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Modified Stent Design for a Coronary Bifurcation Lesion

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Modified Stent Design for a Coronary Bifurcation Lesion

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By

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I. Abstract

Currently, 18.2 million adults aged 20 and older are diagnosed with Coronary Artery Disease (CAD) (Benjamin et al., 2019).. Stenosis is the most common intervention. However, when a patient has a bifurcated artery, treatment becomes more difficult and is often unsuccessful. This project created a new stent and balloon complex that was tested in vitro using a gel phantom artery model. Two separate prototypes have been created and tested so far, with improvements made upon each. Testing is still underway with Prototype 2.

II. Background

Coronary artery stenosis is one of the most common issues that cardiologists treat. In coronary artery stenosis, an atherosclerotic plaque constricts blood flow. And, in the most severe cases, complete blockage of blood flow due to plaque build-up within the artery leads to a heart attack. Several advancements have been made in intervention efforts. Coronary artery bypass surgery used to be the only treatment option, but for the last three decades, coronary stents have revolutionized how physicians treat coronary artery disease and heart attacks. A deflated balloon is placed inside the stent, which is then inserted into the artery through an incision. Tubing connects the balloon/stent complex to a pressure source so that when pressure is applied, the balloon expands and the stent deploys. The stent stays in place, and the balloon is removed.

However, complex areas of stenosis, such as a bifurcation lesion, are more difficult to treat. A bifurcated artery is one that is branched, usually with plaque at the branching point.

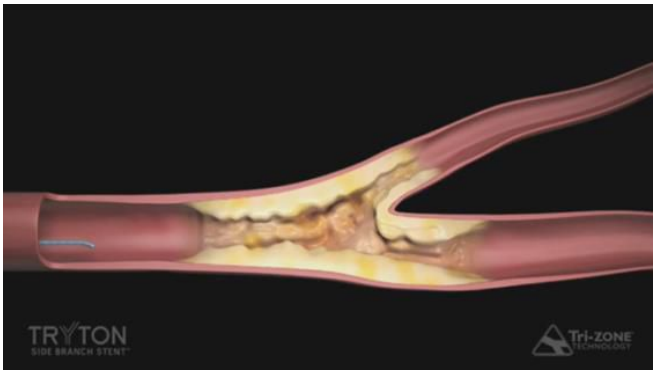

Figure 1. Depiction of Bifurcation Lesion.

These lesions account for approximately one-fifth of all coronary stenosis, but are a medical issue for which no “perfect” solution currently exists (Antoniadis et al.,

2015). This project specifically targets bifurcations with a Medina classification geometry (1, 0, 0) (Louvard & Medina, 2015). The most common intervention is to deploy two separate stents, but this can be technically time-consuming and complicated, and the rates of restenosis are high (Aoki, 2006). Bifurcation vessels are difficult to treat because no two vessels are the same. Each has different properties and different amounts of blockage, which prevents researchers from finding one true solution. The most common method used to treat these vessels is to insert one wire and stent into the main branch, and a second wire and stent into the side branch (Sawaya et al., 2016). This process is not easy to complete, and these vessels typically have higher rates of restenosis and thrombosis as opposed to one-branch blockages.

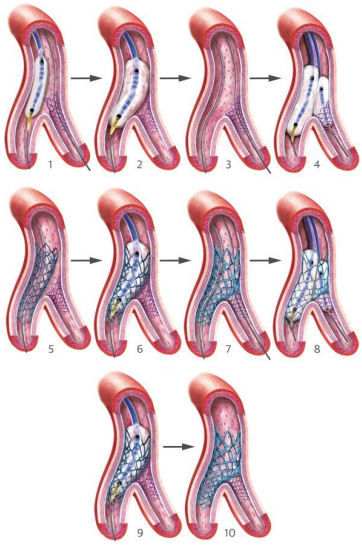

Figure 2. Step-by-step technique using two stents.

III. Initial Proposal

This project was in collaboration with the University of Utah. There were two main aims of this project: to develop a Finite-Element (FE) modeling system in order to predict the outcome

of our stent-phantom model, and to create the physical stent-phantom model to test. Researchers in Utah were responsible for creating the FE model, and all of our data was shared with them for this purpose. The main aim of this project was to simplify the process of repairing bifurcation vessels, as well as increasing the success rate of these repairs and decreasing rates of restenosis and thrombosis. In addition, the FE component was added so that patient-specific models and stents can be created in the future (Jensen & Timmins, 2016).

IV. Prototype Version 1 (2018)

The first version of the balloon-stent complex was completed in 2018. The stent itself was designed on the SolidWorks engineering software, then produced by manufacturers using an oxygen-laser cutter at Hi-Tech Welding in Lee's Summit, Missouri. The stent was made of stainless steel 316L, and was originally cut into a flat dimension before being welded into a cylindrical shape. The initial stent balloon was purchased from Nordson Medical and was made from Polyethylene Terephthalate (PET), a stiff and clear plastic. PET has a good glass transition temperature (exact values are between 73-78 degrees Celsius), which means that the material easily melts into a "viscous liquid" that can easily be molded into a new shape, especially with blow molding. This property is beneficial in this case because the PET is able to be heated at a low temperature, then air blows it into a balloon shape (Polyethylene, n.d.).

Next, a crimper was used to make the stent as compact as possible. The balloon was then inserted into the stent, and then the balloon-stent complex was placed within the phantom. The balloon was attached to an inflator using PET tubing, and the inflator was pumped up to 11 atm. This was a very crude model. The stents themselves had many issues, mainly that there was a large amount of porous residue, or slag, on all surfaces of the stents. Because of this, the welds were unable to hold at several different points. In addition, the porous edges were so sharp that

they pierced some of the balloons. All of the stents in this first prototype broke during the crimping process or while they were being deployed.

V. Prototype Version 2 (2019)

After the first round of stents was created, we tried to make optimal changes in order to reduce the number of breaks that were occuring. First, a change was made in the laser-cutting technique of the steel pieces. The second group of stents were cut using a nitrogen laser, rather than one that uses oxygen. The oxygen laser had caused an oxidation reaction with the steel, which was forming the slag on the stents (Wiley, 2017). A benefit to the oxygen laser was that it cut somewhat quicker than the nitrogen, and it was also cheaper. Second, we employed a tactic called passivation in order to remove the remaining slag (excess metal). This slag was pretty sharp and was causing issues with the stent balloons, as well as causing the stents to break in some places. The passivation method involves soaking the stents in a solution of water and citric acid, and eventually the particles will break off.

The passivation method is very simple. We placed the stents into two different groups, one as a control and one as a test group. First, I weighed all of the stents and wrote down identifying characteristics of all of them. Then, I soaked them in a solution of bleach and water, and tried to brush away some of the metal particles. Next, I placed the control group in a beaker filled with distilled water. Then, I combined another beaker of distilled water with citric acid—proportion was 10% citric acid compared to the weight of the water. I placed both beakers on a hot plate, set at 150 degrees Celsius, for thirty minutes. At the end of the thirty minutes, I took them off the hot plate, rinsed all the stents again with distilled water, and weighed them again. The following data shows the mass of each stent, before and after passivation. The results of Experiment 1 were stents that had already been laser-welded together, forming a cylindrical shape, but had already been deployed and possessed some damages. The stents were divided into

the control group and the test group. Experiment 2 tested stents that had not been welded yet, so the steel was in a flat sheet. Experiment 3 stents were also from the first group (oxygen-laser cut), but they had not yet been deployed.

	Stent #	Mass Before	Mass After	Percent Change
Control Group	**15**	**0.7131g**	**0.7116g**	**0.21%**
	14	**0.7190g**	**0.7172g**	**0.25%**
	4	**0.7205g**	**0.7191g**	**0.19%**
	6	**0.7177g**	**0.7157g**	**0.28%**
Test Group	**16**	**0.7165g**	**0.6873g**	**4.08%**
	1	**0.7163**	**0.6904g**	**3.62%**
	10	**0.7195g**	**0.6956g**	**3.32%**
	7	**0.7206g**	**0.6928g**	**3.86%**

Table 1. Experiment 1.

Stent #	Mass Before	Mass After	Percent Change
1	0.6763g	0.6566g	2.91%
2	0.8000g	0.7665g	4.19%
3	0.7074g	0.7041g	0.47%
4	0.7654g	0.7333g	4.19%
5	0.7437g	0.7228g	2.81%
6	0.7392g	0.7150g	2.08%
7	0.7150g	0.7077g	1.02%
8	0.7102g	0.7089g	0.18%
9	0.8575g	0.8461g	1.33%
10	0.7602g	0.7442g	2.10%
11	0.7022g	0.7021g	0.01%
12	0.7280g	0.7205g	1.03%
13	0.8299g	0.8176g	1.48%
14	0.7123g	0.7095g	0.90%
15	0.7916g	0.7485g	5.44%

Table 2. Experiment 2.

Stent #	Mass Before	Mass After	Percent Change
3	0.7148g	0.6889g	3.62%
5	0.7185g	0.6946g	3.33%
11	0.7209g	0.6948g	3.62%
12	0.7189g	0.7084g	1.96%
13	0.7174g	0.6946g	3.18%

Table 3. Experiment 3.

This data shows that there was a decrease in mass among all stents in Experiment 1. It was a small difference with this group, since it was the control group, but water still had a small effect. The test group, using the citric acid passivation technique, had a large impact on the decrease in mass. With Experiment 2, there was a discrepancy in the temperature. The temperature was set to 150 degrees Fahrenheit because that was the temperature given in the original instructions I found. However, I completed the passivation process again with the same stents at a temperature of 150 degrees Celsius. As seen in the results, there was not a huge change in mass of these stents. But, the nitrogen laser-cutter was more successful for this round of stents, so there was not much metal to dissolve anyway. Experiment 3 was performed using the original batch of stents, so there was more slag than Experiment 2. I set the temperature at 150 degrees Celsius for Experiment 3. Experiment 3 removed more slag relative to Experiment 2.

The next step to prepare the stents for deployment was to crimp them so they would be able to fit into the phantom arteries. To do this, we used the Edwards SAPIEN 3 Lifescience TAVR crimper. The goal was to crimp them down to a diameter of 8 millimeters, which was approximately 31 degrees on the machine. The secondary goal of the crimping experiment was to crimp the stents without any breakages, which had also been a problem in the first round. The following data shows the various measurements taken when crimping the stents. None of the stents in this group were broken, which was a huge success.

Stent #	Initial Diameter (mm)	Final Diameter (mm)	Initial Angle (degrees)	Final Angle (degrees)
1	16.34	8.41	86	35
2	16.07	8.75	94	35
3	16.99	8.53	95	35
4	15.72	8.66	95	35
5	15.7	8.49	90	35
6	16.53	8.44	85	35
7	16.48	8.48	90	35
8	15.64	8.57	95	35
9	16.1	8.26	90	35
10	16.79	8.57	90	35
11	16.06	8.53	90	35
12	16.2	8.57	90	35
13	15.75	8.82	95	35
14	16.12	8.9	95	35
15	16.19	8.6	95	35

Table 4. Data from stent crimping.

The next process was creating new balloons. In the previous version, balloons had been ordered from a medical supply company, but the company ran out of stock. It was also in the initial project proposal to create a machine that would form these balloons. The first step was to prepare the parasons that would serve as the balloon molds. They were formed using PET tubing with a 0.19 inch outer diameter and male Luer locks and they were connected using Loctite 401.

The glue on the parasons dried for approximately forty-eight hours, and then they were able to be blown into a balloon.

The basic concept for the balloon-forming machine was to insert the parason into the mold, with a 3D printed piece made of resin connected on each side to try to reduce movement. The mold was connected to a heater, which was pre-heated to 180C. The parason was placed inside for twenty seconds, then removed, then placed back inside the mold for twenty more seconds. At the end of the second heating, the valve of the attached air compressor was opened for approximately half a second in order to "blow up" the balloon. Multiple trials were performed, but few balloons were actually suitable for the experiment. There were several issues and inconsistencies with version 1.0 of the machine. First, the pararsons were too wobbly inside the machine. It was hard to place the securing end pieces within the time constraints. Also, it was difficult to consistently time each trial perfectly because the pieces would get stuck inside the mold. Also, the machine was built on the floor, so it was difficult to see inside the machine. Because of all of these inconsistencies, many different types of balloons were formed.

Figure 3. Sample balloon.

Even though the majority of the balloons were not fit to be used, data was still collected on them so as to improve the second version of the balloon-forming machine. During the initial testing, all of the balloons were filled completely with water and attached to the inflator. The inflator used in these tests was an actual inflator used in hospital stent deployments, and the packaging advised for the pressure to reach 12 atm. Collaborators at the University of Utah advised for the goal pressure for the balloons to be fully expanded to be 11 atm.

There were some issues with this experiment as well. Some of the balloons burst before reaching 11atm, and some of the Luer locks were not glued properly and broke off from the parason in the middle of the expansion. Each balloon was assigned a letter and a number. G represented a good balloon, M was a mediocre balloon, and B were the bad balloons. They were randomly assigned a number. The bad balloons were so poorly misshapen that they were not expanded at all. The length before expansion was tested on all G and M balloons. For most of the balloons, the following measurements were also taken: diameter at the resting state, length and diameter when the pressure had reached 11 atm, and the length and diameter of the balloon after the balloon had been expanded and the pressure was released. For the balloons that burst, the thickness in the middle of the balloon and at each were recorded. An asterisk represents balloons that burst during expansion.

Balloon ID:	Length Before:	Diameter Before::	Length During:	Diameter During:	Length After:	Diameter After:
G1	69mm	14.14mm		18.2mm		
G2*	90mm	14.45mm		18.72mm		
G3*	59mm			17mm		
G4*	69mm	11.46mm				
G5	92.5mm	10.92mm		19.30mm		
G6	83.42mm	17.15mm		18.16mm		
G7	93.47mm	14.12mm	120.56mm	17.4mm	109.5mm	15.7mm
G8	86.23mm	13.27mm	104.96mm	16.9mm	97.42mm	16.06mm
M1	85mm	14.52mm	102.84mm	17.4mm	94.35mm	15.64mm
M2*	73.5mm	14.52mm				
M3	127.07mm	14.88mm	148.3mm	18.0mm	135.1mm	16.5mm
M4	123.78mm	14.16mm	151.14mm	16.66mm	138.5mm	15.51mm
M5	80.73mm	11.5mm	108.33mm	15.69mm	100.25mm	13.97mm
M6	76.69mm	14.12mm	96.34mm	17.49mm	88.22mm	15.54mm
M7	88.03mm	15.72mm	100.69mm	16.41mm	94.11mm	15.39mm

Table 5. Balloon Experimental Data-Length and Diameter
Key: G-Good
M-Mediocre
B-Bad
*Denotes balloon burst before all measurements were taken

Balloon ID:	Middle Thickness 1:	Middle Thickness 2:	End Thickness Average 1:	End Thickness Average 2:
G1				
G2*	0.17mm	0.02mm	0.62mm	0.61mm
G3*	0.22mm	0.13mm	0.58mm	0.67mm
G4*	0.01mm	0.09mm	0.76mm	0.47mm
G5				
G6				
G7				
G8				
M1				
M2*	0.08mm		0.20mm	0.13mm
M3				
M4				
M5	0.32mm	0.13mm	0.37mm	0.67mm
M6	0.03mm	0.16mm	0.69mm	0.99mm
M7	0.11mm	0.46mm	0.93mm	0.48mm
B1	0.17mm	0.17mm	0.51mm	0.25mm
B2	0.20mm	0.04mm	0.32mm	0.24mm
B3	0.04mm	0.10mm	0.22mm	0.18mm

Table 6. Balloon Experimental Data-Thickness
Key: G-Good
M-Mediocre
B-Bad
*Denotes balloon burst before all measurements were taken

The next step after testing the capabilities of these balloons was to prepare them for actual deployment within the phantom. First, when the balloons were deflated, they naturally folded into a three-fold shape. In order to combat this, the balloons were filled with water again, until they were in the resting state capacity, and then were wrapped with rubber bands. Once the water was removed, the balloons folded into a more crinkly, less rigid shape.

VI. Phantom Deployment

The phantoms were created from an expandable gel that has a Young's Modulus similar to that of a coronary artery. Young's Modulus is a term that defines the stiffness of a material. The gel used is called "Gel 0" and has a Young's Modulus of 0.248MPa. This gel's stiffness is most similar to the known value of the actual artery, which is 0.39∓0.07 MPa^3 (Claes et al., 2010).

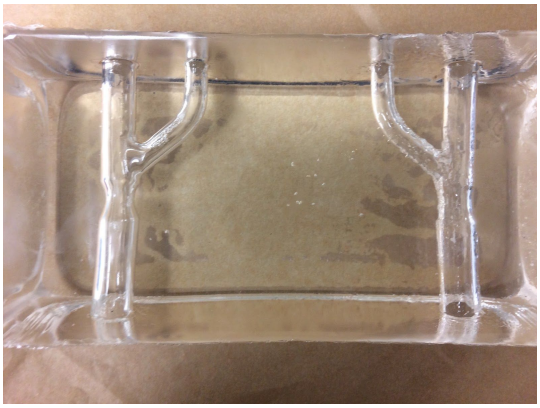

Figure 4. Phantom coronary arteries.

These phantoms are produced by members of our lab group. Data is available and a publication is pending. This method is similar to other methods using ballistic gels (Morrow et al., 2016). In the experiment testing the balloons, a few balloons burst that had potentially been nicked by the metal in the stents. So, before the balloons were placed inside the stents, they were

wrapped in a piece of white copy paper, and then shimmied into the stent. Once the balloon was inside, the paper was removed.

The initial proposal was to test stents in phantoms with no stenosis, and then 25%, 50%, and 75% stenosis. The phantoms take several days to set, so this first test only used the phantom with 50% stenosis. The phantoms were heated with a heat gun in order to ensure maximal visibility during the deployment. Each stent-balloon complex was placed inside the phantom artery in a certain position, so that the area between the second and third metal division was placed right where the side branch artery was connected. The inflator was filled completely up with water, and then connected to the balloon with tubing and the Luer lock. Then, deployment began.

The inflator could not hold enough water to completely deploy the balloon to 11 atm, so the inflator had to be detached midway through deployment, around 6 atm. However, the stent did not seem to expand much after 6 atm, so potentially the calculations were off for creating this model seven times larger than normal. This deployment was repeated three additional times with three different stents, phantoms, and balloons. The results for deployment with 50% stenosis are as follows:

- Trial 1: Stent 1, Balloon G1, Phantom 1
    - The pressure reached 6 atm at its highest point. The Luer lock at the end of the balloon tubing broke off, so this balloon was not able to reach 11 atm. Also, there was not enough water inside the inflator to fully reach 11 atm.
- Trial 2: Stent 2, Balloon G5, Phantom 2
    - The balloon was filled with water to its resting state and was deployed a small amount before placing inside the phantom. Again, the balloon reached 6 atm, but the Luer lock broke off at this point.

- Trial 3: Stent 3, Balloon G6, Phantom 3
    - The balloon expanded completely to 11atm, but then burst after approximately one second.
- Trial 4: Stent 4, Balloon G7, Phantom 4
    - The balloon reached 11 atm, and was able to stay deployed at this point for a significant amount of time.

VII. Future Work

There is still future work to be done on this project. In order to test all possible scenarios, the balloon-stent complex needs to be tested in phantoms with the different variations of stenosis, both 25% and 75%, along with a phantom with no stenosis. To do this, more balloons and stents will have to be made. The balloon-forming machine V2.0 is in current production, but it had not been completed by the publication of this paper. Due to the inconsistencies with version 1 discussed earlier, there are several adjustments that need to be made to the new version. First, the machine needs to be placed at eye-level so that it is easier to see the parasons and move them in and out of the machine. Also, the machine needs a base plate with stoppers around the edges so as to raise the entire machine off of the work surface. The main change that needs to be made is creating a more efficient system to move the parason in and out of the heating unit. At this stage, the idea is to create a "train track" of sorts that can easily move the parason back and forth. There will also be 3D-printed pieces within the heating unit that will stop the parason at the correct point within the heating unit. We also hope to make tapered balloons, which were called for in the initial proposal.

VIII. Conclusion

Coronary artery disease is an ongoing issue that has been an increasing problem, even since 2016 since this project proposal was first created. Bifurcated arteries make interventions

difficult, but we hope that our project will contribute to lower rates of restenosis and more successful operations. There is still work to be done, as technology is rapidly changing and new interventions are made.

IX. References

Antoniadis, A. P., Mortier, P., Kassab, G., Dubini, G., Foin, N., Murasato, Y., … Chatzizisis, Y. S. (2015). Biomechanical Modeling to Improve Coronary Artery Bifurcation Stenting. *JACC: Cardiovascular Interventions*, *8*(10), 1281–1296. doi: 10.1016/j.jcin.2015.06.015

Aoki, J. (2006). Long term follow-up after drug-eluting stent implantation and early experience with endothelial progenitor cell capture stent . Retrieved from https://www.researchgate.net/publication/34707904_Long_term_follow-up_after_drug-eluting_stent_implantation_and_early_experience_with_endothelial_progenitor_cell_capture_stent

Benjamin, E. J., Muntner, P., Alonso, A., Bittencourt, M. S., Callaway, C. W., Carson, A. P., … Virani, S. S. (2019). Heart Disease and Stroke Statistics-2019 Update: A Report From the American Heart Association. *Circulation*, *139*(10), e56–e528. doi: 10.1161/CIR.0000000000000659

Claes, E., Atienza, J.M., Guinea G.V., Rojo, F.J., Bernal, J.M., Revuelta, J.M., and Elices M. (2010). Mechanical Properties of Human Coronary Arteries. *Conference proceedings:…Annual International Conference of the IEEE Engineering in Medicine and Biology Society.* 3792-3795. doi: 10.1109/IEMBS.2010.5627560

Figure 1. Depiction of a Bifurcation Lesion. Reprinted from *BusinessWire* for Tryton Medical, Inc. 2017. Retrieved from

https://www.businesswire.com/news/home/20170306005114/en/Tryton-Medical-Receives-FDA-Approval-Tryton-Side.

Figure 2. Step-by-step Provisional Technique using two stents. Reprinted from "Contemporary Approach to Coronary Bifurcation Lesion Treatment," by F.J Sawaya et al., 2016, *JACC: Cardiovascular Interventions, 9 (18),* 1864. Retrieved from https://www.sciencedirect.com/science/article/pii/S1936879812005572.

Jensen, M., & Timmins, L. J. (2016). AHA Project Proposal.

Louvard, Y., & Medina, A. (2015). Definitions and classifications of bifurcation lesions and treatment. *EuroIntervention*, *11*(V). doi: 10.4244/eijv11sva5

Polyethylene Terephthalate (PET): A Comprehensive Review. (n.d.). Retrieved from https://omnexus.specialchem.com/selection-guide/polyethylene-terephthalate-pet-plastic

Sawaya, F. J., Lefèvre, T., Chevalier, B., Garot, P., Hovasse, T., Morice, M.-C., … Louvard, Y. (2016). Contemporary Approach to Coronary Bifurcation Lesion Treatment. *JACC: Cardiovascular Interventions*, *9*(18), 1861–1878. doi: 10.1016/j.jcin.2016.06.056

Wiley, B. (2017). Oxygen vs. Nitrogen: Laser Cutting Assist Gases. Retrieved from https://www.wileymetal.com/oxygen-vs-nitrogen-laser-cutting-assist-gases/