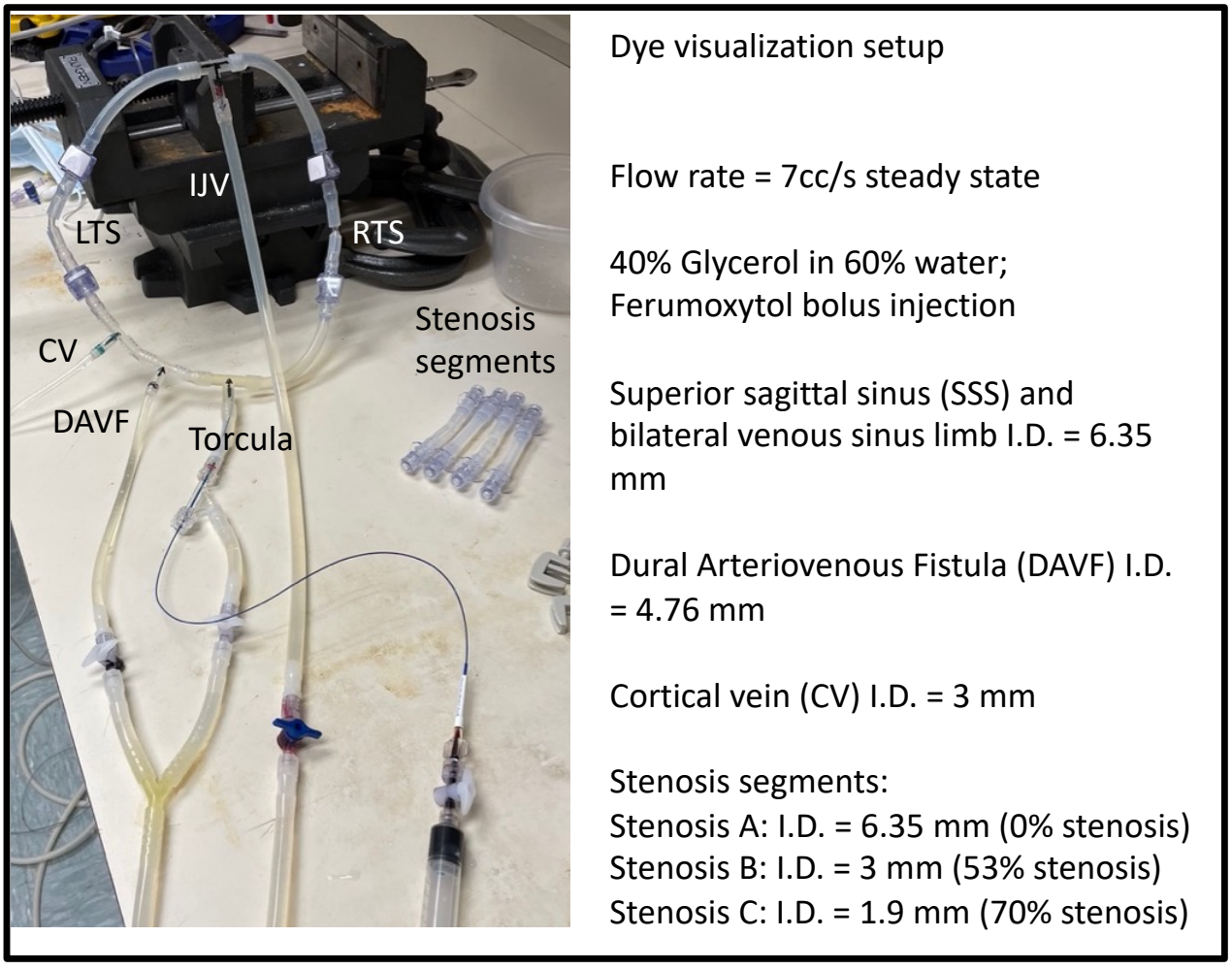


Figure 3. DAVF tubing prototype built in lieu of 3D printed model. The transparent tubing allows excellent visualization of hemodynamics within the model. The model facilitates exchanging left and right transverse sinus (LTS and RTS respectively) sections with varying degrees of stenosis segments (0%, 50% and 70% stenosis). Conditions and parameters for dye visualization experiment setup are shown here. The blood analog solution (mixture of 40% glycerol and 60% water by volume) flows from SSS into Torcula at the characteristic venous flow rate of 7 cc/s where it splits to pass through left and right venous sinus limbs. CV and DAVF sections are designed to drain into the left limb. CV is connected to pressurized saline bag to determine the optimal pressure and flow rate required to mimic in vivo conditions. The blood analog solution will drain out of the model through the internal jugular vein (IJV), back to the reservoir connected to a programmable rotary pump (not shown in the figure).

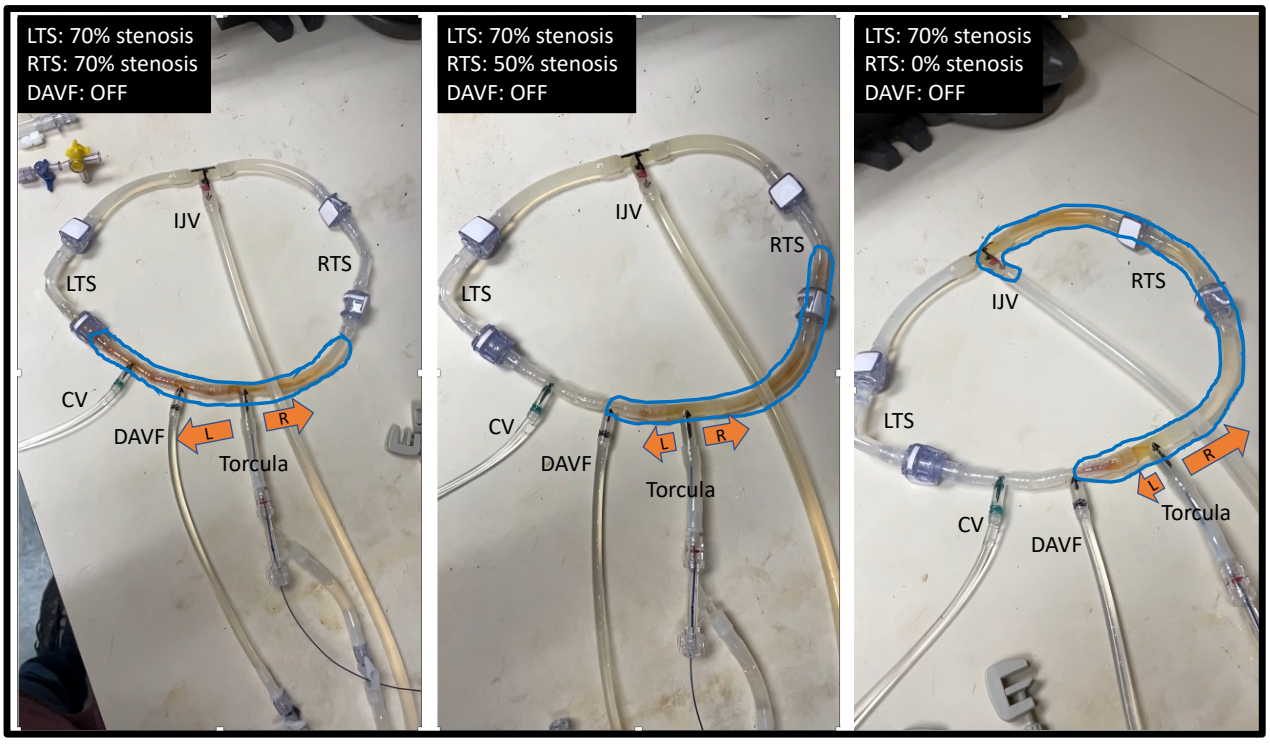


Figure 4. Dye visualization experiment. We are currently performing flow optimization experiments with our tubing prototype. The figure illustrates flow through the model when the degree of right transverse sinus (RTS) stenosis is varied between 70% (left frame), 50% (middle frame) and 0% (right frame) stenosis while the left transverse sinus (LTS) stenosis was kept constant at 70%. A bolus of Ferumoxytol was injected into the torcula using a catheter while the flow through DAVF was turned OFF. The flow of Ferumoxytol could be easily visualized (highlighted in blue) in the transparent model. When both sides were stenosed equally (left frame), the flow rate on either side seemed to be similar as indicated by the length of orange arrows. When the RTS stenosis was reduced to 50% (middle frame), the flow rate was marginally higher on the less stenotic right side. And when the RTS stenosis was eliminated (right frame), the flow rate of the dye was significantly faster on the right side as indicated by the length of the orange arrow, as well as the extent of the blue highlighted region encompassing Ferumoxytol. The CV was connected to a saline bag and was pressurized to 300 mmHg. This pressure turned out to be quite high as we didn't notice any back flow into the CV even under bilateral high-risk stenosis (70% LTS and 70% RTS) with DAVF turned ON (not shown in the picture).

3) Key outcomes: Development and testing of in vitro flow models is completed.
4) Goals not met: Nothing to report.

Subtask 2 (4 - 48 months): Develop additional models as needed throughout the time period to investigate unanticipated in vivo findings.

1) Specific objectives: This activity is proposed to be performed as needed in months 4 - 48.
2) Major activities:
   - Based on the feedback from the experiments performed in the Major Task 1 - Subtask 1, we incorporated additional elements into our prototype design (Figs. 5 and 6). We tested this modified prototype by conducting a carefully designed manometry experiment to study the impact of varying degrees of transverse sinus stenoses on the flow within the cortical vein under the absence/presence of DAVF. The results of this study are presented in Fig. 7.
   - We redesigned our flow circuit by adding a human-sized silicone model of the venous system (United Biologics, Irvine, CA) that comprises of the femoral veins, venacava, right heart, pulmonary artery, and bilateral subclavian veins. We also incorporated a flow pump (Flowtek 125, United Biologics, Irvine, CA) capable of circulating the flow at

any desired pulsatility (0 – 200 beats per minute) and flow rate (0.1 - 300 cc/s) settings. This design further allowed us to integrate our cerebral venous vasculature models and mimic the flow physiology between the head and the body. We prototyped our cerebral venous sinus model (Fig. 5) such that it represents the Superior Sagittal Sinus and bilateral transverse sinuses draining into the subclavian veins of the body model through the respective internal jugular veins. We designed the venous sinus model in a modular fashion with individual segments representing transverse sinuses, sigmoid sinuses and internal jugular veins with inlet ports that are customized to mimic the cortical vein and DAVF.

- We calibrated the pump and the system to obtain flow rates and pressures representative of the physiological state of the body. Sample venous pressures from this setup are shown in the Fig.7.

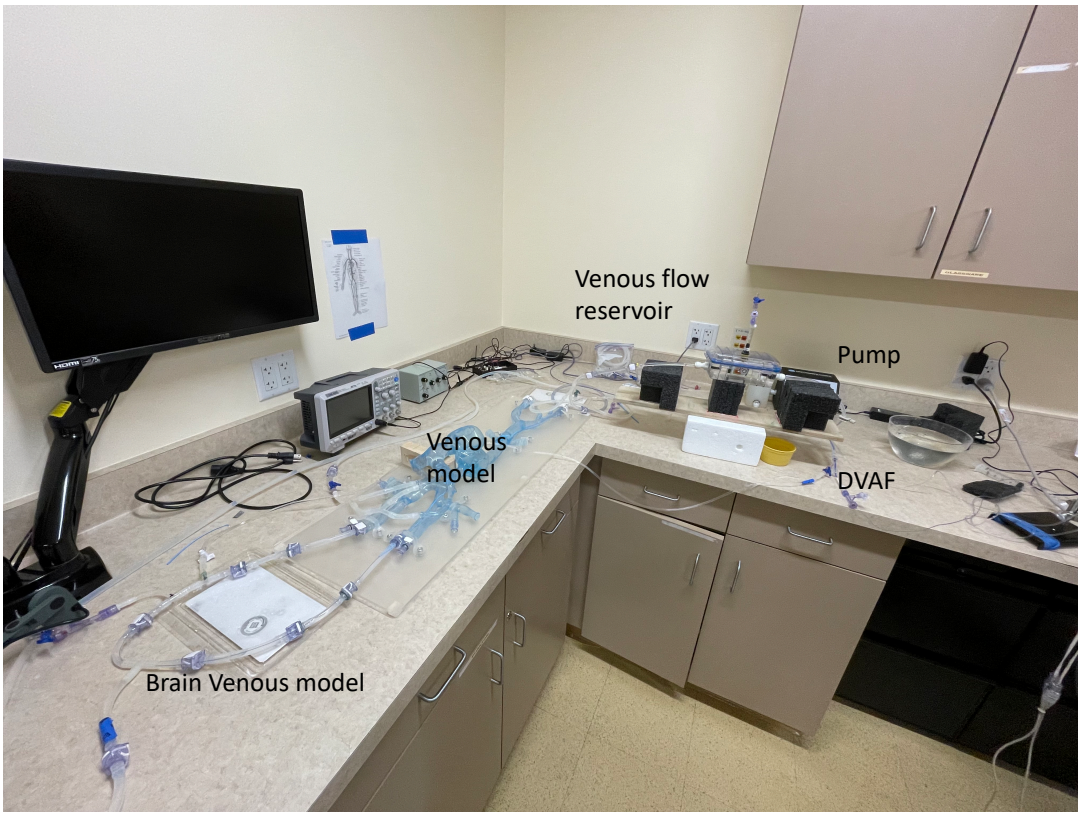


Figure 5. DAVF prototype built to simulate physiological conditions of the body. Like previous model the transparent tubing allows visualization of hemodynamics within the model. The model facilitates exchanging left and right transverse sinus (LTS and RTS respectively) sections with varying degrees of stenosis segments (0%, 50% and 70% stenosis) as well as the ability to test various configurations of the cortical vein and DAVF. Additionally, this model allows us to get the accurate pressures and flowrates of the venous system.

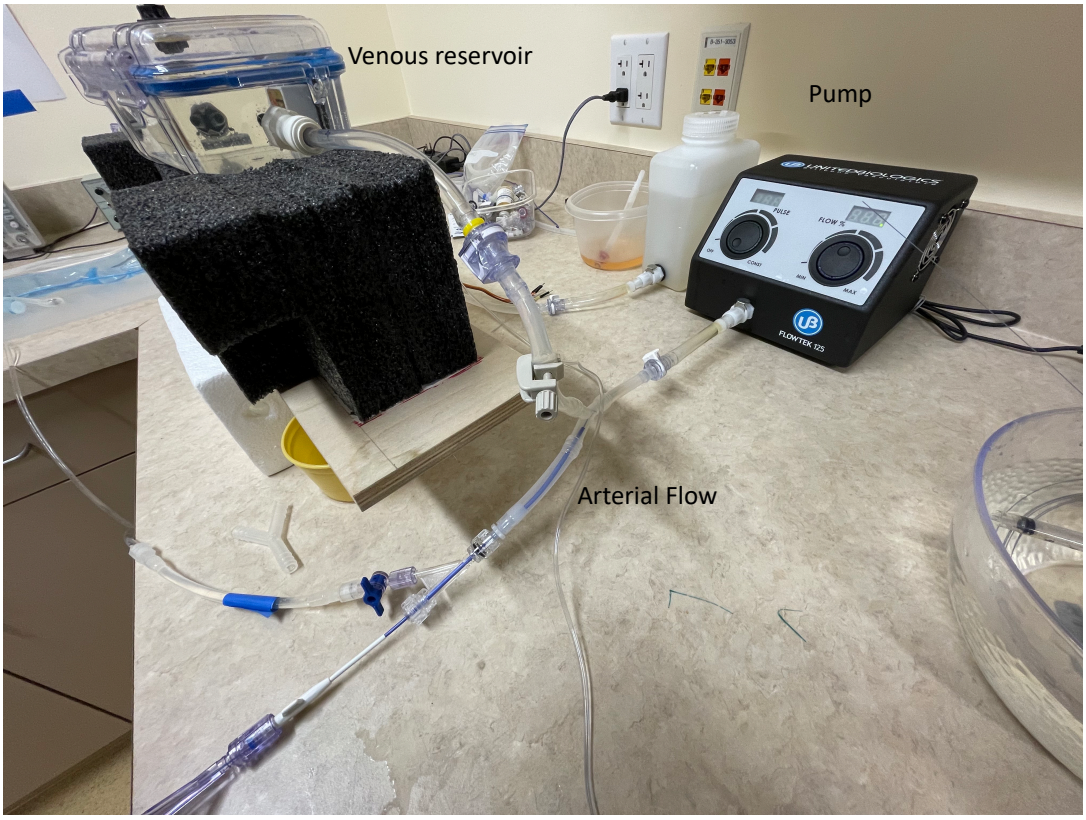
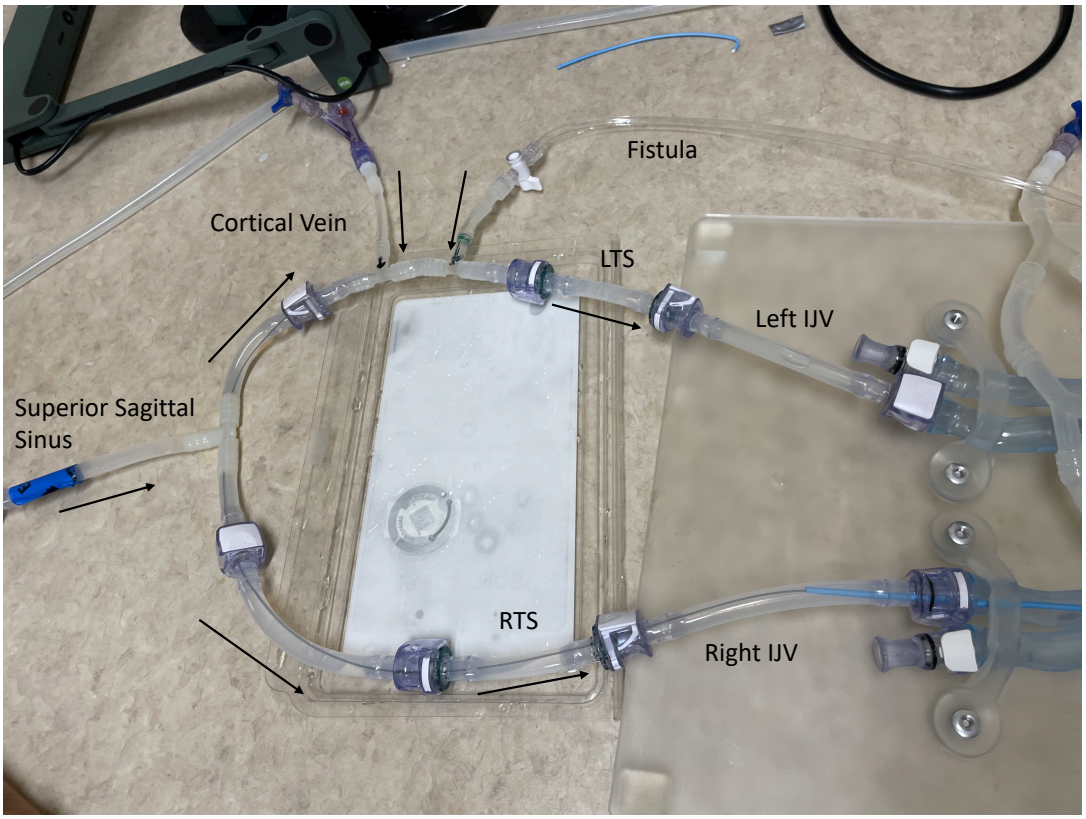


Figure 6: The blood analog solution (mixture of 40% glycerol and 60% water by volume) flows from pump into the arterial flow which bifurcates into vessel simulating the DAVF and another main vessel supplying the venous reservoir simulating the arterial and capillary system of the body. This reservoir functions to lower the pressures to those of the venous system in the body and supply the body and the cerebral venous systems of the model.



Venous flow = 7cc/sec
Venous mean pressures = 10-15mmhg
Cortical Vein Flow rate = 0.7cc/sec
Cortical Vein pressure = 10-16mmhg
DVAF pressure = 120/40 mmhg

Figure 7: One of the branches from the venous reservoir supplies the Superior Sagittal Sinus (SSS). The SSS bifurcates into the left and right cerebral venous systems. Both the sides have interchangeable components that allow the fistula and

cortical vein (CV) to be swapped and tested at various configurations. CV flow is supplied by a pressurized saline bag to mimic the pressure and flow rate in vivo. The DAVF (fistula) is supplied through the arterial branch from the pump directly.

3) Key outcomes: The modified prototype proved to be a better approximation of the in vivo DAVF condition. This version of the prototype facilitated the use of patient characteristic flow rates within the venous outflow tract and the cortical vein. The pump used to circulate flow within the DAVF segment could deliver a variable flowrate and pressure. In the next iteration, we will test this model with various degrees of stenosis and a variable flow rate to quantitatively determine the effect of the DAVF in addition to its presence on the cortical vein.
4) Goals not met: Nothing to report.

Milestone #1: Submit manuscript describing in vitro flow models of DAVF.

The manometry data from our in vitro models is encouraging. We will next perform dye visualization studies to validate our manometry observations. This will provide us ample data to submit a manuscript as proposed. For this time period, this is reported as a goal in progress.

Major Task 2: Optimize 7T and 3T acquisitions using in vitro models.

Subtask 1 (1 - 6 months): Optimize imaging acquisition techniques using first in vitro models. Imaging techniques include phase contrast, pseudo-continuous arterial spin labelling, time of flight MRA, and 4D flow (3D velocity encoding across time).

1) Specific objectives: Compare hemodynamic variables obtained from MRI acquisitions with direct measurements and setting in the models. Perform repeated test measurements for a total of 27 acquisitions. Variables measured: (i) degree of outflow stenosis, (ii) flow velocity, (iii) venous pressure at the site of the fistula, (iv) venous pressures throughout the system, (v) volumetric flow rate of DAVF contributions, (vi) turbulent kinetic energy, (vii) cortical vein flow direction, and (viii) cortical vein pulsatility.
2) Major activities: We are simultaneously executing Major Task 1 - Subtask 2 and Major Task 2 – Subtask 1. We have our modified version of the prototype ready for scanning. We are scheduled this quarter to acquire 7T and 3T MRI data using this model to tune VENC, spatial resolution, and acceleration factors for determining the blood flow in the native dural venous sinuses. We will also perform testing using arterial input that is 50% above and below the derived in vivo values from step 3 once we upgrade our DAVF pump. We will then proceed to obtain pressure maps in this model at 7T and 3T to compare with catheter-based manometry experiments.
3) Key outcomes: Nothing to report.
4) Goals not met: We report this goal as partially met. We expect to scan the model using 3T and 7T MRI this quarter.

Milestone #2: Submit manuscript describing MRI imaging of in vitro DAVF models

Once all the goals in Major Tasks 1 and 2 are met, we will prepare and submit the manuscript as proposed. For this time period, this is reported as a goal in progress.

Major Task 3: Conduct initial feasibility studies to visualize large DAVF hemodynamics

Subtask 1 (1 - 3 months): Submit documents for local IRB review

1) Specific objectives: Submit documents to local IRB review.
2) Major activities: We worked with our institutional IRB to pursue this activity.
3) Key outcomes: We received the approval from local IRB.

4) Goals not met: Nothing to report.

Subtask 2 (3 - 6 months): Submit IRB approval and necessary documents for HRPO review.

1) Specific objectives: Submit IRB approval and necessary documents for HRPO review.
2) Major activities: We worked with our local IRB and HRPO to submit the IRB approval and all the required documents for HRPO review.
3) Key outcomes: We received the approval from HRPO.
4) Goals not met: Nothing to report.

Milestone #3: HRPO approval received.
We achieved this milestone. For this time period, this is reported as completed.

Subtask 3 (6 – 9 months): Image first 3 subjects with large DAVF and review data for quality and consistency in group review sessions.

1) Specific objectives: Recruit and image first 3 subjects with large DAVF using 3T/Gadolinium and 7T/Ferumoxytol. Schedule a group review of the data from the first three subjects. Process and analyze 4DFlow and ICOSA6 datasets obtained at 3T.
2) Major activities: We completed imaging of the first three subjects and are in the process of scheduling group review sessions to review the data (n=3).
3) Key outcomes: We completed imaging our first three subjects with 3T MRI.
4) Goals not met: None of our first three subjects were imaged using 7T MRI with Ferumoxytol.

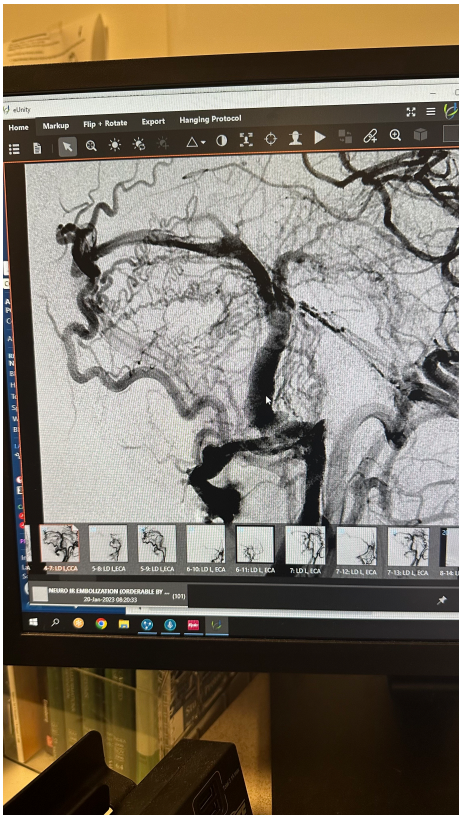
Subtask 4 (6 – 10 months): Address any issues discovered in Subtask 3 using computational fluid dynamics (CFD) and/or dye visualization experiments and optimize techniques.

1) Specific objectives: Review the data from the benchtop models and the first three subjects to determine if there's a need for any optimization using CFD and dye visualization experiments.
2) Major activities: Determine the need for optimization of the CFD and/or dye visualization experiments. In Major Task 1 Subtask 2, the mini peristaltic pump used to circulate flow within the DAVF segment was only capable of delivering a fixed flow rate of 1.5 cc/s. To better approximate the flow rate of the DAVF segment, we purchased a new pump (United Biologics Flowtek 125) that's capable of providing a variable pulsatile flow rate to quantitatively determine the effect of the DAVF in addition to its presence on the cortical vein.
3) Key outcomes: Nothing to report.
4) Goals not met: This goal is reported as complete.

Subtask 5 (6 – 12 months): Compare data obtained at 7T and 3T with DSA data.

1) Specific objectives: Obtain anonymized DSA data for the first three patients acquired at the time of treatment. Compare the DAVF segment(s) identified on DSA images with corresponding MRI data obtained at 3T and 7T.
2) Major activities: Identified DAVF segments and Cortical vein on DSA and MRI images in low and high-risk fistula patients. Analyze hemodynamics of the DAVF segment from 4D flow and ICOSA6 obtained at 3T vs. DSA datasets.

A



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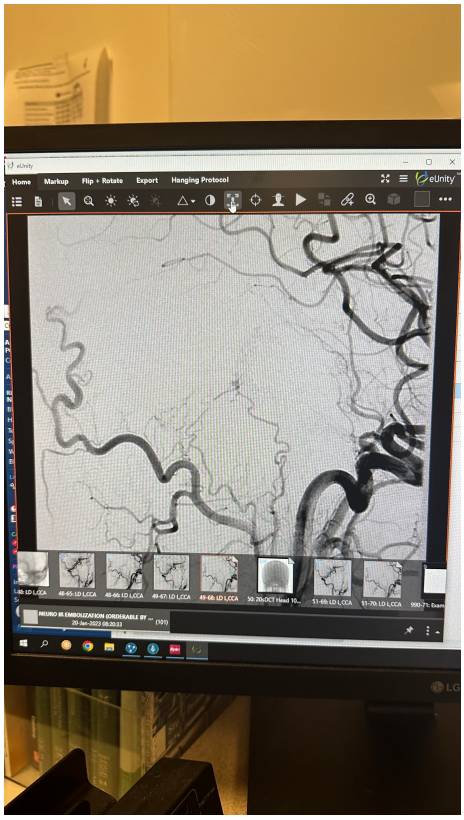
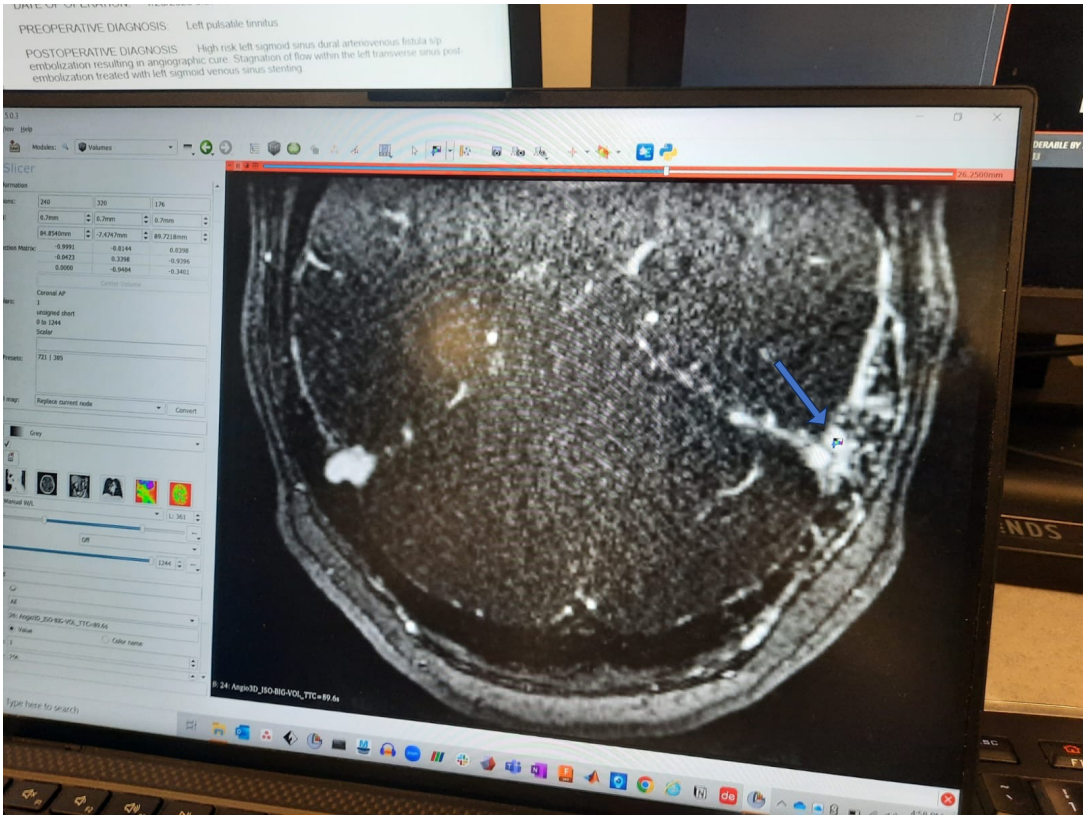


DSA Images – Pre-op and post-op. Patient with High risk DVAF

A. DSA image of a patient with high-risk fistula as visible using a contrast agent pre-op displaying backflow.
B. Post-op images of the same patient with high-risk fistula, displaying no backflow

Figure 8: DSA images of the patient with high-risk DAVF identifying segments of the fistulae and cortical vein.



MRI of the Same patient with the DVAF identified.

Figure 9: MRI Scan of the same patient identifying the high-risk DVAF segment.

3) Key outcomes: Identify the presence/absence of CVD on 3T and 7T MRI data corresponding to the DSA images.
4) Goals not met: This goal is reported as completed. We did not acquire 7T MRI data due to the reasons explained in Subtask 3. Therefore, we compared the 3T MRI dataset against DSA dataset for the first three subjects.

Major Task 4: Ongoing enrollment of subjects

Subtask 1 (12 – 48 months): Scan additional 37 subjects and review data for quality and consistency in group session

1) Specific objectives: Keep recruiting the subjects and review the data in periodic group sessions.
2) Major activities: We are closely tracking the number of patients scheduled for DAVF treatment at Site-1. We expect to have majority of them consent to the study and be on track with our projected recruitment volume by the end of the next two quarters (Y3-Q2). Analyze hemodynamics of the DAVF segment from 4D flow and ICOSA6 obtained at 3T vs. DSA datasets.
3) Key outcomes: Identify the presence/absence of CVD on MRI data corresponding to the DSA images for each subject.
4) Goals not met: This goal is reported as in progress. We've had a slower recruitment of subjects than anticipated and couldn't recruit any during the last quarter (Y2-Q3) of 2022 due to staffing issues at Site-2. We are addressing the staffing concerns with our contingency plan laid out in the previous quarterly report. Consent for contrast administration needs to be obtained by a physician. We are collaborating with the neuroradiologists at Site-2 to receive their assistance with consenting patients until additional radiologists are hired (Abdominal and Body Radiologists at Site-2 who helped us before with consenting have since left in Y2-Q1. The hiring status hasn't changed since our last update). To avoid overburdening the nurses at Site-2 who are primarily tasked with patient care, we were in the process of establishing nursing support to infuse Ferumoxytol through a paid service - UCSF Clinical Research Services (CRS). This ensures we have nurses specifically scheduled for contrast administration and patient monitoring when we need them rather than relying on the patient care nursing staff. We are pleased to report that the on-demand nursing support is mostly established now.

Subtask 2 (12 – 48 months): Compare data obtained at 7T with DSA and catheter measurements.

1) Specific objectives: We needed to first perform a Ferumoxytol dose-ranging study to determine the amount of USPIO that maximizes T1-enhancement without T2* loss before we can image our subjects at 7T. As such, we didn't acquire data at 7T yet.
2) Major activities: We did two dose-ranging studies on both the phantom and in vivo subjects on the 7T scanner and are analyzing this data currently to determine the optimal dose of Ferumoxytol. Once we determine the optimal dose of Ferumoxytol required to image the cerebrovasculature, we will proceed with imaging the DAVF subjects at both 3T and 7T MRI. To help with acquisitions, experiments, and analysis of the data acquired with 3T and 7T, we recruited a post-doctoral researcher with a clinical background (Haider Ali, MBBS) who also has MRI research experience. We are pleased to report that Dr. Ali has joined our team and started working with the PI on this project from August 1st, 2023. He will extend his help to acquire the imaging data from the subsequent studies and analyze the hemodynamic descriptors extracted from these data sets. Both Dr. Saloner and Dr. Amans will directly oversee the work of this scientist.
3) Key outcomes: Nothing to report.

Goals not met: This goal is reported as in progress.

STATUS:

			Enter information regarding number of subjects				
HRPO Protocol Number	**Protocol PI Name**	**Organization (Site)**	**# Target**	**# Enrolled**	**# Completed**	**# Screened**	**# Recruited**
HRPO Log Number E02403. 1a	Matthew Amans, MD	University of California, San Francisco	18 of 40	7 of 18	6 of 18	6 of 18	7 of 18

Demographics

DAVF Enrollment Report										
Racial categories	**Not Hispanic or Latino**			**Hispanic or Latino**			**Unknown / Not Reported Ethnicity**			**Total**
	Female	**Male**	**Unknown / Not Reported**	**Female**	**Male**	**Unknown / Not Reported**	**Female**	**Male**	**Unknown / Not Reported**	
American Indian /Alaska Native	0	0	0	0	0	0	0	0	0	0
Asian	5	1	0	0	0	0	0	0	0	6
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	0
Black or African American	0	0	0	0	0	0	0	0	0	0
White	1	0	0	0	0	0	0	0	0	1
More than One Race	0	0	0	0	0	0	0	0	0	0
Unknown or Not Reported	0	0	0	0	0	0	0	0	0	0
Total	6	1	0	0	0	0	0	0	0	7

Summary

We are on track with the stated goals and subtasks as listed in this report. We learnt a great deal from the experiments with our initial prototype in Major Task 1 - Subtask 1, and incorporated design changes into our next iteration as reported in Major Task 1 – Subtask 2. We will image this modified prototype as described in Major Task 2 – Subtask 1. We have completed Major Task 3 – Subtasks 1 through 4. We couldn't acquire 7T datasets as initially planned under Major Task 3 – Subtask 4 as we were waiting for the results of our dose-ranging study. For Major Task 4 - Subtask 1, we recruited 7 of

18 subjects (4 subjects in the current quarter) and are still delayed with our subject enrollment as per the approved SOW. We are ramping up our recruitment efforts with the plans laid out in Subtask 1 and expect to be on track with the projected volume of subjects within the next two quarters (Y3-Q2). We expect to be on track with the tasks laid out in Major Task 4 – Subtask 2 by the end of the next quarter, Y3-Q1.

Conclusion
This is our eighth quarterly report (Y2 – Q4), and it reflects our progress with respect to the approved SOW.

What opportunities for training and professional development has the project provided?
Nothing to Report

How were the results disseminated to communities of interest?
Nothing to Report

What do you plan to do during the next reporting period to accomplish the goals?
We are back on track with respect to the recruiting activities as mentioned in the Major Task 4 and will continue recruiting subjects at the current pace to perform studies as planned in Subtasks 1 - 2 during the next reporting period (Y3-Q1).

4. **IMPACT:** D*escribe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:*

What was the impact on the development of the principal discipline(s) of the project?
Nothing to Report

What was the impact on other disciplines?
Nothing to Report

What was the impact on technology transfer?
Nothing to Report

What was the impact on society beyond science and technology?
Nothing to Report

5. **CHANGES/PROBLEMS:**

Changes in approach and reasons for change.
Nothing to Report

Actual or anticipated problems or delays and actions or plans to resolve them.
Nothing to Report

Changes that had a significant impact on expenditures
Nothing to Report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Nothing to Report

Significant changes in use or care of human subjects

Nothing to Report

Significant changes in use or care of vertebrate animals
Nothing to Report

Significant changes in use of biohazards and/or select agents
Nothing to Report

6. PRODUCTS: *List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."*

Publications, conference papers, and presentations:
Nothing to Report

Journal publications.
Nothing to Report

Books or other non-periodical, one-time publications.
Nothing to Report

Other publications, conference papers and presentations.
Nothing to Report

Website(s) or other Internet site(s).
Nothing to Report

Technologies or technique.
Nothing to Report

Inventions, patent applications, and/or licenses.
Nothing to Report

Other Products.
As a part of the Major Task 1, this project resulted in generation of 3D printed vitro flow models, and acquisition of a pulsatile circulating flow pump (United Biologics Flowtek 125).

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?
For the dates: 04/01/2023 – 06/30/2023, please see the efforts of individuals in the table below.

Name	Project Role	Researcher Identifier	% Effort	Contribution to Project
Haider Ali, MBBS	Postdoctoral Scholar		66.67%	Dr. Haider continues to perform updates to the prototypes, vessel segmentation and prints flow models as needed. As well

				assist in scans and experiments.
Adelyn Tu-Chan, DO	Physician		5.00	Dr. Tu-Chan continues to oversee the subject recruitment.
Fei Jiang, PhD	Co-I		2.00	Dr. Jiang has assisted the PI in the several complex statistical analyses that will be used to best identify if MRI can accurately detect high risk features in DAVF.
Dimitrios Mitsouras, PhD	Associate Professor		17.10	Dr. Mitsouras helps with image acquisition, reconstruction and processing activities at Site-2.
David Saloner, PhD	PI – Site 2		12.70	Dr. Saloner continues to oversee the imaging and analysis activities at Site-2.
Matthew Amans, MD	PI – Site 1		20.00	Dr. Amans continues to oversee the activities at Site-1 including subject recruitment.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
Nothing to Report

What other organizations were involved as partners?
Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS

Nothing to Report

9. APPENDICES:

Nothing to Report