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1. BACKGROUND ON CARDIOVASCULAR BIO-SOLID MECHANICS

1.1. Introduction

Biomechanics seeks to understand the mechanics of living systems. The cardiovascular system may be studied from two biomechanical perspectives – solid mechanical and fluid mechanical. The former deals with the behavior of the blood vessels themselves while the latter deals with the flow of blood and how that may affect blood and the vessels. In this section, we will study the cardiovascular system from the solid mechanical perspective.

Bio-solid mechanics is the study of forces, motion and strength of biological tissues and organs. Examples of bio-solid mechanics range from the study of the forces on a geriatric hip, the forces on blood vessels due to blood pressure, the mechanical properties of the walls of the chambers of the heart, dynamics of human gait etc.

Although the cardiovascular system encompasses the heart, heart valves and blood vessels, in this section we will focus on the mechanics of the blood vessel (vascular) wall. We will study the intrinsic mechanical properties of the blood vessel, its response to forces acting on it, how these are affected by affliction of vascular diseases and briefly discuss the mechanics of artificial blood vessels. The goal is to provide a first look at the science behind this emerging field.

1.2. Significance

The function of the cardiovascular system is to facilitate the supply of blood to all parts of the body – a chiefly mechanical activity. Biomechanical studies help us understand its normal function, predict changes due to alterations, assess severity of certain diseases and help propose methods of artificial intervention. Its utility therefore is particularly significant for cardiovascular medicine.

Biomechanics has helped address clinical problems in the cardiovascular system with the intervention and analysis of prosthetic heart valves, heart assist devices, extracorporeal circulation, the heart-lung machines, and hemo-dialysis machines. It played a major role in advancing the art of heart transplantation and artificial heart replacement, the problem of postoperative trauma, pulmonary edema, pulmonary atelectasis, arterial pulse-wave analysis, phonoangiography, and in understanding/treating diseases like atherosclerosis and aneurysms.
2. INTRODUCTION TO SOLID MECHANICS

In the fields of statics and dynamics, the forces in a system of solid objects are analyzed under the presumption that the solid objects themselves are rigid bodies with no particular properties of their own. Solid mechanics is the logical next step to these fields. Here, we attempt to account for the individual properties of the solid objects in addition to studying the system they exist in.

2.1. Relevant quantities in solid mechanics

2.1.1. Stress

Stress is a measure of internal forces induced in a body due to external forces acting on it. It is a quantity associated with every point in a body being subjected to external forces. In a one-dimensional problem, stress may be thought of as force normalized to cross-sectional area. In the example shown in Figure 1, a solid bar of cross-sectional area, A is extended in one direction by a force F – an experiment called as uni-axial extension. The stress in the solid bar is uniform and equal to the ratio of F over A. In three dimensions however, at any given point, stress can vary depending on the plane and direction of interest and thus it has 9 components. In this section, we will mostly confine to looking at stress uni-dimensionally.

\[ \text{Stress, } \sigma = \frac{F}{A} \]

2.1.2. Strain

Strain is a measure of internal deformation of a body subjected to external forces or deformation. In the above example, uni-dimensional strain would be defined as the ratio of the change in length to the original length – in other words, the % extension of the bar. It is also associated with every point in a body and has nine components in 3-dimensions like stress.

\[ \text{Strain, } \varepsilon = \frac{l - L}{L} \]

2.1.3. The Elastic curve

The elastic curve is the relationship between stress and strain for a material. In the above example, if we continue to extend the bar until it breaks, record the stress and strain at each increment of extension, graph the data with strain on the X axis and stress on the Y axis, we end up with the elastic curve. For most Engineering materials, the elastic curve (also called the stress-strain curve) will appear like Figure 3. Stress will raise linearly with strain until the bar begins to break, upon which, the stress will rise irregularly with strain until it
almost fully breaks, upon which stress will drop drastically until the bar separates into two pieces. The linear portion of the stress strain curve is called the elastic region. Sometimes, the term elastic curve is also used to refer only to this elastic region of the stress strain curve.

2.1.4. Young’s Modulus

The Young’s modulus, E is a measure of the stiffness of a solid body. Quantitatively, it is the slope of the elastic region of the stress strain curve (see Figure 3). For most material, it is therefore, simply the ratio of stress and strain. In other words, it is the constant of proportionality between stress and strain leading to the following relationship, called the Hooke’s Law.

\[ \sigma = E \varepsilon \]

Young’s modulus is also referred to as the ‘elastic modulus’, ‘elasticity’, and occasionally as just ‘stiffness’.

2.1.5. Strength

The strength of a material is defined as the maximum stress the material can withstand prior to failure (breaking). A ‘stronger’ material will likely withstand much greater stress (or force) before failing as compared to a ‘weaker’ material. The strength of a material is not necessarily related to its Young’s modulus. Sometimes, a material may be very stiff (read high Young’s modulus), yet fail at fairly low stress (read low strength) and vice versa.

2.1.6. Compressibility

Compressibility is the ability of a material to undergo change in volume when subjected to external forces and deformations. It is not to be confused with the ability to squeeze a material in one or two directions. Even if we can squeeze a material in one direction with ease, if it expands in other directions to ensure a more-or-less constant volume, then it has low compressibility. In other words, compressibility is the ability to compress (or expand) a material in all directions simultaneously.

2.1.7. Poisson’s ratio

Poisson’s ratio allows us to quantify compressibility and is defined as the ratio of the resultant strain in lateral directions due to induced strain in the primary direction. In the example of uniaxial extension, the bar while extending in one direction (say the ‘primary direction) may typically compress itself in the other directions (say ‘lateral directions’) to facilitate this extension. The poisson’s ratio is the ratio between the strain in the lateral direction (\( \varepsilon_l \)) to that in the primary direction (\( \varepsilon_p \)). Thus, when a material does not compress in a lateral direction while extending in the primary direction, then the poisson’s ratio is zero and the tissue is perfectly compressible. However, when the material compresses itself in the lateral direction just enough so that the volume of the material does not change, the poisson’s ratio will be equal to 0.5 (this can be derived mathematically) and the material is said to be perfectly incompressible. Poisson’s ratio therefore will vary between 0 and 0.5.

\[ \gamma = \frac{-\varepsilon_l}{\varepsilon_p} \quad \{ 0 \leq \gamma \leq 0.5 \} \]

Figure 4. Poisson’s ratio
2.1.8. Anisotropy
Anisotropy is the ability of a material to behave differently in different directions. A material that behaves similarly in all directions is called an isotropic material. Many engineering materials are manufactured to have isotropic properties (steel) while some are manufactured to be deliberately anisotropic (fiber reinforced composites).

2.1.9. Viscoelasticity
Viscoelasticity is the ability of a material to exhibit both solid-like and fluid-like behavior. If we think of fluids as materials that flow, then the peculiar behavior of some solids that also under the right conditions, flow maybe described as viscoelastic. Typically, such behavior would be because the material itself may have both solid and fluid contents. A chewed bubble gum is an example of a viscoelastic material.
3. INTRODUCTION TO BIO-SOLID MECHANICS

In bio-solid mechanics, we adopt the methodology and standards of classical mechanics to study the function of biological tissues and organs while attempting to account for their biological nature wherever possible.

3.1. Elasticity of soft and hard biological tissues

In the human body, there are many soft (artery, skin, muscle, etc.) and hard tissues (bone, trachea etc.), each associated with distinct mechanical behavior. While there are many facets to mechanical ‘behavior’, we will focus on comparing the elastic behavior of soft and hard tissues to those of engineering materials to get a first look at how different biological tissues are. The following figure compares the elastic curves between various solid materials.

![Figure 5. Comparison of stress-strain curve for steel, dry bone, blood vessel, skin width, skin length](image)

3.2. Complexities in mechanical behavior of soft tissues

Adopting principles from classical mechanics to study soft tissues is easier said than done. Many basic assumptions about material behavior that are taken for granted in engineering may not be appropriate for bio-solids. Below we touch upon a few of these.
3.2.1. Nonlinearity
A striking contrast between the stress-strain relationship for steel and blood vessel is the fact that the latter is substantially nonlinear. Since the Young’s modulus is defined as the slope of the elastic curve, physically, this would mean that unlike a typical engineering material, the stiffness of the vascular tissue actually increases as it is being stretched. The implications are enormous. First, the term, ‘stiffness for a blood vessel’ would carry no meaning since it is not a constant. How then can we quantify the stress-strain relationship now that the classical equation, $\sigma = E\varepsilon$ is inapplicable? What would be the quantity that will be indicative of its elastic behavior? And most importantly, why is it nonlinear? Indeed, these are some of questions that we will attempt to address in this section of the course (see Section 5.1.2. Reason for the nonlinearity of the stress-strain curve).

3.2.2. Heterogeneity
The biologic soft tissue is a heterogeneous material consisting of a complex arrangement of many individual components (cells, muscles, fibers, etc.) each with its own unique mechanical behavior. This is quite unlike any engineering materials, thus leading to substantial additional complexity in how well we can study and understand them. How do we study a heterogeneous material when we are yet to understand fully what it is made of? The answer may lie in educated approximation. A blood vessel for example, is structurally very complex. Yet, if we can get some idea of how it behaves as a whole tissue, then that may itself be sufficient to study (to a degree of accuracy) its behavior, how these are affected by disease and predict its performance after surgical or pharmacological intervention. In this section we will attempt to do precisely that.

3.2.3. Active nature
Another aspect where biological soft tissues part company significantly from passive engineering materials is in the fact that they are active, live tissues that are constantly nourished, rejuvenated and remodeled by the body. Much recent research in biomechanics has concentrated on attempting to model this active nature of biological tissues. In the section, we will touch upon this aspect of the soft tissue.
4. THE ARTERIAL SYSTEM

4.1. Overview

The vasculature is a complex architecture of blood vessels that carry blood to and from various organs of the body. The blood vessels may be classified based on their sizes, function and proximity to the heart. Typically, they fall under one of the following 7 categories and the path of blood flow is as shown in the following figures.

<table>
<thead>
<tr>
<th>Vessel</th>
<th>Aorta</th>
<th>Artery</th>
<th>Arteriole</th>
<th>Capillary</th>
<th>Venule</th>
<th>Vein</th>
<th>Vena cava</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wall Thickness</td>
<td>2mm</td>
<td>1mm</td>
<td>20µm</td>
<td>1µm</td>
<td>2µm</td>
<td>0.5mm</td>
<td>1.5mm</td>
</tr>
<tr>
<td>Lumen</td>
<td>25mm</td>
<td>4mm</td>
<td>30µm</td>
<td>8µm</td>
<td>20µm</td>
<td>5mm</td>
<td>30mm</td>
</tr>
</tbody>
</table>

Figure 6. Classification of blood vessels, their function and the corresponding blood pressures.
4.2. Structural elements of vascular wall

While there are many structural components in the wall of a blood vessel, we will briefly discuss here a few that are biomechanically relevant and provide some idea of its microstructure. It has to be noted that although the microstructure varies greatly between different kinds of blood vessels, these components exist in all kinds of vessels albeit in varied amounts.

4.2.1. Endothelial Cell (EC)
- Cells lining the inner wall layer of blood vessels
- prevent thrombosis and entry of blood borne bacteria to vascular wall etc.
- regenerate if injured
- mechanical properties are negligible
- Very sensitive to shear stress and so very relevant in biomechanical studies
- 50 x 10 x 2 µm; 10^5 cells/cm^2 - tend to align in the direction of shear stresses

4.2.2. Elastin
- Taut tubular fiber
- Highly elastic; low stiffness (50 N/cm2)
- Bears the load under physiological conditions
- Ligamentum Nuchae (runs along top of neck of horses and cattle) is made almost fully of elastin
- Can stretch up to 60% and remain elastic

4.2.3. Collagen
- Tortuous, thick fiber
- High stiffness
- Responsible for structural integrity of vessel
- Rat’s tail is made almost fully of collagen
- Not always wavy, but is wavy in vascular tissues and skin

4.2.4. Smooth Muscle Cell (SMC)
- Involuntary muscle cells
- Responsible for ‘active’ properties of blood vessel wall
- Difficult to measure mechanical properties
- \( E \approx 1 \text{ N/cm}^2 \)

4.2.5. Ground Substance (GS)
- Kind of a glue that keeps all components together

4.3. Layered microstructure of the vascular wall
The blood vessel wall consists of three layers - the intima, media and adventitia. The thickness of these layers may vary from one kind of vessel to another, however, the exist in all the blood vessels and are made up mostly of various amounts of the above structural components.

4.3.1. Intima
- Inner most layer
- Mostly endothelial cells
- Very little collagen (debated)

4.3.2. Media
- Middle layer
- Usually thickest layer
- SMCs 33%; GS 6%; Elastin 24%; collagen 37%
- Most of collagen and elastin in this layer

4.3.3. Adventitia
- Outer layer
- Mostly collagen
- Fibroblasts 9%; GS 11%; elastin 2%; collagen 78%
5. MECHANICAL CHARACTERISTICS OF THE VASCULAR WALL

Understanding the mechanical characteristics of the normal vascular wall can provide us a reference to compare, quantify and evaluate the performance of the arteries when affected by diseases, predict performance after surgical or pharmacological interventions, develop new methodologies for treating them and help identify the desirable characteristics of artificial blood vessels. There are many facets to ‘mechanical property’. In this introductory class, we will focus mainly on the elastic behavior and briefly go over a few other characteristics.

5.1. Elasticity of the vascular wall

Vascular elasticity – the ability of the blood vessel to resist deformation – may be studied by performing a simple experiment called the uni-axial extension.

5.1.1. Uni-axial extension test

Uniaxial extension is the test mentioned in the earlier section, where a solid body is extended until failure. To perform uniaxial extension on an artery, we would first cut the artery open longitudinally and then grip it between clamps, attach the clamps to a testing apparatus. Then the tissue will be slowly (typical speeds of 3mm/min) extended. The apparatus consists of force and displacement transducers that record the force and displacements at regular intervals (typically once every second) to a connected computer. The tissue is gradually extended until it finally tears, upon which the experiment is completed. The figure on the right illustrates this with images taken during an actual test.

5.1.2. Reason for the nonlinearity of the stress-strain curve

The striking nonlinearity of the stress-strain relationship shown above is rather typical of all blood vessels, skin, and indeed, most other soft tissues like tendons and ligaments, albeit to varying degrees. In all cases, the tissue seems to get stiffer as it is being stretched (note the increasing slope in figure above). The logical next question is why? What makes the blood vessel “stiffen-up” as it stretches? Does the shape of this curve tell us anything? What if we find the curve for one artery slightly different in shape than the other? Can we infer anything about the differences in the structure or function between these arteries? We will now explore these questions and attempt to physically interpret the nonlinearity of the elastic curve for the blood vessel.
To understand why the vascular wall behaves the way it does, we should look at what it is made of. Although there are many micro structural components in the vascular wall, the mechanical strength and the ability to bear a load is mostly derived from two vital components – the elastin and collagen fibers. As mentioned earlier, when the artery is initially un-stretched, the compliant elastin fiber is typically taut, while the stiff collagen fiber is tortuous as illustrated in the figure on the right. It is this underlying microstructure that leads to a nonlinear elastic curve during uni-axial extension.

Let us consider a few hypothetical cases and perform some thought experiments.

**Case 1. Tissue made of a single elastin fiber – hypothetical**

Let us say, we perform uniaxial extension on this tissue made of a single elastin fiber. Since elastin is taut at zero-load, when the tissue is stretched, the single elastin fiber will resist the load and therefore, the stress will increase linearly with strain, although with a low slope since as we discussed earlier, elastin is a fairly compliant fiber. For now, we will not consider what will happen to the curve when the elastin fiber gets torn, since we are only trying to understand the ‘elastic region’ of the stress-strain curve.

**Case 2. Tissue made of a single collagen fiber - hypothetical**

When we perform uniaxial extension on this tissue, since collagen is tortuous at zero load, it will offer no resistance to extension up until the point where it does get taut, following which it will offer stiff resistance owing to its relatively higher mechanical stiffness. The stress-strain curve therefore, will be horizontal at zero-load up until the collagen fiber becomes taut, and then rise linearly with a high slope.
Case 3. Tissue made of one elastin and one collagen fiber – hypothetical

In this case, during the initial stages of extension (or strain), only the taut elastin fiber will resist the extension (or bear the load), while the tortuous collagen fiber offers no support except to continue to get less and less tortuous. In this region, stress will rise linearly with strain with a low slope. However, once the extension is large enough that the collagen fiber also becomes completely taut, then it too will start to resist extension (i.e. bear the load). The stress would then rise more sharply (i.e. with a much higher slope), albeit, linearly.

Case 4. Tissue made of 3 taut elastin fibers and 3 collagen fibers of varying waviness – hypothetical

In a blood vessel, the amount of ‘waviness’ or tortuosity of the individual collagen fibers is not the same. We therefore consider 3 collagen fibers of varying degrees of waviness as shown in the figure. In this case, stress will initially rise linearly at low slope (due to the resistance of the three taut elastin fibers) until the first collagen fiber becomes taut upon which it will get ‘recruited’ to start bearing the load. Here upon, stress will start to rise a little more steeply (slope of curve increases). With increasing extension, the second fiber gets taut, upon which it too gets recruited to load bearing, thus increasing the slope even further. Eventually, the third collagen fiber too gets recruited, upon which the stress would have reached its maximum slope and will rise linearly at this slope until tear.

Case 5. Tissue made of many taut elastin fibers and collagen fibers of varying waviness – true scenario

Now we consider the true scenario where a vascular tissue is really made of countless numbers of elastin and collagen fibers – indeed it is practically impossible to separate them into individual fibers. In this case the least tortuous collagen fiber gets recruited very early during extension and gradually, one after the other, collagen fibers of different degrees of tortuosity get recruited. Simultaneously, the slope of the stress-strain curve will also rise gradually, until all the collagen fibers get recruited, upon which the curve will rise linearly with strain until tear. This process will
therefore result in a nonlinear elastic curve whose slope rises smoothly until close to failure. This gradual inclusion of individual collagen fibers to load bearing is termed, ‘collagen recruitment’.

We can see therefore, why the underlying microstructural layout of elastin and collagen fibers leads to the ‘stiffening of artery with extension – something that may have seemed rather strange initially. It is noteworthy that the above rationale was proposed and demonstrated as early as 1957 by Roach and Burton (Roach, M.R. and A.C. Burton. The reason for the shape of the distensibility curves of arteries. Can. J. Biochem. Physiol. 35:681-90, 1957). Although their initial thoughts have been refined and better understood by many later works, this initial publication was perhaps one of the most quoted on this subject. Herein, lies also a good demonstration of how biomechanics parts company with classical solid mechanics in how we understand and interpret the behavior of biological tissues.

5.1.3. Estimating elastin-collagen contents from elastic curve

Based on what we know about how the underlying microstructure affects the stress-strain curve of a blood vessel, it is possible to conversely use the stress strain curve to predict the underlying microstructure and function. Because, the elastin-collagen complex determines the stress strain curve, we can use this curve to study their relative contents in the tissue.

In a typical stress-strain curve, we could expect to see an initial low slope straight line (sometimes referred to as the ‘toe region’), followed by a nonlinear rise in stress and then a final high-slope straight line leading to failure. We know that the toe region is due only to the elastin fibers in the tissue. If the number of elastin fibers in the tissue were to be lower, we would expect that the initial resistance to deformation would be lower resulting in a lower slope. Therefore, it is reasonable to take the slope of the toe region as indicative of the amount of elastin in the tissue. Similarly, the final slope of the curve, just prior to failure would be indicative of the combined stiffness of all the elastin and collagen fibers. Therefore, the difference between the final and initial slope of the curve will be equal to the
stiffness of all the load bearing collagen fibers in the tissue and therefore, indicative of the collagen content in the tissue.

We have now a macroscopic method of obtaining some measure of the relative amounts of elastin and collagen in the tissue without studying it microscopically. But the real utility actually comes in comparing tissues based on their stress-strain curves. An illustration of its use is provided in a later section (see 6.1.3. Mechanical properties of AAA).

The above approach however has its limitations. For one, how well can we know when the toe region ends and the nonlinear region begins? How sure are we that, there were no collagen fibers that were taut right form the beginning? Did all the collagen fibers get recruited to load bearing before the tissue specimen failed? These are questions that have been and are being studied in the field of vascular mechanics today.

5.2. Other mechanical characteristics of vascular wall

5.2.1. Viscoelasticity

The blood vessel wall is viscoelastic. Viscoelasticity is the property of the artery to exhibit both solid and fluid behavior owing to its biphasic microstructure. Solid behavior refers to its ability to exhibit a certain resistance to deformation like an elastic body. Fluid behavior refers to its ability to ‘flow’ due to sustained force. Thus when a constant force is exerted on an artery over an extended period of time, it will first deform like an elastic body, and then continue to deform or ‘flow’ for a finite period. If the artery were to be perfectly elastic, it would simply deform at the instant when force is exerted, but will NOT continue to deform further over time. Its deformation will remain constant. However, experiments have clearly demonstrated that the vascular tissue is viscoelastic.

The simplest method of obtaining a measure of the viscoelasticity of an arterial wall is to perform a creep test. In this test, the artery is first cut longitudinally and made into a flat rectangular strip. Next, it is subjected to a constant force and the deformation is continuously measured over time. If the artery is viscoelastic, it will continue to deform over time, but not indefinitely. Instead deformation will stop after reaching a finite value. Using the recorded data, a time-deformation graph is drawn. This graph is indicative of the viscoelasticity of the artery. By obtaining time-deformation curves for a normal and a diseased artery, it is possible to evaluate the effect of the said disease on the viscoelasticity of the arterial wall.

5.2.2. Anisotropy

The blood vessel wall is significantly anisotropic. Experiments have shown that a typical vascular tissue is slightly to significantly stiffer in the circumferential direction than in longitudinal direction. In some cases though, it is stiffer longitudinally. Experiments to study anisotropy of vascular elasticity have ranged from testing tissues oriented in different directions and comparing stress-strain curves to performing bi-axial experiments where the tissue is simultaneously stretched in two directions and the bi-axial stress strain curves compared. Studies on anisotropy of vascular viscoelasticity have been rare.

5.2.3. Incompressibility

The blood vessel wall has been shown to be almost incompressible. As mentioned earlier, the incompressibility of the vascular wall does not men, it cannot be squeezed or extended in one or two directions. It just means that, when the artery is deformed in one direction, an opposite
deformation will take place in the other directions in such a way that the volume of the tissue remains a constant. This effect can be observed in the sequence of images in Figure 8. Note that as the artery is extended from its initial state, there is a corresponding decrease in the width of the specimen. Indeed, a rigorous calculation of the volume of the specimen at various stages (by measuring the length, width and thickness at each increment of extension) would have revealed that the volume remains a constant.

5.2.4. Residual stress
Residual stress is a stress that exists in an uncut tubular artery even when it is under zero pressure. We know these stresses exist because, when a small piece of tubular artery under zero pressure is cut longitudinally, it springs open as shown in Figure 11. The only explanation for this behavior is that the artery must have been under circumferential stress prior to it was cut, which may have subsequently been relieved by the cut. But this seems to violate one of the basic and seemingly accurate assumptions in classical solid mechanics that a body will be under stress only if there are external forces acting on it. How do we explain the phenomenon of residual stress in arteries? Decades of research have helped us understand why they may be important, but we do not yet know fully how they came to exist, except that they do. We can get a measure of these residual stresses by determining the amount of opening of the artery upon being cut. Thus, an artery that opens more than another may be thought of as having a higher residual stress in its zero-pressure tubular state. The ‘amount’ of opening is quantified by determining the opening angle, θ as shown in figure 11.

![Figure 11. Demonstration of residual stress in the artery following a longitudinal cut.](image)
6. MECHANICS OF VASCULAR DISEASE STATES

Cardiovascular disease is the leading cause of death in the United States. Most of the illness associated with the heart is due to some form of disease in the coronary blood vessels that supply blood to the heart muscles. Thus the study of vascular disease occupies an important place in the improvement of health care in the United States. Given the essentially mechanical nature of their functions, study of the biomechanical aspects of these diseases is indispensable. In the earlier sections, we looked at the behavior of a normal blood vessel. In this section, we will study how their mechanical properties are affected due to affliction of two major vascular diseases – aneurysm and atherosclerosis.

6.1. Aneurysm

6.1.1. Background

Aneurysm is a gradual dilation of an artery over a period of years that will eventually rupture, if untreated. It affects the aortas, arteries and even arterioles. Although it may occur in any portion of the arterial system, they predominantly afflict the abdominal aorta and the cerebral arteries (brain arteries). In this section, we will focus on the abdominal aortic aneurysm (AAA).

AAA is the thirteenth leading cause of death in the United States. It afflicts about 3-5% of the population. The abdominal aorta is a major blood vessel in the abdominal region of 2 cm diameter. When afflicted with aneurysm, the aorta can grow (at the rate of 0.5 cm/year) to as large as 6-10 cm eventually leading to rupture. Rupture is a catastrophic event that is most often fatal (70% mortality according to some estimates).

But it does not occur in an expected fashion. For instance, it is not necessarily related to the size of the AAA. In some patients, AAA of 4cm diameter has ruptured; while in others the AAA has remained unruptured until they grow as large as 10 cm. Indeed they have been compared to a time bomb – with no way of knowing when it will explode. If detected in time, it can be treated surgically by replacing the AAA with an artificial conduit (vascular graft). However, surgery itself is risky to the patient and hence is only best performed when rupture is imminent. Thus, if one can develop a methodology to predict AAA rupture risk, then it can be a valuable tool for the physician who can then plan the surgical intervention accordingly. Currently our ability to predict AAA rupture risk remains poor.

It is strongly believed that biomechanical modeling of the AAA may be the key to predicting its rupture. In the following sections, we will briefly go over some of the biomechanical issues related to AAA.
6.1.2. Pathogenesis of AAA
The pathogenesis of the AAA is not yet fully clear, although some theories have gained more credibility than others. Some of these more accepted theories are:
- Elastin degradation causes expansion; collagen degradation causes rupture
- Atherosclerosis causes wall weakening; sustained pressure on weakened wall causes further loss of wall integrity and eventually expansion
- Genetic predisposition: Connective tissue disorder

Irrespective of which of these theories are true, it is generally accepted (based on morphometric studies) that the aneurysmal aortic wall contains substantially lesser amounts of elastin and moderately lesser amounts of collagen.

6.1.3. Mechanical properties of AAA
Prior to developing biomechanical models that may predict AAA rupture, it is first important that we understand how the mechanical properties of the aortic wall are affected due to aneurysm formation and progression. Here again, we will focus on the elastic curve. It is possible to obtain strips of the AAA wall from patients undergoing surgery. These tissues may be subjected to uniaxial extension test to obtain the elastic curve. Figure 13 shows a comparison between the elastic curves for a normal and aneurysmal abdominal aorta. Note that the curve for the aneurysmal tissue is 1) shifted to right; 2) has lower peak stiffness (slope before failure); and 3) lower strength (stress before failure). Indeed all these observations are to be expected given what we know of the depletion of elastin and collagen contents in AAA tissue.
- The curve is shifted to the right because of elastin depletion since that would cause some of the previously tortuous collagen fibers to become taut, thus leading to greater stiffness even during early extensions.
- The peak stiffness or the slope of the curve at the end of the elastic region is lesser in the AAA because of depletion of elastin and collagen contents (mainly collagen depletion) since fewer fibers would mean lesser resistance to deformation and therefore lower stiffness
- The strength of the AAA tissue is decreased again due to fewer elastin and collagen fibers in the tissue. It is believed that the strength of the AAA wall continues to decrease as the AAA grows larger and may explain why aneurysmal wall ruptures while a normal aortic wall doesn’t. Information on the AAA wall strength is also critical while developing models to predict rupture risk.
6.1.4. Stress in the AAA wall

The stress in the abdominal aortic wall is also known to increase with aneurysm formation and growth. Note that the one-dimensional definition of stress as the ratio of force to cross-sectional area is inapplicable here because the force on the aortic wall itself is uniformly distributed (as blood pressure) and occurs in a direction normal to the tissue unlike in an uni-dimensional problem where the force is in the plan of the tissue. In this case, aortic wall stress may be determined by considering the vessel as a cylindrical thin walled membrane and using the law of Laplace.

\[
\sigma = \frac{pR}{t} \quad \text{(for a cylinder)}
\]

where, \( \sigma \) is the circumferential stress (also called ‘hoop stress’)
- \( p \) is the blood pressure (normal systolic \( BP = 120 \, \text{mmHg} = 1.6 \, \text{N/cm}^2 \))
- \( R \) is the radius of the vessel (1 cm for normal abdominal aorta)
- \( t \) is the wall thickness (0.15 cm for normal abdominal aorta)

Thus the circumferential stress for a normal abdominal aorta would be,

\[
\sigma = \frac{1.6 \times 1}{0.15} = 10.7 \, \text{N/cm}^2
\]

Now consider what happens when this vessel grows to say, 5 cm in diameter. The stress would then increase to,

\[
\sigma = \frac{1.6 \times 2.5}{0.15} = 26.7 \, \text{N/cm}^2
\]

However, the above calculation would be true only if the vessel continues to have a cylindrical shape. Clearly as seen in Figure 12, the AAA seems closer to a sphere than a cylinder. The law of Laplace for circumferential stress a sphere is a slightly different from that of a cylinder and is given by,

\[
\sigma = \frac{pr}{2t} \quad \text{(for a sphere)}
\]

Thus, we can use the above formula for a more accurate estimate for stress in the 5 cm AAA.

\[
\sigma = \frac{1.6 \times 2.5}{2 \times 0.15} = 13.3 \, \text{N/cm}^2
\]

Notice that the stress isn’t as high as calculated earlier. This is owing to the fact that the AAA while increasing its diameter changed its shape to a sphere rather than remain a cylinder. Indeed, it has been speculated this is an attempt in the remodeling process of the body to minimize the stress on the wall, so that the AAA growth may be kept in check. In fact, even the law of Laplace for a sphere
may not be the most accurate for calculating stress since the AAA isn’t close to a sphere either although it may very well be a better approximation than a cylinder. Indeed a typical AAA has a rather irregular shape, which may (and does) have significant effect on the stresses in the wall. The above computations are to provide a first look at how stresses may be calculated in AAA and used to address clinical problems related to this disease.

Much recent research in AAA biomechanics has focused on determining stress distributions in the AAA wall by taking into account the complex shape of the AAA, which if accomplished to a high degree of accuracy may be used by surgeons as a tool to evaluate rupture risk of AAA patients.

6.2. Atherosclerosis

6.2.1. Background
Atherosclerosis is perhaps the most common cardiovascular disease wherein some arteries start ‘thickening’ until they eventually occlude, causing a cessation of blood flow. This severely affect the organs perfused by these arteries leading to severe illness to the patient. Atherosclerosis affects large (aorta), medium size (renal, carotid) and even small muscular arteries (coronary vessels). This process happens over a period of 50 to 60 years and seems to get particularly severe with age. ‘Heart disease is typically due to atherosclerosis of coronary vessels which supply blood to the heart muscles.

6.2.2. Pathogenesis of atherosclerosis
For atherosclerosis too, many theories have been proposed with regard to what it is and how it was formed. Atherosclerosis may be

- A deposition of fibrous substances (a pulpy mass) composed of numerous cholesterol crystals, fatty granules and calcium salts
- An inflammatory process from within intima – an intimal connective tissue cell proliferation
- Purely cholesterol deposits
- Response to injury

6.2.3. Biomechanical issues in atherosclerosis
Most research on atherosclerosis have rightfully concentrated on the fluid mechanical aspects since there seems to be both a logical rationale and statistical correlation between aspects of blood flow and incidences of atherosclerosis. Some solid mechanical aspects such as the viscoelastic and elastic properties of Atherosclerotic tissues may be relevant, although such studies have been relatively few.
Shown below is an elastic curve for an atherosclerotic tissue with a calcification (a stiff, almost bone-like deposit within the atherosclerotic tissue). The physical implications for this curve are not particularly significant. Studies on the viscoelasticity of these tissues have also been performed and it is generally noted that the atherosclerotic tissues are typically a lot less viscoelastic than normal ones.
7. VASCULAR GRAFTS AND STENTS

Vascular grafts are alternative conduits for blood flow that are implanted to replace a diseased (due to aneurysm or atherosclerosis) artery. A vascular graft may be an artificial tube made of synthetic material, a vein taken from a less sensitive portion of the patient, an artery taken from an animal or a tissue engineered artery-like tube grown in a lab.

Stents are tubular metallic wire mesh used to keep blood vessels (or sometimes other vascular grafts) open.

7.1. Vascular Grafts

Vascular grafts may be used to either bypass or completely replace an occluded vessel, or inside an aneurysmal artery in such a way as to exclude the aneurysm from the blood flow (see illustrations on right). In the case of a bypass graft, a hole is made to a side of the parent artery proximal (upstream) to the occlusion and one end of the graft is sutured. A similar suture is made at the other end distal (downstream) to the occlusion. This is also called, a ‘side-to-side anastomosis’. In case of an aneurysm, the aneurysm is first cut open, and the graft is directly sutured to the proximal and distal portions of the aneurysm. This is called an ‘end-to-end anastomosis’.

The material of the vascular graft may be one of many. Listed below is a description of the various types of vascular grafts.

7.1.1. Synthetic Vascular graft

One of the most commonly, the synthetic vascular grafts are either woven/knitted fabric (Dacron) or made of a polymer material (polytetrafluoroethylene - PTFE). They are used to replace large and medium sized arteries to fix both atherosclerotic and aneurysmal arteries

Pros: ability to manipulate size, reliability, and high tensile strength

Cons: Being an artificial material, their blood incompatibility leads to many post implant problems. Further, they are typically very stiff compared to the parent vessel leading to suture line stresses and causing turbulence to blood flow (a phenomenon known as compliance mismatch).

7.1.2. Autograft

Autografts are vessels that are taken from other ‘less critical’ portions of the same patient’s body and implanted in place of a diseased artery. For example, the most common grafts used to bypass an occluded coronary artery are saphenous veins (vein in the leg) and internal mammary arteries (artery in the chest). They are usually used to replace small arteries only. Current clinical data show that these arteries are reliable for 10-15 years, upon which they may need another replacement.

Pros: Compliant; Do not induce an immune response since the tissue is not foreign to the body
Cons: In case of the more popular saphenous veins, the vein is unused to arterial BP (recollect that the BP in the veins is much lower – Figure 6). The increased wall stresses cause undesirable genetic events to take place that may cause the blood flowing through it to clot or induce the deposition of plaque on the graft walls.

7.1.3. Allograft
Allografts are vessels taken from other humans or cadavers, instead of that particular patient. They are also used in small arteries. The pros and cons are similar except the increased risk of triggering an immune response in the body.

7.1.4. Xenograft
Xenografts are vessels taken from a different species, say pigs, and used in humans. These are not used so often these days, but have been utilized to replace many large, middle or small arteries.

Pros: More readily available; mechanical properties may be similar; more deeply studied and understood than human arteries

Cons: Species-to-species differences may lead to unforeseen consequences; triggers some immune responses; sometimes these grafts also develop the same problem as the parent vessel

7.1.5. Bioresorbable vascular graft
The bioresorbable vascular grafts are in the developmental stage. These are perhaps the most futuristic of vascular grafts. The goal here is to actually ‘grow’ a vascular graft using tissue-engineering techniques and attempts are underway to do so both in-vivo and in-vitro. In the in-vitro approach, a tube made of a biodegradable material (poly glycolic acid polymer) is seeded with a thin layer of endothelial cells and perfused in a tissue bath under appropriate conditions of temperature and pressure. Gradually, the cells would seep into the material and a tissue would start to form on both sides of the biodegradable tube. The new tissue will slowly dissolve away the biodegradable material. In a few weeks, the biodegradable material will be completely dissolved and washed away leaving behind a fully grown blood vessel with a microstructural content similar to a parent vessel. In the in-vivo approach, the biodegradable tube is implanted just like any other vascular graft. Due to blood perfusion and coming in contact with bodily tissues, cells would similarly seep into the tissue leading to complete degradation and formation of a new biologic tube in its place. The above sounds easy enough in theory, but in practice, substantial difficulties have arisen in scientists’ ability to seed the inner layer with cells (they get washed away due to shear stresses). Further, the structural properties of the biologic tissue is far lower than expected which leads to their failure. Current efforts are underway to work around this problem, although the progress has been disappointing. Recent reports suggest that there has been some success in duplicating the media and adventitia, but not the most important intima.

Pros: The ideal vascular graft; Can be grown to suit any specific artery for a patient; abundant availability

Cons: The pros are worth noting only when it can actually be done. For now, its only in theory and progress has been disappointing.
7.2. Stents

Stents are metallic wire meshes used to hold open arteries or other vascular grafts. Traditionally, they have been used to hold open partially or (in rare cases) fully occluded blood vessels (mostly coronary arteries). The architecture of the metallic wire mesh is arranged such that the stent itself may be squeezed into a tube of very low radius. However, if it is expanded (say by inflating a balloon inside it), the stent will stay expanded and will not shrink back. The stent with a balloon inside is usually inserted endovascularly via an incision in the radial artery (artery in the upper arm) and guided through to the coronary vessel (with the aid of x-ray diagnostics) where it is first placed as shown in figure below. Then the balloon is inflated making the stent to expand. The stent will then push open the vessel wall. The wire mesh has sufficient radial rigidity to resist closing back, thus permanently opening up the vessel and allowing normal blood flow to resume.

A major advantage of using stents to open up occluded vessels rather than a by-pass graft is that the surgery itself is minimally invasive. The patient is least inconvenienced by the small incision in the arm unlike in the case of the vascular graft where the heart has to be exposed first to perform the by-pass surgery. Some problems with this approach though are, inadequate (or degrading) radial strength of the stent may cause it to close back; reoccurrence of atherosclerosis since it doesn’t stop plaque from forming over the porous wire mesh, etc. It is usually not used for severe cases of atherosclerosis, except when the patient is too weak to take the risks of conventional by-pass surgery.

Recently, a new type of stent has been gaining popularity. Rather than a strategic alignment of wire mesh architecture, these stents are simply made of a special material called shape memory alloys (also called smart materials – Ni-Ti alloys; commercial name, Nitinol). These stents have the capability to shrink into a tiny piece at low temperatures and stay expanded at body temperatures. Thus the stents are maintained at low temperatures and quickly inserted into the occluded location upon which they automatically expand under body temperature thus forcing the vessel open.

Stents have been further used as a lining for vascular grafts used to fix AAA. These grafts require greater radial stiffness and using the stent around the (inside of the) graft provides that additional radial rigidity. The use of Nitinol stents with Dacron grafts to fix AAA endovascularly is one of the most exciting areas of vascular surgery today.

Figure 18. Illustration of a stent being inserted in an occluded coronary artery