CHAPTER 2

MODELING OF AORTIC WALL

There are many systems in the body. System that plays important rule for enriched nutrient blood flows to organs is cardiovascular system. Steady flow of blood through organs must be effectively adjusted by arterial system which can adapt the flow as pulse of blood cyclically pumped by the heart. Therefore, it is necessary to study the properties of the blood vessels to monitor the system to be in normal working conditions. The mechanical properties of blood vessels are shown by the stress and strain, which represents the pressure of blood flow and movement occurred by this pressure. Therefore, we had concept to develop a model for predict this stress and strain.

However, one of the main advantages of this research is to be able to continue to human. So, surgery should be avoided. Advanced imaging inside the body, such as X-ray, MRI or Ultrasound is useful at least to avoid the pain. The imaging and developed modeling will be together to develop a model for more realistic. The results based on information of patient can help physicians in the diagnosis easier.

In this chapter, the basics of the circulatory system, anatomy, histology, physiology of blood vessel and modeling the artery wall as well as ultrasound imaging of the vessel wall must have been understood. This chapter starts from the blood circulation which leads to the arterial system and to understand the anatomy, histology and physiology and this understanding is then used to develop the model.

The following are method for modeling, defining shape, the assumptions. Of course, that would be based on the biological knowledge. This part describes the relationship of pressure on the movement of vessels that is the diameter or radius of the artery. The stress and strain, which represent the pressure and the movement, are related by the constitutive law which base on the continuum mechanics. Dimension and the number of layers that make up the artery will be discussed in the final.

2.1. Circulatory system

Understanding the behavior of the cardiovascular system in both of anatomy and physiology is essential to access functional mechanism of aortic vessels, factors that cause the disorder and to develop mechanical modeling of aortic vessels.

Circulatory system has the heart acted as an important organ and vascular system circulated blood from heart through various sizes of arteries which can be show in Figure 2.1. The heart and vascular system connect together as network that transports blood to nourish all cells in body.

The functions of the circulatory system are to transfer nutrients to the tissues of the body, to remove waste product from the organism, to transfer hormones from one part to another part of the body and normally it is to maintain a proper state of fluid in body tissues.

The circulatory system consists of two components of circulation as shown in Figure 2.1 which are the pulmonary circulation which circulate between heart and lungs and the systemic circulation which circulate between heart and cells of the entire body. Since in systemic circulation blood flow through entire tissues except lungs systemic circulation could be called greater circulation or peripheral circulation.

Functions of each part in circulatory system can be described as following. Function of arteries is to transfer high pressure blood to tissues and therefore arterial wall is strength for serving high velocity of flow in arteries. Arterioles are terminal and smallest for arterial system before blood reaches to capillaries. Capillaries enable to exchange water, nutrients, electrolyte, hormone between blood and surrounding tissues. Wall of capillaries is so very thin. Venules collect blood from capillaries and gradually coalesce to be larger vein. Functions of vein are to act as conduit passed blood from small veins return to the heart and as major reservoir of excess blood. Because of low blood pressure in small veins, wall of vein is thin. Volumes of blood in each component have different percentage, i.e. about 84% of the whole blood in the body is in systemic circulation by in arteries, arteriole and capillaries, vanules and vein are 13%, 7% and 64%, respectively. And the rest of 16% of the whole blood in the body is in the heart and lung those are 7% and 9%, respectively. The volume of blood pumped by the left ventricle from the heart in one contraction called stroke volume. Stroke volume depends on blood volume in ventricle before contraction. Normally, stroke volume is around 80 milliliters for a cardiac cycle. The heart have to pump approximate 60 times to push red blood completely flow a loop. As mentioned, circulatory system constructs with two major components that are the heart and vascular system. The heart is an organ that drives the system. However, vascular system is importance for the system as well to transport blood to entire body. If dysfunction occurs with any position in the vascular network, damage would occur at that tissue or organ.

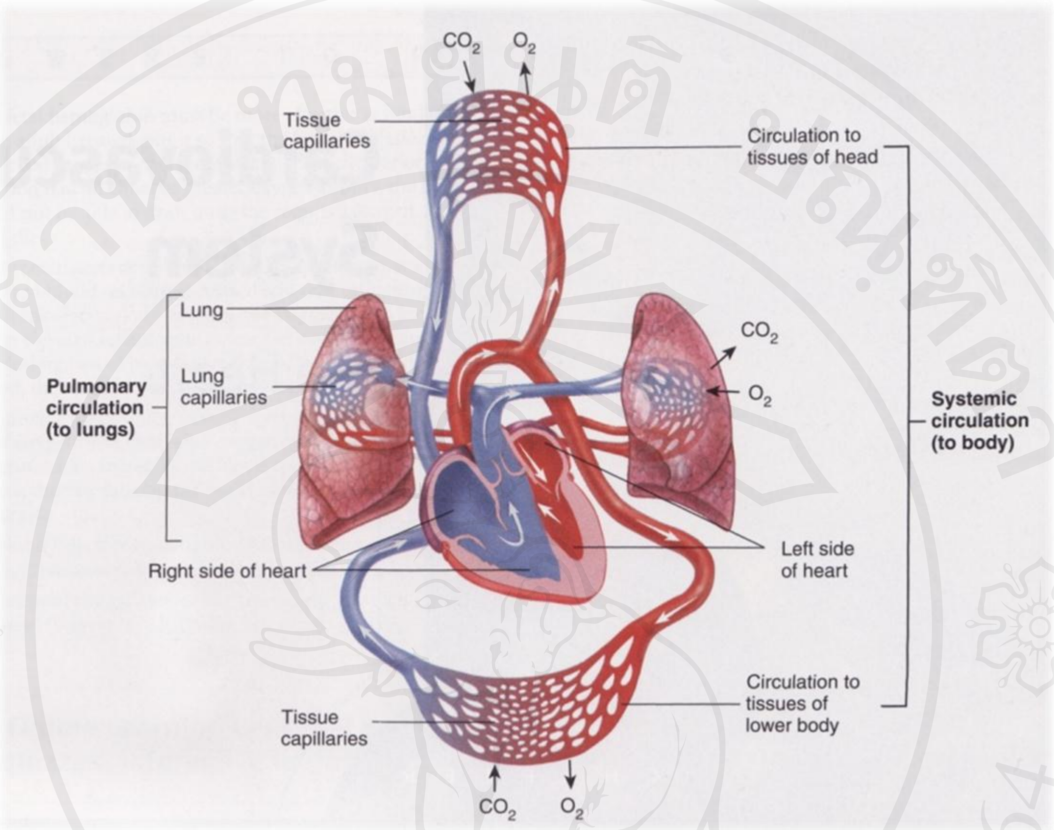

Figure 2.1 Circulatory system (Seeley, 2003)

Characteristic of flow out and flow in to the heart is one direction controlled by effective valves. Although, cardiac output comes out from the heart as pulse, inflation and contraction of the aorta wall acted as elastic material could effectively control form of the flow to steady flow. Consequently, blood is moved with high velocity to aorta and bunches of arterial artery where diameter decrease and thickness of wall decrease as well. Structures of arteries change along with distance from the heart. Structure of the aorta is respected as highly elastic material when related with artery. More far from the heart, the arteries represent as more muscle material.

It could be noted that, aortic vessel has important rule to transfer blood from the heart and adapt form of blood flow to be steady flow and then transfer to arterial network. It is important to understand anatomy, histology and material properties of aortic wall as well as diseases and abnormalities which could be occurred with the aortic vessel. Those abnormalities affect on functionality and material properties which lead to setting of theoretical framework and solving using engineering knowledge.

2.2. Anatomy and physiology of arterial wall

The typical histological and anatomical structure of an arterial wall is shown in Figure 2.2. The arterial wall could be considered by its structure as a number of layers which is made up of three major layers of intima, media and adventitia and two other layers of endothelium and internal elastic lamina (IEL). From the lumen side outward, the five layers of arterial wall are following by endothelium, intima, internal elastic lamina (IEL), media and adventitia. The innermost layer, endothelium, is a single layer of endothelial cells lining as interior surface of arterial which could be elongated in the same direction of blood flow (Yang and Vafai, 2006) and directly contacts to blood flow in the lumen forming as an interface between the circulating blood and other layers of arterial wall. Intima, the innermost major layer, both connective tissue and smooth muscle are presented. Intima grows with age or disease conditions and consequently might become more significant in mechanical behavior of arterial wall. The internal elastic lamina separates the intima from the media. The media, the thickest layer, is consist of alternating layers of smooth muscle cells and elastic connective tissue and arrangement form of its components gives the media high strength and ability to resist load. The media layer is surrounded by loose connective tissue, the adventitia. The adventitia is the outermost layer of arterial wall which is composed of fibrous tissue containing elastic fibers, lymphatic and the occasional nutrient vessels. In high level of pressure, the adventitia change to be like a stiff tube to prevent the artery from rupture.

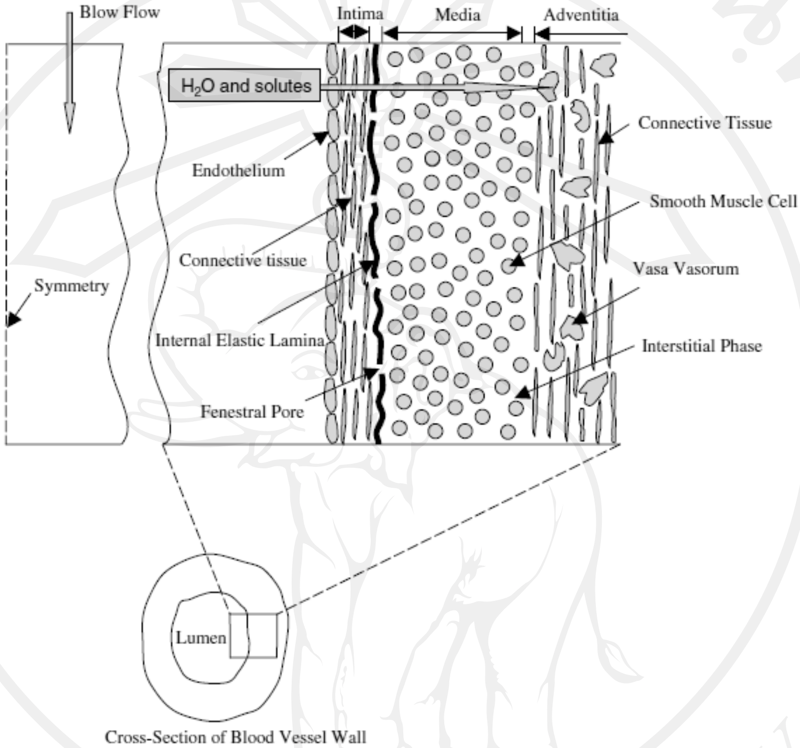

Figure 2.2 Transverse section of a large artery (Ai and Vafai, 2006)

2.3. Material model of arterial wall

Study of the mechanical properties of arterial wall is important because mechanical properties influence arterial physiology, initiation and propagate of arterial diseases. Stress and strains in arterial wall are important factors for understanding mechanics of arteries. Knowledge of the mechanical properties of the wall can use to analyze stress and strain. This section, we review the methodologies used to determine the elastic properties of arterial wall.

2.3.1. Measurement of pressure and diameter of arterial wall

There are several previous studies attempted to investigate relationship of pressure and diameter and meachanical properties of arterial wall (Peterson *et al.*, 1960; Bergel, 1961a; Bergel. 1961b; Patel *et al.*, 1963; Fung, 1967; Pagani *et al.*, 1979; Armentano *et al.*, 1995; Hardt *et al.*, 1999; Guo and Kassab, 2004). Measurement of arterial elasticity had started by study *in vitro*. *In vitro* is Latin language referred to study in experimental biology which arterial vessel has been isolated from its biological context for more convenient analysis. One of the simplest methods is uniaxial tensile testing as illustrated in Figure 2.3. Arterial vessel is cut as flat strip or long cylindrical specimens and is applied uniaxial force. The force and specimen deformation are measured.

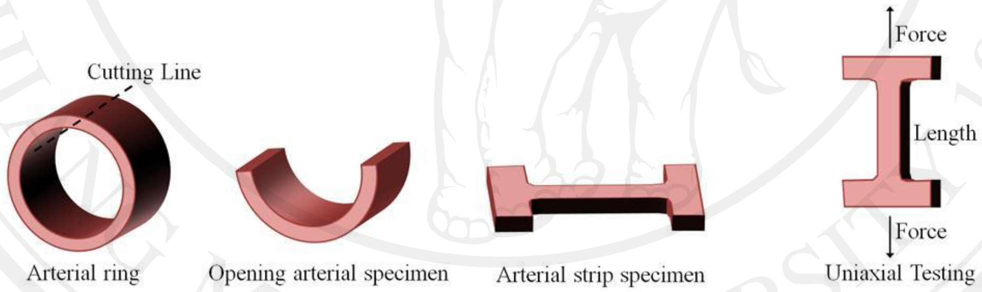

Figure 2.3 Uniaxial testing of arterial strip specimen

In uniaxial test, force is steadily increase and applied to longitudinal direction of specimen which means that force is applied in circumferential direction of arterial specimen in Figure 2.3. Applied force results specimen deformation. The specimen deformation is measured. By this method, it provides relation between stress and strain where stress is force divided by specimen cross-sectional area and strain is specimen elongation divided by reference specimen length. Forces have developed for multiaxial stresses in arterial walls. For instance biaxial testing, as illustrated in Figure 2.4, this kind of testing can apply forces in circumferential and longitudinal directions simultaneously.

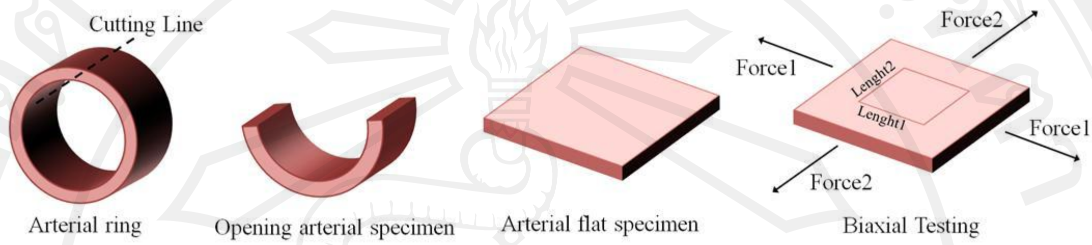

Figure 2.4 Biaxial testing of arterial flat specimen

Despite uniaxial and biaxial testing of arterial strip specimen and arterial flat specimen are often performed, pressure and diameter relationship obtained from tubular segments of arterial vessel are more realistic. *In vitro* studies with tubular specimen had been performed (Patel et al., 1963; Begel, 1961; Begel, 1961; Guo and Kassab, 2004). For instance, Begel (1961) had attempted to study elastic properties of arterial wall. Tubular specimen of arterial wall was studied with apparatus as shown in Figure 2.5. Sinusoidal variations in volume of arterial wall occurred due to a steady pressure of 100 mmHg by a cam-operated pump and changes in radius of the specimen are detected with a collimated light beam and a photomultiplier tube.

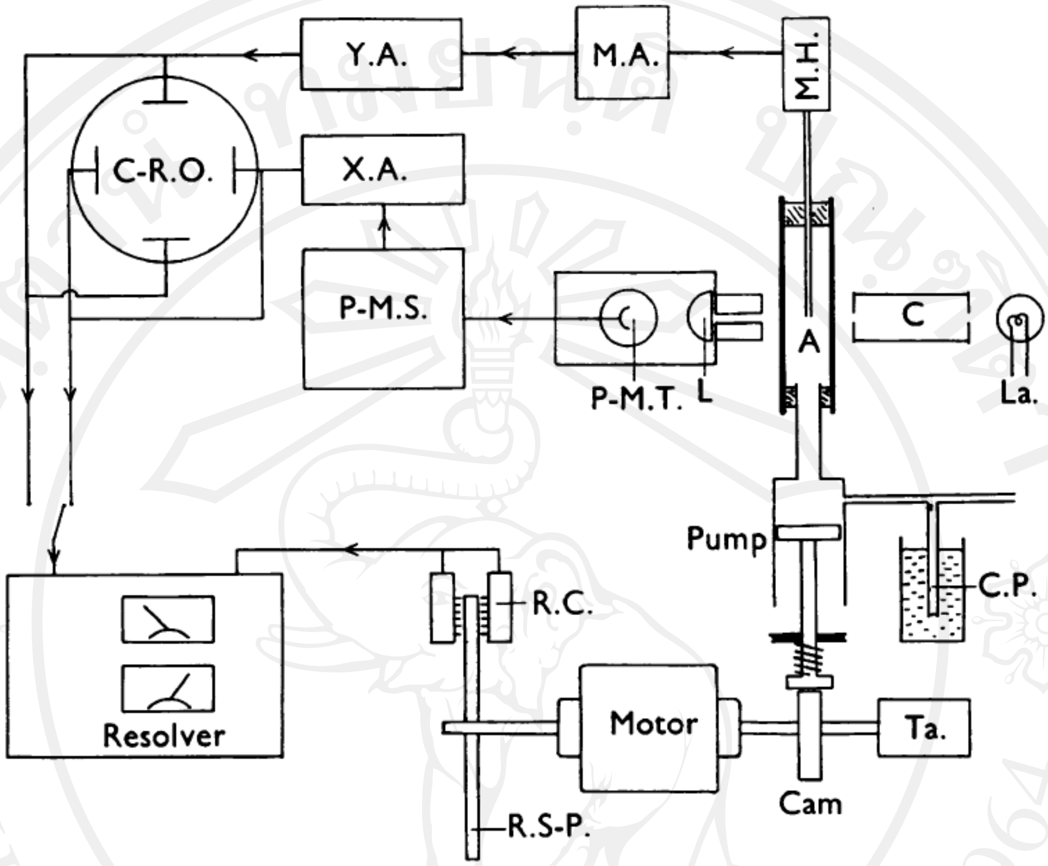

Figure 2.5 Formalized diagram of the apparatus. A, arterial specimen; C, collimating tube; La, light source; C.P., mercury-column manostat; Ta, tachometer; R.S-P., resolver switch-plate; R.C., resolver contacts; L, lens; P-M.T., photomultipier tube; P.M.S photomultipier power supply; M.H., manometer transducer head; M.A., manometer amplifier; X.A., X amplifier; Y.A., Y amplifier; C-R.O., cathode-ray oscilloscope. (Bergel, 1961).

There are various devices for measurement of wall diameter during test. These include still camera, movie camera, sonomicrometer etc. These methods have been further applied to *in vivo* animal experiment which is more realistic. In contrast to *in vitro*, the term of *in vivo* refers to study in experimental biology which arterial vessel live in their normal, intact state. In recent years, video dimension analyzers have been widely used because they are convenient to use. There are some researchers who had studied pressure and diameter of arterial wall by using *in vivo* invasive method (Hardt *et al.*, 1999; Pagani *et al.*, 1979; Peterson *et al.*, 1960; Armentano *et al.*, 1995). For example, intravascular ultrasound as shown in Figure 2.6 had been used for measure of arterial diameter.

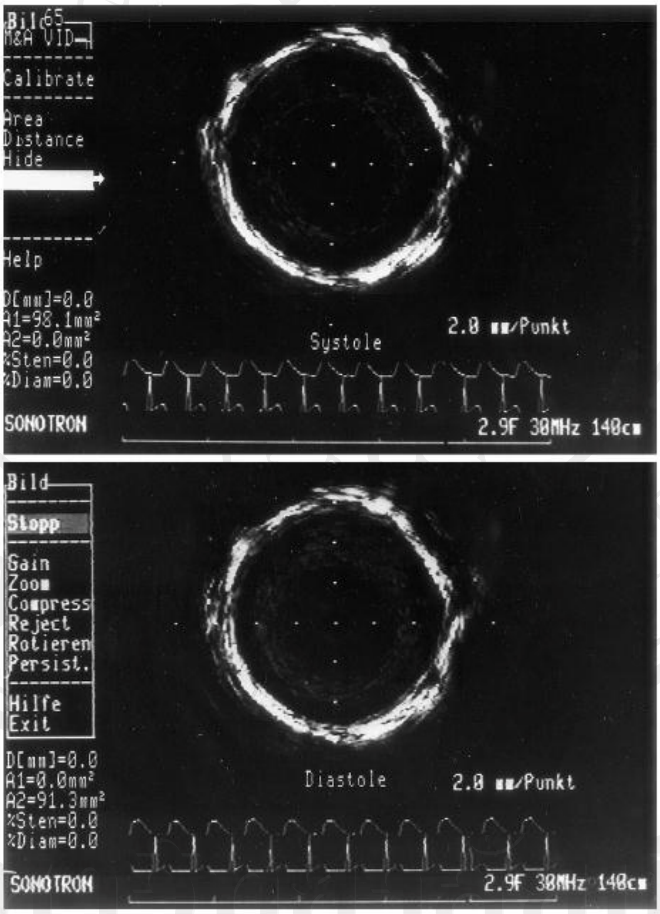

Figure 2.6 Representative example of systolic (top) and diastolic (bottom) images of abdominal aorta recorded with intravascular ultrasound (IVUS). Boundaries of inner lumen are clearly detectable. (Hardt et al., 1999)

Intravascular method has shown as feasible and reliable method for the investigation of changes in aortic wall mechanics. As a recent in ultrasonic technique, diameter and wall thickness of arterial wall could be measure non-invasively with good precision (Konofagou and Opair, 2000; Konofagou *et al.*, 2001; Konofagou and Hynynen, 2002; Harrigan and Konofagou, 2004). Elastic properties of arterial wall can be described quantitatively based on this *in vivo* non-invasive method. Most recent, *in vivo* characterization of the aorta wall stress and strain relationship (Dapinid *et al.*, 2010) had been revealed. *In vivo* non-invasive method by using high frame rate of ultrasound imaging can provide displacement information of abdominal aortic vessel and can be effectively employed to observe one dimension stress and strain relationship. By this point of view, it obviously seen that *in vivo* non-invasive method is reasonably used for further study on multi dimensions of arterial wall especially in three principal directions of radial, axial and circumferential direction respected to geometry of arterial wall.

2.3.2. Characteristic of arterial wall

From the fact that arterial wall consists of several biological basic elastic material such as elastin, collagen, smooth muscle cell, these constituents certainly affect its mechanic behavior and the stress and strain relationship as well. Arterial wall undergo large deformations when subjected to physiological loading like most soft biological tissue (Fung 1990; Fung 1993; Fung 1997; Humphey and Delange, 2003). Arterial response to applied load of luminal pressure while increasingly greater load, or stress, had been observed disproportionate increases in extension, or strain. Behavior of stress and strain response thus tends to exhibit as nonlinear material.

Another important characteristic exhibited by solid under certain conditions is elastic behavior. Although an elastic behaviors suggests that a material responses instantaneously to an applied load, behavior of large arterial wall exhibits nearly elastic behavior because of small hysteresis (Holzapfel *et al.*, 2004) occurred between loading and unloading in stress and strain curve. The nearly elastic behavior of arterial wall is called pseudoelastic which was defined by Fung. Constitutive equations for this behavior are introduced for instance in Table 2.1.

According to arterial constituents, the arterial wall can be presented influents both of isotropic and anisotropic material (Holzapfel *et al.*, 2000). Each layer of arterial wall composed of non-collagenous fibers and two families of collagen fibers which can be treated as isotropic and anisotropic materials, respectively. Arrange of collagen fibers in the reference configuration and histological images of intimal strip, medial strip and adventitial strip with circumferential orientation are shown in Figure 2.7. The overall response of each layer is therefore orthotropic.

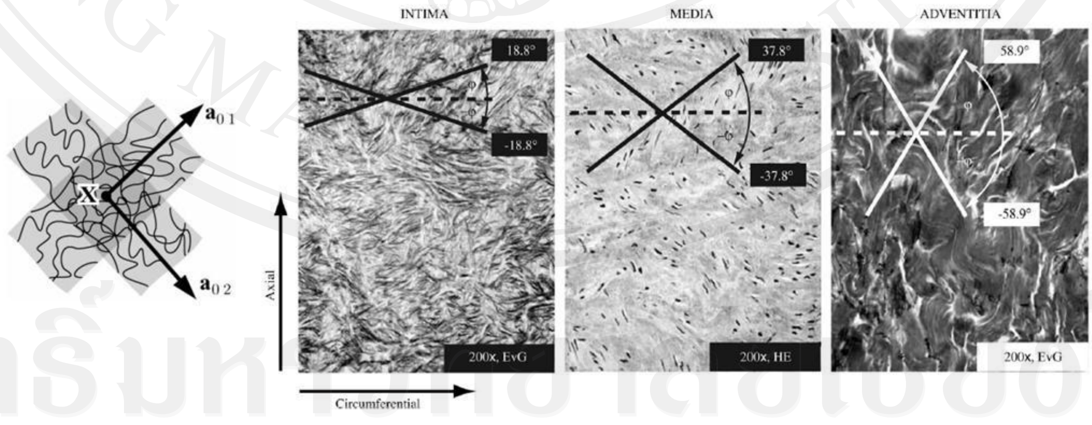

Figure 2.7 Arrange of collagen fibers in the reference configuration (adapted from Holsapfel (2001)) and histological images of intimal strip, medial strip and adventitial strip with circumferential orientation (adapted from Holzapfel (2006)).

When arterial wall is subjected to load, the arterial wall deforms which its shape and volumes are changed. The volume of arterial wall changes about 0.13-1.26% (Carew *et al.*, 1968; Chuong and Fung, 1984) while arterial segment was inflated by pressure of 181 mmHg and while arterial wall was subjected by compressive stress of 10 kPa. Although the arterial wall is slightly compressible, it can be considered as practically incompressible material. The fact that arterial wall preserves its volume is general used to simplification on constitutive equations to describe mechanical properties of arterial wall.

As mentioned, the arterial wall is heterogeneous, nonlinear and anisotropic material. A single-strain energy function cannot be applied to present behavior throughout the arterial wall. Von Maltzahn et al., (1984) had attempted to model arterial wall as two layers model for study elastic properties of media and adventitia of carotid artery. In their study, constitutive equation in exponential form proposed by Fung is employed with a parameter set to study stress distributions of monolayered arterial wall and this type of constitutive equation is also employed with two parameter sets referred to media and adventitia to study stress distribution of two-layer arterial wall in all three directions of radial, axial and circumferential directions across arterial wall. Discontinuous of the stresses exist at the boundary of intact layers. This similar approach was followed by Sokolis (2010). Discontinuous of the stresses existed at the boundary of intact layers is also found. There is lack of mechanical model of more than two-layer arterial wall, three dimensions of geometry and three dimensions of constitutive equation which related stresses and strains because one of important reasons for the model that it is experienced with a number of three dimensions material parameters for each layer needed to estimate prior.

2.3.3. One, two and three dimension constitutive equations

To specify the properties of aortic vessel, constitutive equations are employed. There are many constitutive equations used to descript the properties especially Hookean elastic solid which relate stress and strain relationships as can see good description of mechanic properties for general engineering material. However, the properties of the aorta cannot be simple described.

The characterization of the stress and strain relationship of the arterial wall has been investigated for decades. For instance, simplest method to descript stress and strain relationship is consideration the vessel wall as thin wall. This method can presents simple stress and strain relationship which used for prior study of blood vessel by using Laplace's Law which relates relationship between radial stress occurred from luminal pressure and circumferential stress by assumption that the circumferential stress is nearly constant. The circumferential stress $\sigma_{\theta\theta}$ and circumferential strain $\varepsilon_{\theta\theta}$ could be expressed as in following equations.

$$\sigma_{\theta\theta}=\frac{P_i r_i}{h},\ \varepsilon_{\theta\theta}=\frac{r_{mean}-R_{mean}}{R_{mean}} \tag{2.1}$$

Stress and strain are easier express as tensors and because the aortic vessel is not rigid body, there is moving boundary changing by time, stress and strain can be express in configurations as Figure 2.8. The nonlinear relationship of stress and strain response can determine by using strain energy function. From the first derivative of strain energy function respected to the Green-Lagrange strain tensor $\boldsymbol{E}$, the second Piolar-Kirchoff stress can be obtained and consequently can be transformed to

Cauchy stress which expresses stress relative to current configuration. There are some strain energy functions in two and three dimensional formulations which appropriate for analysis of thick wall tube and use to determine stress and strain of arterial wall shown in Table 2.1.

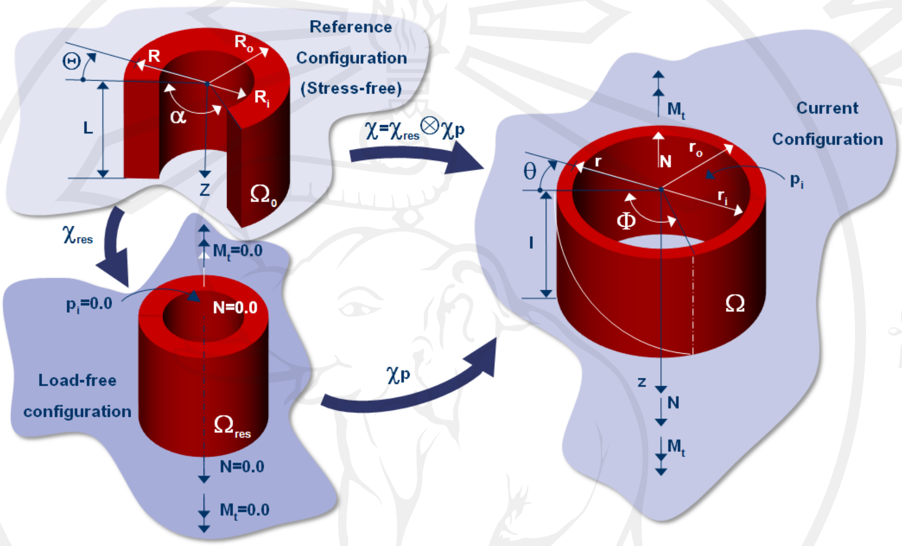

Figure 2.8 Arterial ring in the reference configuration, in load-free configuration and in current configuration (adapted from Holzapfel *et al*. (2000))

Using strain energy function generally involves with a number of parameters. These parameters cannot be chosen arbitrary (Fung,1990; Holzapfel *et al.*, 2000; Humphrey and Delange, 2004). Optimization process must be performed within range that parameters have convexity of strain energy contour in plane of $E_{\Theta\Theta}$ and E_{ZZ}. Our preliminary study of aortic wall as thin wall and thick wall presents in Appendix; A.1. stress and strain analysis of abdominal aortic vessel: a case of three dimensional geometry simulation and A.2. a comparative study of stress and strain analysis of murine abdominal aortic wall based on ultrasound data: cases of thin wall and thick wall.

Table 2.1 Strain energy functions for study mechanical properties of arterial wall

Source of strain energy function	Dimension of formation	Strain energy function	Note	Parameter
Vaishnav *et al.* (1973)	2	$\bar{\Psi} = c_1\bar{E}_{\Theta\Theta}^2 + 2c_2\bar{E}_{\Theta\Theta}\bar{E}_{ZZ} + c_3\bar{E}_{ZZ}^2 + c_4\bar{E}_{\Theta\Theta}^3 + c_5\bar{E}_{\Theta\Theta}^2\bar{E}_{ZZ} + c_6\bar{E}_{\Theta\Theta}\bar{E}_{ZZ}^2 + c_7\bar{E}_{ZZ}^3$	-	c_1, c_2, c_3, c_4, c_5, c_6, c_7
Fung *et al.* (1979)	2	$\bar{\Psi} = \frac{1}{2}c\{\exp(\bar{Q}) - 1\}$	$\bar{Q} = b_1\bar{E}_{\Theta\Theta}^2 + b_2\bar{E}_{ZZ}^2 + 2b_4\bar{E}_{\Theta\Theta}\bar{E}_{ZZ}$	c, b_1, b_2, b_4
Takamizawa and Hayashi (1987)	2	$\bar{\Psi} = -c\mathrm{Ln}(1 - \bar{\psi})$	$\bar{\psi} = \frac{1}{2}b_1\bar{E}_{\Theta\Theta}^2 + \frac{1}{2}b_2\bar{E}_{ZZ}^2 + b_4\bar{E}_{\Theta\Theta}\bar{E}_{ZZ}$	c, b_1, b_2, b_4
Delfino *et al.* (1997)	3	$\bar{\Psi} = \frac{a}{b}\left\{\exp\left[\frac{b}{2}(\bar{I}_1 - 3)\right] - 1\right\}$	$\bar{I}_1 = 2(\bar{E}_{\Theta\Theta} + \bar{E}_{RR} + \bar{E}_{zz}) + 3$	a, b
J.D. Humphey (1995)	3	$\bar{\Psi} = \frac{1}{2}c\{\exp(\bar{Q}) - 1\}$	$\bar{Q} = b_1\bar{E}_{\Theta\Theta}^2 + b_2\bar{E}_{ZZ}^2 + b_3\bar{E}_{RR}^2 + 2b_4\bar{E}_{\Theta\Theta}\bar{E}_{ZZ} + 2b_5\bar{E}_{ZZ}\bar{E}_{RR} + 2b_6\bar{E}_{RR}\bar{E}_{\Theta\Theta} + b_7\bar{E}_{\Theta Z}^2 + b_8\bar{E}_{RZ}^2 + b_9\bar{E}_{R\Theta}^2$	c, b_1, b_2, b_3, b_4, b_5, b_6, b_7, b_8, b_9

2.4. Ultrasound imaging of arterial wall

In order to assess displacement of the arterial wall, a motion estimation technique has been applied to determine displacement of arterial wall based on ultrasound imaging (Konofagou and Ophir, 2000). The basic of ultrasound imaging are presented in this section.

In various clinical applications, ultrasound is used to produce two dimensional imaging of the body soft tissue including arterial blood vessel by using high frequency sound wave (Wells, 2006; Roman *et al.*, 2006). This imaging is used for diagnosis and guidance of treatment procedures. The advantages of ultrasound are that ionizing radiation to produce images is not required which is safe technology, ultrasound provide images in real-time and the image resolution is suitable to use in clinical applications. Moreover, ultrasound is less expensive technique comparing to others in the similar capability and versatile. Ultrasound does not damage tissue with ionizing radiation which is a great advantage over x-ray imaging technology. Ultrasound can be used in any of several modes depending on the interest. Ultrasound wave is sound waves above the frequency that human can hear. In the other word, wave frequency of ultrasound is above 20 thousand hertz. Frequencies between 1 and 10 Megahertz are generally used as medical ultrasound. Although higher frequencies of ultrasound waves provide more detailed imaging, the waves are more readily absorbed and cannot deeply penetrate into body. Ultrasound imaging in large arteries is therefore generally performed at frequencies between 2-5 Megahertz. There are two components in an ultrasound scanner. First, the transducer, it produces sound wave which penetrate body and receives reflected echoes. Second, the data processing unit computer, it organizes the data into an image on screen. Transducers are built around piezoelectric ceramic chips which transmit waves and receive wave by react to electric pluses by producing sound wave and react to sound wave by producing electric pluses, respectively. The transducer is supplied by bursts of high frequency electric pluses to produce scanning sound waves and then receives returning echoes, translates the returning echoes back into electric pulses and sends the returning echoes to data processing computer. Sound waves travel through all tissue of body at speed about 1,500 m/s. Each echo can be received and plotted on the screen as distance into the body and as a point of varying brightness. The echoes are translated into an image by using this way.

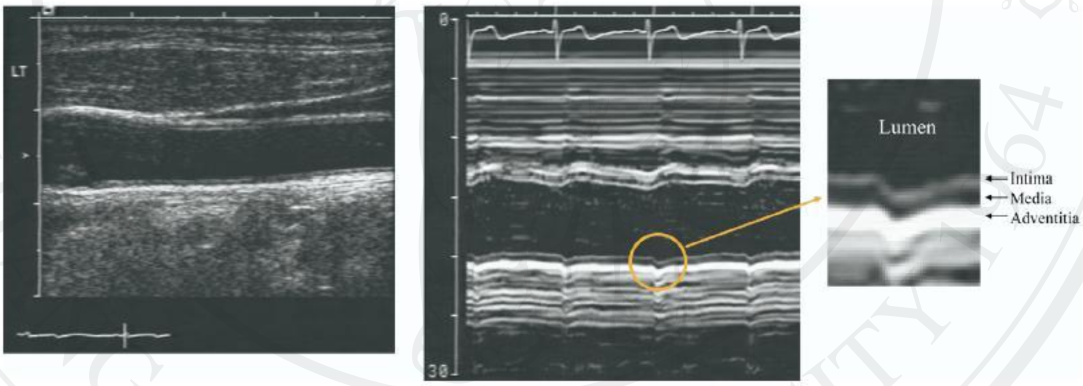

Figure 2.9 B-mode (Left) and M-Mode (Right) image of distal common carotid artery (Roman *et al.*, 2006).

There are several different modes of ultrasound used in medical imaging (Yadav *et al.*, 2011) as following. Firstly, A-mode, it is the simplest type of ultrasound. A single transducer scans a line through body. Echoes plotted on screen in function of depth. This method is suitable use to measure distances within the body and size of internal organ. Secondary, B-mode, in B-mode a linear arrays of transducers simultaneously scans a plane through the body. Two dimensional imaging can be displayed on screen. The other, M-Mode, it displays sequence of B-mode scans enables doctors to see and measure range of motion because organ boundaries that produce reflections move relative to the probe. The several modes of ultrasound imaging named as capital alphabets A-, B- and M- so come from amplitude, brightness and motion, respectively. Images of B-mode and M-mode are shown as instance in Figure 2.9. It is therefore extremely challenging to model three dimensional stress and strain based on advantages of this *in vivo* non-invasive ultrasound imaging.

2.5. Summary

Circulatory system has the aortic vessel as an important part in carrying blood from pulsatile flow from the heart which acts as pump to steady flow in an organ. It is different from other engineering materials. Aortic vessels is biological tissue which not lies on Hooke's law, the expression of the stress and strain on the non-linear elastic model has been demonstrated. The response of the artery could be clearly identified that the load and unloading paths show only small hysteresis. Stress and strain behavior of arterial wall hence involve with elastic deformation under the pressure load. Within the range of pressure considered in this study, the aortic vessel could be considered as incompressible material. According to this reason, extending the developed mechanical modeling from only one or two dimensions to completely three dimensions seems to be possible. The heterogeneity of the aortic can be reasonable considered as multi homogeneous layers by histology of the aorta which simplifies complex constituents of the blood vessels to simple systemic. And of course, the *in vivo* non-invasive imaging of ultrasound can be useful in the modeling.

Ultrasound imaging provides as input information for mechanics model to explain the normality of the blood vessels, which aid in medical diagnosis. These conclusions lead to a mechanics model which is described in the next chapter.