Influence of plaque-components on the
stability of an atherosclerotic lesion

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# Table of Contents

1 Introduction ................................................................. 3
  1.1 Current Research .................................................. 3
  1.2 Objectives ............................................................ 4
  1.3 Outline ............................................................... 4

2 Background .................................................................. 5
  2.1 Coronary Heart Diseases .............................................. 5
  2.2 Atherogenesis ........................................................... 6
  2.3 Atherosclerotic Plaque ............................................... 8
  2.4 Plaque Rupture ........................................................ 10
  2.5 Consequences ........................................................ 11

3 Methods and Techniques ................................................... 12
  3.1 Assumptions Geometry ................................................. 12
  3.2 Finite Element Modelling ............................................. 16
  3.3 Structural Analysis ................................................... 22

4 Results ......................................................................... 25
  4.1 Introduction ............................................................. 25
  4.2 Analyzes ................................................................. 28

5 Conclusion and Discussion ................................................... 35
  5.1 Introduction ............................................................. 35
  5.2 Discussion .............................................................. 37
  5.3 Limitations and Continuation ....................................... 37

A ANSYS files ................................................................. 39

B CT filter .......................................................................... 45

Bibliography .................................................................... 49
Preface

This research was performed at the Petit H. Parker Institute of Bioengineering and Bioscience, a joint department of the Georgia University of Technology (GeorgiaTech) and the Emory University School of Medicine in Atlanta, USA. The study was part of the master program of Biomedical Engineering at the Eindhoven University of Technology (TU/e) in the Netherlands. I should mention that I was supported AMC Research in Amsterdam, TU/e and GeorgiaTech.

My study contributes to a research project guided by RP Vito. The research group consists of approximately 10 researchers, varying from PhD to bachelor students, and are working with mechanical aspects of coronary atherosclerosis. It is part of a large scale research program by the Bioengineering Research Partnership (BRP), a group of investigators from both Emory and GeorgiaTech with WR Taylor as principal investigator.

I would like to thank Raymond Vito, my supervisor at GeorgiaTech, for his many suggestions and constant support during this research. I am also thankful to Peter Carnell for his interest in my work and for supplying me with some results of his work, which gave me a better perspective on my own results. Without his encouragement and his many useful hints, I would have never got this far. I should really thank Donna Brown, Carlijn Bouten, Frans van der Vosse and Bas de Mol for making a study abroad really happen.

Of course, I am grateful to my family and friends for making my time in the USA really great, and for supporting me at all times. Last but not least, I owe a lot to my Dutch colleague Ivo Willems, who not only made my stay in Atlanta really great, but also shared with me his knowledge of finite element analysis and provided many useful references and friendly encouragement.

Eindhoven,
Ewout van der Laan
Chapter 1

Introduction

1.1 Current Research

According to estimates of the American Heart Association for 2002\(^1\), 12.6 million Americans have a type of coronary heart disease. That is more than 4% of the entire population of the United States, a number that will not differ from the rest of the Western countries. Although the death rate from heart attack declined with 25% the last decade \([13]\), coronary heart disease caused more than 500,000 deaths in 1999. It is thereby the single leading cause of death in America today. Fortunately, changes in western lifestyle, advanced diagnostic methods and more adequate treatments cause a steady decline of the number. But still more research is needed to fully understand the genesis, development and consequences of these diseases. With this knowledge adequate diagnosis and treatment methods can be developed.

In the past, many 2D-models have been presented in which the role of certain plaque constituents were investigated \([16, 8, 23, 7, 12]\). Also, ways to identify the plaque morphology are studied \([23, 11, 19]\). Throughout the years more insight in the mechanical behavior of plaque structure is gained \([2, 9]\). So, over the past decades a more consistent picture of the atherosclerotic lesion and plaque vulnerability is arising. Researchers agree that successfully coupling of experimental data with modelling will lead to a complete understanding of vascular mechanical behavior.

The research group of dr. Vito is currently working on a project that will investigate the influence of morphological differences in atherosclerotic plaques. A 3D finite element model of such a plaque will be created from images of a fixed artery that are obtained by micro-computed tomography (μCT) scans. μCT-scanning provides detailed information about the interior microstructure of tissue, in general with a spatial resolution of 100 μm. It is capable of 3D

\[^1\text{http://www.americanheart.org}\]
reconstruction without disruption or destruction of tissue like standard histomorphometric procedures. Unfortunately, it cannot sufficiently distinguish between the different components of a plaque (e.g. lipid and collagen), because the attenuation does not differ enough. Therefore, staining techniques are used and applied on cross-sectional slices of the same fixed artery. With a complex process of slicing, fixing and staining, it is possible to indicate the areas with the tissue of interest and thus to provide the histology data. The images from CT and the histology data from the sliced artery are combined to reconstruct a realistic 3D model of the artery. In this model the different plaque components are incorporated which legitimate an extensive analysis.

1.2 Objectives

This study, as a preliminary part of the research mentioned above, focusses on a simplified model of a coronary artery cross-section. The objective is to construct a 2D finite element model of a human coronary artery based upon images of cross-sections found in literature. In addition, structural analysis on the influence of morphology on plaque stability will in the first place help gain experience in working with finite element method, could also confirm existing theories on plaque stability and may finally provide new perspectives for further research in this group.

A second objective is to use 2D micro-CT images from an artery to reconstruct a 3D FE model, where at this point the artery is considered to be homogenous, so with no distinction between its components. This can be seen as an experimental phase in the research, and - although promising - is therefore included in the appendix. In further research this method may be used and be coupled with the histology data to obtain a true 3D representation of a human coronary atherosclerotic artery.

1.3 Outline

This report will discuss how such a simplified 2D model is created step-by-step. Some physiological background on the issue with regard to atherosclerosis and plaque rupture will be provided in chapter 2. Based on this knowledge, some basic assumptions will be made with respect to building the finite element model. These assumptions, the model and the analysis can be found in chapter 3. The results of this analysis are shown in the following chapter. Some conclusions are drawn and a discussion of the research and its outcome follows in chapter 5. As explained above, additional research has been done on importing $\mu$CT-images into finite element modelling and the result of this is put in an appendix.
Chapter 2

Background

2.1 Coronary Heart Diseases

Coronary atherosclerosis is the most frequent cause of ischemia of the heart, the clinical outcome of coronary heart diseases [4]. Atherosclerosis (AS) is a type of arteriosclerosis, which is the general term for the thickening and hardening of arteries. It comes from the Greek words athero (meaning gruel) and sclerosis (hardness). Atherosclerosis affects large and medium-sized arteries. The type of artery and the location where the plaque develops varies in each person. It is a process that comprises fatty build-ups in the arteries and thereby narrowing the lumen. Although the build-ups are essentially soft tissue, atherosclerosis is considered as hardening of the artery.

Atherosclerosis is a slow, progressive disease that often starts in childhood. In some people this disease progresses rapidly in their third decade. With others it doesn’t become threatening until they are in their fifties or sixties. Therefore coronary atherosclerotic disease is predominantly an asymptotic process. The reduced flow to the heart presents clinically as angina pectoris and can be stable for many years. Disruption and fissuring of the thickened wall, a so-called rupture, could lead to thrombosis and acute coronary syndromes, like myocardial infarction and sudden death. The following sections will describe the main principles and processes that are held responsible for the initiation, progress and consequences of atherosclerosis as far as known today.
2.2 Atherogenesis

The induction of atherosclerotic lesions in the arteries, that is atherogenesis, often starts in the early years of life. It can be found in many arteries of the human circulation, but in this thesis the coronary arteries are of interest because clinical significant events are primarily caused by coronary atherosclerosis.

The sequence of events leading to atherosclerosis is complex, and includes the interaction of several processes. Many pathophysiological studies and vascular research led to a hypothesis formulated by Ross [18]. It states that endothelial cell damage results in a response-to-injury. The reaction to this damage is a precursor in the evolution of atherosclerosis. The damage may be caused a number of factors, but mostly it is due to the endothelial sensitivity to stresses and its apoptotic responses. Therefore, it is generally assumed that atherosclerosis arises through the following two mechanisms: inflammatory and mechanical mechanisms [18].

Inflammatory mechanisms

The most recent version of the Ross hypothesis emphasizes the endothelial dysfunction rather than damage. Free radicals, hypertension, diabetes mellitus, infections, genetic alterations or injury are possible causes for this dysfunction. Circulating vasoactive and toxic materials may cause modifications in the endothelial function. But the major cause of injury to the endothelium are the low-density lipoproteins (LDL), like cholesterol. That is why elevated levels of LDL in the blood (hypercholesterolemia) is detected in almost 50% of patients with some kind of cardiovascular disease (CVD).

When a LDL becomes trapped in an artery, it undergoes oxidation and becomes internalized by macrophages due to receptors on the surfaces. These cells are now called foam cells. Removal of modified LDL is an important protective initial role of the macrophage. LDL itself may stimulate the replication of macrophages out of monocytes and the entry of new monocytes. Antioxidants like vitamin E have an anti-inflammatory effect and increase the resistance of LDL to oxidation (in proportion to the vitamin E concentration).

Endothelial dysfunction leads to compensatory responses. If the inflammatory response does not remove the offensive agents, it stimulates fibrogenesis and migration and proliferation of vascular smooth muscle cells (VSMC). The fibrogenesis results in large amounts of collagen in the lesion. In addition to VSMC, macrophages and lymphocytes also participate in lesion formation and in the modification of its composition [1]. At the same time, fat builds up within and around these cells and form the connective tissue. All of these components together comprise the extracellular matrix (ECM). Metalloproteinases (MMP) are enzymatic enzymes...
that selectively digest the individual components of the ECM. For example, MMP-1 breaks down the fibrillar collagen and thus the vessel integrity and are undoubtedly very important in the research of atherosclerotic stability.

The innermost layer of the artery becomes markedly thickened by these accumulating cells and surrounding material. The build-up that results is called plaque. When the lumen diameter of the vessel stays constant, the process is called positive remodelling because there is a compensatory enlargement of the lumen. At a certain point, the arterial wall can no longer compensate and this luminal restriction causes alteration of blood flow, thus decreasing the oxygen supply. This is known as negative remodelling (detectable by angiography). When the consequent stenosis is sufficiently severe, the plaque may partially or totally block the blood’s flow through an artery causing ischemia.

![Figure 2.1: Process of atherosclerosis](image)

**Hemodynamic factors**

Studies have shown that the location of plaque often involves regions of flow with a high Reynolds-number, that is near branches where the velocity gradients of the flow are small. The effect of this low velocity should be an increase in transport rate of especially lipids.
A recent in vitro study showed that low mean shear stress favors monocytes to bind to endothelial cells [20]. Plaques tend to develop in locations where wall shear stress is relatively low and changes of direction in the course of the cardiac cycle. Such regions are sites of increased residence for particles in the circulation. That is, particles tend to remain in this area during several cardiac cycles, exposing the area to increased contact with reagents compared to sites of elevated and unidirectional shear stress.

It is proposed that shear stress oscillations, which are heart rate dependent, enhances plaque localization. This occurs in those regions of the arterial tree, where flow reversal during end systole is a characteristic feature of the flow velocity profile. With alterations in the flow of blood, specific adhesion molecules form on the endothelium that are responsible for the migration of monocytes and T-cells. Also, shear stress responsible elements (SSRE) in the arterial wall contribute to this [18].

![Figure 2.2: Process of Atherosclerosis (http://www.americanheart.org)](http://www.americanheart.org)

### 2.3 Atherosclerotic Plaque

As explained earlier, there are a number of inflammatory and hemodynamic factors that can be held responsible for the origin of atherosclerotic plaque, which mainly consists of fatty deposits in the arterial wall. Besides these fatty substances, there are a lot of other molecules that are of importance in the plaque build-up and stability. The following table sums up these components and explains their function in a few words.
Collagen: Mostly collagen I; it is not equally present in the plaque and it hardens the plaque locally \[17\].

Calcium: Results in stiffening and extra strength. Although coronary artery calcification is associated with severe cardiovascular prognosis, the influence of calcium on the stability of the plaque is questionable.

Vascular smooth muscle cells (VSMC): They have a constructive role. The populations of VSMC and macrophages strongly vary across the plaque cap.

Macrophages: They have a destructive role by inducing collagen breakdown. With more macrophages, the plaque weakens locally.

Endothelial cells (EC): The response to damage or dysfunction of these cells are primarily the cause of atherogenesis.

Metalloproteinase (MMP): Regions of MMP activity potentially increase the susceptibility of atherosclerotic lesion to complications associated with plaque rupture \[9\]. Evidence has been presented \[14\] that overexpression of MMP colocalizes with regions of high stresses.

LDL: These are held responsible for the initiation of atherosclerosis and are involved right from the early stages. High concentrations of LDL in the blood definitely influence the progress of AS. Further, oxidized LDL regulates MMP-9 expression.

Monocytes: They induce MMP-1 and MMP-3 secretion by VSMC. They are present in all stages of the atherosclerosis and are precursor of macrophages.

T-cells: They migrate into the arterial cells together with monocytes. They replicate in the lesion as well as monocyte-derived macrophages. T-cell activation by macrophages or VSMC through oxidized LDL results in the secretion of cytokines that amplify the inflammatory response. In this way they contribute to instability of the lesion \[10\].

Platelets: They adhere to dysfunctional EC, collagen and macrophages, while releasing growth factors and cytokines. They are very important in maintaining vascular integrity.

For simplicity, in literature the plaque is often sectioned into a number of components. The first one being the lipid pool where LDL cholesterol is internalized by macrophages - the foam cells - and is therefore sometimes called the necrotic core. Secondly, the accumulation of collagen and fibrous tissue is called the fibrous cap. We define a fibrous cap as a distinct layer of connective tissue covering the lipid core. The fibrous cap consists purely of smooth muscle cells with varying degrees of infiltration by macrophages and lymphocytes. Thus, a fibrous
Cap atheroma may have a thick or thin cap overlying a lipid-rich core [23]. Fibrous caps vary widely in thickness, cellularity, matrix, strength and stiffness, but they are often the thinnest in at their shoulder region, where disruption most frequently occurs [5]. Thirdly, advanced lesion are often characterized by large concentrations of calcium, called the calcified region. Although coronary artery calcification with worse cardiovascular prognosis, the influence of calcification on bio-mechanical plaque stress is questionable [8].

2.4 Plaque Rupture

Stable advanced lesion usually have uniformly dense fibrous caps [18]. The unstable atheroma characteristically has a thin, eccentric fibrous cap and a large necrotic core of lipid and cellular debris. This plaque configuration is particularly unstable because large mechanical stresses develop in the thinnest portions of the fibrous cap over the lipid pool. It is suggested that uneven thinning often occurs at the shoulder of the cap, where macrophages enter, accumulate and are activated [18]. Low density lipoprotein cholesterol in the lesion plays a significant role in most or all of these processes, and our current understanding of the unstable atheroma is consistent with the clinical successes of lipid-lowering therapy [12].

It seems that there are critical stages in the progress of the disease where the lesion becomes unstable or vulnerable. This means that the tissue matrix could rupture, and this disruption could lead to a thrombus. Although many aspects have been studied intensively throughout the past decades, the exact mechanism that causes the disruption is not yet fully understood. Therefore, a proper quantitative definition of a plaque that is about to rupture, the so-called plaque vulnerability, is still not present. In order to define a plaque more quantitatively, three stages of development are describe [17]:

**Stage III** lipid pool > 40% of the area or the macrophage density is five times the density of endothelial cells (EC) or there is evidence of previous thrombotic material.

**Stage II** lipid pool > 20% of the area or the macrophage density equals the density of the endothelial cells.

**Stage I** the development is less advanced. In addition, the different stages could also be indicated by + or - representing a positive or negative remodelling.

It has been postulated that there are three features of a vulnerable plaque: the lipid pool, the presence of a thin fibrous cap and a region of inflammatory cells.
Earlier studies suggested that reducing the fibrous cap thickness dramatically increases peak circumferential stress in the plaque [15] and thus plaque instability [5]. From a recent study of > 200 sudden death cases, ≈ 60% of acute thrombi resulted from rupture of thin cap atheroma [23]. This could explain why the cause of myocardial infarction is not always detectable on angiography, which only shows stenosis severity. An increase in fibrosis and its related adventitial thickening is associated with greatly negative remodelling [21]. The mechanisms of fibrous cap thinning is not known. There is, however, evidence for extensive apoptosis of smooth muscle cells within the cap of advanced atherosclerosis. A thin fibrous cap would rupture because its inability to maintain the cap matrix.

Large lipid pools can already be found in the stages of positive remodelling [21] but are also common features of a ruptured lesion [8]. Other factors that contribute to instability include inflammation and infiltration of macrophages and lymphocytes [10]. MMP activity in the lesion breaks down the structural integrity of extracellular matrix (ECM) [9] and are recognized markers for vulnerability. Of all the morphological features associated with rupture, cap thinning seems to be be he most critical [10].

### 2.5 Consequences

The understanding of the pathology of the atherosclerotic lesion is still continuing to grow. It has become clear that not all abnormalities of the vascular system have clinically significant effects. Coronary atherosclerosis can progress and be stable for decades, often with angina pectoris (chest pain) as the most significant complaint as a result of a reduced oxygen supply to the heart. Ischemia of the heart on the other hand, does often result in irreversible damage. There are two things that can happen when a plaque is vulnerable, that is bleeding (hemorrhage) into the plaque and the formation of a blood clot (thrombus) on the plaques surface. If either of these occurs and blocks the entire artery, the oxygen supply to the heart muscle is reduced and a heart attack may occur. If the oxygen supply to the brain is cut off, a stroke is the clinical outcome. Lack of oxygen supply to the extremities could result in gangrene.

It is widely accepted that, although the exact process of atherosclerosis is not yet understood, there are a number of risk factors: age, male, blood pressure, hypertension, smoking, familial hyperlipidemia, elevated levels of fasting LDL such as cholesterol [23]. Cigarette smoke greatly aggravates and speeds up the growth of atherosclerosis in the coronary arteries, the aorta and arteries of the legs.
Chapter 3

Methods and Techniques

It is generally assumed that local tissue stress in the plaque area strongly contribute to the plaque instability. Finite element models are a useful tool in analyzing stress distributions. But unfortunately, not many three dimensional FE models are present that relate high stress regions and morphology. As mentioned in chapter 1.2, Vitos group is trying to build such an extensive model. This study is a start in this attempt and focusses on creating a simplified cross-section of a heavily stenosed coronary artery. Before describing the steps to build such a representation of a diseased vessel wall, some assumptions have to be made with regard to its geometry and the finite element modelling.

3.1 Assumptions Geometry

This section will describe the geometrical simplifications of a plaque that were made based on literature. As proposed in chapter 2.3, a lesion can roughly be sectioned in the following artery components:

- Lumen Area (LA)
- Fibrous Cap Tissue (FC)
- Lipid Pool (LP)
- Calcified Region (CA)
- Disease-free tissue (DF)

These components will be used in the basic geometry. The disease-free tissue (DF) consists of the adventitia, the media and cellular fibrosis, but are considered as one for simplicity. The adventitia and the media together form the wall area (W), which will be used later on in some calculations.
There is a great number of studies [6, 8, 10, 13, 16, 15, 23, 14, 22, 24] that present cross-sectional images of a stenotic artery. Not all studies make use of this same differentiation of components, some are more complicated while others confine themselves to a few components. The images in this studies are obtained by a number of methods, e.g. from intravascular ultrasound (IVUS) or by digitizing histological cross-sections. Some of them are shown in figure 3.1 and are partially used to define the geometry created in this study.

![Cross-sections](image)

**Figure 3.1:** Cross-sections

Before designing a simplified representation of such an artery, some preconditions are formulated with respect to the morphology. There has to be little calcification, as the emphasis will be on the lipid pool and the fibrous cap. An artery with advanced stenosis and an eccentric lumen area are desired, because arteries in advanced stages of atherosclerosis are less stable. Furthermore, an asymmetrical fibrous cap is a precondition, as this often yield interesting stress distributions. Lastly, a large asymmetrical lipid pool is often related to progressive atherosclerosis and is therefore also included.

Considering all this, the model shown in figure 3.2(a) has become the Basic Geometry (BG), which meets simplicity and reality. The values of the dimensions from figure 3.2(b) can be found in table 3.1. The vessel radius is the only dimension that is more or less estimated (2.0 mm). The other dimensions are chosen such that the area of the component agrees with areas found in literature. These areas are found in table 3.2, and are build up as follows.

The plaque area (PA) is the sum of areas of the lipid pool, the calcification, de fibrous cap and the disease-free zone minus wall area. So, \( PA = LP + CA + FC + DF - W \)

The lipid pool, the calcification and the fibrous cap are percentages of the plaque area. The
percentage stenosis (lumen reduction) is defined as the ratio of the plaque area and the total area minus the wall area: \( \text{Stenosis} = \frac{PA}{(Total - W)}. \)

This Basic Geometry will be used to build a finite element model. The next section will describe the steps taken to create this model and the choices that were made with respect to elements and material properties.

<table>
<thead>
<tr>
<th>Description</th>
<th>Parameter</th>
<th>Value [(\mu m)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vessel radius</td>
<td>r1</td>
<td>2000</td>
</tr>
<tr>
<td>Lumen radius</td>
<td>r2</td>
<td>1000</td>
</tr>
<tr>
<td>Wall thickness</td>
<td>r3</td>
<td>400</td>
</tr>
<tr>
<td>Lipid pool distance</td>
<td>r5</td>
<td>250</td>
</tr>
<tr>
<td>Lipid pool thickness</td>
<td>r6</td>
<td>700</td>
</tr>
<tr>
<td>Lipid pool size (a)</td>
<td>r7</td>
<td>1500</td>
</tr>
<tr>
<td>Lipid pool size (b)</td>
<td>r8</td>
<td>1500</td>
</tr>
<tr>
<td>Cap thickness</td>
<td>r9</td>
<td>250</td>
</tr>
<tr>
<td>Calcification thickness</td>
<td>r10</td>
<td>150</td>
</tr>
</tbody>
</table>

Table 3.1: Dimensions of Basic Geometry

<table>
<thead>
<tr>
<th>Constituent</th>
<th>Basic Geometry</th>
<th>Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plaque area</td>
<td>39%</td>
<td>35% [1]</td>
</tr>
<tr>
<td>lipid pool</td>
<td>26%</td>
<td>22% [1], 23% [8]</td>
</tr>
<tr>
<td>fibrous cap</td>
<td>17%</td>
<td>11% [1]</td>
</tr>
<tr>
<td>calcification</td>
<td>8%</td>
<td>7% [1], 5% [8]</td>
</tr>
<tr>
<td>Stenosis (lumen reduction)</td>
<td>61%</td>
<td>79% [1], 70% [15], 75% [16]</td>
</tr>
</tbody>
</table>

Table 3.2: Areas of Basic Geometry
Figure 3.2: The Basic Geometry of a coronary artery
3.2 Finite Element Modelling

Finite element analysis was performed with the finite element package ANSYS® 6.0 on a computer workstation Pentium® Xeon. This section will describe which steps were taken to achieve a model that could represent an advanced atherosclerotic plaque. A condition of the model is that the areas of all the components can be varied, without changing the shape of the area. This means that the geometry can easily be adjusted in order to analyze the influence of different morphologies on the stress.

The standard procedure in ANSYS to build such a model is generally represented by the following steps:

1. Enter preferences
2. Build or import a geometry
3. Elements
   (a) Material properties
   (b) Element-type
   (c) Real constants
   (d) Elements Coordinate System
4. Meshing
5. Boundary Conditions
6. Solve

Step 1 & 2
The only preference is that a non-linear structural analysis will be performed. The BG is drawn by defining keypoints, then lines through these points and finally areas enclosed by the lines. All the commands that are used to create these points, lines and areas are gathered in a so-called ANSYS batch-file. This batch-file is saved as "geo.dat". All the coordinates of the keypoints are expressed in terms of variables. These variables are the dimensions $r_1 - r_{10}$ shown in figure 3.2(a). The mechanism will not be discussed in detail, but the advantage of this method is that the geometry or morphology can easily be varied by changing the values of these variables. The shape of the plaque constituent will more or less stay the same, while its area or the distance between the different area can vary. The values of these variables are saved in a separate input-file called "init.dat". The geometry of the artery can now be build from scratch by running a program-file called "Just_geo.inp" from ANSYS which
calls "init.dat" for the variables, and "geo.dat" to build the geometry. This structure of working with input-, batch- and program-files can be found in figure 3.5.

**Step 3a)**

The next step concerns the elements. First of all, the material properties of the different plaque constituents have to be defined. Because a static pressure load is applied, no parameters associated with time-varying viscoelastic effects were required and the material is assumed to be incompressible. The different arterial tissues are often considered as nonlinear and anisotropic. Often, the structures of plaque and artery are assumed to have identical mechanical properties in axial and circumferential direction, which differ from properties in the radial direction [3, 16, 15]. This is called transversely isotropic or orthotropic behavior. Unfortunately, non-linear material properties combined with orthotropic behavior would yield too complex a model in the scope of this research. Therefore, non-linear isotropic incompressible material properties are assumed. This is a valid assumption, since only the properties of the fibrous plaque differ significantly in the radial and circumferential direction.

In earlier studies [2], a bi-linear isotropic approach is used and the material properties proposed in that specific article will be used here. Optimizing the results of deformation experiments yielded bi-linear stress-strain curves. Material properties for each constituent are defined by the break-point strain $\epsilon_1$ (normal strain) and the two moduli $E_1$ and $E_2$ for strains less than and greater than $\epsilon_1$ respectively [2]. Unfortunately, this model cannot directly be implemented in ANSYS. The finite element software requires that the elasticity modulus $E$ at zero strain ($\epsilon = 0$) is not lower than any value of $E$ for $\epsilon > 0$. The bi-linear model presented by Beattie does not meet this requirement. Therefore a large modulus $E_0$ is introduced for very small strains ($\epsilon_0 \leq 10^{-6}$). This meets the requirements of ANSYS but does not effect the solution. In addition, ANSYS does not accept fully incompressible ($\nu = 0.5$) materials, so incompressibility is imposed by opposing $\nu = 0.49$. When the four material models are entered in ANSYS, they can be connected or linked to the individual plaque areas.

Table 3.3 illustrates the resulting material parameters for the LP, FC, CA and the DF. Figure 3.3 (a) shows the stress-strain curve of the lipid pool and also illustrates that the influence of $E_0$ in this bi-linear model can be neglected. In figure 3.3 (b), a detail ($\epsilon \leq 2 \cdot 10^{-5}$) of this curve can be seen which also shows $E_0$.

**Step 3b, 3c & 3d)**

The following step is defining the element type which will be used to mesh the geometry. ANSYS provides numerous elements for almost every type of application. Firstly, the model here will use non-linear material properties, as explained above. ANSYS suggests to use quadratic structural elements for irregular structures. A quadratic element is also known as a curved element or an element with mid-side nodes. Secondly, degenerate elements are desirable when working with irregular structures. A degenerate element has the shape of a
Figure 3.3: Material properties of the lipid pool

(a) Stress-strain curve

(b) Detail of the stress-strain curve for very small strain-values
tetrahedra or triangular in stead of a cube or a square respectively. Thirdly, assumed is that the arterial wall will be fixed in the axial direction which means that there are two degrees of freedom (DOF): the x- and y-direction. Hence, a structural degenerate quadratic 2D element is chosen - that is a 3-noded element - known as element type Plane82.

When considering the real constants for our element-type, there is no consensus in literature whether to assume plane stress [24] or plane strain [3,15,17]. The assumption of plane stress was made because stress in axial direction can be neglected compared to stress in circumferential direction. Finally, a cylindrical element coordinate system would be a natural choice considering the geometry of the vessel. The origin is the center of the vessel and the boundary of this vessel is then defined by Γ(r, θ) = (r₁, θ).

**Step 4**

When it comes to mesh the model, ANSYS provides automated meshing, with the options free meshing vs. mapped meshing. For irregular structures, free meshing often provides more accurate results. Another feature is smart-sizing, where ANSYS chooses the appropriate element-size for each element separately. High-result regions will now have more elements in order the increase reliability. Figure 3.4 shows the mesh as performed by ANSYS, and approximately 1000–1500 elements were used, dependent on the chosen values of the variables. Equal to what is done in step 1 and 2, all the commands given in step 3 and 4 are saved in an ANSYS batch-file called "mesh.dat". Now a new program-file is saved: "just_mesh.inp", which does the same as "just_geo.inp" but also calls this new batch-file "mesh.dat". Again, the structure of all this is shown in figure 3.5.

**Step 5**

The last step before solving the model comprises the definition of boundary conditions. Two types of boundary conditions can be discerned. Firstly, essential boundary conditions, which must be specified. In this model three points at the outer boundary of the vessel are chosen to specify this type of boundary condition. With a cartesian coordinate system (x, y), the keypoints (−r₁, 0) and (r₁, 0) are constraint in the y-direction and keypoint (0, r₁) in the

<table>
<thead>
<tr>
<th>Constituent</th>
<th>E₀</th>
<th>E₁</th>
<th>E₂</th>
<th>ε₀</th>
<th>ε₁</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid pool</td>
<td>4.0⁻²</td>
<td>3.81⁻³</td>
<td>3.88⁻²</td>
<td>10⁻⁶</td>
<td>0.182</td>
</tr>
<tr>
<td>Disease-free zone</td>
<td>0.25</td>
<td>6.15⁻²</td>
<td>0.245</td>
<td>10⁻⁶</td>
<td>0.137</td>
</tr>
<tr>
<td>Fibrous cap</td>
<td>2.0</td>
<td>0.483</td>
<td>1.82</td>
<td>10⁻⁶</td>
<td>0.082</td>
</tr>
<tr>
<td>Calcification</td>
<td>11</td>
<td>3.99</td>
<td>10.7</td>
<td>10⁻⁶</td>
<td>0.053</td>
</tr>
</tbody>
</table>

Table 3.3: Elasticity moduli [MPa] and break-point strains [-]
x-direction. This prevents the model from rotating when a load is applied, but the model will still be able to expand. Secondly, natural boundary conditions are specified. Here the boundary which encloses the lumen area is chosen to specify a surface load. This surface load is a constant pressure of 100mm Hg (13.3 kPa in SI) directed from the lumen towards the tissue. The value of this load is assigned to a variable in the input-file "input.dat".

Step 6)
The last step is to simply solve the problem created in the preceding steps. Because the problem is nonlinear, the pressure will be nonlinear with respect to the velocity field $\vec{u}$ due to the presence of the product $\vec{u} \cdot \nabla \vec{u}$. This implies that the equations have to be solved in an iterative procedure. Many different choices can be made, but ANSYS makes use of the Newton-Raphson iteration process.

The Newton-Raphson iteration process can be outlined by considering a scalar nonlinear equation $f(x) = 0$. Let $\hat{x}$ denote the solution, and $x_i$ an estimate of this solution obtained at the $i$-th iteration. The iteration process may be summarized as:

1. Given an initial estimate $x_0$ of the solution $\hat{x}$,
2. Find an approximation of the error by solving

$$f(x_i) + \frac{df}{dx} \delta x_i = 0$$

with $\delta x = \hat{x} - x_i$ the error in the estimate $x_i$ compared to the exact solution $\hat{x}$.
3. Update the estimate of the solution

$$x_{i+1} = x_i + \delta x_i$$
4. If not converged, repeat form step 2, else stop.

A nodal tolerance of 0.1N was used to solve the FE model. ANSYS needed on the average between 10 – 20 iterations before the solution was converged.

![Software structure to create the model](image-url)

Figure 3.5: Software structure to create the model
3.3 Structural Analysis

This section will describe the analyzes that were performed on the 2D model that is defined previously. For each test, the values of some variables were altered and the new stress distribution was observed. Earlier is stated that fibrous cap thickness and lipid pool size have a big influence on the stress distribution and hence plaque stability. The focus will therefore be on these two areas, but also other factors will be considered.

In all cases the values from the BG were taken and one or more variables were changed. The pressure is 100 mm HG (13.3kPA) in all cases, except for test 6. The material properties are the same as defined above and only differ in test 7. The following tests are defined:

1. **FC thickness**
   Thin caps are known to be a high stress region. Therefore, the fibrous cap thickness is varied:
   
   \[ r_9 = 25 - 350 \text{ µm} \]
   
   The distance between LA and LP is kept at 500 µm, so \( r_5 = 500 - r_9 \).

2. **LP size** (figure 3.6)
   The lipid pool is a large area of soft tissue, and therefore greatly influences the stress distribution. The lipid area is varied for three different values of the fibrous cap thickness.
   
   LP area: \( 0.47 - 2.23 \text{ µm}^2 \) (by varying \( r_6, r_7 \) and \( r_8 \))
   
   - \( r_9 = 50 \)
   - \( r_9 = 100 \)
   - \( r_9 = 150 \)

3. **Distance LP - FC** (figure 3.7)
   
   - \( r_5 = 14 - 457 \text{ µm}, r_9 = 50 \)
   - \( r_5 = 20 - 462 \text{ µm}, r_9 = 100 \)
   - \( r_5 = 23 - 461 \text{ µm}, r_9 = 150 \)

4. **Omitting LP** (figure 3.8)
   Because the LP could be an important factor, its interesting what the stress in the plaque area would be if the LP is omitted. The distance between LA and LP is kept at 500 µm, so \( r_5 = 500 - r_9 \). So, this test is the same as test 1, except for the absence of LP.
   
   \( r_9 = 25 - 350 \text{ µm}, \) no LP
5. **Omitting CA**
In literature, the contribution of CA to a unstable plaque is still doubtful. Therefore, test 1 is repeated with no calcified region.

\[ r_9 = 25 - 350 \ \mu m, \text{ no CA} \]

The distance between LA and LP is kept at 500 \( \mu m \), so \( r_5 = 500 - r_9 \).

6. **Lumen pressure**
High blood pressure is a known risk-factor of atherosclerosis. The tests are performed with different (constant) lumen pressures, again for three different values of the fibrous cap thickness.

Pressure = 64.8 – 112.5 mm Hg (9 – 15 kPA)

- \( r_9 = 50 \)
- \( r_9 = 150 \)
- \( r_9 = 250 \)

7. **Hardening LP**
Changing the material properties could tell something about the influence of the LP. The lipid pool is hardened like it is calcifying, by increasing \( E_1 \) and \( E_2 \) for three different FC thicknesses.

\[ E_{LP, 1} = 0.381 - 3,810 \ kPa \]
\[ E_{LP, 2} = 3.88 - 38,800 \ kPa \]

- \( r_9 = 25 \)
- \( r_9 = 75 \)
- \( r_9 = 125 \)

Figure 3.6 - figure 3.8 give an idea of some of the tests. The results of all the tests can be found in the next chapter.
Figure 3.6: Varying LP size (test 2)

Figure 3.7: Varying the distance LP - FC (test 3)

Figure 3.8: Omitting the LP (test 4)
Chapter 4

Results

4.1 Introduction

When the solution has converged, the last result is read. As mentioned before, the stress could be an important marker for plaque stability. One can look at the direction of the stress in the high result areas by plotting the principal stresses $\sigma_1$, $\sigma_2$ and $\sigma_3$. The three (perpendicular) planes on which these stresses work each have zero shear stress by definition. The highest stresses were with no exception directed circumferential, and are of course tensile stresses (figure 4.1).

Figure 4.1: Vector plot of the principal stresses
Generally, Von Mises stresses give a good indication of the total stress on an element. They are also called equivalent stresses ($\sigma_{SEQV}$ or $\sigma_E$) and are therefore often used in this kind of analyzes. The von Mises is known as follows:

$$
\sigma_E = \sqrt{\left(\sigma_1 - \sigma_2\right)^2 + \left(\sigma_2 - \sigma_3\right)^2 + \left(\sigma_3 - \sigma_1\right)^2} / 2
$$

(4.1)

It incorporates all of the three principal stresses. Next thing is to look at the location of the highest stress point. In almost all cases they were present at the plaque cap center on the lumen-tissue boundary - indicated in figure 4.3(a) - or at the shoulder of the cap - shown in figure 4.3(b). In some of the following results, it is indicated in the graphs where the highest stress occurs. Because the location of the highest stress point varies, it could be helpful to focus on one specific point in the model, and observe how the stress reacts to the morphological changes. This is done for test 1, where the stress distribution along the y-axis is considered besides the value of the overall maximum stress.

Because the stresses in the area around the lumen - and especially the FC - are so high, the distribution of stress in the remaining part of the plaque area have become invisible. Therefore, figure 4.3(c) shows this low-stress distribution for the BG. It is clear that the lower stresses can be found in the area between FC and LP, and some in the CA.

Finally, the displacement is illustrated in figure 4.2. It shows the sum of displacement ($\bar{u} = \sqrt{u_x^2 + u_y^2}$) with a maximum of about 0.6 mm, in the case of the BG.

Figure 4.2: Displacement plot of BG
Figure 4.3: Examples of Von Mises stress distributions for some arbitrary geometries
4.2 Analyzes

1. FC Thickness

Figure 4.4 clearly shows that the maximum stress in the fibrous cap rises exponentially with thinning of the plaque cap. Also, when the thickness falls below 200µm, the maximum stress shift from the shoulder to the center of the cap. At FC = 175µm, the stress decreases less than 5% while the cap thickness doubles. Because the point of maximum stress shifts at 200µm, the stress distribution has been analyzed at one specific location, that is along the y-axis. The maximum stress along the y-axis is also found at the border of the tissue and the lumen in the plaque cap. It relates to the FC thickness just like overall maximum stress does. In figure 4.5 the nodal plot of the Von Mises stress is shown for this test for FC thicknesses of 25 and 350µm.

![Fibrous cap thickness](image)

Figure 4.4: Result of the influence of FC thickness
Figure 4.5: Nodal plot of Von Mises stress for different FC thicknesses
2. LP Size

This figure shows the influence of the LP on the maximum stress value that can be found in the tissue. It is clear that a larger necrotic core has a negative effect on the plaque stability. But this effect is little: when the LP area increase almost fivefold, the maximum stress rises with about 10% in all the three cases ($FC = 50$, 100 and 150 $\mu m$). But there is a fixed distance of 250$\mu m$ between LP and FC, which could prevent the interference of the LP on the cap stress. Therefore, in the next test this distance will be varied to see how important the location of the LP is.

![Figure 4.6: Result of the influence of LP size](image-url)
3. Distance LP - FC

When moving the LP closer to the FC, the stress in the fibrous cap rises as illustrated in figure 4.7. The area of LP stays constant, and with a FC-thickness of 50µm the maximum stress increases with almost 20% when the LP is sited just above the fibrous cap. For a thicker FC this stress increases with only 10%.

![Lipid pool closer to lumen](image)

Figure 4.7: Result of the influence of LP - FC distance
4. Omitting LP
When the LP area has the same material properties as DF, it is assumed that there is no LP present at all in the atherosclerotic plaque. One can expect a decrease in stress according to test 2. So the stress for different FC is compared to the results from test 1, and the decrease in maximum stress is shown in figure 4.8. It follows that for a thin cap ($FC \leq 150\mu m$) there is a decrease in stress of about 10%.

![Chart showing decrease in stress for different FCs](image)

Figure 4.8: Result of the omitting the LP

5. Omitting CA
Similar as what is done in test 4, the CA area now has the same material properties as the DF area, which is equal to omitting the CA. Again, test 1 is repeated but this yielded no significant changes. With omitting the CA, there was an average increase in stress of 0.6% ($\pm 0.2\%$).
6. Lumen pressure

Hypertension is often marked as a factor that increases the chance of plaque rupture. Therefore, the lumen pressure is varied. It is trivial that the stress and strain in the tissue will follow the raise in pressure. Therefore, the principal circumferential stress is normalized by dividing it by the pressure. This yields a graph that can been seen in figure 4.9. The normalized stress in the cap increases with 10-15% when the pressure almost doubles.

Figure 4.9: Result of the influence of lumen pressure
7. Hardening LP
From post mortem studies it is known that the necrotic core composition can be very different. It varies from very soft (lipid-rich) to hardened (calcified). Figure 4.10 show what happens when this core calcifies. The third dot from the left in this graph represent the material properties similar to LP from the BG. The most right dot represent the properties similar to CA. In the change of the necrotic core from lipid-like properties to calcification, the stress in the cap significantly decreases (almost 90% for $FC = 25\mu m$). The figure gives the effect of lipid core composition on wall stress distribution. One can see that for FC smaller than 50$\mu m$, the value of $\sigma$ exponentially increases with decreasing $E_{core}$.

![Lipid pool calcifies](image)

**Figure 4.10:** Result of the influence of LP hardening
Chapter 5

Conclusion and Discussion

5.1 Introduction

This chapter will shortly draw conclusions from the results that were presented in section 4.2 with respect to the FC and the LP. Furthermore, it will discuss the objectives formulated in section 1.2 and how well the results connect with earlier studies. Next it will be discussed whether the many assumptions made throughout this paper are all defensible. Which results are be erroneous or could be at least doubtful and which kind of improvement could be made? Finally, are there results that could be useful for further research and what kind of research could that be?

- Cap Thinning: Fibrous cap thickness seems to play a very important role as expected, and peak circumferential stress could be a determining factor in the mechanisms leading to the rupture of the atherosclerotic plaque. At a certain critical value, which is around 150$\mu$m, the peak stress quickly rises as shown in figure 4.4 and the plaque is vulnerable. This value agrees with Ohayon [16], which addresses a value of 120$\mu$m as being a critical value. Also Loree [15] found a similar curve for the peak stress related to the cap thickness. Virmani [23] defined a thin cap however as $<65\mu m$ thick. The cap thickness can be accurately measured with intravascular ultrasound (IVUS) techniques and may therefore become a clinical index of plaque vulnerability [16].

The location of peak stress probably shifts from the center to the shoulder of the cap as a result of the sharp corner of the cap shoulder. When the cap thicknesses increases, the peak stress will tend to move to this irregular geometry. Artery tissue however will never has these distinct boundaries of different tissues but consist of smooth transitions
between the different types of tissue. They will therefore never have these high stresses caused by irregular shapes.

A physiological increase of arterial pressure causes a raise in normalized peak stress ($\sigma_P$), but it does not affect thin caps more than thick caps (10-15% in all cases). So, arterial pressure does not seem to be not a very important cause of elevated peak stress value. But hypertension acts in another way. It alters the shear stress acting on the artery wall and causes abnormal velocity profiles. Note that a pressure value of 15 kPa maximum was applied, while patients suffering from hypertension could have arterial pressures up to 25 kPa.

A calcium deposit does not seem to play a role. Omitting the calcification did not result in different stress distributions compared to the same situation where the calcium was present. Probably, the stiff fibrous cap is able to take the pressure load by itself and because of its arc shape there is little strain in the calcified region. Figure 4.3(c) showed that little stress could be found in the CA, but is negligible compared to cap stresses. Also Huang concluded that calcification does not seem to decrease the mechanical stability of the coronary atheroma, in contrast to lipid pools which dramatically increases the stresses [8]. In addition, Veress stated that calcium buried deep in the lesion would have little effect on the overall stability of the lesion [22].

In all of the tests, we see higher peak stresses in the cap atheroma when the cap thickness reduces. The next section will discuss how the lipid pool affects the stability.

- Lipid pool: It is generally assumed that the lipid core greatly determines the plaque stability. The results in this study however do not affirm this. An increase in lipid pool size (fivefold) yields a rise in peak stress of only 10%. So maybe the lipid pool is not located close enough to the cap. One could imagine that a large area of soft tissue will force the surrounding tissue to take over the stress. Test 3 showed that a necrotic core sited very close to a thin fibrous cap gave an increment of peak stress with 20%. For thicker caps the LP location is of less importance.

The same occurs when the LP is omitted in test 4. Only for very thin caps the stress decreases (10%). Hence, it can be concluded that the lipid pool influences the plaque stability, but only when the plaque cap is thin. Also, the thin cap itself is already a cause of vulnerability. So overall, this study does not stress the importance of LP like others concluded. Test 7 showed that a very lipid-rich core could affect the plaque stability, but again, only for thin caps.

Hence, the effect of omitting the LP is little for thick caps.
5.2 Discussion

In conclusion, the morphology of the plaque constituents is of great importance when considering stress distribution in the lesion. It has been proven that fibrous cap thickness is a strong marker for high circumferential stress in the lesion. Although peak stress distribution largely determines plaque stability, vulnerability and the formation of thrombi, it is only a result of morphological changes in the process of atherosclerosis. These changes have numerous causes, and deeper insight in these processes atherogenesis might be of more value than analysis of the rupture event.

This structural analysis was designed to understand more of the structure of the lesion and the impact of some bio-mechanical factors on the stability of plaques. So, this study improves the knowledge on mechanisms of plaque rupture and could be very useful for diagnosis of vulnerable lesion. The mechanisms by which a plaque ruptures, involved in acute coronary syndromes, still have to be clarified and predictability to be improved.

The objectives formulated in section 1.2 were to construct a 2D finite element model of a human coronary artery and to investigate the influence of morphology on plaque stability. This goal is achieved and furthermore, experience is gained in working with finite element method, existing theories on plaque stability are partially confirmed and new perspectives are provided for further research in this group.

The second objective was to use 2D micro-CT images from an artery to reconstruct a 3D FE model, where at this point the artery is considered as to be homogenous, so with no distinction between its components. The conversion of micro-CT to a finite element model did work, and the software worked well. The small error that came up in 3D is easy to eliminate, but due to the limited time that was given, this still has to be done in the future.

5.3 Limitations and Continuation

Many aspects of the finite element model are simplified. It was not possible in the limited time that was given to use a realistic cross-section of a coronary artery, which has been the biggest limitation of the model. The simplified geometry contains errors, but does make clear some of the basic principles about stress in an stenosed artery. In addition, an artery will have smooth transitions between different components, e.g. the fibrous cap and the lipid pool. This model has distinct borders between the different constituents, which will generate erroneous results. Furthermore, the bilinear material model has proven to be accurate, but the assumption of isotropic material behavior could greatly influence the results. Similar
analyzes in earlier studies assumed a tenfold difference of the Youngs modulus in radial and circumferential direction. This has to be incorporated in further studies.

The research that follows on this study, will extend the model to a three-dimensional, realistic finite element model. It will need a more complex and a more extensive material model, and a time-varying load condition like a sine wave.
Appendix A

ANSYS files

init.dat

!-------------------DIMENSIONS -------------------------------
  r1=2000  r2=1000  r3=400  r5=350  r6=700
  r7=1500  r8=1500  r9=150  r10=150

p1=(r3+r2-r1)
p2=(p1+r2)
p3=(p2+r9+r5)
p4=(p3+r6)

!-------- lumen pressure ---------
pres = 13.3e-3  !MPa = 100 mm HG

!----------------------------------------
!--------- BILINEAR MODEL FROM BEATTIE 1996:  ---------
!----------------------------------------

! m__ are the moduli of the material (3 in each material)
! eta_ are the strain values at which the E-modulus changes
! s_mat_ are the stress that correspond to the strains/moduli

eta = 1e-8 !

---------- Material 1 = lipid pool ----------------------
eta1= 0.182 m10 = 0.04 m11 = 0.00381 m12 = 0.0388 nu1 = 0.499

!---------- Material 2 = disease-free ----------------- 
eta2= 0.137 m20 = 0.25 m21 = 0.0615 m22 = 0.245 nu2 = 0.499
Material 3 = fibrous cap

\[ \eta_3 = 0.082 \quad m_{30} = 2 \quad m_{31} = 0.483 \quad m_{32} = 1.82 \quad \nu_3 = 0.499 \]

Material 4 = calcification

\[ \eta_4 = 0.053 \quad m_{40} = 11 \quad m_{41} = 3.99 \quad m_{42} = 10.7 \quad \nu_4 = 0.499 \]

Connect areas to mat-prop

A1=2
A3=1
A4=4
A5=3

A1=everything on the inside  A2=circle in the middle  A3=big area in the upper region  A4=little area on top of A3  A5=area around lumen

buildgeo.dat

/prep7

!============== GEOMETRY CONSTRUCTION ===============

====== Create outer border ==========

p1=(r3+r2-r1)  p2=(p1+r2)  p3=(p2+r9+r5)  p4=(p3+r6)

====== Create lumen area ================

FLST,2,2,8 FITEM,2,0,p1,0 FITEM,2,0,p2,0 CIRCLE,P51X, , ,360,10,

====== Create keypoints for lipid ========

K,41,2*r7,p3-0.25*r6,0, K,42,r7,p3+0.6*r6,0, K,43,0,p3+r6,0,
K,44,-1.5*r8,p3+r6,0, K,45,-3*r8,p3+0.8*r6,0, K,46,-4*r8,p3,0,
K,47,-3*r8,p3-0.75*r6,0, K,48,-1.5*r8,p3-0.25*r6,0, K,49,0,p3,0,
K,50,r7,p3,0,

====== Create spline through keypoints ========

FLST,3,7,3 FITEM,3,41 FITEM,3,42 FITEM,3,43 FITEM,3,44 FITEM,3,45
FLTEM,3,46 FITEM,3,47 BSPLIN, ,P51X

FLST,3,6,3 FITEM,3,46 FITEM,3,47 FITEM,3,48 FITEM,3,49 FITEM,3,50
!======= Create keypoints for calcification ==============
K,54,0.75*r7,p4,0, K,55,0,p4+r10,0, K,56,-1.5*r8,p4+r10,0,
K,57,-2.75*r8,p4,0,

!==== Create spline through keypoints ====================
FLST,3,6,3 FITEM,3,42 FITEM,3,54 FITEM,3,55 FITEM,3,56 FITEM,3,57
FITEM,3,45 BSPLIN, ,P51X

!====== Divide line ======================================  
FLST,2,1,4,ORDE,1 FITEM,2,33 FLST,3,1,4,ORDE,1 FITEM,3,32
LSBL,P51X,P51X, , ,KEEP

!========== Fibrous cap ==================================
K,58,0,p2+r9,0, K,59,r2,p1+0.65*r2+r9,0, K,60,-r2,p1+0.5*r2+r9,0,
K,61,r2+0.1*r2,p1+0.15*r2,0, K,62,-r2-0.1*r2,p1+0.15*r2,0,
FLST,3,7,3 FITEM,3,16 FITEM,3,62 FITEM,3,60 FITEM,3,58 FITEM,3,59
FITEM,3,61 FITEM,3,26 BSPLIN, ,P51X

!========Create areas ====================================
FLST,2,10,4 FITEM,2,1 FITEM,2,2 FITEM,2,3 FITEM,2,4 FITEM,2,5
FITEM,2,6 FITEM,2,7 FITEM,2,8 FITEM,2,9 FITEM,2,10 AL,P51X
FLST,2,20,4 FITEM,2,11 FITEM,2,12 FITEM,2,13 FITEM,2,14 FITEM,2,15
FITEM,2,16 FITEM,2,17 FITEM,2,18 FITEM,2,19 FITEM,2,20 FITEM,2,21
FITEM,2,22 FITEM,2,23 FITEM,2,24 FITEM,2,25 FITEM,2,26 FITEM,2,27
FITEM,2,28 FITEM,2,29 FITEM,2,30 AL,P51X
FLST,2,7,4 FITEM,2,35 FITEM,2,38 FITEM,2,39 FITEM,2,36 FITEM,2,37
FITEM,2,31 FITEM,2,34 AL,P51X
FLST,2,2,4 FITEM,2,32 FITEM,2,37 AL,P51X
FLST,2,11,4 FITEM,2,13 FITEM,2,12 FITEM,2,11 FITEM,2,30 FITEM,2,29
FITEM,2,28 FITEM,2,27 FITEM,2,26 FITEM,2,33 FITEM,2,14 FITEM,2,15
AL,P51X

!==== Overlap area’s and remove lumen =====================
FLST,2,1,5,ORDE,1 FITEM,2,1 FLST,3,1,5,ORDE,1 FITEM,3,2
ASBA,P51X,P51X, , ,KEEP
matmesh.dat

/PREP7

ET,1,PLANE82 local,11,1

!=================================================================================================
!============= Calculate strain-stress curves =================
!=================================================================================================

s1mat1 = eta*m10 s2mat1 = (eta1-eta)*m11 s3mat1 = (1-eta1)*m12

s1mat2 = eta*m20 s2mat2 = (eta2-eta)*m21 s3mat2 = (1-eta2)*m22

s1mat3 = eta*m30 s2mat3 = (eta3-eta)*m31 s3mat3 = (1-eta3)*m32

s1mat4 = eta*m40 s2mat4 = (eta4-eta)*m41 s3mat4 = (1-eta4)*m42

!=================================================================================================
!====== Bilinear material properties ===========================
!=================================================================================================

TB,MELA,1,1,3 TBTEMP,0 TBPT,,eta,s1mat1 !4E-010
TBPT,,eta1,s2mat1 !0.000693 TBPT,,1,s3mat1 !0.0317

TB,MELA,2,1,3 TBTEMP,0 TBPT,,eta,s1mat2 !2.5e-9
TBPT,,eta2,s2mat2 !8.43e-3 TBPT,,1,s3mat2 !2.11e-1

TB,MELA,3,1,3 TBTEMP,0 TBPT,,eta,s1mat3 !2e-8
TBPT,,eta3,s2mat3 !3.96e-2 TBPT,,1,s3mat3 !1.67

TB,MELA,4,1,3 TBTEMP,0 TBPT,,eta,s1mat4 !1.1E-007
TBPT,,eta4,s2mat4 !0.211 TBPT,,1,s3mat4 !10.1

!=================================================================================================
!========= Linear isotropic behavior ===========================
!=================================================================================================
MPTEMP,,,,,,,, MPTEMP,1,0 MPDATA,EX,1,,m10 MPDATA,PRXY,1,,nu1
MPTEMP,,,,,,,, MPTEMP,1,0 MPDATA,EX,2,,m20 MPDATA,PRXY,2,,nu2
MPTEMP,,,,,,,, MPTEMP,1,0
MPDATA,EX,3,,m30 MPDATA,PRXY,3,,nu3
MPTEMP,,,,,,,, MPTEMP,1,0 MPDATA,EX,4,,m40 MPDATA,PRXY,4,,nu4

!=================================================================
!=========== AREA ATTRIB =========================================
!=================================================================

!============== Area 1 ===========================================
CM,_Y,AREA ASEL, , , , 1 CM,_Y1,AREA CMSEL,S,,,Y CMSEL,S,,,Y1
AATT, A1, , 1, 11, CMSEL,S,,,Y CMDELE,,,Y CMDELE,,,Y1

!============== Area 3 ===========================================
CM,_Y,AREA ASEL, , , , 3 CM,_Y1,AREA CMSEL,S,,,Y CMSEL,S,,,Y1
AATT, A3, , 1, 11, CMSEL,S,,,Y CMDELE,,,Y CMDELE,,,Y1

!============== Area 4 ===========================================
CM,_Y,AREA ASEL, , , , 4 CM,_Y1,AREA CMSEL,S,,,Y CMSEL,S,,,Y1
AATT, A4, , 1, 11, CMSEL,S,,,Y CMDELE,,,Y CMDELE,,,Y1

!============== Area 5 ===========================================
CM,_Y,AREA ASEL, , , , 5 CM,_Y1,AREA CMSEL,S,,,Y CMSEL,S,,,Y1
AATT, A5, , 1, 11, CMSEL,S,,,Y CMDELE,,,Y CMDELE,,,Y1

!=================================================================
!================ MESHEN =========================================
!=================================================================
SMRT,1 MSHAPE,1,2D MSHKEY,0 SMRTSIZE, ,0.25,1,2,10,15,1.5,0,0,4,0
FLST,5,4,5,ORDE,3 FITEM,5,1 FITEM,5,3 FITEM,5,5
CM,_Y,AREA ASEL, , , ,PS1X CM,_Y1,AREA CHKMSH,'AREA' CMSEL,S,,,Y
ACLEAR,,,Y1 AMESH,,,Y1 CMDELE,,,Y CMDELE,,,Y1 CMDELE,,,Y2

/GO EPLOT FINISH

solve.dat

/PREP7
!========== BOUNDARY CONDITIONS =========================
!=========================================================

!========== Nodal Displacement ==========================

FLST,2,2,3,ORDE,2 FITEM,2,3 FITEM,2,-4 /GO DK,P51X,0,0,UX, ,
, , 

FLST,2,2,3,ORDE,2 FITEM,2,1 FITEM,2,6 /GO DK,P51X,0,0,UY, ,
, , 

!========== Nodal pressure ==============================

FLST,2,20,4,ORDE,2 FITEM,2,11 FITEM,2,-30 /GO SFL,P51X,PRES,PRES,

!========================================================
!================ SOLUTION AND POSTPROCESSING =============
!========================================================

/SOLU NLGEOM,1 NSUBST,10,500,5,1 SOLVE /GO

/POST1 SET,LAST

/EFACE,1 AVPRIN,0, , PLNSOL,S,1,0,1

/contour,1,10,0,0.05

/replot FINISH

complete.inp

/clear,start

/TITLE,Simplified plaque geometry

/TRIAD,OFF

/PREP7

ANTYPE,0

!===== Load parameters ===============================

/INPUT,'init','dat','.\input\','', 0

/INPUT,'buildgeo','dat','.\input\','', 0

/INPUT,'matmesh','dat','.\input\','', 0

/INPUT,'solve','dat','.\input\','', 0 SAVE
Appendix B

CT filter

The second objective formulated in section 1.2 was to use micro-CT images from an coronary artery to reconstruct a 3D finite element model. The images were provided by L. Lowder from Dr. Vito’s research group, and an example can be seen in figure B. The artery does not have a typical circular shape because the tissue was not pressure-fixed before scanning. This means that the artery is in a relaxed condition unlike a vessel in vivo, where it is constantly subjected to a certain pressure. Fortunately, at this point the method is of more interest than obtaining physiological correct results. The actual problem is to convert the shape of the vessel wall to a finite element package, and stack the images to reconstruct teh vessel in 3D. One can divide the problem in 4 steps:

1. The images contain too much information since we are only interested in the shape of the vessel wall. Hence, the images have to be decreased to a 2-bit contour image.

2. The contour plot needs to be smoothed, because very sharp curves and corners will lead to erroneous results in FE.

3. The images are standard graphic images (bitmaps) while ANSYS is restricted to import IGES files only (an AutoCad format). So, the contour plots have to be converted.

4. Finally, the images have to be stacked. This can be done in ANSYS or before step 3.
Figure B.1: Cross-section of a coronary artery (micro-CT)

In order to perform the first two steps, a software program is written in Matlab. The graphic user interface is shown in figure B.2. It can be run from the Matlab command prompt and is called "CTgui.m".

Procedure of handling CT-images: Start program by typing CTGui in the Matlab command prompt. Make sure that the path is the same as the directory where the program files are.

- File - Open: Load the image
- Resize: Omits borders of the image to save CPU time
- Fill border: Fills the surroundings of the image with lumen by clicking on the lumen-area
- Debris: Erases debris, dots and air bubbles. Draw a closed area around the AOI with the mouse and right-click when finished
- Done: Filter the image by adjusting the slider values to smooth the edge
- Contour: Create contour-lines and save the image in the tiff format

The software package MIMICS ® from Materialise is able to generate a IGES file from a contour plot. After loading the produced TIFF-file, MIMICS transforms the contour lines

\(^1\)The image must be an uncompressed TIFF image which can be checked in Paint Shop Pro e.g.
Figure B.2: Interface for the filter software

to polylines, which can be saved in the IGES-format. This file-format can be imported in ANSYS, the area enclosed by the lines can now be defined and meshed into elements. One can see this in figure B.3(a). A little test with this mesh has been done, analogue to the tests performed in chapter 3. The result of this is shown in figure B.3(b).

The first two steps can be repeated for all the cross-sections of an artery. MIMICS is able to stack these images and convert the contour lines to one IGES-file. Unfortunately, a small error occurred in the last step. The individual poly-lines in ANSYS did not have the same starting and end point, and the lines cross themselves.

To conclude, the matlab program CTGui works pretty well in this situation, and can be used in further research. When desirable, its simple to different types of filters can be chosen and implemented in the code. MIMICS is a powerful and useful software package, and is able to convert regular images to formats suitable for finite element software. Some work has to be done when it comes to 3D modelling, because some small errors occurred in this final step.
Figure B.3: FE model of a smoothed micro-CT image
Bibliography


