Design Validation of a Multi-Stage Gradually Deploying Stent

Dillon J. Despain

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Design Validation of a Multi-Stage Gradually Deploying Stent

Dillon J. Despain

A thesis submitted to the faculty of
Brigham Young University
in partial fulfillment of the requirements for the degree of
Master of Science

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ABSTRACT

Design Validation of a Multi-Stage Gradually Deploying Stent

Dillon J. Despain
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Master of Science

In-stent restenosis (ISR) induced by intimal hyperplasia is a common challenge to angioplasty, a common treatment for reopening narrowed vasculature via the use of rapidly deploying stents. High impact stresses from current stent deployment processes have been linked to intimal hyperplasia; thus, a stent that is gradually deployed over a longer period of time holds potential to mitigate these stresses. This work hypothesizes that resorbable polymeric links can be used as a triggering mechanism to enable repeatably controlled deployment of a compliant nitinol stent design with the eventual goal of reducing intimal hyperplasia. The aims of this work include the structured design process and design validation of such a stent.

A structured design process was used to develop a multi-stage, gradually deploying nitinol stent in which PDLG (DL-lactide/Glycolide copolymer) bioresorbable links constrained specific mechanical cells within the stent geometry, thus limiting initial deployment to an intermediate diameter and allowing for secondary gradual deployment as the PDLG degraded via a combination of bioresorption and creep. A finite element analysis was carried out to design the link geometry to hold the stent at an intermediate stage (90% of final diameter) upon initial deployment, and enable a gradual secondary deployment phase lasting several minutes. Prototypes were then manufactured and the design was validated in a flow chamber mimicking the conditions of human blood flow and temperature. Using a camera and image processing methods, the diameter increase of the stents was tracked over time to characterize the secondary gradual deployment process of the stents.

Results showed the links constrained the stents to an initial ~90% diameter upon initial deployment, followed by a gradual, secondary deployment with an average 63.2% rise time of 16.2 minutes. Creep was observed to be the primary driver of the gradual deployment, followed by subsequent bioresorption of the material. All prototypes exhibited gradual secondary deployment without any visible delamination of the bioresorbable links from the stent struts.

Based on these findings it can be concluded our hypothesis has been demonstrated, and that a feasible gradually deploying stent design has been mechanically validated, preparatory to pre-clinical studies of its efficacy. Prior to clinical application, future in vivo work is needed to compare actual ISR rates with this stent design to other commonly used stent designs in preclinical trials. In addition, further preclinical work is needed to compare ISR rates through several stent design parameters such as initial deployment diameter, gradual deployment rate, final deployment diameter, and stent sizes to give insights into the optimal stent design. We anticipate that this gradually expanding stent design could reduce in-stent restenosis and improve clinical outcomes.

Keywords: hyperplasia, stent, bioresorbable, PDLG, restenosis, angioplasty
ACKNOWLEDGEMENTS

I would like to recognize the amazing undergraduates Diego Leon, Allison Larsen, and Jemi Ong for their problem-solving and stellar attitudes they brought to this project. I also would like to acknowledge Corbion for sending us several samples of bioresorbable materials and Darrell Skousen for the baseline reference stent design. Finally, many thanks to my thesis committee chair, Dr. Anton Bowden for his engineering expertise and wise counsel. I would also like to thank the other members of my graduate committee, Dr. Brian Jensen and Dr. Scott Thomson for their time and assistance in reviewing the content of the thesis.

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1 INTRODUCTION

This thesis describes the structured design and design validation of a novel multi-stage gradually deploying stent. Specifically, a design was developed in which PDLG (an 85:15 ratio DL-lactide/Glycolide copolymer) bioresorbable links attached to a self-expanding nitinol stent to constrain the initial deployment to an intermediate diameter. This design allowed for gradual deployment to then occur as the bioresorbable PDLG links expanded due to material strength degradation and mechanical creep. Twelve prototypes were manufactured and tested in a flow chamber that mimicked human blood conditions. The time course of the gradual deployment of the stents was measured using quantitative videography and subsequently analyzed.

Chapter two presents a background on the physiology and causes of intimal hyperplasia as well as a literature review on current stent technologies used to address stent-induced intimal hyperplasia. Further, it details the design process used in selecting the final stent design used in this thesis.

Chapter three presents the main work of this thesis. It contains the method and validation of the multi-stage gradually deploying stent design, specifically bioresorbable material selection, finite element analysis, manufacture, and verification of twelve prototype stents in a blood-like flow chamber. Chapter three will be submitted as a paper to a peer-reviewed journal. The work done in Section 3.3.2 to analyze the degradation behavior of the bioresorbable
materials was done by a team of researchers under Dr. Anton Bowden prior to this work. The data was analyzed in this thesis to select the appropriate material and is relevant to the paper, therefore it was included. Co-authors include Diego Leon, Jemi Ong, Allison Larsen, and Anton E. Bowden.

Chapter four concludes this thesis and suggests future work and direction related to this research. In particular, it points towards the further testing of design parameters and verification in preclinical, in-vivo testing.
2 BACKGROUND

Coronary artery disease is the leading cause of death in the world, with over 8.14 million deaths annually [1]. Myocardial infarction, commonly known as a heart attack, is a symptom of coronary artery disease and frequently occurs due to a buildup and rupture of atherosclerotic plaque [2]. Percutaneous coronary intervention, also known as coronary angioplasty, is the most common medical procedure related to myocardial infarction prevention in which a stent is deployed to reopen the artery. Approximately 5 million procedures are performed annually [3]. Angioplasty is also used in other areas of the body in response to plaque-induced stenosis [4] [5].

2.1 Causes and Effects of Intimal Hyperplasia

While arthroscopy is proven to be a practical and effective method of fighting myocardial infarction, the complications and adverse effects of the procedure, mainly in-stent restenosis (ISR) induced by intimal hyperplasia, limit the use of this method. Intimal hyperplasia is the thickening of the blood vessel walls in response to vessel injury [6]. The walls of blood vessels are composed of three layers: intimal, medial, and adventitial. Smooth muscle cells are housed in the medial layer, patterned in longitudinal and circumferential orientations interlaced with collagen and elastic fibrils. The intimal layer, or intima, comprises the inner layer and is composed of a specialized extracellular matrix [7, 8]. The interaction between the smooth muscle cells and the matrix of the intima keeps the veins and arteries in a balanced state, with controlled
growth of the muscle cells. Molecules synthesized in the endothelial cells of the intima (i.e. heparin) inhibit the growth and migration of smooth muscle tissue [9, 10]. These endothelial cells are essential for the balance between smooth muscle propagation and inhibition, allowing the blood vessels to function effectively.

Injury to the intima and damage to the endothelial cells induces the production of various molecules which can degrade the extracellular matrix of the intima [11]. With the degraded intima matrix and the production of growth inhibitors from the endothelial cells reduced, smooth muscle tissues from the media grow and migrate into the intima and intrude on the blood vessel [12]. Along with the migration of smooth muscle cells, intimal hyperplasia signifies an increase in extracellular matrix after the initial smooth muscle tissue migration, with stable intimal volume being 20% muscle tissue and 80% extracellular matrix [13].

While the stent compacts the plaque buildup in the blood vessel, it causes fracturing and fissuring of the vessel wall. ISR can restrict the blood flow in the cardiac arteries by a 50% reduction in luminal diameter. Restenosis occurs in approximately 20% of patients who undergo angioplasty with a traditional metal stent, and a majority of these patients requires subsequent angioplasty procedures within 6 months [14, 15].

2.2 Current Stent Solutions for Intimal Hyperplasia

The two common types of stents are plastically deforming (e.g., stainless steel), and self-expanding (e.g., nitinol). For both types, the area of arterial stenosis is pre-dilated via balloon angioplasty, i.e. the surgeon rapidly deploys a small balloon, expanding the closed artery. For plastically deforming types, the stent is similarly deployed via balloon angioplasty and rigidly holds open the artery. For self-expanding types, a crimped stent is deployed by removing
an outer sheath and the stent deploys via the intrinsic hyper-elastic properties of the material. The deployment rate is rapid on the surrounding arterial walls. Current stent technologies developed to address restenosis rates caused by intimal hyperplasia include drug eluting stents, fully biodegradable stents, and variations in stent geometry.

Drug eluting stents have had a large effect (13-24% reduction) on ISR rates by releasing molecules that inhibit smooth muscle propagation [16]. Current medical practice recommends the use of drug eluting stents almost exclusively over bare metal stents [3]. However, drug eluting stents still have high rates of intimal hyperplasia and can lead to serious medical complications [17].

To reduce the negative effects and long-term pathobiological response of a metallic implant residing in the arteries, fully biodegradable polymeric stents have been developed. Most recently, Abbott Vascular developed and tested a device made from biodegradable poly-lactic acid. However, as they are not as strong as metallic stents, they require thicker geometry and are more susceptible to fractures. These negatives showed an increase in myocardial infarction and cardiac death and were discontinued [3]. Biodegradable metal stents, most commonly using Magnesium and Forum based alloys, are being developed to overcome the challenges of fully biodegradable polymeric stents. However, the main challenge with biodegradable metal stents is achieving heterogeneous corrosion of the stent geometry. Especially under the influence of intimal hyperplasia, it is difficult to control the uniform degradation of the stent, as areas of high stress experience a greater corrosion response [17]. Heterogeneous corrosion can allow breakage and release of portions of the stent into the vascular system.

Several geometric design factors affect stent thrombosis rates. Strut thickness has a negative effect on healing and leads to a higher risk of neointimal hyperplasia [18]. Though
thinner struts have a greater risk of fracture, the optimization of strut thickness to radial stent strength has contributed to the reduction of adverse responses. A stent design that has less obstruction to blood flow and hemodynamics results in a better pathobiological response [3].

Several studies have linked the medical complications categorized by intimal hyperplasia are linked to the stresses of the stent during its rapid deployment process. Timmons et al. performed an in vivo analysis that compared the pathobiological response of different stent designs that imposed different levels of stress on porcine arteries [19]. Similarly, Freeman et al. showed that oversizing the diameter of initial stent deployment significantly increased the total thickness and neointimal hyperplasia after 30 days in porcine models [20]. Another study showed a stress threshold for hyperplasia and demonstrated that strut geometry had a significant impact on intimal proliferation [21].

In addition to high initial stresses of stents, several studies suggest that prolonged, gradual inflation times for balloon angioplasty lead to better outcomes [22-25]. In particular, a few studies compared restenosis rates using a computerized, controlled balloon expansion versus standard rapid expansion, with a similar strategy of reducing trauma to the intima layer of the arteries caused by mechanical stress [26-28]. The patients who underwent angiography with the computerized, gradual balloon had a significantly lower rate of restenosis (greater than a 10% reduction). The effect was even greater in patients who also underwent stenting [26].

Though both initial stent stresses, as well as the rate of deployment, have an impact on the rates and severity of restenosis, no current known stent technology leverages a multi-stage, gradual stent deployment. Similar to computer-controlled gradual balloon angioplasty, a multi-stage, gradually deploying stent design could reduce the initial impact stress and then allow the
collagen and extracellular matrix cells to adapt and relax as the stent gradually opens the vessel walls over a prolonged course of time.

Thus, this aim of this thesis was to design, prototype, and mechanically validate such a stent that potentially reduces mechanical trauma to the intima by leveraging a multi-stage, gradual deployment process.

2.2.1 Design Exploration

The overall design ideology developed leverages a multi-stage approach in which the stent is rapidly deployed to an intermediate diameter upon initial release. This initial expansion provides adhesion of the stent to the occluded artery. After this initial rapid deployment, the stent would begin its gradual deployment to fully open the occluded artery and allow blood flow.

![Figure 2-1: Initial concept design regimes for the gradually deploying stent](image)
There were several concepts that were researched as possible solutions to the multi-stage deployment process desired for the stent. These ideas were generalized into three categories: mechanical attachments, external bands, and composite beams (Figure 2-1).

The principal characteristic of mechanical links was the unification of struts using bioresorbable material bonds. Each attachment method used the strength of the bioresorbable material to prevent parts of the stent from opening until properly dissolved into the blood stream.

External bands introduced the possibility a deployment regulator that could be implemented universally around the diameter of the stent. Upon deployment, it was designed to retain an intermediate-stage diameter of any given type of stent. The external bands would be synthesized out of a flexible bioresorbable polymer and secured about a semi-crimped stent and would enable a gradual deployment as each band degraded.

Composite beams incorporated the use of either metal deposition, a polymer coating, or a ceramic coating in order to increase the stiffness of the stent. The additional stiffness would reduce the radial force of the stent and prevent it from superseding the arterial resilience.
Analogous to the external bands, this concept enables a gradual deployment of the stent as the bioresorbable material is absorbed into the bloodstream, reducing the stiffness of the stent (Figure 2-2).

2.2.2 Final Design Selection

Four of the underlying concepts explored in Figure 2-1 were selected for final feasibility consideration: Design 1: geometric links that attached and constrained stent geometry mechanically; Design 2: extruded links that constrain certain regions of the stent geometry via extruding melted bioresorbable material; Design 3: external bands applied radially to constrain expansion; Design 4: a composite beam stent leveraging a polymer coating.

Table 2-1: Design methodology for the selection of the bioresorbable link design

<table>
<thead>
<tr>
<th>Design Requirements</th>
<th>Design 1</th>
<th>Design 2</th>
<th>Design 3</th>
<th>Design 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predictability of Stent Expansion</td>
<td>0</td>
<td>0</td>
<td>-</td>
<td></td>
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<tr>
<td>Variability</td>
<td>+</td>
<td>0</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Conservation of Stent Integrity</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Manufacturability</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
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<tr>
<td>Invasiveness</td>
<td>0</td>
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<tr>
<td>Sum +</td>
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<td>Sum -</td>
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</table>
A list of pragmatic design requirements was developed to select a final design: (1) predictability – the ability to adjust design geometry to adjust the expansion rate, (2) variability – the ease of controlling variability among samples, (3) conservation of stent integrity – how much the polymer application would impact the underlying stent shape and function, (4) manufacturability – the ease and time required to manufacture a sample, and (5) invasiveness – the extent the added polymer would affect the surrounding arterial wall. Each design was evaluated against these criteria with a +/- design evaluation matrix shown in Table 2-1. A “+” designation indicates a design that is more desirable than the reference design (in this case, the reference design is Design 1), a “-” designation indicates a design that is less desirable than the reference design, and a “0” designation indicates no difference between designs.

Design 2 (restriction of stent geometry by links applied via heated extrusion) was selected as having the most attractive design regime. This was the design that was analyzed, prototyped, and mechanically validated in this work. See Figure 3-2 for a final rendering of this design.
3 DESIGN VALIDATION OF A MULTI-STAGE GRADUALLY DEPLOYING STENT

3.1 Abstract

In-stent restenosis induced by intimal hyperplasia is a common problem with angioplasty in treating atherosclerotic plaque. High impact stresses from current stent deployment processes have been linked to intimal hyperplasia; and we hypothesize that the use of gradually deploying stent could mitigate these stresses. This work aims to design and validate such a gradually deploying stent with the eventual goal of reducing intimal hyperplasia. A design was developed for a multi-stage, gradually deploying stent in which PDLG (an 85:15 ratio DL-lactide/Glycolide copolymer) bioresorbable links constrained specific stent cells limiting initial deployment to an intermediate diameter, allowing for secondary gradual deployment as the PDLG degraded via a combination of bioresorption and creep. A finite element analysis was carried out to design the geometry of the links to hold the stent closed on initial deployment. The prototypes were then manufactured and validated in a flow chamber mimicking the conditions of human blood flow using a camera to analyze diameter increase. Results showed the links constrained the stents to an initial ~90% diameter upon initial deployment, followed by a gradual, secondary deployment with an average 63.2% rise time of 16.2 minutes. Creep appeared to be the primary driver of the gradual deployment, followed by subsequent bioresorption of the material. Based on these
findings it can be concluded that a gradually deploying stent design has been biomechanically validated, preparatory to pre-clinical studies of its efficacy.

3.2 Introduction

Coronary Artery Disease is the leading cause of death in the world, with over 8.14 million deaths annually [1]. Myocardial infarction, commonly known as a heart attack, is a symptom of coronary artery disease and frequently occurs due to a buildup and rupture of atherosclerotic plaque [2]. Percutaneous coronary intervention, also known as coronary angioplasty, is the most common medical procedure related to myocardial infarction prevention in which a stent is deployed to reopen the artery. Approximately 5 million procedures are performed annually [3]. Angioplasty is also used in other areas of the body in response to plaque induced stenosis [4, 5].

3.2.1 Causes and Effects of Intimal Hyperplasia

While angioplasty has been proven to be a practical and effective method of fighting myocardial infarction, the complications and adverse effects of the procedure, mainly in-stent restenosis (ISR) induced by intimal hyperplasia, limit the use of this method. Intimal hyperplasia is the thickening of the blood vessel walls in response to vessel injury [6].

The intimal layer of the blood vessel, or intima, comprises the inner layer and is composed of a specialized extracellular matrix [7, 8]. The interaction between the smooth muscle cells and the matrix of the intima keep the veins and arteries in a balanced state, with controlled growth of the muscle cells. Injury and damage to the intima cause smooth muscles cells to migrate along with an increase in extracellular matrix [12, 13].
When the stent compacts the plaque buildup in the blood vessel, it causes fracturing and fissuring of the vessel wall at variable depths. ISR can restrict the blood flow in the cardiac arteries by a 50% reduction in luminal diameter. Restenosis occurs in approximately 20% of patients who undergo angioplasty with a traditional metal stent, and a majority of these patients require subsequent angioplasty procedures within 6 months [14, 15].

Several studies have shown that medical complications categorized by intimal hyperplasia are linked to the stresses of the stent during its rapid deployment process. Timmons et al. performed an in vivo analysis that compared the pathobiological response of different stent designs that imposed different levels of initial stresses on porcine arteries. After 28 days inside porcine models, testing showed a significant correlation between the magnitude of stress-induced on the artery wall and the severity of neointimal hyperplasia [19]. Similarly, Freeman et al. showed that oversizing the diameter of initial stent deployment significantly increased the total thickness and intimal hyperplasia after 30 days in porcine models [20]. Another study identified a stress threshold for hyperplasia and found that strut geometry had a significant impact on intimal proliferation [21]. The majority of stent cases (>90%) are over expanded upon initial deployment [29, 30].

In addition to high initial stresses of stents, several studies suggest that prolonged, gradual inflation times for balloon angioplasty lead to better outcomes [22-25]. In particular, a few studies compared restenosis results using a computerized, controlled balloon expansion versus standard rapid expansion, with a similar strategy of reducing trauma to the intima layer of the arteries caused by mechanical stress [26-28]. The patients who underwent angiography with the computerized, gradual balloon had a significantly lower rate of restenosis (greater than a 10% reduction). The effect was even greater in patients in stenting procedures [26].
Both stent deployment forces, as well as their rate of application have a significant impact on the rates and severity of intimal hyperplasia. We hypothesize that by controlling the deployment rate of the stent, excessive injury to the intima could be avoided, and in-stent restenosis rates reduced.

Thus, the purpose of the present work was preclinical design, prototyping, and design validation testing of a stent that reduces initial stresses by leveraging a gradual deployment process. Specifically, this work demonstrates a novel stent is feasible with the following design requirements: (1) have a rapid deployment to contact the arterial wall, (2) exhibit a secondary gradual deployment, and (3) deploy in a timescale feasible for patients and doctors.

3.3 Methods

3.3.1 Gradual Deployment Mechanism Design

The overall design ideology developed leveraged a multi-stage approach in which the stent would be rapidly deployed to an intermediate diameter upon initial implantation in the artery. The design was such that this intermediate diameter would provide enough contact with the artery upon initial deployment as to prevent stent migration yet minimize initial deployment force. After this rapid initial deployment, the stent would begin its secondary, gradual deployment to its final diameter until it fully opened the occluded artery.

The super-elastic (fully recoverable deformation to 9% strain) and shape memory properties as well as the biocompatibility of nitinol made it an ideal material for the gradually deployable stent, with bioresorbable links limiting initial deployment. Nitinol stents are commonly used due to their super-elastic properties and biocompatibility [31]. After initial
Implantation in the artery, the super-elastic properties would cause a constant pressure on the bioresorbable links. This would prolong mechanical deployment by leveraging a time-dependent degradation in material stiffness and strength due to bioresorption or mechanical creep.

The nitinol stent design used in this study was a custom stent based on previous work in our lab [32], but the deployment mechanism for the gradually deployable stent is largely agnostic to underlying stent design. The cell pattern for our specific design was an open-closed pattern using brides between open cells. This pattern allows the stent to maintain its shape and for complex motion such as twisting and bending. The bridges are slightly thinner than the struts and provide an extra degree of motion when the stent undergoes a twisting transformation (Figure 3-1). The pattern allows sections to be closed and held, limiting the diameter upon initial deployment of the stent. The physical prototype stents were made out of laser cut nitinol (Admedes, Inc., Pforzheim, Germany). A stent outer diameter of 12mm was selected, a typical diameter size used in peripheral angioplasty.

Figure 3-1: Geometry definitions of the stent design (left) and a 12mm laser cut nitinol stent used in this study (right)
Figure 3-2 shows a rendering of the final concept design for the gradually deployable stent design. Bioresorbable links are applied via extrusion across the bridges of the closed stent cells, with the entire stent remaining closed until implantation in the artery. Upon initial deployment, the links constrain the stent to an initial diameter large enough to create coercion with the atrial wall but to reduce initial impact. As the strength of the bioresorbable links degrades, the stent cells begin to gradually open until the stent reaches its final diameter to fully reopen the narrowed artery. The links are eventually fully absorbed into the bloodstream over a larger timescale, leaving the bare nitinol stent as a permanent implant.

Figure 3-2: The stent before deployment with the bioresorbable links shown across the bridges (left), after initial deployment constrained to an intermediate diameter by the links (center), and the final diameter after gradual, secondary deployment due to the strength degradation of the bioresorbable links (right)

3.3.2 Bioresorbable Material Selection

The first material requirement was that the bioresorbable material be safely absorbed into the bloodstream (i.e. nontoxic) and degrade gradually. Second, the material needed sufficient
strength to hold the stent struts closed before initial deployment in the artery. Third, the material needed to adhere well to the nitinol stent, as lack of adherence is a risk for embolism either during initial deployment or after gradual degradation. Finally, the timeline of degradation needed to be a balance between an infinite deployment time and a finite time frame that coincided with surgical expediency (e.g., minutes to hours) and recovery time. The deployment was designed to be short enough that the surgeon could verify radiographically that the stent was fully deployed, well-situated, and stable before releasing the patient to return home, ideally before the patient left the operating room.

Three candidate biocompatible polymers were tested in this study to find the degradation of the Ultimate Strength: PLA (polylactic acid), PDLG 8531 (85:15 ratio DL-lactide/Glycolide copolymer), and PDLLA (poly D,L-lactic acid) from Corbion, Inc., Amsterdam, Netherlands. These polymers are currently used for medical applications, including drug delivery, due to their degradation properties and safety when used in the human body [33-35].

Tensile test samples were created by melting the polymer samples into sheets approximately 1 mm thick. The sheets were then cut using a laser cutter into dog-bone shapes. The dog bones had a designed cross section of 1mm x 2mm, with the working area being 3.73mm long. The samples were numbered randomly, and the cross-sectional dimensions were measured before incubation. In order to match the Reynolds number of the flow system with that of blood in the coronary artery, a SeaFlow aquatic pump (Model SFDP1-012-035-21) was used to induce a flow of approximately 0.8 L/min throughout the system. The Reynolds number of the coronary artery has a normal range of about 120 to 1500 [36]. Due to the complexity of the trays, evaluating the flow rate was calculated using the thickness of a single dogbone for the critical length, \( x \), in the Equation 3-1.
\[ R_e = \frac{ux}{v} \]

(3-1)

This resulted in a range of 0.7-8.8 L/min. The flow rate throughout the system was reduced to approximately 0.8 L/min to minimize turbulence.

Samples were removed periodically for tensile testing. The tensile testing was performed on a tensile tester outfitted with an incubator that allowed the samples to be pulled in solution and at temperature (Figure 3-3).

Figure 3-3: Dog-bone sample holding fixture and tray (top). The flow system consisted of four tanks connected in series to a circulation pump and filled with Earle's Balanced Salt Solution (bottom left) and tensile testing apparatus (bottom right).
Testing started from day 0 (samples which were not placed in the incubator) to day 59, with test frequency biased towards the beginning of testing. Before testing, samples had their cross-sectional dimensions measured to track swelling of the polymers. Samples were pulled at 1mm/min, except for the final three tests of PDLG, which were pulled at 10mm/min due to the high amount of strain needed to reach the ultimate tensile strength. The ultimate tensile strength was calculated using the cross section measured immediately prior to testing and the largest force measured on the tensile testing machine. Young’s modulus was found using the cross section measured before testing and using 3.73mm as the original length. Each test was comprised of six samples per polymer.

Figure 3-4: Tensile strength and modulus degradation of PLA, PDLLA, and PDLGA over time
The PDLG was selected as the preferred candidate for the multi-stage stent gradual deployment mechanism. After 3-6 days, both the tensile strength and elastic modulus degraded substantially, reaching close to zero (Figure 3-4). At this stage, the samples were extremely elastic, but it is important to note that there were no breakages that would cause a potential embolism in the artery or hinder the deployment of the stent. Both the PLA and the PDLLA had no significant changes in modulus or strength following 59 days in the incubator, indicating that degradation rates of these materials was infeasible for a gradually deploying stent.

3.3.3 Finite Element Analysis

An FEA was used as an initial design tool to appropriately size the PDLG link geometry, specifically the cross-sectional area, to be sufficient in preventing plastic deformation caused by initial deployment forces from the stent. The simulations were done using ANSYS Mechanical APDL (see Appendix A for MAPDL script).

Due to the repeating pattern of the stent, a half cylinder geometry with one and half cells of the baseline nitinol design was used with symmetry conditions on the top, bottom, and along the transverse plane of the model. Steady state, static simulations were used. Nitinol’s material and super-elastic properties were simulated similar to other FEA analyses done with nitinol [37-39], but using the super-elastic material capabilities available with ANSYS MAPDL. This simulation used 625 and 645MPa for the austenite to martensite phase transition with 345 and 325MPa for the martensite to austenite phase transformation. The PDLG link material properties were an elastic modulus of 1.6GPa and a Poisson’s ratio of 0.35.

A first simulation was done to obtain the compressed stent geometry and determine the forces required to hold the closed cells together. The stent geometry was meshed with 11,398
SOLID185 elements. A series of linear actuator elements (LINK11 elements) were attached to the outside of each bridge on the closed cells of the stents. Actuator elements allow for an input displacement and the output of resultant forces. A total of six actuator elements were used and displaced to bring the bridges of the closed cells together. Due to the large deflection required to compress the stent, nonlinear geometry settings were used. The resultant forces in actuator elements (16.5N per each compressed stent cell) and compressed stent geometry were then extracted.

A second simulation was done to determine maximum stresses in the links due to the opening of the stent. The compressed geometry of the stent was imported and meshed (11398 SOLID185 elements). The geometry of the bioresorbable links was imported, meshed (151718 SOLID185 elements), and coincident nodes merged to the nitinol stent mesh. Finally, the extracted actuator forces were reversed and reapplied to the stent bridges, such that the closed cells applied the opening force against the PDLG link mesh (Figure 3-5).

Several link geometries were iterated to determine the appropriate dimensions to be used in the prototypes. The final selected cross section of the PDLG link design was 1.5x1.6mm (cross sectional area of 2.72 mm²) per link. This resulted in a max Von Mises stress on a single link of 5.7 MPa, with the max stress at the center of the links, between the bridges of the closed cell. The length of the link past the edges of the bridges did not change the stress, as the max stress occurred along the center plane of the cross section, interior to the bridges. The yield stress of PDLG in body-like conditions is approximately 20-30MPa [40]. The cross-sectional area of the links was selected to result in a factor of safety of 3-4 while attempting to minimize the external invasiveness of the links on the stent.
Figure 3-5: Stent FEA. (a) Mesh of uncompressed stent geometry. (b) Compressed stent with stresses without links. (c) Mesh of links attached to mesh of compressed stent. (d) Stent stresses reversed and constrained by links.

3.3.4 Manufacturing Process

The raw PDLG flakes were processed into 1.75mm filament cartridges using a heated aluminum mold at 175°C (Figure 3-6). The volume of the cartridges (16mm³) was designed to be relatively close to the volume of one link segment (13.2mm³). A system was designed to close the desired stent struts together, align a mold around the closed section, and inject the PDLG cartridges into the mold to form the links around the nitinol. A laser cutter was used to cut two 15x50mm mold halves out of acrylic and then engrave a 3x1.5mm rectangle to a 1.6mm depth. The cross-sectional area of the links between the bridges (1.5x1.6mm) were made to match the
dimensions simulated in the FEA, however, the ends of the links were rounded to reduce the total volume of PDLG material required.

Figure 3-6: Raw PDLG flakes and PDLG filament cartridges

Figure 3-7: Stent manufacturing system. (a) Metal segments design used to compress the closed cells around the bridges. (b) Acrylic mold halves aligned on either side of the bridges. (c) Laser-cut acrylic molds and metal alignment segments. (d) Mold system on a nitinol prototype.
Two thin metal segments were created to hold the bridges together to compress the closed cell. This aligned the two acrylic mold halves around the bridges to extrude the PDLG links into place (Figure 3-7). A 3D printing extruder (MYNT3D) was used to extrude the PDLG around the bridges of the closed cell. The mold and metal segments were removed after cooling. The PDLG was extruded at 215°C. A total of twelve prototypes were created, each with six PDLG links (Fig. 8).

Figure 3-8: Creation of prototypes. (a) Extruder used to melt PDLG onto stent. (b) Extruding the PDLG into mold system. (c) Single PDLG link. (d) Finished PDLG stent prototype with six links.
3.3.5 Gradual Deployment Characterization

To validate the secondary, gradual deployment characteristics of the prototype stents in a similar environment to the bloodstream, an experimental flow system was created simulating conditions of a typical coronary artery [41]. The Reynolds number of a coronary artery is in a normal range of about 120 to 1500 [36]. Earle’s Balanced Salt Solution (EBSS) was used as the fluid and kept at 37°C with a temperature sensor/heater system (Inkbird ITC-308 Digital Temperature Controller, Hamilton Beach 22 Quart Roaster Oven). The flow rate was monitored with a digital flow meter. A flow rate of 2.0 L/min was used that resulted in a Reynolds number of 380 around the stent (see Equation 3-2).

\[
Re_{stent} = \frac{(\rho_{EBSS} \times velocity_{EBSS} \times D_{stent})}{\mu_{EBSS}}
\]  

(3-2)

Where, \(Velocity_{EBSS} = \frac{Flow\ Rate_{EBSS}}{Flow\ Area_{EBSS}}\)

This Reynolds number calculation used a EBSS density of 1002 kg/m³, EBSS dynamic viscosity of 7.028e-4 Pa-s, flow rate of 2.0 L/min, an area of EBSS flow of 0.0015 m², and a characteristic length of 12 mm. The characteristic length \((D_{stent})\) was approximated by using the fully expanded diameter of the stent.

The flow cell was designed to hold four prototype stents per trial and were fixed parallel to the flow of the EBSS with no external resistance on stent deployment (Figure 3-10). The stent holding fixture was designed so the stents could be rapidly lowered into the EBSS. Image capture began immediately after submersion.
Figure 3-9: Verification system
A machine vision camera (Basler Scout) was used to take images of the stent prototypes every two minutes until full deployment. The images were processed in MATLAB (Mathworks, Inc.) using a binarize grayscale filter with a 0.8 cutoff threshold. The average diameter across the stent was then found using a custom boundary detection method (see Appendix B). This was done for the four stents per each image (Figure 3-11).
3.4 Results

3.4.1 Initial Deployment Behavior

Before placement in the flow system, the nitinol prototypes were allowed to sit for over 24 hours at the intermediate stage (see Figure 3-2) in air at room temperature. For all 12 prototype stents, the PDLG links showed no deformation or creep but held the selected stent cells at the intermediate diameter verifying that the initial stent forces were below the yield stress of PDLG links. In addition, the stents were then placed in an air-temperature controlled room at 37°C for several hours. None of the prototypes showed any creep or expansion. The average intermediate diameter of the stents was 10.9mm (std. dev. of 0.216mm), or 91.2% of the final deployment diameter (12mm).

3.4.2 Secondary, Gradual Deployment Behavior

For all 12 prototypes, secondary, gradual deployment of the stent began immediately following placement in the EBSS until the final diameter was reached (Figure 3-12). The expansion of the stent occurred due to the gradual stretching of the links at their center, between the bridges of the closed cells. Each of the twelve stent prototypes followed a secondary, gradual deployment. The gradual stretching of the links occurred between the bridges of the closed cells. The links remained coherent and attached to the nitinol stent throughout the duration of the testing period (24 hours), without any visible loss of large PDLG particles into the EBSS flow or readily observable changes to the EBSS.
Figure 3-12: Photographs of stent after rapid initial deployment and placement into the flow cell (top) and after secondary, gradual deployment (bottom). Note: the end of the top right link is deformed but remains attached to the stent.

To adjust for differences in initial diameter of the 12 stent prototypes, the expansions were normalized with the method described in Equation 3-3. An exponential model was then fit to the data with a least-squares optimization (see Figure 3-13 and Equation 3-4). The expansion data of each prototype was linearly interpolated between the two-minute intervals for rise time calculations. The prototypes had an average 63.2% rise time of 15.34 minutes and an average time to 97% expansion of 51.21 minutes. See Table 3-1 for results from each individual trial.

\[
\text{Normalized Expansion} = \frac{\text{diameter} - \min (\text{diameter})}{\max (\text{diameter}) - \min (\text{diameter})}
\]  

\[
N = -e^{-0.0670t (\text{min})} + 1.0
\]  

Where \( N \) = normalized expansion
Table 3-1: Deployment statistics for individual stent prototypes

<table>
<thead>
<tr>
<th>Stent Prototype</th>
<th>Time to 97% Expansion (min)</th>
<th>63.2% Rise Time (min)</th>
<th>R2 Fit to Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30.77</td>
<td>12.25</td>
<td>0.92</td>
</tr>
<tr>
<td>2</td>
<td>79.51</td>
<td>28.63</td>
<td>0.75</td>
</tr>
<tr>
<td>3</td>
<td>51.24</td>
<td>9.96</td>
<td>0.93</td>
</tr>
<tr>
<td>4</td>
<td>28.05</td>
<td>12.45</td>
<td>0.92</td>
</tr>
<tr>
<td>5</td>
<td>62.17</td>
<td>13.17</td>
<td>0.95</td>
</tr>
<tr>
<td>6</td>
<td>36.06</td>
<td>9.71</td>
<td>0.90</td>
</tr>
<tr>
<td>7</td>
<td>63.68</td>
<td>26.01</td>
<td>0.80</td>
</tr>
<tr>
<td>8</td>
<td>57.96</td>
<td>15.62</td>
<td>0.99</td>
</tr>
<tr>
<td>9</td>
<td>43.28</td>
<td>19.54</td>
<td>0.95</td>
</tr>
<tr>
<td>10</td>
<td>40.14</td>
<td>7.68</td>
<td>0.79</td>
</tr>
<tr>
<td>11</td>
<td>51.59</td>
<td>5.85</td>
<td>0.75</td>
</tr>
<tr>
<td>12</td>
<td>70.02</td>
<td>23.27</td>
<td>0.82</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td><strong>51.21</strong></td>
<td><strong>15.34</strong></td>
<td></td>
</tr>
<tr>
<td><strong>STD. Deviation</strong></td>
<td><strong>16.08</strong></td>
<td><strong>7.40</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Fit Model</strong></td>
<td><strong>52.37</strong></td>
<td><strong>14.93</strong></td>
<td></td>
</tr>
</tbody>
</table>
3.5 Discussion

The gradual deployment of the stents was triggered by a combination of hydration in the EBSS medium and the temperature of 37°C. The time to 97% stent deployment was an average of 51.21 minutes while material testing indicated that significant tensile strength degradation occurred after a few days. This indicates that the constant force from the closed cell bridges on the PDLG links created a gradual creep strain triggered by a combination of hydration in the EBSS and the high temperature of 37°C, rather than by tensile strength degradation. This is consistent with previously reported work by Bartkowiak-Jowsa et al., who compared the strength degradation and creep of PDLG under similar fluid (pH and temperature) and load (15% vs 19% of ultimate tensile strength) conditions. Their research showed that strength degradation in PDLG occurred after several days [40], similar to the strength testing results from the present
work. In contrast, their testing of PDLG showed a rapid creep strain rate under constant loading, reaching similar strains in less than 60 minutes. Other researchers have also confirmed high creep rates in PDLG at human blood temperature [42, 43]. Consequently, the mechanism of secondary, gradual deployment of the prototype multi-stage stents designed in this study is primarily driven through creep strain in the PDLG links triggered by submersion in EBSS at 37°C. This design study did not aim to have any specific deployment timeline other than to keep the timeline within a reasonable post-surgical observation time window but was intended to validate the design as a feasible method for a gradually deploying angioplasty stent design. With respect to this goal, the timeline for deployment was deemed successful and ready for future preclinical study.

There are several limitations to the present work. First, the present work consists solely of design and design validation testing, which was performed ex vivo, and did not measure or compare actual ISR rates. While the ex vivo validation in this work was done to simulate blood conditions, in vivo preclinical testing will need to be completed and remains a topic for future work. Second, the results from the present work are strictly limited to a single size (12 mm diameter) stent. While it is anticipated that a scaled version of the multi-stage, gradually deploying stent would function similarly at other sizes, this has not yet been validated, and some optimization of link geometry would likely be required to balance creep expansion effects with mechanical property degradation due to material resorption. We anticipate that smaller stents with the same number of links would likely have longer gradual expansion rates due to lower stresses, while larger stents would deploy more quickly.

In summary, in contrast to all known current stent designs which exhibit a virtually instantaneous deployment and deformation on the vessel wall, the deployment of the designed,
multi-stage, gradually deploying stent presented here occurs on an extended timescale, dramatically reducing the rate of force application on the intima. It is hypothesized that this change may reduce intimal hyperplasia due to stent damage of the intima. This hypothesis will be tested through future investigations in our laboratory.
4 CONCLUSION AND FUTURE WORK

This thesis outlines the design, testing, and verification of a multi-stage, gradually deployable stent and demonstrates this design is biomechanically feasible. The prototype stents analyzed showed an instantaneous initial deployment constrained to an intermediate diameter by bioresorbable PDLG links. Gradual deployment then occurred until the stents reached their final deployment diameter. We anticipate that this stent design could be a potential solution to reducing ISR rates and improving clinical outcomes.

Future work is needed to perform a longer-term material degradation test on the PDLG links after gradual deployment. The stents in this work were removed from the simulated blood flow after reaching a steady-state diameter. In theory, after the secondary expansion the PDLG links would be removed due to material degradation and reabsorption into the bloodstream, eventually leaving the bare nitinol stent as a permanent implant. To verify the modes of material failure in the PDLG, and confirm that total, gradual resorption of the PDLG links does not lead to delamination from the underlying stent, the stents need to be analyzed until the PDLG is fully absorbed and removed from the stent. Premature delamination of large PDLG particles from the base nitinol stent could have negative consequences such as the risk of potential embolism.

Another limitation of this work is that design testing was performed ex vivo. Though experimentation simulated conditions within the human vasculature, in vivo experimentation is required to quantify stent biomechanical behavior such as stent integrity and deployment.
behavior within real biological systems and blood flow. The stents studied ex vivo were allowed to expand freely without the external resistance of the arterial wall, which could have a significant effect on expansion behavior. Any differences in deployment behavior would need to be characterized and resolved. In addition, this work did not quantify actual reductions in intimal hyperplasia or in-stent restenosis behavior within an actual blood vessel, as the scope of this work was merely to design and validate a multi-stage gradually deploying stent. Future work will be needed to deploy this stent design, in comparison to other commonly used stent designs, in preclinical trials to characterize physiological blood vessel response differences and any reduction in intimal hyperplasia.

Further research is needed to optimize several stent design parameters not yet considered. This work validated only a single stent diameter and length. Specifically, quantification of ISR rates through several stent design parameters such as initial deployment diameter, final deployment diameter, and differing stent lengths will give insights into the optimal stent parameters. In vivo work is needed to quantify the initial diameter needed to adhere fully to the embolism, while reducing initial impact stress, as well as the optimal final stent diameter needed to reduce in-stent restenosis but fully open the occluded artery. While the design used in this study proved that gradual stent deployment triggered by the body is feasible, the optimal rate of this gradual deployment in the body has not been determined. The rate of deployment of this design occurred within tens of minutes, however, longer expansion times may be necessary to reduce intimal hyperplasia. Conversely, shorter times may be sufficient in reducing ISR, yet allow for more practical use by physicians. The rate may be adjusted with actual geometry changes to the PDLG links, or through changes in material properties, such as polymer ratios or
different bioplastics. Additionally, the underlying metal stent geometry such as cell spacing, structure, pattern, thickness, etc., could be adjusted resulting in different physiological responses.

Finally, a more effectively controlled manufacturing process will need to be developed. This would include more precise control of PDLG extrusion temperature, cooling time, and PDLG link dimensions. This would reduce variation across gradually deploying stent prototypes and allow for a more effective adjustment of deployment parameters.

In conclusion, in contrast to all other known stent designs that target the negative effects of intimal hyperplasia induced ISR, this thesis proposes a novel design solution to this problem through a multi-stage gradually deploying stent. The results of this work show that such a stent design is biomechanically feasible and ready for validation in preclinical testing.
REFERENCES


APPENDICES

This section includes all of the appendices for this work. Appendix A includes all of the coding script used in ANSYS Mechanical APDL to compress the stent, extract forces, attach the link mesh, and re-expand the combined meshes. Appendix B contains the MATLAB code used to parse the image, run image processing, and extract stent diameter from the captured images.
APPENDIX A. ANSYS MECHANICAL APDL SCRIPT

!!! Compress Link !!!

!! Preprocessor Commands
/CLEAR
/BATCH
! /COM,ANSYS RELEASE 13.0 UP20101012 21:42:02 06/07/2014
/CWD,'C:\Users\Dillon\OneDrive\Stent\FEA'
/PREP7

!! Set Element Types
ET,1,SOLID185
ET,2,LINK11
R,1,1E9,0,0,
~PARAIN,'Multistage_10_double_side_12','x_t',,SOLIDS,0,0
/NOPR
/GO
*SET,SCALE,3.6363636

!! Material Properties
MPTEMP,,,,,,
MPTEMP,1,0
MPDATA,EX,1,,40.8E9
MPDATA,PRXY,1,,.3
TB,SMA,1,1,6,
TBTEMP,0
TBDATA,,625E6,645E6,345E6,325E6,.04,1
!! Define Linear Actuator Elements
K,1671,0,-.002*SCALE,.001566*SCALE
K,1672,0,-.002*SCALE,-.001566*SCALE
K,1673,0,.000694*SCALE,.001566*SCALE
K,1674,0,.000694*SCALE,-.001566*SCALE
lstr,1668,1666
lstr,747,752
lstr,759,1673
lstr,764,1674
lstr,1660,1671
lstr,1662,1672

!! Mesh
ESIZE,.000045*SCALE,0,
LESIZE,2330, , ,2, , , ,1
VSWEEP,1
FLST,5,6,4,ORDE,2
FITEM,5,2506
FITEM,5,-2511
CM,_Y,LINE
LSEL, , , ,P51X
CM,_Y1,LINE
CMSEL,S,_Y
CMSEL,S,_Y1
LATT,1,1,2,,
CMSEL,S,_Y
CMDELE,_Y
CMDELE,_Y1
FLST,5,6,4,ORDE,2
FITEM,5,2506
FITEM,5,-2511
CM,_Y,LINE
LSEL,,P51X
CM,_Y1,LINE
CMSEL,,_Y
LESIZE,_Y1,.0018*SCALE,,1
ALLSEL,ALL
FLST,2,6,4,ORDE,2
FITEM,2,2506
FITEM,2,-2511
LMESH,P51X
ALLSEL,ALL

!! Constraints
FLST,4,19,1,ORDE,16
FITEM,4,3443
FITEM,4,-3444
FITEM,4,4449
FITEM,4,-4450
FITEM,4,4453
FITEM,4,-4454
FITEM,4,8083
FITEM,4,8084
FITEM,4,8087
FITEM,4,8088
FITEM,4,8091
FITEM,4,-8092
FITEM,4,8095
FITEM,4,-8097
FITEM,4,10105
FITEM,4,-10108
CP,1,UY,P51X
FINISH
/SOL

DA,828,UX,
DA,829,UX,
DA,830,UX,
DA,833,UX,
DA,832,UX,
DA,831,UX,
DL,439, ,UZ,
DL,73, ,UZ,
DL,1753, ,UZ,
DA,834,UY,
DA,835,UY,
DL,1541, ,UY,
DL,2162, ,UY,

FLST,2,4,1,ORDE,2
FITEM,2,14502
FITEM,2,-14505
D,P51X, , , ,UX, , , ,

nsubst,20, , ,1
NLGEOM,ON

!! Displacements
! *SET,DD,-750E-6*SCALE
*SET,DD,-750E-6*SCALE
*SET,DD1,DD*.25
SFE,5693,1,PRES,,DD1,,
SFE,5694,1,PRES,,DD1,,
SFE,5695,1,PRES,,DD1/2,,
SFE,5696,1,PRES,,DD1/2,,
SFE,5697,1,PRES,,DD1/2,,
SFE,5698,1,PRES,,DD1/2,,
LSWRITE,1,

*SET,DD1,DD*.5
SFE,5693,1,PRES,,DD1,,
SFE,5694,1,PRES,,DD1,,
SFE,5695,1,PRES,,DD1/2,,
SFE,5696,1,PRES,,DD1/2,,
SFE,5697,1,PRES,,DD1/2,,
SFE,5698,1,PRES,,DD1/2,,
LSWRITE,2,

*SET,DD1,DD*1
SFE,5693,1,PRES,,DD1,,
SFE,5694,1,PRES,,DD1,,
SFE,5695,1,PRES,,DD1/2,,
SFE,5696,1,PRES,,DD1/2,,
SFE,5697,1,PRES,,DD1/2,,
SFE,5698,1,PRES,,DD1/2,,
LSWRITE,3,
!! Solve
LSSOLVE,1,3,1

!!! Post Forces in Actuator Elements !!!

!! Find Actuator Element Forces
/POST1
ESEL,S,ENAME,,LINK11
NSLE
ETAB,FORCE,SMISC,1
PRET,FORCE

!! Find Actuator Element Strokes
/POST1
ESEL,S,ENAME,,LINK11
NSLE
ETAB,STROKE,NMISC,3
PRET,STROKE

!! Outputs
! 3.3 MM STENT
PRINT ELEMENT TABLE ITEMS PER ELEMENT

***** POST1 ELEMENT TABLE LISTING *****

<table>
<thead>
<tr>
<th>STAT</th>
<th>CURRENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>ELEM</td>
<td>FORCE</td>
</tr>
<tr>
<td>5617</td>
<td>-0.66068</td>
</tr>
<tr>
<td>5618</td>
<td>-1.2806</td>
</tr>
</tbody>
</table>
5619  -1.3686
5620  -1.3834
5621  -0.70751
5622  -0.70802

MINIMUM VALUES
ELEM  5620
VALUE  -1.3834

MAXIMUM VALUES
ELEM  5617
VALUE  -0.66068

! 12 MM STENT
PRINT ELEMENT TABLE ITEMS PER ELEMENT

***** POST1 ELEMENT TABLE LISTING *****

STAT  CURRENT
ELEM  FORCE
5693  8.6612
5694  16.214
5695  16.560
5696  16.846
5697  8.5912
5698  8.4057

MINIMUM VALUES
ELEM  5698
VALUE  8.4057
MAXIMUM VALUES

ELEM    5696
VALUE   16.846

!!! Import and Mesh Link Geometry !!!

/CLEAR

/CWD,'C:\Users\Dillon\OneDrive\Stent\FEA'
~PARAIN,'links','x_t',"\SOLID MODELS\",SOLIDS,0,0

/PREP7
ET,1,SOLID185

*SET,SCALE,3.6363636

!! Material Properties
MPTEMP,,,,,,
MPTEMP,1,0
MPDATA,EX,1,,1.6E9
MPDATA,PRXY,1,,.35

!! Mesh
ESIZE,.000045*SCALE,0,

CM_,Y,LINE
LSEL, , ,P51X
CM_,Y1,LINE
CMSEL,,_Y
!*
LESIZE,_Y1,,1,1,1,1
!* 
MSHAPE,1,3D
MSHKEY,0
!* 
FLST,5,6,6,ORDE,2
FITEM,5,1
FITEM,5,-6
CM,_Y,VOLU
VSEL,,P51X
CM,_Y1,VOLU
CHKMSH,'VOLU'
CMSEL,S,_Y
!* 
VMESH,_Y1
!* 
CMDELE,_Y
CMDELE,_Y1
CMDELE,_Y2
!* 

FINISH
/SOL
FLST,2,4,5,ORDE,4 
FITEM,2,1161
FITEM,2,1379
FITEM,2,1638
FITEM,2,2082
!* 
/GO
DA,P51X,UX,0
FINISH

!/PREP7
!CDWRITE,DB,'CDB FILES/links','cdb','",""

!!! Merge Links to Stent !!!

clear
/CWD,'C:\Users\Dillon\OneDrive\Stent\FEA'

/INPUT,'links','cdb','C:\Users\Dillon\OneDrive\Stent\FEA\CDB FILES',, 0
/INPUT,'DB_deformed12','cdb','C:\Users\Dillon\OneDrive\Stent\FEA\CDB FILES',, 0
eplot

/PREP7
NUMMRG, NODE, 1.0E-8

EDELE, 5693
EDELE, 5694
EDELE, 5695
EDELE, 5696
EDELE, 5697
EDELE, 5698

!! FORCES
*SET,F5693,-8.6612
*SET,F5694,-16.214
*SET,F5695,-16.560
*SET,F5696,-16.846
*SET,F5697,-8.5912
*SET,F5698,-8.4057

! 5693
FLST,2,1,1,ORDE,1
FITEM,2,4459
!*
/GO
F,P51X,FZ,-F5693

FLST,2,1,1,ORDE,1
FITEM,2,4460
!*
/GO
F,P51X,FZ,F5693

! 5694
FLST,2,1,1,ORDE,1
FITEM,2,3580
!*
/GO
F,P51X,FZ,-F5694

FLST,2,1,1,ORDE,1
!!! Expand Stent !!!

!! FORCES
*SET,F5693,-8.6612
*SET,F5694,-16.214
*SET,F5695,-16.560
*SET,F5696,-16.846
*SET,F5697,-8.5912
*SET,F5698,-8.4057
! 5693
FLST,2,1,1,ORDE,1
FITEM,2,4459
!*
/GO
F,P51X,FZ,-F5693

FLST,2,1,1,ORDE,1
FITEM,2,4460
!*
/GO
F,P51X,FZ,F5693

! 5694
FLST,2,1,1,ORDE,1
FITEM,2,3580
!*
/GO
F,P51X,FZ,-F5694

FLST,2,1,1,ORDE,1
FITEM,2,3557
!*
/GO
F,P51X,FZ,F5694

! 5695
FLST,2,1,1,ORDE,1
FITEM,2,3542
!*  
/GO
F,P51X,FX,-F5695

! 5696
FLST,2,1,1,ORDE,1
FITEM,2,3535
!*  
/GO
F,P51X,FX,-F5696

! 5697
FLST,2,1,1,ORDE,1
FITEM,2,4449
!*  
/GO
F,P51X,FX,-F5697

! 5698
FLST,2,1,1,ORDE,1
FITEM,2,4454
!*  
/GO
F,P51X,FX,-F5698
/SOL
SOLVE
!!! Final Plots !!!

/POST1
!esel,s,,,5698,87002
esel,s,,,30693,43440

cm, myelem,elem

cmsel,s,myelem,elem

plnsol,s,eqv

/triad,off

/VIEW,1,,1
/ANG,1
/ANG,1,-30,ZS,1
/ANG,1,-30,ZS,1
/ANG,1,-30,ZS,1

/POST1
nsel,s,,,20759
nsel,a,,,20764
nsel,a,,,20765
nsel,a,,,20779

PRNSOL,S,PRIN
%% Master File %%%

clc;
clear;

numFiles = 51;

image_analysis_4;
image_analysis_5;
image_analysis_6;
image_analysis_7;
image_analysis_8;
image_analysis_9;

smooth_data;

flatten_arrays;

normalize_array;

data_fit;

plot_all;

%% Trials 1-4 %%%

% Specify the folder where the files live.
myFolder = 'C:\Users\Dillon\Desktop\Stent Images\trial4';

% Check to make sure that folder actually exists. Warn user if it doesn't.
if ~isfolder(myFolder)
    errorMessage = sprintf('Error: The following folder does not exist:
    
    uiwait(warndlg(errorMessage));
    return;
end
% Get a list of all files in the folder with the desired file name pattern.
filePattern = fullfile(myFolder, '*.tiff');
theFiles = dir(filePattern);

% initialize image processing bounds
ybounds = 394:600;

x_start = 110;
x_width = 40;
x_dist = 330;

xbounds = [x_start:x_start+x_width;
x_start+x_dist+60:x_start+x_dist+x_width+60;
x_start+x_dist*2-30:x_start+x_dist*2+x_width-30;
x_start+x_dist*3+60:x_start+x_dist*3+x_width+60];

% initialize arrays
time_array = zeros(numFiles,1);
time = 0;
avg_stent_diameter_array = zeros(numFiles,4);
v_array = zeros(4,4);

for k = 1 : 1: numFiles
    % parse through images in folder
    baseFileName = theFiles(k).name;
    fullFileName = fullfile(myFolder, baseFileName);
    fprintf(1, 'Now reading %s\n', fullFileName);

    I = imread(fullFileName);

% binarize the image
BW = imbinarize(I,0.80);

time_array(k) = time;
time = time + 2;

for m = 1 : 4
    % find average diameter across xbounds
    [avg_stent_diameter,v] = find_stent_diameter(BW,xbounds(m,:),ybounds);
    v_array(:,m) = v;
    avg_stent_diameter_array(k,m) = avg_stent_diameter;
end

% for display
imshow(BW);
plot_capture_box(avg_stent_diameter_array(k,1),xbounds(1,:),ybounds,v_array(:,1),'g')
plot_capture_box(avg_stent_diameter_array(k,2),xbounds(2,:),ybounds,v_array(:,2),'r')
plot_capture_box(avg_stent_diameter_array(k,3),xbounds(3,:),ybounds,v_array(:,3),'b')
plot_capture_box(avg_stent_diameter_array(k,4),xbounds(4,:),ybounds,v_array(:,4),'m')

drawnow;
%     pause
end

array.array_1 = avg_stent_diameter_array(:,1);
array.array_2 = avg_stent_diameter_array(:,2);
array.array_3 = avg_stent_diameter_array(:,3);
array.array_4 = avg_stent_diameter_array(:,4);
t.time_array1 = time_array;
t.time_array2 = time_array;
t.time_array3 = time_array;
t.time_array4 = time_array;

%% Trials 5-6 %%%

% Specify the folder where the files live.
myFolder = 'C:\Users\Dillon\Desktop\Stent Images\trial5';

% Check to make sure that folder actually exists. Warn user if it doesn't.
if ~isfolder(myFolder)
    errorMessage = sprintf('Error: The following folder does not exist:
    %s', myFolder);
    uiwait(warndlg(errorMessage));
    return;
end

% Get a list of all files in the folder with the desired file name pattern.
filePattern = fullfile(myFolder, '*.tiff');
theFiles = dir(filePattern);

% initialize image processing bounds
ybounds = 394:600;

x_start = 110;
x_width = 50;
x_dist = 330;
xbounds = [65:65+x_width; 1080:1080+x_width];

% initialize arrays
time_array = zeros(numFiles,1);
time = 0;
avg_stent_diameter_array = zeros(numFiles,2);
v_array = zeros(4,2);

for k = 1 : 1: numFiles
    % parse through images in folder
    baseFileName = theFiles(k).name;
    fullFileName = fullfile(myFolder, baseFileName);
    fprintf(1, 'Now reading %s
', fullFileName);

    I = imread(fullFileName);

    % binarize the image
    BW = imbinarize(I,0.80);

    time_array(k) = time;
    time = time + 2;

    for m = 1 : 2
        % find average diameter across xbounds
        [avg_stent_diameter,v] = find_stent_diameter(BW,xbounds(m,:),ybounds);

        v_array(:,m) = v;
        avg_stent_diameter_array(k,m) = avg_stent_diameter;
    end
end
imshow(BW);
plot_capture_box(avg_stent_diameter_array(k,1),xbounds(1,:),ybounds,v_array(:,1),'g')
plot_capture_box(avg_stent_diameter_array(k,2),xbounds(2,:),ybounds,v_array(:,2),'r')

drawnow;
%
pause
end

array.array_5 = avg_stent_diameter_array(:,1);
array.array_6 = avg_stent_diameter_array(:,2);

t.time_array5 = time_array;
t.time_array6 = time_array;

%%% Trial 7 %%%%

% Specify the folder where the files live.
myFolder = 'C:\Users\Dillon\Desktop\Stent Images\trial6';

% Check to make sure that folder actually exists.  Warn user if it doesn't.
if ~isfolder(myFolder)
    errorMessage = sprintf('Error: The following folder does not exist:
%s', myFolder);
    uiwait(warndlg(errorMessage));
    return;
end

% Get a list of all files in the folder with the desired file name pattern.
filePattern = fullfile(myFolder, '*tiff');
theFiles = dir(filePattern);

% initialize image processing bounds
ybounds = 394:600;

x_start = 90;
x_width = 40;
x_dist = 330;

xbounds = [x_start:x_start+x_width];

% initialize arrays
time_array = zeros(numFiles,1);
time = 0;
avg_stent_diameter_array = zeros(numFiles,4);
v_array = zeros(4,1);

for k = 1 : 1: numFiles
   % parse through images in folder
   baseFileName = theFiles(k).name;
   fullFileName = fullfile(myFolder, baseFileName);
   fprintf(1, 'Now reading %s\n', fullFileName);

   I = imread(fullFileName);

   % binarize the image
   BW = imbinarize(I,0.80);

   time_array(k) = time;
time = time + 2;

for m = 1 : 1
    % find average diameter across xbounds
    [avg_stent_diameter,v] = find_stent_diameter(BW,xbounds(m,:),ybounds);

    v_array(:,m) = v;
    avg_stent_diameter_array(k,m) = avg_stent_diamter;
end

% for display
imshow(BW);
plot_capture_box(avg_stent_diameter_array(k,1),xbounds(1,:),ybounds,v_array(:,1),'g')

drawnow;
%    pause
end

array.array_17 = avg_stent_diameter_array(:,1);

t.time_array7 = time_array;

%%% Trials 8-9 %%%

% Specify the folder where the files live.
myFolder = 'C:\Users\Dillon\Desktop\Stent Images\trial7';

% Check to make sure that folder actually exists. Warn user if it doesn't.
if ~isfolder(myFolder)
errorMessage = sprintf('Error: The following folder does not exist:
%s', myFolder);
uiwait(warndlg(errorMessage));
return;
end

% Get a list of all files in the folder with the desired file name pattern.
filePattern = fullfile(myFolder, '*.tiff');
theFiles = dir(filePattern);

% initialize image processing bounds
ybounds = 394:600;

x_start = 110;
X_width = 40;
x_dist = 330;

xbounds = [x_start+x_dist+90:x_start+x_dist+90+x_width;
x_start+x_dist*2:x_start+x_dist*2+x_width];

% initialize arrays
time_array = zeros(numFiles,1);
time = 0;
avg_stent_diameter_array = zeros(numFiles,4);
v_array = zeros(4,2);

for k = 1 : 1: numFiles
    % parse through images in folder
    baseFileName = theFiles(k).name;
    fullFileName = fullfile(myFolder, baseFileName);
    fprintf(1, 'Now reading %s\n', fullFileName);
I = imread(fullFileName);

% binarize the image
BW = imbinarize(I,0.80);

time_array(k) = time;
time = time + 2;

for m = 1 : 2
    % find average diameter across xbounds
    [avg_stent_diameter,v] = find_stent_diameter(BW,xbounds(m,:),ybounds);

    v_array(:,m) = v;
    avg_stent_diameter_array(k,m) = avg_stent_diameter;
end

% for display
imshow(BW);
plot_capture_box(avg_stent_diameter_array(k,1),xbounds(1,:),ybounds,v_array(:,1),'g')
plot_capture_box(avg_stent_diameter_array(k,2),xbounds(2,:),ybounds,v_array(:,2),'r')
drawnow;
% pause
end

array.array_8 = avg_stent_diameter_array(:,1);
array.array_9 = avg_stent_diameter_array(:,2);

t.time_array8 = time_array;
t.time_array9 = time_array;

%% Trials 10-11 %%%

% Specify the folder where the files live.
myFolder = 'C:\Users\Dillon\Desktop\Stent Images\trial8';

% Check to make sure that folder actually exists. Warn user if it doesn't.
if ~isfolder(myFolder)
    errorMessage = sprintf('Error: The following folder does not exist:
%s', myFolder);
    uiwait(warndlg(errorMessage));
    return;
end

% Get a list of all files in the folder with the desired file name pattern.
filePattern = fullfile(myFolder, '*.tiff');
theFiles = dir(filePattern);

% initialize image processing bounds
ybounds = 394:600;

x_start = 110;
x_width = 40;
x_dist = 330;

xbounds = [x_start+x_dist-50:x_start+x_dist-50+x_width;
             x_start+x_dist*2-60:x_start+x_dist*2+x_width-60];

% initialize arrays
time_array = zeros(numFiles,1);
time = 0;

avg_stent_diameter_array = zeros(numFiles,4);
v_array = zeros(4,2);

for k = 1 : 1: numFiles
    % parse through images in folder
    baseFileName = theFiles(k).name;
    fullFileName = fullfile(myFolder, baseFileName);
    fprintf(1, 'Now reading %s
', fullFileName);

    I = imread(fullFileName);

    % binarize the image
    BW = imbinarize(I,0.80);

    time_array(k) = time;
    time = time + 2;

    for m = 1 : 2
        % find average diamter across xbounds
        [avg_stent_diameter,v] = find_stent_diameter(BW,xbounds(m,:),ybounds);

        v_array(:,m) = v;
        avg_stent_diameter_array(k,m) = avg_stent_diameter;
    end

end

% for display
imshow(BW);
plot_capture_box(avg_stent_diameter_array(k,1),xbounds(1,:),ybounds,v_array(:,1),'g')
plot_capture_box(avg_stent_diameter_array(k,2),xbounds(2,:),ybounds,v_array(:,2),'r')

drawnow;

array.array_10 = avg_stent_diameter_array(:,1);
array.array_11 = avg_stent_diameter_array(:,2);
array.array_11(40:end) = array.array_11(40);

array.array_10 = avg_stent_diameter_array(:,1);
array.array_11 = avg_stent_diameter_array(:,2);
array.array_11(40:end) = array.array_11(40);

t.time_array10 = time_array;
t.time_array11 = time_array;

%% Trial 12 %%%

% Specify the folder where the files live.
myFolder = 'C:\Users\Dillon\Desktop\Stent Images\trial9';

% Check to make sure that folder actually exists. Warn user if it doesn't.
if ~isfolder(myFolder)
    errorMessage = sprintf('Error: The following folder does not exist:
    \n%s', myFolder);
    uiwait(warndlg(errorMessage));
    return;
end

% Get a list of all files in the folder with the desired file name pattern.
filePattern = fullfile(myFolder, '*.tiff');
theFiles = dir(filePattern);

% initialize image processing bounds
ybounds = 394:600;
x_start = 160;
x_width = 40;
x_dist = 330;

xbounds = [x_start+x_dist*2:x_start+x_dist*2+x_width];

% initialize arrays
time_array = zeros(numFiles,1);
time = 0;
avg_stent_diameter_array = zeros(numFiles,4);
v_array = zeros(4,1);

for k = 1 : 1: numFiles
    % parse through images in folder
    baseFileName = theFiles(k).name;
    fullFileName = fullfile(myFolder, baseFileName);
    fprintf(1, 'Now reading %s
', fullFileName);

    I = imread(fullFileName);

    % binarize the image
    BW = imbinarize(I,0.80);

    time_array(k) = time;
    time = time + 2;

    for m = 1 : 1
        % find average diameter across xbounds
        [avg_stent_diameter,v] = find_stent_diameter(BW,xbounds(m,:),ybounds);
    end
end
v_array(:,m) = v;
avg_stent_diameter_array(k,m) = avg_stent_diameter;
end

% for display
imshow(BW);
plot_capture_box(avg_stent_diameter_array(k,1),xbounds(1,:),ybounds,v_array(:,1),'g')
drawnow;
% pause
end

array.array_12 = avg_stent_diameter_array(:,1);
t.time_array12 = time_array;

%% Extract Stent Diameter %%

function [avg_stent_diameter,v] = find_stent_diameter(BW,xbounds,ybounds)
stent_diameter_array = zeros(size(xbounds,2),1);
v = zeros(4,1);

for j = xbounds
    vector = BW(ybounds,j);

    v1 = find(~vector, 1,'first');
    v2 = find(~vector, 1,'last');
if j == xbounds(1)
    v(1:2) = [v1,v2];
elseif j == xbounds(end)
    v(3:4) = [v1,v2];
end

stent_diameter_pixel = v2-v1;
stent_diameter_array(j+1-xbounds(1)) = stent_diameter_pixel;
end

avg_stent_diameter = mean(stent_diameter_array);
end

%% Plot Capture Box %%

fn_a = fieldnames(array);
fn_t = fieldnames(t);

%% Initial Stent Diameter
initial_diameter = zeros(12,1);
for i=1:12
    diameter_array = percent_diameter(array_flat.(fn_a));
    initial_diameter(i) = diameter_array(1);
end
mean_initial_diameter = mean(initial_diameter)

%% Rise Times
normalized_array = zeros(12,1);
time_97 = zeros(12,1);
time_constant = zeros(12,1);
for i=1:12

    normalized_array = array_normalize.(fn_a{i});
    time_array = t.(fn_t{i});

    n_97 = find(normalized_array > .97, 1);
    n_tau = find(normalized_array > .632, 1);

    time_97(i) = time_array(n_97);
    time_constant(i) = time_array(n_tau);
end

mean_time_97 = mean(time_97)
std_time_97 = std(time_97)

mean_time_constant = mean(time_constant)
std_time_constant = std(time_constant)

% Fit Data Parameters
n_97_fit = find(datafit > .97, 1);
n_tau_fit = find(datafit > .632, 1);

time_97_fit = time_array(n_97_fit)
time_constant_fit = time_array(n_tau_fit)

%% Force Curve ANSYS

x = [750e-6,650e-6,550e-6,450e-6,350e-6,250e-6,150e-6,50e-6,50e-7];
x_norm = normalize(x);
y_force = [16.2,15.0,13.7,12.1,10.2,7.8,4.8,1.7,.16];
y_stress = [0.26795E+008,0.24827E+008,0.22799E+008,0.19783E+008,0.16566E+008,0.12672E+008,0.78407E+007,0.26890E+007,0.27271E+006]/(1e6)*(5.7e6/.26795e8);

fun = @(b,time) b(1)*exp(b(2)*time) + b(3);

x0 = [1,1,0];
x1 = [10,10,10];

[b_force,residual] = lsqcurvefit(fun,x0,x_norm,y_force);
b_stress = lsqcurvefit(fun,x1,x_norm,y_stress);

forcefit = fun(b_force,x_norm)';
stressfit = fun(b_stress,x_norm)';

fig = figure(1);
left_color = [0 0 0];
right_color = [0 0 0];
set(fig,'defaultAxesColorOrder',[left_color; right_color]);

yyaxis left
plot(x_norm,y_force,'b')
hold on
% plot(x_norm,forcefit,'k')
xlabel('Percent expansion (%)')
ylabel('Stent opening force (N)')

yyaxis right
% plot(x_norm,y_stress,'r')
% hold on
% plot(x_norm,stressfit,'g')
xlabel('Percent expansion (%)')
ylabel('Link stress (MPa)')
ylim([0 6.35])

A = (1.6/1000)*(1.7/1000)
F = 16.2;

S = F/A

function norm_array = normalize(array)

    norm_array = (array - max(array))./((array(end))-max(array));
end

%%% Smooth Data %%%%
%% Initial Stent Diameter
initial_diameter = zeros(12,1);
for i=1:12
    diameter_array = percent_diameter(array_flat.(fn_a{i}));
    initial_diameter(i) = diameter_array(1);
end

mean_initial_diameter = mean(initial_diameter)
std_initial_diameter = std(initial_diameter)

%% Rise Times
normalized_array = zeros(12,1);
time_97 = zeros(12,1);
time_constant = zeros(12,1);
for i=1:12
    normalized_array = array_normalize.(fn_a{i});
    time_array = t.(fn_t{i});
    time_array_inter = 0:.01:100;
    normalized_array_inter = interp1(time_array,normalized_array,time_array_inter);
    n_97 = find(normalized_array_inter > .97, 1);
    n_tau = find(normalized_array_inter > .632, 1);
    time_97(i) = time_array_inter(n_97);
    time_constant(i) = time_array_inter(n_tau);
end

mean_time_97 = mean(time_97)
std_time_97 = std(time_97)

mean_time_constant = mean(time_constant)
std_time_constant = std(time_constant)

% Fit Data Parameters

datafit_inter = interp1(time_array,datafit,time_array_inter);
n_97_fit = find(datafit_inter > .97, 1);
n_tau_fit = find(datafit_inter > .632, 1);

time_97_fit = time_array_inter(n_97_fit)
time_constant_fit = time_array_inter(n_tau_fit)

%% Force Curve ANSYS

x = [750e-6,650e-6,550e-6,450e-6,350e-6,250e-6,150e-6,50e-6,50e-7];
x_norm = normalize(x);
y_force = [16.2,15.0,13.7,12.1,10.2,7.8,4.8,1.7,.16];
y_stress = [0.26795E+008,0.24827E+008,0.22799E+008,0.19783E+008,0.16566E+008,0.12672E+008,0.78407E+007,0.26890E+007,0.27271E+006]/(1e6)*(5.7e6/.26795e8);

fun = @(b,time) b(1)*exp(b(2)*time) + b(3);

x0 = [1,1,0];
x1 = [10,10,10];

[b_force,residual] = lsqcurvefit(fun,x0,x_norm,y_force);
[b_stress,residual] = lsqcurvefit(fun,x1,x_norm,y_stress);

forcefit = fun(b_force,x_norm)';
stressfit = fun(b_stress,x_norm)';

fig = figure(1);
left_color = [0 0 0];
right_color = [0 0 0];
set(fig,'defaultAxesColorOrder',[left_color; right_color]);

yyaxis left
plot(x_norm,y_force,'b')
% hold on
% plot(x_norm,forcefit,'k')
xlabel('Percent expansion (%)')
ylabel('Stent opening force (N)')

yyaxis right
% plot(x_norm,y_stress,'r')
% hold on
% plot(x_norm,stressfit,'g')
xlabel('Percent expansion (%)')
ylabel('Link stress (MPa)')
ylim([0 6.35])

A = (1.6/1000)*(1.7/1000)
F = 16.2;

S = F/A
function norm_array = normalize(array)

    norm_array = (array - max(array))./((array(end))-max(array));
end

%% Trim Arrays %%%

array_flat = array_smooth;

fn_a = fieldnames(array_flat);
fn_t = fieldnames(t);

for i = 1:12
    %     plot(t.(fn_t{i}),array_smooth.(fn_a{i}));

    temp_array = array_smooth.(fn_a{i});

    temp_array_diff = diff(temp_array);
    n = find(abs(temp_array_diff) < .01, 1);

    %     pause(0.3);

    temp_array_flat = temp_array;
    if(~isempty(n) && i~=11)
        temp_array_flat(n(1):end) = temp_array(n(1));
    end

    array_flat.(fn_a{i}) = temp_array_flat;
```matlab
% plot(t.(fn_t{i}),temp_array_flat);
% pause(0.3);
end

%%% Normalize Expansion %%%

array_normalize = array;

fn_a = fieldnames(array);

for i = 1:12

    array_normalize.(fn_a{i}) = normalize(array_flat.(fn_a{i}));

end

function norm_array = normalize(array)

    norm_array = (array - min(array))./((array(end))-min(array));
end

%%% Fit Model Curves %%%

fun = @(b,time) b(1)*exp(b(2)*time) + b(3);
fn_a = fieldnames(array_normalize);
fn_t = fieldnames(t);
```
%% Fit for Each Trial
array_fit = array;

b_single = zeros(12,3);
Rsq_single = zeros(12,1);

for i=1:12
    data = array_normalize.(fn_a{i});
    time = t.(fn_t{i});
    x0 = [-1,-1,0];

    [b_single(i,:),residual] = lsqcurvefit(fun,x0,time,data);

    datafit = fun(b_single(i,:),time);

    SStot = sum((data-mean(data)).^2);    % Total Sum-Of-Squares
    SSres = sum((data(:)-datafit(:)).^2); % Residual Sum-Of-Squares
    Rsq_single(i) = 1-SSres/SStot;               % R^2

    array_fit.(fn_a{i}) = datafit;
end

%% Fit for All Trial
Rsq_tot = zeros(12,1);
data = zeros(10,51);
time = zeros(10,51);
for i=1:12
    data(i,:) = array_normalize.(fn_a{i});
    time(i,:) = t.(fn_t{i});
end

x0 = [-1,-1,0];

[b_sum,residual] = lsqcurvefit(fun,x0,time,data);

datafit = fun(b_sum,time(1,:))';

for i=1:12
    data_i = data(i,:);
    SSStot = sum((data_i-mean(data_i)).^2);    % Total Sum-Of-Squares
    SSSres = sum((data_i(:)-datafit(:)).^2); % Residual Sum-Of-Squares
    Rsq_tot(i) = 1-SSres/SSStot;               % R^2
end

%%% Plot All Trials and Model %%%

figure(21)
fn_a = fieldnames(array);
fn_t = fieldnames(t);

LineType = '.-';
MarkerSizeDot = 12;
MarkerSizeTri = 4;
colormap = [0 0.4470 0.7410
 0.8500 0.3250 0.0980
 0.9290 0.6940 0.1250
 0.4940 0.1840 0.5560
 0.4660 0.6740 0.1880
 0.3010 0.7450 0.9330];

colororder(colormap)

plot(t.(fn_t{1}),array_normalize.(fn_a{1}),'.-','MarkerSize',MarkerSize);
hold on
plot(t.(fn_t{2}),array_normalize.(fn_a{2}),'.-','MarkerSize',MarkerSize);
plot(t.(fn_t{3}),array_normalize.(fn_a{3}),'.-','MarkerSize',MarkerSize);
plot(t.(fn_t{4}),array_normalize.(fn_a{4}),'.-','MarkerSize',MarkerSize);
plot(t.(fn_t{5}),array_normalize.(fn_a{5}),'.-','MarkerSize',MarkerSize);
plot(t.(fn_t{6}),array_normalize.(fn_a{6}),'.-','MarkerSize',MarkerSize);
plot(t.(fn_t{7}),array_normalize.(fn_a{7}),'^-','MarkerSize',MarkerSizeTri,'MarkerFaceColor',colormap(1,:));
plot(t.(fn_t{8}),array_normalize.(fn_a{8}),'^-','MarkerSize',MarkerSizeTri,'MarkerFaceColor',colormap(2,:));
plot(t.(fn_t{9}),array_normalize.(fn_a{9}),'^-','MarkerSize',MarkerSizeTri,'MarkerFaceColor',colormap(3,:));
plot(t.(fn_t{10}),array_normalize.(fn_a{10}),'^-','MarkerSize',MarkerSizeTri,'MarkerFaceColor',colormap(4,:));
plot(t.(fn_t{11}),array_normalize.(fn_a{11}),'^-','MarkerSize',MarkerSizeTri,'MarkerFaceColor',colormap(5,:));
plot(t.(fn_t{12}),array_normalize.(fn_a{12}),'^-','MarkerSize',MarkerSizeTri,'MarkerFaceColor',colormap(6,:));

plot(time(1,:),datafit,'r-','LineWidth',3.0)
xlabel('Time (minutes)')
ylabel('Percent expansion (%)')
ylim([0 1.1])
xlim([0 100])
% grid on

legend('Trial 1','Trial 2','Trial 3','Trial 4','Trial 5','Trial 6','Trial 7', ...
'Trial 8','Trial 9','Trial 10','Trial 11','Trial 12','Fit model')

%% Compute Trial Statistics %%%

fn_a = fieldnames(array);
fn_t = fieldnames(t);

%% Initial Stent Diameter
initial_diameter = zeros(12,1);
for i=1:12

diameter_array = percent_diameter(array_flat.(fn_a{i}));
initial_diameter(i) = diameter_array(1);
end

mean_initial_diameter = mean(initial_diameter)

%% Rise Times
normalized_array = zeros(12,1);
time_97 = zeros(12,1);
time_constant = zeros(12,1);
for i=1:12

    normalized_array = array_normalize.(fn_a{i});
time_array = t.(fn_t{i});

    n_97 = find(normalized_array > .97, 1);
n_tau = find(normalized_array > .632, 1);

    time_97(i) = time_array(n_97);
time_constant(i) = time_array(n_tau);
end

mean_time_97 = mean(time_97)
std_time_97 = std(time_97)

mean_time_constant = mean(time_constant)
std_time_constant = std(time_constant)

% Fit Data Parameters
n_97_fit = find(datafit > .97, 1);
n_tau_fit = find(datafit > .632, 1);

time_97_fit = time_array(n_97_fit)
time_constant_fit = time_array(n_tau_fit)

%% Force Curve ANSYS
x = [750e-6,650e-6,550e-6,450e-6,350e-6,250e-6,150e-6,50e-6,50e-7];
x_norm = normalize(x);
y_force = [16.2,15.0,13.7,12.1,10.2,7.8,4.8,1.7,.16];
y_stress = [0.26795E+008,0.24827E+008,0.22799E+008,0.19783E+008,0.16566E+008,0.12672E+008,0.78407E+007,0.26890E+007,0.27271E+006]/(1e6)*(5.7e6/.26795e8);

fun = @(b,time) b(1)*exp(b(2)*time) + b(3);

x0 = [1,1,0];
x1 = [10,10,10];

[b_force,residual] = lsqcurvefit(fun,x0,x_norm,y_force);
[b_stress,residual] = lsqcurvefit(fun,x1,x_norm,y_stress);

forcefit = fun(b_force,x_norm)';
stressfit = fun(b_stress,x_norm)';

fig = figure(1);
left_color = [0 0 0];
right_color = [0 0 0];
set(fig,'defaultAxesColorOrder',[left_color, right_color]);

yyaxis left
plot(x_norm,y_force,'b')
% hold on
% plot(x_norm,forcefit,'k')
xlabel('Percent expansion (%)')
ylabel('Stent opening force (N)')

yyaxis right
% plot(x_norm,y_stress,'r')
% hold on
% plot(x_norm,stressfit,'g')
xlabel('Percent expansion (%)')
ylabel('Link stress (MPa)')
ylim([0 6.35])

A = (1.6/1000)*(1.7/1000)
F = 16.2;

S = F/A

function norm_array = normalize(array)

    norm_array = (array - max(array))./((array(end))-max(array));
end