Design and Development of Auxetic Coronary Stent for the Treatment of Coronary Heart Diseases

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ISLAMABAD
2014

In the name of Allah, the most

Beneficent and the most Merciful

Declaration

It is hereby declared that this research study has been done for partial fulfillment of requirements for the degree of Master of Science in Biomedical Engineering. This work as not been taken from any publication. I hereby also declared that no portion of the work referred to in this thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning.

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Dedicated ….

To a Person who is "The Rehmat" for all the universe,

And

To our Parents and to whom we love and respect

Acknowledgement

First of all I am very thankful to Almighty Allah, The Kind and The Merciful, who gave me an opportunity to join the degree course of MS at National University of Sciences and Technology (NUST) Islamabad and make me able to complete this thesis work successfully.

I take immense pleasure to thank my Supervisor Dr. Murtaza Najabat Ali for providing me this opportunity to work under his supervision. I owe a great deal of gratitude to him and for the encouragement, valuable guidance and timely suggestions rendered in the completion of this work.

I am highly indebted to NESCOM for providing me facility and support for completion of this research.

Finally, I would like to thank all faculties in department for their consistent support and guidance.

FAISAL AMIN

LIST OF PUBLICATIONS

Patents

1. *Murtaza Najabat Ali, Umar Ansari, Muhammad AsimMinhas, Faisal Amin, WakeelShahid, Jamal Saeed (2014) "ANISOTROPIC STENT DEVICE FOR THE TREATMENT OF CORONARY HEART DISEASE",* **26/2014**

Journal Publications

1. Faisal Amin, Murtaza Najabat Ali, Umar Ansari, Mariam Mir, Muhammad AsimMinhas and WakeelShahid, NoamanUl-Haq (2014),*"Auxetic Coronary Stent Endoprosthesis: Fabrication and Structural Analysis",* Journal of Applied Biomaterials & Functional Materials;

2. Murtaza Najabat Ali, Faisal Amin, Umar Ansari, Muhammad AsimMinhas (2014), "*Anisotropic Coronary Stent Device: Fabrication and Structural Analysis*",WIT Transactions on Engineering Sciences;

3. Faisal Amin, Murtaza Najabat Ali, Mariam Mir, Umar Ansari (2014), "*Emerging Approach for Treating Complications Associated with Pertrochanteric Fractures: A Review*", Minerva Ortopedica E Traumatologica;

4. Faisal Amin, Murtaza Najabat Ali, Muhammad AsimMinhas (2013), "*An Evolutionary Appraisal of the Efficacy of Coronary Artery Stents relevant to the Treatment of Coronary Heart Diseases*", International Journal of Biomedical and Advance Research, Vol.4 Issue 1;

5. Tehreem Jamil, Mariam Mir, Faisal Amin, Umar Ansari, Murtaza Najabat Ali (2014), "*Fabrication and mechanical testing of synthetic cervical anterior longitudinal ligament",* POLIMERY Journal;

6. M.N.Ali, Faisal Amin (2014), "*Smart stent: A new concept for the treatment of central airway obstructions",* NUST Journal of Engineering Sciences, Vol. 5 No.1, pp. 27-34.

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LIST OF ABBREVIATIONS

CHD	Coronary Heart Diseases
PTCA	Percutaneous Transluminal Coronary Angioplasty
NPR	Negative Poisson's Ratio
CAD	Computer Aided Design
PCI	Percutaneous Coronary Intervention
PLLA	Poly L-Lactic Acid
POBA	Plain Old Balloon Angioplasty
CATH LAB	Catheterization Laboratory
BMS	Bare Metal Stents
DES	Drug Eluting Stents
ISR	In-Stent Restenosis
CNC	Computer and Numerically Controlled
H_2O_2	Hydrogen Peroxide
BF_3	Boron Trifluoride
NaOH	Sodium Hydroxide
H_3PO_4	Phosphoric Acid
H_2SO_4	Sulphuric Acid
SEM	Scanning Electron Microscope

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ABSTRACT

Cardiovascular heart disease in the present era is one of the leading health problems and needs considerable healthcare resources to avoid these issues. This thesis is focused on new coronary stent development based on Auxetic geometry that causes the stent to exhibit negative Poisson's ratio. Vascular system of the body shows anisotropic characteristics whereas commercially available coronary stents have isotropic properties. This results in a mismatch between stent isotropic-anisotropic properties and arterial wall which is not favorable for mechanical anchorage of available commercial available coronary stent with the arterial wall. It is believed that with inherent anisotropic mechanical properties the Auxetic coronary stent will have good mechanical anchorage with arterial wall. The Auxetic design was fabricated through laser cutting and surface treatment was performed via acid pickling and electropolishing process and followed by heat treatment. The mechanical performance of Auxetic coronary stent was analyzed through invitro mechanical analysis. Scanning electronic microscope (SEM) was used to determine fabrication processes effects on the Auxetic stent topography. The invitro mechanical analysis shows that Auxetic stent design will effectively maintain the luminal patency of the coronary artery. Also, it will prevent the stent migration problem by expanding in both radial and longitudinal directions, thus Auxetic coronary stent showed no foreshortening. The Auxetic stent bulges outwards when it is radially expanded through an inflated balloon by virtue of its synclastic behavior.

CHAPTER 1

INTRODUCTION

1.1. Introduction

Coronary Heart Diseases (CHD) in this present era are one of the foremost healthcare problems and require much attention and care to avert from this problem. The leading complications of coronary heart disease are the angina pectoris and myocardial infarction caused by a disease known as atherosclerosis. This disease lead towards the stenosis where the fats or plaques are accumulates under coronary artery endothelium layer. This deposition in turn blocks the coronary artery and not allows smooth flow of blood to the walls of the heart. Consequently, disturbing the coronary artery luminal patency.

The treatment of atherosclerosis coronary artery is carried out by deploying the coronary stent in the stenosed artery. "A stent is a small medical device comprising of expandable mesh like tubular structure that when implanted act as a scaffold and maintains the luminal patency of stenosed artery by opening the narrow coronary artery ". So, having no obstruction the oxygen rich blood then smoothly flow through the artery. The chances of above complications are greatly minimized by the procedure of stents intervention. Corrosion resistant stents such as 316L stainless steel and cobalt-chromium alloy are clinically deployed to reinstate luminal patency of coronary arteries. Percutaneous Transluminal Coronary Angioplasty (PTCA) is an stenting technique in which coronary stent is deployed and positioned in the stenosed artery. Designs of many metallic coronary have been developed with different structural and mechanical properties.

For clinical applications a good platform is provided by 316L type stainless steel. Studies have illustrated that design of stent has great influence on late lumen loss along with neointimal proliferation which eventually affect the requirements of post intervention procedure and rate of

restenosis. It is also revealed that design of stent also affected the platelet activation and thrombogenesis. Nevertheless, the problems such as restenosis, migrations collapses and thrombosis are still common.

A stunning new field of venture is to study Auxetic structures exhibiting negative Poisson's ratio (NPR). These structures have the ability to contract under uniaxial compression in the transverse direction and when stretched it expand radially. There are some models of rigid mechanics that provide as models for designs and structures. Like in Auxetic materials the behavior of Auxetic in geometry based models are also scale independent that at any level it can be operate with deformation mechanism as well as with similar geometry combination. Both geometric features and deformation mechanisms are mainly associated with auxeticity of a system and the models such as rotating rigid unit models allowed this behavior to exhibits and subsequently because of the unit models stretching and rotating the deformation then occurs in a system.

This thesis presents the design and fabrication of a new coronary stent design with Auxetic geometry for the treatment of coronary artery disease of the heart. The new coronary stent design complements the body's vascular system anisotropic properties. Based on previous studies, we can hypothesize that the new Auxetic design of stent will allow good anchorage with arterial walls. When expanded through an inflated balloon, the special feature of this design allows maintaining vascular patency by expanding in two directions simultaneously The design of Auxetic geometry of the present coronary stent build with plurality of unit cells interconnected with the help of horizontal and vertical edges to form struts and hinges. The single unit structure of the stent formed by four angulated squircles along with a hollow diamond.

1.2. Objective of the Study

The objective of this study is to design and fabricate Auxetic coronary stent that avert the localized constriction of blood flow in the coronary artery of the heart. The Auxetic design was developed on AUTOCAD software and the fabrication process was carried out through Laser cutting, Surface treatment and Annealing process. This new Auxetic coronary stent will might

effectively maintain the luminal patency of the coronary artery by expanding in both radial and longitudinal directions and will reduce the chances of restenosis. Furthermore, present coronary stent will also have good mechanical adherence with arterial wall because of its inherent anisotropic property.

1.3. Approach and Methodology

- Problem area was selected;
- Literature was studied about the coronary stents and compile data on all possible process routines and design;
- Possible design for Auxetic coronary stent was selected and implemented on computer aided design (CAD) tool with design specific dimensions;
- Fabrication of the prototype of the Auxetic coronary stents was carried out;
- Analysis on the fabrication processes results as well as on invitro mechanical analysis and surface morphology analysis were evaluated;
- Lastly. Thesis write up then carried out.

1.4. Thesis Overview

- In this chapter with an introduction that includes the objective, approach and methodology and overview of the thesis is presented.

- Chapter 2 presented the literature view about the coronary stents with their implantation techniques, applications, history and brief description about the types of coronary stents available commercially.

- Chapter 3 concentrates on the design along with methodology that was carried out for the fabrication of Auxetic coronary stent.

- Chapter 4 describes the results obtained on the work described in chapter 3 along with in-vitro mechanical analysis and surface morphology analysis.

- Chapter 5 illustrates the discussion on the salient features of the results.

- Conclusion is presented based on the outcome of the research work.

CHAPTER 2

LITERATURE REVIEW

2.1. Introduction

The origin of coronary heart disease (CHD) is mainly the atherosclerosis where there is development of deposits of plaques below the endothelium that eventually narrowing the vessels of blood and reduce or resist the flow of oxygen rich blood to the heart walls as shown in figure 1. The back push of walls of vessel of the plaque and reopening of artery are the imperative treatment of coronary heart disease (Gott, 2012). Clinical reports revealed that cardiovascular related diseases are the main worldwide health care dilemma at the present decade. At the arterial walls the basis for formation of thrombus is the buildup of fats, cholesterol, fats etc that block arteries as well as slender the vessels lumen (Basu, 2012).

Blood vessels narrowing because of atherosclerotic possess a pain upon breakdown of tissue as shown in vascular disease because of the buildup of fatty plaques and blood movement constraint to the tissues (Gage, 2003). To deal with this problem, the well proficient and supportive device is the coronary stent (Basu, 2012). Narrowing arteries (stenosis) that delivers blood to the tissue of heart apparently causes the angina and myocardial infarction. Over the years for coronary heart disease treatment the percutaneous coronary intervention (PCI) is stunning alternate to surgical revascularization (Kraitze, 2008).

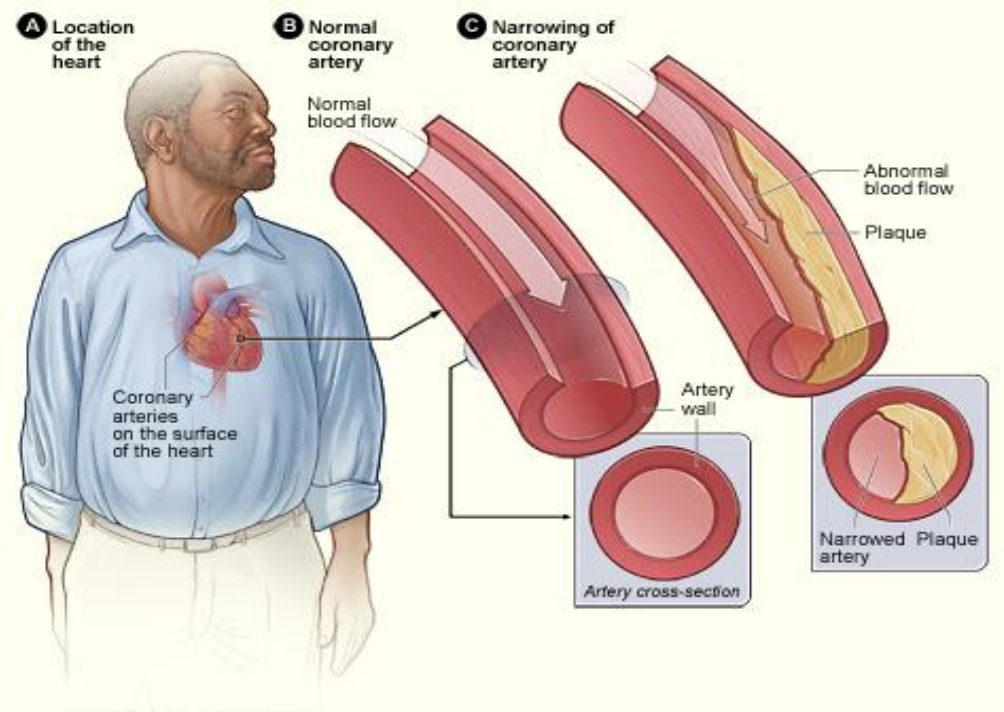

Figure 1. Showing, (A) Heart location (B) Normal Coronary artery (C) Narrowed coronary artery by plaque (NIH, 2012).

2.2. Historical Background

Charles Theodore Dotter and Melvin P. Judki in 1964 introduced the first angiography and thereafter thirteen years of first angioplasty Andreas Gruntzig performed the first balloon angioplasty that step ahead towards cure of coronary intervention (Garg, 2010). Many designs of metallic stents have been developed and introduced by researchers to increase the performance of vascular stents following the idea of these stents (Venkatraman, 2003). In 1977, a new treatment of coronary artery was introduced by Gruentzig who successfully in structure lesion employed the percutaneous transluminal coronary balloon angioplasty procedure. In this method of treatment when balloon dilate the structure lesion broadens due to which the flow of blood get improves. In this treatment method the flow of blood improves when the structure lesion broadens after the dilation of balloon (Kwon, 2012).

Duke Stent, a biodegradable stent was first introduced in 1980s which was formed by woven strands of poly l-lactic acid (PLLA) polymer. In human the first biodegradable stent implanted

that had helical coil zigzag design was Igaki–Tamai stent (Venkatraman, 2003). The complication rates was appreciable minimizes due to the introduction of stenting in 1993. The complications which reduce by stents are elastic recoil of wall of vessel, closure of acute and subacute vessel**,** intimal dissection and minimize the rates of restenosis after angioplasty (Kraitze, 2008).

2.3. Stenosis and Restenosis

Stenosis is an abnormal condition where the arteries turn to tapered or narrowed by the accumulation or backing of fat or cholesterol which ultimately not permit the blood flow to the heart walls. The normal function of the heart affects severely when hearts arteries get constrict and therefore become fatal. The technique for stent implantation to treat cardiac vessels stenosis is Percutaneous Transluminal Coronary Angioplasty (PTCA) which make use of intervention of stent is a stunning replacement to medical therapy and surgical revascularization. In the body into a natural passage a stent that is mounted on balloon catheter is introduced that provides support as well as mechanical assist to the diseased vessel and work against ultimately to the induced diseased that caused constraint of localized flow. This stent usually broaden the wall of vessels and compact the plaque subsequent to position into an artery. The important advantage is that they do not necessitate open surgery of heart (Basu, 2012). Because of efficient progress and foreword of coronary stents through stenting procedure into the medical practice of several years of endeavor made it promising to get over or minimizes these complications (Paszenda, 2010).

Re-narrowing of blood vessels which reduces the lumen size and constraint blood movement after the intravascular procedure is the Restenosis. It is usually explained and distinguished by remodeling of artery and intimal hyperplasia. Restenosis occurs by amalgamation of mechanical reaction along with a biological reaction to percutaneous coronary intervention (PCI) (Kraitze, 2008). The restenosis problems occur in plain old balloon angioplasty (POBA) treatment was minimizes through treatment of coronary stent for the first time when in 1986 Wall stent was implanted (Garg, 2010).

2.4. Stents

Stents are considered as essential intravascular implants for cardiovascular heart disease treatment (Paszenda, 2010). Stents are arrangements of mesh like structures that radially expand at the site of narrowing vessel to stabilize the patency of vessels (Gott, 2012). These small implants have features of tiny sized, cylindrical design scaffolding. A type of metal that opened area that is active after it is inserted into stenosed coronary vessel. The technique for the coronary heart disease treatment in order to open the coronary arteries is the Percutaneous Transluminal Coronary Angioplasty (PTCA) (Paszenda, 2010) as presented in Figure 2.

The significant feature in the effectiveness of the surgical procedure is the stents expansion that primarily based on material along with geometry of stent as well as on the deformation (Migliavacca, 2005). Bare metal or first generation stents were designed and developed with fully mechanical functionality. Later, second generations stents which were drug eluting stents reduces the restenosis and in turn restrain the inflammation (Gott, 2012).

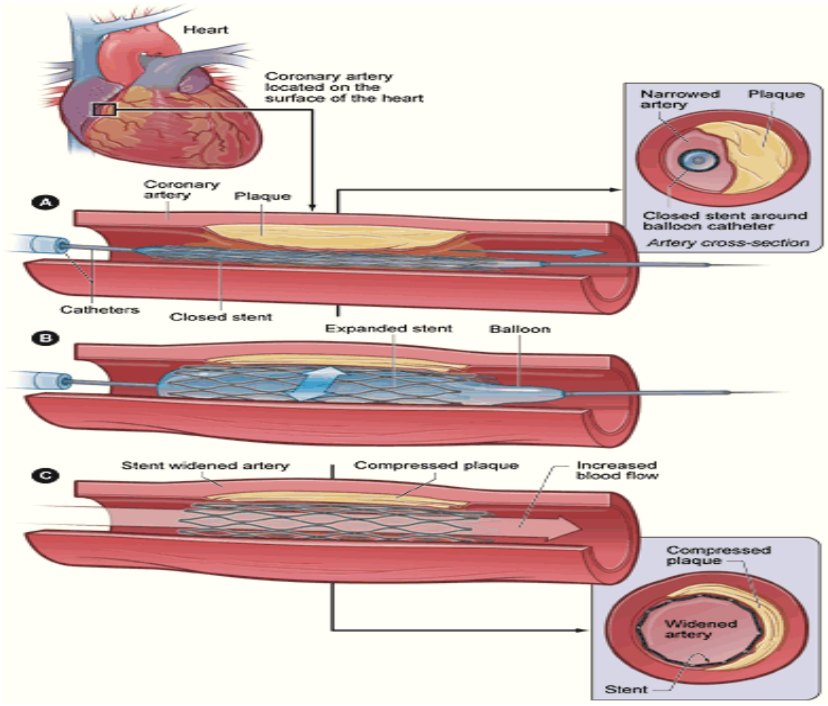

Figure 2. Percutaneous Transluminal Coronary Angioplasty (PTCA), (Schmidler, 2010).

When insert into vessel lumen stents open previously blocked pathway after it is expanded by Percutaneous Transluminal Coronary Angioplasty (PTCA) procedure. Mainly stents are fabricated from polymer filamentous and metals. In various areas of studies stents were giving preference over balloon angioplasty owing to its acute and long term benefits (Kraitze, 2008). According to many engineering entities stents are classified that contrived biocompatibility, outcome and characteristics (Sangiorgi, 2006). The ideal characteristics reported are (Sangiorgi, 2006) low unconstrained profile, high radial strength, trackable, low surface area, radio-opaque, biocompatible, thromboresistant, circumferential coverage, reliably expandable (Sangiorgi, 2006).

Due to the design, form factor and mechanical act the requirement of stents varies and also put few restrictions on the progression of manufacturing and assembly that are mainly applied on them. Metal and laser cutting is mostly utilized for the development of majority of coronary stents that usually form a mesh like shape (Takahata, 2004). The stent design pyramid illustrates in figure 3.

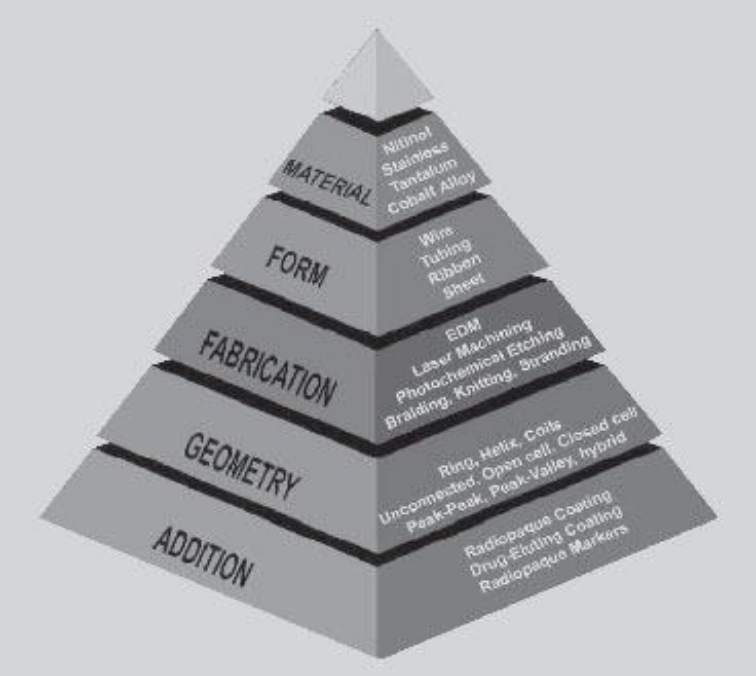

Figure 3. Stent design pyramid (Sangiorgi, 2006)

2.5. Coronary Stents

Implantation of coronary stents is an important part of interventional procedures for percutaneous revascularization. Over balloon angioplasty the importance of coronary stenting because of two significant assessments that is reduction in restenosis and recurrence of intercession that require in focal lesions as well as in large coronary arteries. The existing coronary stents that is bare metal stents and drug eluting stents are made with different materials and designs (Sangiorgi, 2006). It was eastablished that the stenting has improves the coronary intervention protection and rate of success of short term. Remodeling of negative arterial, Neointimal hyperplasia (Migliavacca, 2004) and elastic recoil (Mintz, 1997) – (Sangiorgi, 1999) are the important three pathogenic factors related to restenosis. Moreover, stents have the potential to reduce and counteract elastic recoil and arterial remodeling respectively however, the restenosis still exists because of neointimal hyperplasia (Migliavacca, 2004) – (Schwartz, 2001).

2.6. Coronary Stent Implantation Technique

Deployment of coronary stent is carried out in hospital in specialized dedicated room called as Catheterization Laboratory (CATH LAB). Coronary stent deployment and insertion method steps are explained below;

1. As after local anesthetic given, a small incision is made in groin femoral artery and then a catheter sheath introducer inserted. Next, through the sheath a guiding catheter is passed through the heart as presented in figure 4.

2. Through the guiding catheter sometimes a contrast dye is administered that let the artery to observe through the angiography machine.

3. The doctors then advance through guiding catheter to the narrowed artery.

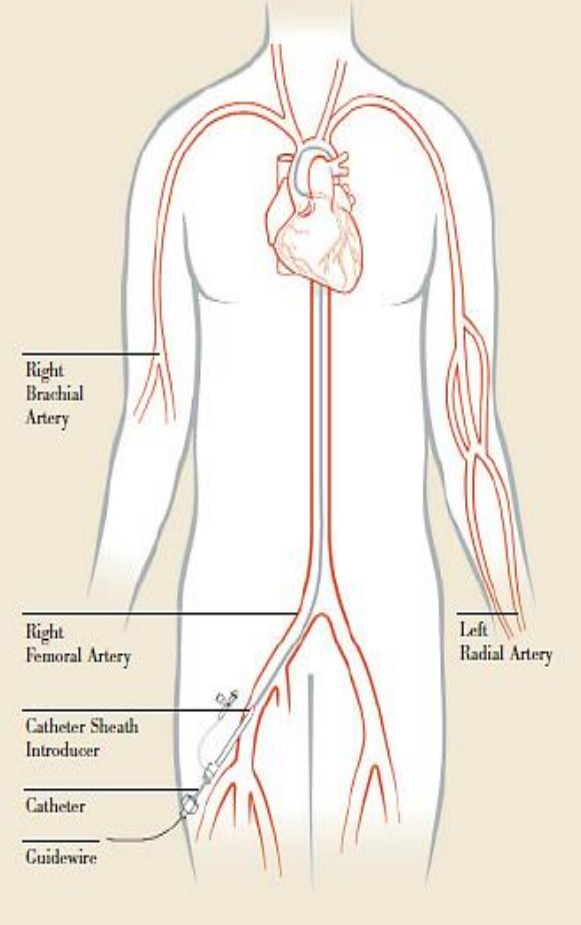

Figure 4. Coronary Stent insertion site (UCHD)

4. Now the coronary stent is mounted on balloon catheter and position it at the blockage artery as shown in figure 5.

5. After the balloon catheter is inflated, the stent get expanded and positioned there.

6. The balloon catheter is deflated and removed once the coronary stent adjust in the artery.

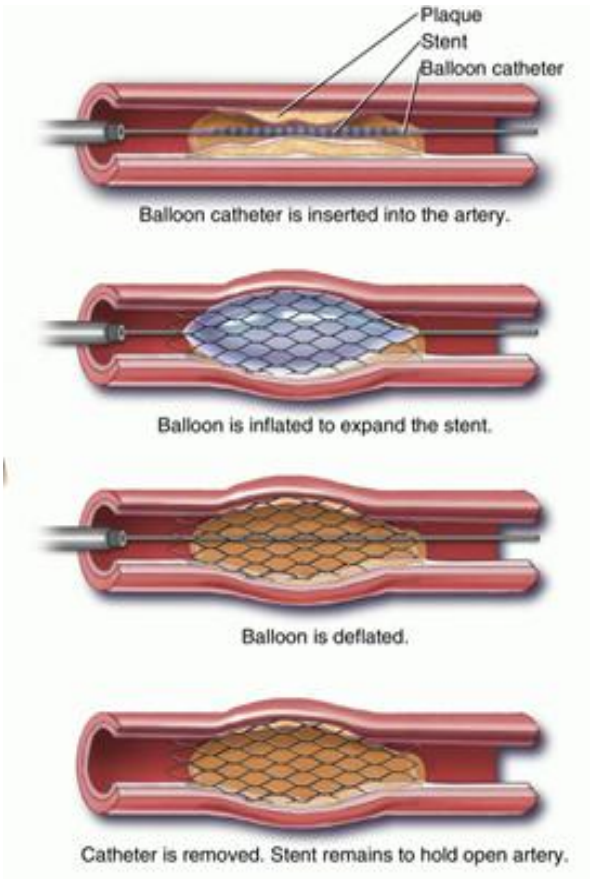

Figure 5. Coronary stent implantation (CMVM. 2014)

2.7. Types of Coronary Stents

Based on the expansion modality, the availability of coronary stents are in two types such as balloon expandable stents and self expandable stents (Migliavacca, 2004). Due to material characteristics the balloon expandable stents through the balloon inflation are deformed plastically, even after the balloon is deflated the stent retains its expanded shape, apart from slight recoil formed by deformation. Self expanding stent in expanded shape are developed which is compressed to hold in a delivery system and after it is released from delivery system it has the ability to spring back to preset diameter (Gage, 2003), (Sangiorgi, 2006). Placement complication mainly cause by the self expanding stents and cause shortening at deployment however due to emerging of new designs this effect has been minimize whereas high stiffness

shows by balloon expandable stents (Gage, 2003). For balloon expandable stents the ideal material for manufacture should hold low yield stress as well as have high elastic modulus. Balloon expandable stents are of small diameters that are deployed at the target side within the lumen of vessel after it is mounted on balloon catheter. On other side, functionally the self expanding stents depends on elastic properties of materials and these materials must also hold high yield stress and low elastic modulus (Sangiorgi, 2006). Nowadays cardiologists have variety of coronary stents for implantation. Coronary stents that are most widely used are new biodegradable polymers drug eluting stents (DES) and bare-metal stents (BMS) (Garg, 2010).

2.7.1. Bare Metal Stents

Metals are available in balloon expandable and self expandable. Expansion of metal stent is based on the principle of plastic deformation. Some of the main disadvantage associated with metals stents includes thromobogenicity, fear for metal hypersensitive, immunological response irritation. Stents that are made of metals have the capacity to hold drug delivery locally with less thrombogenic like materials such as polymer coatings (Kraitze, 2008). In the beginning, the majority of the stents that were fabricated was stainless steel stents and named as bare metal stent (BMS). In grouping with immunological response the body affects inflammatory mediators by metal stents that eventually allow neointimal hyperplasia (Curcio, 2010), (Tan, 2013). For the fabrication of metal stents, its selection is mainly based on strength, malleability, memory and elasticity. Materials that are mainly used include stainless steel, tantalum and nitinol alloys (Kraitze, 2008).

To increase the quality as well as performance of vascular stents researchers have developed and presented various metallic stents design since the starting of stents development. It has been revealed that intracoronary stenting played a vital in reducing the closure of vessel and rapid occurring of restenosis. Despite of high rate of success In-stent restenosis is still considers a major obstacle. Moreover, along with issue of compliance disparity among the stent and artery wall metallic prosthesis effects are little identified for long term therefore consideration is essential to improve new metals stents (Venkatraman, 2003).

2.7.1.1. Cobalt - Chromium Alloy Stent

Cobalt-chromium alloys are the material of choice for the coronary stents because of its association among struts thickness and to In-Stent Restenosis (ISR) rates. As compared with the stainless steel this alloys high strength levels and high attenuation of x ray (Martin, 2011). Currently cobalt alloys are not in clinical trial but they are also readily available for coronary intervention. Cobalt alloy also provides better radiopacity.

2.7.1.2. Nitinol (Nickel Titanium) Alloy Stent

Since balloon expandable stents dominating the markets of stents but there is also used of self expandable stents manufactured from nickel titanium (nitinol) (Panescu, 2004). Nitinol made through balance titanium and 55 wt %. Below the room temperature this type of stent is crimped over delivery system easily and until expand it strike the wall. The nitinol stents design includes Sheet-based Stent Designs, Wire-based Stent Designs and Tube-based Stent Designs (Stoeckel, 2004) as presented in figure 6.

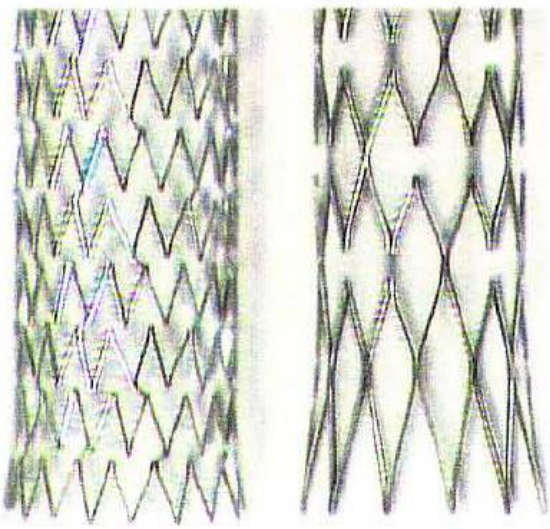

Figure 6. Laser cut Nitinol stents (Stoeckel, 2004)

2.7.2. Metal Bioabsorbable Alloy Stents

Two categories of bioabsorbable metal alloys includes are bioabsorbable magnesium stent and bioabsorbable iron stent.

2.7.2.1. Bioabsorbable Magnesium Stent

Due to metallic nature, biocompatibility and higher radial strength Magnesium stents as presented in figure 7 has advantages over polymeric stent (Shabto, 2014). Bioabsorbable WE43 magnesium-alloy stent name as AMS stent has the same strength as 316L stainless steel (Martin, 2011). In the PROGRESS-AMS trial of 63 patients, the first metallic bioabsorbable stent having thickness of 165 μm was implanted (Ormiston, 2009). During the trials it was absorbed that magnesium stents undergoes rapid absorption in humans and lasted for about days or weeks. However, serious cardiac events were resulted therefore more PCI were performed in 15 patients in early months of procedure (Ormiston, 2009). And 45% patients got PCI procedure later. The magnesium stent within 4 months easily degraded. Currently many investigations are in process for AMS stent for degradation of long time with alteration in their mechanical properties (Martin, 2011).

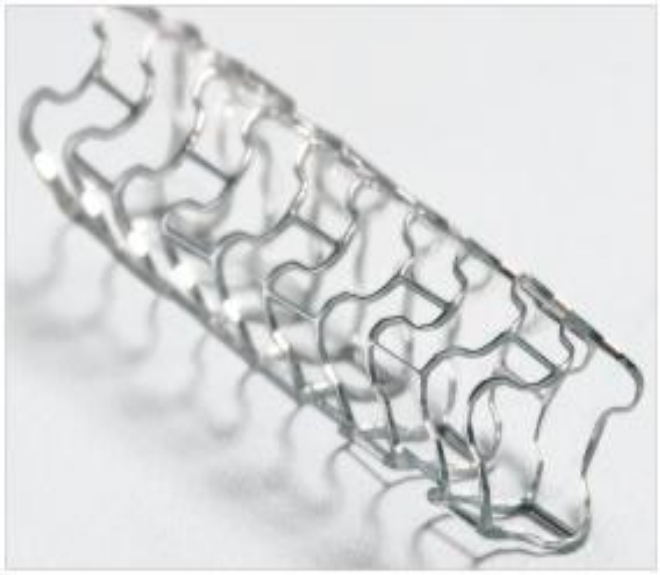

Figure 7. Magnesium stent (Shabto, 2014)

2.7.2.2. Bioabsorbable Iron Stent

(Peuter et al, 2001) carried out experimental studies on 100-120 μm thickness bioabsorbable iron stent. This stent was manufactured with 41mg pure iron that is equal to the iron in use by human orally and deployed into descending aorta of white rabbits in New Zealand (Shabto, 2014). During the follow up of 6 to 18 months there was no information on thrombosis after the implantation but on other side, the animals experienced destruction of internal membrane of arteries (Shabto, 2014).

2.8. Drug Eluting Stents

"A drug eluting stent is device that into bloodstream releases single or multiple agents that are bioactive". In-stent restenosis eliminates when the agent deposited to the affected tissue. Drug eluting stents reduces the side effects as well as provide a high drug concentration at the site if deployment of tissue (Kraitze, 2008). Drug-eluting stents (DESs) prevail internationally in cardiology world due to its use in lessening the restenosis in the CHD treatment. DES introduces vital revolutions in the field of cardiology intervention. For restenosis prevention the drug required an anti migratory and anti proliferative effect and increases re-endothelialization prevents late thrombosis (Patel, 2012).

The ideal drug eluting stent has better radial strength, large surface area and flexible. The drug in DES is supplied over the target lesion by a gap that is formed in between the stent struts. Material of stent, properties of electrophysiological and stent biocompatibility greatly influence the neointimal proliferation. In the past except the poly-l-lactate biodegradable stent (Sangiorgi, 2006), (Tamai. 2000), there was enlarge proliferation of neointimal due to inflammatory reaction. Polymer coating, drug and stent are the three main components of drug eluting stents (Van der Hoeven, 2005). Drug-eluting stents (DES) have greatly replaced Bare metal stents to decreases the risk chances of in stent stenosis (ISR) (Hossfeld. 2013). BMS provided the platform for DES that coated with drug formulation. Three generations of drug eluting stents are presented in Figure 8.

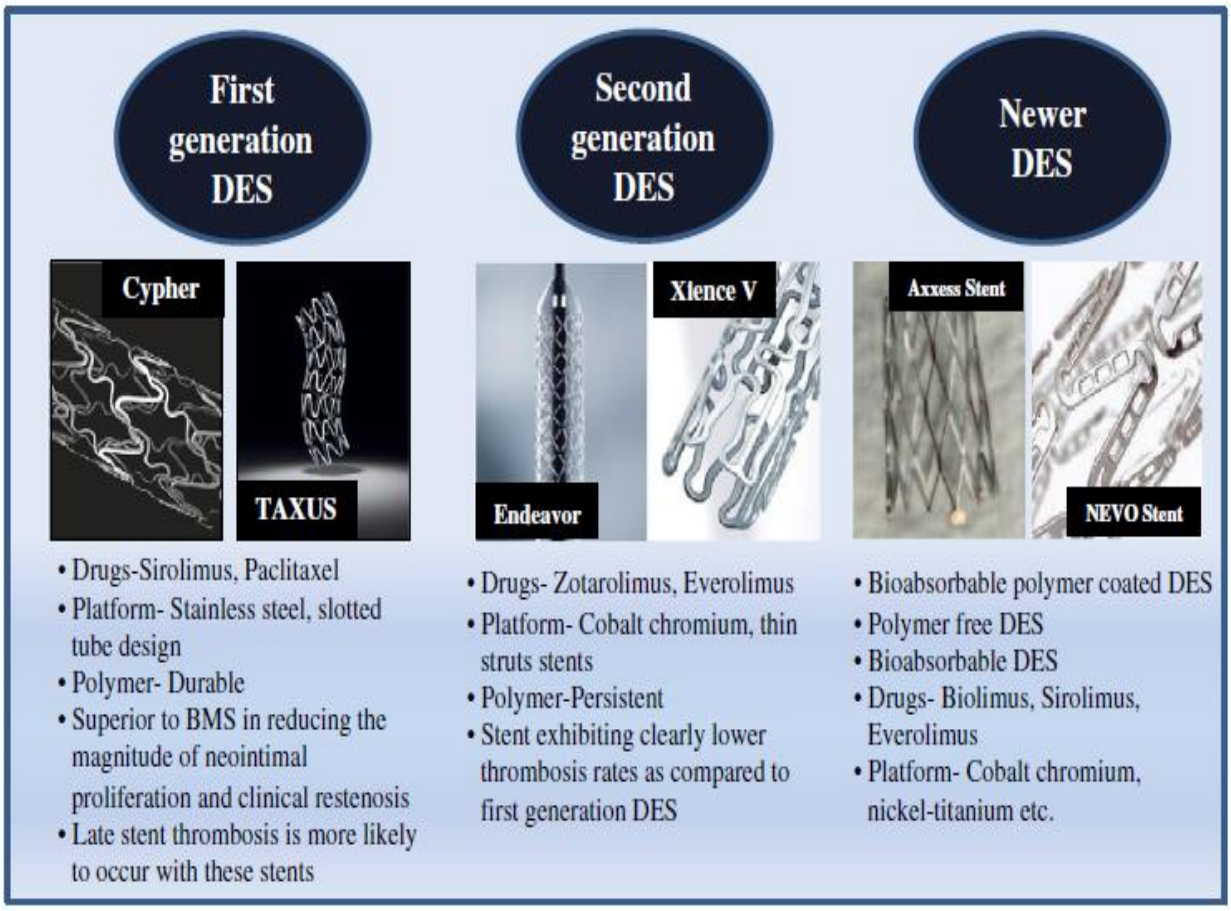

Figure 8. Three generation of drug eluting stents (Schofer, 2003)

2.9. Auxetic

In the field of new biomedical devices and implants an emerging progression is the development of Auxetic structures that demonstrate negative Poisson's ratio. "Negative Poisson's Ratio (NPR) is a property of a system which when stretched becomes wider and when compressed becomes narrower; this phenomenon is the opposite of positive Poisson's ratio ". Devices having negative Poisson's ratio is capable to radially expand when stretched and it contracts under uniaxial compression in the transverse direction (Attard, 2009). Auxetic geometry introduced into

biomedical implants will reduce the tissue adhesion damage when deployed at the site of injured tissue and will enhance and improve the device mechanical and physical properties. Auxetic behavior are scale independent in geometry based models like an Auxetic material so with mechanism of deformation along with same combination of geometry it can be maneuver at any stage. Moreover, due to negative Poisson's ratio effect the device geometric features exhibit deformation once subjected to uniaxial loads.

The behavior of Auxeticity can be achieved in macro, micro and nano-scale levels. Both features of the geometry and mechanisms of deformation are mainly associated with auxeticity of a system and the models such as rotating rigid unit models allowed this behavior to exhibits and subsequently because of the unit models stretching and rotating the deformation then occurs in a system (Attard, 2009). Therefore, Auxeticity is because of the freedom of degree of geometric internal structures that allowed them to get deform (Blumenfeld, 2005).

CHAPTER 3

METHODOLOGY

3.1. Auxetic Coronary Stent Design Considerations

The Auxetic structure design of the present coronary stent constructed with the interconnection of unit cells as shown in figure 9a. These unit cells interconnected through horizontal and vertical vertices in order to form hinges and struts of the coronary stent. A design of single unit shown in figure 9b, formed with the help hollow diamond and four angulated squircles.

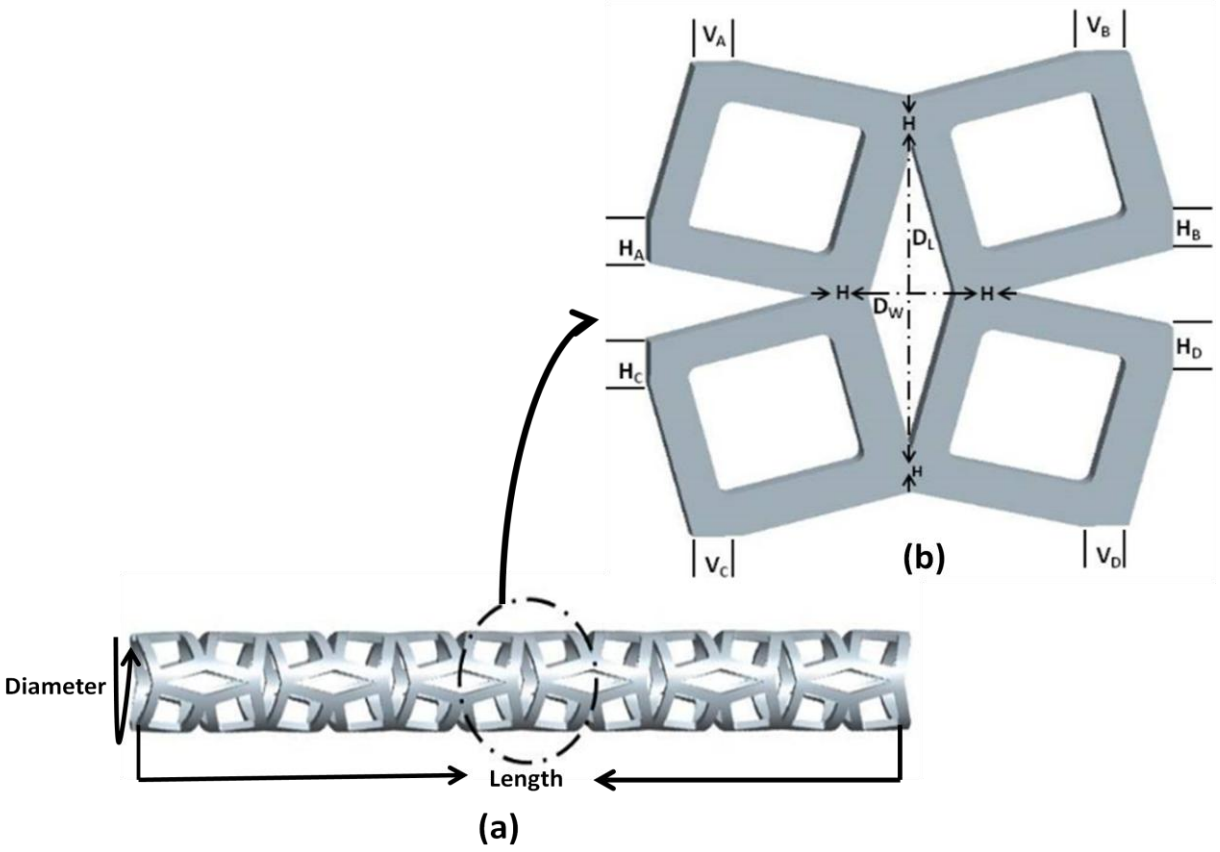

Figure 9. (a) Auxetic coronary stent design (3D model) (b) Single unit cell.

In the horizontal direction, the adjacent unit cells are joined by the horizontal vertices (H_A, H_B, H_C and H_D) of the unit cells and in the vertical direction, the adjacent unit cells are joined through the vertical vertices (V_A, V_B, V_C, V_D) of the unit cells, thus creating the unit cells arrays in the horizontal and radial directions. In the plurality of unit cells, length (D_L) and width (D_W) remains similar in the design. Auxetic coronary stent dimensions were 1.8mm diameter, 0.14mm strut thickness and 18mm length.

3.2. Fabrication of Auxetic Coronary Stent

A biocompatible 316L stainless steel material was utilized to carried out the fabrication of Auxetic coronary stent. This material is being used widely in the other biomedical implants and in the fabrication of coronary stents because of its stable and effective physical and mechanical properties which adhere properly with the blood environment at the site of blood tissue interaction. Figure 10, illustrates the order of the fabrication process route employed for the Auxetic coronary stent.

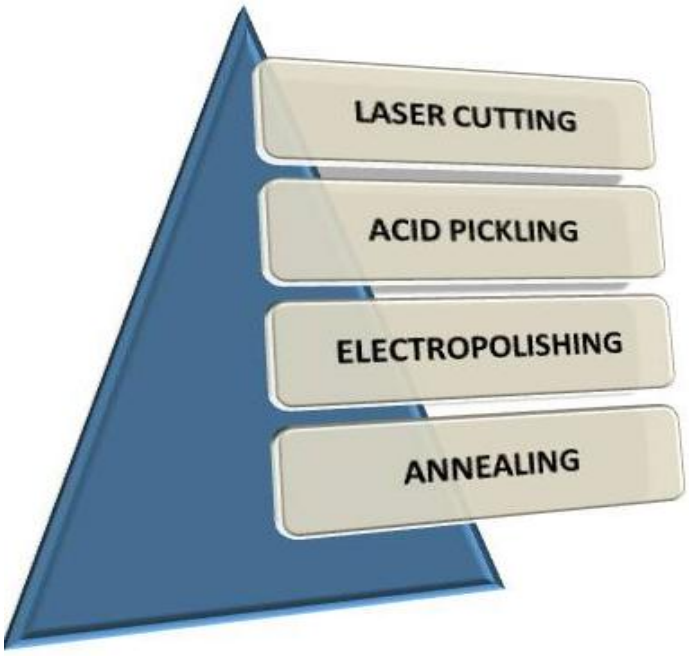

Figure 10. Steps of the adopted fabrication route

3.2.1. Laser Cutting Process

The laser cutting process was the first step in the fabrication of Auxetic coronary stent. The geometric structure of the coronary stent was first designed on AUTOCAD software which was then converted into a computer and numerically controlled (CNC) CAGILA program. In the horizontal and vertical axes, the new Auxetic stent design contains arrays of diamonds and squircles. Laser equipment STARCUT 12FM pulsed Nd:YAG (Rofin Baasel, Germany) was employed for 316L stainless steel tube cutting. Figure 11, illustrates the cutting of coronary stent. The laser cut stent was the examined under the optical microscope (LEICA, GERMANY) for monitoring of design features, welding spots and micro cracking.

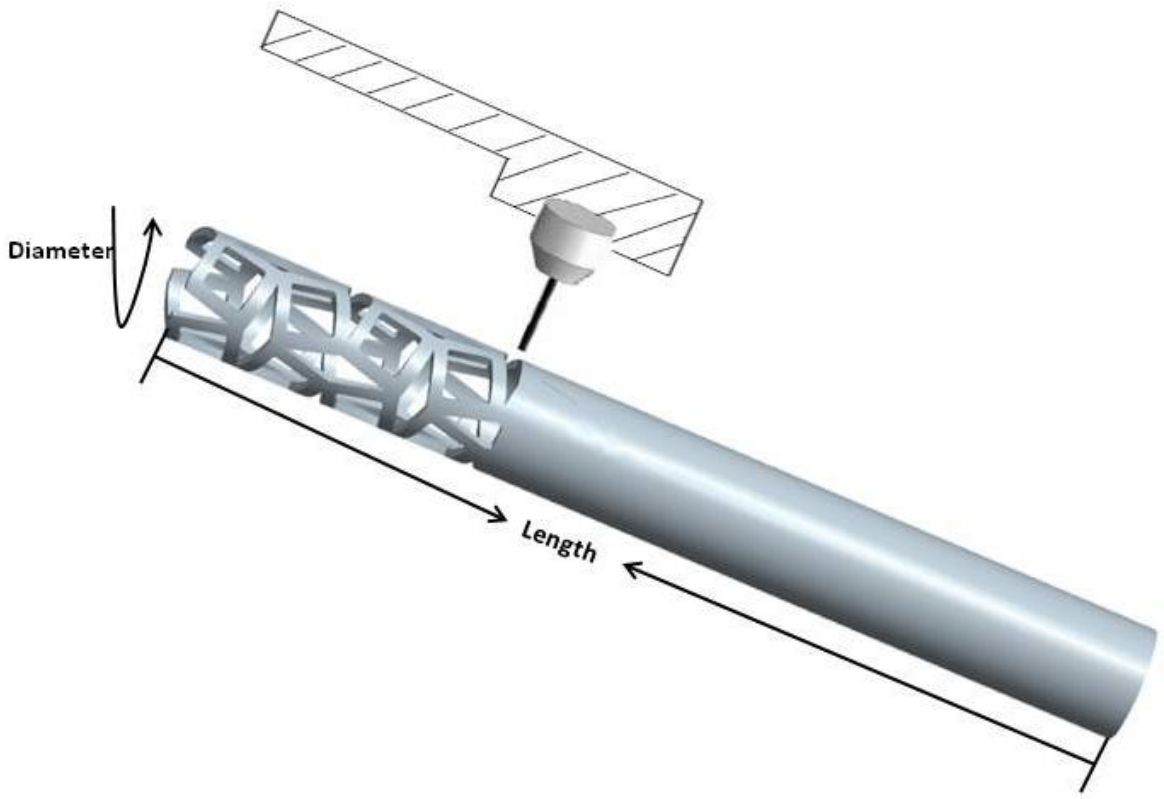

Figure 11. Illustrates the cutting of coronary stent by CNC laser cutting machine.

3.3. Surface treatment of Auxetic coronary stent

3.3.1. Acid Pickling process

Acid Pickling process was deployed to effectively eliminate the oxide scales and slags that were formed after the laser cutting process via immersed the Auxetic coronary stents into acid pickling solution. This process from the stent primarily eradicates the unwanted material. Figure 12, illustrates flow chart of the acid pickling process steps. The mixture of Hydrogen Peroxide (H_2O_2) and Boron trifluoride (BF_3) was prepared for acid pickling solution. The Auxetic coronary stent were then submerged into 150ml solution of acid pickling and ultrasonicated. Subsequently, the coronary stents were then dried in the oven for 10 min at temperature 90 °C after they were rinsed with propanol for 30 sec. The pickled Auxetic stents were then placed into petri dish for further surface treatment procedures. Figure 13, shows the images of Acid pickling process of Auxetic coronary stents.

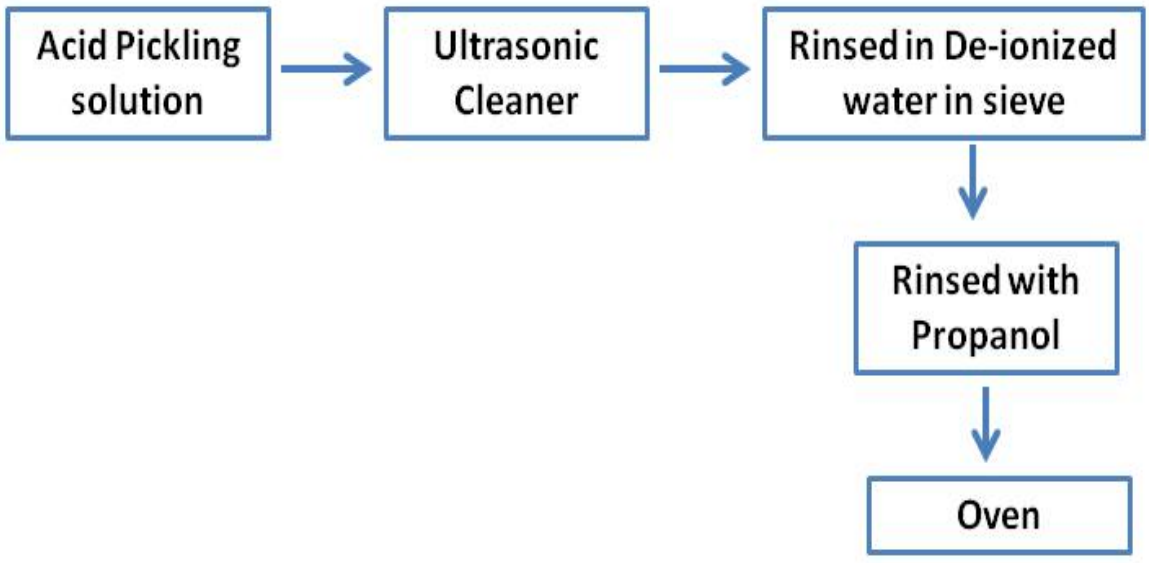

Figure 12. Flow chart of the acid pickling process steps

Figure 13. Acid pickling process of Coronary stents, (a) Acid pickling solution preparation, (b) Stents in ultrasonic cleaner, (c) stents rinsed in the sieve, (d) Stents after rinsing with propanol, (e) Sieve having stents is placed into an oven, (f) Acid pickled stents in Petri dish.

3.3.2. Electropolishing

The next step that was employed for the surface treatment was the electropolishing of the Auxetic stents. The use of this method was to reduce the strut thickness, to make the smooth stent surface and round-off edges effectively. The electropolishing setup is shown in figure 14. The basin contains the electrolyte solution whereas sink contains de-ionized water. The stent was polarized to the desire level of voltage and current after the power was provided to the Auxetic stent which acts as anode. Constant temperature was provided to the basin contained electrolyte solution through electrode heater. The time controller of the electropolishing setup supplied polishing time to the Auxetic stents whereas the electrodes acted as cathode inside the basin.

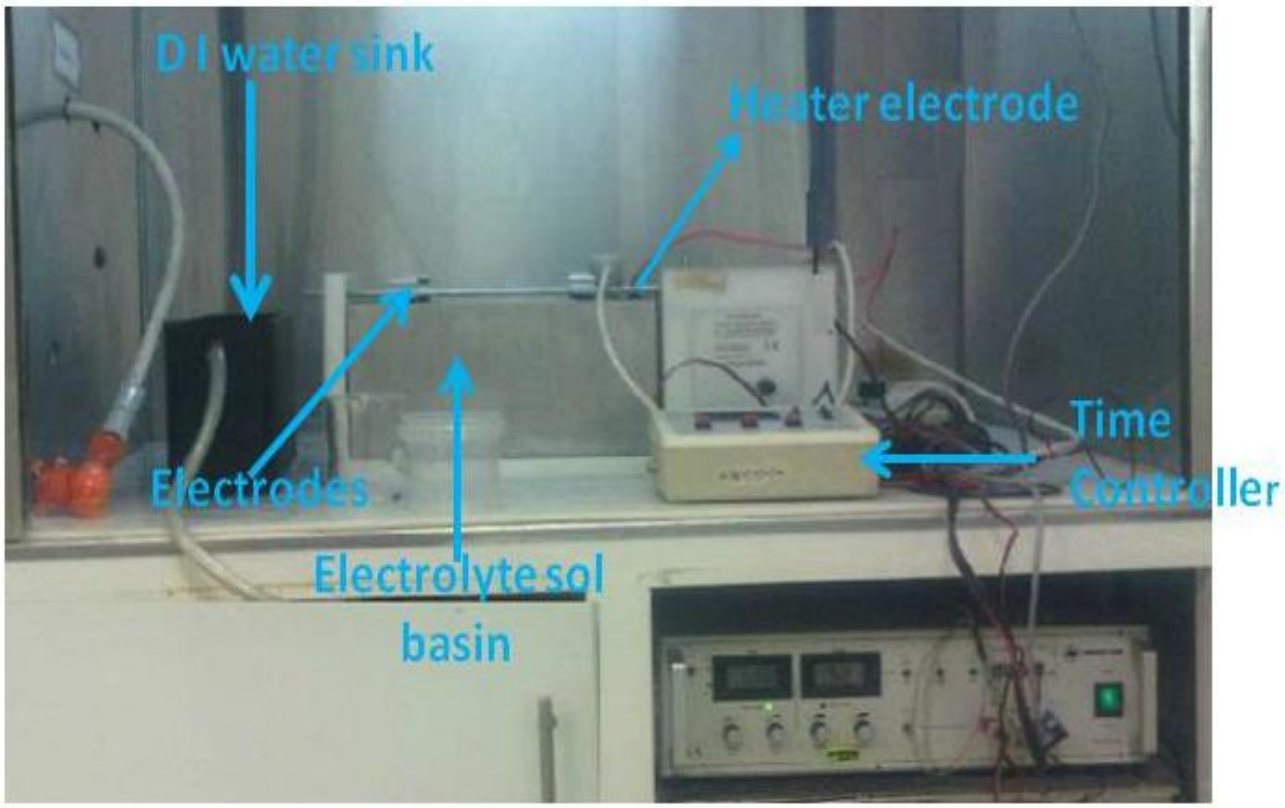

Figure 14. Electropolishing Setup

Figure 15, illustrates the flow chart of electropolishing process steps. Electrolyte solution contained sodium hydroxide (NaOH), phosphoric acid (H_3PO_4) and water. The temperature of the electrolyte solution was set to 70 °C. After completion of the polishing cycle the stents were rinsed for 28 min with a solution containing 13 ml sulphuric acid (H_2SO_4) and de-ionized water and then ultrasonicated. Afterwards the Auxetic stents were dried into oven for 2 hours at 90 °C.

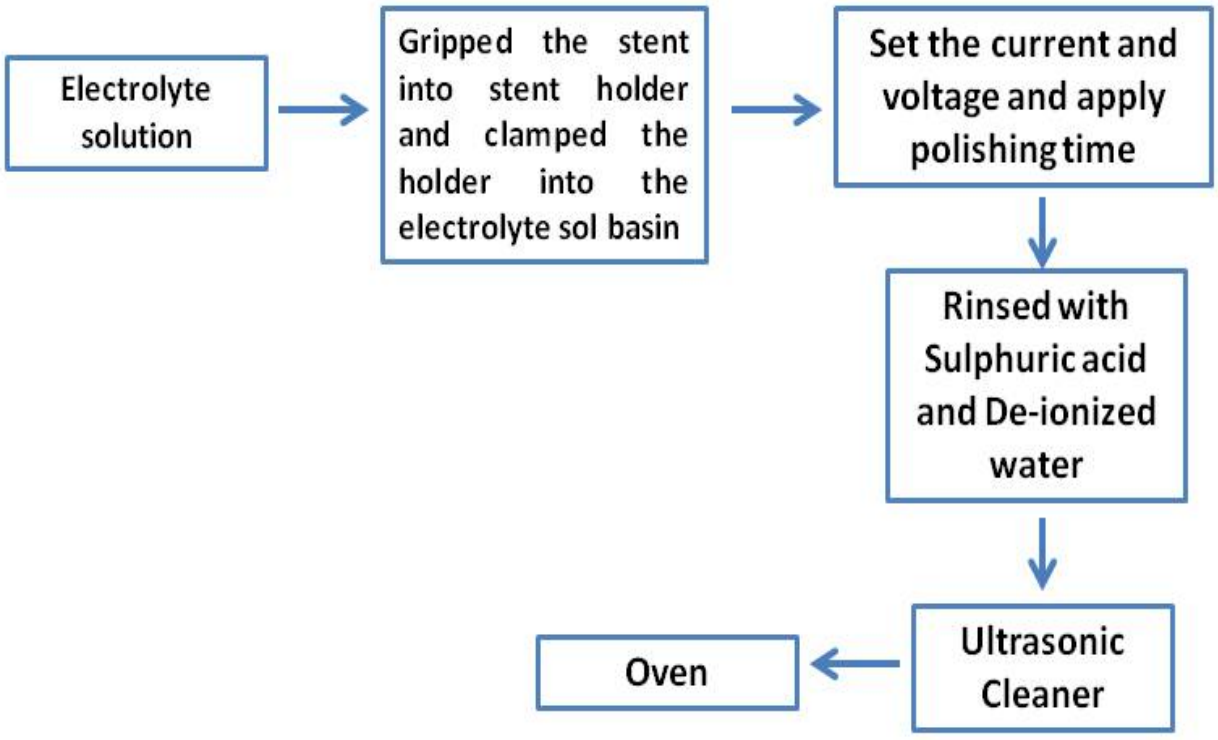

Figure 15. Flow chart of Electropolishing Process Steps

3.4. Annealing

The as-polished Auxetic stents were subsequently annealed to enhance their ductility and make them soften. This was performed in a vacuum furnace (CARBOLITE, GERMANY). Figure 16, shows the annealing setup for Auxetic coronary stents. This process was performed by placing the coronary stents into quartz bolts. After setting of parameters such as heating rate, temperature increment and time, the furnace headed forward towards quartz boltz for specific time and returns back to its original position when temperature of quartz bolts attained to 960 °C with heating rate of 30 °C/min. After the furnace returned back to its original position the fan then starts to cool quartz bolts until the temperature reaches to the room temperature. The dwelling time within a quartz boltz of the Auxetic coronary stents was 3.5 hours.

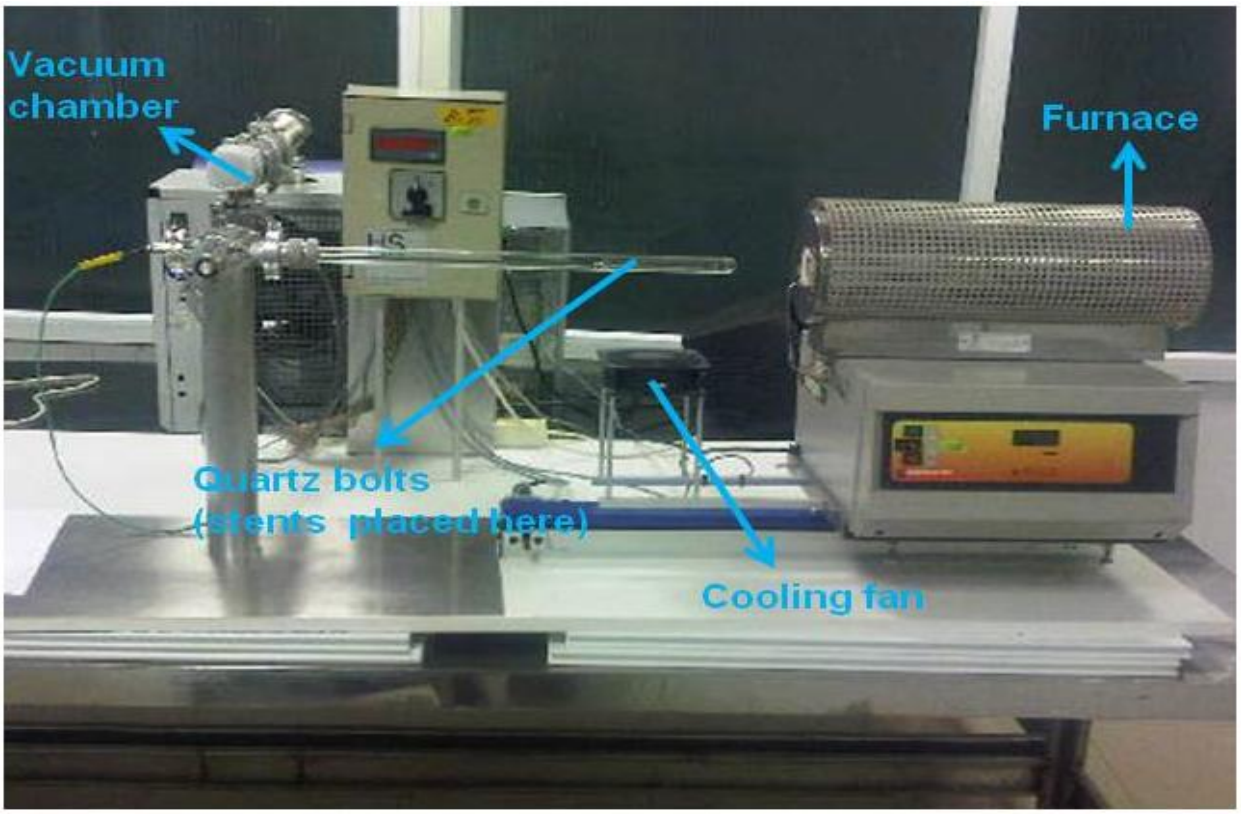

Figure 16. Annealing Setup

CHAPTER 4

RESULTS

4.1. Auxetic Coronary Stent Design Formation

The Auxetic design pattern that consists of diamonds and squircles was formed by the interpolation of tubing movements in rotational and linear directions by the laser machine. The laser cut Auxetic coronary stent design pattern was examined through optical microscope and is depicted in Figure 17 below. No micro cracking and welding spots were found along the struts of the present coronary stent. However, sharp edges were found and slags were also attached at the cutting zone and inside the laser cut coronary stent. The main laser cutting parameters for Auxetic design pattern formation are mentioned in Table 1.

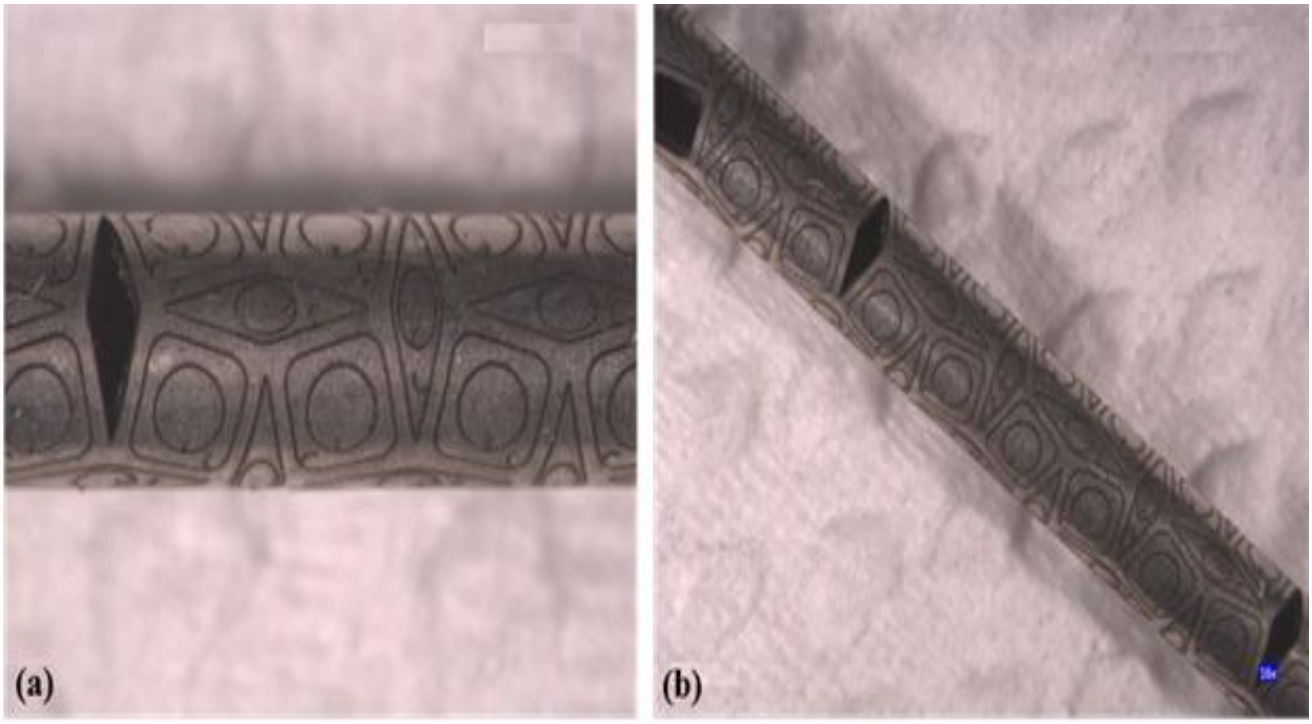

Figure 17. (a) Closer view of laser cut stent, and (b) Full view of laser cut stent

Table 1- Process Parameters of the laser cutting of 316L Auxetic stent

Units	Process Parameters	Values
V	Voltage	534
W	Average Power	2.0
ms	Pulse Width	0.1
mm/sec	Cutting Speed	4

4.2. Effect of Acid Pickling on the Auxetic Coronary Stent Design

The struts of the Auxetic stent and the unit cells (consists of hollow diamonds and squircles) were obviously seen after acid pickling as revealed in figure 18. After acid pickling process the Auxetic stent strut thickness was reduced by 1μm. Additionally, even though after acid pickling process the surface of the Auxetic stents was still coarse, but the surface irregularities were removed effectively. The parameters involved in elimination of oxides and slags are given below in Table 2.

Table 2- Specifications for Acid pickling process

Units	Components/Parameters	Amount/Quantity
ml	Pickling sol BF_3	146
ml	Oxidizing Agent H_2O_2	4
Min	Time	37
°C	Temperature	40
D.I Water and Oven parameters		
°C	D.I Water Temperature	60
μS	D.I Water Conductivity	0
°C	Oven Temperature	90
Min	Oven Drying Time	10

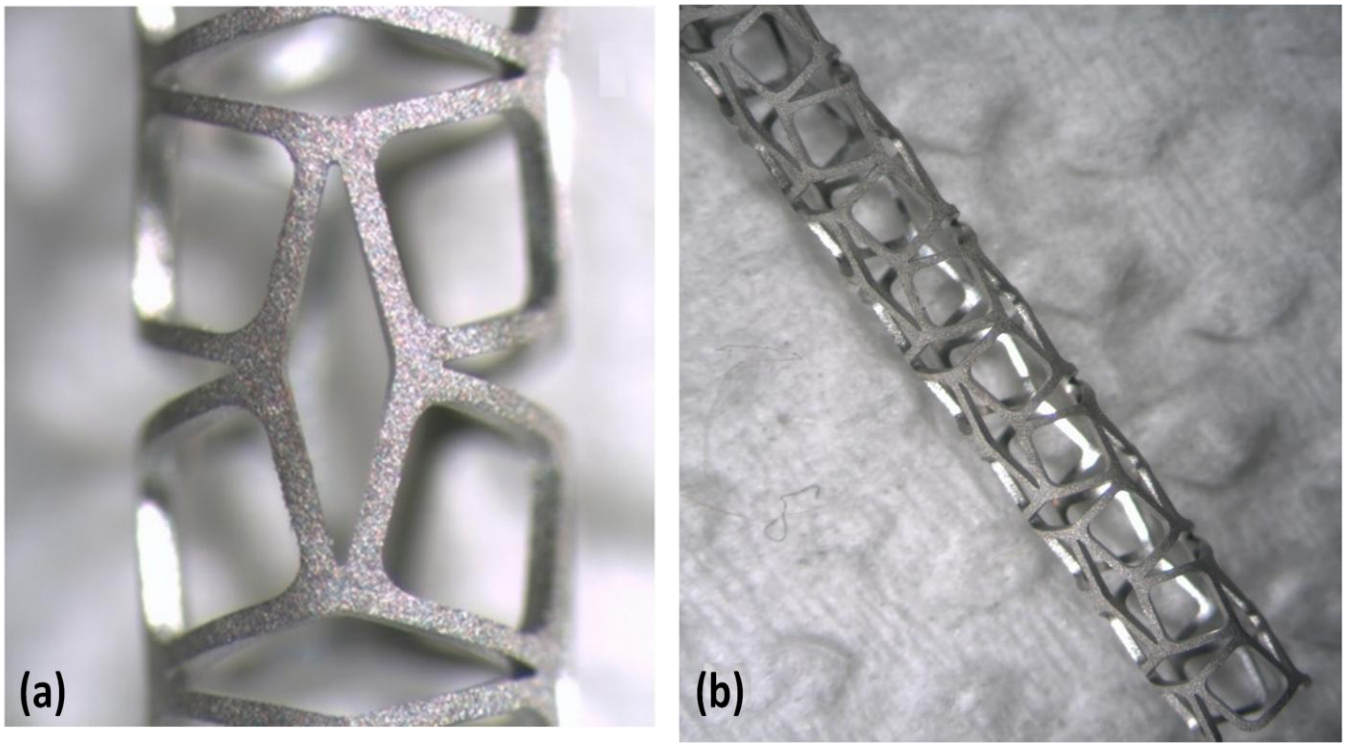

Figure 18. (a) Single unit cell, (b) Full length Acid Pickled Auxetic coronary stent.

4.3. Auxetic Stent Surface Smoothness and Profile

The elimination of peaks and valleys (i.e. surface roughness) from the surface was attained by applying the appropriate parameters of the electropolishing as given in Table 3. Figure 19, depicted that after electropolishing surface definition and stent characteristics were greatly improved.

Table 3- Specifications for surface smoothness

Units	Parameters	Values
A	Current	5.6
V	Voltage	5.8
Seconds	Polishing time	84

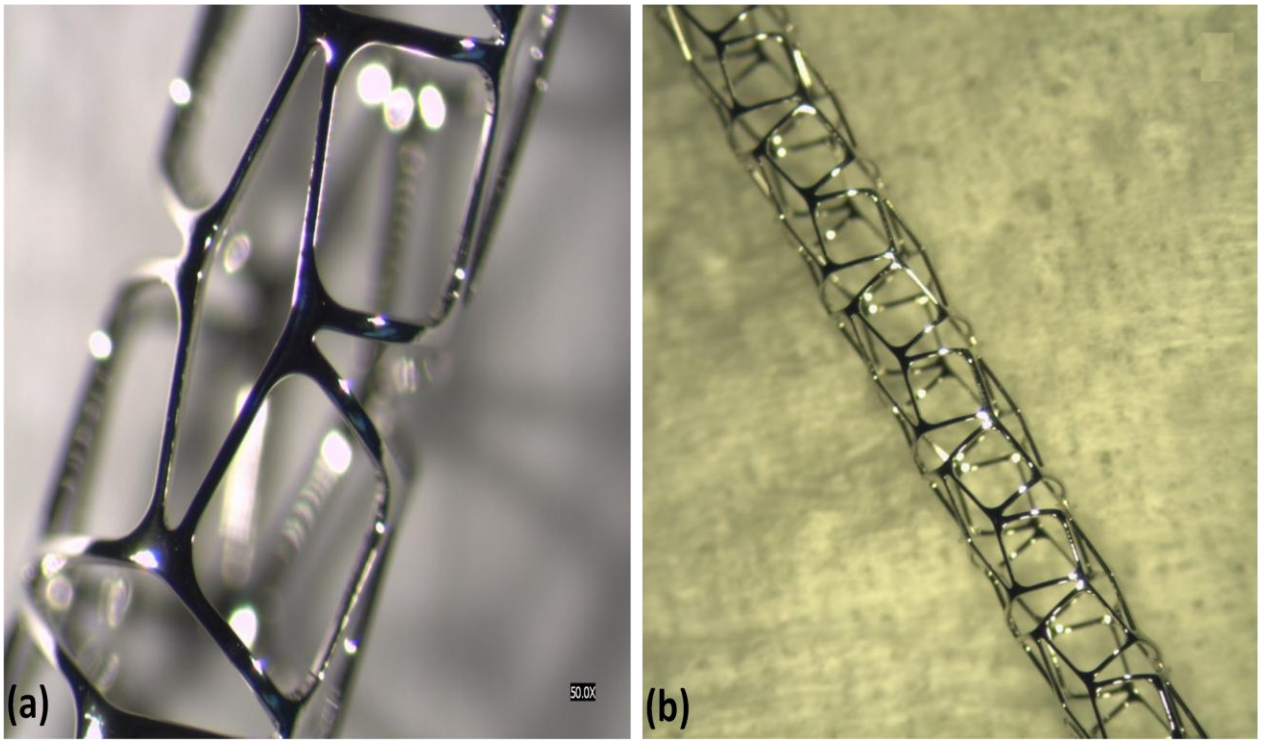

Figure 19, (a) Single unit cell, (b) Full length Electropolished coronary stent

The as-pickled Auxetic stent having sharp flat geometrical features were changed into well rounded edges as shown in the scanning electron microscope (SEM) micrographs (SEM, JEOL-instrument JSM-6490A) below in figure 20. The parameters such as current, voltage and time controlled the profile of Auxetic coronary stent. To accomplish the smoothness of surface and desired thickness of strut, other parameters were varied while the voltage was kept constant. Current was supplied for transfer material to cathode from anode (Auxetic stent) and to attain smoothness of surface by the elimination of peaks and valleys. Consequently, the thickness of the strut width of the Auxetic coronary stent was reduced from 140 μm to 85 μm with a polishing time of 84 sec. as illustrated in Figure 21.

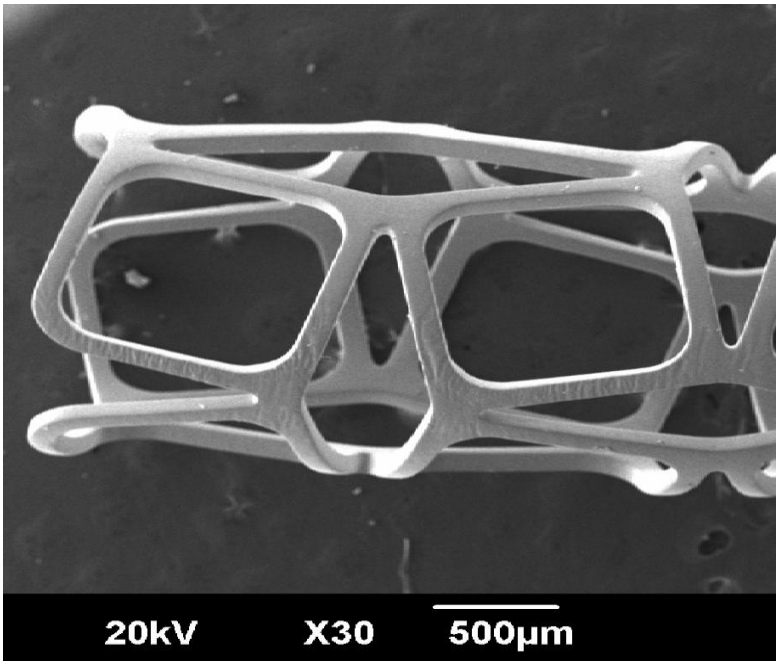

Figure 20. SEM micrograph showing polished stent with round edges

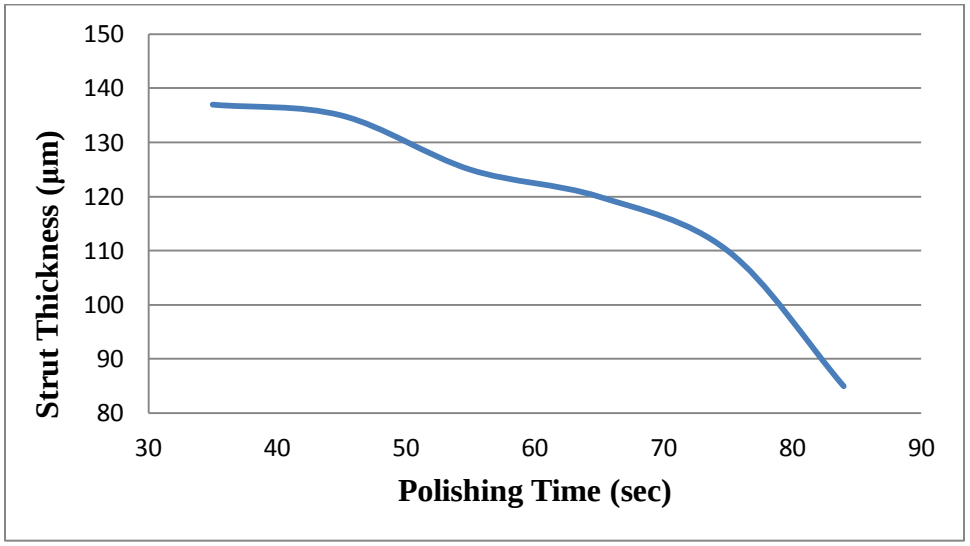

Figure 21. Plot showing Polishing time for the reduction of strut thickness of Auxetic stent

4.4. Effectiveness of Annealing on Auxetic Coronary Stent

It was ascertained that the Auxetic stents heat treatment through annealing was very effective and not only improved the stents quality but improved the mechanical properties (i-e internal stresses were eliminate and become more ductile when subjected to balloon expansion) of the stent as shown in figure 22. This was validated (in section 4.7) by using Angioplasty balloon catheters while subjecting the Auxetic stents to balloon expansion.

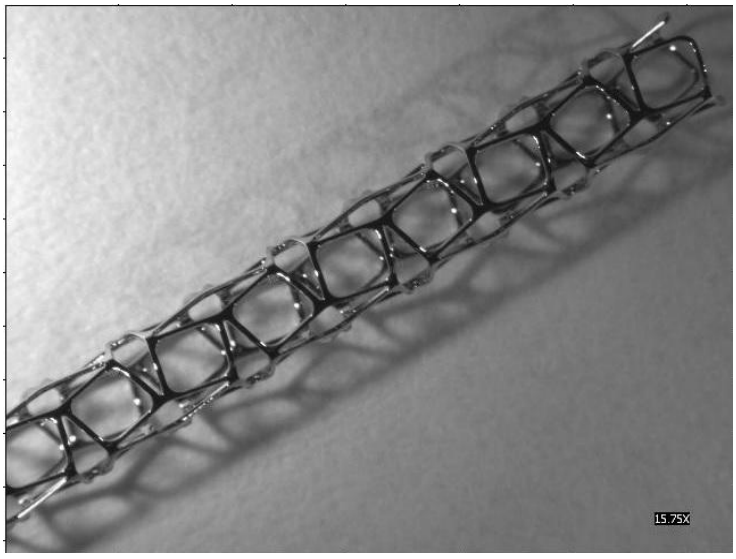

Figure 22. Annealed Auxetic coronary stent

4.5. Analysis of Strut Width Thickness Reduction

The reduction in Auxetic stent strut thickness is tabulated after laser cutting, acid pickling and electropolishing of the stent in Table 4 below. The reduction in strut thickness of the stent was calculated by using an equation 1. The plot in figure 23 shows the data of eight stents and revealed that there is no variation in the strut width thickness after each fabrication step as the material rate of removal was fairly controlled in each process steps. It was established that since there was no change in strut thickness after lasercutting of the stent, the reduction in strut

thickness was observed after acid pickling and electropolishing processes and was 0.71% and 38.4% respectively.

$$\boldsymbol{Reduction} = \frac{\boldsymbol{width\ before - width\ after}}{\boldsymbol{with\ before}} \qquad (\mathbf{1})$$

Table 4: Strut width thickness reduction

Stents	Strut width thickness (µm)	Reduction (%)
Laser cut	140	----
Acid Pickled	139	0.71
Electropolished	85	38.4

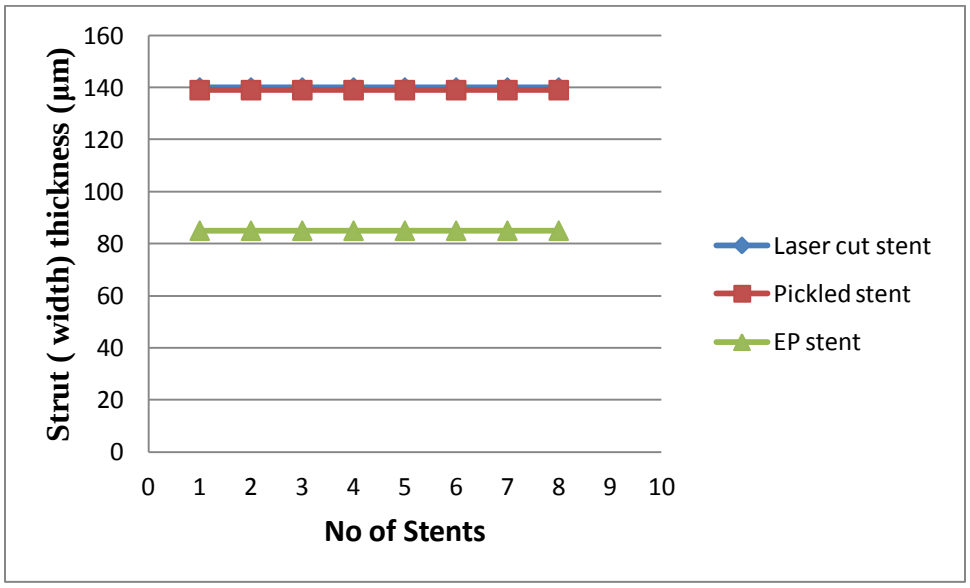

Figure 23. Plot showing strut width thickness reduction

4.6. In-vitro Mechanical Analysis of Auxetic Coronary Stent

4.6.1. Diameter and Length Size Before and After Expansion

In-vitro test was employed to examine the behavior of Auxetic coronary stent before and after expansion. Auxetic stent inflation and deflation was carried out experimentally with the help of inflation device and the results were observed under optical microscope. Actual length and diameter was measured before applied any pressure to the Auxetic coronary stent mounted on the balloon catheter. The Auxetic coronary stent expansion was examined after the pressure was given with 1 atm increments. The compliance data related to unexpanded and expanded Auxetic stent illustrates in Table 5. This data revealed that the Auxetic coronary stent expanded in both radial and longitudinal directions. Graphical representation of radial expansion profile is shown in figure 24.

Table 5: Compliance Data Before and After Expansion

	Pressure (atm)	**Diameter (mm)**	**Length (mm)**
Before Expansion	0	1.68	18.01
After Expansion	1	1.71	18.01
	2	1.80	18.05
	3	2.01	18.08
	4	2.25	18.12
	5	2.32	18.18
	6	2.50	18.22
	7	2.61	18.27
	8	2.78	18.31

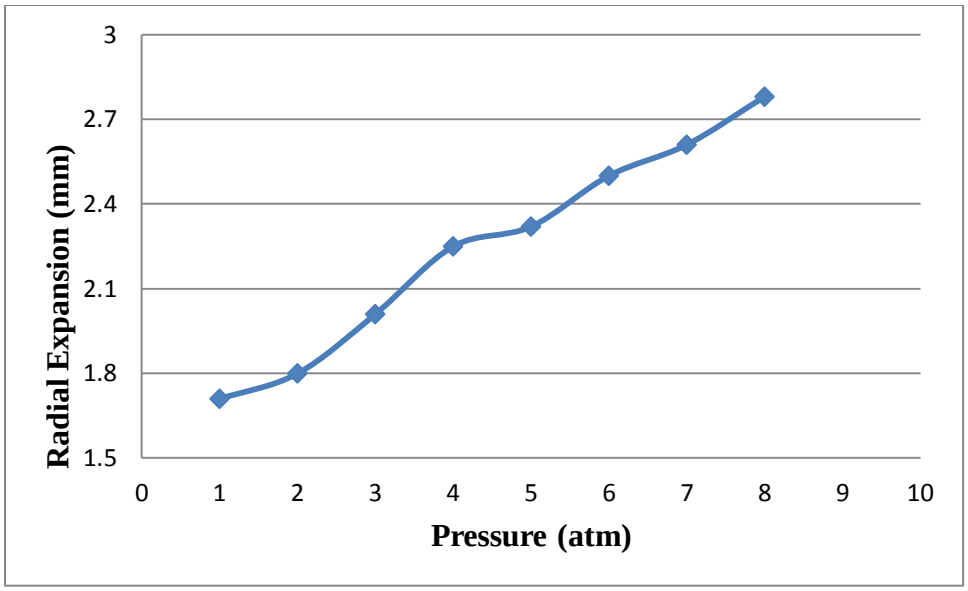

Figure 24. Radial expansion profile of Auxetic coronary stent

4.6.2. Foreshortening

The Auxetic coronary stent foreshortening was examined and observed to be zero percent. Because of the auxeticity of coronary stent design that causes no foreshortening, which in turn allowed the Auxetic coronary stent to expand in longitudinal direction, as illustrates in figure 25, where it was obvious that there is no foreshortening in the Auxetic coronary stent but it expanded in the longitudinal direction.

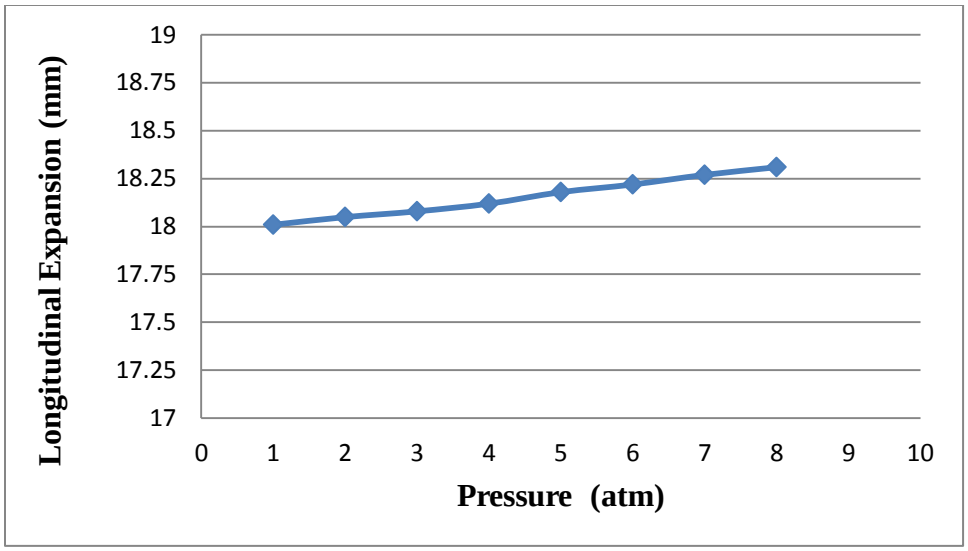

Figure 25. Longitudinal expansion profile of Auxetic coronary stent

4.6.3. Elastic Recoil

The elastic recoil test was carried out by reversed the inflation device pressure from 8 atm to 0 atm. No damage along the struts of the stent was found during this test. Table 6, illustrates the observed measurement for elastic recoil of the Auxetic coronary stent.

Table 6. Measurement of elastic recoil test.

Pressure (atm)	Diameter (mm)	% Recoil
8	2.78	
0	2.69	3.3 %

4.7. Surface Morphology Analysis

An analysis on the surface morphology of the Auxetic coronary stent was carried out via Scanning Electron Microscope (SEM) to analyze the effects of fabrication processes on the

Auxetic stent topography presented in section 2. The SEM micrographs of the Auxetic stent inner luminal surface shown in figure 26 were taken at 850 and 1500 times magnification and they illustrates that there was deposition of irregular and porous oxide layer on the inner surface of the stent.

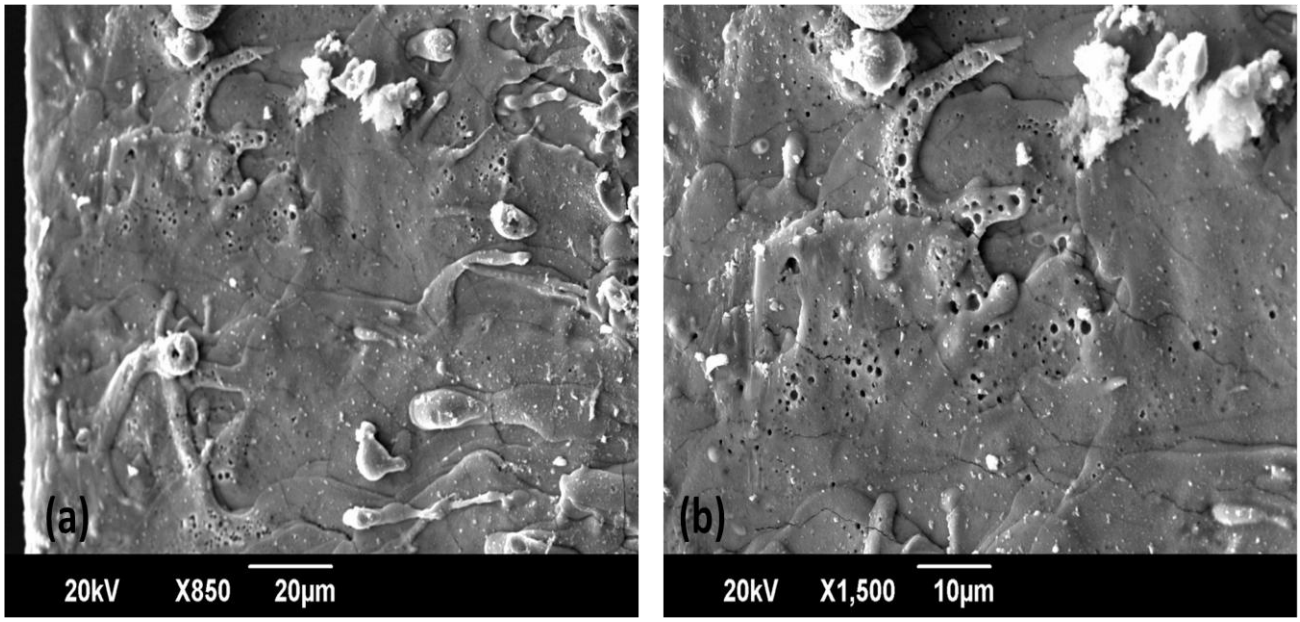

Figure 26. SEM micrographs showing irregular and porous oxide layers on the inner surface of the stent.

The SEM micrograph of the electropolished Auxetic stent shown in Figure 27 (a) was taken at 1200 times magnification. The micrograph presented that surface of the stent was efficiently improved and also showed smooth surface devoid of any porous deposited layer. It was apparent from the SEM micrograph that definition of the diamonds and squircles of the Auxetic design was fairly clear and there were also fairly rounded off edges eliminating the chances of causing any injury to the coronary artery. The SEM micrograph taken at 850 time magnification presented in figure 27 (b) show quite apparent grain boundaries of the Auxetic stent. In the SEM micrographs the brightness of surface and luster revealed that electropolishing or passivation was performed effectively that not only improved the structural definition of the stent but also made the Auxetic coronary stent corrosion resistant.

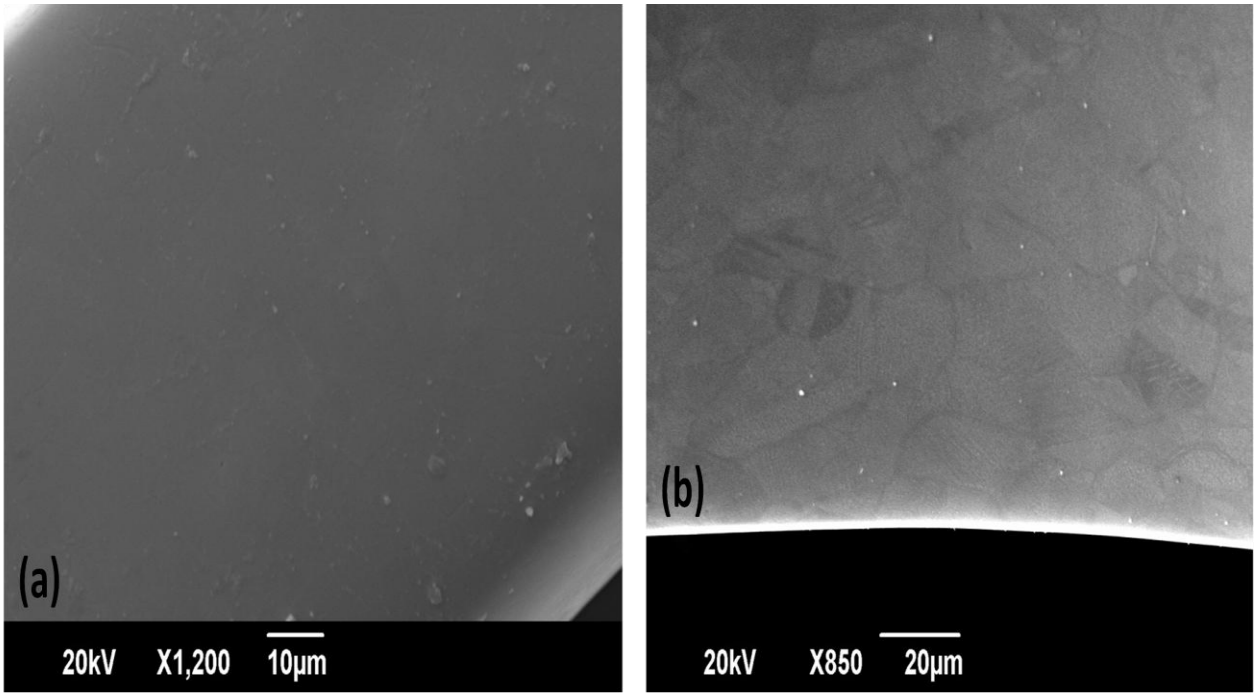

Figure 27. SEM micrographs showing electropolished Auxetic stent (a) smooth surface, (b) apparent grain boundaries.

It was observed from the SEM micrographs of the annealed stent captured at 850 and 1200 times magnification shown in figure 28 that the heat treatment of the Auxetic stent reduces the size of the grain boundaries which in turn introduced ductility into the Auxetic coronary stent that eventually also improved the structural integrity of the Auxetic stent. This improvement in mechanical properties is very critical, since by balloon expansion the Auxetic stent will be deployed into coronary and through plastic deformations in radial and longitudinal directions the Auxetic stent will acquire anchorage with surrounding tissue.

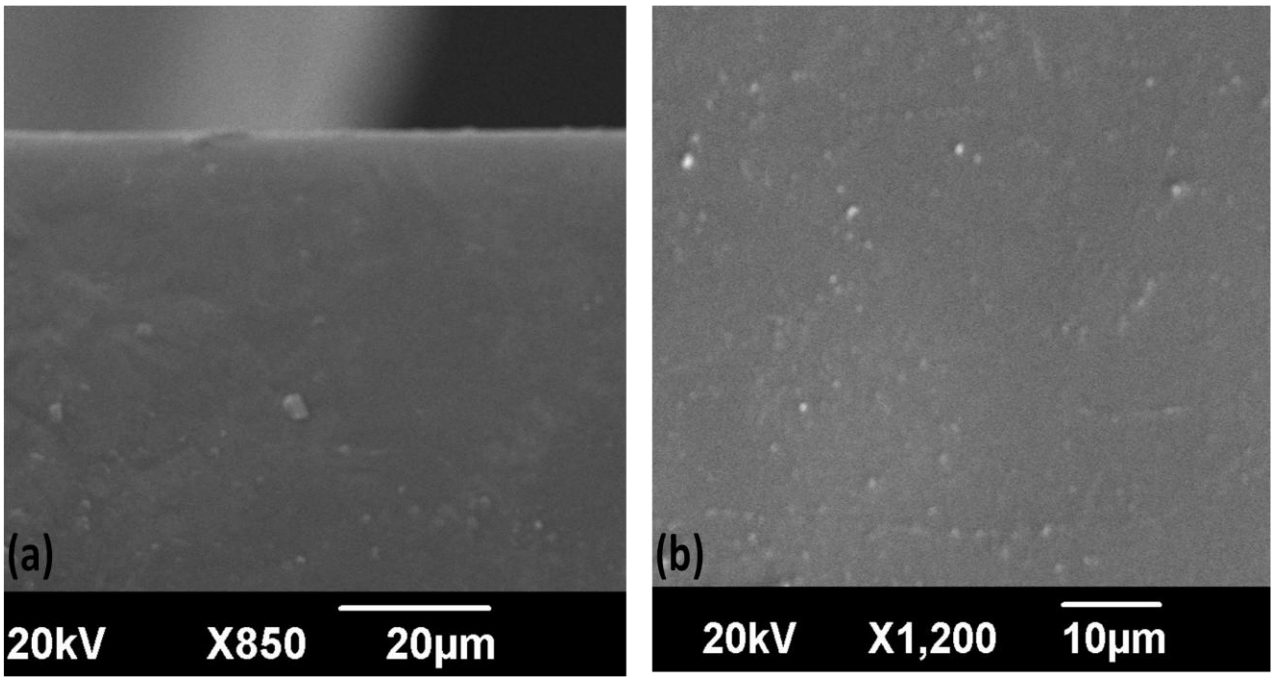

Figure 28. SEM micrographs showing surface of annealed stent.

CHAPTER 5

DISCUSSION

5.1. Effect of Laser Cutting on Auxetic Design Coronary Stent

After lasercutting, a mesh like Auxetic structure was created consisting of diamonds and squircles where struts were only left solid. Along the struts of Auxetic stent no micro cracking or welding spots were found. However it was found that the edges are sharp and slags and oxides layers are formed inside the lumen and on outer surface of the stent which are clearly visible in SEM micrograph as shown in figure 29.

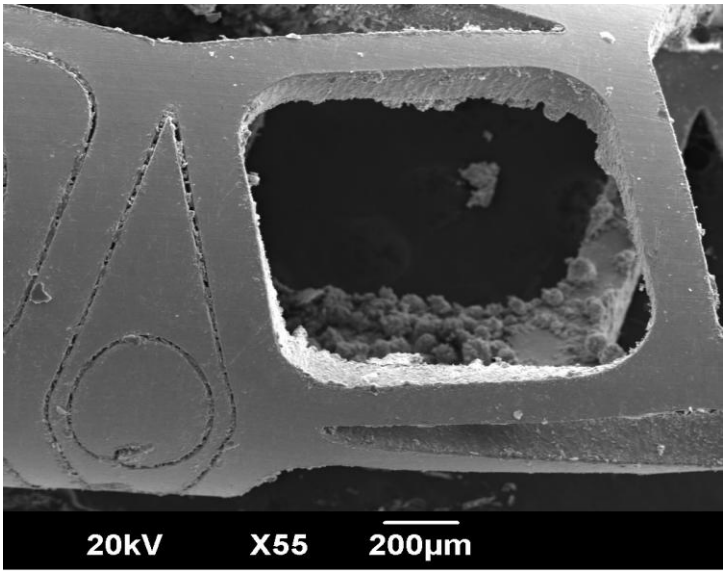

Figure 29. SEM micrograph showing, Slags and Oxide deposits inside the stent lumen.

5.2. Removal of Slags and Oxides

When the acid pickling procedure was applied to the coronary stents, the residual slags, metal oxides and unwanted material were effectively removed. The plurality of Auxetic structure unit

cells containing diamonds and squircles are clearly seen and observed in figure 30. For this Auxetic design, temperature and time that influenced the pickling rate were parameters that played an essential role in the subtraction of surface irregularities and in the proper elimination of the slags.

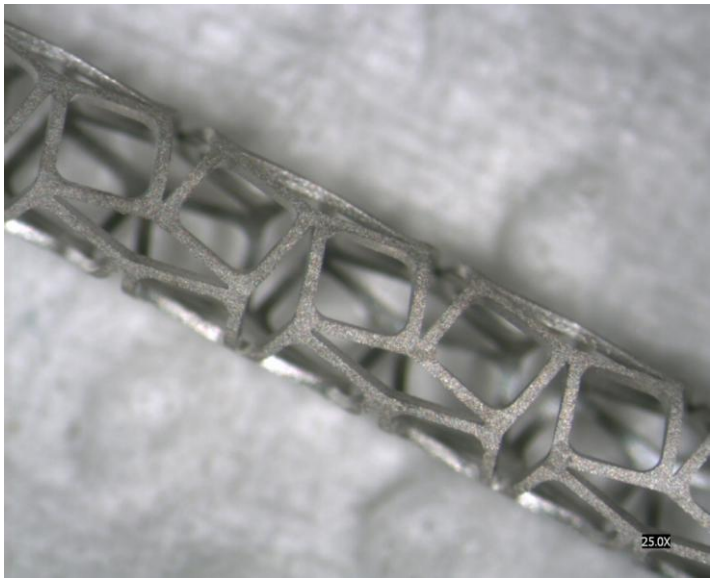

Figure 30. Pickled Auxetic stent showing slags and oxides were removed

5.3. Achievement of Surface Smoothness

The surface roughness of the as-pickled Auxetic stent is considerably replaced with smooth, bright surface of the Auxetic stent after electro polishing process as seen in figure 31. The smoothness of surface and reduction in material was achieved by the supply of direct current to the anode (i-e Auxetic stent), so that to the desired level of voltage and current it polarized the Auxetic stent. Therefore, anodic polarization effects subsequently started metal material transmitting to cathode (stainless steel plate) from anode which established anodic leveling and anodic brightness and eradicate peaks and valleys from the rough surface of the Auxetic stent. Polishing time was a very critical parameter for rounding of the sharp edges (as shown in figure 31) and for reducing the strut thickness of the Auxetic stent.

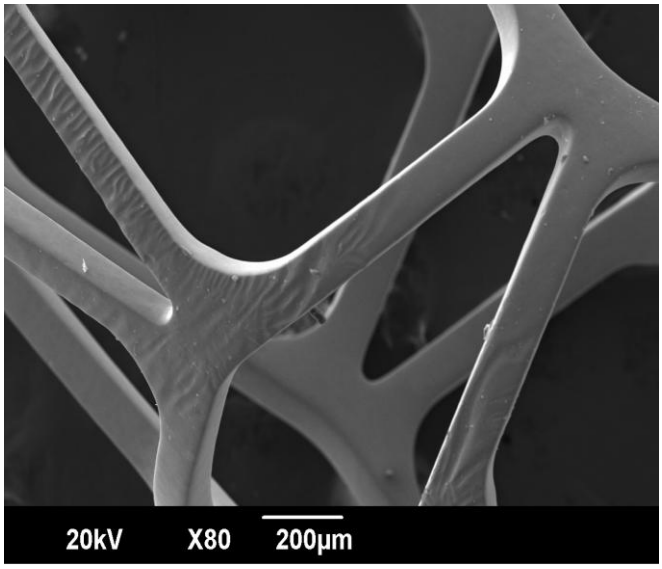

Figure 31. Electropolished Auxetic stent showing surface smoothness and round edges

5.4. In-vitro Mechanical Analysis of Auxetic Coronary Stent

Figure 32, shows Auxetic coronary stent expansion at different pressures which was experimentally carried out in section 4.6.1. When the pressure was applied a horizontal diamond widens gradually with increasing pressure and rotates the squircles whereas simultaneously, the vertical diamonds widen as shown in optical image and SEM micrograph in figure 33. The Auxetic coronary stent expansion in both radial and longitudinal directions will have mechanical anchorage with arteries walls and due to its Auxetic design it will retain the luminal patency of the coronary heart. Auxetic stent having this feature have an advantage over the existing stents, due to their isotropic property the existing available coronary stents have a mismatch between wall of artery and structure of stent, which is because these stents do not have favorable anchorage with the wall of arteries.

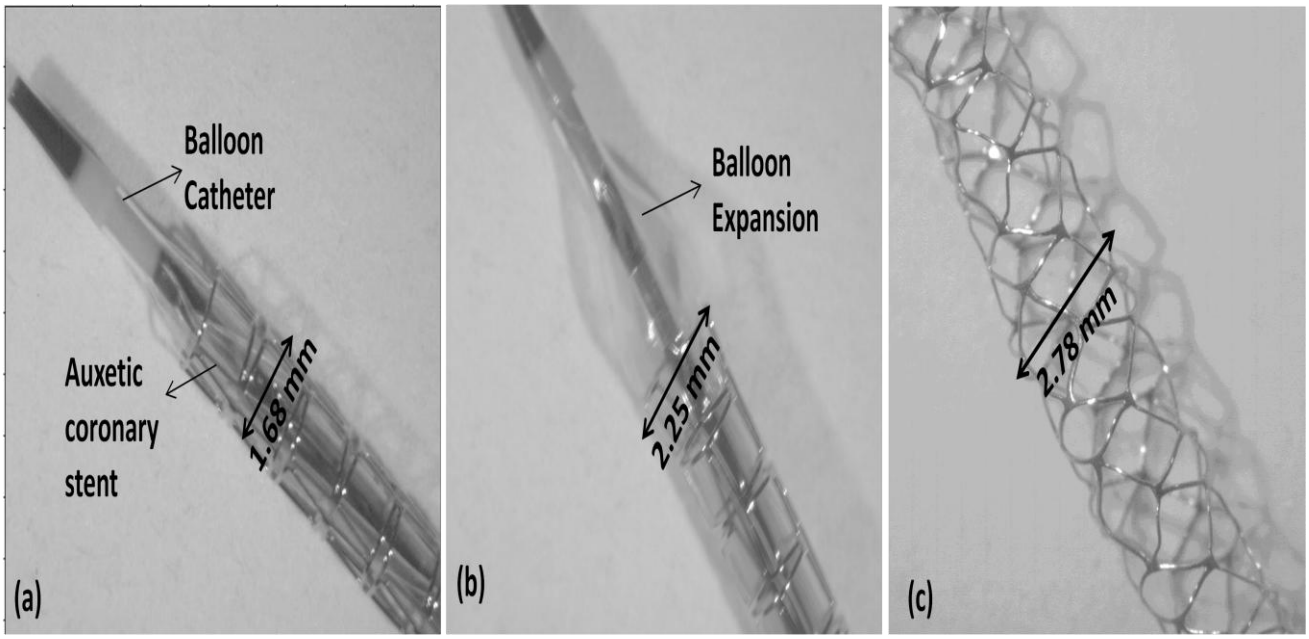

Figure 32. : Expansion of Auxetic coronary stent (a) Pressure at 0 atm (b) Pressure at 4 atm (c) Pressure at 8 atm

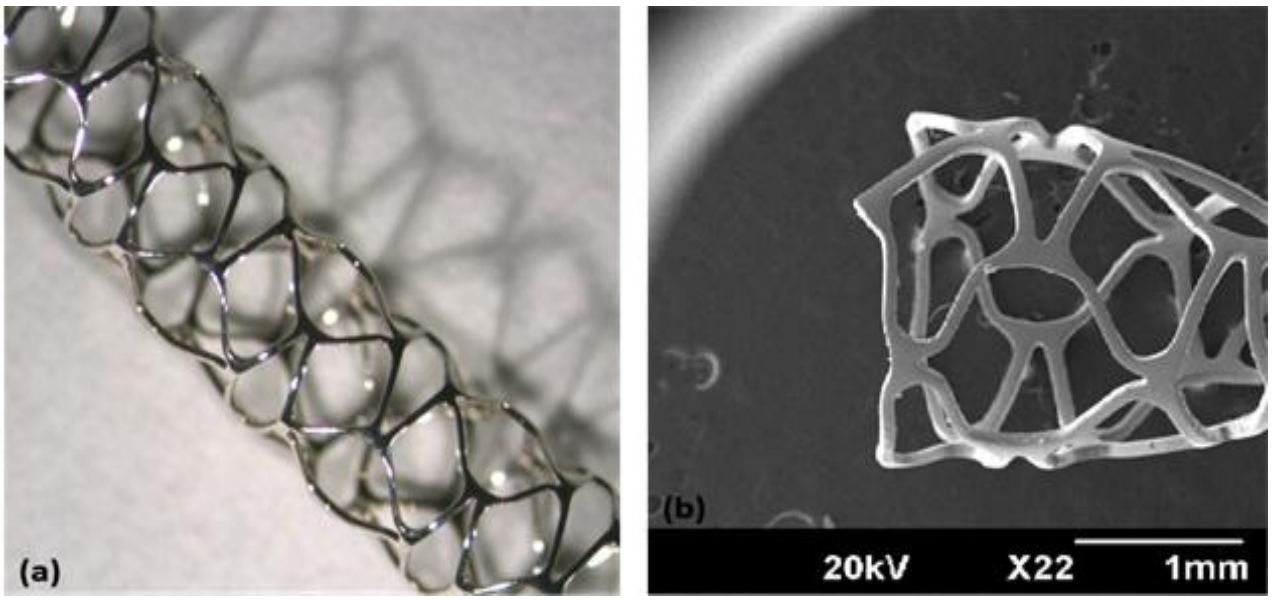

Figure 33. Expanded Auxetic coronary stent unit cell where horizontal diamond widens and squircles rotates.

Due to the longitudinal expansion there is no foreshortening in the Auxetic coronary stent. So, over the existing coronary stents this is an advantage of Auxetic coronary stent where foreshortening cause the problem of stent migration. Having no foreshortening in the present stent will might avert the stent from migration problem while expanded in the coronary artery which in turn will reduces the chances of thrombogenesis and restenosis in the coronary artery. The 3.3 % elastic recoil shows that the luminal patency will effectively maintain by the Auxetic coronary artery. Hence, for the clinicians minimum elastic recoil would be favorable to increase the inflation pressure in comparison with diameter of coronary artery therefore at the site of tissue blood interaction Auxetic coronary stent will adhere properly with the blood environment.

5.5. Surface Morphology

Surface morphology through Scanning Electron Micrographs (SEM, JEOL-instrument JSM-6490A) presented in section 4.8, determined the effects of fabrication processes of the Auxetic coronary stent. Figure 9, depicts the formation of porous oxide layers inside surface of the stent. This deposition was due to the reaction of oxygen with the elemental contents of the 316L stainless steel. The pickling solution was easily absorbed by these pores which facilitated the removal of slags and oxide layers from the inner stent surface as well as from the outer surface of the Auxetic stent.

The SEM micrographs of electropolished stent depict the surface smoothness and round off edges of the Auxetic coronary stent. The surface roughness was much apparently improved than the pickled stent due to the controlled parameters such as current, voltage and polishing time which were executed efficiently to achieve the inside and outside smooth surface of the Auxetic coronary stent. From the SEM micrograph it is evident that there are no indications of roughness on the surface however grain boundaries are formed after the electropolishing. Moreover, the electropolishing also created great impact on the edges of the squircles and diamonds that make it more fairly round edges. In order to prevent perforation and injury to the surrounding arterial wall the rounded edges are desirable in case of Auxetic coronary stent.

A protective oxide layer is formed on the 316L stainless steel Auxetic stent which made the stent intrinsically corrosion resistant due to presence of high chromium content along with other elemental constituents such as iron, molybdenum and nickel. But when stent is subjected to highly corrosive blood environment this protective layer usually wears off with time. Therefore, the corrosion resistance of the Auxetic stents was enhanced by subjecting the stents into highly oxidizing environment and for this purpose the Auxetic stents were dipped into sulphuric acid (H_2SO_4), and it was also reported in the past by (Parsapour, 2007). The brightness of surface and luster revealed that electropolishing was performed effectively that not only improved the structural definition of the stent but also made the Auxetic coronary stent corrosion resistant. The annealed process makes the Auxetic stent ductile and made it balloon expandable. It was also notice that the size of the grain boundaries reduced through annealing process that eventually improved the overall surface topography and structural integrity of the Auxetic coronary stent.

CONCLUSION

This thesis is associated with the design and development of new Auxetic coronary stent for the treatment of coronary heart disease. It is proposed that by virtue of having suitable mechanical properties the arterial wall will have good mechanical anchorage with the new balloon expandable Auxetic stent. Due to Auxetic design the stent has anisotropic properties that make it great match for coronary vessel anisotropic structural properties. When expanded radially through balloon catheter the Auxetic stent size increases in both radial and longitudinal directions and thus exhibits no foreshortening. It is believed that Auxetic stent will prevent the problem of stent migration and will effectively maintain the luminal patency of the coronary artery due to the Auxetic property of the stent design.

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