DISLOCATION STUDIES ON 8MM PDA DEVICES IN RIGID WALLED MODELS

An Undergraduate Research Scholars Thesis

by

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Submitted to the Undergraduate Research Scholars program at
Texas A&M University
in partial fulfillment of the requirements for the designation as an

UNDERGRADUATE RESEARCH SCHOLAR

Approved by Research Advisor: Dr. Duncan Maitland

May 2019

Major: Biomedical Engineering

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ABSTRACT

Dislocation Studies On 8mm PDA Devices in Models

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Patent ductus arteriosu is a condition wherein the ductus arteriosus, the natural port between the aorta and pulmonary artery during canine fetal development, fails to spontaneously close shortly after birth. The post-natal patent duct allows left to right shunting of the blood that sparks a blood volume overload into the left ventricle of the heart and excess blood flowing into the lungs [1]. If not promptly treated, this can lead to complications such as cardiac arrhythmias, heart failure, and in the worst case, death.

The research objective of this study is to investigate the ability of an occlusion device to remain stationary in an in vitro model of the ductus arteriosus under both physiological resting and accelerated blood pressures compared to current market devices. Current results indicate that, compared to the other current patent ductus arteriosus treatment options, the nitinol foam cage device is suitable at remaining stable.

ACKNOWLEDGEMENTS

I would like to thank my Research Advisor Dr. Duncan Maitland, and my lab mentors Dr. Mark Wierzbicki and Dr. Brandis Keller for their guidance and support throughout the course of this research.

NOMENCLATURE

PDA	Patent Ductus Arteriosus
NFC	Nitinol Foam Cage
SMP	Shape Memory Polymer
WA	Wide Ampulla
MDD	Minimal Ductal Diameter
ACDO	Amplatzer Canine Duct Occluder

CHAPTER I

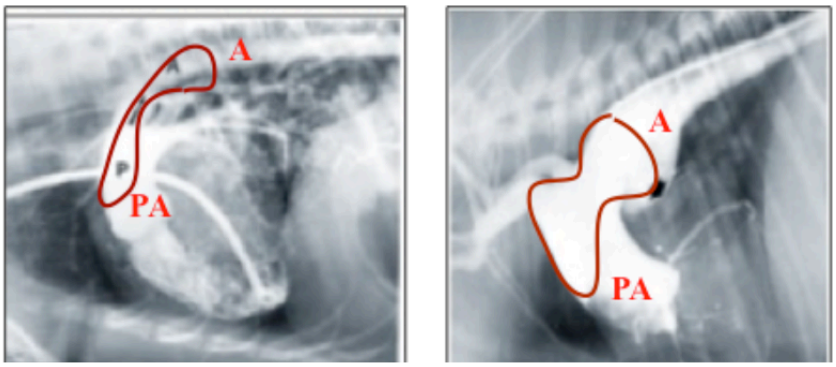
INTRODUCTION

The ductus arteriosus is the vascular structure that connects the proximal descending aorta to the roof of the main pulmonary artery during canine fetal development [6]. After birth, the vessel spontaneously closes due to increased arterial oxygen tension, allowing blood to flow to the now newly inflated lungs.

In utero, the canine fetus does not require 100% of the lung to function normally, as blood is mostly shunted right to left from high resistance in cardiopulmonary circulation [9]. Patent ductus arteriosus, or PDA, occurs when the duct fails to close just after birth which allows blood volume overload into the left ventricle of the heart and excess blood flowing into the lungs [8].

PDA accounts for about 30% of all congenital cardiovascular diseases observed in canines each year. Both canine weight and state of the cardiovascular health can contribute to variations in severity of the issues that arise from this disease. However, complications are more likely to manifest later in life, such as cardiac arrhythmias, congestive heart failure, and in the worst case, death [3].

The most common cases of PDA in canines occur in the Tapered Cylinder (IIA) and Tapered Cone (IIB) shapes of the ductus arteriosus as shown **Figure 1.**



[8] **Figure 1**. Tapered Cylinder and Tapered Cone canine morphologies
A = Aorta
PA = Pulmonary Artery

Treatment options include both invasive and minimally invasive techniques. The first is surgical ligation, a process in which the ductus is literally sutured and closed using ligatures such as sutures [8]. It is an extremely expensive and invasive procedure, a burden on both owner and canine. The second is the Amplatzer Canine Duct Occluder (ACDO), a trans catheter device designed to create cross sectional overage to the duct in order to completely occlude flow. The ACDO device is highly successful at remaining stable, but is also cost prohibitive for pet owners.

While the ACDO is effective, there have been very few investigations launched to study the variations of device size, migration, and ease of delivery using the technique of catheter occlusion [1]. This has led to the development of a third treatment option, the Nitinol Foam Cage (NFC) device used in this study, designed to remain stable under normal and accelerated physiological conditions.

The research conducted in this study will the effectiveness of this occlusion device (under various forces and pressures), to remain stationary in a mock ductus arteriosus configuration. The ductus arteriosus is an area in the cardiovascular system

often exposed to both extremely high and fluctuating flow. It would be ideal for the implanted device to be able to experience these pressures and remain stable in the body.

This will be done using a peristaltic flow loop set up to imitate the steady blood flow rate in the body. A motor will provide the driven flow and 2 pressure transducers will measure and track the pressure gradient across the device and model. gradient across the device and model. The mobile behavior of the device will be observed and recorded over time.

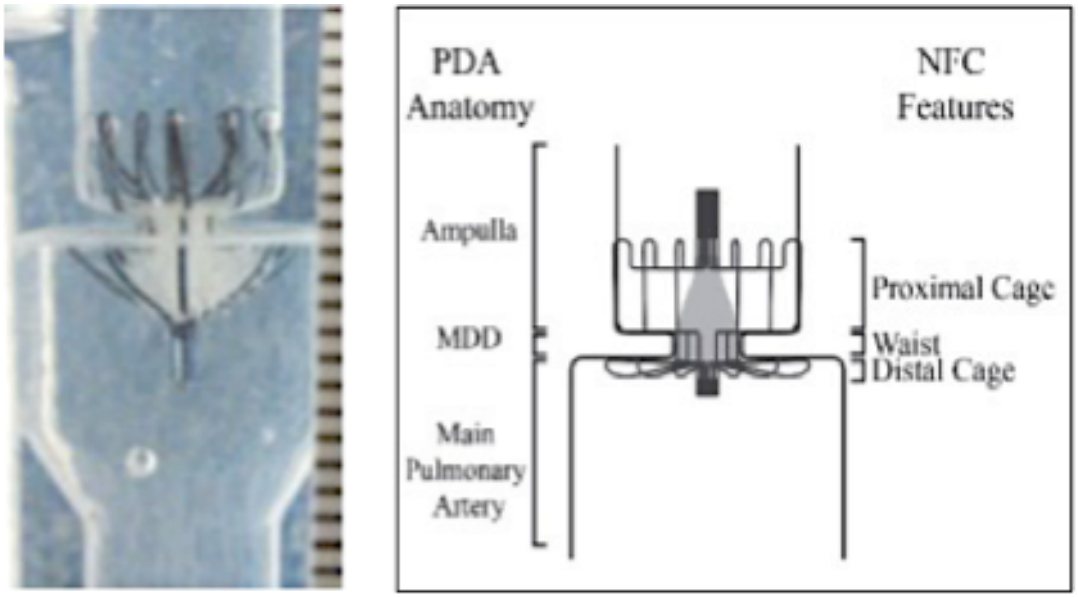
The expected outcomes of this research study should be a series of tests proving how varying forces and pressures could compromise the secures position of the deployed device in the model, and hopefully provide a demonstration of the device's ability to remain stable under external stresses.

CHAPTER II

METHODS

Device Fabrication

The nitinol foam cages (NFC) were fabricated by cutting ten radial slots into a nickel titanium alloy tube using an Excimer laser [5]. The tube was 5/8" long, with a 0.044" outer diameter and 0.041" inner diameter, with 0.002" wall thickness. The tubes were then cleaned of debris and soaked in isopropyl alcohol. A custom designed shape setting fixture was then used to compress the tube, allowing the individual struts to expand out into the desired cage shape, shown in Figure 2. Once the tube was fixed into the final shape, the entire mold was annealed in a furnace at 550 °C for 25 minutes.



[**5] Figure 2** shows a sketch of the device in relation to the model

Foam Preparation

The NFC device employs shape memory polymer foam (SMP) mechanical property modifications to improve upon stability and foam capacity [5]. The SMP is polyurethane foam, which makes for better capability to occlude flow across the NFC device. In order to make the foam pieces that are deployed into the device, a large piece of "raw" foam is cut to a desired size and put through two mechanical reticulation processes to open the pore membranes for flow.

The foam was then cut into cylinder sand twisted onto a steel wire. The foams were then crimped at 100 degrees Celsius, deforming them into a secondary shape that is much smaller than the original configuration. Cooling the foams at 0 degrees Celsius will allow them to hold this secondary shape, before being loaded into to the NFC devices to be used during . The "crimped" form allow for easy catheter delivery, however prior to starting tests, the foam was allowed to expand completely within the device while in water.

The proximal side of the device anchors the foam to the side of the model, and the distal side allows for device positioning and security. A laser welder was then used to weld a threaded end piece to the proximal side of the NFC, as well as a distal metal cuff to provide a barrier for the foam to be inserted later and provide visualization under fluoroscopy.

Model Construction

Ampulla morphology and size can vary from canine to canine. The most common cases of PDA in canines occur in the Tapered Cylinder (IIA) and Tapered Cone (IIB) shapes. Three different ductal morphology models were used to represent PDA in the experiments. They were based on both the normal physiological configuration of the duct

(4 mm diameter duct), and an oversized shape (6.5mm diameter duct). These included a cylindrical ampulla (IIA), conical ampulla (IIB) and wide ampulla (WA) model [5]. Each shape is outlined in **Figure 3** below.

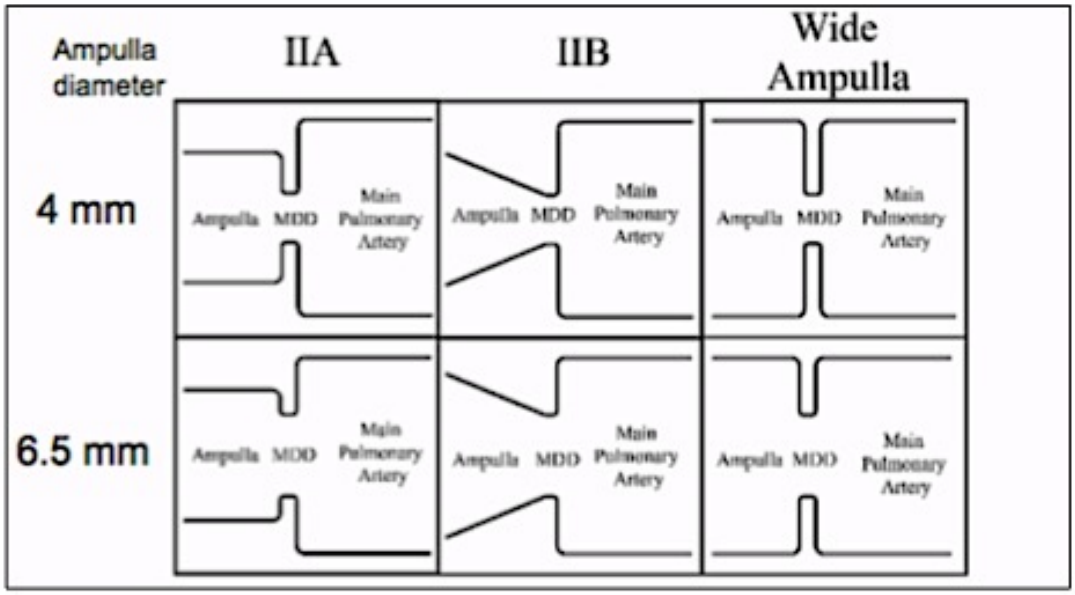


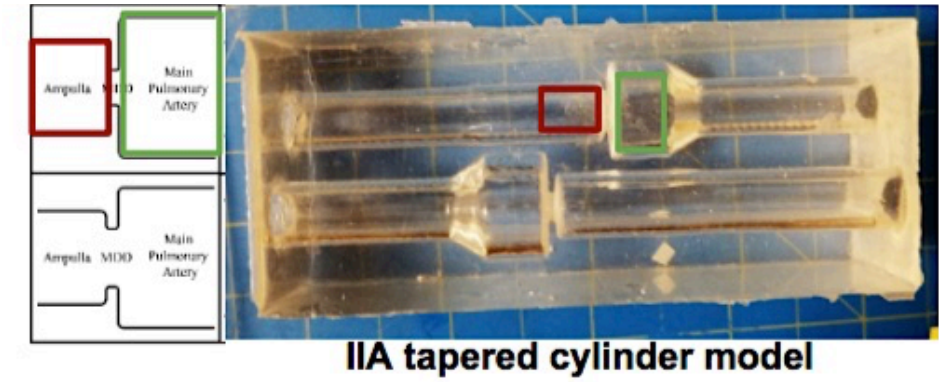
Figure 3. PDA morphologies used in rigid models

The rigid walled model parts were designed using the 3D CAD design software SolidWorks. The entire model consists of a block of PDMS with 2 “vessel” lumen shapes molded in the middle, one with a minimal ductal diameter (MDD) of 4mm, and the other with an MDD of 6.5mm. Both model types had a 3/8-inch inlet and outlet diameter.

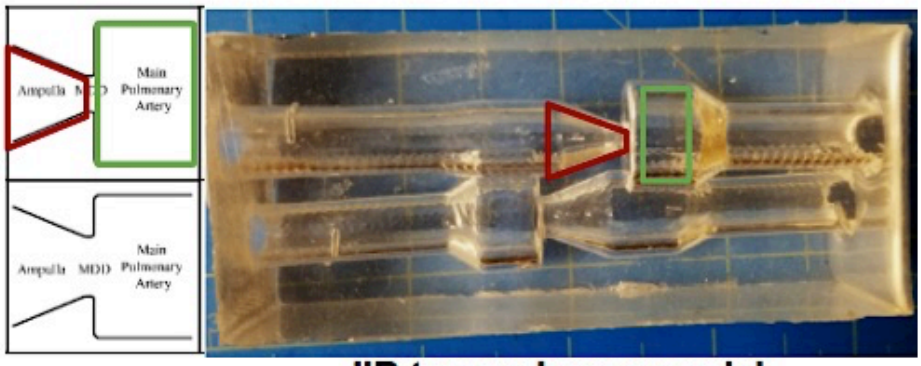
The CAD modeled lumen pieces were 3D printed and vapor polished in acetone. A rectangular prism shaped mold was sealed together, with each lumen piece glued vertically to the base. A PDMS mixture with a 20:1 base to curing concentrate ratio was then poured into the mold and allowed to cure at 80 C for 3 hrs.

Once this was complete, the outer mold was taken apart, and the model was put in a base bath to dissolve out the 3D printed lumen material. Then the leftover mold was put

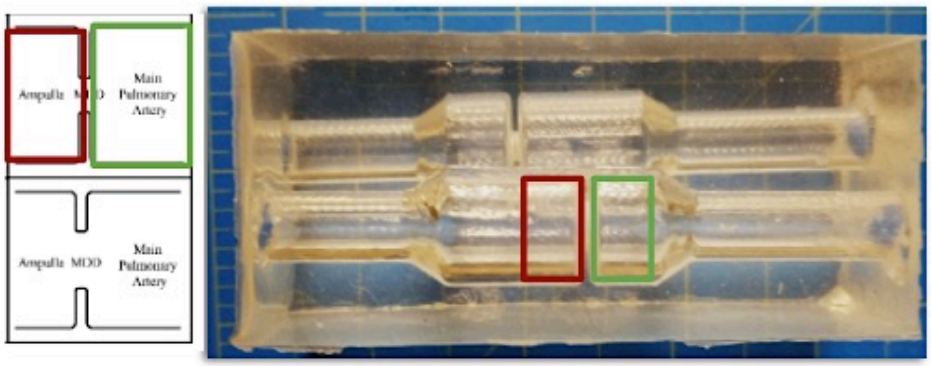
under vacuum suction to clear any lasting debris from the curing process. **Figure 4** shows the finished model types.



IIA tapered cylinder model



IIB tapered cone model



Wide Ampulla model

Figure 4 shows completed PDMS models

Dislocation Tests

In order to study how the effects of force and pressure can dislodge the model in vitro, a peristaltic flow loop applied at a steady blood flow rate of physiological pressure (i.e. 100

mmHg/min). Each model is inserted into the loop with the device installed. Water is pumped through the loop at increasing pressures for a total of 5 minutes. **Figure 5** below demonstrates how the flow loop system was set up.

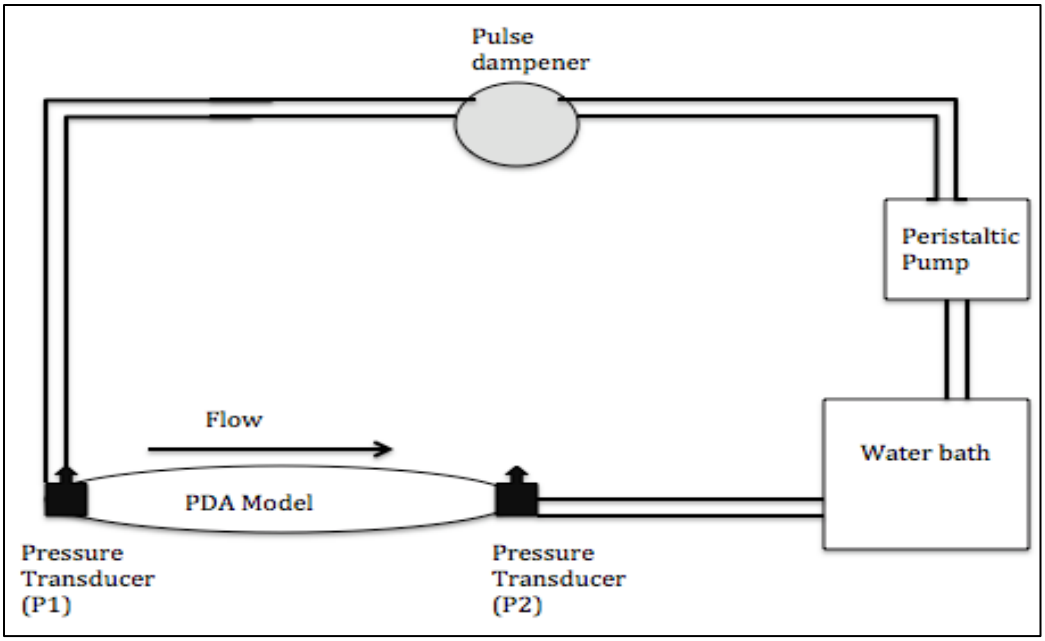


Figure 5. Flow loop used to study device displacement

3 devices were developed with the exact same dimensions and materials. All were tested for each model type to provide repetitive data to do accurate comparisons across each trial for each model type.

Pressure transducers (P1 and P2) measured the pressure of the water at either side of the model. The difference was measured and recorded using Labview software. Two series of tests were run for model with each device, once at physiological pressure (100 mmHg), and once more at 2x physiological pressure (200 mmHg). Images were taken at each minute mark to review how much migration occurs over time.

CHAPTER III

RESULTS AND DISCUSSION

Initial migration testing was conducted with individual flexible models made of 10:1 PDMA ratio. This meant the models were capable of bending and expanding to a higher degree compared to the rigid models, made of a 20:1 PDMS ratio. The purpose of fabricating the flexible models was to provide a better likeness to an actual vessel and how they expand. However, upon analyzing the pressure drop across the device recorded in Labview versus the real time flow rate, there was shown to be an artificial inflation of pressure. To fix this, rigid models were fabricated with a higher PDMS ratio that still allowed for expansion and proved more durable.

Each model type (IIA, IIB, WA) underwent migration testing for 5 and 10 minute time periods. All models were held at 100 mmhg (physiological pressure) for 5 minutes. If able, some models were then held at 200 mmhg for another 5 minutes. Only the 4mm models for all types could be tested for a full 10-minute time period since these models could withstand up to 2x physiological pressure without expanding too much. The 6.5mm models were only able to reach physiological pressures for up to 5 minutes. Above 100 mmhg, the software could not pick up data accurately and the 6.5mm models were at risk of rupturing.

At each 1-minute mark during the 5 or 10-minute trial period, an image was taken of the device in the model. Using the ImageJ program, the total amount of movement was determined by analyzing the images at the 0 minute, 5 minute, and if applicable, 10 minute mark and measuring the difference in placement of the device along the model.

Figures 6 and 7 show a comparison of migration patterns across each model type, both rigid and flexible.

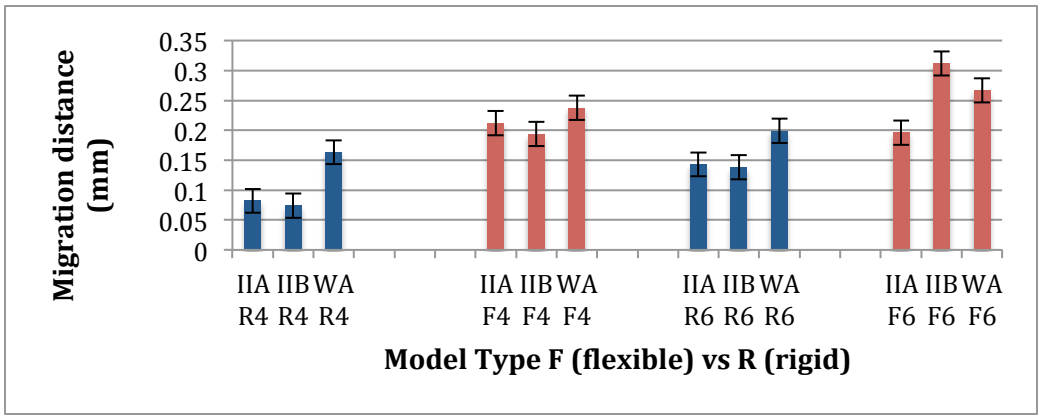


Figure 6 shows the total migration by the 5 minute mark for both rigid (blue) models and flexible (red) models.

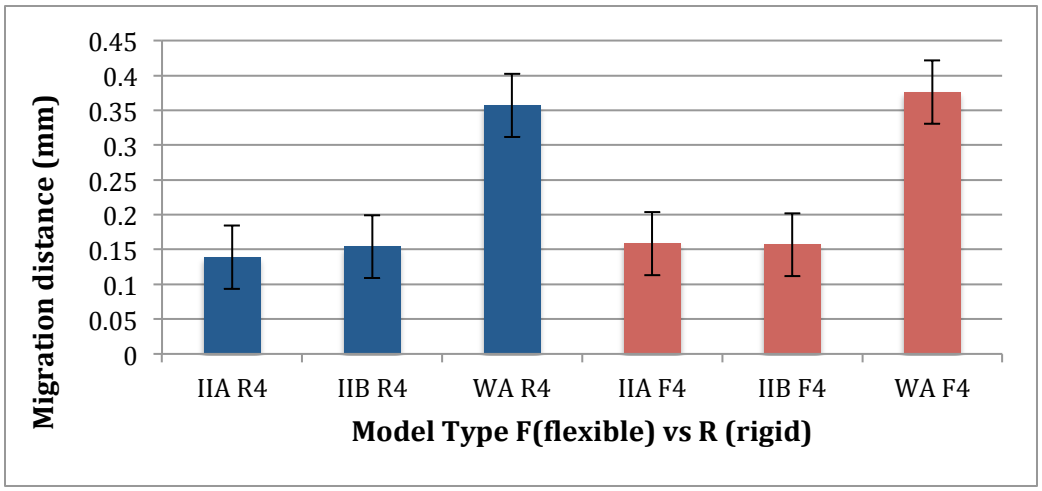


Figure 7 shows the total migration by the 10 minute mark for both rigid (blue) models and flexible (red) models.

As shown in the graphs above, there is a discernable trend between model type and migration. The NFC devices proved to be the most capable of remaining stable in the IIA and IIB 4mm model types. For the WA model, the NFC device showed a much higher average migration distance trend.

Between the flexible and rigid models, the flexible models seem to display a higher rate of migration. This could be due to the fact that the flexible models were able

to expand more, allowing for more room for displacement, or the pressure inflation across the model that allowed for exposure to greater pressures. **Figures 8 and 9** below show the trend between pressure drop and migration across all models.

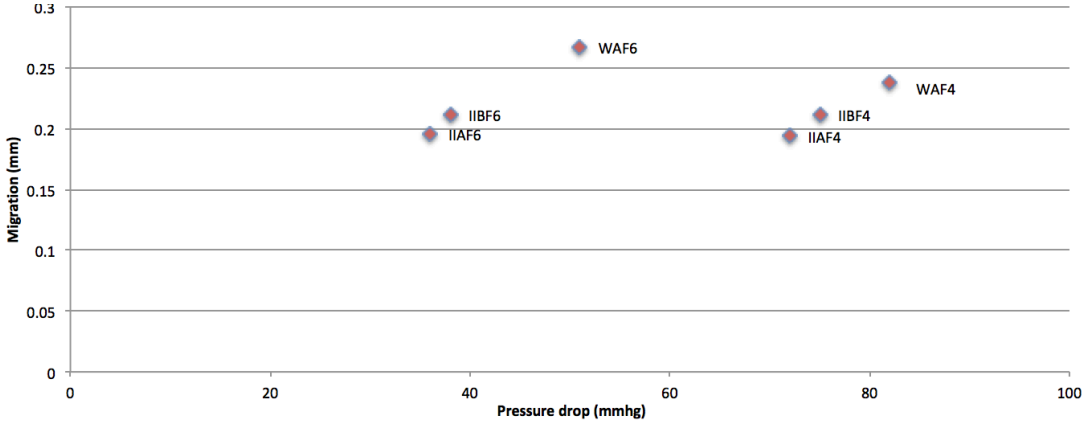


Figure 8 shows the average migration of each flexible model as associated with total pressure drop at both 5 and 10 minutes

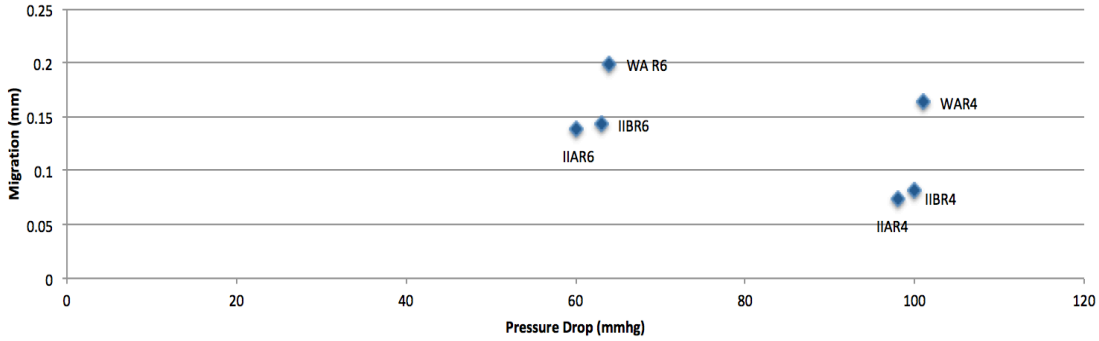


Figure 9 shows the average migration of each rigid model as associated with total pressure drop at both 5 and 10 minutes

There is a distinct pattern in how increased pressure affects the amount of migration in all model types, both flexible and rigid. The higher the pressure drop, the more migration occurred, particularly in the WA model for both flexible and rigid model types. This may be due to the fact that the WA models have an expanded ampulla diameter and the current device model doesn't allow for wider cage expansion in enlarged aortic morphologies.

Figure 10 below shows the trend between average migration and pressure drop for the IIA 4 mm rigid model.

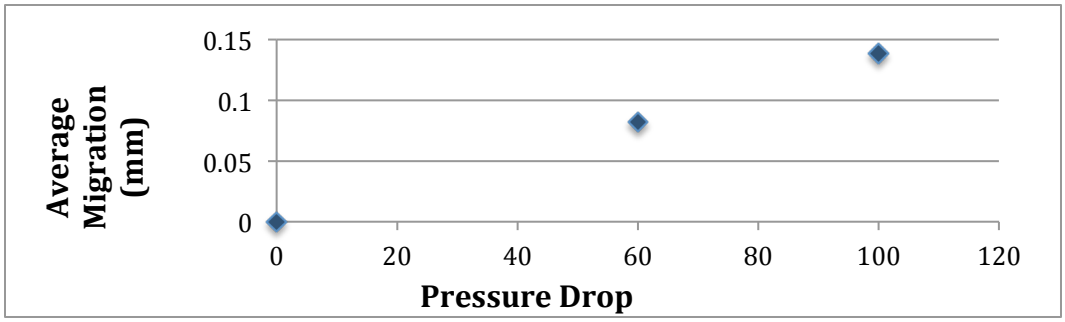


Figure 10 shows the migration at the 0, 5, and 10 minute marks and the associated pressure drops.

CHAPTER IV

CONCLUSION

Based on the results collected by the dislocation studies, we are able to conclude that the NFC device is suitable at staying in place under physiological pressures in the most common canine minimal ductal diameters (MDD) or morphologies (IIA, IIB or WA). However, the NFC device was rendered not suitable for use under accelerated pressures in the oversized MDD at any morphology.

Both flexible and rigid model types were developed and tested at the same pressures for all testable NFC devices. The data above indicates that the flexible model types were less capable at remaining in place and had a much higher rate of migration than the rigid model types.

It is important to note that the NFC device is at risk of slight migration after being positioned in the model, however the incidence rate does not even breach 20%. As discussed in previous literature involving the ACDO device, migration of this device is often a late and rare complication. The NFC device is self expanding and exerts a radial force against the endothelial wall, which by design, is to minimize displacement. Should any serious migration occur, treatment can be easily managed by conservative, non invasive surgical treatment.

Future work aims to investigate device alterations to allow for stable deployment in the wider duct models by accounting for wider cage expansion and larger tube struts, as well as improving upon the flexible model type design to provide for a larger range of testable environments.

REFERENCES

[1] "Angiographic classification of the isolated, persistently patent ductus arteriosus and implications for percutaneous catheter occlusion." *The American Journal of Cardiology,* Excerpta Medica, 22 Apr. 2004, Sept. 2017

[2] Faella, H. J. and Hijazi, Z. M. (2000), Closure of the patent ductus arteriosus with the Amplatzer PDA device: Immediate results of the international clinical trial. Cathet. Cardiovasc. Intervent., 51: 50–54. doi:10.1002/1522-726X(200009)51:1<50::AID-CCD11>3.0.CO;2-6

[3] Matsui, H, et al. "Morphology of the patent arterial duct: features relevant to treatment." *Images in Paediatric Cardiology*, Medknow Publications & Media Pvt Ltd, Jan. 2008, www.ncbi.nlm.nih.gov/pmc/articles/PMC3232584/.

[4] Mueller,S et al. "Adult patent ductus arteriosus ; An unusual cause of heart failure in an octogenarian female. *Wiener klinische Wochenschrift.,* U.S National Library of Medicine, Dec. 20. 2016, ww.ncbi.nlm.nih.gov/pubmed/27565643. Accessed 16 Sept. 2017

[5] Wierzbicki, Mark, "An experimental canine patent ductus arteriosis occlusion device based on shape memory polymer foam in a nitinol cage." *Journal of the mechanical Behavior of Biomedical Materials, Elsevier, 25 July 2017,* www.sciencedirect.com/science/article/pii/S1751616117303193. Accessed 17 Sept. 2017

[6] Scheider, Douglas J., and John W. Moore. "Patent Ductus Arteriosus." *Circulation,* American Heart Association,Inc., 24 Oct. 2006, circ.ahajournals.org/content/114/17/18733.short. Accessed 16 Sept 2017

[7] Zulgarnain, A, et al. "Comparison of effectiveness and cost of patent ductus arteriosus device occlusion versus surgical litigation of patent ductus arteriosus*." Pakistan journal of medicinal sciences*., U.S National Library of Medicine, Dec. 20. 2016, ww.ncbi.nlm.nih.gov/pubmed/27648051. Accessed 16 Sept. 2017

[8] Pam White, Can Vet J. 2009 Apr; 50(4): 401–404

[9] Katz ES, Tsiamtsiouris T, Applebaum RM, et al. Surgical left atrial appendage ligation is frequently incomplete: a transesophageal echocardiograhic study. J Am Coll Cardiol 2000;36:468-71. 10.1016/S0735-1097(00)00765-8. Accessed 12 February 2018

[10] Hassine M., Hamdi S., Mlayeh D., Jomaa W., Ben Hamda K., Gamra H., Maatouk F. Percutaneous closure of persistent ductus arteriosus in low-weight infants | La fermeture percutanée du canal artériel persistant chez les enfants de faible poids Archives de Pediatrie, Volume 24, 2017