A CONTINUUM MECHANICS MODEL FOR THE ARTERIAL WALL GROWTH AND REMODELING UNDER HYPERTENSION

A Dissertation

by

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ABSTRACT

Hypertension is a chronic disease that one has higher blood pressure than normal. Since it is highly related to cardiovascular diseases, which is the culprit of death over the world, it is important to study hypertension, and it has been treated as an important topic for several decades.

In this study, we formulate nonlinear elasticity equations in the current configuration to model an idealized arterial wall under hypertension, using two material models. Under the conjectures that nature tries to adjust the circumferential stress arising from hypertension by growth and remodeling, we illustrate the growth and remodeling reduce the elevated circumferential stress and see the outcome of controlling the stress.

We made a conclusion that in order to have the preferred circumferential hoop stress, which is the circumferential hoop stress at the normal blood pressure, remodeling and growth are both needed.

DEDICATION

To my family members, who always love and believe in me.

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TABLE OF CONTENTS

Page

ABSTRACT ii

DEDICATION iii

ACKNOWLEDGMENTS iv

TABLE OF CONTENTS v

LIST OF FIGURES vii

LIST OF TABLES viii

1. INTRODUCTION 1

    1.1 Histology of Arteries [5, 6, 7, 8, 9] 2
    1.2 Literature Review 3
    1.3 Thesis Outline 4
    1.4 Purpose and Goal 5

2. MECHANICS : ELASTICITY 7

    2.1 Kinematics and Kenetics 7
    2.2 Constitutive Relation 7
        2.2.1 Incompressible Neo-Hookean Model 8
        2.2.2 Incompressible Holzapfel-Ogden Model 8
    2.3 Residual Stress 10
    2.4 Semi-inverse Approach 12
        2.4.1 Elasticity in the Current Configuration 14
    2.5 Manage Stress : Growth and Remodeling 16

3. BALANCE OF LINEAR MOMENTUM 17

4. NUMERICAL EXPERIMENT 20

    4.1 Result using Neo-Hookean Model 20
        4.1.1 Growth 23
        4.1.2 Remodeling : Change Opening Angle 25
        4.1.3 Both Growth and Remodeling 25
    4.2 Result using Holzapfel-Ogden Model 27
        4.2.1 Growth 28

4.2.2 Remodeling : Change Opening Angle 30
4.2.3 Both Growth and Remodeling 31

5. CONCLUDING REMARK 34

5.1 Summary of the experiments 34
5.2 Future Work 35
5.2.1 Future work for more directly related to this dissertation 35
5.2.2 Requirement/Request for the Ultimate Future work 35

REFERENCES 37

APPENDIX A. DETAILS OF COMPUTATIONS 42

A.1 Derivative of a tensoral valued function 42
A.2 Gradient of the vector valued function in the cylindrical coordinates 42
A.3 Solve the equation (2.9) 43

LIST OF FIGURES

FIGURE Page

2.1 Diagram of Cross Section of the Arterial Wall 12

4.1 Hoop stress vs. radius at the intermediate configuration using Neo-Hookean Model . 21

4.2 Hoop stress vs. radius when pressure 0 and 0.06 using Neo-Hookean Model 22

4.3 Hoop stress vs. radius when pressure 0, 0.06, 0.075, 0.09, and 0.12 using Neo-Hookean Model 22

4.4 Hoop stress vs. radius when growth happens at the inner wall, by 0%, 5%, 10% using Neo-Hookean Model 24

4.5 Hoop stress vs. radius when growth happens at both the inner and outer wall, by 0%, 5%, 10% using Neo-Hookean Model 24

4.6 Hoop stress vs. radius as opening angle varying with fixed pressure and area using Neo-Hookean Model 26

4.7 How much angle changes for each pressure and increased area using Neo-Hookean Model 26

4.8 Hoop stress vs. radius when pressure 0, 0.25, 0.3125, 0.375, and 0.5 using Holzapfel-Ogden Model 28

4.9 Hoop stress vs. radius when growth happens at the inner wall using Holzapfel-Ogden Model 29

4.10 Hoop stress vs. radius when growth happens both the inner and outer wall using Holzapfel-Ogden Model 30

4.11 Hoop stress vs. radius as opening angle varying with fixed pressure and area using Holzapfel-Ogden Model 31

4.12 How much angle changes for each pressure and increased area using Holzapfel-Ogden Model 32

LIST OF TABLES

TABLE Page

4.1 Triplet (Pressure, Area, Opening Angle) having target hoop stress using Neo-Hookean Model 27

4.2 Triplet (Pressure, Area, Opening Angle) having target hoop stress using Holzapfel-Ogden Model 33

1. INTRODUCTION

Hypertension is a chronic disease that one has higher blood pressure than normal blood pressure. There are several standards to diagnose hypertension depending on organizations or countries. In 2017, the American College of Cardiology (ACC) and the American Heart Association (AHA) released new guidelines for hypertension; having systolic and diastolic blood pressure above 130/80 mmHg is stage 1 hypertension, above 140/90mmHg is stage 2 hypertension, and above 180/120 mmHg is hypertensive crisis. Previously, they define hypertension if systolic and diastolic pressure is above 140/90 mmHg. European and Korean Organizations still define hypertension as having systolic/diastolic blood pressure greater than 140/90 mmHg.

Hypertension is a common public health problem. According to AHA, it is estimated that over 100 million Americans have hypertension. This is not a problem only of the American or Western countries. Many Asian countries have developed hypertension problems as well. For example, South Korea has 49.2% prevalence of hypertension if it applies the AHA/ACC guideline [1], which is nearly half of the adults in Korea, [2] .

While many people underestimate the importance of hypertension in the sense that hypertension does not have severe symptoms for some cases, it is highly important to study hypertension since it increases the incidence and the risk of cardiovascular diseases. It is well known that many cardiovascular diseases are affected by elevated blood pressure [3]. High blood pressure raises the mortality rate of cardiovascular diseases such as aneurysms, strokes, and heart attacks. Moreover, those cardiovascular diseases are leading causes of death over the world [4].

Therefore, studying hypertension is an important subject that may benefit plenty of people as well as is associated with the most dangerous diseases. In my dissertation, I intend to provide a mathematical model about the growth and remodeling of the artery due to hypertension.

1.1 Histology of Arteries [5, 6, 7, 8, 9]

There are roughly two types of arteries: elastic and muscular arteries. Elastic arteries are usually located near the heart so that it may take blood from the heart directly and have a comparatively large diameter. For example, the aorta and the pulmonary artery are elastic arteries. Muscular arteries are positioned closer to the arteriole, which means it is far away from the heart, and it has a relatively smaller diameter. The radial arteries and femoral arteries are examples of muscular arteries.

Both types of arteries have three layers: the intima, the media, and the adventitia. The intima, which is the innermost layer of the artery, consists of the endothelial cells, the basal lamina, and the subendothelial layer. Endothelial cells play a role in regulating the transport of substance between the arterial wall and the lumen, which means the internal space of the tubular structure in biology. The basal lamina, which is composed of collagen type IV, supports the structure, and the subendothelial layer has layers comprised of smooth muscle cells, collagen, and elastin. The middle layer is called the media. Components of the media are also smooth muscle cells, collagen fibrils, and elastin. While the intima is structurally similar regardless of types of arteries, the media of the elastic artery has different structures from those of the muscular artery. In the elastic artery, the media has several sublayers. The basic unit is made up of one layer of an elastic lamina, smooth muscle cells, and the second layer of elastic lamina. Over this unit, there is another unit, and collagen fibers are embedded between those units. However, there is a single thicker smooth muscle cell layer between the internal elastic lamina and the external elastic lamina in the muscular artery. The smooth muscle cells in the media align helix-like but almost circumferential, so they help to sustain circumferential loads. The volume of media is about 80 percent of the arterial wall, which is the thickest among these layers. Lastly, the outermost layer is called the adventitia, the components of which are collagen (mostly type I), elastin, nerves, fibroblasts, and vasa vasorum, which feed the wall of the artery. Its boundary is obscure but smoothly attached to its outside tissues. The adventitia of an elastic artery takes about 10 percent of the whole artery wall, and muscular arteries have a bit thicker adventitia layer than what elastic arteries have.

1.2 Literature Review

Mechanobiology is the study of a biological process arising from mechanical stimuli. Many researchers investigate the growth and remodeling of biological tissues in the sense of mechanobiology [10, 11, 5, 12, 13, 14, 15, 9, 16, 17, 18, 19, 20]. Plant growth, bone growth, remodeling of heart and tumor all these subjects are involved in mechanobiology. This project, which focuses on how much the arterial wall gets thicker and/or changeable in response to high blood pressure, is also one example of mechanobiology.

Among those topics, let me introduce some studies which are more closely related to the arterial wall.

Residual stress is a stress when the body does not have external loads. It has been studied for decades experimentally [21] and theoretically [22, 23], whereas it is sometimes disregarded for setting a model due to difficulty and ignorance of computing residual stress. Fung [21] showed the existence of residual stress by cutting a thin slice of arterial wall segments radially. Once cutting the specimen, it opens up despite any external loads not given. Hoger et al. [22, 23, 24, 25] explain the importance of the virtual stress-free configuration in order to handle residual stress.

The Holzapfel-Ogden model [10] considers arteries as composites, which is that two families of collagen fibers are embedded in isotropic base materials, which are called the extracellular matrix in biology. The strain energy function of the Holzapfel-Ogden model consists of two parts. The isotropic part corresponds to the neo-Hookean model, and the anisotropic part corresponds to an exponential stiffness form.

Taber and Humphrey [12] discussed a model of how residual stress in soft tissue arises as a natural process of growth; by comparing their model result and experimental data, they show the growth of arteries depends on stress.

Zulliger et al. [26] proposed a new strain energy function that is similar to the Holapfel-Ogden model but includes the waviness feature of collagens.

In [11], Hariton et al. present a stress-modulated remodeling model of an artery. They considered that circumferential stress affects the reorientation of the collagen families in an artery. That

is the angle of the fibers are considered in the model.

In addition, the review paper [27] handled biological growth and remodeling ranging from current developments to avenues to further developments. They especially mentioned the issue of choosing a configuration when a biological tissue is growing. The use of elasticity formulated in the current configuration helps tackle the issue of incompatible growth of soft tissues.

A constrained mixture theory, which was proposed by Rajagopal and Humphrey in 2002, [16] assumes that the soft tissue and each component in it deformed together, but each constituent has its own properties, including natural configuration separately. Based on [16], there were many following studies [28, 29, 30].

1.3 Thesis Outline

If arteries undergo chronic hypertension, arteries may add mass or change the mechanical properties such as residual stress in order to handle abnormal blood pressure, as a part of homeostases (the state that living tissues maintain the steady internal conditions.) Here, adding mass is usually referred to as growth, and changing the mechanical properties of an artery (with little change in mass) is referred to as remodeling. To explain a series of this process, I compose the sections as follows.

In section 2, I describe basic elasticity. It starts with providing a basic definition of mechanical concepts. Two constitutive relations are described: the neo-Hookean and the Holzapfel-Ogden model. Residual stress, which is an unavoidable mechanical property of the arterial wall, is explained in the section.

Section 3 gives us the governing equation. By the balance of linear momentum, we have the partial differential equation. We use the boundary conditions in this project to be traction-free at the inner and outer wall at the intermediate configuration and pressurized at the inner wall, and traction-free at the outer wall at the current configuration. In vitro, the surrounding of the specimen is air, and no external force is given; it is natural to take the traction-free condition at the intermediate configuration, and we can control to impose pressure at the inner and outer wall for the current configuration since we simulate the in vitro experiments. Other soft tissues surround

the blood vessels in vivo so that they may have different boundary conditions.

In section 4, numerical experiments are conducted. For both the neo-Hookean and the Holzapfel-Ogden models, I mainly show how much growth and residual stress changed to bring down the hoop stress (circumferential stress) when mildly to highly pressurized at the inner wall. We end up get the results that one of growth and remodeling can still cope with the increased hoop stress, but a more effective way to tackle this issue is combining both growth and remodeling.

In section 5, I summarize the numerical experiments and provide the discussion.

1.4 Purpose and Goal

Having a mathematical model serves the following purposes in general. First, we can understand more and better the given situation. Secondly, one can predict after the event happens. Lastly, one may be able to control the event or to provide treatments for the event or issue. My goal for this project is to provide a mathematical model for the growth and stiffening of the arterial wall caused by hypertension. I would mainly focus on describing the situation using the mathematical model. Better understanding will help us move forward to prediction, control, and treatments for hypertension.

Many studies show that arteries are layered, anisotropic, heterogeneous, slightly compressible [31, 32, 33, 34], elastic or viscoelastic bodies [35, 36]. As mentioned in section 1.2 histology, an arterial wall has three layers, but depending on research, some researchers choose a one-layered, or two-layered model [8]. Sometimes, slightly compressible bodies are treated as incompressible bodies [35].

To set up our mathematical model, we idealize that arteries are one-layered, isotropic/anisotropic (depending on constitutive model), incompressible hyperelastic body, and the geometry we take for this project is an axisymmetric cylindrical tube. This is mainly because of simplicity. In detail, a one-layered model comes from the feature that the media takes the most of the arteries in terms of volume, and there is experimental evidence that the media changes the most among three layers depending on hypertension [9]. An axisymmetric cylindrical geometry will give us a way to handle our PDE for writing in terms of r, in the current configuration. One can choose an isotropic model

if only the extracellular matrix of arteries is taken into account. An anisotropic model such as the Holzapfel-Ogden model is used here when considering the arterial wall to be a composite material consisting of fiber-reinforced extracellular matrix.

To sum up, in this work, a hyperelastic, isotropic/anisotropic, incompressible model on an axisymmetric cylindrical tube will be utilized in order to see how hypertension affects growth (change in mass of an artery) and remodeling (change in residual stress of an artery) in the current configuration.

2. MECHANICS : ELASTICITY

Soft tissues are often modeled by elastic bodies, [5, 7, 11, 27, 33]. Likewise, the arterial wall in our project is assumed as an elastic material. Especially, the stress-strain relationship of the arterial wall is derived from the strain energy function. That is, the arterial wall is hyperelastic. In this section, we start with classic concepts of continuum mechanics and those will be helpful tools to understand the force and deformation of elastic bodies.

2.1 Kinematics and Kenetics

Let $\mathcal{B}$ be a reference configuration, and $\mathcal{B}_t$ be the current configuration, which are embedded in a three dimensional Euclidean Space. A point $\boldsymbol{X} \in \mathcal{B}$ and $\boldsymbol{x} \in \mathcal{B}_t$ are a material point, and the spatial point according to the $\boldsymbol{X}$ at time t by a mapping, respectively. The smooth mapping $\boldsymbol{\chi} : \mathcal{B} \to \mathcal{B}_t$ such that $\boldsymbol{x} = \boldsymbol{\chi}(\boldsymbol{X}, t)$ where $\boldsymbol{x} \in \mathcal{B}_t, \boldsymbol{X} \in \mathcal{B}$ is called a motion. Then, the deformation gradient we denoted by $\boldsymbol{F}$ is defined as $\boldsymbol{F}(\boldsymbol{X}) := \nabla\boldsymbol{\chi}(\boldsymbol{X}, t)$. Also, the displacement is $\boldsymbol{u} = \boldsymbol{x} - \boldsymbol{X}$. In the spatial description of the displacement is, $\tilde{\boldsymbol{u}} = \boldsymbol{x} - \boldsymbol{\chi}^{-1}(\boldsymbol{x})$.

The Cauchy stress tensor $\boldsymbol{T}$, is given by the function of the deformation gradient. i.e. $\boldsymbol{T} = \hat{\boldsymbol{T}}(\boldsymbol{F})$. Arteries are hyperelastic, which means the Cauchy stress tensor, $\boldsymbol{T}$, is defined as a function of the gradient of strain energy function, $W = \hat{W}(\boldsymbol{F})$. The Cauchy stress is

$$\boldsymbol{T} = J^{-1}\partial_{\boldsymbol{F}}\hat{W}(\boldsymbol{F})\boldsymbol{F}^T, \tag{2.1}$$

where $J = det\boldsymbol{F}$.

2.2 Constitutive Relation

Constitutive relations in solid mechanics relate stresses and strains. If we define the strain energy function of the material, then we can get the relation between stress and strain, by the hyperelasticity. Although mechanically real arteries are slightly incompressible, we idealize that an arterial wall is incompressible like many previous works ([37, 38, 19, 32, 39, 40, 41]). The

reason why we choose the arterial wall to be incompressible is that the soft tissue is composed largely of water and it leads to simplification of certain key computations. We'll use the neo-Hookean Model ([34]) for assuming arteries isotropic, and the Holzapfel-Ogden Model ([10]) for assuming arteries anisotropic to illustrate how the arterial wall reacts to the hypertensive blood pressure.

2.2.1 Incompressible Neo-Hookean Model

The neo-Hookean model is frequently chosen as a simplistic model of soft tissue. In particular, the extracelluler matrix is often modeled as neo-Hookean. Also, it gives us intuition about the stress-strain relation and how much remodeling/stiffening is needed to control the stresses. A strain energy function of the incompressible neo-Hookean material is

$$\boldsymbol{W}(\boldsymbol{F}) = \frac{\mu}{2} tr(\boldsymbol{F}\boldsymbol{F}^T) \tag{2.2}$$

along with the incompressibility constraint $det\boldsymbol{F} = 1$. Note that $tr(\cdot)$ is the trace of the input.

By the hyperelasticity (2.1) and the tensoral derivative (A.1), the Cauchy Stress $\boldsymbol{T}$ is

$$\boldsymbol{T}(\boldsymbol{F}) = \mu \boldsymbol{F}\boldsymbol{F}^T - p(r)\boldsymbol{I} \tag{2.3}$$

where p is the Lagrange multiplier enforcing the incompressibility.

2.2.2 Incompressible Holzapfel-Ogden Model

The Holzapfel-Ogden Model is for an anisotropic material. Areteries are commonly considered as anisotropic since components like fibers are not isotropically oriented over the cell. Especially, Holzapfel et al. [10] considered the arterial wall structures in a way that in the extracellular matrix which is an isotropic material, two collagen fiber families are embedded, which lead to anisotropic property of the artery. Those two families of the collagen fibers are placed in a helix-like shape, and the angle between them differs depending on arteries. Here, we choose the angle between them 29° from the data in Holzapfel's, [10].

The strain energy function for the Holzapfel-Ogden model is defined as

$$\Psi(I_1, I_4, I_6) = \Psi_{iso}(I_1) + \Psi_{aniso}(I_4, I_6)$$

where

$$I_1 = tr\boldsymbol{C},\ I_4 = \boldsymbol{C} \cdot A_1,\ I_6 = \boldsymbol{C} \cdot A_2,\ \boldsymbol{C} = \boldsymbol{F}^T\boldsymbol{F}.$$

A_i's are obtained by the following process.

$$A_i = \boldsymbol{a}_i \otimes \boldsymbol{a}_i,\ i = 1, 2.$$

$$\boldsymbol{a}_i = \boldsymbol{F}\bar{\boldsymbol{a}}_i,\ i = 1, 2,$$

where

$$\bar{\boldsymbol{a}}_1 = \begin{pmatrix} 0 \\ \cos\beta \\ \sin\beta \end{pmatrix},$$

and

$$\bar{\boldsymbol{a}}_2 = \begin{pmatrix} 0 \\ \cos\beta \\ -\sin\beta \end{pmatrix}.$$

Here, $\bar{\boldsymbol{a}}_i$'s are unit vectors in the direction of fibers in the reference configuration and β is the angle between those unit vectors. Additionally, the anisotropic contribution of the strain energy function is a Fung-type exponential model. The anisotropic contribution of the strain energy function is,

$$\Psi_{aniso}(I_4, I_6) = \frac{k_1}{2k_2} \sum_{i=4,6} \{\exp[k_2(I_i - 1)^2] - 1\}.$$

$$\Psi_{aniso}(\boldsymbol{C}) = \frac{k_1}{2k_2} \sum_{i=1,2} \{\exp[k_2(\boldsymbol{C} \cdot A_i - 1)^2] - 1\}.$$

We can rewrite the function in terms of deformation gradient $\boldsymbol{F}$:

$$\Psi_{aniso}(\boldsymbol{F}) = \frac{k_1}{2k_2} \sum_{i=1,2} \{\exp[k_2(\boldsymbol{F}^T\boldsymbol{F} \cdot A_i - 1)^2] - 1\}.$$

The isotropic part of strain energy function is the same as the neo-Hookean, $\Psi_{iso}(\boldsymbol{F}) = \frac{c}{2} tr\boldsymbol{F}\boldsymbol{F}^T$.

Therefore, the Cauchy stress is

$$\boldsymbol{T} = \frac{1}{J}[\partial_{\boldsymbol{F}}\Psi_{iso}(\boldsymbol{F}) + \partial_{\boldsymbol{F}}\Psi_{aniso}(\boldsymbol{F})]\boldsymbol{F}^T - p(r)\boldsymbol{I},$$

where $J = det\boldsymbol{F}$ and p is a Lagrange multiplier.

$$\begin{aligned} \boldsymbol{T}(\boldsymbol{F}) &= c\boldsymbol{F}\boldsymbol{F}^T \\ &+ 2k_1 \sum_{i=1,2} \{(tr[\boldsymbol{F}A_i\boldsymbol{F}^T] - 1) \times \exp[k_2(tr[\boldsymbol{F}A_i\boldsymbol{F}^T] - 1)^2]\boldsymbol{F}A_i\boldsymbol{F}^T\} - p(r)\boldsymbol{I}. \end{aligned} \tag{2.4}$$

2.3 Residual Stress

When stress still exists but there is no involved strain, we say the body is residually stressed. Residual stress in biological materials is important since it is well known that residual stress in elastic arteries is not negligible [33], and it highly affects the stress-strain relation of the elastic body.

$\tau := \hat{\boldsymbol{T}}(\boldsymbol{I})$ where $\boldsymbol{I}$ is the identity tensor is called the residual stress in $\mathcal{B}$. If $\hat{\boldsymbol{T}}(\boldsymbol{I}) = 0$, then $\mathcal{B}$ is called a natural configuration. In other words, a natural configuration is in a stress-free condition. In addition, in this work, a natural configuration is also load-free; there are no external traction and body forces. The residual stress τ satisfies the equilibrium condition; $Div\tau = 0$ in the

body $\mathcal{B}$, and traction-free on the boundary of the body; $\tau \boldsymbol{n} = 0$ on $\partial\mathcal{B}$, where $\boldsymbol{n}$ is normal unit vector to the boundary $\partial\mathcal{B}$.

Gorb and Walton [33] bring the concept of the natural response function (with subscript N) and for a multiplicative model like Fung-type model, use the following natural strain energy function $\hat{W}_N(\cdot)$.

$$\hat{W}_R(\boldsymbol{C}; \tau) = \hat{W}_N(\boldsymbol{F}_R^T \boldsymbol{C} \boldsymbol{F}_R)$$

where $\boldsymbol{F}_R = \boldsymbol{T}_N^{-1}(\tau)$ where τ is a residual stress. Once we apply this idea to (2.3) and (2.4), the equation (2.3) becomes

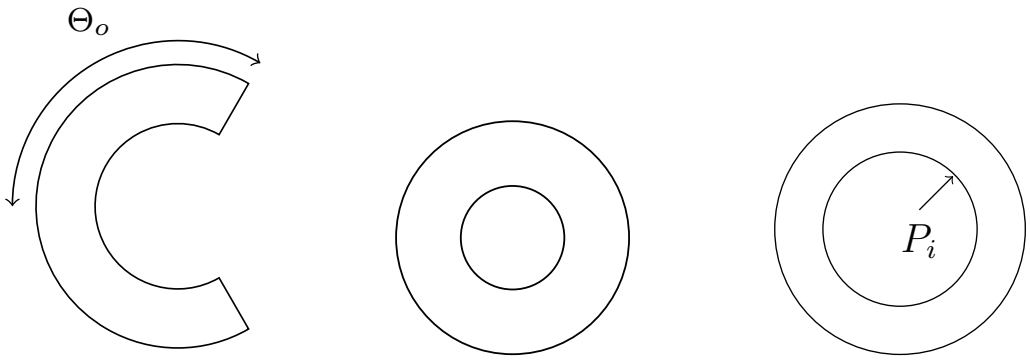
$$\boldsymbol{T}(\boldsymbol{F}\boldsymbol{F}_R) = \mu \boldsymbol{F}\boldsymbol{F}_R(\boldsymbol{F}\boldsymbol{F}_R)^T - p(r)\boldsymbol{I}, \tag{2.5}$$

and the equation (2.4) becomes

$$\begin{aligned}\boldsymbol{T}(\boldsymbol{F}\boldsymbol{F}_R) = {} & c\boldsymbol{F}\boldsymbol{F}_R(\boldsymbol{F}\boldsymbol{F}_R)^T \\ & + 2k_1 \sum_{i=1,2} \{(tr[\boldsymbol{F}\boldsymbol{F}_R A_i (\boldsymbol{F}\boldsymbol{F}_R)^T] - 1) \times \exp[k_2 (tr[\boldsymbol{F}\boldsymbol{F}_R A_i (\boldsymbol{F}\boldsymbol{F}_R)^T] - 1)^2] \boldsymbol{F}\boldsymbol{F}_R A_i (\boldsymbol{F}\boldsymbol{F}_R)^T\} \\ & - p(r)\boldsymbol{I}.\end{aligned} \tag{2.6}$$

The existence of residual stress can be confirmed by experiment ([21, 42]). In particular, Fung and colleague collected specimens from animals. They take thin slices of arteries in a ring shape. Then, they cut those rings radially, and the sliced arteries open up as a result. Since the arteries are intact and unloaded in the experimental setting, this result shows us that residual stress leads to the arterial wall open up.

An idealized model of the Fung experiments visualizes arterial rings as slices from an axisymmetric cylindrical tube, Figure 2.1. Let (R, Θ, Z) be the natural configuration (stress free), (ρ, ϑ, ζ) be the intermediate configuration (residually stressed but not loaded) and (r, θ, z) be the current configuration (loaded), represented as figure (a), (b), and (c) respectively. In short, Fung's experiments are the process of figure (b) to figure (a). They cut the intact unloaded artery (figure (b)



(a) (R, Θ, Z) (b) (ρ, ϑ, ζ) (c) (r, θ, z)

Figure 2.1: Diagram of Cross Section of the Arterial Wall

in Figure 2.1) radially. Then the vessel opens up until the residual stress is released (figure(a) in Figure 2.1). Although in order to release all residual stress, several cuts might be needed [12, 43], we assume that a single radial cut produces a natural configuration. Θ_o is called an opening angle, where we put the center of an artery at the origin and choose the angle between the negative x-axis to the ray passing the cutting segment of the artery for easier computation. From figure (b) to (c) is the process of pressurizing, which is needed for our numerical experiment, not related to Fung's. P_i is pressure given in the inner wall. Fung et al. assumed that the residual stress in the intermediate configuration can be modeled by the following deformation from the natural configuration (a) to the intermediate configuration (b).

$$\rho = \rho(R)$$
$$\vartheta = \frac{\pi}{\Theta_0}\Theta$$
$$\zeta = \Lambda Z.$$

2.4 Semi-inverse Approach

The semi-inverse approach is a method of simplifying challenging nonlinear elastic boundary value problems [5]. As mentioned above, we idealize the artery wall as an axisymmetric cylindrical tube. In addition, applying the semi-inverse approach to the problem under consideration, we

modeled the deformation from the intermediate configuration to the current configuration (the motion from figure(b) to figure(c)) is

$$r = r(\rho)$$

$$\theta = \vartheta$$

$$z = \tilde{\lambda}\zeta$$

where $\tilde{\lambda}$ is the axial stretch from the intermediate configuration to the current configuration.

The residual deformation gradient $\boldsymbol{F}_R$ is

$$\boldsymbol{F}_R = \begin{pmatrix} \dfrac{\partial \rho}{\partial R} & 0 & 0 \\ 0 & \dfrac{\rho\pi}{R\Theta_0} & 0 \\ 0 & 0 & \Lambda \end{pmatrix}.$$

The deformation gradient $\boldsymbol{F}$ from intermediate configuration to current configuration is

$$\boldsymbol{F} = \begin{pmatrix} \dfrac{\partial r}{\partial \rho} & 0 & 0 \\ 0 & \dfrac{r}{\rho} & 0 \\ 0 & 0 & \tilde{\lambda} \end{pmatrix}.$$

In addition, by the incompressibility, we have $det(\boldsymbol{F}_R) = 1$ and $det(\boldsymbol{F}) = 1$. Thus, we get the relation between R , ρ and r as follows.

$$\frac{\partial \rho}{\partial R} = \frac{R\Theta_0}{\rho\pi\Lambda}.$$

$$\frac{\partial r}{\partial \rho} = \frac{\rho}{r\tilde{\lambda}}.$$

$$R(\rho) = [R_i^2 + \frac{(\rho^2 - \rho_i^2)\pi\Lambda}{\Theta_o}]^{1/2}. \tag{2.7}$$

2.4.1 Elasticity in the Current Configuration

Historically and most commonly, the governing equations in nonlinear elasticity are formulated to relative to a reference configuration. As mentioned, in the important survey paper [27], it would be very advantageous to formulate mechanical equations modeling soft biological tissue in the deformed (current) configuration. A key contribution of this dissertation is to carry out that challenge. Consequently, from here on, we formulate our model of the mechanics of the arterial wall in the current configuration. To that end, we apply the semi-inverse approach to modeling the deformation from the intermediate configuration (b) to the current configuration (c), by assuming the displacement from the intermediate configuration to the current configuration has the form

$$\tilde{\boldsymbol{u}}(r, \theta, z) = \eta(r)\boldsymbol{j}_1(\theta) + \lambda z \boldsymbol{j}_3$$

where $\{\boldsymbol{j}_1(\theta), \boldsymbol{j}_2(\theta), \boldsymbol{j}_3\}$ is a basis for cylindrical coordinates on the current configuration (c). That is,

$$\boldsymbol{j}_1(\theta) = \cos(\theta)\boldsymbol{e}_1 + \sin(\theta)\boldsymbol{e}_2,\ \boldsymbol{j}_2(\theta) = -\sin(\theta)\boldsymbol{e}_1 + \cos(\theta)\boldsymbol{e}_2,\ \boldsymbol{j}_3 = \boldsymbol{e}_3$$

where $\{\boldsymbol{e}_1, \boldsymbol{e}_2, \boldsymbol{e}_3\}$ denotes the natural basis for the Euclidean space.

Since $\boldsymbol{F} = (\boldsymbol{I} - grad\tilde{\boldsymbol{u}})^{-1}$, and

$$grad\tilde{\boldsymbol{u}} = \eta'\boldsymbol{j}_1 \otimes \boldsymbol{j}_1 + (\frac{\eta}{r})\boldsymbol{j}_2 \otimes \boldsymbol{j}_2 + \lambda \boldsymbol{j}_3 \otimes \boldsymbol{j}_3,$$

the deformation gradient $\boldsymbol{F}$ can be written in terms of displacement as the following.

$$\boldsymbol{F} = \boldsymbol{F}^T = \frac{1}{1-\eta'}\boldsymbol{j}_1 \otimes \boldsymbol{j}_1 + \frac{1}{(1-\frac{\eta}{r})}\boldsymbol{j}_2 \otimes \boldsymbol{j}_2 + \frac{1}{1-\lambda}\boldsymbol{j}_3 \otimes \boldsymbol{j}_3. \tag{2.8}$$

Again, the incompressibility, $det\boldsymbol{F} = 1$ along with the equation (2.8) gives us

$$\frac{1}{(1-\eta')(1-\frac{\eta}{r})(1-\lambda)} = 1. \tag{2.9}$$

Then we can obtain the algebraic formula for η by solving the differential equation (2.9).

$$\eta(r,c) = r - \sqrt{c + \frac{r^2}{1-\lambda}}. \tag{2.10}$$

In Johnson's dissertation [13], the integration constant c is fixed by $r_o^2\lambda/(1-\lambda)$ because she assumed that there is no displacement at the outer wall. However, in this dissertation, we don't assume the outer wall is not moving. Rather, we take a traction-free condition after pressurized as well, which will be given in the section 3. Therefore, we keep integration constant c.

Lastly, consider the definition of the displacement,

$$\rho(r) = r - \eta(r,c), \tag{2.11}$$

we can get the ρ in terms of r and c.

We plug the deformation gradient, transpose of the deformation gradient (2.8), and the definition of displacement (2.11) in the Cauchy stress using the neo-Hookean relation (2.5) and the Holzapfel-Ogden relation (2.6). Finally, the extra term of the Cauchy stress $\boldsymbol{T}$ (the term not involving Lagrange multiplier) becomes in terms of r, η (including integration constant c), which is presented in the current configuration.

The Cauchy Stress for the incompressible neo-Hookean Model in terms of r is

$$\boldsymbol{T}(r) = \mu \begin{pmatrix} \frac{1}{1-\eta'}\frac{\rho(r)\pi}{R(\rho(r))\Theta_0\Lambda} & 0 & 0 \\ 0 & \frac{1}{(1-\frac{\eta}{r})}\frac{\rho(r)\pi}{R(\rho(r))\Theta_0} & 0 \\ 0 & 0 & \frac{1}{1-\lambda}\Lambda \end{pmatrix}^2 - p(r)\boldsymbol{I}. \tag{2.12}$$

The Cauchy Stress for the incompressible Holzapfel-Ogden Model in terms of r is obtained by

the same way, and we omit writing.

2.5 Manage Stress : Growth and Remodeling

How does an arterial wall behave if hypertension continues? We conjecture that the artery originally has preferred circumferential stress, and the arterial wall tries to bring the circumferential stress down to the preferred stress when it detects chronic hypertension. Since it is well known that hypertension accompanies with arterial wall thickening and stiffening in many cases from the many clinical data [44], the reasonable guesses about how arterial wall handle abnormal stress is growth and remodeling.

The opening angle in the Fung model of residual stress can be viewed as a measure of a level of residual stress. In this work, a change in residual stress without changing mass is what is meant by remodeling.

Adding mass or volume corresponds to growth. We show that the arterial wall can mitigate the increase in circumferential stress due to hypertension through thickening resulting from growth. A major result in this present work is to analyze the effectiveness of both growth and remodeling in reducing the elevated circumferential stress due to hypertension.

By the balance of linear momentum, $div\boldsymbol{T} = 0$.

$$\frac{\partial \boldsymbol{T}_{rr}}{\partial r} + \frac{1}{r}\frac{\partial \boldsymbol{T}_{\theta r}}{\partial \theta} + \frac{\partial \boldsymbol{T}_{zr}}{\partial z} + \frac{\boldsymbol{T}_{rr} - \boldsymbol{T}_{\theta\theta}}{r} = 0$$

$$\frac{\partial \boldsymbol{T}_{r\theta}}{\partial r} + \frac{1}{r}\frac{\partial \boldsymbol{T}_{\theta\theta}}{\partial \theta} + \frac{\partial \boldsymbol{T}_{z\theta}}{\partial z} + \frac{2\boldsymbol{T}_{r\theta}}{r} = 0$$

$$\frac{\partial \boldsymbol{T}_{rz}}{\partial r} + \frac{1}{r}\frac{\partial \boldsymbol{T}_{\theta z}}{\partial \theta} + \frac{\partial \boldsymbol{T}_{zz}}{\partial z} + \frac{\boldsymbol{T}_{rz} - \boldsymbol{T}_{\theta\theta}}{r} = 0.$$

Since $\boldsymbol{T}$ is a diagonal matrix in our case, we only have

$$\frac{\partial \boldsymbol{T}_{rr}}{\partial r} = \frac{\boldsymbol{T}_{\theta\theta} - \boldsymbol{T}_{rr}}{r}. \tag{3.1}$$

The boundary conditions that we have in the current configuration are pressure, P_i, which is given at the inner wall (which imitates blood pressure in vivo), and traction-free at the outer wall.

$$\boldsymbol{T}_{rr}(r_i) = -P_i, \tag{3.2}$$

and

$$\boldsymbol{T}_{rr}(r_o) = 0. \tag{3.3}$$

By taking the integration with respect to r,

$$\boldsymbol{T}_{rr}(r) - \boldsymbol{T}_{rr}(r_i) = \int_{r_i}^{r} \frac{\boldsymbol{T}_{\theta\theta} - \boldsymbol{T}_{rr}}{x} dx. \tag{3.4}$$

Now, $\boldsymbol{T}$ is a function of c and r since the displacement η depends on c and r. Then plugging $r = r_o$ in equation (3.4) with the boundary conditions (3.2) and (3.3) gives us the following.

$$Pi = \int_{r_i}^{r_o} \frac{\boldsymbol{T}_{\theta\theta} - \boldsymbol{T}_{rr}}{x} dx. \tag{3.5}$$

The left hand side of the equation (3.5) is a function of r_i, r_o, and c. Additionally, r_o depends on r_i by the incompressibility. Thus, we have two unknowns r_i, c in equation (3.5). If we assume the inner radius in the intermediate configuration can be measured by the experiment, then one can get one more equation for finding r_i and c. Consider the definition of the displacement, $\rho = r - \eta(r)$, then the second equation is

$$\rho_i = r_i - \eta(r_i, c). \tag{3.6}$$

Then we solve this system of equations (3.5) and (3.6).

Lagrange multiplier is derived from the equation (3.4). With boundary condition $\boldsymbol{T}_{rr}(r_i) = -P_i$, and the Cauchy stress in terms of r, the equation (2.12) , we have

$$\left(\frac{1}{1-\eta'} \frac{\rho(r)\pi}{R(\rho(r))\Theta_0 \Lambda} \right)^2 - p(r) = \int_{r_i}^{r} \frac{\boldsymbol{T}_{\theta\theta} - \boldsymbol{T}_{rr}}{x} dx - P_i,$$

if we use neo-Hookean Model.

For convenience, let denote the extra term of Cauchy stress by $\boldsymbol{T}^{ex}$.

$$\boldsymbol{T}^{ex}_{rr}(r) - p(r) = \int_{r_i}^{r} \frac{\boldsymbol{T}_{\theta\theta} - \boldsymbol{T}_{rr}}{x} dx - P_i.$$

Then, Lagrange multiplier is

$$p(r) = \boldsymbol{T}^{ex}_{rr}(r) - \int_{r_i}^{r} \frac{\boldsymbol{T}_{\theta\theta} - \boldsymbol{T}_{rr}}{x} dx + P_i, \tag{3.7}$$

and the integrand of the right hand side of the equation (3.7) is actually written as only extra term of Cauchy stress.

$$\frac{\boldsymbol{T}_{\theta\theta} - \boldsymbol{T}_{rr}}{x} = \frac{\boldsymbol{T}^{ex}_{\theta\theta} - p(r) - (\boldsymbol{T}^{ex}_{rr} - p(r))}{x} = \frac{\boldsymbol{T}^{ex}_{\theta\theta} - \boldsymbol{T}^{ex}_{rr}}{x}.$$

Hoop stress function is finally defined in terms of fully r and c. Therefore, we can get the hoop stress at a point in the current configuration.

$$\boldsymbol{T}_{\theta\theta}(r) = \boldsymbol{T}^{ex}_{\theta\theta}(r) - p(r). \tag{3.8}$$

4. NUMERICAL EXPERIMENT

When we conduct the numerical experiment, we set a hypothetical arterial wall. The first thing to know is we assume we know the radii at the intermediate configuration. It is reasonable to assume that one knows the geometry of intermediate configuration since one could measure the inner and outer radii from experiments in vitro. Here we adopt some values from page 337 in Humphrey's book [5]; $\rho_i = 0.00139$ m and $\rho_o = 0.00199$ m. Then we choose axial stretches $\Lambda = 1$ and $\tilde{\lambda} = 1$ for our intuitive and computational convenience. Lastly, we choose the initial opening angle $\Theta_o = \frac{3}{4}\pi$. We are using two material models: the neo-Hookean and the Holzapfel-Ogden Models, but they are non-dimensionalized by the shear modulus.

4.1 Result using Neo-Hookean Model

To complete the knowledge of residual stress, we need to compute the inner and outer radii (R_i, R_o) of the natural configuration. It should start with the deformation from the natural configuration to the intermediate configuration. This deformation also needs to satisfy the relation of equation (3.5). Thus, we have the following.

$$0 = \int_{\rho_i}^{\rho_o} \frac{\boldsymbol{T}_{\vartheta\vartheta} - \boldsymbol{T}_{\rho\rho}}{x} dx. \tag{4.1}$$

Also, the integrand in the equation (4.1) is a function of (R_i, R_o), then it becomes in terms of only R_i due to the incompressibility (see equation (2.7).) We can get R_i and R_o if we solve the equation (4.1) with incompressibility. Finally, we fully achieve information about the residual stress of the beginning stage. The following figure 4.1 is the circumferential stress at the intermediate configuration through the arterial wall. i.e., it is when zero pressure is given at the inner wall of arteries. As we can see in this graph, the inner half of the arterial wall is compressive, and the outer of it is tensile.

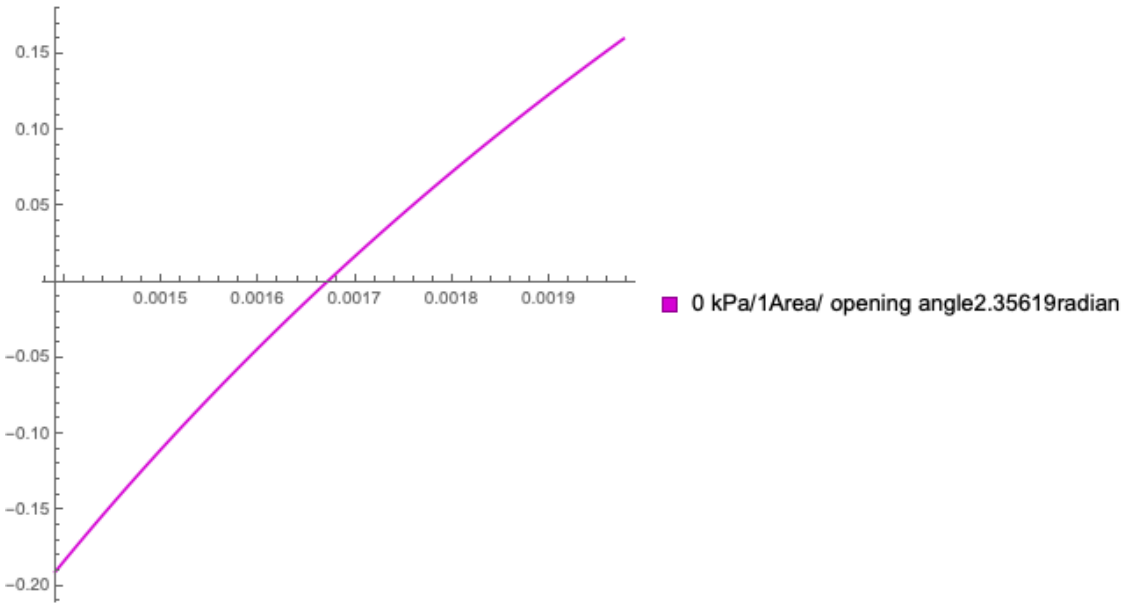


Figure 4.1: Hoop stress vs. radius at the intermediate configuration using Neo-Hookean Model

Secondly, we need to set up a target value, so called preferred stress. We assign 0.06 as normal blood pressure for the neo-Hookean model since the hoop stress graph after loaded 0.06 is non-negative; in other words, the minimum hoop stress when applying pressure 0.06 is above zero, which means the arterial wall after pressurizing is totally tensile. Note that the upper line in figure 4.2 is the hoop stress with the normal blood pressure, and the lower line is the hoop stress graph at the intermediate configuration (i.e. the same line with figure 4.1) for comparison. If we compute the hoop stress values , the minimum hoop stress value at the loaded configuration applying normal blood pressure is 0, and the maximum hoop stress value at the loaded configuration applying normal blood pressure is 0.2908. These minimum and maximum hoop stress values are set to be our target values.

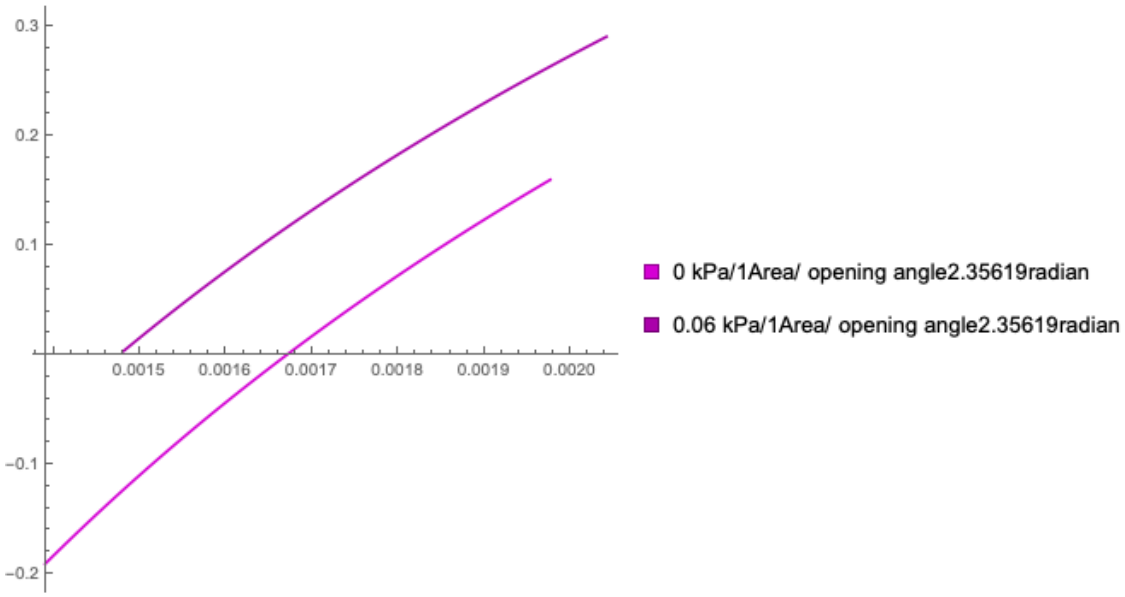


Figure 4.2: Hoop stress vs. radius when pressure 0 and 0.06 using Neo-Hookean Model

Now, we are applying higher pressures than our normal blood pressure, which are 0.075, 0.09, and 0.12. Figure 4.3 shows that the arterial wall has a higher maximum hoop stress as pressure increases. The bottom two lines are the same as figure 4.3 for comparison, and the upper three lines are as pressure increased by 25%, 50% and 100% respectively from the middle line to the most upper line.

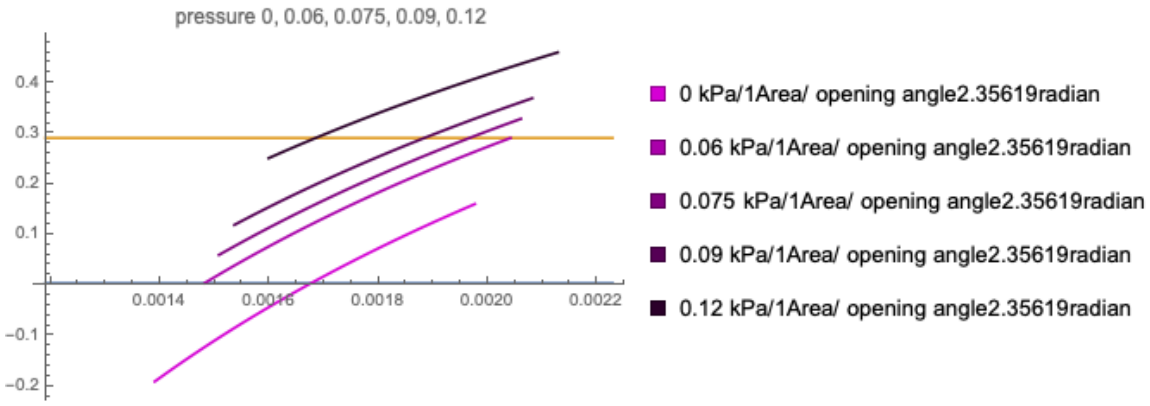


Figure 4.3: Hoop stress vs. radius when pressure 0, 0.06, 0.075, 0.09, and 0.12 using Neo-Hookean Model

Initially, we want to control the elevated maximum hoop stress by growth and remodeling. Our goal is to find how much growth or remodeling is needed to bring the increased maximum hoop stress arising from hypertension down to the target maximum hoop stress value.

4.1.1 Growth

As we mentioned above, because we simplify the arterial wall as homogeneous, growth can be represented by adding mass/volume if we assume the density of arteries is a constant. Especially if we set the axial stretch as 1, then adding an area of the cross-section of an artery is enough to illustrate a growth. Thus, after pressurizing, we increase the area of the cross-section of the arterial wall. Then, we obtain new inner and outer wall radii in the following two ways. If growth happens only at the inner wall,

$$r_i^{new} = r_i - x, \;\; r_o^{new} = r_o$$

where x such that

$$IncreasedArea = ((r_o)^2 - (r_i - x)^2) \cdot \tilde{\lambda},$$

and if growth happens at both the inner and outer wall with a same length,

$$r_i^{new} = r_i - x, \;\; r_o^{new} = r_o + x$$

where x such that

$$IncreasedArea = ((r_o + x)^2 - (r_i - x)^2) \cdot \tilde{\lambda}.$$

These new radii allow us to find the hoop stress using equation (3.8).

The following graphs are hoop stresses at a certain level of load along with increasing area. Note that I present only when pressure is 0.09, but other cases with different pressures also have similar trends.

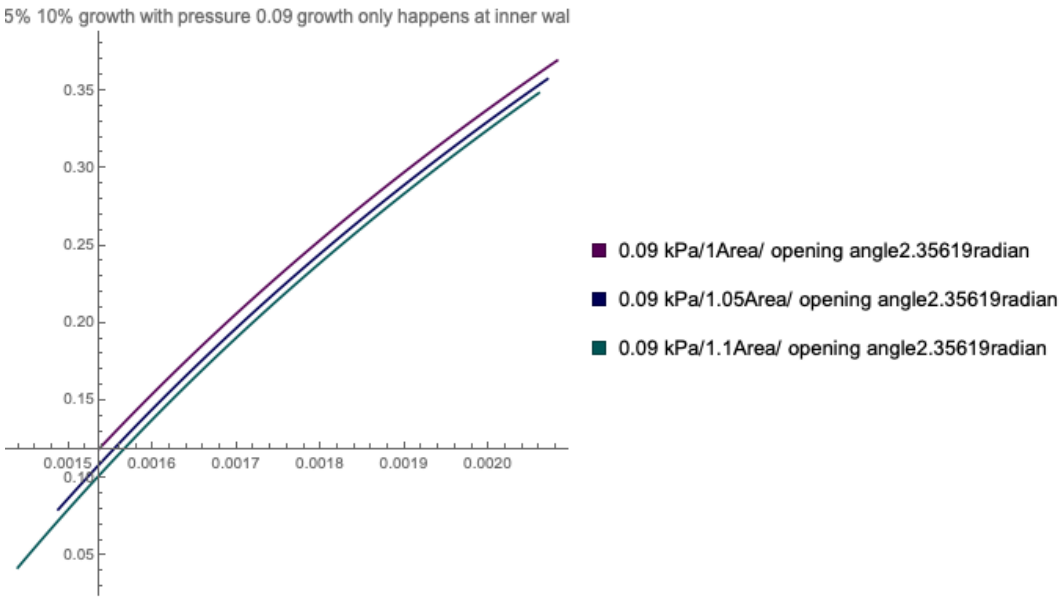


Figure 4.4: Hoop stress vs. radius when growth happens at the inner wall, by 0%, 5%, 10% using Neo-Hookean Model

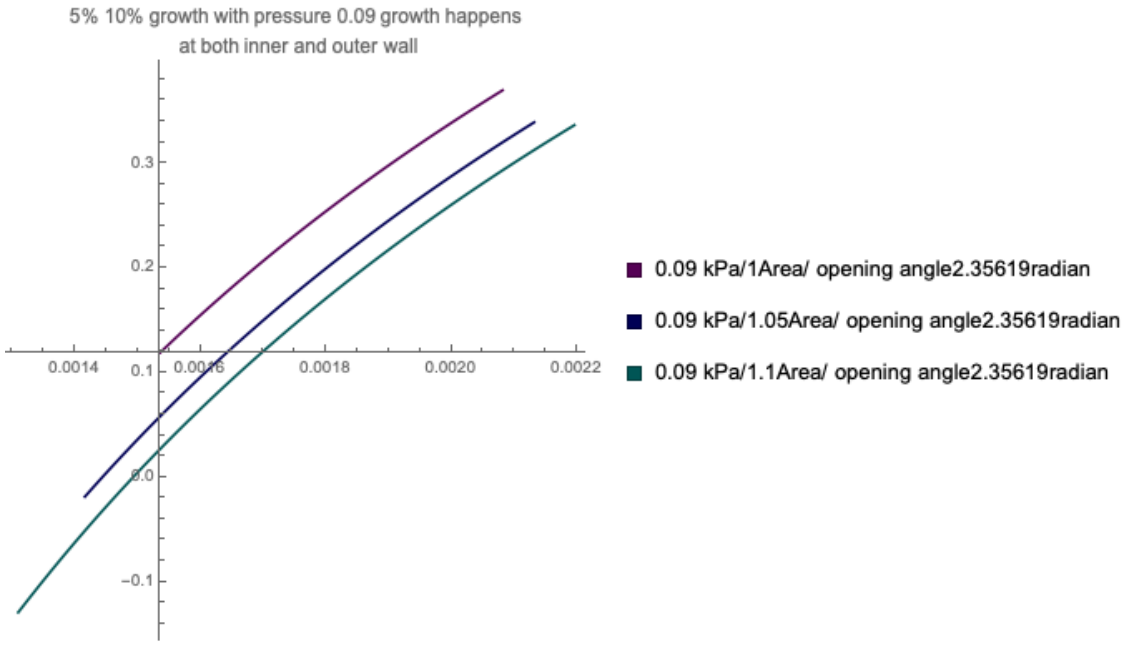


Figure 4.5: Hoop stress vs. radius when growth happens at both the inner and outer wall, by 0%, 5%, 10% using Neo-Hookean Model

As we can see in figure 4.4, as growth happens at only the inner wall, the hoop stress graphs are shifting down and the maximum hoop stress decreases. Growth doesn't guarantee that maximum hoop stress is always getting smaller due to where the growth happens. Figure 4.5 shows that when the arterial wall growth occurs at both the inner and outer wall, the maximum hoop stress reduces in the beginning stage of growth, but later it does not bring down maximum hoop stress.

Secondly, only growth may bring down maximum hoop stress to our target value. However, often it brings hoop stress too much down so that the arterial wall is compressive partly, which is represented by the negative values of the lefthand side of the green line in Figure 4.5.

4.1.2 Remodeling : Change Opening Angle

As mentioned in the previous sections, we treat changing opening angle as a type of remodeling. So, we conduct numerical experiments according to having different opening angles.

Figure 4.6 displays that the hoop stress vs. radius as opening angle changed by 0% (i.e. before remodeling happens), 5% and 10% when having fixed pressure and no growth. This figure shows that when there is no growth, but only changes in opening angle (remodeling,) the hoop stress graph has a less steep slope, which means increasing opening angle leads to reducing maximum hoop stress but making the minimum hoop stress increase.

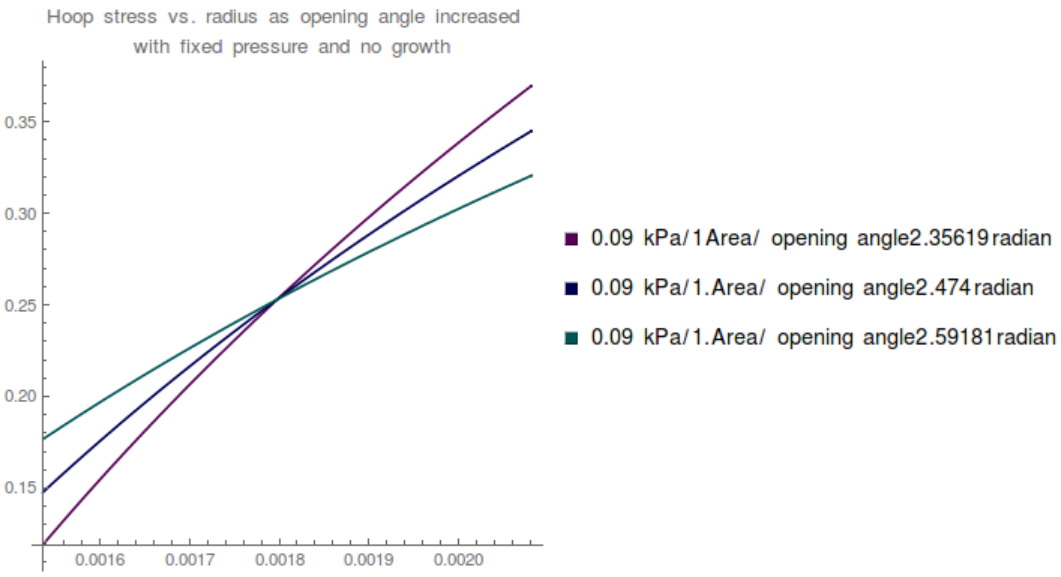
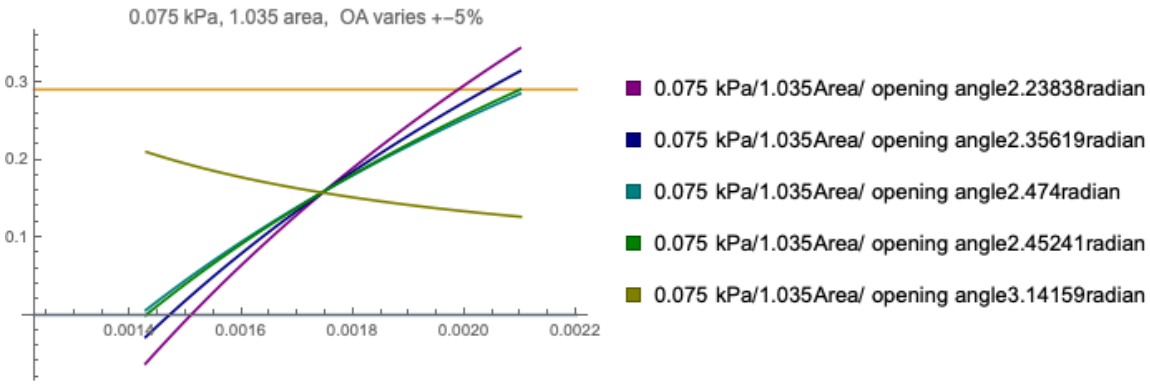


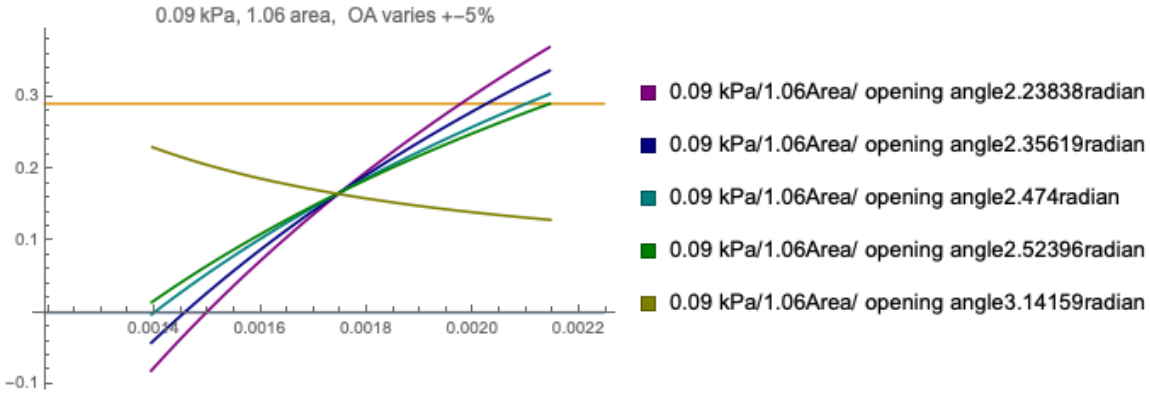
Figure 4.6: Hoop stress vs. radius as opening angle varying with fixed pressure and area using Neo-Hookean Model

4.1.3 Both Growth and Remodeling

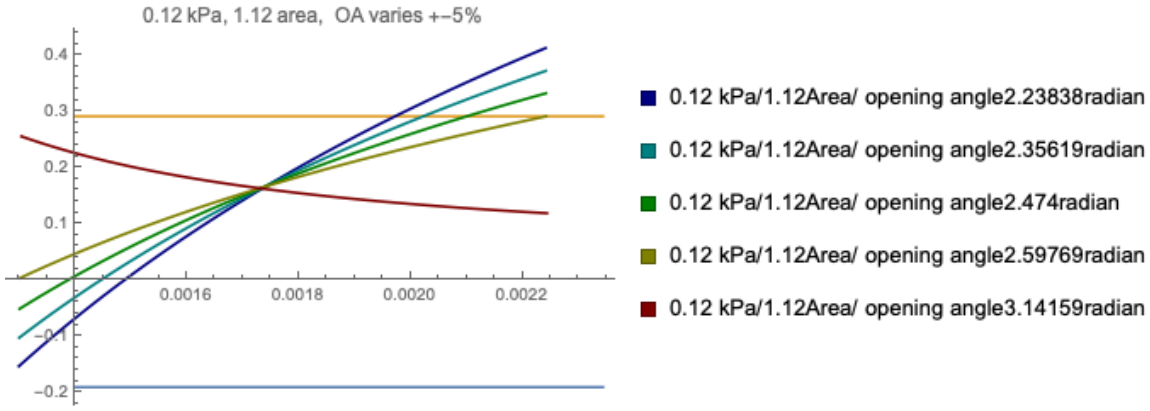
As we can see in the previous sections, growth and remodeling individually have an impact on reducing the maximum hoop stress, but using only one of them cannot bring hoop stress down to the target value. Therefore, we conduct experiments with both growth and remodeling. Figure 4.7 shows the hoop stress at the certain level of pressure and growth by changing opening angles.



(a) 1.25Pressure, 1.035Area



(b) 1.5Pressure, 1.06Area



(c) 2.0Pressure, 1.12Area

Figure 4.7: How much angle changes for each pressure and increased area using Neo-Hookean Model

Table 4.1 displays the values of how much area and opening angle need to be increased to match the target values as pressure increased from the experiments of figure 4.7. Here, the target

values are the maximum and minimum hoop stress under normal pressure.

Pressure	0.06	0.075	0.09	0.12
Area	A	$1.035A$	$1.06A$	$1.12A$
Opening Angle	Θ_o	$1.0408\Theta_o$	$1.0712\Theta_o$	$1.1025\Theta_o$

Table 4.1: Triplet (Pressure, Area, Opening Angle) having target hoop stress using Neo-Hookean Model

When pressure is 25% increased, if area increased by 3.5% and opening angle increased 4.08%, then the hoop stress value will match to the target values. When pressure is 50% increased, if area increased by 6% and opening angle increased 7.12%, then the hoop stress value will match to the target values. When pressure is 100% increased, if area increased by 12% and opening angle increased 10.2%, then the hoop stress value will match to the target values.

4.2 Result using Holzapfel-Ogden Model

Holzapfel and Ogden used $c = 3$ kPa, $k_1 = 2.3632$ kPa, and $k_2 = 0.8393$ (no dimension) in their paper [10]. So here we choose the same values but non-dimensionalize the equation by c. In code, we use $c = 1$, and $k_1 = 2.3632/3 = 0.7877$. Figure 4.8 has 5 hoop stress lines; the lowest line is hoop stress distribution at the intermediate configuration, and the second lowest line is when the pressure is normal. Note that we choose 0.25 as the normal pressure for the same reason as the neo-Hookean model; the arteries are tensile through the wall after pressurizing. Thus, we set a normal blood pressure for Holzapfel-Ogden model as 0.25. Also, the top three lines are when pressure is increased by 25%, 50% and 100% from the bottom, respectively. Basically, we carry out the same experiments as the neo-Hooken model but using the above constants and the Holzapfel-Ogden model.

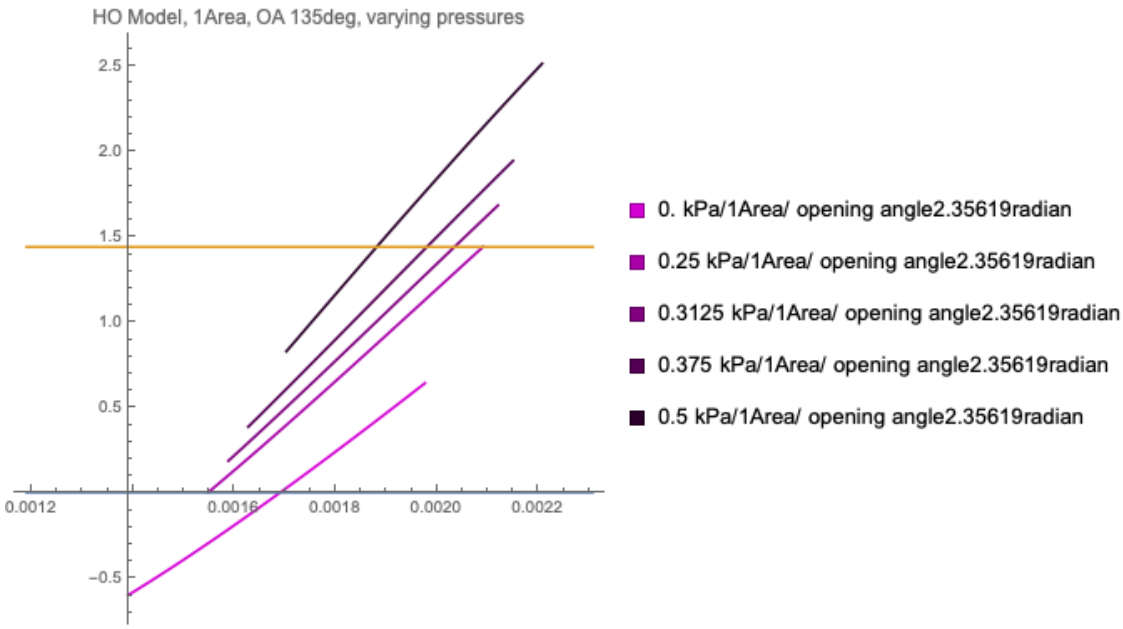


Figure 4.8: Hoop stress vs. radius when pressure 0, 0.25, 0.3125, 0.375, and 0.5 using Holzapfel-Ogden Model

4.2.1 Growth

Figure 4.9 and figure 4.10 show that the hoop stress graphs while growing happens at a certain level of pressure and an opening angle using the Holzapfel-Ogden model. Similar to the result of using the neo-Hookean model, as area increases (i.e., growth), the maximum hoop stress values get smaller than the previous level of growth in general. However, either it is not enough to reach the hoop stress value at the normal pressure or the arterial wall becomes compressive at the inner wall.

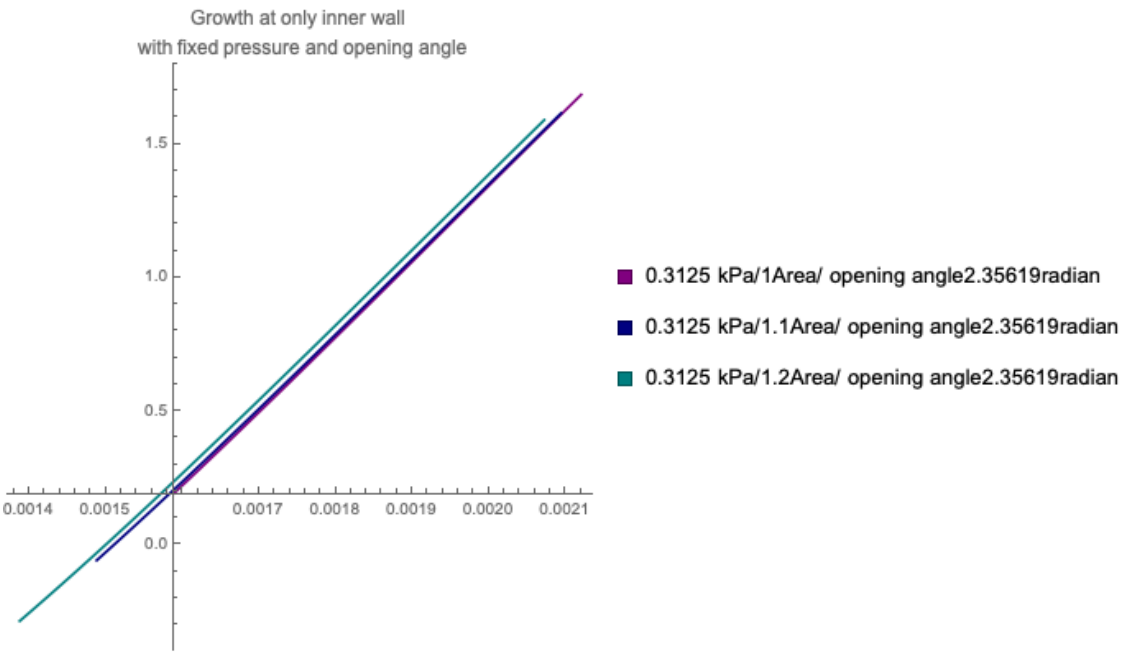


Figure 4.9: Hoop stress vs. radius when growth happens at the inner wall using Holzapfel-Ogden Model

In particular, if growth occurs at both the inner and outer wall (see figure 4.10), the maximum hoop stress decreases in the early stage, but at some point, the wall grows too much so that it is beyond the preferred maximum hoop stress.

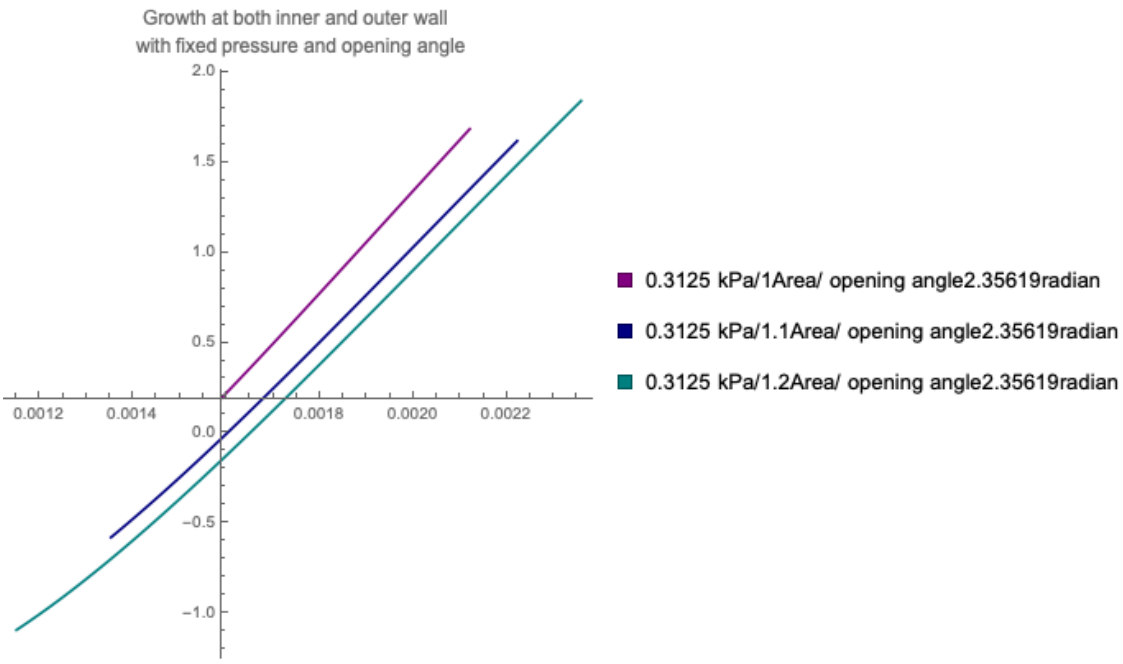


Figure 4.10: Hoop stress vs. radius when growth happens both the inner and outer wall using Holzapfel-Ogden Model

4.2.2 Remodeling : Change Opening Angle

Holzapfel-Ogden Model shows a similar result for the remodeling as well; as opening angle increases, hoop stress decreases. Figure 4.11 is hoop stress as the opening angle increased by 5% and 10% when pressure is 0.375 without growth. Likewise, the cases of other pressures have similar trends, so we skip presenting.

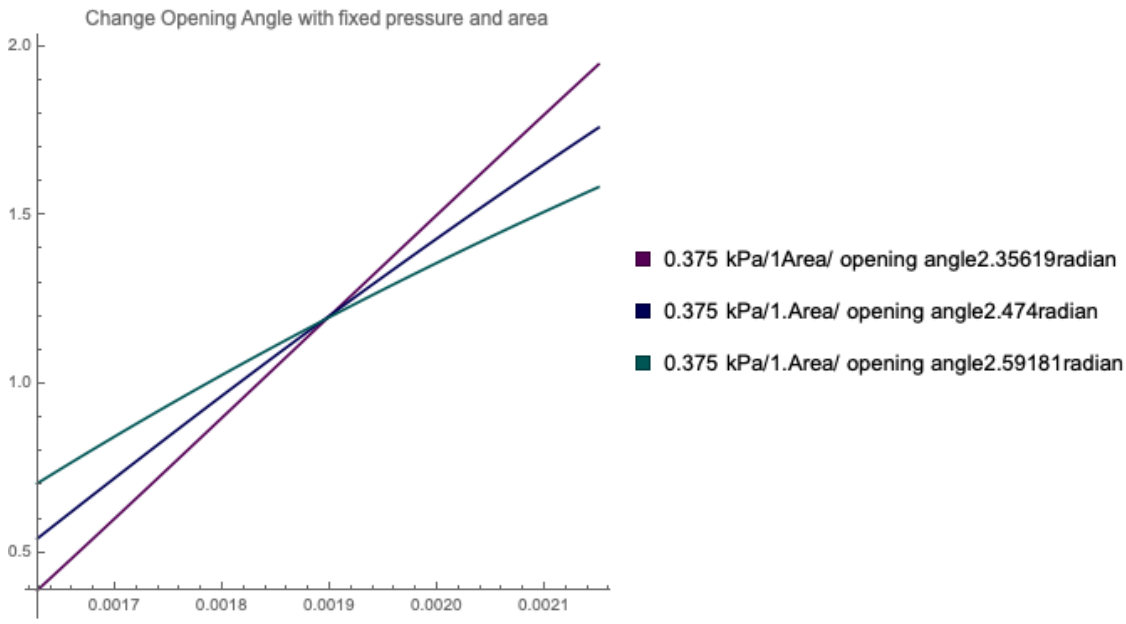
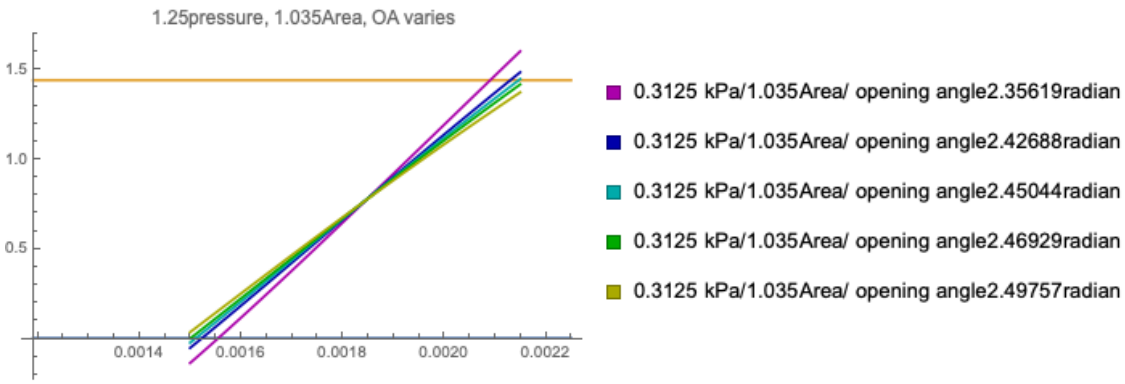


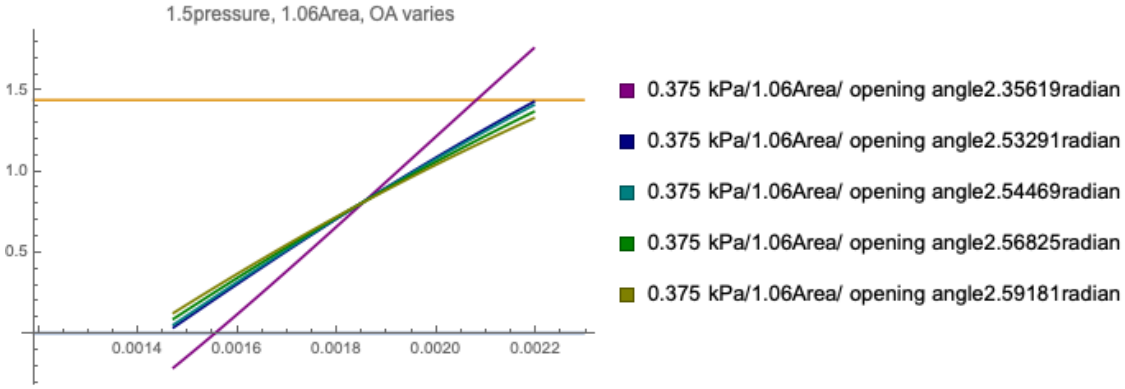
Figure 4.11: Hoop stress vs. radius as opening angle varying with fixed pressure and area using Holzapfel-Ogden Model

4.2.3 Both Growth and Remodeling

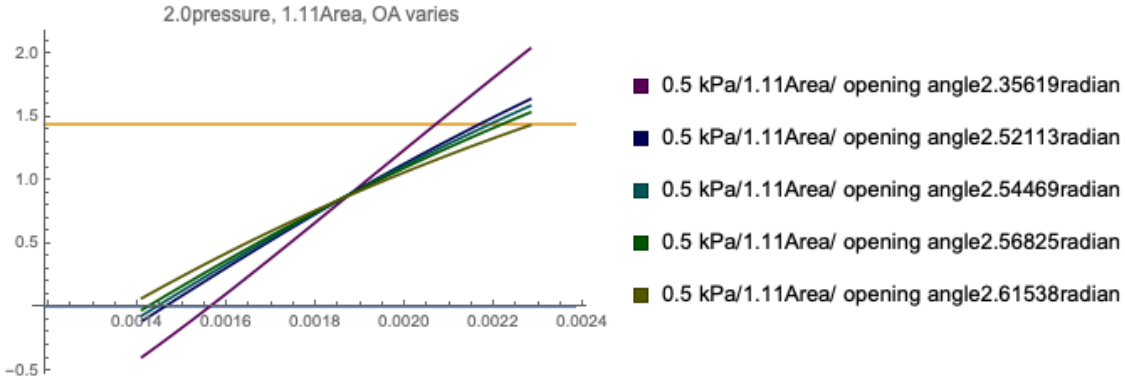
Figure 4.12 represents the hoop stress at a certain level of pressure and growth according to the change of opening angle.



(a) 1.25Pressure, 1.035Area



(b) 1.5Pressure, 1.06Area



(c) 2.0Pressure, 1.11Area

Figure 4.12: How much angle changes for each pressure and increased area using Holzapfel-Ogden Model

Table 4.2 shows that the area, opening angle and pressure which are needed to reach the maximum and minimum hoop stress of the setting that area is A, opening angle is Θ_o and pressure is normal. As pressure increased, the area and opening angle need to be increased to get the same

value of hoop stress of normal pressure. That is, growth and remodeling both are necessary.

Pressure	0.25	0.3125	0.375	0.5
Area	A	$1.035A$	$1.06A$	$1.11A$
Opening Angle	Θ_o	$1.048\Theta_o$	$1.075\Theta_o$	$1.11\Theta_o$

Table 4.2: Triplet (Pressure, Area, Opening Angle) having target hoop stress using Holzapfel-Ogden Model

5. CONCLUDING REMARK

We have discussed ways that the arterial wall controls elevated hoop stresses due to hypertension. First, we formulate a stress-strain relation using nonlinear elasticity. Our material body is incompressible, isotropic and anisotropic, and residually stressed. Also, the geometry we used is an axisymmetric cylindrical tube. Then semi-inverse approach helps us formulate the circumferential stress function in terms of r, which is in the current configuration. In particular, we simulate the situation that the arterial wall is traction-free at the boundary of the intermediate configuration, and the internal pressure is given at the inner wall of the current configuration and traction-free at the outer wall.

5.1 Summary of the experiments

In both isotropic and anisotropic cases, in general, growth can reduce the circumferential stress, but whether or not it does can be influenced by where growth occurs. When growth happens, the inner and outer radii in the deformed configuration can change. We consider two possibilities. One is during growth, the outer radius remains fixed, and only the inner radius changes in the deformed configuration. The second case is that during growth, the inner and outer radii change at the same rate. In our results, if growth only changes the inner radius, then the maximum hoop stress decreases with growth. In contrast, if both inner and outer radii change at the same rate, in the initial face of growth, the maximum hoop stress reduces; if growth exceeds a certain level, then the maximum hoop stress increases again. It shows that growth alone cannot bring the maximum hoop stress to the target value. Also, growing mostly gives us a compressive arterial wall near the inner wall while pressurizing.

Secondly, if the opening angle increases, which we define as remodeling in this dissertation, then the maximum hoop stress decreases. Precisely, the hoop stress graph is flatter than that of the previous level of opening angle. In other words, changing the opening angle is not only reducing the maximum hoop stress but also increasing the minimum hoop stress.

Therefore, we start to combine growth and remodeling, and it successfully restores the maximum hoop stress when we use both methods together. Also, it leads to the arterial wall not compressive at the inner wall, which is the desired state after loading.

5.2 Future Work

5.2.1 Future work for more directly related to this dissertation

The easiest thing we can do next is to release our idealization. For example, the followings are all our options: using the generalized tube, taking the mechanical features like slightly compressible, and/or introducing the two-layered, three-layered model, using different constitutive relations.

We have talked about there exists a triplet (pressure, growth, and remodeling) that makes arteries have normal circumferential pressure. We have not confirmed there are other triplets to have the same situation. If they exist, choosing the "best" triplet will be the next question.

We may complexify the geometry of an artery from a cylinder to a tube having bifurcation, which is actually the location that vascular diseases like aneurysms take place. As another option, we can implement numerical experiments using a periodic function of pressure instead of having a constant inner pressure, which is a closer simulation of heart pumping.

It will be interesting to couple modeling the arterial wall with blood flow as the review paper [45] suggested. In this case, the advantage of the usage of the current configuration will be emphasized.

5.2.2 Requirement/Request for the Ultimate Future work

More work is needed to better understand the mechanobiology of residual stress in the arterial wall. In particular, it is insufficiently understood how the cells (fibroblasts and smooth muscle cells) in the arterial wall modify the residual stress through the synthesis of collagen and cell hypertrophy (cell growth) and hyperplasia (cell division). Once we better understand these processes, we can then create more complex models for making predictions of the rate at which these mechanobiological mechanisms can mitigate the effects of chronic hypertension. If there were studies about the rates of growth in an arterial wall under hypertension or the rates of remodeling,

we could build a time-dependent model so that we can get a more precise prediction in terms of time. The rate of adding/increasing mass may replace the rate of growth like in [12, 13]. Studying the rate of remodeling can be demanding because there is no consistent definition of remodeling over the field, and there are too many factors that can change the mechanical properties.

All the above cases are ultimately to simulate and illustrate the event more realistically to predict the next steps or the next outcomes. More accurate models eventually provide proper treatments or prevent disease outbreaks, and so on. The mathematical framework is more indispensable when it comes to predict events without expensive experiments or inevitable damages on specimens. However, to be confirmed the framework is reasonable, we must cooperate with experiments in the laboratory. It will be important that collaborating with mathematical, experimental, and clinical studies.

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APPENDIX A

DETAILS OF COMPUTATIONS

A.1 Derivative of a tensoral valued function

$$D_{\boldsymbol{F}}\phi(\boldsymbol{F})[\boldsymbol{H}] = \partial_{\boldsymbol{F}}\phi(\boldsymbol{F}) \cdot \boldsymbol{H}, \text{ for every } \boldsymbol{H} \in \mathcal{T}^2.$$

If $\phi(\boldsymbol{A}) = tr(\boldsymbol{A})$, then $D_{\boldsymbol{A}}tr(\boldsymbol{A})[\boldsymbol{H}] = tr\boldsymbol{H}$.

If $\phi(\boldsymbol{A}) = \boldsymbol{A}\boldsymbol{A}^T$, then $D_{\boldsymbol{A}}\phi(\boldsymbol{A})[\boldsymbol{H}] = \boldsymbol{A}\boldsymbol{H}^T + \boldsymbol{H}\boldsymbol{A}^T$.

If $\psi(\boldsymbol{A}) = tr(\boldsymbol{A}\boldsymbol{A}^T)$, then

$$D_{\boldsymbol{A}}\psi(\boldsymbol{A})[\boldsymbol{H}] = tr(\boldsymbol{A}\boldsymbol{H}^T + \boldsymbol{H}\boldsymbol{A}^T) = 2\boldsymbol{A} \cdot \boldsymbol{H}$$

Thus,

$$\partial_{\boldsymbol{A}}\psi(\boldsymbol{A}) = 2\boldsymbol{A}. \tag{A.1}$$

A.2 Gradient of the vector valued function in the cylindrical coordinates

A vector values function $\boldsymbol{v} = v_r\boldsymbol{j}_1(\theta) + v_\theta\boldsymbol{j}_2(\theta) + v_z\boldsymbol{j}_3$, where $\{\boldsymbol{j}_1(\theta), \boldsymbol{j}_2(\theta), \boldsymbol{j}_3\}$ is a basis for cylindrical coordinates.

$$\nabla\boldsymbol{v} = \frac{\partial v_r}{\partial r}\boldsymbol{j}_1(\theta) \otimes \boldsymbol{j}_1(\theta) + \frac{1}{r}(\frac{\partial v_r}{\partial \theta} - v_\theta)\boldsymbol{j}_1(\theta) \otimes \boldsymbol{j}_2(\theta) + \frac{\partial v_r}{\partial z}\boldsymbol{j}_1(\theta) \otimes \boldsymbol{j}_3$$

$$+\frac{\partial v_\theta}{\partial r}\boldsymbol{j}_2(\theta) \otimes \boldsymbol{j}_1(\theta) + \frac{1}{r}(\frac{\partial v_\theta}{\partial \theta} + v_r)\boldsymbol{j}_2(\theta) \otimes \boldsymbol{j}_2(\theta) + \frac{\partial v_\theta}{\partial z}\boldsymbol{j}_2(\theta) \otimes \boldsymbol{j}_3$$

$$+\frac{\partial v_z}{\partial r}\boldsymbol{j}_3 \otimes \boldsymbol{j}_1(\theta) + \frac{1}{r}\frac{\partial v_z}{\partial \theta}\boldsymbol{j}_3 \otimes \boldsymbol{j}_2(\theta) + \frac{\partial v_z}{\partial z}\boldsymbol{j}_3 \otimes \boldsymbol{j}_3.$$

A.3 Solve the equation (2.9)

$$\frac{1}{(1-\eta')(1-\frac{\eta}{r})(1-\lambda)} = 1.$$

$$(1-\eta')(1-\frac{\eta}{r}) = \frac{1}{(1-\lambda)}.$$

Let $\tilde{\eta} = r - \eta$.

$$\tilde{\eta}'\tilde{\eta} = \frac{r}{(1-\lambda)}.$$

$$\frac{(\tilde{\eta}^2)'}{2} = \frac{r}{(1-\lambda)}.$$

Take integral with respect to r,

$$\tilde{\eta}^2 = \frac{r^2}{(1-\lambda)} + c.$$

$$\tilde{\eta} = \pm\sqrt{\frac{r^2}{(1-\lambda)} + c.}$$

$$r - \eta = \pm\sqrt{\frac{r^2}{(1-\lambda)} + c.}$$

$$\eta = r \mp \sqrt{\frac{r^2}{(1-\lambda)} + c.}$$

We need to choose $-$ sign since the definition of displacement is $\eta(r) = r - \rho$,

The square root part is positive, and $0 < \rho_i \leq \rho \leq \rho_o$.

Therefore,

$$\eta = r - \sqrt{\frac{r^2}{(1-\lambda)} + c.}$$