Development of Reinforced Metal Tubing for Vascular Applications

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Declaration

I certify that this research work titled *"Development of Reinforced Metal Tubing for Vascular applications"* is my own work. The work has not been presented elsewhere for assessment. The material that has been used from other sources it has been properly acknowledged/ referred.

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Abstract

Coronary artery diseases remain one of the leading causes of mortality, with the incidence of death rate being 20% in Pakistan. The disease causes deposition of plaque on the lumen of the blood vessels that narrow the coronary arteries (blood) hindering the blood flow to the heart and rest of the tissues. The treatment procedure of the disease involves delivering the expandable device (balloon/stent) to the target region. Guide catheters plays a crucial role for the advancement of these treatment devices (stent/balloon). Guide catheters are hollow tubular structures of 100-110 cm in length, which are required to provide support, and facilitate the delivery of the stent/balloon at the target region. The guide catheter is made to enter the body via the wrist/femoral artery. From here, it traverses all the way to the heart while passing through blood vessels of varying diameter, and a tortuous anatomy of the body. In fact, the pathway of the guide catheter is not a straight, rather a curved path. It is important for the guide catheter to have certain mechanical characteristics to reach the heart without causing any vascular trauma. The performance of the guide catheter heavily relies on its braided shaft, and the outer jacket. Spontaneous movement of the catheter due to its instability, coronary dissections due to a high push force, and arterial spasms resulting from the friction are a few common problems of guide catheters used commercially. The current research is focused on catering these challenges by optimizing the pitch of the braided shaft and jacketing the shaft with a polymer unique to commercial catheters. In order to find the best guide catheter to meet the challenges presented in the literature, three guide catheters of varying pitch were designed, and coated with a polyimide jacket material. The protypes were tested for performance under mechanical, and physically testing and the candidate performing the best was selected. The guide catheter that performed the best in providing the longitudinal stiffness, reducing the friction, and decreasing the push force was chosen, and bench tested.

CHAPTER 1: INTRODUCTION

The research work in this dissertation is carried out to resolve the guide catheter issues and reduce the number of cardiovascular diseases holistically. The objective of the research incudes to the study the effect of picks per inch of the braided shaft on performance of the guide catheter, and how polyimide influence this behavior.

1.1. Background

Over the past few decades, our lifestyle has changed tremendously. The exclusion of physical activity, and the inclusion of poor dietary patterns has lead to a boom in cardiovascular diseases. Cardiovascular diseases as the name suggests is the group of disorders relating to the heart, and the blood vessels. It includes abnormal heart rhythms, atherosclerosis, coronary artery diseases, heart attack, pericardial disease, rheumatic heart disease, etc. Around 17.9 million people died due to cardiovascular diseases in 2019, alone that represents 32% of all global deaths (Organization, 2020).

1.1.1. What is a Coronary Artery Disease (CAD)?

Among the other cardiovascular disease, coronary artery disease is the most common, and one of the leading causes of death all around the globe. The disease is caused by plaque deposition within the lumen of the artery. As a result, the arterial lumen is reduced, and becomes narrow, making it difficult for the oxygen, and nutrients to pass through the vessels and reach the heart and body tissues. The depiction of same is shown in the Figure 1.1. The incidence of CAD in Pakistan is (Barolia et al., 2017)26.9 with a mortality rate of 20% (Barolia et al., 2017).

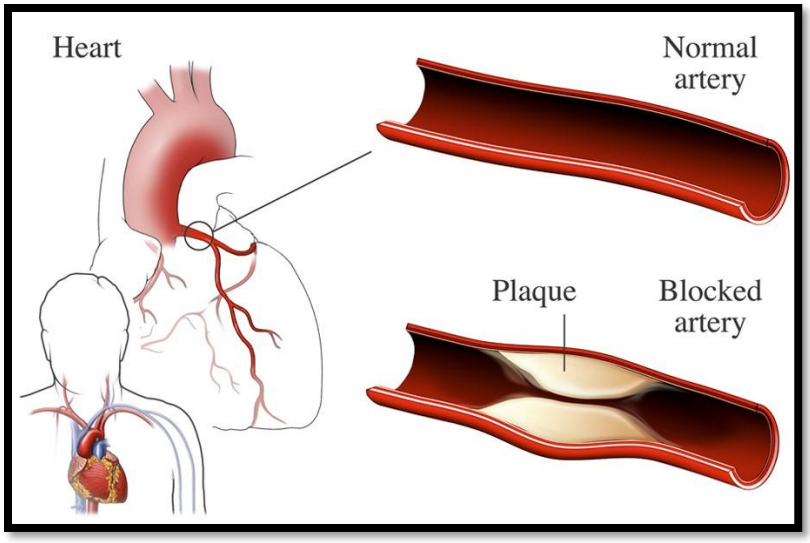

Figure 1.1: Normal vs Blocked Artery (NIH, 2022).

1.1.2. Treatment of Coronary Artery Disease

With the earlier, and accurate treatment it is possible to reduce the rate and prevent deaths resulting from CAD. Percutaneous Coronary Intervention (PCI) is the gold standard for treating coronary artery disease (Ali et al., 2012). This treatment procedure involves the delivery of expandable therapeutic devices (a balloon or a stent) to the target region that widen the otherwise narrow blood vessel. During the treatment procedure, an incision is made either on the wrist or the leg. Next, a hollow tube, called guide catheter is passed to the coronary ostium of the heart, near the blocked region of the arteries. Next a guide wire is made to enter the blood vessels passing through the guide catheter. Finally, the therapeutic device, is passed through the lumen of the guide catheter, and over the guide wire to reach the blocked region here plaque deposition is present. The stent or the balloon then expands to treat the diseased region of the heart
(Ali et al., 2012), as depicted in Figure 1.2.

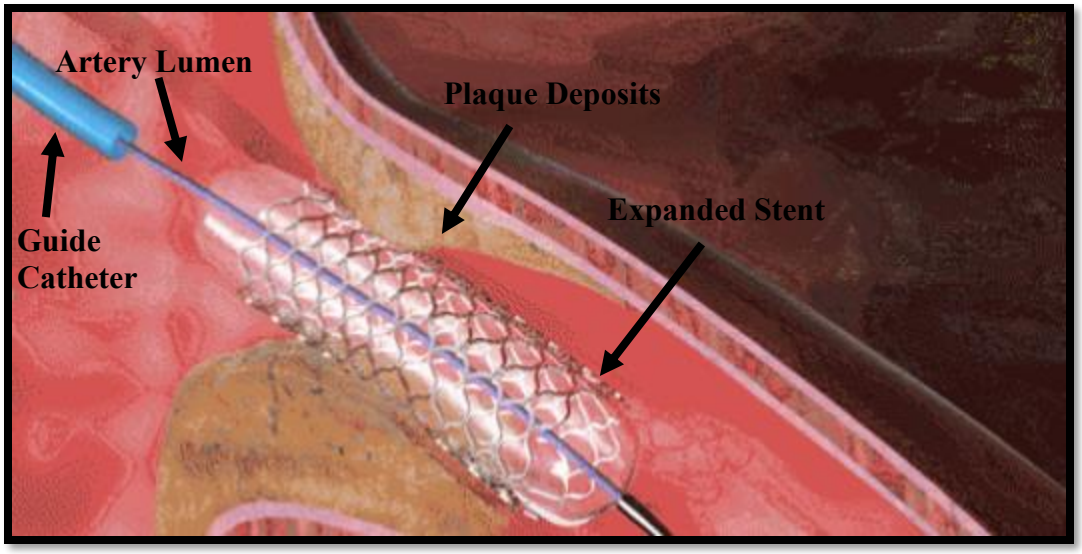

Figure 1.2: Guide catheter delivery the stent during PCI

Therefore, the treatment of coronary artery disease relies heavily on the accurate positioning and functioning of a guide catheter (Topaz et al., 1990).

1.1.3. Current Guide Catheters

A guide catheter is the hollow tube that has three layers, an inner lumen, middle reinforcement braided shaft, and the outer polymer jacket. The mechanical performance of the guide catheter depends on the middle, and the outer layer. The commercially available guide catheters use a flat stainless-steel wire that are intertwined to form a crisscross pattern (braided) tube making the middle reinforcement shaft. The number crosses in inch of the braid are crucial in governing the mechanical performance of the catheter. The choice of the type of the braided shaft, and the polymer material for the outer jacket depends on the type of lesion present, and the treatment desired.

1.2. Research Objective:

The research was aimed at studying the effects of picks per inch of the braided shaft on the performance of the guide catheter. To achieve this, three types of polyimide guide catheter prototypes were developed varying in pitch of their braided shafts. The guide catheters were expected to possess following characteristics:

a. Stiffness in longitudinal direction
b. Lower coefficient of friction
c. Jacket material of high polarity
d. Lower advancement force

CHAPTER 2: LITERATURE REVIEW

Coronary artery disease is the number one killer worldwide. The disease has killed 360,900 people lost their precious lives due to CAD in 2019, in United States (CDC, 2022). On the top of it, the onset of the disease can begin as early as 20 years of age. CDC reports that 18.2 million people are suffering from coronary artery disease at the age of 20 and more. It is also reported that out of 10 deaths due CAD, two of them are of the people less than 65 years age (CDC, 2022). The gravity of the situation requires, both the earlier diagnosis, and the earlier treatment. While the treatment of CAD involves delivering the therapeutic device to the target region that then open-up the narrow or the blocked vessels.

2.1. Understanding The Guide Catheter

As mentioned, the guide catheter plays a crucial role in delivering these devices to the target site. A guiding catheter is inserted into a peripheral artery and progressed through the aorta via a guidewire until the distal end of the guiding catheter is engaged with the proper coronary ostium in a normal coronary angioplasty procedure. The guiding catheter's stiff main body component provides enough "pushability" and "torqueability" to allow it to be inserted a peripheral artery, manipulated and twisted in the vasculature to place the distal end of the catheter near to a specific coronary artery. Due to the complex nature of intravascular catheter paths, it is critical that an intravascular catheter be directed by torquing its proximal hub and that the torque be delivered to the distal end in a timely manner. Furthermore, the catheter must be strong enough in the longitudinal direction to avoid kinking or folding as it travels through the circulatory system. It should also include a lubricious core lumen to make it easier to insert a guidewire or another catheter or device through it. A relatively thin wall is required by the desirable features of a catheter with a small outer diameter (O.D) and a large inner diameter (I.D). Maintaining the appropriate torqueability and pushability properties of a thin wall catheter necessitates a lot of creativity in the material formulation and fabrication processes (Ali et al., 2012).

Good guide assistance (also known as backup support) is required for efficient stent distribution. The capacity of the guide catheter to stay in place and offer adequate stability for the progression of interventional equipment is key to good guide support (Takeshita et al., 2008).

A typical guide catheter is a 100-115 cm long, hollow tubular structure of 2-2.2 mm in diameter. It has two distinct ends, a proximal and the distal end. The end of the catheter that the physician's hold to manipulate the position of the catheter is called the proximal end, whereas the end of the catheter that enters the body is called the distal end (Kucklick, 2012). This end has a radiopaque tip attached that helps visualizing the position of the guide catheter when inside the body. A hub is present at the proximal end that's maintains the catheter integrity. A typical catheter structure is shown in the Figure 2.1.

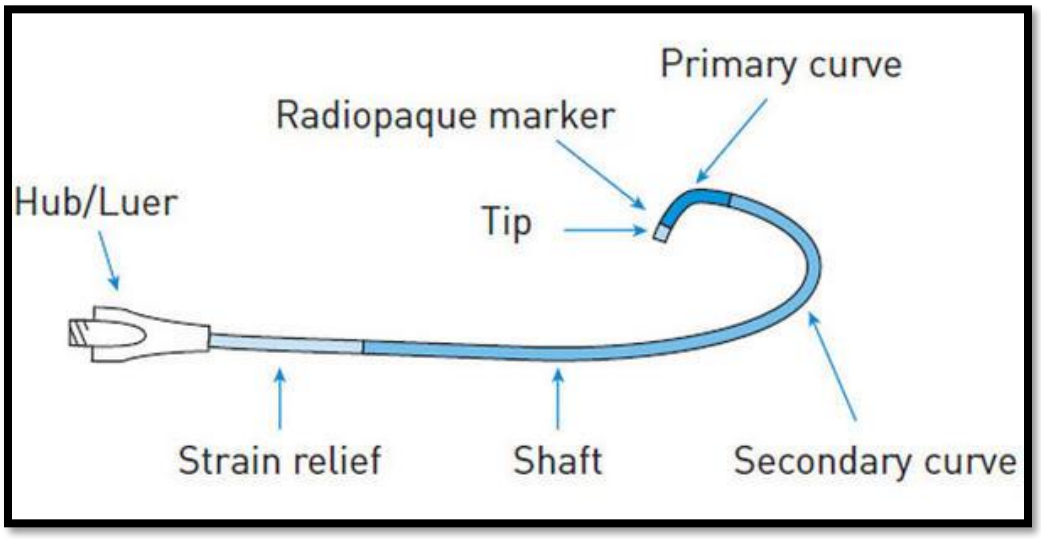

Figure 2.1: Guide catheter physical construction

The primary and secondary curve of the catheter above are shaped. Usually, the guide catheter has following shapes; Judkin's right, Judkin's left, Amplatz left and Hocket stick (Figure 2.2). Each shape plays an important role in accessing the coronary ostium.

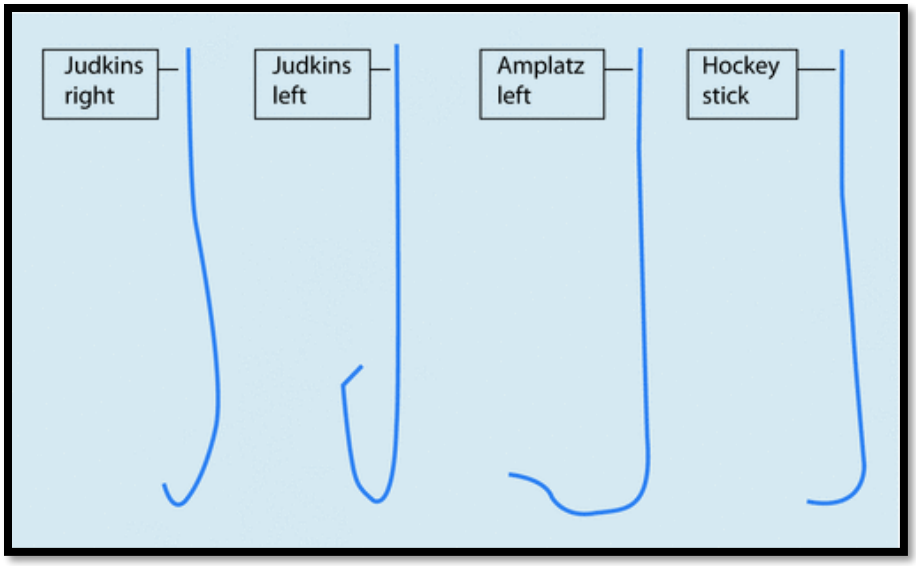

Figure 2.2: Guide catheter shapes

Anatomically, the guide catheter has three layers in its construction. A lubricious PTFE inner layer, a stainless-steel braided layer, and an outside polymer jacket are the three layers that make up a guiding catheter. The stainless-steel coating stiffens the catheter to let the device move through, but it makes the guide more difficult to engage than a diagnostic catheter. Compared to similar diagnostic catheters, guides have a shorter, more angulated tip and a greater internal diameter (Kucklick, 2012). The increased internal diameter makes it easier to deliver equipment and inject contrast.

2.1.1. Stainless-Steel Layer

The middle of the guiding catheter, which is made up of stainless steel is braided. It involves intertwining of stainless-steel wires into a braided tubular structure, using a large machine called braider. The carrier is the major component of the braider that determines the size of the braided tube that results. The machine has eight or sixteen circularly rotating carriers (Kocaturk et al., 2009). The carrier also maintains the bobbin and wire together, correcting for changes in length while maintaining consistent tension and maintaining control if the wire breaks. The carriers are equipped with 80- or 120-millimetre gear (Melenka et al., 2017). The size of the shaft on the guide catheter determines the option. The braiding point is connected to the carrier through bobbins. It gathers the wire's various strands and weaves them together into a strong braid. The triaxial wheels

beneath the braider contribute to the final design of the braid. The braided wire is made by winding many strands of thin, flexible wire around a core on spools that rotate fast in a circular pattern, weaving the wire together and molding it into a flexible and robust braid (Melenka et al., 2017). This is how a resultant braided tubular structure looks as shown in the Figure 2.3:

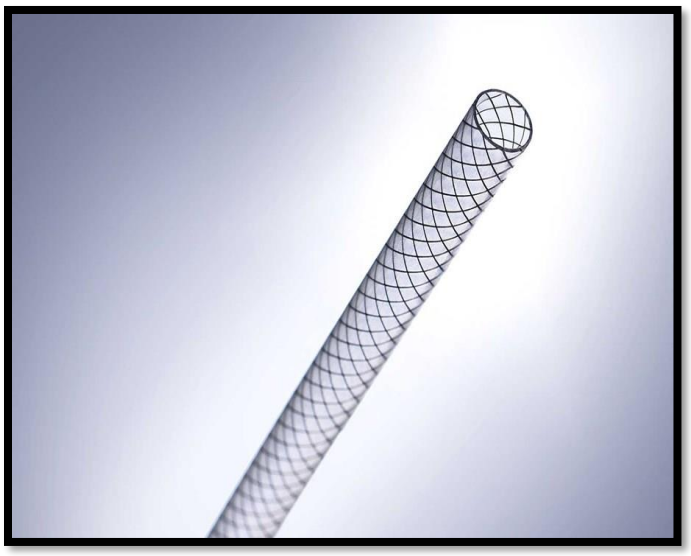

Figure 2.3: A typical briaded shaft

The braided tubular structure that makes the shaft of the catheter has three important features governing the mechanical performance of the guide catheter.

- Wire Type
- Pitch
- Braid Pattern

Wire Type

The two types of stainless-steel wires usually employed in the braided shaft are either round, or flat. Each of these wires have their own important characteristics in imparting the mechanical properties to the guide catheters. For instance, if the round wire is chosen for the braided shaft, then it should be taken into consideration that round wire increases the flexibility of the braided structure, but at the cost of overall profile (Kucklick, 2012). Whereas, the flat wire may not add much to the flexibility, but it does not increase the overall profile/thickness of the

catheter. Additionally, it enhances the kink-resistance properties of the catheter indicating better abilities at avoiding necking (Mukherjee et al., 2011)

Pitch

Pitch of the catheter is number of times the wire crosses an inch along the length of the braided shaft. Increasing the crosses per inch increases the flexibility of the braided shaft, whereas a smaller number of crosses in an inch decreases the flexibility but increases the stiffness of the catheter. The number of crosses or the pitch is also referred as picks per inch. Picks per inch (PPI) also affect the pushability, and kink-resistance properties of the braided shafts. With increase in number of the picks per inch, the pushability of the braided shaft increases but its ability to avoid the kinks also decreases (Peterson et al., 2003).

One of the easiest ways to manipulate the catheter properties is changing the pitch of the braided shafts. The current commercial catheters have their pitch in the range of 60-90 per inch. However, since the properties affected by the picks per inch come in contradicting manner, catheter design engineers have to carefully take into consideration the properties desired by the catheter before deciding on the braided shaft pitch (Lynn et al., 2019).

Braid Pattern

Just as the pitch of the catheter can be optimized, the way in which stainless-steel wires intertwine with each-other also varied in numerous patterns. However, the three basic and widely used braid patterns include, Figure 2.4 (Lynn et al., 2019) (Ayranci et al., 2008):

a. **One over-two and under-two:** This is a desirable pattern when catheter is required to deliver a high pushability and maximum dispersion
b. **Two-under-two, over-two**: This pattern is superior in torqueability, and kink-resistance
c. **One-under-one, over-one**: When maximum rotational force at the prximal end is required from the force applied at the distal end, then one-under-one, over-one is opted in the braided shafts.

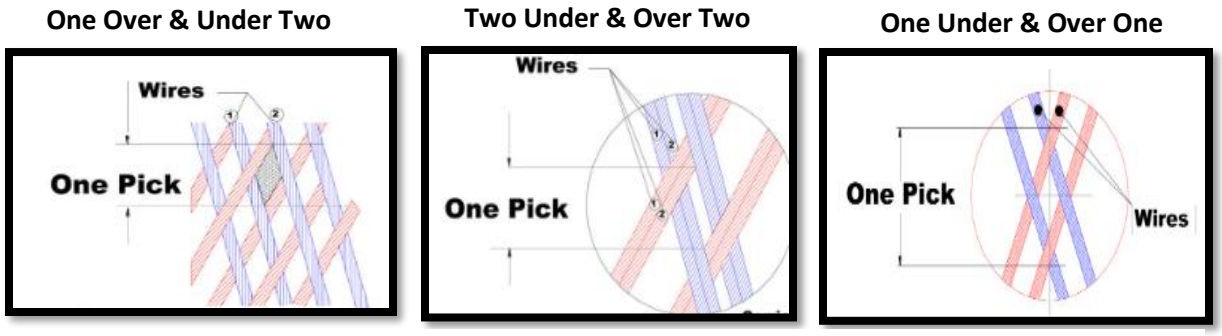

Figure 2.4: Braided shaft typical patterns

2.1.2. Outer Polymer Layer

The outer jacket of the catheter also plays an integral role in governing the mechanical performance of the behavior. This layer, which is mostly polymer, affects the pushability and stiffness of the guide catheter. Since this is the layer that is in direct contact with the blood cells, it is important that the layer has lower friction so that it exerts lower forces on the wall of the vessels. The insertion of the guide catheter inside the body is a painful procedure. Owning to the high friction of the device, it can cause vascular trauma, including coronary artery dissections, arterial spasms, and bleeding (Collins, 2019) (Julia Merkle; Christopher Hohmann;, 2017). A lubricious surface, along with kink-resistance, flexibility, pushability and ability to endure arterial compressional stress are the prime functional requirements of the guide catheters.

Therefore, an adequate understanding of catheter design is essential to develop the device having optimal properties. Nylon, and PEBAX® are the most widely used polymers for the outer jacket layer of the guide catheter. The two materials had been the top choices because of their flexural values that are quite low and help the vascular catheters to traverse the tortuous anatomy of the body. However, keeping in consideration, the problems of arterial dissections, and arterial spasms due toa high frictional forces, the use of the Nylon, and PEBAX® has to be reconsidered.

Polyimide in this regard has an imide functional group, Figure 2.5. A condensation process between an aromatic anhydride group and an aromatic amine produces the imide group. This group has a high thermal stability. Aliphatic imides are feasible, but they have less heat stability, which is one of the main reasons to employ an imide-type polymer. Polyamide–imides (PAIs) are thermoplastic amorphous polymers with important features such as remarkable chemical resistance, outstanding mechanical strength, high thermal stability, and excellent electrical characteristics. Thus, imide has two acyl groups bonded to the same nitrogen atom (McKeen, 2012).

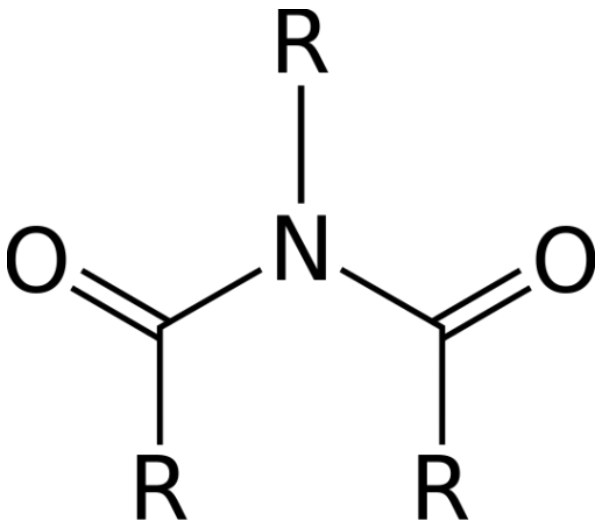

Figure 2.5: Functional group imide structure

The acyl group in imide is polar making polyimide an attractive choice for the guide catheter. Additionally, the polar of the polyimide also ensures that is hydrophilic signifying that would exert less frictional forces on vessel walls during insertion (McKeen, 2012). An extensive comparison of Nylon, Pebax, and polyimide yields following properties (Watanabe et al., 1968) (DataSheets; MicroLumen, 2011):

Table 2.1: Comparison of Properties of Nylon. Pebax, and Polyimide

Properties	Pebax	Nylon	Polyimide
Tensile Break Strength (MPa)		82	96
Coefficient of Friction	1.0	1.5	0.5
Contact Angle (Degree °)	76	72.4	68
Modulus of Elasticity (MPa)	259	900	1,970
Biocompatible	✔	✔	✔

CHAPTER 3: MATERIALS AND METHODOLOGY

This chapter discusses the materials chosen for the braided shaft and the outer jacket while demonstrating why they were the right choice for the current study, and the mythology adapted to develop the protype and its testing.

3.1. Stainless Steel 304 As a Choice of Material for Braided Shaft

Designing the medical devices require a vast knowledge of material science to overcome the posed challenges, and to meet the industry standards. Therefore, scientists are cautious to employ the use of diverse materials and select the one suited the best. Stainless steel 304 is the most common choice of braided shaft for catheters. The stainless steel 304 has the combined properties of steel and 304 grade that includes, a high modulus of elasticity which is crucial in ensuring a high push and torqueability. Moreover, the low carbon content of the stainless steel makes it excellent choice for braided shafts since it ensures that it's corrosion resistance (Geantă et al., 2013).

The assurance that the stainless-steel catheter will not chemically react with bodily tissue or sterilisation products makes Stainless 304 the ideal material for the braided shaft of the guiding catheter (Geantă et al., 2013).

3.2. Polyimide As a Choice of Material for Braided Shaft

Considering the challenges encountered by commercially available guiding catheters, following was the selection criteria for the jacket material of the guiding catheter, Figure 3.1:

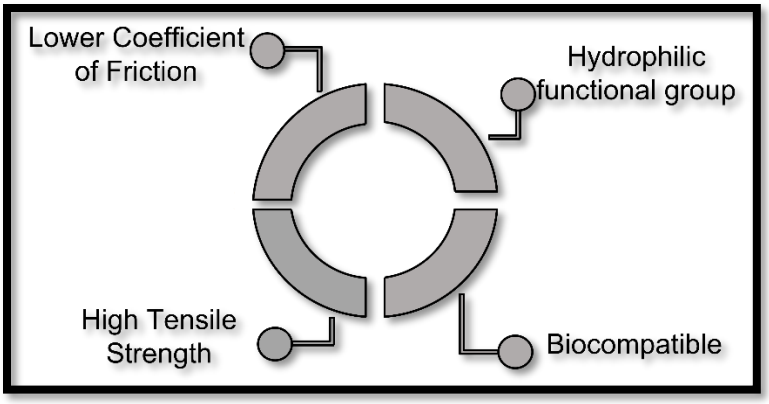

Figure 3.1: The selection criteria for outer jacket of the guiding catheter

Therefore, polyimide was chosen as the potential material of the outer jacket. Polyimide has imide as its main functional group, which is polar, and hydrophilic. The contact angle in this regard for polyimide is 75.8^{o}. It has also a lower coeffecient of friction of 0.5 that ensures a smoother advancement of the catheter into the blood vessels (Lin et al., 2020).

The overall goal of the research was to study the effect of picks per inch on the mechanical performance of the guiding catheter. For that, the pitch of the braided shaft of the catheter was optimized by choosing three types of picks per inch and comparing them to evaluate the mechanical behavior. Braiding of stainless-steel wires and extrusion of polyimide tubes were done for this purpose, followed by lamination of the catheter assembly. The braided shaft design was inspired by an exhaustive literature research and market survey that indicated that only catheters with 60-90 picks per inch were being used. Following the design assessment, the research moved on to the guide catheter prototype development. This thesis therefore compares the three different guide catheters, namely 50 picks per inch, 100 picks per inch, and 140 picks per inch.

3.3. Braiding for 50 PPI, 100 PPI, and 140 PPI Braided Shafts

A 6 French (Fr) stainless steel braided catheter prototype was built following these steps. stainless steel wires (0.001"*0.003") (0.0005"*0.0025"), and (0.0005"*0.0025") for 50 PPI, 100 PPI, and 140 PPI braided shaft were used. Using the standard vertical Steeger's braider (as shown in the Figure 3.2), a braid pattern of one-wire-over two and under
two was produced for each of the three braided shafts.

Figure 3.2: Vertical Steeger's braided

The inner layer of the catheter was made of polytetrafluoroethylene (PTFE) lined polymer tubing. The braided shafts were braided over this layer. The resultant shafts out of these steps are shown in the Figure 3.3 below:

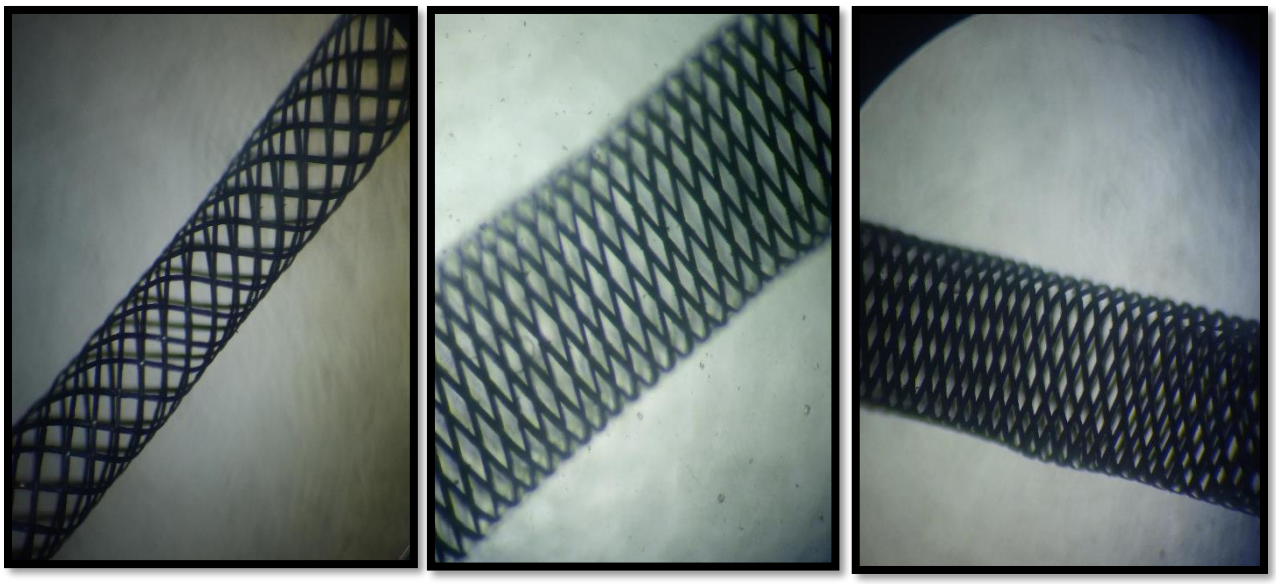

Figure 3.0.3: Resultant braided shafts used for this study. From left to right – 50 PPI, 100 PPI and 140 PPI.

3.4. Polyimide Coating Over Braided Shafts

Polyimide was extruded following the conventional extrusion process. The schematic process of extrusion is shown in the Figure 3.4.

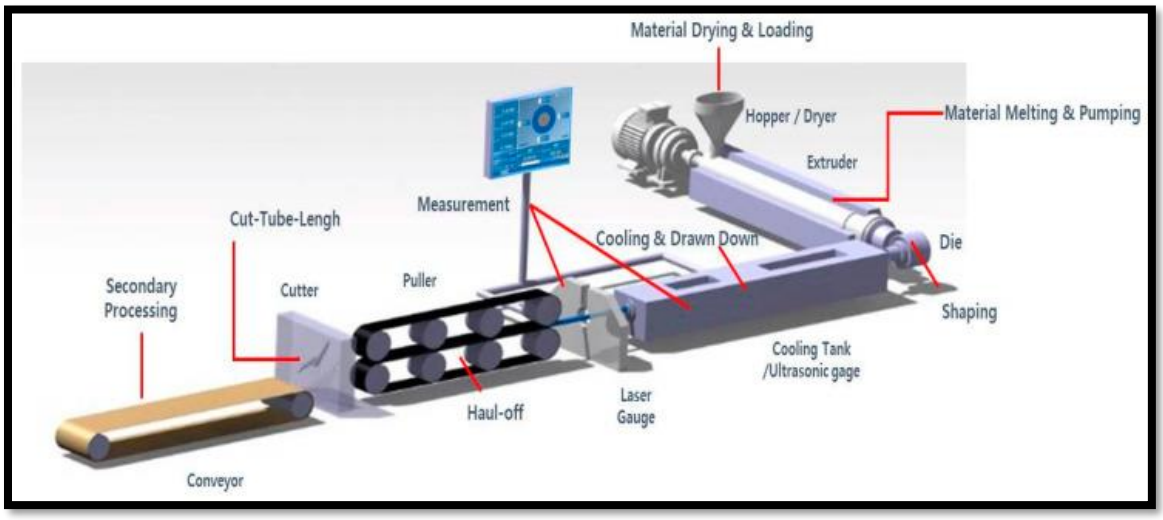

Figure 3.4: Schematic extruder diagram

The extruder's hopper is injected with dried and dehumidified polymer. The polyimide polymer then flows toward the barrel. Furthermore, as a screw and a barrel. The heat of friction between the screw, the polymer, and the inside wall of the barrel melts the polymer as it moves. The melted polymer is passed through the tip and die, which forms the initial shape. The polymer will now be quenched and hardened in the cooling tank. In the conveyor system, the puller eventually pulls the tube and cuts it to the correct length. During extrusion, the measurement instrument is utilised to determine the wall thickness and tube diameter. The end-product, a polyimide tube, (using extruder, as shown in figure) which was extruded over the braid.

The catheter assembly was then heated using a heat shrink sleeve during the reflow lamination process. The heat shrink layer forced the liquified sheath layer material to become intact with the flat wires and the inner liner during the melt process. The resultant tube after the polyimide over it looked like the one shown in the Figure 3.5 below:

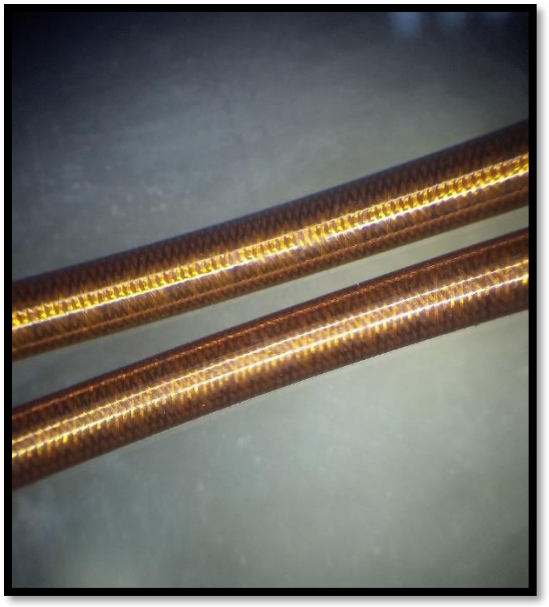

Figure 3.5: Microscopic view of polyimide over the braided shaft

3.5. Catheter Prototype Development

Once the polyimide was successfully extruded over the braided shaft having the inner PTF liner, the tubular structure was processed for catheter development with attachment of a hub, shaping, and tip fabrication.

- ***Hub Attachment****:* Using the loctite, a medical grade glue, a female luer lock, polycarbonate, was attached at proximal end of the tubular structure, as shown in the Figure 3.6. Hub facilitates the easier manipulation of the catheter while preventing the damage that may be caused due to handling.
- ***Shaping****:* The prototype was placed in Judkin's Right die for shaping for some time, and then heated using a thermoforming machine at Medical Device and Development Center, NUST. Since, the polyimide has a higher melting temperature, the prototype was heated at 125°C for 25 minutes to be shaped as Judkin's Right. The catheter was withdrawn from the thermoforming machine and finally from the forming die once the distal shaping process was completed.
- ***Tip***: As polyimide has greater stiffness, it was essential to make the tip of the catheter soft so that if, and when the guiding catheter enters the vascular may not cause vascular trauma.

Hence, the prototype was further heated with a small piece of pebax (2 mm) on the distal end, at 180°C for 2 minutes (Figure 3.7).

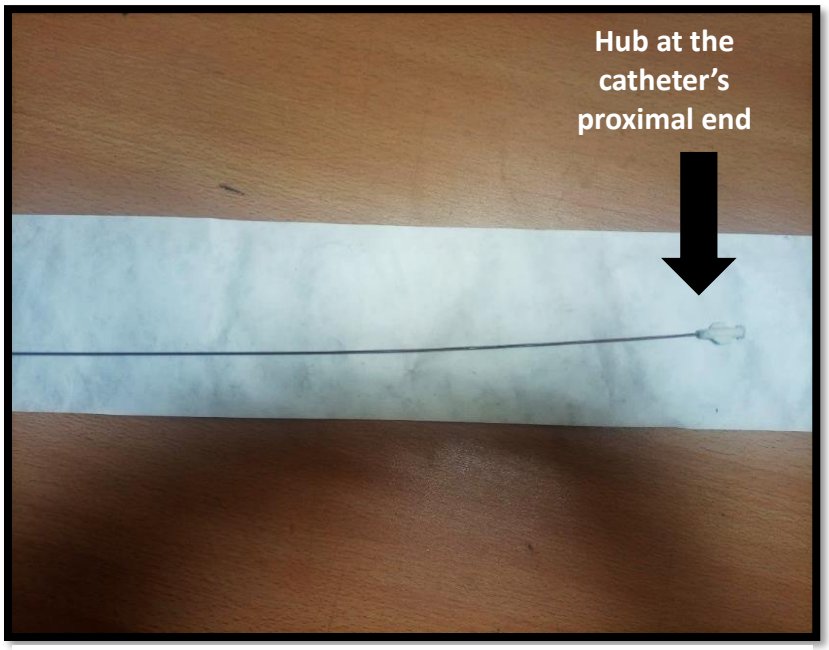

Figure 3.6: Hub attached to the proximal end of the catheter

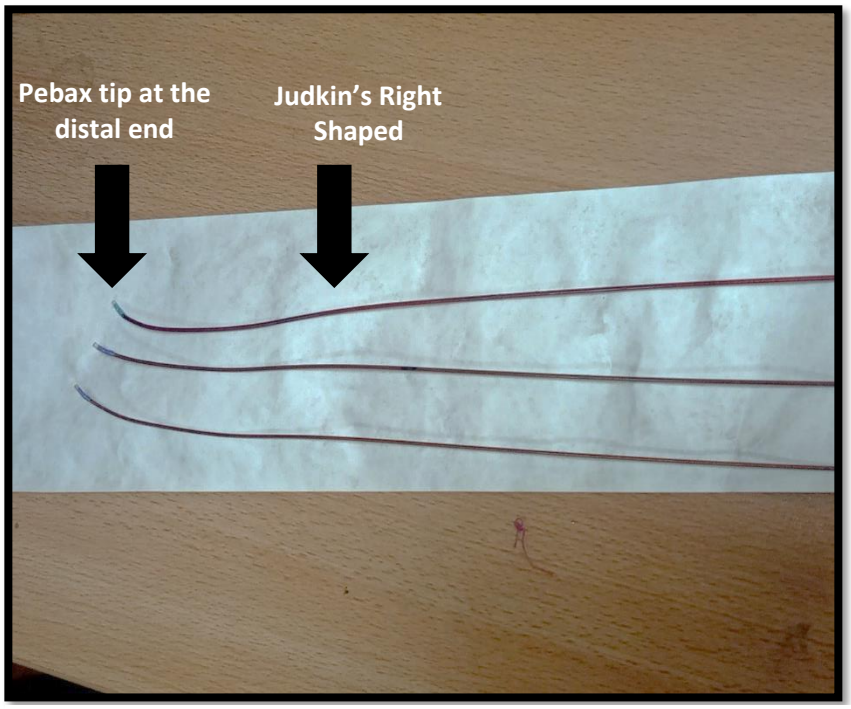

Figure 3.7: Shaped guide catheter with a pebax tip attached to its distal end.

Finally, the prepared guide catheters were subjected to characterization, and invitro testing to analyze their performance.

The developed guide catheters are serial coded in this dissertation for the ease of understanding, as follows:

Table: 3.1: Codes for guide catheter prototypes

Code	Pitch Type	Outer Jacket
GC-1	50 PPI	Polyimide
GC-2	100 PPI	Polyimide
GC-3	140 PPI	Polyimide

3.6. Guide Catheter Characterization

Since the guiding catheter was subjected to high temperature for quite some time, it was important to determine if the desired characteristics of the catheter (polyimide) were still intact, before proceeding to the in-vitro testing (Ray et al., 2018). Fourier Transform Infrared Spectroscopy (FTIR), and Wettability tests were done for the said purpose.

3.6.1. Fourier Transform Infrared Spectroscopy (FTIR)

FTIR spectroscopy is a technique for determining organic and inorganic compounds, as well as their chemical characteristics (Asensio et al., 2009). The guiding catheters were subjected to Fourier transform infrared (FTIR) spectroscopy (PerkinElmer; Spectrum 100 FTIR spectrophotometer) to see if the polyimide retained its functional groups and their interactions after heating (at 256 scans, 8 cm^{-1}. resolution). The chemical interaction between the carbon atoms present in imide group of the polyimide was investigated.

3.6.2. Wettability Test

The hydrophilicity of the polyimide was tested using a contact angle study of the processed

guiding catheter (McPhee et al., 2015). The contact angle was measured optically using the VCA System from AST Products, which uses a telescope goniometer. A section of the guiding catheter was placed on the stage and lighted with the VCAOptima's light source, followed by the placement of a 100 µl syringe needle at the proper distance. On the guiding catheter, a 25 µl distilled water droplet was placed. When the water droplet landed on the catheter's surface, the CCD (charged coupled device/ camera) took a dynamic image at 30 FPS (frames per second). The formed droplet over the catheter was used to determine the tangent line.

3.7. In-*vitro* Testing

In-*vitro* testing of guiding catheters were carried out to determine the efficacy of the catheters and establish their performance effectiveness. Overview of these tests is represented in figure 3.9.

3.7.1. Mechanical Testing

This section details in vitro mechanical testing that was carried out to assess the proposed catheter's stability, bending, and flexibility.

1. **Tensile Testing**

   The tensile strength test was used to measure the catheters' longitudinal stiffness, and ductility behavior of each of the samples.

Protocol:

The bare braids and prepared catheters were tested according to the BS EN ISO 10555-2013+A1:2017 standard ("ISO 10555-1:2013+A1:2017,"). The stress-strain curve for the test specimen was obtained using SHIMADZU (Tokyo, Japan), (Figure 3.9). The tensile strain was applied to a tiny section of roughly 2 inches of both the braid and the prepared catheter until the test specimen was broken into two or more pieces. The process entails measuring the gauge length (the distance between the apparatus's two jaws), then applying tensile strain at a unit strain rate of 20 mm/mm of gauge length. The maximum tensile force achieved at the point of breakage was recorded.

Figure 3.9: Tensile test being carried out on the braided shaft and the guide catheter

2. 3-Point Bending Test

A 3-Point bending test was performed for both the braids, and the set of the guide catheters to determine the bending stiffness.

Protocol:

The test specimen was loaded onto the 3-point fixature, according to ASTM standard (ASTM). They were bend by the force applied on the top, and midway between the lower spans. The bending stiffness was determined by plotting the force-displacement curve (Figure 3.10). Fix span length method was used as it allows force-displacement comparisons that are independent of the span length. The test specimens were maintained at room temperature (37^{o}C). The test was started with a small pre-load and results were corrected accordingly. Force was applied at a deflection rate of 50 um till the braid was bent to 0.5 mm displacement.

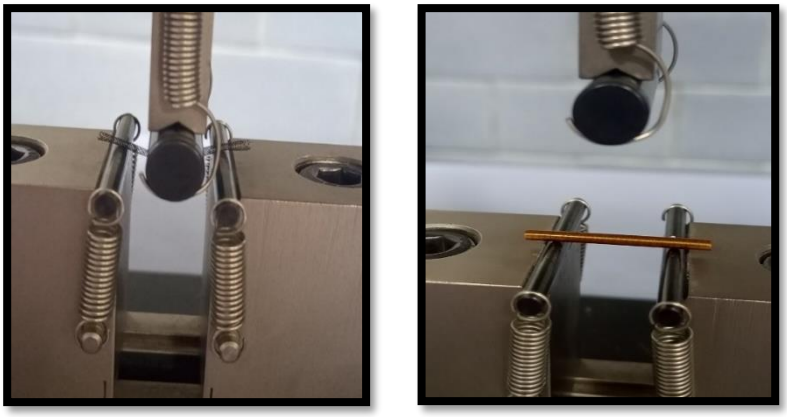

Figure 3.10: 3-Point Bending test being carried out for braided shaft and the guide catheter

3. Flexibility Test

The test was conducted to determine the average flexural force of all three-guide catheter samples.

Protocol:

EN 13868 ("EN 13868:2002,") was used carry out the flex test for the guiding catheter. Guide catheters were tested in anticlockwise orientation, from 90^0 to 0^0) using a cantilever attached to a 1000g load cell on a two-point bend testing machine (MDDC, NUST), (Figure 3.11).

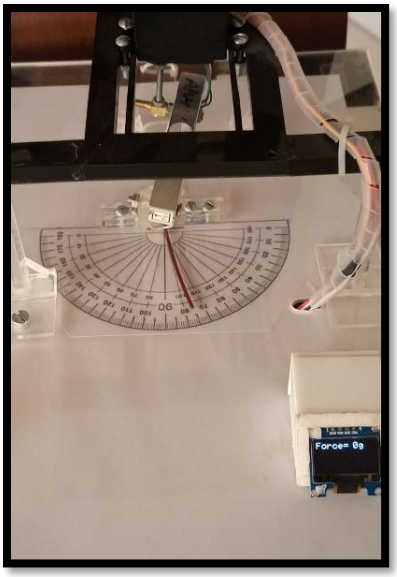

Figure 3.11: Apparatus used for flexural test

3.7.2. Physical Testing

This section details in-*vitro* kink resistance testing and pushability/advancement force testing for the polyimide based guiding catheters.

1. Pushability Test

The test was carried out to determine the force required to advance the guide catheter through vascular anatomy that the catheter traverses during the treatment procedure.

Protocol:

The pushability / advancement force experienced by guiding catheters was evaluated on (Figure 3.12) Catheter Trackability Testing Machine (CTTM) (MDDC, NUST). During this test, guiding catheters were made to pass through the mock arterial vascular system designed as per ASTM-F2394 standards. The advancement for the guiding catheter was set at 15mm/sec. The leur lock at the proximal and of the guiding catheter was firmly attached to the force gauge of CTTM. This force gauge had the measuring capacity of up to 10N. The reading was recorded as the force between the guiding catheters and inner walls of the vascular system.

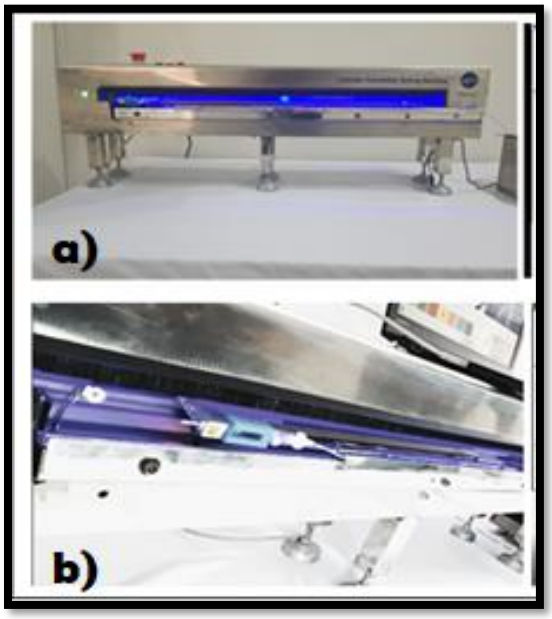

Figure 3.12: a) Catheter Trackability Machine. b) Side-view of the CTTM with catheter inserted.

3.7.3. Biocompatibility Testing

Following two tests were conducted to assure that the develop guiding catheter was suitable for the use within the body cells.

1. Hemolysis Test

The hemolysis assay is a frequently used method for determining the hemocompatibility of materials that come into contact with blood (ASTM). To determine the effect of stainless steel and the polyimide together, on RBCs test samples were placed in direct contact with blood cells The haemolytic activity of samples was measured against positive and negative controls (0.5% Triton-X) (PBS Solution) (Figure 3.13).

Protocol:

First, 30ml fresh human blood was taken in an ETDA tube, which contained anticoagulants that prevented the blood from clotting. After drawing blood, the plasma and blood cells were separated by centrifugation at 5000rpm for 5 minutes. Plasma was removed from the tube, and the remaining RBCs were rinsed in PBS solution before centrifugation to remove any leftover plasma. After that, samples were placed in tubes and incubated at 37^{o}C for three hours in a solution made with PBS and blood cells in a 1:3 ratio. After incubation, centrifuge the samples again for quantitative UV analysis to determine the hemolysis percentage. While qualitative analysis is performed without the use of a centrifuge**.**

Figure 3.13: Hemolysis test being carried out. In the picture, PBS solution, and the sample after couple of centrifuge rounds.

2. Corrosion Resistance Test

Corrosion can decelerate the catheter life during packaging, and storage. Corrosion can release toxins create adverse biological effects. When a catheter is corrosion resistant, it will not release adverse biological effects when it comes in contact with the ionic contrast.

Protocol:

The protocol ("ISO 10555-1:2013+A1:2017,") involved immersion of the catheter samples in saline solution for five hours. Next, the samples were dipper in boiling water for 30 minutes, followed by their incubation for 48 hours at 370c. Samples were then allowed to dry at room temperature, and inspected under the Olympus digital microscope at 280 x magnification (Figure 3.14).

Figure 3.14: Steps for corrosion test with pictorial representation

3.7.4. Bench Testing

If the guide catheter is to be used for the PCI procedure, it is essential to determine its ability to deliver the contrast agent, and flow rate test of the contrast. Both of the tests were conducted according to the ISO 10555-1:2013 “Intravascular catheters – Sterile and single–use catheters ("ISO 10555-1:2013+A1:2017,").

1. Liquid Leakage Under Pressure

The test was conducted to determine if the guide catheter allows the media to reach the target site.

Protocol:

The test involved connecting the catheter hub to the pressure infusion pump via leak-proof connection. The pressure apparatus was filled with distilled water while catheter’s distal end was occluded with small mandrel piece. The pressure of 300 kPa was applied and maintained for 30 seconds (Figure 3.15).

Figure 3.15: The pressure apparatus used for the liquid leakage test

2. Flow Rate Test

The test was conducted to ensure that the catheter may produce accurate visual depiction of the vasculature. This is important for right interpretation of the health of the vessels as well to determine the accurate position of the catheter.

Protocol:

Catheter was connected with a constant level tank ("ISO 10555-1:2013+A1:2017,") Distilled water was flown through the catheter, for one minute and collected in a measuring flask. The efflux was measured gravimetrically, (Figure 3.16).

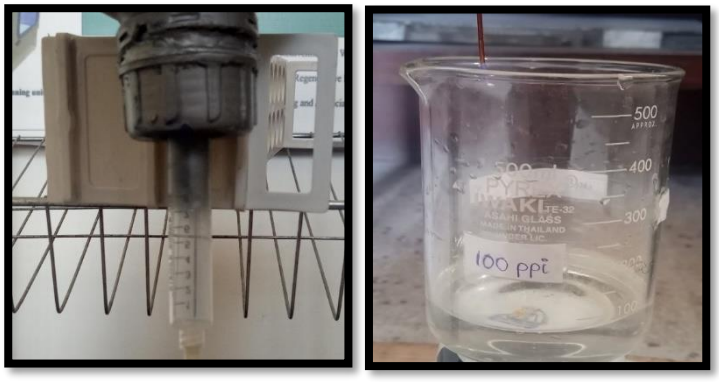

Figure 3.16: Left – glimpse of the apparatus used for measuring flow rate. Right – measuring beaker to collect the efflux coming out of the tank.

CHAPTER 4: RESULTS & DISCUSSION

This chapter discussed the results of the tests done to find out which pitch of the polyimide guide catheter worked best according to the desired properties.

4.1. Characterization

Characterization was carried out to determine the polarity, and hydrophilicity nature of the polyimide guide catheters (Asensio et al., 2009) (McPhee et al., 2015).

4.1.1. FTIR Results

Polyimide's imide group is extremely polar. The undamaged imide groups were seen in the FTIR results (Figure 4.1). The o-carboxylic amide was converted to the imide ring. The

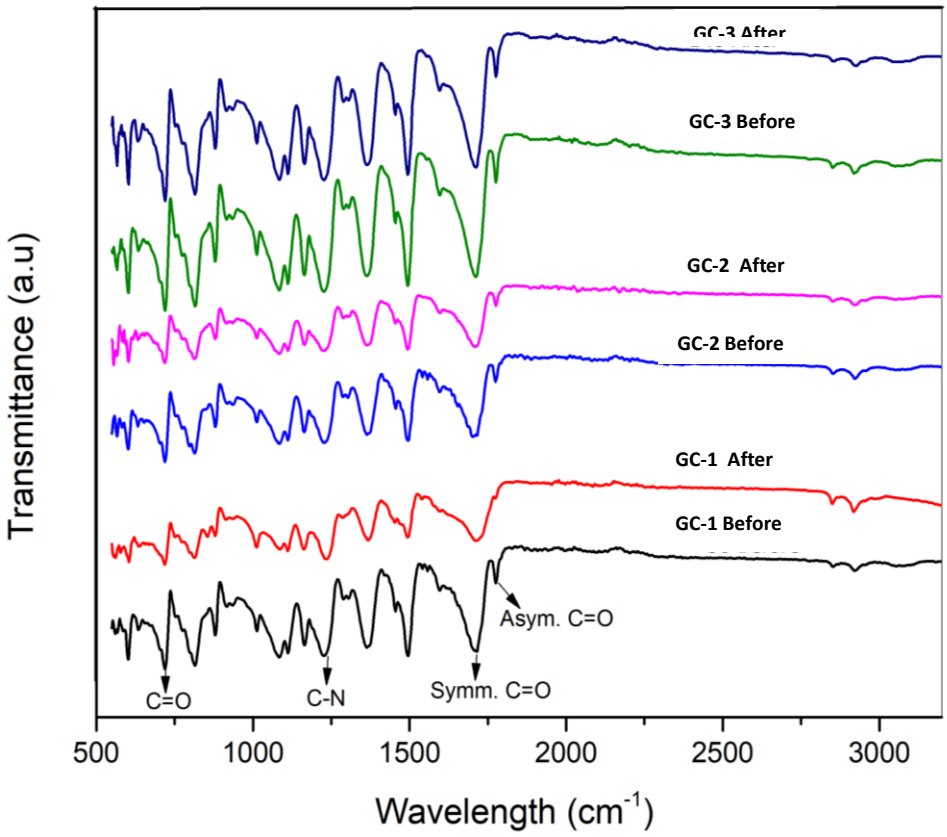

Figure 4.1: The presence of symmetrical and asymmetrical C=O, along with the C-N bonds, before and after the heating of the guide catheters are the indicative of the imide group.

disappearance of the amic-acid bands at 2500- 3500 cm-1 demonstrates this. The appearance of distinctive asymmetrical C=O at 1775, symmetrical C=O stretch at 1713, C-N stretch at 1382, and C=O bending at 745 are evidence of imide group (Dhakshnamoorthy et al., 2012).

4.1.2. Wettability Results

All the samples exhibited their hydrophilic nature before, and after the heating process (Table 4.1). However, it should be noted that the contact angles had increased after the heating

Table 4.1: Contact angles of GC-1 (top), GC-2 (middle), and GC-3 (bottom) before, and after the heating.

Samples	Before Heating	After Heating
GC-1	49.3°	60.6°
GC-2	48.6°	71.6°
GC-3	53.6°	55.2°

process for all three catheters indicating a decrease in the hydrophilicity of the guiding catheters, as the angle for the hydrophilic has to be less than 90^{o} and the angle greater than 90^{o} indicates hydrophobic nature of the materials. The pictorial representation of these angles is also displayed in Figure 4.2.

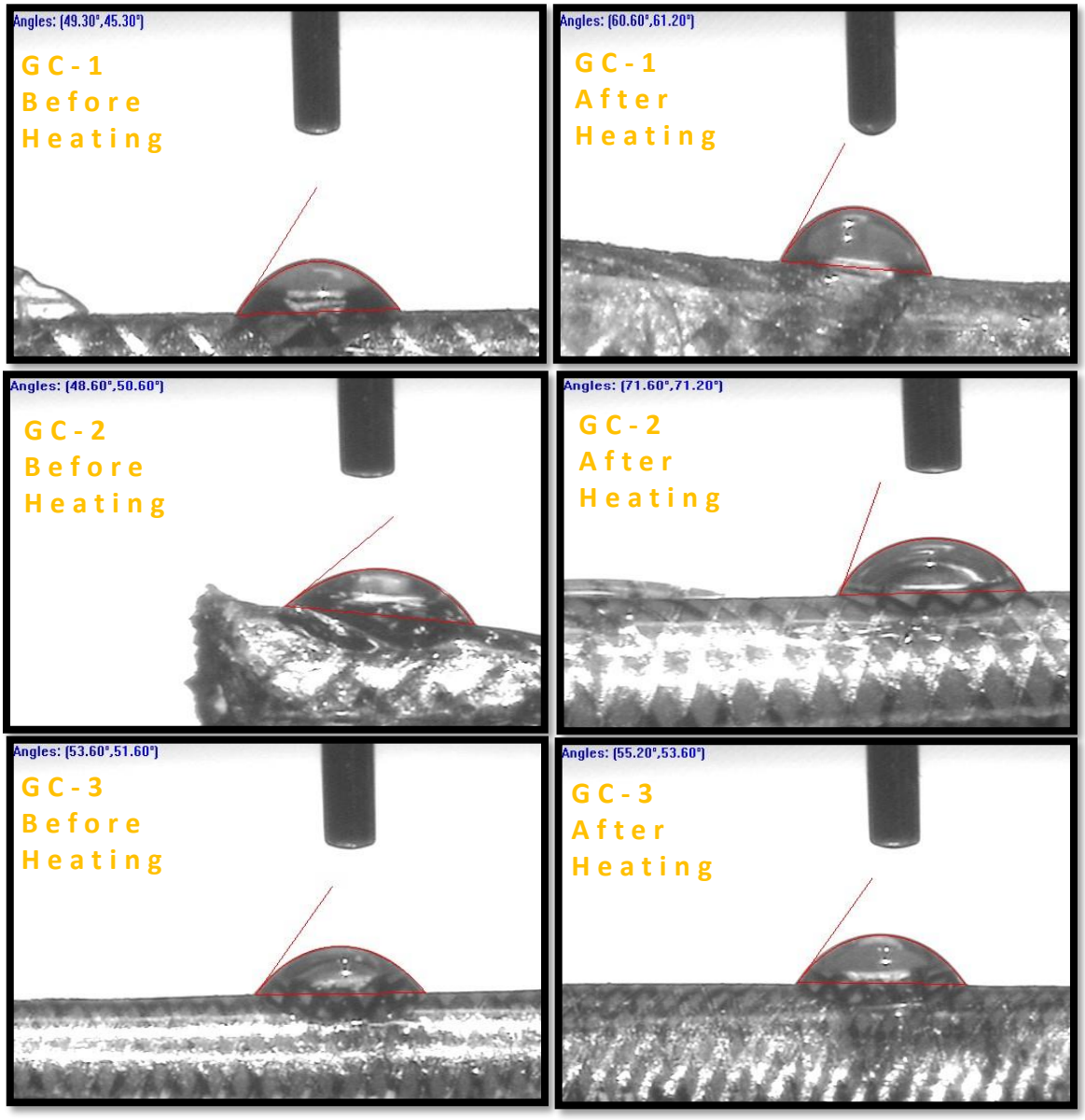

Figure 4.2: Contact angles of the guide catheters before, and after the heating.

4.2. Mechanical Testing

It was carried out to determine how would the catheter mechanically behave when inside the vascular curvatures.

4.2.1. Tensile Testing

All three braids and the guide catheters were used in the tensile testing. Three pieces of guide catheters were tested until the test specimen were broken. As a result, stress-strain curve was generated, as shown in the Figure 4.3. In this work, a SHIMADZU AG-X plus series tensile tester was used. GC-3 braid has the highest tensile strength of 5.7 N/mm^2 with GC-1 being the second one 5.1 N/mm^2 and, GC-3 braid with the least tensile strength 2.0 N/mm^2 (Figure 4.3, left). With the addition of polyimide jacket over them, the braided shaft's ultimate tensile strength enhanced extravagantly which is representative of how strong polyimide is as a polymer. As per the literature, the steeper the slope, the stiffer the material. Hence, GC-3 is the stiffest material among the test catheters, with GC-1 being the second. The stress-strain curve also yielded the ultimate tensile strength for the catheters, 100.6, 83.4, and 132.3, respectively. It is also noteworthy, that the GC-3 exhibited the ductile behavior that indicates that it is better at resisting the kinks (Figure 4.3, right).

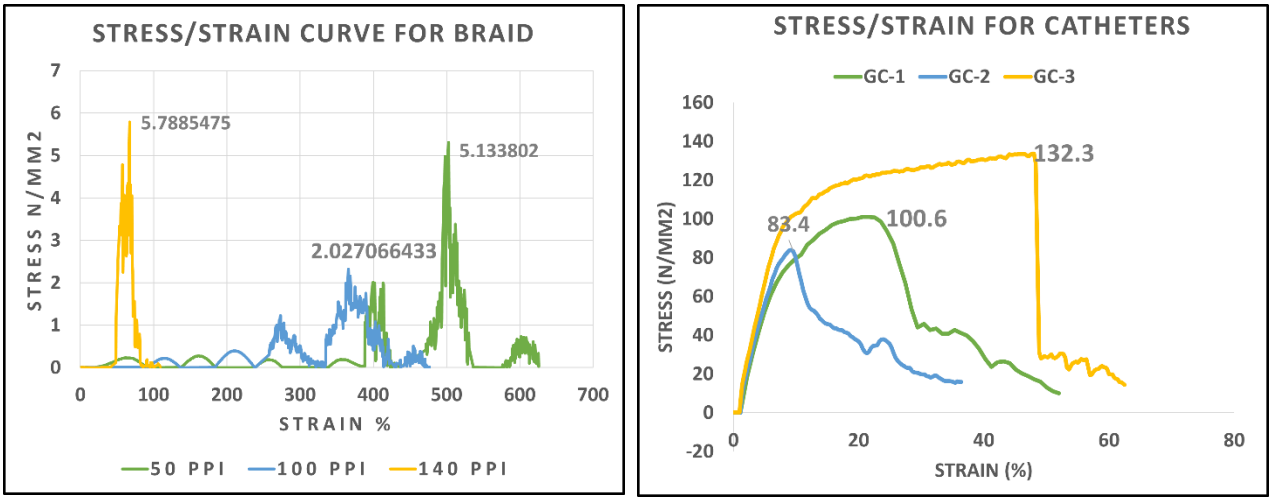

Figure 4.3: Tensile results of braids, and the catheters

4.2.2. 3-Point Bending Results

3-point bending test was also conducted for both, the braids and the catheters. The results are shown in the Figure 4.4. Since the catheter is meant to traverse the tight anatomy of the vascular system, it is crucial to have the guide catheter with no high bending stiffness. Figure 4.4 shows the bending stiffness for the braids, where force is depicted against the five displacement points. The lower value of force at any point indicates lower bending stiffness. Thus, at lower displacement values, braid with 50 picks per inch had lower force, and at the higher displacement values, the

braid with 140 picks per inch exhibited lower stiffness. Figure 4.4 displays the bending stiffness of the guide catheter samples. The steeper the slope, the higher the bending stiffness is for the catheter (Wang et al., 2017). Hence, GC-3 had the least bending stiffness which means that s the most suitable choice for the guiding catheter in terms of the bending stiffness.

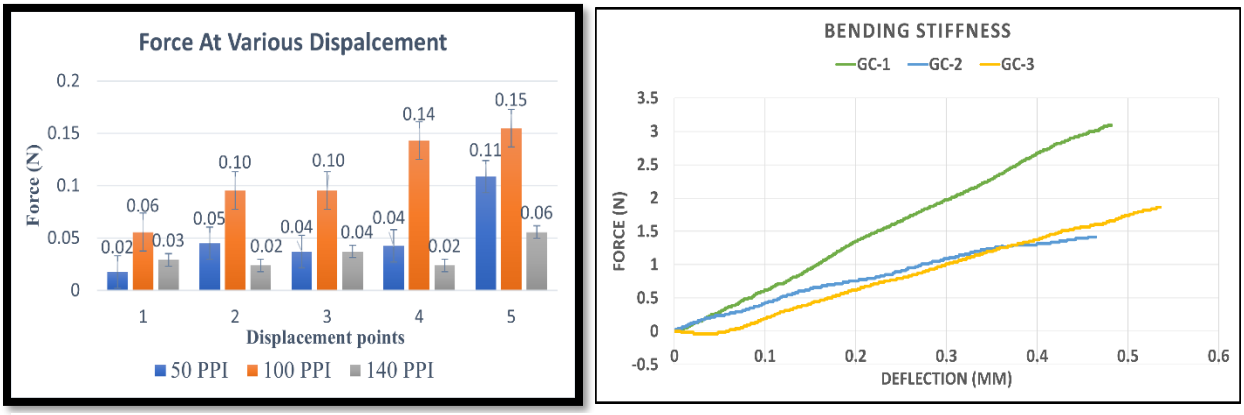

Figure 4.4: Left - Bending stiffness results for the braids. Right- Bending stiffness results for the catheters

4.2.3. Flexibility Test Results

The test was conducted to determine the average flexural force for each catheter. The force recorded as a result is displayed in Figure 4.5. As the catheter traverses the coronary arteries, they are required to exert lesser force on the blood vessels to avoid any vascular trauma. GC-1 exhibited an average force of 231.3 g, GC-2 recorded the force of 174.6 g and GC-3's force was 153 g. This explains that GC-3 is going to exert lesser force on the vessels as compared to the other guiding catheters, and it is better in terms of flexibility.

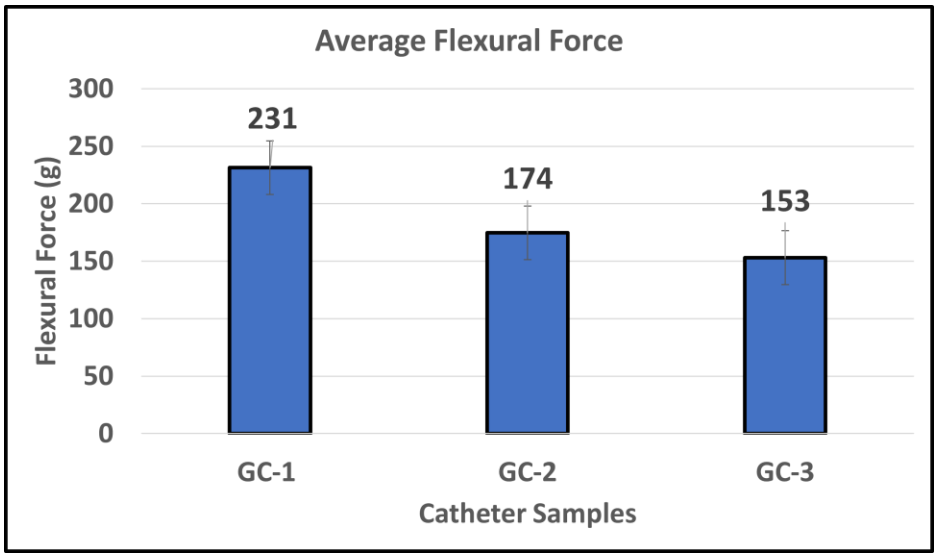

Figure 4.5: Flexural rigidity force for the guide catheter samples

4.3. Physical Testing

The catheters were subjected to the physical testing in order to determine the pushability force that is required to advance them through the blood vessels.

4.3.1. Pushability Test Results

The force exerted by the physicians to travel the catheter to the target blockage site is called pushability. As the push force of the catheter rises, the catheter becomes more prone to kinking (Schmidt et al.).

The test was performed to evaluate the real-time resistive force that the catheter may encounter in the vascular model. During the time when the sample guiding catheters were traversing the mock vascular track, GC-1 encountered an average of 591 g force, GC-2 force was 605 g whereas the GC-3 experienced the least force of 568 g (Figure 4.6). This means that when moving to the target site, it requires lesser force to make GC-3 enter the blockage site, and therefore there is less chance of damage to the blood vessels. Similarly, the CTTM also recorded the force required to withdrawal the guide catheters form the coronary arteries which also needs to be less to avoid arterial spasms. This force was also recorded to be lesser for GC-3 than GC-2, but a bit more than

GC-1. Coronary arteries can bear the maximum force of 1000g. Since, the force was least for GC3, it can be concluded that it is most effective to minimize the cases of arterial spasms.

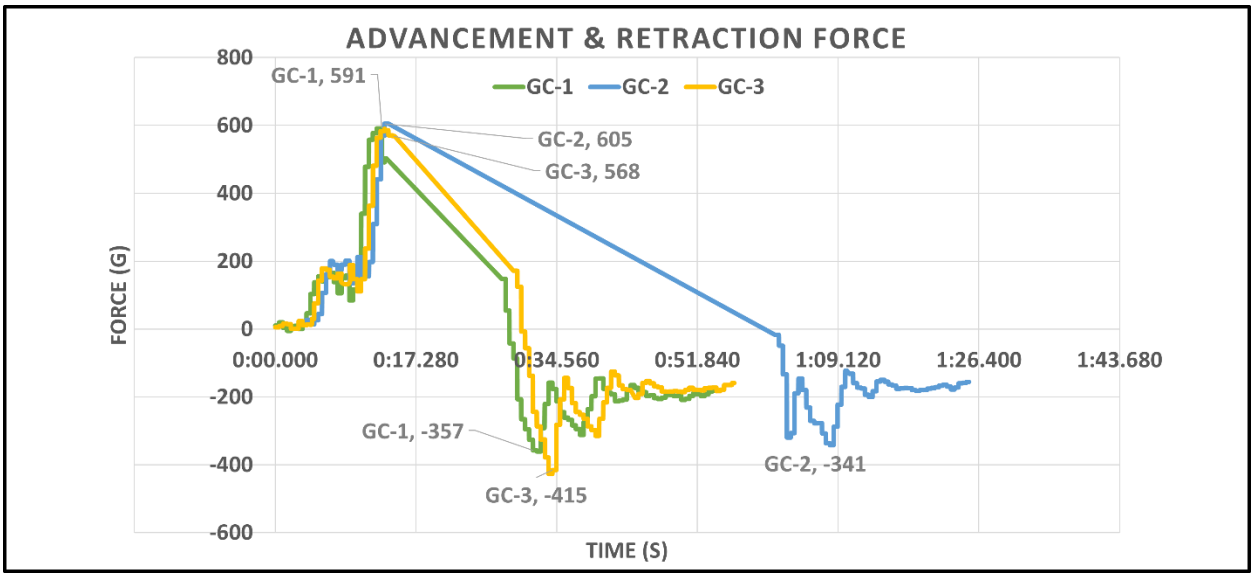

Figure 4.6: The values in positive are for advancement force, while the values in negative are for retraction/withdrawal force.

Considering the results for the tensile testing, bending testing, flexibility testing, and the pushability testing it is evident that GC-3 has performed better rest of the two catheters. Hence, GC-3 was selected as the catheter of the choice and to cater the problems mentioned in the chapter 2 of this research. Therefore, GC-3 was tested for biocompatibility and bench testing to determine its efficacy for the use in coronary arteries.

4.4. Biocompatibility

4.4.1. Hemolysis Results

According to the ASTM F756 standards the hemolytic activity of the biomaterial has to be less than 2% for it to be considered as non-hemolytic. Whereas, if the results show the hemolytic activity between 2% to 5% than the material is slightly hemolytic. 5% and more hemolytic percentage is the indicative of the material as hemolytic. The results of hemolysis test in this study

were evaluated in two both, quantitatively, and qualitatively (ASTM). The qualitative analysis involved the visual inspection of the test where supernatant was observed, Figure 4.7.

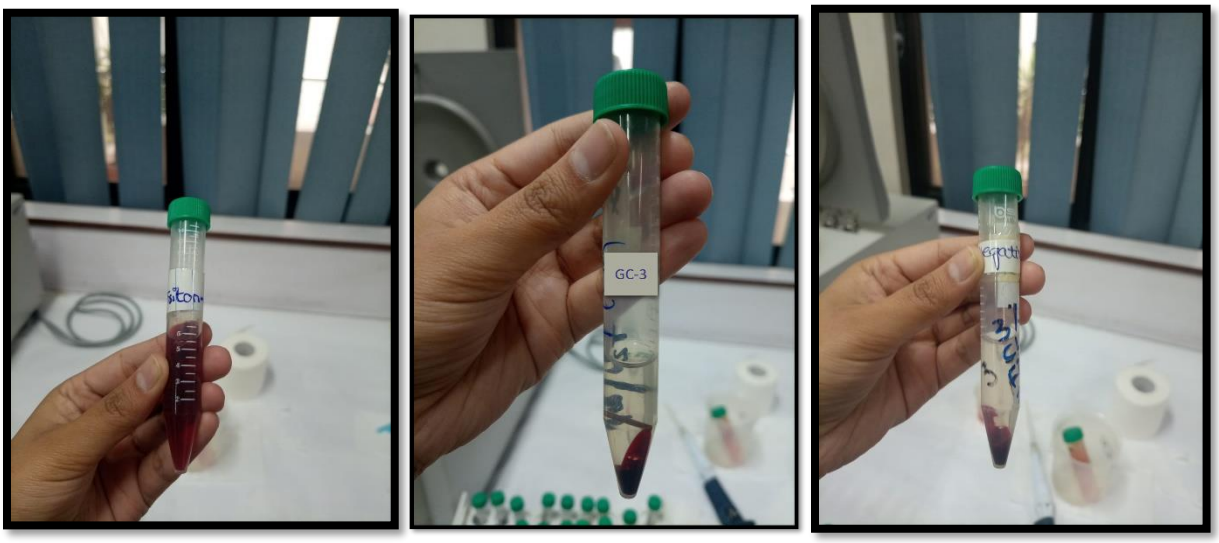

Figure 4.7: Left – Positive control, Middle – GC-3 with clear supernatant, Right – Negative control with clear supernatant

The clear supernatant at the end of the result showed that the GC-3 was non-hemolytic. The positive control had dark color, whereas negative control also showed clear supernatant. The quantitative analysis was carried out using UV spectrophotometry at 550 nm. As seen in the Figure 4.8, the hemolytic activity exhibited by GC-3 was 0.62%. Thus, it is safe to use and would not cause blood cells disruption.

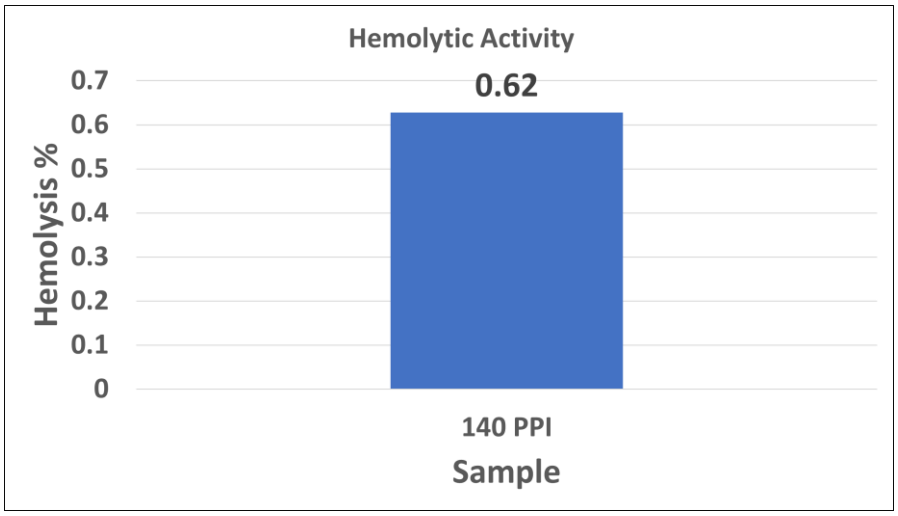

Figure 4.8: Hemolytic activity of GC-3

4.4.2. Corrosion Resistance Test Results

GC-3, the polyimide-based catheter, having the 140 picks per inch didn't show any signs of corrosion after the test was completed. As shown in the Figure 4.9 below, before, and after results for the stainless-steel braid were same when inspected under the microscope.

Figure 4.9: Left in the figure features a snippet from the braided shaft of GC-3 before the corrosion resistance test, and right sides of the figure exhibits the braided shaft after the corrosion resistance test.

4.4. Bench Testing Results

4.4.1. Liquid Leakage Under Pressure Results

While the catheter's both ends were closed, it was observed for the signs of the leakage using a paper which was wiped all over the catheter. No signs of wettability were found at any point along the length of the catheter. Moreover, the pressure deflection needle didn't go back to zero as shown in the Figure 4.10.

Figure 4.10: Pressure needle didn't deflect back showing the liquid was present in the pump even after 30 seconds.

4.4.2. Flow Rate Results

The average liquid (water) flow rate observed for the GC-3 was observed as 96.3 ml/s which is still within the allowable (125 ml/s) according to the literature. The consistent opacification of the coronary arteries with contrast media is one of the most essential variables contributing to high-quality pictures (Jerabek et al., 2018). So, if the guide catheter is to be used for emergency diagnosis purposes, the following flowrate needs to be considered, (Figure 4.11).

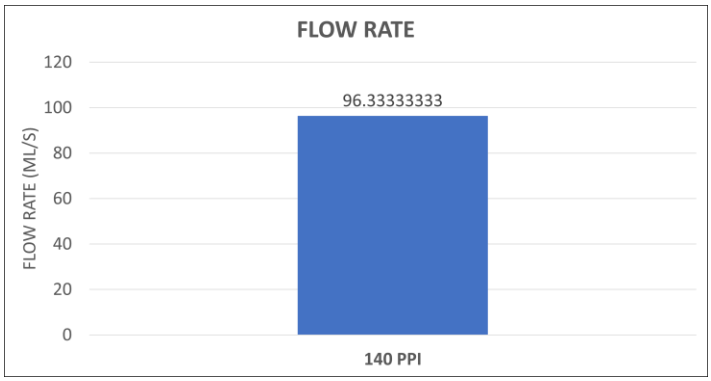

Figure 4.11: Flow rate of the guide catheter with 140 picks per inch

CHAPTER 5: CONCLUSION & FUTURE RECOMMENDATIONS

In this research, guide catheter prototype was fabricated from polyimide and by varying its pitch as it greatly influences the mechanical behavior of the guide catheter. After considering the commercial guide catheter, this research studied the effects of 50 pick count, 100 pick count, 140 pic counts on the catheter behavior. It was found out that most of the mechanical properties are improved by using the guide catheter with 140 picks per inch and polyimide as jacket material. Although, 140 picks per inch guide catheter was better in flexibility, but it was also found to be superior in longitudinal strength imparted by polyimide. Owning to the lower friction of the polyimide (DataSheets). all three guide catheters exhibited a lower advancement force, but being the least in advancement force value, GC-4 (140 picks per inch) was shortlisted as the best in avoiding the arterial spasms. Polyimide along with stainless steel were also tested for their corrosion resistance and hemolytic properties to ensure safety to red blood cells and other parts of the body. They were found to be safe to use for the guide catheter of the choice.

Future Recommendation

The developed guide catheter with 140 picks per inch and polyimide should also be tested for the torqueability as it is also open of the crucial mechanical property for the performance. Due to the unavailability of the equipment, it was not tested in this research. Sophisticated method for kink resistance test is also required that can determine that when the guide catheter is subjected to the advancement force of 500 or more, the polyimide guide catheter having 140 pick count won't neck.

For the more accurate analysis, two primary test benches are necessary.

1. Torque testing
2. In-vivo testing

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