IMPROVING THE NORWOOD PROCEDURE VERIFICATION AND VALIDATION

March 1, 2019

Akshay Thontakudi, Varun Lahoti, Gerardo Molina

Group 17

Contents

INTRODUCTION

Accounting for nearly 23% of neonatal deaths while only present in 0.016% of live births, Hypoplastic Left Heart Syndrome (HLHS) has a disproportionately high death rate.[1] Infants born with HLHS have an underdeveloped left ventricle, preventing blood from reaching all parts of the body. To rectify this condition, surgeons perform the Norwood Procedure to re-purpose the right ventricle to pump blood to the body. During the procedure, surgeons have a small view of the operating field and have only a small window of time to perform the surgery. Thus, the group has engineered a device that would reduce the obstruction of operating field and expedite the surgery.

The verification and validation report overviews any changes to the core project, presents verification and validation plans for the device, describes FDA approval processes, and shows proof-of-concept results.

PROJECT CHANGES

The group made no changes to the need statement, project scope, team responsibilities, or budgetary requests. However, the group changed the name of specification called "occlusion" to "obstruction" to clarify its meaning, as per the recommendation of Professor Klaesner. In addition, a specification for finger cut-out diameter of 30 mm was added to accommodate fingers of all sizes. Furthermore, the group updated its design schedule as shown in Appendix B, allowing for more time to test with 3D prints and pushing back the date at which the group settles on a final design. This is because it is less feasible to obtain a clamp in medical-grade titanium, so the group will focus more on testing the 3D printed versions.

VERIFICATION PLAN

Overview

The verification plan lists each design specification and provides a plan to test it against its corresponding metrics, as shown in Appendix A, outside of a surgical environment. The validation plan covers those specifications that cannot be tested outside of live surgery.

Physiological Constraints

The physiological constraints were made to match the status-quo clamp dimensions. That is, the group would verify that the device fits into an incision of 2 cm^2 clamp an artery with diameter of at most 12 mm. This would be done 3D-printing a complete assembly of the device and seeing if it fits into the incision and can clamp an artery.

Elimination of Blood Flow

The pressure that the device needs to exert is between 300-450 kPa. In addition, this also indicates the amount of pressure that blood flowing through the artery would produce against the walls that are clamped. Therefore two specification meters needed to be tested. First, the force must be translated fully and only to clamping ridges. This would be verified through the stress test analysis heat maps. The second metric is that the ridges can withstand this force. The frictional coefficient for the interaction between every ridge is 0.36.[2] This means that slippage cannot occur at this level of force.

Debris Removal

The actual pump used for debris removal will not be changed. Therefore, the removal rate caused by standard suction power meets the given specification. The tea basket design however, diminishes the removal rate slightly because tissue can occasionally be sucked in and clog the slotted holes that are part of the design. Therefore, a test measuring the average number of slots blocked by suction will be conducted to determine debris removal rate.

Debris removal will be tested in the validations step as well.

Arterial Integrity

This specification is out of the scope of verification. It will instead be proven in the validation plan through the process described.

Weight

To find the device weight, the group would use the Equation 1, where W is device weight, V_{3D} is the volume of the 3D print, and ρ_{Ti} is the density of medical grade titanium.

$$W = V_{3D} \cdot \rho_{Ti} \tag{1}$$

To find the volume, the group would 3D-print the assembled, properly-scaled device. In a liter beaker filled to 750 mL, the group would submerge the device and calculate the difference in volume in milliliters to get the device volume. The device volume of the 3D print and machined titanium are assumed identical because there are no hollow pieces in the 3D print.

Multiplying the 3D print volume times the titanium density, which is $4.54 \frac{g}{cm^3}$, would result in the device weight.[3] The group would verify the weight by comparing it to the ideal weight range shown in Appendix A.

Cost

Verifying cost would entail creating a combined computer-aided design (CAD) assembly of the device, indicating medical-grade titanium as the preferred material, and sending it to Gateway Laser Services (a client-recommended machine shop) and to St. Louis Makes to receive cost estimates. The estimates would be compared to ≤ $1000 metric from the design specifications.

Biocompatibility

Medical-grade titanium does not react with human tissue or fluids after prolonged and frequent contact.[4] The group has thus deemed it biocompatible.

Maneuverability

Testing maneuverability includes verification and validation.

In the verification step, the length, depth, and width of the device tip would be measured, and would be compared to the ensure it is ≤2.8 mm to ensure it meets the design specification for maneuverability as shown in Appendix A.

The validation step would entail garnering feedback when simulating the surgery. This is will be furthered explained the validation plan.

Installation Time

This specification is out of the scope of verification. It will instead be proven in the validation plan.

Comfort

The thickness of the handle will be measured to ensure it is $15-20$ mm in diameter. The cut-outs will also be measured ot ensure it is ≥ 30 mm as specified in Appendix A. In addition, the handle symmetry will be tested to ensure ambidextrous functionality.

Subjective comfort will be explained in the validation section.

Durability

The verification of durability is outside the scope of this project. However, the process outlined for testing durability is as follows. First, most of the degradation of the clamp would occur during the sterilization process. The group would follow the guidelines that the CDC outline for cleaning and sterilizing surgical equipment.[5] According to the client, this clamp will be used 25 times a year, and the specification is for the clamp to last 10 years. Therefore this process will be repeated 250 times to simulate clamp usage over the course of 10 years. In addition, between each sterilization cycle, the clamp tip will be placed in a sample of blood for 30 minutes to simulate the surgery conditions.

Obstruction

A pixel-by-pixel image comparison of the infant chest cavity will be done to measure obstruction. One image will have the currently used clamp and associated suction tubes, while the other image will have the proposed clamp solution in the chest cavity. The percentage of obstruction will be calculated according to Equation 2, where O is the obstruction fraction, C is the number of pixels the clamp takes up, and T is total number of pixels in the chest cavity.

$$O = \frac{C}{T} \tag{2}$$

The differences in this fraction will be used to assess the obstruction reduction the clamp provides.

FINAL VALIDATION PLAN

The validation plan entails Group 17's client Dr. Pirooz Eghtesady operating on two different infant pigs, one with the created device and the other with the clamp used in the status quo. Dr. Eghtesady will perform aspects of the Norwood Procedure on the anesthetized pigs that are relevant to device's testing. Both the existing clamp and the group's device will clamp the pigs' aortas for the duration of the surgery, simulating their use in the Norwood procedure. The aim of the validation is to test design specifications that could not be tested in verification and ensure that the device meets the project scope.

Elimination of Blood Flow

This will be done by clamping a test artery with the blood flow given in the specification of 450 kPa. On the open end of the test artery a graduated cylinder will be placed to catch any blood that passes through the clamp. This graduated cylinder will be accurate to the nearest tenth of a ml. If the amount of blood contained within the tube after the standard procedure time, 30 to 45 minutes maximum, is less than 0.1 mL, the clamp will be validated for elimination of blood flow. The 0.1 mL standard was the client-recommended metric.

Debris Removal

Validating debris removal would entail turning on the device's suction to remove fluids and particulates. The group would use a pressure transducer to measure the pressure of the device's suction over the course of the Norwood Procedure. The transducer's sampling rate would be once per second. The group would find the average pressure and compare it to the 350-450 kPa range, as specified in Appendix A: Updated Design Specifications. If the average pressure is in that range, the group will have validated the debris removal flow rate.

Arterial Integrity

After two infant pigs undergo the Norwood procedure, one with the currently-used clamp and the other with the designed device, the arteries of both pigs will be stained with hematoxylin-eosin. This type of staining will indicate any inflamed cells due to hemorrhaging, edema, congestion, neutrophilic cells, or any cells showing necrosis.[6] Microscopy and a blood assay would show if an increase in acute inflammation or necrosis had occurred, indicating artery damage. If this

is found to be false(using $p<0.5$ for significance), then the clamp would show proper safety to arterial integrity.

Maneuverability

After performing the procedure and examining the device, the surgeon would rank on a 1 (worst) to 5 (best) scale the ease of insertion, general control during surgery, and ease of removal of the device — all with respect to moving around small artery beds. The group will review the survey results and general comments to evaluate and improve maneuverability.

Installation Time

The group will record the amount of time taken to install the clamp while also timing the entire surgery to calculate the percentage of surgery time installation takes. This percentage should not exceed 10%.

Comfort

To measure the subjective component of comfort, a survey will be given to the residents and surgeons post-surgery. The questions include whether it was easy to hold, easy to move around and responsiveness, amongst others. The group will use the feedback to improve the design of the clamp.

Obstruction

When testing the device in simulated conditions, a subjective questionnaire for the surgeons will be used to determine perceived occlusion.

FDA Process

Once the prototype clears the tests outlined above, the next steps are to continue refining the design based on the feedback received and then submit the clamp to the FDA for review as a Class I device. A Class I device is described as one that has low risk to the patient. According to the FDA, surgical clamps fall under this designation. The team would submit a 510(k) report for the device, which would explain how the prototype is similar to other Class I clamps that are being sold, like the Javid clamp.

Because the client is a pediatric cardiothoracic surgeon, the team plans to have him use it in surgery and then write a case report on the merits of the surgical device. This, in combination with the FDA clearance would allow the team to approach surgical device companies in order to structure a licensing deal.

OVERALL PROJECT STATUS

Currently, the group assembled the component CAD files for each part of the device (e.g. handle, 70°clamp angle, Javid-style clamping mechanism) into an assembly file. Screenshots of this file from different angles may be found in the proof-of-concept subsection. The group has 3D printed four iterations of the device and a picture of the most recent one can be found in the proof-of-concept subsection in Figure 2. Furthermore, the group has performed force analyses in AutoDesk Inventor as shown in Appendix C that show the fail strengths of titanium and indicate how force from the handle is transmitted to the device tips.

The next steps for the group are to integrate the debris removal mechanism into the current design, meet with the client to get feedback on the more subjective design specifications (e.g. expected maneuverability, comfort, and ability to maintain arterial integrity), continue testing and modifying the 3D printed device for each design specification, and get a price quote for titanium-machined device.

Proof-of-Concept Results

The screenshot of assembled CAD file of the device can be found in Figure 1.

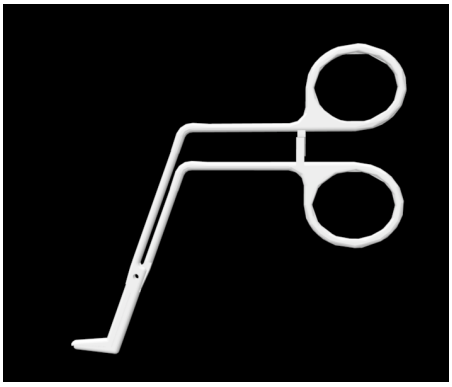

Figure 1: *The fourth iteration of the completely assembled device*

The device has all the functionality specified in the project scope except debris removal, which the group is working to add in the next iteration.

Figure 2 shows the 3D print of the CAD file.

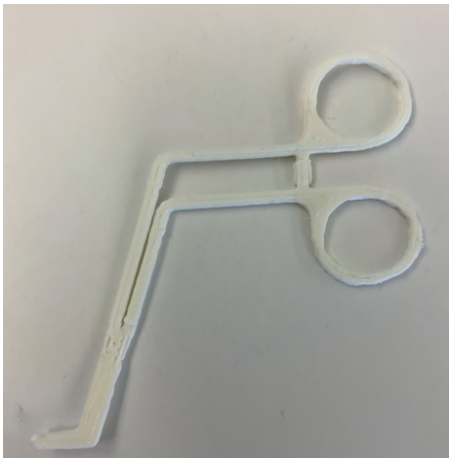

Figure 2: *3-D printed device from the CAD file shown in Figure 1*

Figure 2 shows the properly-scaled device, which has the ability to open and close like similar surgical clamps.

The stress analyses images, descriptions, and results are located in Appendix C. In summary, the results of the test show that device can withstand industry-standard fail strengths and can transmit force from the handle to the tip properly.

REFERENCES

[1] D. S. Fruitman. “Hypoplastic left heart syndrome: Prognosis and management options”. In: *Paediatr Child Health* 5.4 (May 2000), pp. 219–225.

[2] Allan DeMello. *Coefficients of Friction*. Oct. 2010. URL: http://www-eng.lbl.gov/~ajdemell//coefficients_of_friction.html.

[3] *Medical Grade Titanium*. 2017. URL: https://www.americanelements.com/medical-grade-titanium-7440-32-6.

[4] A. T. Sidambe. “Biocompatibility of Advanced Manufactured Titanium Implants-A Review”. In: *Materials (Basel)* 7.12 (Dec. 2014), pp. 8168–8188.

[5] Centers for Disease Control and Prevention. *Infection Control*. 2016. URL: https://www.cdc.gov/infectioncontrol/guidelines/disinfection/sterilization/sterilizing-practices.html.

[6] Carlos Hespanha Marinho Junior et al. “Evaluation of the damage caused by clamping or section of cervical sympathetic nerve in rabbits”. en. In: *Acta Cirurgica Brasileira* 27 (June 2012), pp. 376–382. ISSN: 0102-8650. URL: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0102-86502012000600004&nrm=iso.

APPENDIX A: UPDATED DESIGN SPECIFICATIONS

Table 1: *Modified Specifications used to Prototype Device*

Specification	Metric	Description
Physiological Constraints	Arterial – diameter: 6-12 mm – thickness: 0.4-0.6 mm Incision diameter: 2 cm	Device must suit artery diameters and thickness and fit into operating incision
Eliminate Blood Flow	300-450 kPa	Maximum pressure of the device should be in the range listed in the left column
Debris Removal Flow Rate	40-60 $\frac{ml}{min}$	Device should achieve listed flow rate to match rate of debris generation, and maintain pressure < 1.4 kPa to prevent tears in heart tissue
Arterial Integrity	N/A	Device must not damage or be abrasive to arteries
Weight	50-70 grams	The weight range balances strength and wieldiness
Cost	≤$1000	Cannot cost >$5000 to create as per client request
Biocompatibility	N/A	The device should not react with bodily tissue or corrode
Maneuverability	Device tip width: ≤2.8 mm	Must be able to move around small artery beds
Installation time	≤10% of operation time	Device will not increase operating time more than 10%
Comfort	Device thickness: 15-20 mm, Finger cutout diameter: ≥ 30mm	Device should be comfortable to grasp and have ambidextrous functionality
Durability	10 years	The device should last at least 10 years
Obstruction	20% of operating field	The device should not obstruct more than 20% of the surgeon's operating field

APPENDIX B: UPDATED DESIGN SCHEDULE

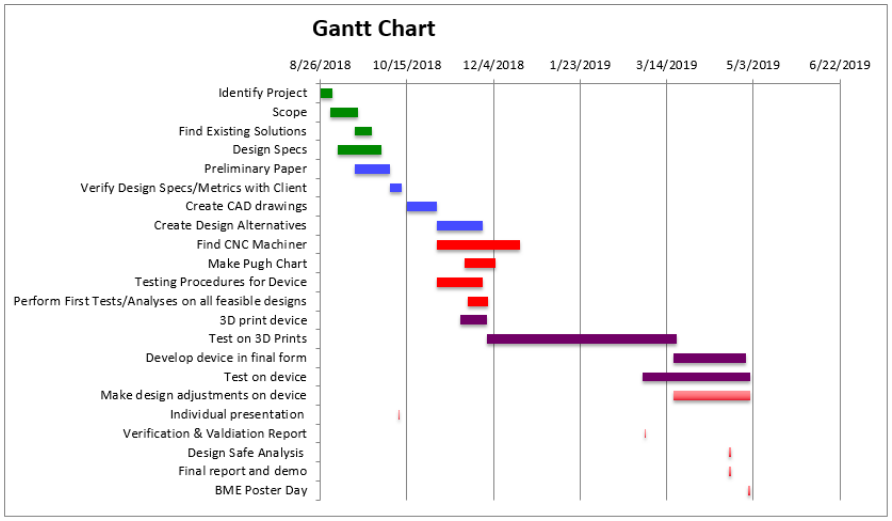

Figure 3: *Updated Gantt Chart for Group 17, showing an elongated time for testing with 3D prints*

APPENDIX C: FORCE ANALYSES

The following is the stress analysis performed used to verify the functionality of the clamp. Note all forces were reduced given the clamp's physical reduction for modeling purposes. These were calculated from the given design specification of eliminating blood flow. The forces applied to the bottom and tap surfaces of the device tips are shown in Figure 4 and 5, respectively.

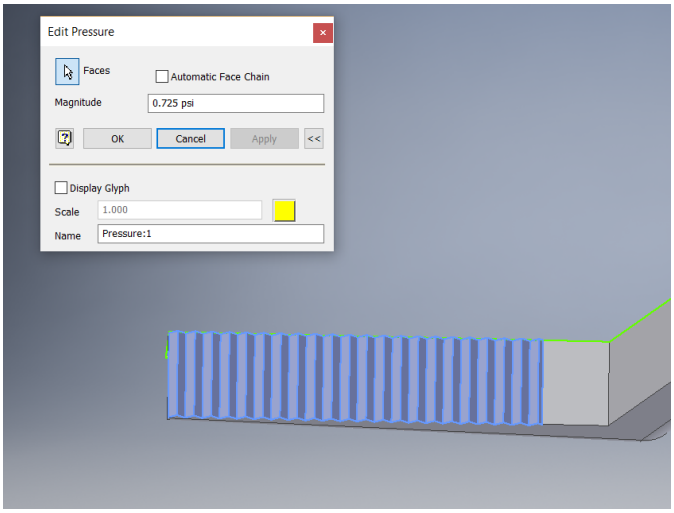

Figure 4: *Force applied to the surface of the bottom device tip*

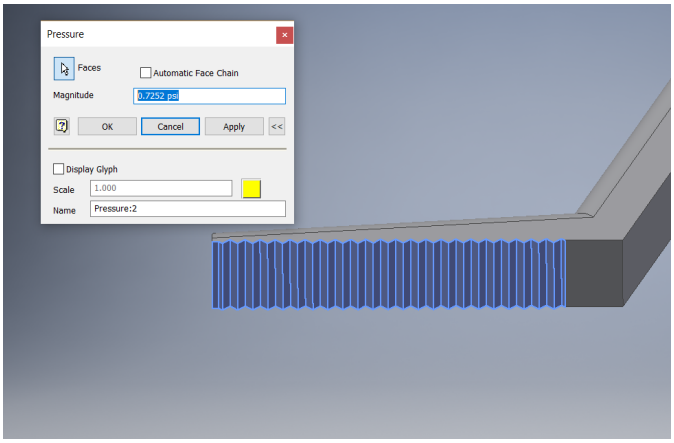

Figure 5: *Force applied to the surface of the top device tip*

These are the forces, 0.725 psi to the top and 0.7252 psi to the bottom, applied in pressure format to the clamp. However, as will be discussed later, the top device tip, shown in Figure 5, is effectively considered fixed in order to simplify for the simulation. Therefore, the force was all realistically presented onto the bottom device tip, shown in Figure 4.

The material choice of titanium and mesh division is shown in Figure 6 and Figure 7, respectively.

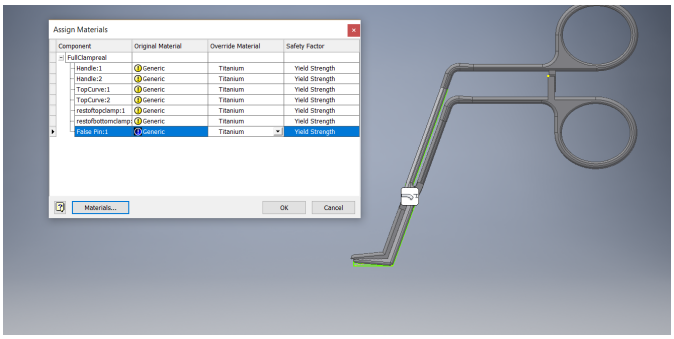

Figure 6: *Setting the material type to titanium for all components of the device*

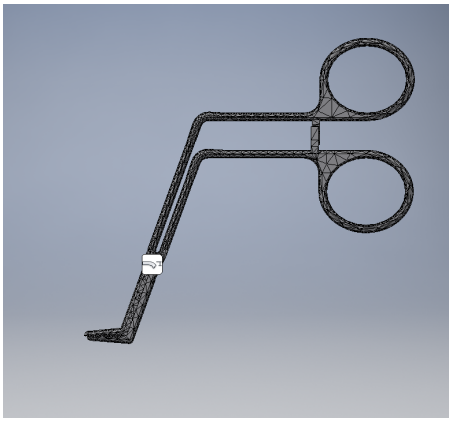

Figure 7: *The mesh division of the device*

The mesh division was done automatically by AutoDesk. Note the fixed constraint near the pin, shown in Figure 8, is designating the fixing of the top handle. The hole where the pin would be also has a pin constraint.

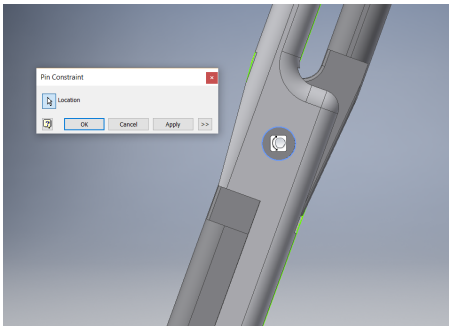

Figure 8: *The device pin constraint*

Figures 9 and 10 show the results of the stress test analyses.

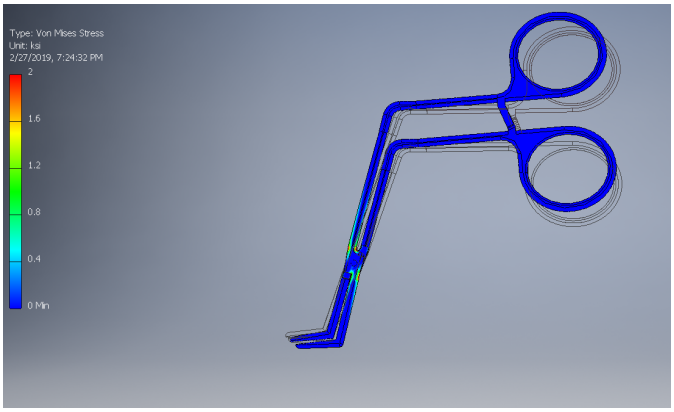

Figure 9: *Stress map of the entire device*

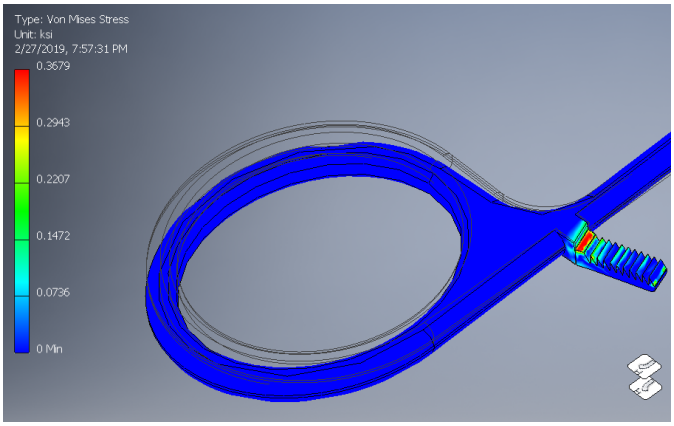

Figure 10: *Stress map of the entire device*

In the first test, as shown in Figure 9, the full clamp view, we can see minor stress felt near the joint, but a majority of the clamp does not deform. The second test, as shown in Figure 10, was done with the exact same conditions, however, the other handle of the clamp was made invisible and the scale was reduced to see the underlying color map of stress felt on the teeth. This was done for enhanced visualization.