SYNTHESIS OF POLYURETHANE SHAPE MEMORY POLYMERS

OVER NICKEL TITANIUM WIRE

An Undergraduate Research Scholars Thesis

by

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ABSTRACT

Synthesis of Polyurethane Shape Memory Polymer Foams Over Nickel Titanium Wire.
(May 2014)

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In this work, the synthesis of ultra-low density Shape Memory Polymer (SMP) foams onto a nickel-titanium backbone wire is achieved, optimized, and characterized for the use in an intracranial aneurysm embolization device. The Biomedical Device Lab (BDL) is developing a new type of cerebral aneurysm embolization device that incorporates a high volume filling shape memory polymer foam onto a shape set nickel titanium (nitinol) backbone. This device seeks to improve upon current methods of endovascular treatment for intracranial aneurysms. This work was completed to streamline the current device fabrication protocol, which includes crimping the shape memory polymer over the backbone wire and fixing it in place with epoxy on the proximal and distal ends. This procedure is tedious, time consuming, and has substantial issues regarding foam slippage along the backbone wire.

The key parameters for this project were to achieve substantial adhesion to the wire without disrupting the foams' physical and chemical properties in the vicinity of the backbone wire. The synthesis of SMP foams onto a backbone wire was achieved by selecting and optimizing a coating used on the nitinol wire to ensure proper foam-wire adhesion. Foam chemistry was slightly altered to make lower viscosity solutions to enable the foaming over the necessary length

of wire.

The process of adhering the foam to nitinol wire during foam fabrication culminated in a formalized standard used to synthesize SMP foams onto nitinol wires. Results have shown successful adhesion and low foam densities in the vicinity of the wire. Density ratios of foam adjacent to the wire in comparison to the bulk foam are uniform, signifying little change in foam density. Pore size ratios show similar results indicating very little difference between the bulk and adhered foam. Volume recovery of the SMP foams was found to be acceptable for device incorporation. In conclusion, foam can be synthesized around appropriately coated nitinol wires without major changes to the material properties of the SMPs or to their performance.

DEDICATION

I would like to dedicate this work to my parents, who have encouraged me through this whole process. I wouldn't be who I am today without their continual support and love.

ACKNOWLEDGEMENTS

First and foremost, I would like to thank Dr. Duncan Maitland who convinced me to undergo this project. I have learned more that I ever would have imagined in the past year in his laboratory, and his continuing support and advice is probably the most valuable thing I have gained while at A&M.

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I would like to thank Landon Nash for sitting with me for hours on end trying to explain basic materials concepts and characterization techniques to me when I first entered the lab and had absolutely no idea what I was doing. He has been a great mentor and teacher to me.

Thank you to everyone in the laboratory who answered my unending questions and helped me with samples, new equipment, and editing of my paper. I have sincerely enjoyed the past year with everyone.

Lastly, I would like to thank my family. They are my examples, my rock, and my cheerleaders. I love you.

NOMENCLATURE

SMP .... Shape Memory Polymer

BDL...Biomedical Device Laboratory

PU .... Polyurethane

TEA.. Triethanolamine

HPED ....N,N,N',N'-Tetrakis(2-Hydroxypropyl)ethylenediamine

TMHDI .... Trimethyl-hexamethylene Diisocyanate

IPDI...Isophorone Diisocyanate

Nitinol .... Nickel-Titanium Alloy (Specific)

NCO ....Isocyanate Groups

OH...Alcohol Groups

PTFE ....Polytetraflouroethylene

FOW.. Foam Over Wire

SEM .... Scanning Electron Microscope

DSC ....Differential Scanning Calorimetry

PBS ....Phosphate Buffer Saline

CHAPTER I

INTRODUCTION

Clinical Motivation

A cerebral aneurysm is a weakening of the neurovascular wall that allows localized dilation and ballooning of the artery. The major cause of aneurysms is unknown but small defects of the vascular wall are suspected to be the cause[1]. Correlations between connective tissue disorders, high blood pressure and cerebral aneurysms have also been found. Aneurysms are susceptible to rupturing due to wall thinning, which causes an intracranial hemorrhage. It is estimated that 30,000 aneurysms rupture in the United States every year[1] and approximately 3-5 million people in America have or will develop an aneurysm in their lifetime[2]. Current aneurysm treatments include surgical clipping and the endovascular delivery of platinum coils to embolize the aneurysm[1]. Surgical clipping includes a craniotomy and although proven effective, is extremely invasive[2]. An endoscopic endonasal approach for aneurysm clipping has been successful, but it is also fairly invasive and requires pedicled nasoseptal flap reconstruction after the aneurysm clipping[3].

Endovascular embolization is now the preferred treatment for many patients[4], and the new device concept of the Biomedical Device Lab attempts to optimize this treatment. The current standard for embolization utilizes platinum coils to occlude the aneurysm and promote thrombogensis[5]. Issues with platinum coils include material cost and a significant incidence of recanalization and retreatments due to coil packing over time. Hydrogel coated platinum wires were developed to reduce aneurysm recurrence rates[6] and are the intermediary device between the platinum coils

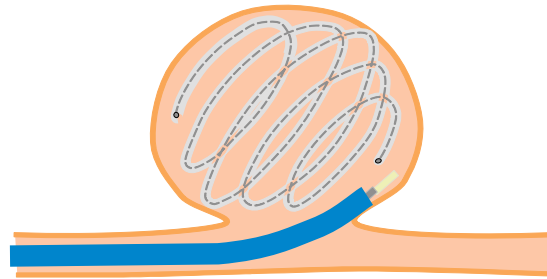embolism treatments and the shape memory polymer coated treatment.

Figure 1: Proposed foam/coil device which intends on using a microcatheter to deliver the device to a sidewall aneurysm and deploy the device while simultaneously actuating the shape memory properties of the foam

The new neurovascular embolism device uses ultra-low density polyurethane shape memory polymer (SMP) foams adhered to a nitinol backbone to occlude the aneurysm[7]. SMPs are a class of smart material that are capable of deforming to a stable secondary shape and recovering to a primary form when exposed to a particular stimulus [7], such as heat. This shape memory property allows for the delivery of a compressed foam to the aneurysm site via micro-catheter and for consistent, high volume recoveries once positioned. This property is demonstrated in Figure 2.
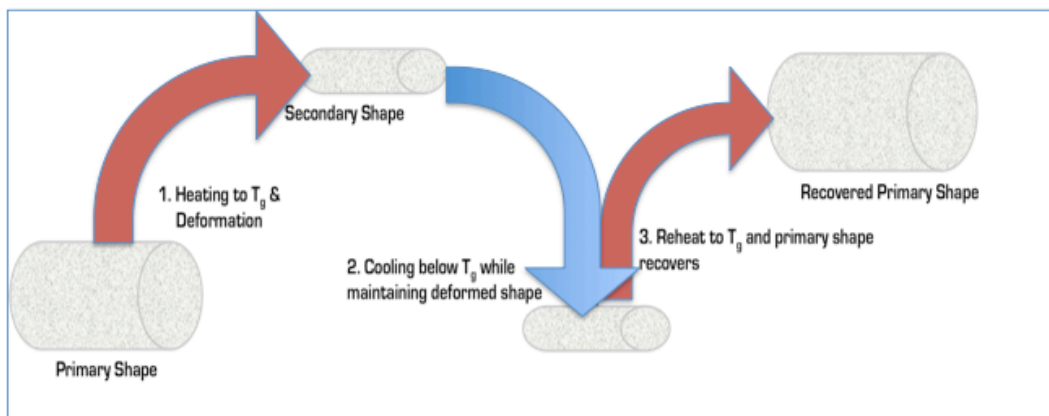

Figure 2: Summary of the shape memory effect

Research Objective

The previous protocol for attaching the SMP foams to the backbone wire was to mechanically crimp and adhere the foam directly to the wire at both ends using epoxy, thus setting the secondary shape of the SMP around the wire. Using this process, the foams had a tendency to slip along the wire and cause multiple problems during delivery of the device to the aneurysm site. For instance, the use of epoxy could be detrimental to the device as a whole because of the possibility for a lack of biocompatibility. Additionally, the use of adhesive increases the minimum compressed diameter of the foam over the wire. This entire process of adhering previously synthesized foam to a wire was extremely tedious and would have required significant optimization.

The proposed process is to synthesize the foams directly over the nitinol backbone wire, while holding the current properties of the foams constant in the immediate vicinity of the wire. The specimen is then cut to the desired diameter using an Excimer Laser or biopsy punch. This eliminates the need to optimize the process of crimping the foam to the wire and alleviates multiple issues within the device design and fabrication, including foam slippage and detachment from the coil.

Preliminary work adding coatings to the nitinol wires for direct foaming was completed to simplify the placement of SMP foam over wire. This research expanded on what has already been discovered and aided in the production of a functional embolic device treatment using shape memory polymer foams synthesized directly onto a nitinol wire and shaped using an Excimer Laser. The axial length of foam/ wire device was approximately 12 cm. The current

foaming process has been refined, and fixtures to optimize the coating and foaming process were created. This was done in order to streamline the manufacturing process to increase the likelihood of this device making it through stringent FDA regulations and ultimately to market. By using this new fabrication protocol, scaling up of the manufacturing of the device for market is much more streamlined instead of having to implementing quality controls at every step. In short, the hope is that a simple, direct application of foam to the backbone wire will streamline manufacture and greatly enhance the speed with which this life saving treatment can be deployed to the general market.

Foam Synthesis

An established protocol for the synthesis of ultra low-density polyurethane shape memory polymer foams was used to create foam for device use[9]. The current method for foam synthesis involves a combination the alcohols triethanolamine (TEA, Sigma Aldrich, St. Louis MO), and N, N, N', N'- Tetrakis (2-hydroxypropyl) ethylenediamine (HPED, Sigma Aldrich, St. Louis MO), in a ratio of 0.32-0.35 to isocyanates to form an NCO premix, or prepolymer. For the purpose of this paper, isophorone diisocyanate (IPDI, TCI America, Tokyo, Japan) with a racemic mixture of 2,2,4-trimethyl-1,6-hexamethyene diisocyanate and 2,4,4- trimethyl-1,6-hexamethyene diisocyanate (TMHDI TCI America, Tokyo, Japan) was used in varying compositions to create the polyurethane (PU) foams. The structure of the alcohol and isocyanate monomers can be seen in Figure 3 below.
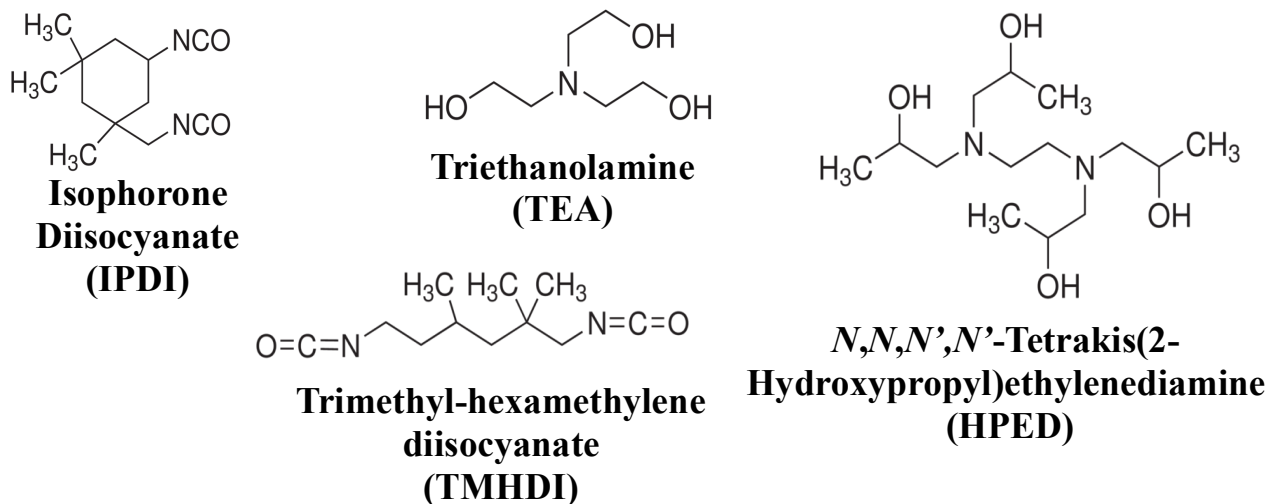

Figure 3: Chemical structures of all monomers used in polyurethane foams and coatings

The range of chemical compositions for foam synthesis used in this experiment can be seen in Table 1.

Table 1: Isocyanate content of the five chemical compositions used in this experiment

Chemical Composition	1	2	3	4	5
IPDI content	0%	5%	10%	15%	20%
TMHDI Content	100%	95%	90%	85%	80%

An isocyanate premix of 32-35% alcohols was allowed to cure for two days in a programmed oven, in which the temperature was ramped to 50°C and subsequently allowed to cool to room temperature. An alcohol premix, containing the balance of remaining OH monomers was created immediately before foaming to react with the excess isocyanates with a 0.96 OH/NCO ratio. The alcohol premix also contained catalysts BL-22 and T-131 as well as the surfactant, DC 5943, for pore stability. Water was added to the OH premix to serve as a chemical blowing agent for the foaming process. Table 2 shows the exact masses of agents added.

Table 2: Exact amounts of accessory chemicals for foaming process of all foam compositions created in this work

	DC 5943	BL-22	T-131	Enovate	Water
Target for one foam	2.8g	0.253g	0.101g	7mL	0.917 g

The OH premix and the NCO premix were combined and mixed for 10 seconds in a speed mixer (SpeedMixer DAC 150 FVZ-K, Flacktek, Landrum, SC), after which the physical blowing agent,

Enovate, was added and the polymer was mixed again for 10 additional seconds. The reaction mixture was carefully transferred into a large bucket containing the coated wires, (See Wire Orientation) which were previously positioned in the bucket, and placed in an oven. As the foam reacted, it experienced about 30x volume expansion and took the primary shape of the container it was reacting in. The foam was allowed to react for 20 minutes at 90°C, after which time the foam was removed from the oven and allowed to cool to room temperature under a fume hood.

Once cooled, the buckets were slightly deformed to release the foams from the container. The wires attached through small holes in the bottom were released, the tape discarded. At this point the foams were simply lifted out of the bucket. The foams were cut in half using the Proxxon Thermocut Hotwire Cutter.

Coating Optimization and Adhesion

The wires required an optimized coating for proper foam adhesion. Test coatings were then ordered from Coatings2Go.com and tested on multiple samples. Without any etching process, a silicone coating, a hydrophilic coating, and a polytetrafluoroethylene (PTFE) coating were applied onto the 0.0035" diameter nitinol wire using a KimWipe. This process was repeated for acid etched wires, which were etched using a mixture of 1:3 ratio of 6M nitric acid and 6M hydrochloric acid. Lastly, a thermoset neat polymer with the same bulk chemical composition as the foam was used as a wire coating. Bare, untreated, and acid etched wires were used as controls for foam adhesion.

Neat coatings were created inside a humidity-controlled chamber in order to reduce isocyanate-reactions with ambient moisture. The four monomers were mixed in stoichiometric amounts with

varying IPDI content congruent to the foam to be created. The monomer target values for all compositions can be seen in Table 3 below.

Table 3: Stoichiometric amounts of monomers for varying IPDI Content in Neat Polymers

0% IPDI	Sample ID		130625AMNCMB01
Components	Target for 1 foam (g)	Scale	Total target value (g)
HPED	9.191	0.25	2.298
TEA	3.080	0.25	0.770
TMHDI	19.729	0.25	4.932
IPDI	0.000	0.25	0.000

5% IPDI	Sample ID		130625AMNCMB01
Components	Target for 1 foam (g)	Scale	Total target value (g)
HPED	9.175	0.25	2.294
TEA	3.074	0.25	0.769
TMHDI	18.710	0.25	4.677
IPDI	1.041	0.25	0.260

10% IPDI	Sample ID		130625AMNCMB01
Components	Target for 1 foam (g)	Scale	Total target value (g)
HPED	9.159	0.25	2.290
TEA	3.069	0.25	0.767
TMHDI	17.694	0.25	4.424
IPDI	2.078	0.25	0.520

15% IPDI:	Sample ID		130625AMNCMB01
Components	Target for 1 foam (g)	Scale	Total target value (g)
HPED	9.143	0.25	2.286
TEA	3.063	0.25	0.766
TMHDI	16.682	0.25	4.170
IPDI	3.112	0.25	0.778

20% IPDI:	Sample ID		130625AMNCMB01
Components	Target for 1 foam (g)	Scale	Total target value (g)
HPED	9.127	0.25	2.282
TEA	3.058	0.25	0.765
TMHDI	15.673	0.25	3.918
IPDI	4.142	0.25	1.036

Once the chemicals were massed and measured, the polymer solution was then mixed for one minute, checked for homogeneity, and mixed again for one minute. The wires to be coated were

strung into a structure as seen in Figure 4, and the polymer coatings were wiped on by hand using a Kim-Wipe.

Figure 4: Structure for coating wires. Wires were strung horizontally across this scaffold and secured on either end; coatings were then be wiped on by hand.

Wire Orientation

To attain ideal foaming, the wire orientation also required optimization. Wires were strung in one bucket transversely to the foaming direction, while the second bucket had wires axial to the foam. This tested the interactions of the foam and wires to determine the least disruptive orientation to foaming. Once determined, an attachment to the foaming vessel was created in order to optimize foam/wire adherence that maintained the stability of the wire.
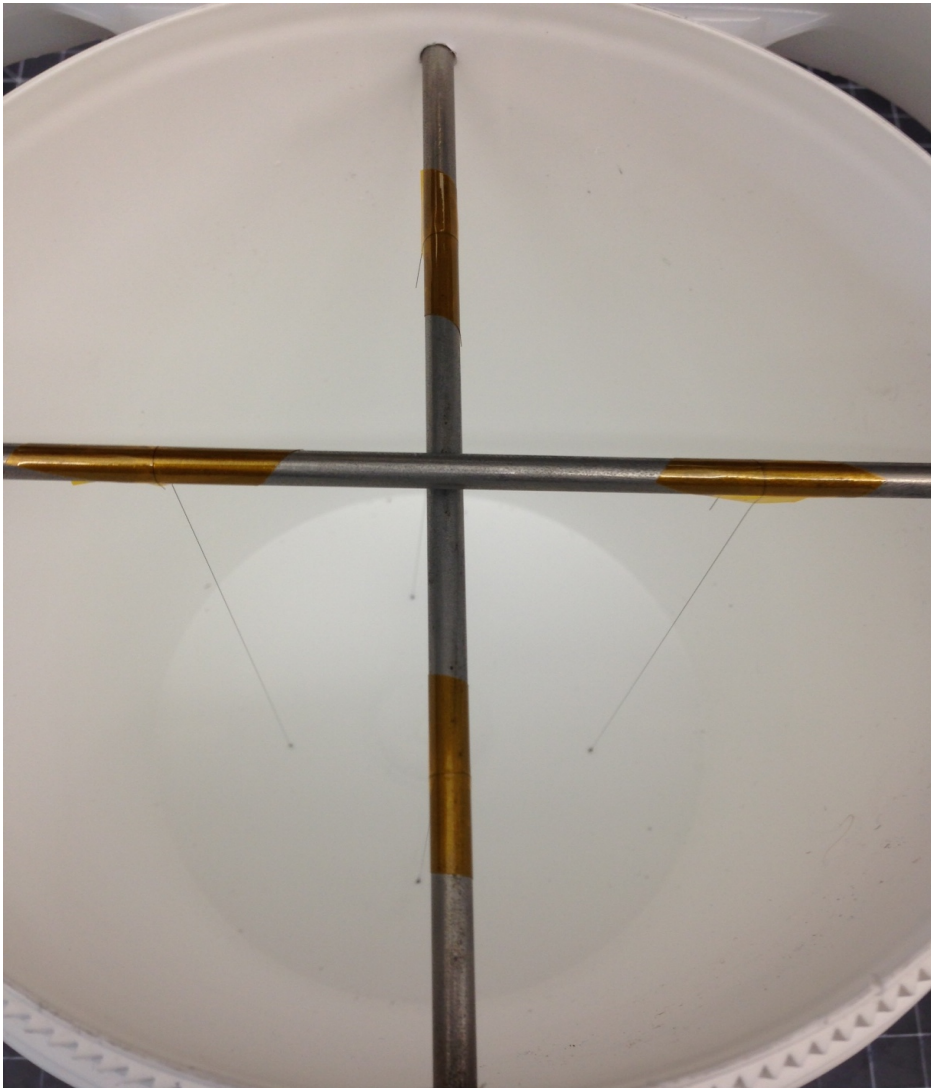
Figure 5: Final foaming vessel, with wires in place.

Microscope Imaging

Microscope imaging was used to determine the homogeneity of the foam surrounding the wire and quantitative data such as density and pore size. Dry volume expansion was then used to further quantify the homogeneity of the foams[12]. After foam synthesis, the wires were cut out of the foam using a Proxxon Thermocut Hotwire Cutter to remove extraneous foam. The sample

was then imaged using a Leica long-range microscope with Jenoptic camera system and the foam morphology surrounding the wire was used to determine the useful length, with a goal of 12 cm, the original (and longest) possible length of the device. 12 cm was a parameter derived from the length of the final geometry of the device, a coil of nitinol wire in the aneurysm. Refer back to Figure 1.

Density Calculations

The ratio of the foam density surrounding the wire to the density of the bulk foam was measured to determine foam homogeneity in the vicinity of the wire. Bulk foam density was calculated by cutting three small squares from the center of the foam, far away from the wires to ensure minimal interference with the general structure and pores of the samples. The length, width, and height of each of the three squares were measured three times and the averages of each dimension were taken. These averages were used to calculate the volume of the foam sample. The sample was then massed and the density was found using Equation 1.

$$\rho = {}^{m}/_{V} \hspace{4cm} \text{Equation (1)}$$

Where ρ is the density, m is the mass, and V is the volume. This process was then repeated for samples taken within 2 mm of the wire for three wires in the foam. The process used to measure the cube volume described above was repeated and each cube was massed. The calculated density was then averaged and then the bulk foam density was divided by the average wire-foam density, resulting in the ratio of the two foam types, as described by Equation 2.

$$Density\ Ratio = {}^{\rho_{Bulk}}/_{\rho_{Wire}} \hspace{3cm} \text{Equation (2)}$$

Where *Density Ratio* is the reported value, ρ_{Bulk} is the bulk foam density, and ρ_{Wire} is the wire foam density.

Pore Size Calculations

Cell images were taken using a Leica long-range microscope with Jenoptic camera system from a sample of foam approximately one cell thick cut transversely to the axis of foaming. The diameter of a specific cell was measured from the collected images, and the diameter of 15 cells was used for the analysis. For non-circular cells, diameters were taken at the longest point between two walls. Calculations assume perfectly circular cell sizes. Pore sizes were calculated using Equation 3:

$$\text{Pore Size} = \frac{\pi}{4}d^2 \hspace{4cm} \text{Equation (3)}$$

Where d is the measured diameter of the cell.

Volume Recovery In Air

Cylindrical samples with a diameter of 6mm and a height of 4 cm were cut from the bulk foam, making sure that the wire was embedded along the axis of the sample. The foams were radially crimped using an ST150-42 Machine Solutions stent crimper to the smallest possible diameter. The secondary morphology was set by maintaining the samples at 100°C while in the primary shape for 20 minutes, then crimping to the smallest possible diameter and subsequently cooling the samples back to room temperature. An image was taken using the Leica long-range microscope with Jenoptic camera system and analyzed for the diameter using Image J software. The samples were actuated at 100°C for 20 minutes in an oven, and allowed to cool to room temperature. Once cooled, the samples were again imaged and analyzed for the final diameter. The volume recovery was calculated using Equation 4.

$$V_E = (^{D_r}/_{D_c})^2 \hspace{4cm} \text{Equation (4)}$$

Where V_E is the volume expansion, D_r is the recovered diameter, and D_c is the crimped diameter.

This was repeated for 5 samples.

Scanning Electron Microscope Images

Scanning Electron Microscope (SEM) images were taken of two samples of wire. The first sample was the uncoated, 0.0035" nitinol backbone wire. The second sample was the same nitinol wire with the addition of a neat polymer coating. The resulting images were analyzed with ImageJ Software to determine the overall change in diameter caused by the addition of the neat polymer coating.

CHAPTER III

RESULTS

Foam Synthesis

Foam Synthesis was completed on a range of chemical compositions (See Table 1). It was noted that as IPDI content increased (15% IPDI and 20% IPDI), the successful length of foam along the wire was lower when holding all other variables constant. The viscosity of the prepolymer increased with increasing IPDI content and resulted in a more viscous reaction mixture than lower IPDI concentrations as the foam progressed up the wire. To account for the increase in viscosity, the ratio of OH/NCO prepolymer was decreased from 0.35 to 0.32. This change produced for a longer successful foam length along the wire as determined by qualitative imaging. A successful foam can be seen below in Figure 6.

Figure 6: Successful foaming vessel, testing two preliminary ways to secure the wires.

It was also discovered that the lower IPDI content foams (0% and 5% IPDI) should have a shorter mixing time than higher IPDI content foams after the addition of the Enovate. The lower IPDI content lends to a lower viscosity prepolymer compared to higher IPDI concentrations (see Figure 1, structure of IPDI). The less viscose foam mixture required less mixing to achieve homogeneity, and rapidly expanded in size. The original 10 second mixing time was reduced to 5 seconds, and this change resulted in greater bulk homogeneity in foam composition, as shown in Figure 7.
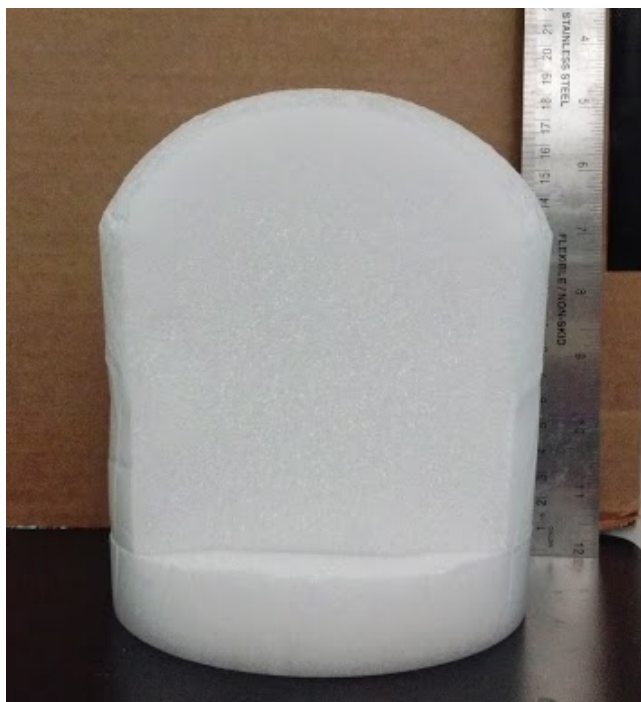
Figure 7: 20 % IPDI Homogenous Foam Sample, Ideal result for all bulk foams

Two different methods of securing wires were tested, shown in Figure 3, in order to determine the best method to attach wires to a foaming vessel. We determined that the top of the foaming vessel needed to secure the coated wires, eliminating as much lateral motion as possible and to

allow gaseous escape during the foaming reaction. Attaching wires to the bucket handle as seen on the left in Figure 3, allowed for forward/ backward movement from the handle, and was not adequate for our purposes. The concept on the right was tedious and wasteful because it required taping spatulas to the top of the foaming bucket. From the given constraints, and the desire to be able to foam over many wires at once, the final structure, as seen in Figure 8, was created with the goal of securing the coated wires to the foaming vessel.
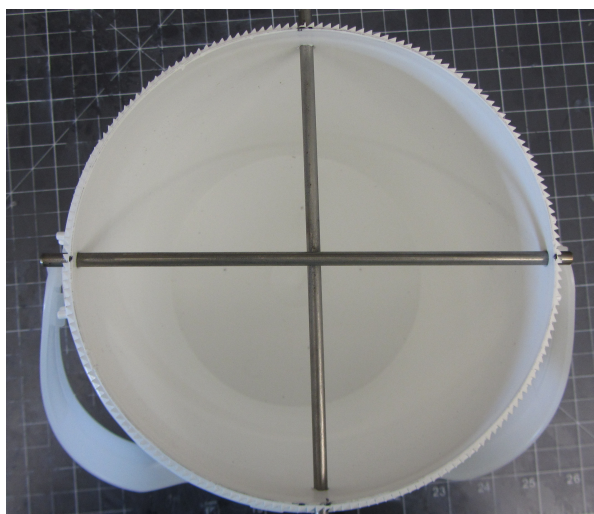
Figure 8: Bucket with upper structure to attach wires.

1mm diameter holes were cut in the bottom of the 2L bucket, 1.5" from the center (halfway between center and outer diameter) at 90° angles from one another. This allowed four wires to be fed through the bottom of the bucket and taped down using Kapton heat-resistant tape. The wires were then pulled taught through the bucket and attached to the steel bars, seen in Figure 8, using the Kapton tape. Figure 5 shows the final structure with wires in place.

Coating Optimization and Adhesion

Multiple coatings were tested in order to optimize foam-wire adhesion, including uncoated (as a control), PTFE, Hydrophillic, silicone, and neat SMP. When uncoated wires were placed in the foaming vessel and foam was synthesized directly onto them, large caverns in the foams surrounding the wires were created. This was due to contrasting chemical compositions of the nitinol wire and PU foams. The silicone, PTFE, and hydrophilic coatings were used to coat the 0.0035" wire following the directions provided by the company. In Figure 9 below shows the qualitative results of the preliminary coatings.
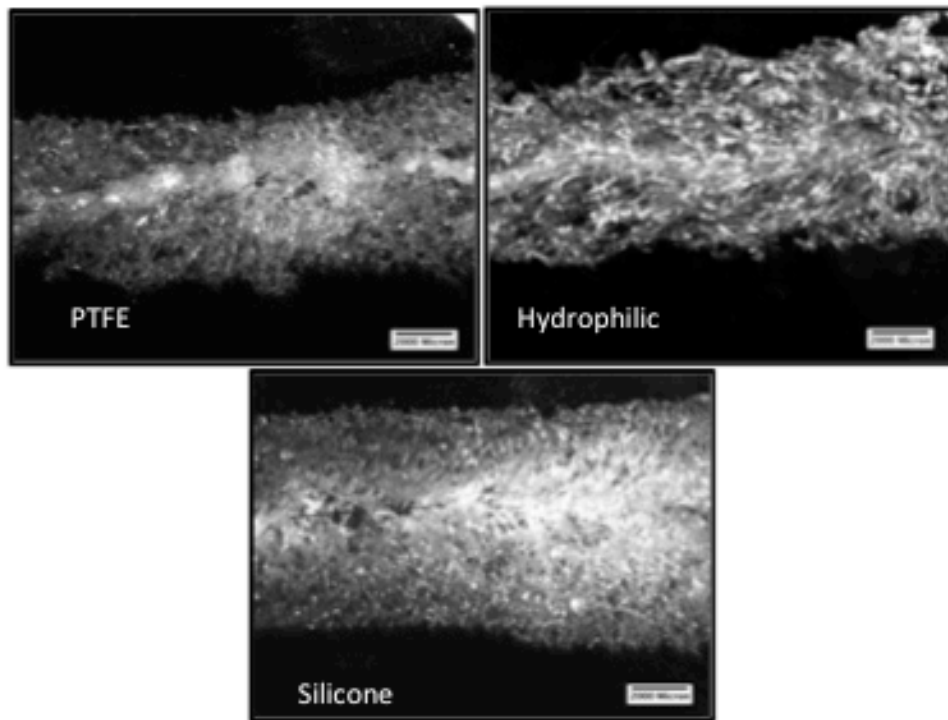
Figure 9: Images of the three preliminary coatings for foam- wire adhesion

It can be seen from each image that the homogeneity of the foam is severely compromised in the

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immediate vicinity of the wire. From this, we determined that the coating of the wire should have an almost identical chemical composition as the foam. Therefore thermoset neat polymer was used as a coating. SEM Images of the uncoated wire can be seen in Figure 10.
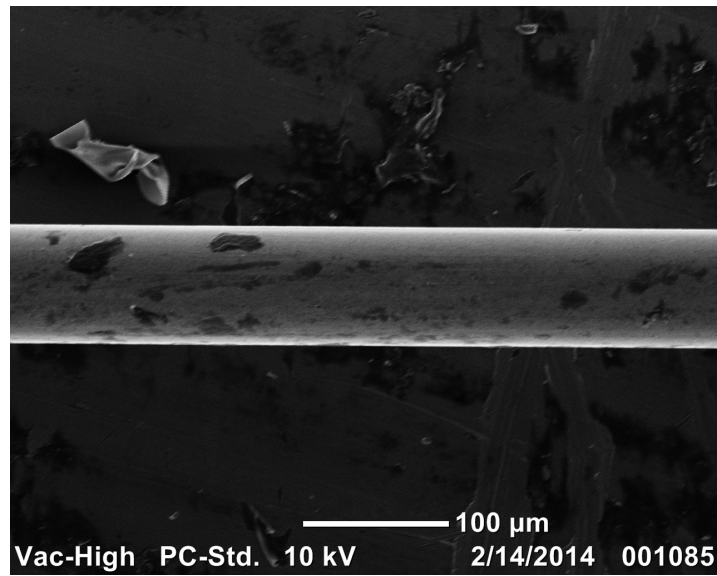

Figure 10: SEM image of an uncoated nitinol backbone wire

An SEM image of the neat polymer coated wire can be seen in Figure 11. The polymer formed an uneven distribution of the polymer along the wire. We later discovered that uneven coatings actually increased homogenous foam adhesion due to the expansion of the foam as it progressed up the wire.
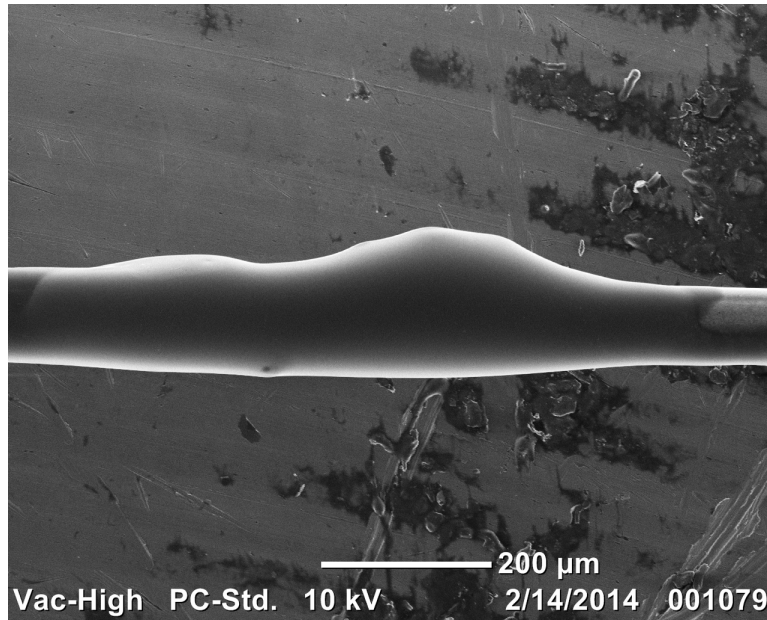
Figure 11: SEM image of a thermoset neat polymer coated nitinol wire.

Additionally, the uneven adhesion caused a varying change in diameter of the wire from the neat polymer. The original diameter of the wire was 0.0035" whereas the highest recorded diameter after two neat polymer coatings was 0.0069". This was almost double the diameter of the wire and could cause significant issues when crimping the foam around the wire because the crimped device diameter should ideally be under 0.016' to accommodate the dimensions of human catheters.

Wire Orientation

At least 4 attempts at wire orientation inside the buckets were foamed and it was determined by inspection that the transverse wires disrupted the foaming process significantly more than the vertical wires. There was a higher probability that the foam would split immediately above transverse placed wires, resulting in poor foam coverage above the wire, as shown in Figure 12.
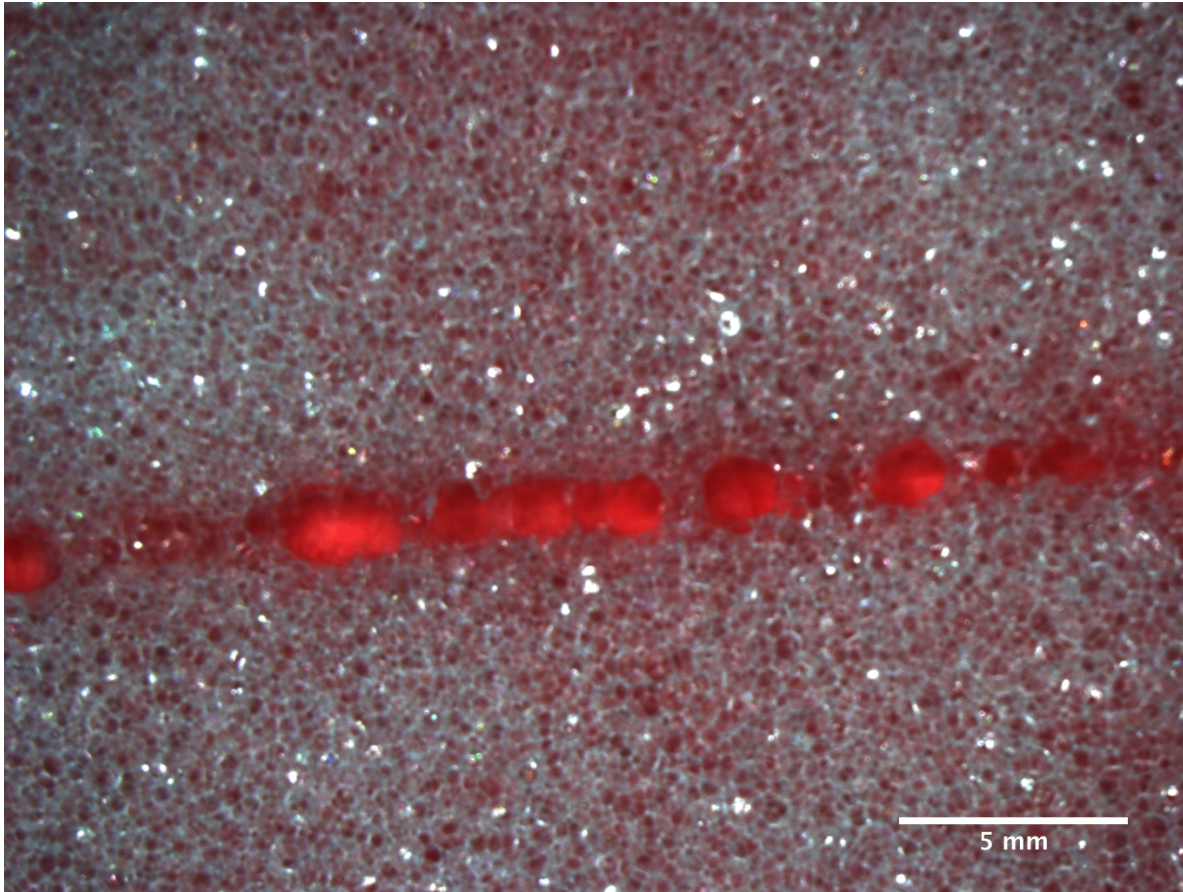
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Figure 12: Transverse image of bulk foam defect caused by transverse wire orientation

Microscope Imaging

Microscope images were used to determine the quality of adhesion of the foam to the nitinol backbone wire. Figure 13 shows a coated wire with adequate adhesion and little foam disruption compared to the previous coating used.
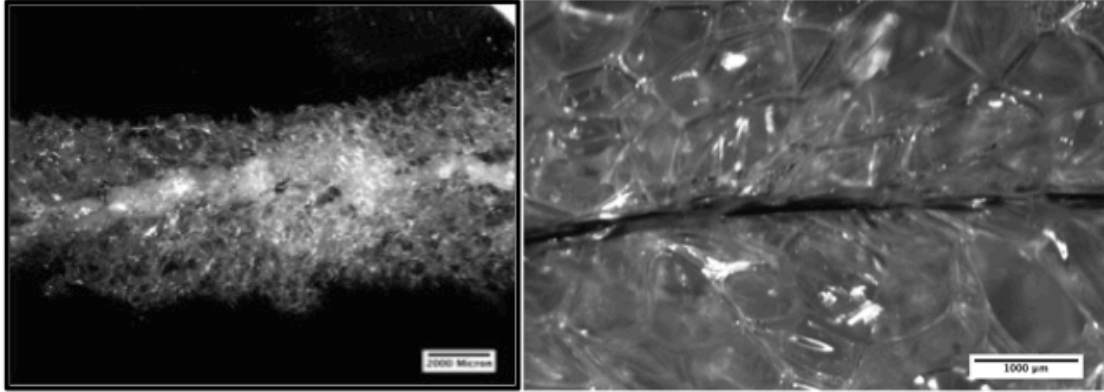
Figure 13: Microscope images of adequate foam-wire adhesion

The microscope camera was also used to record images of the overall FOW structure. The specimen seen in Figure 14 was cut to a diameter of 2.5 mm from the bulk foam using an Excimer Laser.
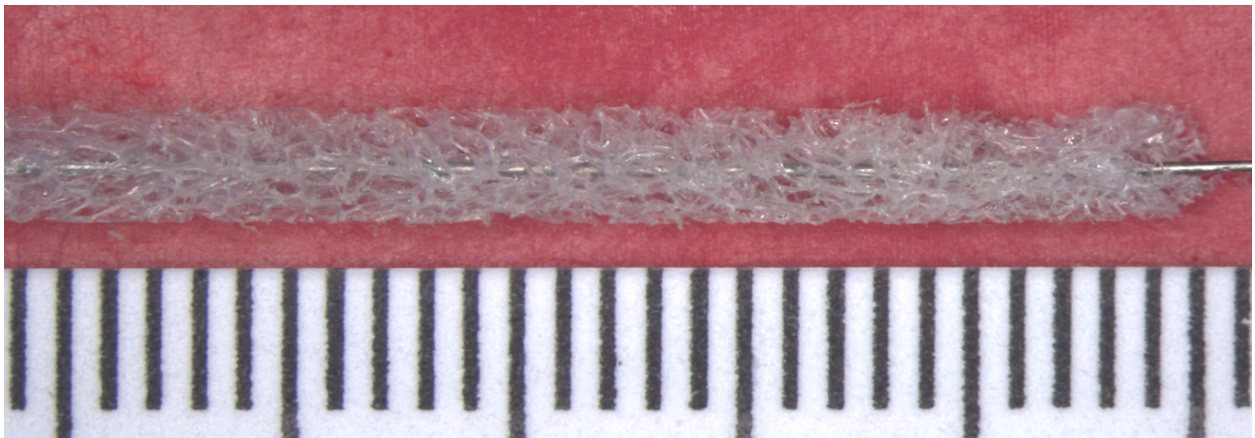

Figure 14: Large scale foam-wire adhesion cut from foam using an Excimer Laser

Density Calculations

The results of the density calculations are summarized in Table 4 below.

Table 4: Results of foam density calculations

Composition	Bulk Density (g/cm^3)	FOW Density (g/cm^3)	Ratio
0% IPDI	0.0107	0.0113	1.0622
5% IPDI	0.0108	0.0109	1.0141
10% IPDI	0.0127	0.0111	1.0207
15% IPDI	0.0120	0.0111	0.9662
20% IPDI	0.0092	0.0093	1.0075

The bulk density was the foam density calculated near the center of the foam, where no wires are present. The foam over wire (FOW) density was calculated using foam taken within 2 mm of the wire. The ratio calculated is the FOW density to the bulk density. The majority (4 out of 5) of the density ratios were greater than one, implying that the foam surrounding the wires was slightly denser than the density of standard foams of the same composition. This was to be expected since the wire causes an imperfection in the foaming area, causing the foam to congregate more around the wire. Maintaining low density in the vicinity of the wire was of paramount importance because it relates to smaller device diameters when crimping. Since the ratio of densities was only slightly larger than one, this parameter was met.

Pore Size Calculations

The data acquired from the pore size experiments are summarized in Figure 15.
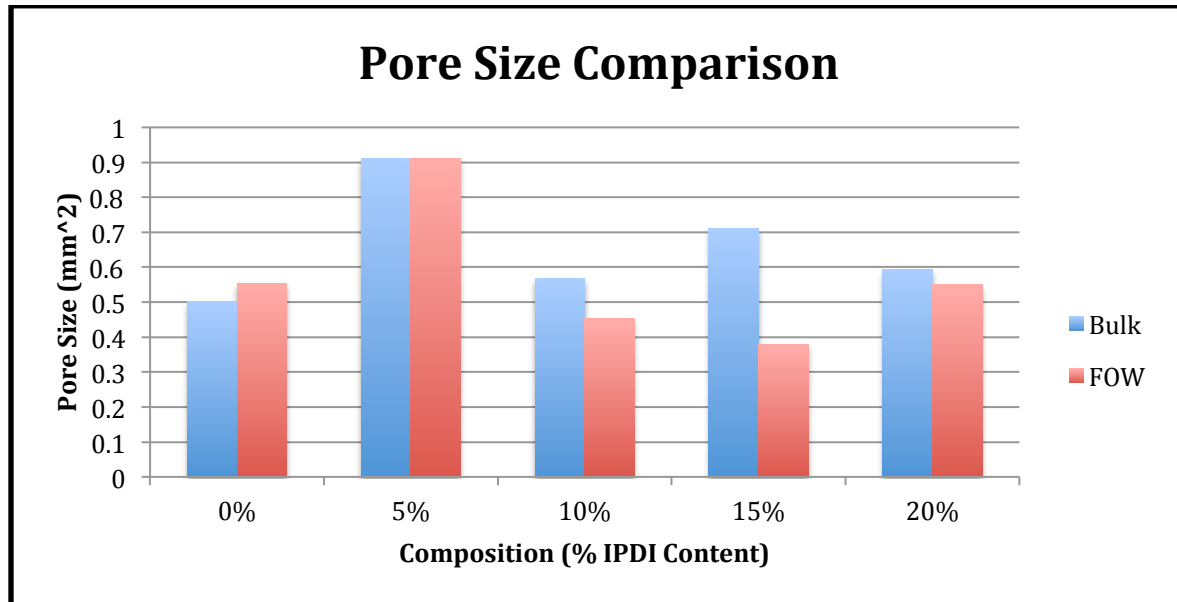

Figure 15: The results of the foam over wire pore size experiment separated by IPDI content, compared to the bulk pore size

The pore size data indicates that there were slightly smaller pores in the FOW samples for the majority of compositions, with the largest difference being the 15% IPDI composition. However, we noted that this composition had irregular data among all the experiments performed. Overall, as expected, pore size decreased slightly in the vicinity of the wire. However since this decrease was minimal, it shouldn't have a significant impact on the device as a whole.

Volume Recovery In Air

The results of the volume recovery experiments in air are summarized in Figure 16 below.
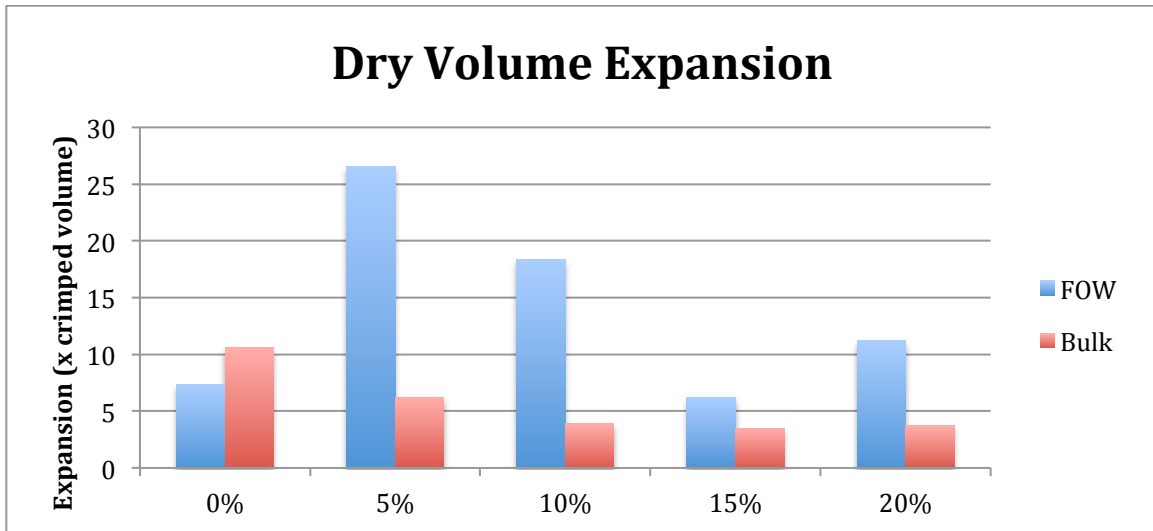

Figure 16: Dry volume expansion data, as compared to bulk foam

The data suggested large variability with possibly of decreasing volume recovery with increasing IPDI content. The data was skewed possibly due to the variability of foam quality around wire, and the position of the wire relative to the center of the foam. When cutting the foam with the biopsy punch, it was difficult to place the wire directly in the middle of the cylinder. The data would have been more accurate if all the samples were cut using an Excimer laser, ensuring the nitinol backbone wire was centered within the foam cylinder. The dry volume expansion data also suggested that adhered foam-wire samples may have better volume expansion than their bulk foam counter-part samples, which is excellent for use of this technology in the overall device. It is also important to note that dry volume expansion behavior was not entirely representative of the clinical uses of this material. Future expansion tests will be conducted in a heated water bath to better represent the aqueous vascular environment.

CHAPTER IV

SUMMARY AND CONCLUSION

Conclusions

This study characterized the efficiency of a new protocol for attaching a shape memory polymer foam to a nitinol backbone for applications in aneurysm occlusion. This was done through qualitative imaging as well as quantitative comparisons of the pore size, density, and dry volume recovery of the newly created specimens to the previous methods. With pore sizes and densities comparable to previously created foams, this change in device fabrication shows promise for future use. The ratio of bulk foam to foam over wire foam is nearly one in all cases, indicating little to no change in the ultra low-density nature of the polymers. Foam over wire pore sizes are comparable to their bulk foam counterparts, indicating little change in the nature of the foams. Volume expansion shows promise with higher dry volume expansion than other bulk foam pieces, but will require further investigation in order to draw a conclusive trend on the data. The change in fabrication protocol was implemented along a wide range of foam compositions, and should be able to be implemented for any new foam composition that the aneurysm occlusion device may see in the near future. Although there is still a large amount of research to be done into the expansion and characterization of the foam over wire device, this protocol change appears to be suitable for the aneurysm occlusion device as a whole. Overall this discovery created a seamless interface between two device components that may allow for a much more rapid prototyping and manufacturing process of the medical device. By streamlining this process, a significant step towards manufacturability has been reached.

Future Work

To ensure that this is an appropriate change and seamless interface of device components, more research should be done in specific areas to fully verify the efficacy of the synthesis of foam directly onto the wires. Differential Scanning Calorimetry (DSC) should be used to confirm that the wet and dry glass transition temperatures of the foam over wire device are similar to that of the previously synthesized foam devices. More research should also be done in the area of expansion, including a larger sample size for the dry volume expansion data. Also, samples should be created in a different manner to ensure homogeneity around the wire. This process should then be repeated in water or phosphate buffer saline (PBS) in order to ensure that volume expansion will remain high under physiological conditions.

REFERENCES

[1] Cerebral Aneurysm Fact Sheet. *National Institute of Neurological Disorders and Stroke.* [Online] September 14, 2011. [Cited: August 4, 2013.]

[2] What You Should Know About Cerebral Aneurysms. *American Stroke Association*. [Online] April 11, 2012. [Cited: September 5, 2013.]

[3] Anand V. Germanwala, M. and M. Adam M. Zanation (2011). "Endoscopic Endonasal Approach for Clipping of Ruptured and Unruptured Paraclinoid Cerebral Aneurysms: Case Report." Neurosurgery.

[4] Molyneux A, Kerr R, Stratton I, et al, for the International Subarachnoid Aneurysm Trial (ISAT) Collaborative Group. International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured aneurysms: a randomised trial. Lancet 2002; 360: 1267–74.

[5] Molyneux AJ, Kerr RS, Birks J, et al, for the ISAT Collaborators. Risk of recurrent subarachnoid haemorrhage, death, or dependence and standardised mortality ratios after clipping or coiling of an intracranial aneurysm in the International Subarachnoid Aneurysm Trial (ISAT): long-term follow-up. Lancet Neurol 2009; 8: 427–33.

[6] Philip M White, S. C. L., Anil Gholkar, Robin J Sellar, Hans Nahser, Christophe Cognard, Lynn Forrester, Joanna M Wardlaw (2011). "Hydrogel-coated coils versus bare platinum coils for the endovascular treatment of intracranial aneurysms (HELPS): a randomised controlled trial." Lancet 377: 1655-62.

[7] Ward Small, I., Pooja Singhal, Thomas S. Wilsona and Duncan J. Maitland (2010). "Biomedical applications of thermally activated shape memory polymers." Journal of Materials Chemistry.

[8] Marilyn Brooks, et al (2013). "Effects of Isophorone Diisocyanate on the Hydrophobicity of Shape Memory Polymers for Cerebral Aneurysm Treatments" Poster presented at undergraduate summer research group poster session, College Station, Texas.

[9] P.Singhal, et al (2013). "Low density biodegradable shape memory polyurethane foams for embolic applications." Acta Biomaterialia.