A REVIEW OF BIOMECHANICS OF ARTERIAL STENT IMPLANTS

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MASTER OF SCIENCE

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ABSTRACT

This work looks to provide a review of modern stents by evaluating the need for them as well as providing a detailed engineering analysis of the conditions they are subjected to. It is estimated that over two million of these devices are implanted in patients annually. Of those implanted, a majority are used in the treatment of arteriosclerosis. This disease causes arterial walls to thicken and toughen leading to restricted blood flow and in extreme cases, complete loss of circulation. Arteriosclerosis and complications arising from it form a leading cause of death in the developed world. Although there are a variety of treatment options available, stents have been successfully used for several decades. The review of numerous technical reports infers that stents must withstand complex multi-axial loading conditions while being able to withstand an immense number of loading cycles, making the design and implementation of stents a significant feat.

ACKNOWLEDGMENTS

I would like to express my gratitude to my advisor, Dr. Karami for his support and guidance throughout this project. In addition to this, I would like to extend my thanks to the North Dakota State University Mechanical Engineering Department who made this opportunity possible.

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1. INTRODUCTION

First conceived in the 1960s and later successfully used in the 1980s, cardiovascular stents have become a modern invention that improves the quality and span of life for millions around the globe [1]. Stents are small mesh tubes that can be inserted into the body and are constructed such that perforations allow them to expand without fracturing. The expansion of these medical devices allows them to open passageways within the body, restoring flow. These devices provide a treatment option for diseases such as arteriosclerosis; a chronic disease that is distinguished by the walls of arteries abnormally hardening and thickening, resulting in a loss of elasticity [2]. Since these changes to the interior walls of arteries ultimately impact blood circulation, and with arteries being the only way for tissues within the body to receive nutrients and oxygenated blood, the potential health impacts are significant. The extremity of which is such that arteriosclerosis and complications arising from it are one of the leading causes of death and disability in the developed world and it can be directly related to half of all deaths within the United States [3]. Although there are several treatment options for these diseases, stents have been successfully used for cases with significant complications for several decades. With stents having such a consequential impact it is crucial for engineers to fully understand the design scenario, allowing for the engineering of highly effective stents with negligible complications. This work looks to review the circumstances driving the need for stents, the conditions they are subjected to, and considerations that must be taken in their design.

2. ANATOMY & PHYSIOLOGY OF HUMAN CARDIOVASCULAR SYSTEM

To understand the need for stents in treating arteriosclerosis one must first have a detailed understanding of the biological structures involved. To function correctly, the tissues of the body must receive vital oxygen and nutrients while having toxins and other wastes removed from them. This process is achieved by the cardiovascular system through blood transport. Within the cardiovascular system there are five primary classes of blood vessels: arteries, arterioles, capillaries, venules, and veins. Arteries carry oxygenated blood away from the heart before branching repeatedly and decreasing in diameter until they become classified as arterioles. These arterioles carry blood into capillaries, allowing diffusion of oxygen and nutrients for carbon dioxide and toxins with the interstitial fluid of cells. After the blood passes through the capillaries, it is now deoxygenated and thus enters the venous system through venules. These venules gradually combine and enlarge to form veins while traveling back to the heart and lungs to be re-oxygenated, restarting the cycle [3]. In general, arteries are thicker and more resilient than veins since they must withstand the high-pressure, pulsatile supply of blood from the heart.

Arterial walls are constructed of three distinct layers; the tunica intima, tunica media, and tunica externa [3]. The innermost layer, the tunica intima, can be further broken down into the endothelial lining, which is surrounded by the internal elastic membrane, a thick layer of elastic connective fibers that circumferentially surrounds the endothelium. In arteries, the endothelium typically has a rippled surface due to vessel constriction. The central layer of an artery, called the tunica media, is made of concentric sheets of smooth muscle cells that are loosely connected with a framework of collagen fibers. Larger arteries may also contain smooth muscle cells arranged longitudinally to the artery. The outermost layer, the tunica externa, is a connective sheath comprised of collagen and elastic fibers. These fibers tend to intertwine with surrounding

tissues to stabilize the blood vessels [3]. Figure 1 visually depicts the structure of artery walls [3].

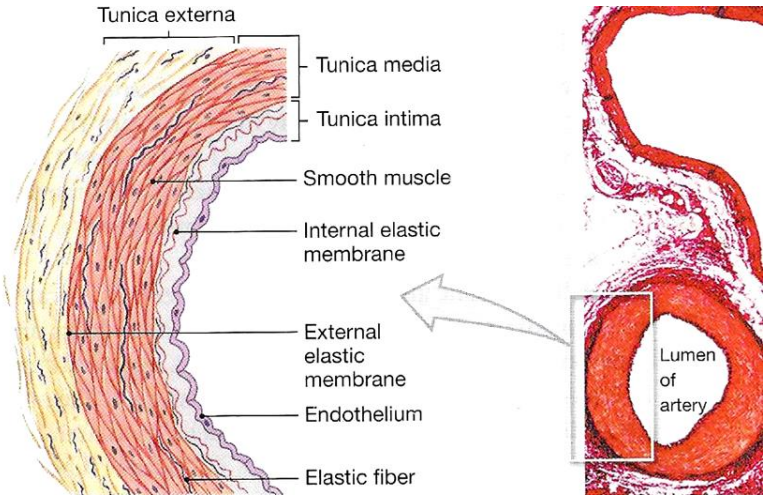

Figure 1. Cross-section of artery wall [3].

The thick, strong walls allow arteries to maintain their circular cross-section when not fully pressurized and the inherent elasticity allows arteries to absorb the pulsatile pressure that is generated by the rhythmic pumping of the heart through expansion and contraction. This process is known as elastic rebound and allows for the high pressures generated during the ventricular systole to be dissipated by dampening the peaks and valleys and ultimately creating a near-continuous blood flow in the arterioles [3]. It should be noted that due to the large diversity of conditions within the human body, different types of arteries exist to best perform the required function. Although the different types of arteries have varying construction and performance, in general they operate the same with this work primarily focusing on the larger arteries where arteriosclerosis is most commonly present.

2.1. Arteriosclerosis

Arteriosclerosis can be broken down into three distinct diseases: atherosclerosis, arteriolosclerosis, and Monckeberg medial calcific sclerosis [3]. Atherosclerosis is the most

common form of arteriosclerosis and is the formation of a lipid lesion in the tunica media of an artery. Arteriolosclerosis is atherosclerosis present in smaller arteries known as arterioles. Monckeberg medial calcific sclerosis, also known as focal calcification, is the formation of calcium salts within arteries. This condition is commonly associated with natural aging processes. It is important to note that the terms arteriosclerosis and atherosclerosis are commonly used interchangeably even though they are distinctly different and that atherosclerosis can initiate the other forms of arteriosclerosis. All forms of arteriosclerosis lead to blood flow restrictions. Arteriosclerosis can affect any artery, but it is most common in the carotid arteries, coronary arteries, renal arteries, and peripheral arteries. Depending on the location that arteriosclerosis is affecting determines the symptoms and potential health effects of the patient. Figure 2 below, depicts the locations of major arteries within the human body [3].

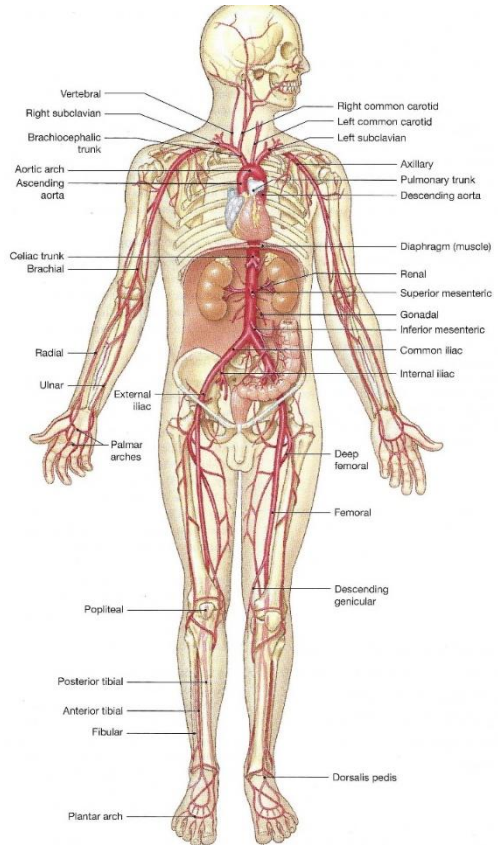

Figure 2. Major systemic arteries [3].

Atherosclerosis occurs when the endothelium becomes damaged, allowing for the accumulation of lipids, but the process tends to be more elaborate than this. The presence of high levels of plasma lipids, particularly cholesterol and high levels of low-density lipoproteins initiate the formation of atherosclerotic lesions [2, 3]. Elevated levels of the substances in the bloodstream cause them to remain in circulation for extended periods. The body reacts to this with monocytes, a specific type of white blood cell that consumes the excess lipids. Once containing lipids, the monocyte cells are known as foam cells. These foam cells then attach to the endothelial lining of the arteries and release cytokines, a protein used in cell signaling. The protein works to stimulate the smooth muscle cells of the tunica media, causing them to divide, grow, and thus thicken the arterial wall. This process continues as more monocytes accumulate in a concentrated area. The endothelial cells eventually begin accumulating lipids as well, forming a mass of tissue that protrudes into the bloodstream known as an atherosclerotic plaque or fatty streak [2, 3]. At this phase of atherosclerosis, there is evidence to suggest that lifestyle changes can reverse this process [3]. If the lesion and elevated lipid levels persist, or if the endothelial cells are further injured, the endothelial cells will continue to accumulate lipids causing them to swell and expose gaps containing collagen fibers from underlying arterial wall layers. The atherosclerotic lesion would now be considered an intermediate or an advanced lesion. The next stage in atherosclerotic lesion growth is known as atheroma. Atheroma is characterized by a continued accumulation of lipids and scar tissue. Continued growth will promote the formation of a fibrous cap over the lesion, known as fibroatheroma. These exposed collagen fibers can allow blood platelets to adhere, forming localized blood clots, known as thrombosis. These localized blood clots create a serious health hazard since they can spontaneously dislodge, travel down the artery, and clog a smaller artery, ultimately restricting or

completely limiting blood supply to a portion of the circulatory system. This atherosclerotic lesion growth process is visually depicted in Figure 3 [4].

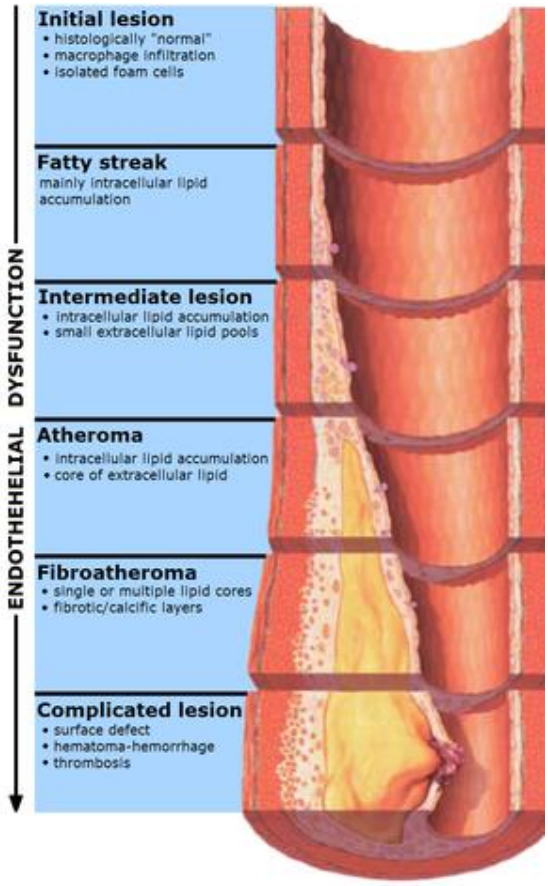

Figure 3. Progression of atherosclerosis [4].

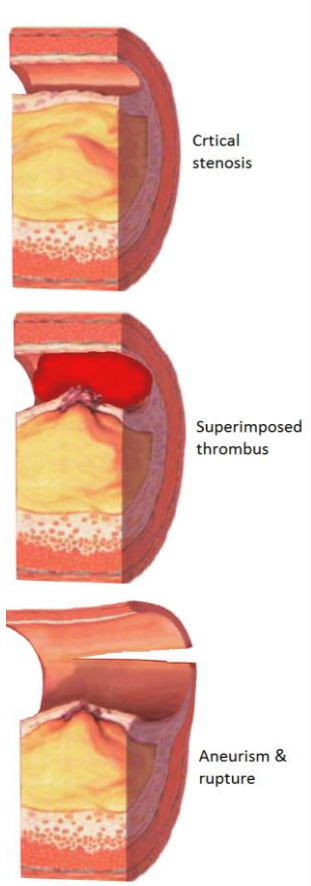

Figure 4. Atherosclerosis complications [4].

As an atherosclerotic lesion grows, the arteries will remodel by distending to negate the impact on flow restriction. This distension of the arterial wall causes them to thin and stiffen, taking away the artery's ability to absorb the pressure pulses of blood flow [2, 5]. Although the arteries can initially remodel to mitigate the effect of the lesion on blood flow, if the lesion continues to grow beyond the maximum distention of the artery it will start to protrude into the blood flow, causing the artery to become stenosed. Atherosclerotic lesions can develop early in life and then remain undetectable for decades as they slowly grow. Once the lesion has reached a critical state, there are four possible outcomes; the lesion ruptures releasing a mass that travels

further down the artery called embolism, critical stenosis occurs creating a condition where the downfield circulatory system does not receive enough blood, thrombosis occurs creating hazardous blood clots, or the weakened arterial wall develops an aneurysm increasing the potential for rupture [6]. Figure 4 visually depicts the possible outcomes of increased lesion growth [4].

Since it is known that atherosclerotic lesions are initiated by mechanical damage to the endothelial surface, the presence of curvature, branching, and bifurcation results in an increased risk of stenosis formation. In the human circulatory system, common areas afflicted by atherosclerosis include the coronary arteries, the subclavian and common carotids, the bifurcation of the common carotid into the internal and external carotids, the renal arteries, and the ileo-femoral bifurcations [3]. These regions all share similar geometries and subsequently undesirable fluid dynamic situations that lead to increased risk of atherosclerotic lesion formation.

2.2. Atherosclerotic Diseases

As mentioned previously, an individual who has atherosclerosis may live a normal life for decades, but when the atherosclerotic lesion grows to a critical size or ruptures the outcome can be life-altering. Although the exact initiation process is not fully understood, several known risk factors include smoking, high amounts of cholesterol and other lipids present in the bloodstream, stress, high blood pressure, and high amounts of sugar present in the blood due to diabetes. Other risk factors include increased age and a family history of atherosclerotic diseases, particularly heart disease [7]. As with all diseases and ailments, the best cure is preventive action. With atherosclerosis a healthy lifestyle can be a major inhibitor. Eating a heart-healthy diet that is low in sodium, added sugar, and solid fats, as well as regular physical activity and

weight control can significantly reduce the risk of atherosclerosis. Avoiding smoking and smoke inhalation are also important to prevent the onset of this disease [7]. When an individual does get atherosclerosis, they will likely not be aware of it until the artery becomes critically narrowed or completely blocked, in which case a heart attack or stroke is likely to occur. More specific symptoms depend on what arteries are being affected. If the coronary arteries are affected, then ischemic heart disease or coronary microvascular disease can form. These are characterized by chest pain, discomfort, shortness of breath, fatigue, and sleep problems due to a lack of oxygen to these muscles. If the carotid arteries become affected, symptoms of a stroke such as sudden weakness, paralysis, confusion, trouble speaking, or trouble seeing are expected. Atherosclerosis affecting peripheral arteries, the arteries supplying blood to limbs, can lead to peripheral artery disease causing numbness and pain as well as infections in extreme cases. Chronic kidney disease can form if the renal arteries become affected. This disease causes tiredness, changes in urination, nausea, swelling of the hands and feet, and trouble concentrating. With so many possible symptoms and locations for atherosclerosis to form, a multitude of diagnosis options are required. Simple blood tests, electrocardiograms, X-rays, and echocardiography can all identify factors indicating the presence of atherosclerosis. Other testing such as Ankle/Brachial Index and Stress Testing can be used to gauge the extent of atherosclerosis by evaluating the efficiency of blood flow. More advanced testing such as Computed Tomography Scan and Angiography can be used to generate computer images of the heart, arteries, as well as analyze the blood flow through them [7].

2.3. Treatments of Atherosclerosis

Once the extent of atherosclerosis is determined, treatment can begin. For atherosclerosis the most important treatment option is to make lifestyle changes to prevent the continued

progression and formation of atherosclerotic lesions. If this is not enough, medications to lower blood pressure, blood sugar levels, prevent inflammation, and blood thinners to prevent blood clots can be prescribed. For more extreme cases surgery may be required. Procedures can be used to open blocked arteries, remove plaque buildup, and insert stents to keep the artery open. Other invasive options include bypass surgery where arteries from other parts of the body are re-attached to bypass the damaged section of artery [7]. The extent of atherosclerosis, the location, and the health of the patient determine the success of the procedures.

If a stent is required, then it is commonly inserted through a process called balloon angioplasty. This process involves a needle being inserted into a major artery, often in a leg near the groin. A catheter with a stent applied over a balloon is then inserted through the needle and pushed to the location of the atherosclerotic lesion. Once in position, the balloon is expanded, subsequently expanding the stent, and thus opening the artery. The balloon is then deflated, and the catheter is removed [1]. A portion of this procedure can be seen in figure 5 [8]. It should be noted that stents are not solely utilized for the treatment of arteriosclerosis, but can also be used to treat aneurysms, open bile ducts, the larynx, or trachea, among other things. This work focuses attention on stents used in arteriosclerosis due to their commonality in medical treatment and because all stents are used to expand passageways indicating that the principles of arterial stents used in the treatment of arteriosclerotic legions can be readily applied to other applications.

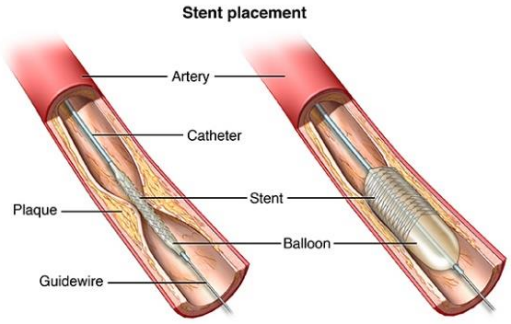

Figure 5. Balloon Angioplasty [9].

3. ARTERIAL STENT IMPLANTS

The first stent implanted in a living human took place in 1986 when Jacques Puel and Ulrich Sigwart successfully implanted a self-expanding stainless-steel stent into a patient to prevent restenosis after a coronary surgery [9,10]. This success was quickly followed by Julio Palmaz and Ricard Schatz who implanted a similar stent in a patient in 1987 using an expandable balloon. The Palmaz-Schatz stent became the first FDA-approved stent in the United States and is the foundation for all modern stents [9]. Since these early successes, stents have since improved significantly due to advances in design, materials, and implementation techniques.

3.1. Stent Geometries

Stents are typically cylindrical in shape and are comprised of one or more structural elements such as splints, fibers, rods, threads, or wires [9]. It is common for the length, diameter, and strut thickness to vary significantly based on the application and manufacturer. Figure 6 depicts several stent structures used in peripheral arteries [11].

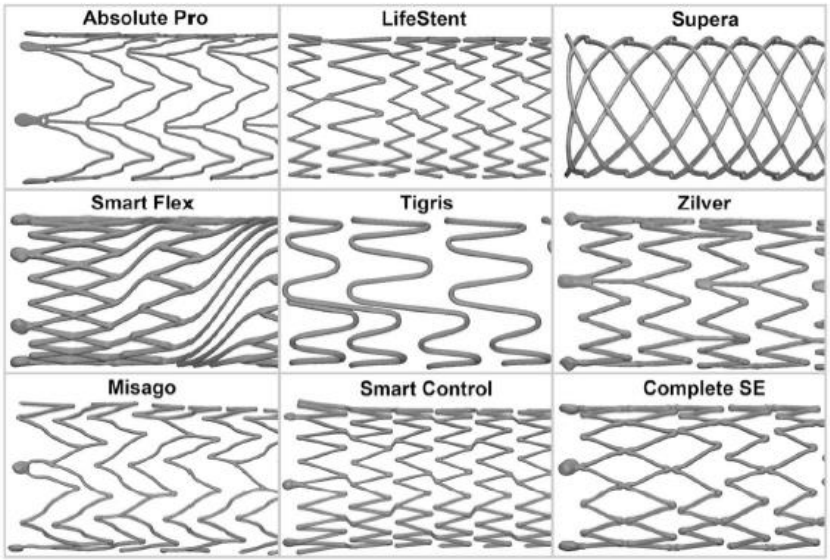

Figure 6. Common peripheral artery stent designs [11].

Though stents often vary in geometry, they must exhibit sufficient mechanical characteristics to be able to stretch, twist, and compress with the vessel it is implanted in, while

providing sufficient radial strength to open it. In addition to this, stents also need to exhibit radio impermeability to prevent transmission of X-rays, be able to compress sufficiently to allow for passage through narrow arteries, and be biocompatible [9]. It has also been shown that the restenosis rates can be dependent on the geometry of the stent due to vascular damage. One geometrical factor known to directly affect restenosis rates is strut thickness. A study comparing the restenosis rates of a 50-micrometer thick strut and a 140-micrometer thick strut found that the 50-micrometer thick strut caused 15 percent restenosis rates while the 140-micrometer thick strut caused 26 percent restenosis rates [9].

3.2. Materials of Stents

Proper material selection for stents has a direct impact on the success of stent implementation and restenosis rates [9,10]. Due to the nature of the corrosive environments found throughout the human body, highly biocompatible and corrosion resistant alloys are of extreme necessity. The Food and Drug Administration does not strictly regulate materials used in medical implants but regulates the devices themselves [12]. Metals are commonly employed in medical implants due to their ideal mechanical properties, which include high ductility while retaining a high toughness and strength. The first stents used were called bare metal stents (BMSs) and were often made from stainless-steel alloys and Nitinol, a nickel-titanium alloy [10].

Stainless steels were some of the first metals utilized in modern medical implants in the early 1900s. Numerous alloys are employed, the most common being 316L. A key attribute of stainless steel is that is has high electrochemical corrosion resistance due to the formation of passive chromium oxide films [12]. Stainless steel has high strength, corrosion resistance, lack of magnetic properties, good formability, and cost effectiveness. Although stainless steel has excellent corrosion properties, it is susceptible to pitting in the presence of chloride and saline

solutions. Other shortcomings of stainless steel include the leaching of toxic chromium and nickel ions and stress shielding, due to its high modulus of elasticity [12]. Stainless steel stents also tend to have poor flexibility which can lead to stent fracture [10].

Nitinol is a shape memory metal alloy named after its composition and place of origin, Nickel Titanium Naval Ordnance Laboratory. This smart material was derived in 1959 and exhibits both a shape memory effect—the ability to be mechanically deformed at a specific temperature, have the external force removed while maintaining the deformed shape, then return to its original undeformed shape when heated—and super elasticity—the ability to withstand large deformations and return to its original shape when the external load is removed—depending on the transformation temperature of the specific alloy. Both unique properties are possible due to the crystal structure change that occurs during Nitinol's phase change between austenite and martensite phases. In biomedical applications it is often the super elastic effects that are leveraged [13]. This super elastic property is characterized by strain recoveries of up to 10 percent which can be 10 to 30 times as much as traditional engineering metals [13].

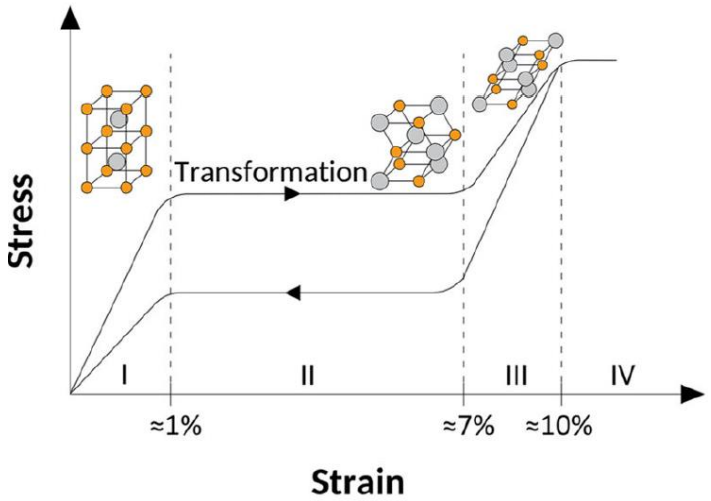

Figure 7. Super elastic deformation behavior [11].

Figure 7 visually depicts this super elastic property, showing a graph of super elastic nitinol stress versus strain curve and how the temperature dependent microstructure of nitinol

influences its response to stress and strain. The four stages shown in this figure show that the super elastic deformation of nitinol is nonlinear and contains significant hysteresis [11]. The first stage in this figure depicts nitinol that is still in its austenite phase undergoing linear elastic deformation with a high modulus. This physical property can be associated with the deformation of the austenite crystal structure's chemical bonds. Once the strain rate approaches one percent, the second yield stage starts, which continues to approximately seven percent strain. This large strain occurs with a minor increase in stress but is not identical to plastic yielding because it occurs due to a crystal structure change and not crystal structure units irreversibly slipping [14]. This structure transition is a transition from austenite to twinned martensite. The third deformation stage is again characterized by an increase in elastic modulus. The deformations in these first three stages are fully recoverable, but it should be noted that the large hysteresis present creates much smaller forces during unloading than initially loaded [11]. The super elastic property of nitinol that is leveraged in stents is only present between the austenite-finish temperature and the martensite forming temperature. These two temperature bounds are determined by the exact alloy composition of the nitinol as well as the heat treatment used during manufacture and are the start position in stage one and the stop position in phase three, respectively. If the temperature is greater than the martensite forming temperature, then nitinol follows a traditional metal alloy plastic deformation after stage one [11]. Titanium and some of its alloys readily form a stable, protective oxide layer when placed in vivo, allowing it to not interfere with biological functions. Nickel however can cause toxicity, cellular damage, and immune responses in patients [11]. The formation of nickel oxide prevents the release of nickel into the patient, allowing nitinol alloys to be acceptable for in vivo applications. Although this is

the case, some studies have shown that the hyper elasticity of Nitinol can increase the risk of nickel leaching out of stents [11].

Later stent designs utilized cobalt-chromium alloys. Similar to stainless steels, cobalt-chromium alloys get their corrosion resistance through the formation of thin chromium oxide films. These alloys are known to exhibit excellent corrosion resistance, even in the presence of chloride ions [12]. Along with excellent corrosion properties, favorable mechanical properties include toughness and elongation. Cobalt-chromium alloys have a higher modulus of elasticity than most medical implant materials. These improved mechanical properties allow cobalt-chromium stents to have thinner struts, thus improving clinical performance [9,10]. Since chromium-cobalt alloys contain toxic elements such as chromium, cobalt, and nickel, corrosion and degradation can be a concern.

Bare metal stents benefit from being simple to design and manufacture but have been known to cause artery damage and restenosis at rates of 20 to 30 percent due to their need to permanently stay within the body once implanted [9,10]. To overcome this, drug-eluting stents were developed. These stents are bare metal stents with medicine that can directly target atherosclerotic lesions [9]. This medicine can be delivered through a variety of techniques such as being contained within degradable polymer coatings or by being placed within micro-pores created on the surface of bare metal stents.

The desire to further improve the quality of life for patients through the reduction of post-implant complications resulted in the concept of decomposable implants. These implants are designed to be bio-resorbable, thus allowing for the complete recovery of blood vessels [9]. These stents can be comprised of either corrodible metallic materials or degradable polymeric materials. Poly-L-lactic acid (PLLA), a thermoplastic polymer, was one of the first polymers

used as a stent material. This polymer is decomposed through the hydrolysis of ester bonds, allowing it to be metabolized into carbon dioxide and water [9,10]. Clinical trials have shown that these stents can provide radial support for 6 months and be completely resorbed in two to three years [9]. Other polymers that are being investigated for biodegradable stents include poly(lactide-co-glycolide) (PLGA), polycaprolactone (PCL), poly-glycolic acid (PGA), and poly(D-lactide) (PDLA) [10]. Biodegradable polymer stents offer advantages in drug delivery and biocompatibility compared to bare metal stents, but at the disadvantage of poor mechanical strength [9,10].

To overcome this, biodegradable metal stents were developed. These stents are commonly made from magnesium and zinc alloys, both essential metals for bodily functions. Magnesium alloy stents exhibit good mechanical properties and are biocompatible due to the fundamental role of magnesium in many physiological functions, but can be harmful in large amounts. To optimize the decomposition of magnesium, special alloys such as WE43 were developed, allowing for slow, even degradation [9,10]. Though zinc is only needed in small amounts within the human body it is still a viable option for biodegradable stents. These stents have numerous advantages when compared to other materials including ideal degradation rates, biocompatibility, and anti-bacterial effects [9,10].

4. BIOMECHANICAL ANALYSIS OF STENTS

4.1. Fluid Dynamics

A thorough understanding of the biofluid mechanics involved with atherosclerosis is essential for proper diagnosis, treatment, and prevention. Given that atherosclerosis causes an artery to become stenosed, thus restricting the blood flow, the fluid mechanics can be modeled as a simplified restricted flow problem. Figure 8 below depicts this simplified flow model where blood flows from the left side at point one before being reduced at point two. It should be noted that point one is upstream of the stenosed portion of the artery in a healthy section of the artery.

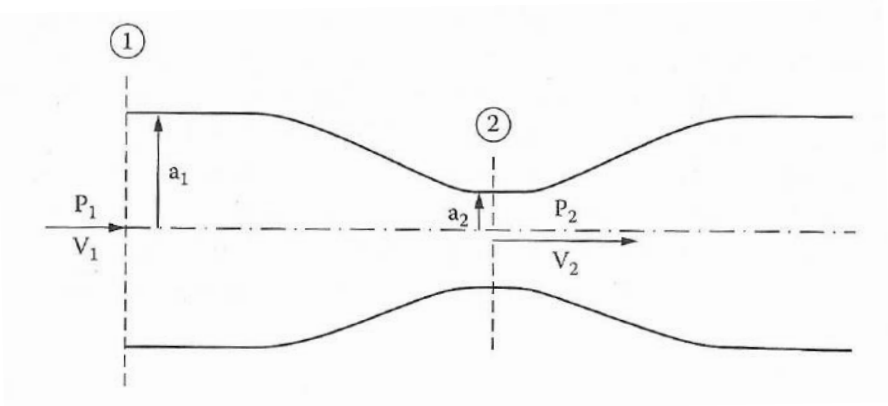

Figure 8. Atherosclerotic artery flow model [2].

As with all closed systems, the principle of Conservation of Mass is valid, allowing for the determination of the blood velocity within the stenosis. This principle states that the mass of a body is constant during motion and can be expressed as the area times the velocity at one point in the flow path being equal to the area times the velocity in another portion of the flow path. This law is mathematically shown in Equation 1.

$$A_1 V_1 = A_2 V_2 \tag{1}$$

If the blood flow through the stenosis is both incompressible and steady, the energy equation shown in Equation 2 can be used to evaluate it. In this expression $P, V,\ z, and\ \gamma$ are the pressure, velocity, location, and specific weight respectively, at the beginning and end points.

$$\frac{P_1}{\gamma} + \alpha_1 \frac{{V_1}^2}{2g} + z_1 = \frac{P_2}{\gamma} + \alpha_2 \frac{{V_2}^2}{2g} + z_2 + h_L \tag{2}$$

The gravitational constant is represented by g, and head loss, h_L, defines the energy loss associated with the viscous dissipation. To adjust for the varying velocity profiles found in fluid flow the kinetic energy coefficients α_1 and α_2 are used. For an ideal case with a uniform velocity profile then kinetic energy coefficients are equal to one, otherwise they are greater than one.

Chandran et al further reduces the energy equation by ignoring viscous dissipation and assuming a uniform velocity profile, allowing the Bernoulli equation to be applied. Gravitational effects and head losses are ignored since they can be deemed negligible due to the short distance of the stenosis. Equation 3 mathematically expresses the Bernoulli equation and in this case, can be reduced to Equation 3.1.

$$P_1 + \frac{1}{2}\rho {V_1}^2 + \rho g h_1 = P_2 + \frac{1}{2}\rho {V_2}^2 + \rho g h_2 \tag{3}$$

$$P_1 + \frac{1}{2}\rho {V_1}^2 = P_2 + \frac{1}{2}\rho {V_2}^2 \tag{3.1}$$

It should be noted that the application of the Bernoulli equation requires the fluid flow to be steady, that is the velocity, pressure, and density are constant and do not change. The flow must also be incompressible, meaning that the density does not change along the streamline. The viscous forces within the fluid flow must also be negligible. Due to the Bernoulli effect and increased flow velocity within the stenosis, there is a pressure drop. In severe cases this reduced pressure can cause arteries to collapse [2]. When exiting the stenosis into a healthy artery the

flow is initially separated due to the high jet momentum. This separated flow region also contains recirculating flow.

Although it is common for atherosclerosis to be analyzed as a nozzle fluid flow problem, stenosed arteries are typically characterized by being highly focal and eccentric, that is they are short in linear length and asymmetric in cross-sectional shape [2]. It is also important to note that the flow path geometry—curved versus straight, branching versus conjoining, and narrowing versus widening—of the artery also impact flow characteristics. One emerging technology that is being applied to biofluid mechanics to help engineers analyze flow is Computational Fluid Dynamics (CFD). CFD allows for high accuracy, patient specific models to be designed and analyzed, as well as the production of detailed flow fields that the blood is subjected to while traveling through diseased arteries. Although CFD methods are a significant improvement over traditional, simplified paper-pencil calculations the approach still has limits. Scientists are continuing to advance it by incorporating the effects of vessel elasticity and cardiac motion including arterial compliance, vessel bending, and cardiac contraction [15]. CFD methods also rely upon the assumption that blood behaves as a Newtonian fluid—a fluid whose viscosity remains constant, regardless of applied shear stress. This assumption is valid in healthy arteries, but the complex flow patterns that atherosclerotic lesions form can invalidate this assumption [15]. Figure 9 illustrates an example of the velocity and pressure distribution of blood traveling through a stent that was obtained through CFD methods [16].

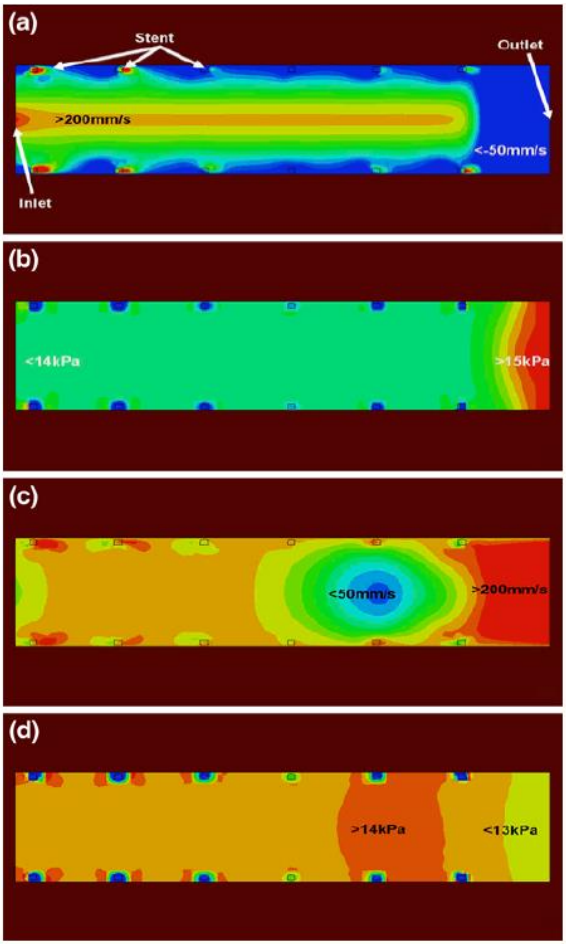

Figure 9. Blood velocity and pressure profiles [16].

Section “A” depicts the velocity profile and “B” depicts the pressure profile during peak systole. The velocity peaks at over 200 millimeters per second entering the region, whereas the outlet is flowing at approximately 50 millimeters per second. The pressure passing through the stent is approximately less than 14 kilopascals whereas it exits greater than 15 kilopascals. Section “C” depicts the velocity profile and “D” depicts the pressure profile during peak diastolic trough.

4.2. Stent Loading Conditions

As introduced earlier, stents and arteries are subjected to a highly rhythmic, pulsatile flow. This motion comes from the systole and diastole cycles of the heart. These cycles create pressure in the arteries and induce radial strain on the artery as well as stents. The pressure generated depends on the distance from the heart as well as the specific artery. Figure 10 depicts the force exerted in a cardiac cycle on a stent in relation to its crimp and deploy forces and strains [13].

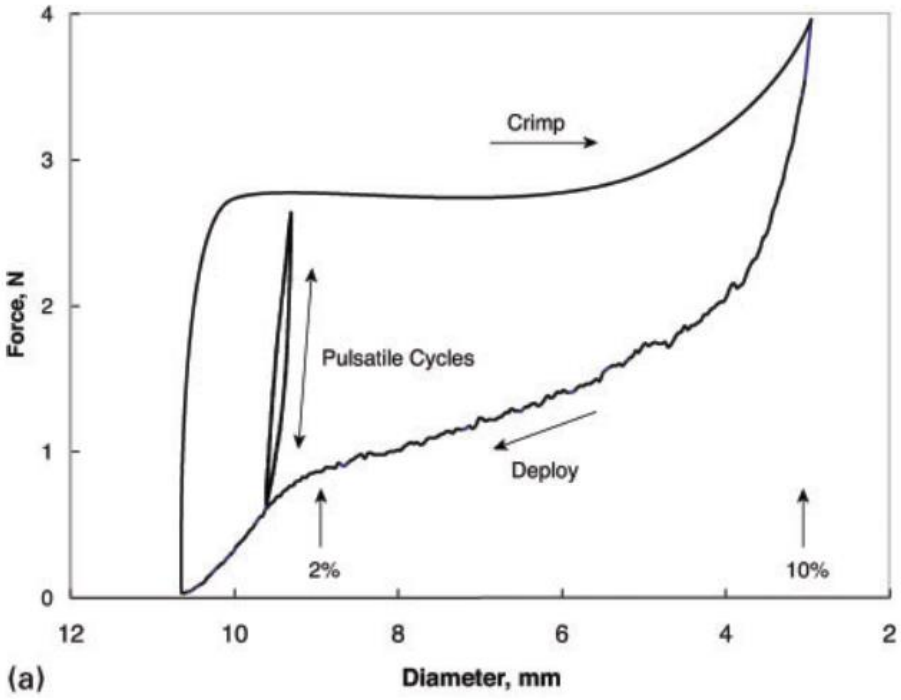

Figure 10. Stress-strain of nitinol stent [13].

As discussed previously, when a stent is inserted into an artery via balloon angioplasty it must first have its diameter reduced to fit. This is the “crimp” and can be done at strain values upwards of 10 percent as indicated by the figure. Once the stent is deployed, it expands until its expansion forces reach equilibrium with the elasticity of the arterial wall. From this state, the cyclic pumping of the systole and diastole exert the pulsatile cycle loop shown.

In addition to being subjected to pulsatile forces, stents must also be able to expand longitudinally, withstand torsion, and bending moments to not break while the body moves. Within the human body, one of the most troublesome regions is the Femoropopliteal Artery due to the high degree of mobility [11]. Figure 11 depicts the femoropopliteal artery; a major artery that travels across the pelvic girdle, femur, and patella, all of which allow a high range of motion.

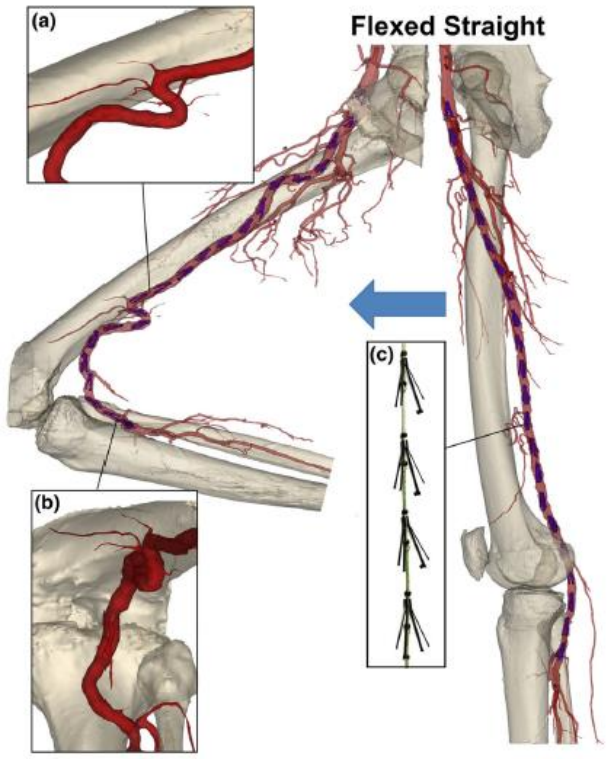

Figure 11. Femoropopliteal artery [11].

Studies looking to evaluate deformations during limb flexion have reported wide ranges in deformations due to the uniqueness of each segment of the femoropopliteal artery, with the more extreme values being at the adductor hiatus and below the kneecap [11]. It should also be noted that these regions are more susceptible to arteriosclerotic diseases due to the complex motion and fluid flow through them. Three studies performed by different groups on range of

motion were evaluated. The first suggested that while traveling from a supine position to a fetal position a torsion of 60° ± 34°, and axial compression of 13% ± 11% were observed within a stent. Another study suggested that a torsional twist of 2 to 4°/cm, an axial compression of 4 to 13%, and a bending radius of 22 to 72 mm occurred during limb flexion. The third group utilized custom markers that did not affect the stent performance and placed these within human cadavers for analysis. These markers were designed to measure axial compression, bending, and twisting of the artery during limb flexion. It was observed that this measuring technique yielded significantly larger values than the previous studies. The axial compression, bending radii, and twist during limb flexion were found to be 9 to 25%, 8 to 27 mm, and 8 to 26°/cm, respectively [11].

4.3. Fatigue Analysis of Stents

Of engineering considerations for stent design, one of the most important is the fatigue life since these implantable medical devices are subjected to millions, even billions, of cycles per year and cannot be readily serviced after being inserted into a patient. This indicates that their fatigue resistance is the dominant factor in characterizing their durability and ultimately the safety of the patient. Of materials used to construct stents, nitinol is a clear outlier and has shown significant promise due to its super elasticity. This property allows stents to be shrunk, inserted into an artery, and expanded. It also allows the stent to return to its original shape after limb flexion. Due to the unique loading, fatigue failure is a common issue in traditional stents, with some reports indicating re-admission rates upwards of 50 percent, whereas early nitinol stent re-admission rates were as low as 18 percent [17, 18].

With each of these loadings occurring every time a limb, muscle, or artery support structure moves and considering the systolic and diastolic pumping of the heart, one can imagine

the multitude of cycles that stents must endure. These loadings add up to subject numerous millions to billions of fatigue cycles on stents in a single year. Regulatory bodies have exact requirements for the fatigue testing and evaluation of stents that include at least 10 years of pulsatile cycling, the equivalent of 4*10^8 cycles. To put this into perspective, if an accelerated test were constructed to simulate the effects of the systole and diastole at a test rate of 65 hertz, it would take approximately 72 days to complete 4*10^8 cycles [14]. Figure 12 depicts loading cycles compiled from various regulatory bodies that stents are subjected to on an annual basis [14].

Loading	Frequency (Hz)	Cycles per year
Diastole–systole	1.2	4×10^7
Musculoskeletal	1	$\sim 0.2 \times 10^7$
Breathing	0.3	$\sim 1 \times 10^7$

Figure 12. Standard in-vivo loading conditions for stents [14].

These cycles and loads are highly dependent upon where the stent is placed in the cardiovascular system. If a 10-year performance evaluation is required, then 4*10^7, 2*10^6, and 1*10^7 cycles would be required for the diastole-systole, musculoskeletal, and breathing conditions, a stent would have to withstand over a half-billion cycles.

Nitinol stent failure has been primarily attributed to crack propagation that is caused by microstructural defects arising from cyclical stress concentrations [11]. Some fracture mechanics and fatigue properties of nitinol that have been characterized show that the transformation between austenite and martensite phases can occur along the tips of cracks, further promoting crack propagation by inducing additional tensile stresses [19]. It has also been observed that crystallographic orientations are highly influential on crack propagation with the energetically preferred orientation occurring at 45° from the drawing direction of the nitinol stent [20]. Due to

the multiaxial loading and material dependent fatigue properties, there is not one predetermined fatigue analysis path.

Studies have shown that the geometry of the stenosis has a significant effect on the fatigue life of the stent [21]. Studies have also shown that the different designs of stents have a significant effect on fatigue life under multi-axial loading conditions. One such study performed found that it is not uncommon for stents to fail much earlier than their expected design life [22]. Figure 13 depicts the data collected from this experiment [22].

Stent model	Fracture under axial compression	Fracture under bending
Luminexx	4/5	5/5
Protégé Everflex	0/5	5/5
Smart Control	0/5	5/5
Xceed	2/9	4/9
LifeStent FlexStar	2/7	0/4
Absolute	1/30	1/30

Figure 13. Stent fracture rates for 10^7 cycles [22].

In the table, the first number represents the number of stents that failed, while the second number corresponds to the total number of stents tested. The experiment was performed by placing each of the stents tested in a silicone tube to model it being placed in an artery. The tube was sized such that there was an oversize ratio of 1 to 1.4. The stents were then loaded with five percent axial compression and 48° bending deformations at a rate of 7 hertz for 10 million cycles or until failure. A 37°C saline solution was also placed in the tube. Every 24 hours of cycling an optical microscope was used to inspect for fractures. Similar tests have been performed by numerous other groups confirming that even though stents are designed to last 10 years or more some fail earlier under the required cycling [11].

With the seeming lack of reliable correlation between design life and actual life that is shown in both experimental setups as well as in vivo testing, attempts at advancing engineering design with computer modeled finite element analysis are being pursued. One such attempt successfully incorporated the complex nitinol mechanical properties into a computer simulated finite element model and was able to accurately predict the fatigue life compared to in vivo testing. The model used the Von Mises yield criterion and elastic-plastic material modeling. Since then, other studies have been performed confirming that detailed finite element models could be used successfully to study in vivo stent failure [11]. Current finite element models have improved upon these earlier models, but the complex nature of stent behavior coupled with complex multi-axial loading still leaves more to learn.

4.4. Corrosion and Biocompatibility of Stents

Another important consideration in stents is biocompatibility; a material's ability to be compatible within a living organism without inducing a toxic or immunological response. In metal implants this property is often directly related to the materials corrosion response. If the metal does corrode, toxic and carcinogenic species can leach into the surrounding tissue and cause significant harm by altering the electrical behavior, changing the chemical environment, and affecting cellular metabolism [12]. Typical allowable corrosion rates within medical implants are around 0.001 millimeters per year [12]. With such potential for cataclysmic consequences and the lack of accessibility, stents must be designed in such a manner that they do not fail or degrade to the point of harm during their intended design life.

To successfully engineer metallic stents that do not prematurely degrade through corrosion mechanisms, it is vital to understand the environment they are subjected to. The human body is a highly diverse system that contains a wide array of corrosive systems that change with

location. The most important characteristics of the body that influence corrosion mechanisms are ion concentrations, dissolved oxygen, and pH levels [12]. Although the body contains numerous unique corrosive environments, it is beneficial that the concentration and distribution of electrolytes are kept constant within the respective region through homeostasis. The primary solvent within the human body is water, which consists of 40 to 60 percent of the weight. Water is an excellent electrolyte in corrosive systems, but its properties are enhanced through the addition of ions. The primary cations found in bodily fluids include hydrogen, sodium, potassium, calcium, and magnesium ions and major anions include hydroxide, bicarbonate, chloride, phosphate, and sulfate ions [12]. Although bodily fluids can consist of diverse combinations of elements, dissolved salts, particularly chloride ions and other halides, are considered to be the most influential on corrosion. Another important factor affecting corrosion is the levels of dissolved oxygen contained in bodily fluids. Oxygen is a key element in most corrosion reactions and is found in varying concentrations throughout the body with varying partial pressures ranging from approximately 267 to 13300 pascals [12]. This large differential can lead to stent surfaces being in contact with varying oxygen concentrations, thus increasing the potential of aeration cell formation. The pH is another significant factor affecting corrosion rates and can range from a strongly acidic 1.5 in the stomach to a mildly basic 7.35 to 7.45 in the blood. Although homeostasis acts to normalize pH levels throughout the body, localized pH levels can drop from approximately 7.4 to as low as 4 and take 10 to 15 days to recuperate. Alternatively, bacterial infections can raise the pH to levels as high as 9 [12]. These significant changes in pH levels can be detrimental to implant performance and lead to severe localized corrosion. Although temperature is normally an important consideration for corrosion, it is generally assumed to be constant at 98.6 degrees Fahrenheit. Biological macromolecules can also

affect local corrosion rates by interfering with the anodic and cathodic reactions of corrosion by altering local chemical properties through oxidation and hydrolytic reactions [12].

5. A PROPOSED SOLUTION

As a mechanical engineer, when presented with a problem the desire to propose a solution can be strong. As such, one was generated and proposed in this paper. It should be noted that the following section reflects the opinions of the author.

When proposing a new solution to a complex problem one must first understand the methods currently being utilized by engineers to handle the problem. From an engineering perspective, the understanding of arterial stents is complex and involves multiple subject areas including material science, corrosion science, mechanical engineering, and biological sciences. Currently, engineers are using a multitude of approaches to mitigate the frequency of failures by using exotic materials such as nitinol, highly engineered stent designs to mitigate fatigue failure, and employing scanning methods to monitor the occurrence of restenosis.

After reviewing a variety of papers, two factors that hinder the design, testing, and ultimately the implementation of stents consistently appear; uncertain fatigue characteristics and unknown, non-replicable in-vivo conditions. Only recently have computational engineering models been generated that reliably correlate theoretical test results to in-vivo tests. Even so, there have been studies that suggest that this is not always the case. To any engineer, this should not come as a surprise since there is always statistical probability, uncertainty, and assumptions present in calculations that can significantly affect results. For example, in the realm of fatigue failure, even a good theoretical life analysis can be off by an order of magnitude or more. This coupled with the complex multi-axial fatigue cycle loading, renders reliable fatigue analysis impossible, at least without significant testing. As with most engineering analyses, thorough theoretical modeling coupled with quality experimental data is required for reliable design. This uncertainty drives a need for better in vivo-testing, but ethical considerations often stand in the

way. With the advent of lab grown specimens and bio 3D printing more reliable in vivo testing should be able to be produced, while remaining ethical.

As previously mentioned, the application of arterial stents is complicated and involves the knowledge of many disciplines to fully comprehend. Regardless of this, it is well understood that motion induced fatigue is one of the leading causes of stent failure. As explained already, complex multi-axial loading conditions often exist in arterial stents with the rhythmic cardiac cycle inducing radial strain and biological motion generating torsion, bending moments, and longitudinal expansion [13, 11]. Regardless of the multi-axial loading conditions that an arterial stent may be subjected to, its sole responsibility is to open the artery and allow blood flow to continue uninterrupted. To do this a stent must stay in place while providing sufficient radial support to open the artery, but no requirements exist to transmit any additional loads. Although this simplifies the loading scenario the stent must still be rigid enough to not buckle or fold while moving with the human body. Most modern stents are precision laser machined from solid metal tubes, commonly made of nitinol, stainless steel, or cobalt-chromium alloys. This is done to remove material from the tube and thus make it artificially elastic. The problem with this is that the starting structure is one homogeneous piece, meaning that if any axial, circumferential, bending, or torsion forces are exerted anywhere on the structure they will be transmitted throughout the entire structure. This forces the entire structure to physically endure every cycle to its fullest potential. Combining the knowledge of the loading conditions, mechanical requirements, and modern stent design one could reasonably deduce that a design that mitigates the transmission of forces could lead to an improved design that ultimately improves the efficacy of stents.

With this understanding, one could design a stent such that certain loads are not transmitted through the structure. There are several ways that this could be achieved, but ultimately all involve designing structures that are free to move in certain directions. One such design could be to make a stent that is comprised of repeating semi-traditionally designed stent structures that are linked together with longitudinally running linkages. In this design every repeating unit is identical and every two combined units have partial freedom of movement. In this case, the linkages would mitigate or altogether eliminate the transmission of any bending or torsional loads while providing full radial support to the artery. The design shown in figure 14 is overly simplified but the benefits of the added freedom of movement can be easily visualized.

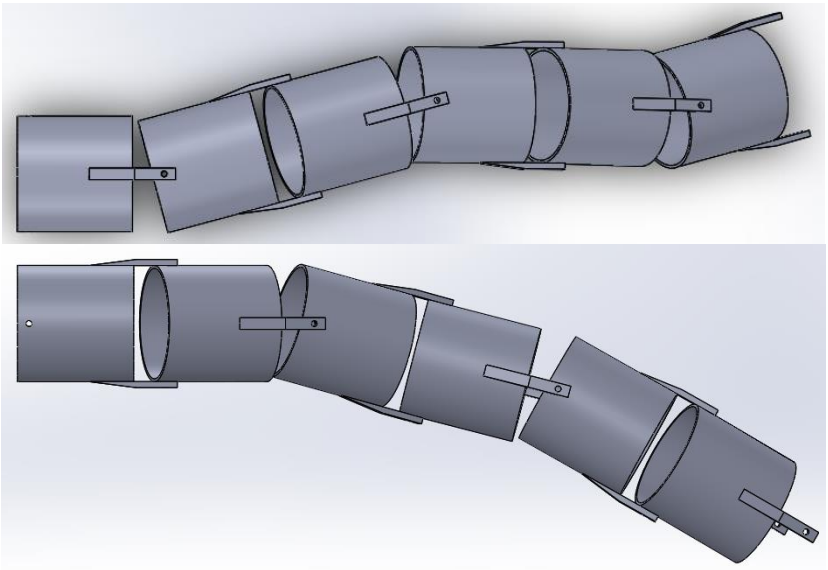

Figure 14. Segmented arterial stent design top and front views.

As with any novel solution, there are often drawbacks. By increasing the number of parts and the precision that they must be assembled, manufacturing costs are likely to increase. Although this is likely to occur, a cost-benefit analysis of this may deem it to be highly beneficial, particularly if stent reliability and longevity increase. Another drawback to these designs is that with moving parts, there will be a dependency between position and fluid flow

characteristics. This not only hinders flow analysis but could lead to the formation of potentially lethal blood clots in the altered fluid flow regions. Yet another possible problem with these designs is that moving components must be present, possibly resulting in wear, and ultimately the release of poisonous ions for certain alloys. A potential solution to this could be to revert to traditional materials such as 316L stainless steel since it rapidly forms protective passive oxide layers or to add wear pads of biocompatible polymer between the connection points.

6. CONCLUSION

With complex multi-axial loading conditions, patient-to-patient diversity, and an immense number of fatigue cycles, the implementation of stents is no small feat. Although clinical trials have indicated that the application of nitinol within stents has driven re-admission rates down from 50 percent of traditional engineering materials to 18 percent, and future implementation of bio-absorbable stents showing even more potential, there is still significant improvement that can and must be obtained. As science and engineering knowledge of materials and the human body continues to advance, the construction and ultimately the success of stents is expected to improve, but for now there are significant engineering limitations due to available materials, the current understanding of fatigue failure of stents, and the in vivo conditions they are subjected to.

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