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Modifications of a Machine to Produce Clinically-Sized Angioplasty Balloons for Bifurcations

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Abstract

Coronary artery disease is the most common form of heart disease and the leading cause of death in the U.S. ("Heart Disease Facts | cdc.gov", 2021). Typically, coronary artery disease is a result of coronary stenosis, constriction of the coronary artery, which can cause heart failure, arrhythmia, or heart attack ("Coronary Artery Disease: Prevention, Treatment and Research", 2021). Angioplasty balloons are a common treatment method for coronary stenosis and work by placing a stent at the lesion site to widen the vessel and promote blood flow. A type of lesion which remains particularly difficult and relatively common to treat is a bifurcation lesion (Rizik, 2021). Current stenting methods for bifurcation lesions use standard-shaped angioplasty balloons and can result in restenosis through overlapping stents or exposed artery locations. In response, tapered balloons that better fit the bifurcation geometry are being examined for potential use in intervention treatments (Uretsky, 2014).

Previous research in this project developed a prototype balloon-forming machine and customizable molds which did produce bifurcation-specific angioplasty balloons (Elmer et. al., 2022). However, the prototype produced balloons that were significantly larger than the typical sizes used in clinical settings. This project examined the effects of reducing the mold size diameter from 16 mm to 9 mm on the machine and balloon forming process. Formation variables, such as heat time, pressure, and temperature, were tested across various ranges, which highlighted issues in the procedure such as tubing dimensions and luer lock connections. These were corrected by developing a new tubing necking device and process to produce tubing with tapered ends. A setting rack was designed to correct luer lock connections. The resulting parisons and procedures were more closely adapted to standard industry practices. Further research and testing will have to be conducted to improve the tubing end seal.

I. Introduction

Coronary artery disease, a type of heart disease, is the leading cause of death in the United States, killing 360,900 people in 2019 alone. Typically, coronary artery disease is a result of coronary stenosis, constriction of the coronary artery, which can cause heart failure, arrhythmia, or heart attack. Angioplasty balloons are a standard method of treatment and function by placing a stent at the lesion site to widen the blood vessel. A catheter with the balloon and stent attached is inserted into the body typically via one of the arteries and navigated up to the diseased coronary artery. Once at the lesion site, the balloon is expanded and in turn presses the stent against the sides of the artery wall, fixing it in place. After the catheter and balloon are extracted, the stent should remain and maintain arterial blood flow through that location. A particularly difficult type of lesion to treat is a bifurcation lesion, due to its complex geometry which varies among patients. Bifurcations are also common areas in the arteries which are affected by coronary artery disease, accounting for approximately 15-20% of interventions (Rizik, 2021). Aspects of the bifurcation to be considered in treatment include branch angles in multiple dimensions, lesion distribution in the main and side branches, and individual parameters, such as diameter, in both branches. A variety of stenting procedures utilizing standard-shaped balloons have been developed to address the bifurcation area; however, these tend to result in either insufficient coverage or overlapping stents, both of which can result in restenosis.

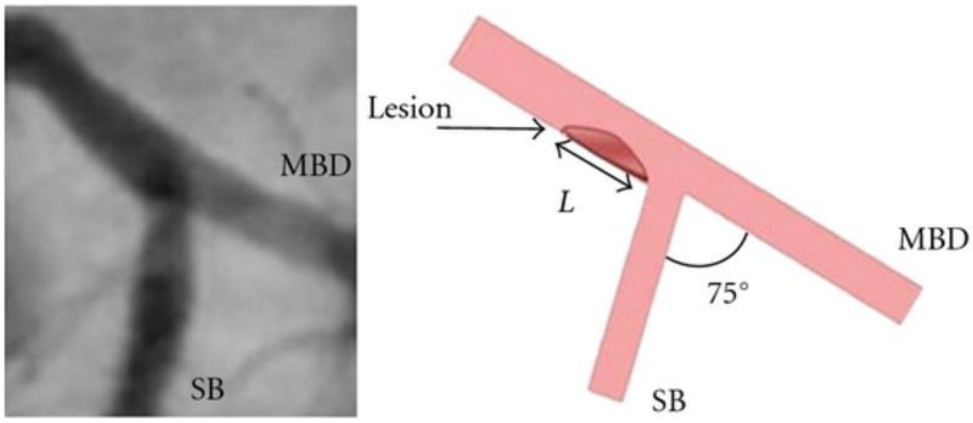

Figure 1. Image of coronary artery bifurcation (left) and corresponding diagram (right) (Molavi-Zarandi et. al., 2012).

To address the issues which hinder the use of standard-shaped balloons in bifurcations, this research project previously developed a balloon forming machine with customizable molds that would allow clinicians to produce angioplasty balloons adapted for each individual patient (Elmer et. al., 2022). The prototype machine manufactured balloons that were significantly larger than the balloons typically used in coronary arteries to allow for easier preliminary testing ("WOLVERINE™ Cutting Balloon -Surgical Dilatation Catheter", 2022). The purpose of this honors thesis project was to resize the molds to form smaller balloons. In doing so, one aspect was to explore how the size reduction affected the balloon forming process and how certain variables such as pressure, heat time, and temperature influenced balloon formation. As these variables were examined, multiple issues were highlighted in the machine and parison-forming process. The size reduction exacerbated certain aspects of the procedure which previously had negligible effect in the initial prototype. This project also examined the presented issues and undertook the necessary research to correct them.

II. Materials and Methods

The prototype machine previously developed relies upon a combination of heat and pressurized air to soften and expand the balloon preforms to fill the inside of a custom 3D printed resin mold. The balloon preform, or parison, are made of polyethylene terephthalate (PET) tubing attached to a luer lock with cyanoacrylate glue. One end of the tube length is inserted inside the luer lock, and the other end is sealed with cyanoacrylate glue. After the parison glue has dried and set, the parison is inserted inside the mold, which has been heated up to a specified temperature by the machine. The open end of the luer lock is attached to an air compressor hose. After heating the parison to the desired pliability, pressurized air is released inside the parison for 1-2 seconds, which expands the tubing and fits it to the inside of the mold. The air is then released from the parison, and the balloon is extracted from the mold.

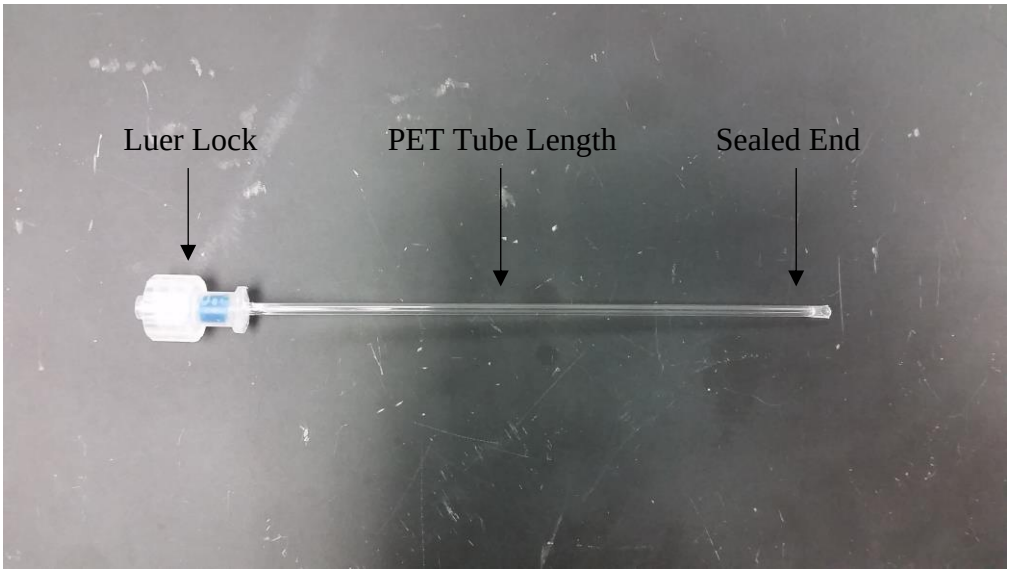

Figure 2. Parison before inflation inside the balloon-forming machine. Consists of a luer lock attached to PET tubing using cyanoacrylate glue.

To examine how a reduction in mold size affected the balloon formation process, the mold was first resized from 16 mm diameter to 9 mm diameter. The new mold was resized in SolidWorks and printed using a resin printer. To examine the effects of heat time, temperature, and pressure, each of these variables was tested over a range of values while holding the other two variables constant. Heat time was tested over a range of 20 to 28 seconds with two-second intervals and a constant temperature of 130°C and pressure of 85 psi. Temperature was tested over a range of 90 to 120°C with 10°C intervals and a constant pressure of 85 psi and a heat time of 30 seconds. Pressure was tested over a range of 55 to 85 psi with 10 psi intervals and a constant temperature of 120°C and heat time of 30 seconds.

The primary corrections developed in this project were a setting rack, necking device, and insertion ramp. The setting rack and insertion ramp were both designed in SolidWorks and printed on a 3D printer from polylactic acid (PLA). The necking device contains a wooden base clamped to the suspended metal base of the balloon-forming machine. Attached to the wooden base, a sliding track runs parallel to the insertion axis of the machine. Two clamps, one on the track and the other fixed to the wooden base, hold the PET tubing horizontal and suspend it inside the heating block of the machine. After the tube is heated to the desired pliability, the mobile clamp slides along the track and pulls the tubing, stretching the portion which was inside the heating block. Both ends of the tubing receive this treatment, leaving a 1 to 3 mm section in the middle untouched.

III. Results

As preliminary pressure, temperature, and heat time testing began, it became apparent that several process details which had an insignificant impact on the larger prototype had more pronounced effects upon the smaller prototype. Most of these issues revolved around the parison. The smaller tubing which was selected for the resized prototype did not properly fill out the mold. During testing, the parison either would not fill the inside of the mold entirely or would inflate both inside and outside the back end of the mold. During pressure testing, pressures of 65 psi and above produced a second inflated portion which developed outside the back end of the mold. This inflation inhibited the extraction of the balloon and resulted in the balloon tearing or stretching. 55 psi was the only setting which did not produce a second inflation; however, the balloon did not properly fill out the mold, only reaching a diameter of 6.7 mm and length of 6.1 mm.

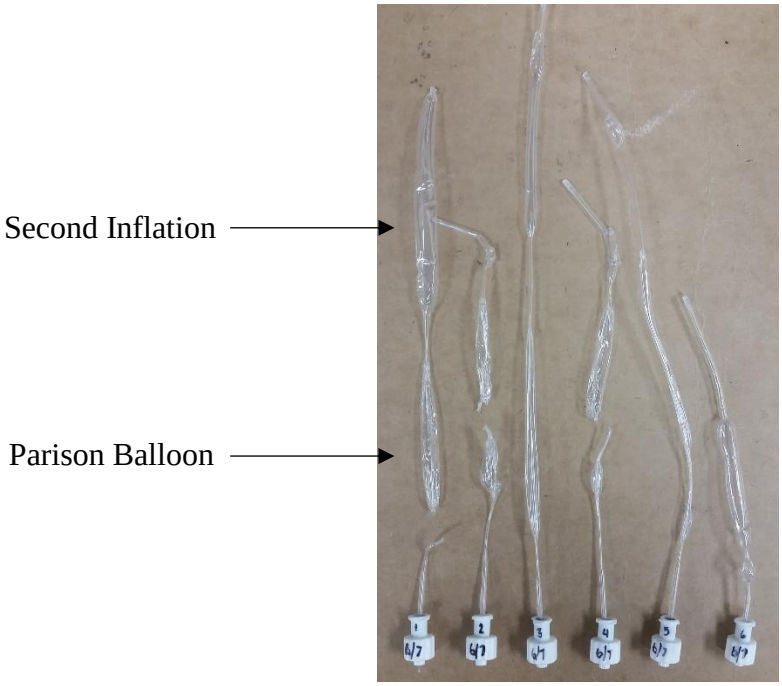

Figure 3. Results of pressure testing with fixed temperature and heat time. From left to right, pressures are 85 psi (x3), 75 psi, 65 psi, and 55 psi respectively.

The temperature testing also saw comparable results. Temperatures of 110°C and above produce the second inflation outside the back end of the mold. However, the 90°C and 100°C settings failed to inflate the parison completely. Unlike the pressure testing, the temperature testing results did not produce a graded response to the change in settings. It either produced two inflations or no inflation at all.

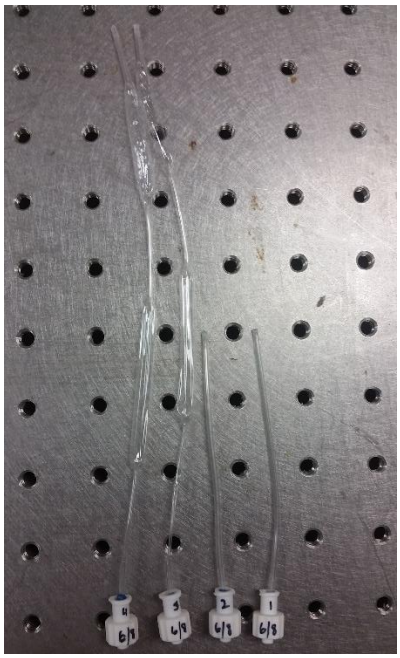

Figure 4. Results of temperature testing with fixed pressure and heat time. From left to right, temperatures are 90°C, 100°C, 110°C, and 120°C.

Heat time testing had similar results to pressure testing. Higher time durations of 24 seconds and above produced a second inflation with the inflation length growing with increasing time. Times of 22 seconds and less did not produce the second inflation; however, they did not fill out the mold completely, with the shorter times corresponding to smaller balloon sizes.

IV. Discussion

As previously mentioned, several issues occurred with the balloon-forming process which had to be addressed. The machine had to manufacture balloons that did not produce a second inflation but properly filled out the mold. Many of these issues stemmed from the parison, including the parison tubing dimensions. To find a solution to this issue, extensive research was conducted into industry practices for the formation of the parison. By incorporating components from industry methods, the developed solution was to take larger tubing and neck down (or reduce the diameter of) the ends by heating and stretching. The resulting tubing diameter decreased from approximately 2.73 mm to 1.54 mm, a reduction of 43.6%. The larger portion in combination with the narrower ends assisted in developing the general shape that the machine mold produced. This step is intended to support the balloon in filling out just the inside of the mold and not extend beyond the mold limits. Another issue that arose from the parison was the connection between the luer lock and the tubing. Cyanoacrylate glue is used to attach the luer lock and tubing, which were initially laid flat on a surface to set. However, this resulted in the tube drying at an angle in the luer lock, which inhibited the insertion of the parison into the smaller machine mold. So, a rack was designed to hold the tubing in a centered position inside the luer lock as it dried, which allowed the resulting parisons to insert into the mold more easily. The rack was designed to hold ten parisons for each drying period.

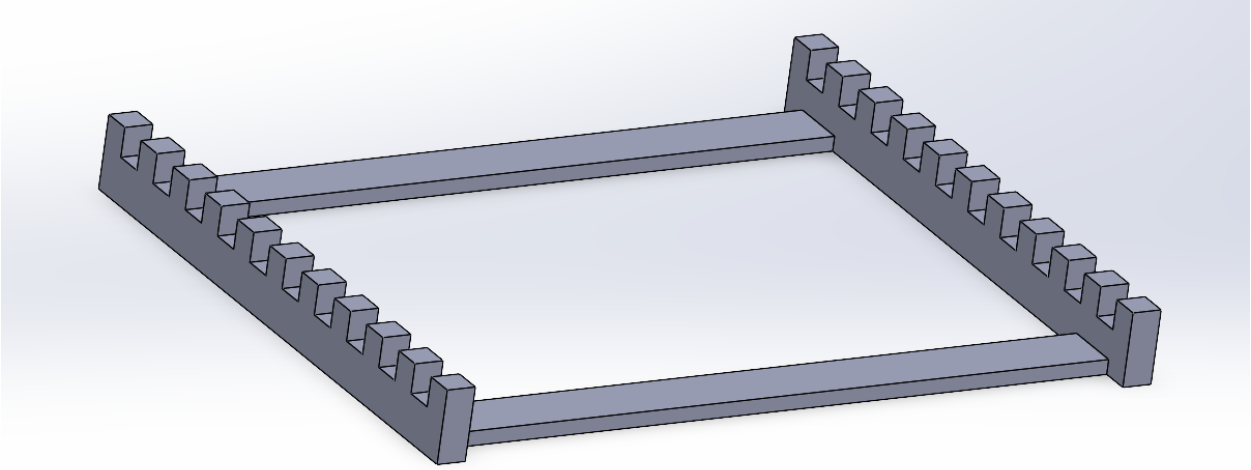

Figure 5. SolidWorks model of the parison setting rack. Designed to prevent parison preforms from setting at an angle in the luer lock.

Despite the issues which hindered the performance of the machine with the reduced mold, some information was gained about how pressure, temperature, and heat time affected the smaller balloon formation. Although all factors had some effect on balloon formation, heat time and pressure appeared to play more significant roles in the process. The lower end of the heat time range produced better balloons with the 22 to 24 second interval performing best. In addition, the lower end of the pressure range performed better in these tests; however, in subsequent tests it was shown that by reducing the heat time, the pressure must be increased to adequately fill the inside of the mold. Temperature was also tested but did not produce the graded results which we saw with pressure and heat time. The plastic requires a certain temperature to adequately soften within the relatively brief time frame the procedure encompasses. Based on the tests, the machine should be set between 110 and 120°C.

One problem involved the necking process for the parison tubing. The initial procedure was manually driven and allowed for some human error to be introduced into the parisons. Two people were required in this procedure as one had to hold the tubing and the other had to assist in the placement of the tubing in the metal block to ensure the tubing was approximately level. As a result, it became apparent that some post-stretched tubing was set at an angle, which hindered the insertion of the parison into the machine. So, an apparatus was developed to stretch the tubing along a level track to make the parisons straight and therefore easy to insert. It consisted of a wooden base and a mounted track and slider to run alongside the metal block. Two clamps held the tubing in place through the heating and stretching process. The resulting parisons were significantly straighter than the previous ones and were much easier to insert into the machine.

Figure 6. Device constructed to sketch larger diameter tubing to obtain tapered ends.

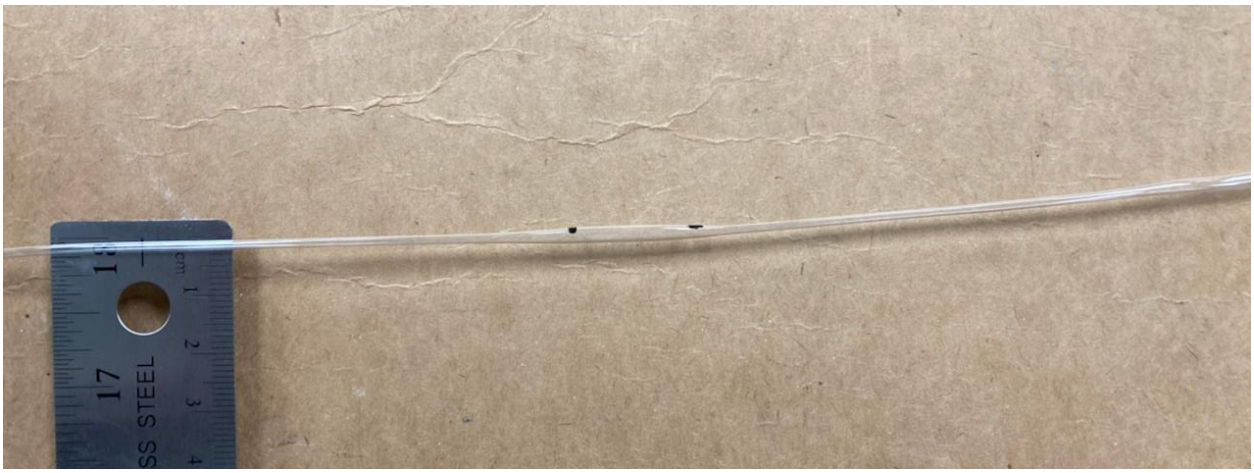

Figure 7. One of the parison preforms after being stretched in the necking device. The area between the two black markings is the original tubing diameter 2.73 mm and the outside tubing has a diameter of approximately 1.54 mm.

Another issue that was addressed was the issue of the tubing diameter. The larger tubing which was initially used in the project produced parisons that had a wall thickness that was too great for angioplasty balloons. A balloon with a large wall thickness is less pliable and is more difficult to insert inside the artery. Visibly, this is marked by an opaquer appearance after inflation. In reviewing the results from the initial prototype machine, it was noted that the diameter-to-wall thickness ratio was very different between the prototype balloons and the smaller balloons. Therefore, an alternative type of tubing with a similar diameter but smaller wall thickness was purchased. The resulting balloons had a smaller wall thickness and a clearer wall appearance. In addition to changing the tubing dimensions, the issue of wall thickness was also addressed by adopting the industry practice of stretching the preform while inflating. The purpose is to exert more control over the parison and balloon shape. Not only is this intended to modify the wall thickness but also assist in shaping the balloon during inflation. Initial results indicate that

stretching may hinder the second inflation from forming outside the back end of the mold; however, further research must be done to perfect this process

One other minor area which was addressed in the project was providing additional aides for quick and easy insertion of the parison into the machine. Since the procedure is highly time-dependent, machine performance is affected by any aspect which slows insertion and extraction. The reduced size mold resulted in a more difficult insertion process given the parison and one end piece must be inserted at the same time. To aid this step, a ramp was designed and 3D printed to provide a support that guided the end piece and parison more easily into the mold opening.

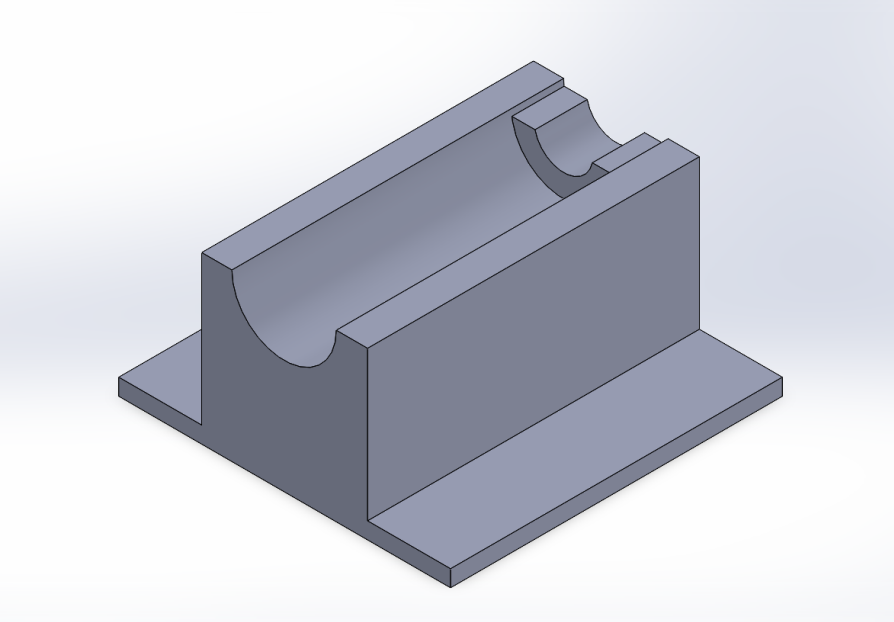

Figure 8. SolidWorks model of ramp designed to assist the insertion of the parison and end piece into the mold.

V. Future Work

Towards the end of this project, a new issue arose with the sealed end of the parison. Following insertion of the parison into the machine, the cyanoacrylate glue appeared to heat and

liquefy, preventing the inflation of the parison. It was speculated that this could be due to continued insertion delays for the parison; however, the seal also began having issues before insertion, which indicated another source for this problem. The seal would not hold up under pressures that it had previously withstood when completely cool. As a result, alternative sealing options are currently being examined and will need to be tested in the future to correct this issue. Future work in this project would also include reducing the mold size again to discover whether additional aspects of the process and machine will be affected on an even smaller scale. Beyond that, the overarching goal of this project is to provide clinicians with the option of customizable angioplasty balloons for use in bifurcations. Additional research and significant testing will need to be conducted to one day place this life-saving technology in the clinical setting.

VI. Conclusion

In conclusion, the reduction in mold size from 16 mm to 9 mm affected multiple aspects of the balloon-forming machine and process, which were addressed in this project. Preliminary pressure, heat time, and temperature testing exposed these issues and provided insight into how the variables influence each other and affect balloon formation. Components of the process were adjusted to match industry practices, including a necking process to develop a preform. The later versions of this preform were made with tubing dimensions that were more closely scaled down from the prototype dimensions, resulting in a smaller balloon wall thickness. The tubing and luer lock connection was improved through a better setting process. The tubing dimensions were altered to produce a balloon with a more appropriate wall thickness. The results of this project have supported the goal of a balloon-forming machine to produce customizable, clinically-sized angioplasty balloons. The results of this project have refined the balloon-forming process to

eliminate issues that arose from the reduction in prototype size, giving further insight into what elements may also need to be re-examined when the machine is resized again.

VII. References

1. Heart Disease Facts | cdc.gov. (2021). Retrieved 10 June 2021, from https://www.cdc.gov/heartdisease/facts.htm

2. Coronary Artery Disease: Prevention, Treatment and Research. (2021). Retrieved 10 June 2021, from https://www.hopkinsmedicine.org/health/conditions-and-diseases/coronary-artery-disease-prevention-treatment-and-research

3. Rizik, D. (2021). Treating Bifurcation Coronary Artery Disease. *Reviews In Cardiovascular Medicine*, *11*(S1), 1-2.

4. Uretsky, B. (2014). Apparatus and method for treatment of bifurcation lesions. United States.

5. Molavi-Zarandi, Marjan & Mongrain, Rosaire & Bertrand, Olivier. (2012). Determination of Flow Conditions in Coronary Bifurcation Lesions in the Context of the Medina Classification. Modelling and Simulation in Engineering. 2012. 10.1155/2012/419087.

6. Athletis™ Ultra High Pressure Balloon. (2021). Retrieved 10 June 2021, from https://www.bostonscientific.com/en-US/products/catheters--balloon/athletis.html?gclid=EAIaIQobChMIkp7ujMLo8AIVmWxvBB0suApOEAAYASAAEgL85fD_BwE

7. AngioSculpt 7 and 8 mm. (2021). Retrieved 10 June 2021, from https://www.usa.philips.com/healthcare/product/HCIGTDASPTASBC/angiosculpt-pta-scoring-balloon-catheter-7-and-8-millimeters?origin=7_700000002118465_71700000075517184_58700006483790368_43700058556410114&dmcm=EAIaIQobChMIpoy968Lo8AIVkm1vBB18Mw2YEAAYASAAEgITdfD_BwE&gclid=EAIaIQobChMIpoy968Lo8AIVkm1vBB18Mw2YEAAYASAAEgITdfD_BwE&gclsrc=aw.ds

8. Elmer, K.M., Bean, M.J., Uretsky, B.F. *et al.* (2022). Customizable Angioplasty Balloon-Forming Machine: Towards Precision Medicine in Coronary Bifurcation Lesion Interventions. *J. of Cardiovasc. Trans. Res.* https://doi.org/10.1007/s12265-022-10229-w

9. WOLVERINE™ Cutting Balloon -Surgical Dilatation Catheter. (2022). Retrieved 26 April 2022, from https://www.bostonscientific.com/en-US/products/balloons-cutting/wolverine-cutting-balloon.html?cid=PPC-accountype:GOOGLE-campaign:WOLVERINE-searchterm:coronary+cutting+balloon-adgroup:Non+Brand-keywordid:p59907741233&gclid=CjwKCAjwsJ6TBhAIEiwAfl4TWKdRN04j_fKii-lJVQEzPax-kc_HNY_j0C2dfhdjeEg8_yjdTB7AVhoC4noQAvD_BwE&gclid=CjwKCAjwsJ6TBhAIEiwAfl4TWKdRN04j_fKii-lJVQEzPax-kc_HNY_j0C2dfhdjeEg8_yjdTB7AVhoC4noQAvD_BwE

VIII. Appendix

Terms:

FD – front diameter; front portion of balloon measured with calipers

MD – middle diameter; middle portion of balloon measured with calipers

BD – back diameter; back portion of balloon measured with calipers

Avg – average; mean of FD, MD, and BD

Double wall – calipers measured both balloon walls when pressed together

A. Pressure Testing Raw Data

Pressure (psi)	**Trial***	**Notes**	**Length (mm)**	**FD (mm)**	**MD (mm)**	**BD (mm)**	**Avg (mm)**	**Double wall (mm)**
85	Fail	second shape	8	5.5	3.64	3.13	4.09	0.03
75	Fail	second shape	N/A	N/A	N/A	N/A	N/A	N/A
65	Fail	second shape	8	4.54	3.19	3.25	3.66	0.15
55	Success		6.1	6.75	6.53	6.82	6.7	0.12

B. Temperature Testing Raw Data

Temperature (°C)	**Trial**	**Notes**	**Length (mm)**	**FD (mm)**	**MD (mm)**	**BD (mm)**	**Avg (mm)**	**Double wall (mm)**
90	Fail	no inflation	N/A	N/A	N/A	N/A	N/A	N/A
100	Fail	no inflation	N/A	N/A	N/A	N/A	N/A	N/A
110	Fail	second shape	5.8	5.93	5.75	5.6	5.76	0.14
120	Fail	second shape	6.4	5.83	5.54	5.56	5.6433333	0.31

C. Heat Time Testing Raw Data

Heat time (sec)	**Trial**	**Notes**	**Length (mm)**	**FD (mm)**	**MD (mm)**	**BD (mm)**	**Avg (mm)**	**Double wall (mm)**
28	Fail	second shape	12.3	6.66	3.17	2.76	4.1966667	0.18
26	Fail	second shape	9.8	4.67	2.81	3.2	3.56	0.24
24	Fail	Second shape	6.8	3.89	5.99	5.7	5.1933333	0.31
22	Success		4.5	4.83	5.63	5.5	5.32	0.04
20	Success	did not fill entire mold	2.6	4.99	5.87	5.1	5.32	0.15

*For trials, it should be noted that “Fail” indicates that a second inflation formed outside the mold or inflation did not occur at all and “Success” indicates that the parison did inflate just in the mold.