CHAPTER 1

INTRODUCTION

1.1 MOTIVATION

Recent reports of World Health Organization indicate that the number of people with cardiac ailments in India is growing alarmingly. If unchecked 50% of the world’s cardiac cases will be from India by the year 2012(). Age is the major risk factor for cardiovascular disease. Changing lifestyles, high stress and sedentary work culture are among the other contributors. So far very little attention has been devoted to aging. It is because age has usually been viewed as a chronological, unpreventable or untreatable risk factor. But, vascular aging is a cardiovascular risk factor as stated by Najjar et al (2005). Vascular aging and vascular disease go together; each has its own contribution to what is presently referred to as ‘cardiovascular disease’. Hence, what clinical people now refer as ‘vascular disease’ must be regarded as the ‘vascular aging-vascular disease interaction’. Though there is significant improvement in cardiovascular treatment, little is done towards the assessment and prevention of these diseases.

1.2 OBJECTIVE

Aging alters the structure and function of large elastic arteries. To understand why age is so closely linked to cardiovascular disease and ultimately to understand the causes and develop cures for this group of diseases, it is essential to understand what is happening in the heart and
arteries during normal aging – aging in the absence of disease. This work focuses on the effects of aging on blood vessels.

The aim of present work is

- to compare the structural and functional modifications of the common carotid artery (CCA), a large elastic artery, in different groups of healthy subjects that differ in age.
- to maintain a database for healthy subjects and thereby, provide caution to subjects with ‘unsuccessful aging’ to meet the cardiologist for further diagnosis and treatment.

Unsuccessful aging does not mean that they have clinical disease, but is viewed as a risk factor for future clinical cardiovascular disease.

1.3 PROBLEM FORMULATION

Age associated modeling of large arteries in healthy persons is manifested by dilatation of the vessel and vessel lumen diameter to characterize vascular aging though two more parameters (intima media thickening and endothelial dysfunction) are also involved as shown by Arno et al (1998). To find the dilatation of the vessel lumen, the distension of the vessel lumen is measured. The diameter of the vessel is also measured.

The CCA is segmented and the boundary of the vessel lumen is extracted. Segmentation is done by two techniques (i) by canny operator, which is combined with other pre, and post-processing techniques for the longitudinal as well as the transversal section of the B-mode image (ii) by Daubechius wavelets and watersheds. This is done for a set of consecutive
frames, 20-30 frames (corresponding to 2-3 cardiac cycles) for each subject. The diameter is measured for each frame and the total variation in the diameter (distension) for each patient is stored. A database is maintained for subjects with different age groups, their diameter and corresponding distension. A back propagation network is trained which takes the inputs, distension and diameter and compares with the database and gives an output informing if the subject has ‘successful’ or ‘unsuccessful’ vascular aging. A system is developed which, when a person walks in, calculates the vascular age from his arterial diameter and distension. The individuals who manifest ‘unsuccessful’ vascular aging might be viewed as having sub clinical vascular disease. They are recommended to meet the physician for further diagnosis and treatment.

1.4 BACKGROUND
1.4.1 Aging

Aging blood vessels are fertile soil in which the seeds of cardiovascular diseases flourish, and therefore, vascular aging contributes to the age-dependent rise in hypertension and atherosclerotic disease and the chronic heart failure or stroke that result from these diseases (Edward 1993). Aging confers an even more risk for these diseases than do other major risk factors, such as smoking, diabetes, or life style. The impact of increasing age on the risk of the occurrence of cardiovascular diseases as well as their severity is mainly due to the age-associated changes in cardiovascular structure or behavior, which is definitely present in every person with cardiovascular disease.

In most of the developing countries, the age profile of the population keeps changing from a pyramidal distribution, in which the young people dominate, to a columnar structure in which the elder people
progressively become more numerous as life expectancy has increased as stated by Lakatta and Levy (2003). This transition, adds more years of life, and at the same time provides a longer period of exposure to the risk factors of cardiovascular diseases. If population levels and risk factors for cardiovascular diseases increase simultaneously due to changes in life-style then, their effect becomes further compounded. Both the amount and duration of exposure to cardiovascular disease risk factors increase, and changes in blood vessels due to the aging process lay the foundation for the cardiovascular epidemic.

The epidemic of cardiovascular diseases is no longer restricted to Western societies. Cardiovascular diseases now spread their roots in India and are expected to surpass infectious diseases as the leading cause of mortality and disability. The major reasons for such changes in the pattern of diseases and the massive increase in heart disease are reported to be: 1) the growing life expectancy; 2) the decreasing infant mortality rate; 3) the decline in infectious disease rate; 4) the increase in gross national product and in per capita income enabling the populations of these nations to adopt the "unhealthy" life-styles and behaviors of the more developed countries; and 5) the interaction among genetic factors and newly altered environment.

Cross-sectional studies in humans have found that wall thickening and dilatation are prominent structural changes that occur within large elastic arteries during aging (Laurent 1996). The age-associated increase in intima-media thickening and endothelial dysfunction are accompanied by both luminal dilatation and a reduction in arterial compliance or distension with an increase in vessel stiffness (Laurent 1996). Still, more recent data from epidemiological studies show that increased large vessel stiffening may also be due to atherosclerosis and diabetes (Ahigren 2002). The link is that stiffness is governed not only by the structural changes but also by endothelial regulation of vascular smooth muscle tone and of other aspects of vascular
wall structure/function. **This gives a clear inference that altered mechanical properties of the vessel wall influence the development of atherosclerosis and the later, via endothelial cell dysfunction and other mechanisms, influences vascular stiffness and hence cardiovascular diseases** (Schmidt-Trucksass 2000).

As the walls of large arteries become stiffer, for a given pattern of left ventricular ejection, central systolic arterial pressure and the pulse pressure increases whereas diastolic arterial pressure decreases (Lakatta 2003). This suggests that altered structure/behavior of the stiff vessel wall is an additional risk factor for future vascular events. Recent studies, in fact, have demonstrated that increased vascular stiffness precedes the development of hypertension (Van Popele 2001). There is a growing body of evidence that increased stiffness and endothelial dysfunction in healthy older persons, and the ensuing increase in systolic and pulse pressure, earlier thought to be part of normal aging are now predicted to be high risk factors for developing cardiovascular disease.

Therefore the current purpose is to understand the age-associated changes in vascular structure and function, in apparently healthy persons. This is then specifically related and conferred to the increased risk for clinical cardiovascular disease occurrence and severity. This goal is pursued to provoke thought regarding the new effort to design the system that elucidates the aspects of aging like age-associated increase in large vessel lumen and stiffness. This aims at creating awareness of those aspects of aging that occur in healthy persons, but confer risk for over subsequent clinical cardiovascular disease.

Arterial tree is not a homogenous system (Bartolotto 1999). Major differences exist in the structure and function of various arteries. The method
for diagnosis of early stage of cardiovascular diseases is proposed to measure the physical and mechanical properties of the arterial wall i.e., diameter and change in diameter (distension) of the arterial wall. From the viewpoint of clinical investigation, the simplest approach for studying structural changes of large arteries with aging is the measurement of lumen diameter in various populations (Laurent 1996); for studying functional change, the distension of the artery which is directly related to the elasticity, may be measured. Studies reveal that elastic arteries better suit the purpose than muscular arteries like femoral artery as they are not clearly altered by age (Benetos 1993). Common carotid artery is an elastic artery. Also, long-term outcome of patients with carotid artery disease rests on modifying risk factors for circulation problems that can also lead to blockage in heart and leg arteries (Stephanian 2005). Moreover the association between carotid and coronary atherosclerosis has helped to focus on common carotid artery. CCA diameter increases as a consequence of hypertension and may also increase as the thickness of the arterial wall increases due to atherosclerosis and plaque deposits (Polak 1996). Therefore it is suggested that CCA is a highly compliant artery for the study of elastic properties like distension. The distension of an artery during a cardiac cycle depends on the elastic characteristics of the vessel wall. Distension is the change in diameter of the artery from diastole to systole. Diastole is the relaxation of heart muscles and systole is the contraction of heart muscles during pumping of blood.

1.4.2 Carotid System

Blood vessels are hollow tubes that carry blood through miles and miles in a never-ending stream. If all the blood vessels could be taken and lined up, they could reach about 60,000 miles long in a child and 100,000 miles in an adult. Blood vessels form a closed system of tubes that carries blood away from the heart, transports it to the tissues of the body and then
returns it to the heart. The blood vessels carry blood between the heart, different tissues and organs of the body. There are three types of blood vessels: arteries, veins and capillaries. These blood vessels have the ability to expand to allow more blood to flow through them. They can also contract to help control the flow of blood. The blood flows through the big arteries into smaller ones. The smallest arteries, called arterioles, direct the blood flow into capillaries. The capillaries connect to the smallest veins called venules. The veins then return the blood to the heart.

The arteries are elastic, muscular tubes that carry the blood from the left ventricle of the heart to the capillaries. The walls of the arteries are thicker than the other vessels because of the high pressure. The largest artery is the aorta, which is about 1 inch in diameter. The wall of an artery has three coats, with the innermost coat being the endothelium. The endothelium is a continuous layer of cells that line the inner surface of the entire cardiovascular system. Normally the only tissue that blood comes in contact with is the endothelium. The hollow center through which blood flows is called the lumen. The outer layer of tissue called adventitia varies a lot between different arteries and contains fibro elastic tissue, nutrient vessels and nerves. It also connects the artery with its surrounding tissues. The muscular middle layer consists mostly of smooth muscle cells and various elastic tissues. Figure 1.1 shows the structure of the artery. Arteries are generally classified as elastic and muscular arteries:

- Elastic arteries are bigger arteries. These have more elastic materials in their walls and conduct large amounts of blood away from the heart.
• Muscular arteries – once the blood has reached the general region it is aimed for, smaller arteries take over, such as radial artery. These have more smooth muscles.

**Figure 1.1 Structure of the artery**

In healthy subjects the mechanical properties of elastic arteries like the carotid artery and aorta are age dependent (Ahigren 2002). In contrast, muscular arteries, like the common femoral artery are not clearly affected by either age or gender. The main reason for choosing carotid artery for this study is that carotid disease could indicate the presence of severe Coronary Artery Disease (CAD), a leading cause for stroke and heart attack. The combination (Kallikazaros 1999) of carotid disease with impaired left ventricular systolic performance could predict the presence of severe CAD. Also the absence of carotid disease in a patient with normal left ventricular systolic performance may reflect the absence of severe CAD.

Figure 1.2 shows the Carotid system located in the neck. This contains the Carotid communis (CCA), which branches into Carotid interna
(Internal carotid artery) and Carotid externa (External Carotid artery). The left Carotid communis artery is the second branch from the arch of the aorta. It divides into Carotid interna and externa the same way as the right Carotid communis. The Carotid interna artery supplies blood to structures inside the skull like most of the cerebrum of the brain. It also supplies blood to the eyeballs, ears, and external nose. The general distribution of the Carotid externa artery is to structures external to the skull.

![Carotid system diagram](image)

**Figure 1.2 The Carotid system**

A stroke occurs when the blood supply to parts of the brain is suddenly interrupted, (ischemic stroke), or when a blood vessel in the brain bursts, spilling blood into the spaces surrounding brain cells (hemorrhagic stroke). For all types of medical intervention, treatment must be given immediately, as neuronal death progresses quickly after the onset of symptom. The most common form of stroke is ischemic stroke, which occurs when an artery becomes blocked, suddenly decreasing or stopping the blood flow. Blood clots are the most common cause of artery blockage and brain
infarction. Ischemic strokes can also be caused by stenosis. This kind of stroke accounts for approximately 75 percent of all strokes (Stephanian 2005).

Carotid stenosis refers to the blockage and narrowing of the Carotid artery. This blockage is caused by fatty build-up called plaque and is also referred to as arteriosclerosis. This fatty material accumulates in the inner lining of blood vessels and results in narrowing and irregularity of the artery as seen in Figure 1.3. The complex structure of the plaque cause heterogeneous stress-strain states, which may ultimately lead to rupture and the formation of blood clots that can flow up to the brain and cause ischemic stroke.

The arterial system can be considered as an elastic chamber, which represses the blood volume in systole and delivers a suppressed, almost constant flow to the capillaries in diastole. The circulation system is a network of elastic tubes with complex geometry and non-linear elastic properties. It is therefore a very complicated system to model. For practical reasons it can be sufficient to describe the mechanics of the vessel wall as a function of pressure and diameter.

Figure 1.3 Diseased artery
Many medical conditions, such as arteriosclerosis, change the mechanical properties of the vessel walls, which is why physicians study parameters like compliance and distension (Laurent 1994). The build-up of plaque makes the wall stiffer which decreases the distension. With this idea, this work proposes to measure the diameter and distension and thus infer on the risk factors of cardiovascular diseases.

1.4.3 Ultrasound Imaging

Ultrasound is a popular medical imaging modality because it is non-invasive, versatile, with no known side effects, and the equipment used for ultrasonic scanning is small and inexpensive relative to other options. A distinguishing feature of ultrasound images is the oriented “speckle texture” produced by the physics underlying the data acquisition (Brunner 2002). Due to its orientation, which changes somewhat across the image, the speckle energy is typically concentrated in certain spectral regions. Speckle is caused by scattered reflections produced by features that are small with respect to the wavelength. These multiple small reflections result from a rough scattering surface with fine scattering structures.

Ultrasound includes all sound waves above the frequency of human hearing—about 20 thousand Hertz, or cycles per second. Medical ultrasound generally uses frequencies between one and 10 million Hertz (1-10 MHz). Higher frequency ultrasound waves produce more detailed images, but are also more readily absorbed and so cannot penetrate deep inside the body. Carotid ultrasound imaging is performed at frequency of 7.5 MHz. Table 1.1 shows the various transducer frequencies used in ultrasound imaging and their penetration levels.
### Table 1.1 Ultrasound Transducer frequency

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<th>Low resolution</th>
<th>2.0 MHz</th>
<th>High penetration</th>
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<tr>
<td>High resolution</td>
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<td>Low penetration</td>
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An ultrasound machine consists of two parts: the transducer and the analyzer (Ohanyido 2005). The transducer, produces the sound waves that penetrate the body and also receives the reflected echoes. Transducers are built around piezoelectric ceramic chips. (Piezoelectric refers to electricity that is produced when pressure is put on certain crystals such as quartz). These ceramic chips react to electric pulses by producing sound waves (they are transmitting waves) and react to sound waves by producing electric pulses (receiving). Bursts of high frequency electric pulses supplied to the transducer cause it to produce the scanning sound waves (Hall 1993). The transducer then receives the returning echoes, translates them back into electric pulses and sends them to the analyzer—a computer that organizes the data into an image on a television screen.

Because sound waves travel through all the body's tissues at nearly the same speed—about 3,400 miles per hour—it takes few microseconds for each echo to be received. This can be plotted on the screen as a function of distance of penetration into the body. The relative strength of each echo, a function of the specific tissue or organ boundary that produced it, can be plotted as a point of varying brightness. In this way, the echoes are translated
into a picture. Tissues surrounded by bone or filled with gas (the stomach, intestines and bowel) cannot be imaged using ultrasound, because the waves are blocked or become randomly scattered.

Four different modes of ultrasound are used in medical imaging:

- **A-mode.** Amplitude Modulation. This is the simplest type of ultrasound in which a single transducer scans a line through the body with the amplitudes of the returning echoes plotted on screen as a function of time. This method is used to measure distances within the body and the size of internal organs. Therapeutic ultrasound aimed at a specific tumor or calculus is also A-mode, to allow for pinpoint accurate focus of the destructive wave energy.

- **B-mode.** Brightness Modulation. In B-mode ultrasound, a linear array of transducers simultaneously scans a plane through the body that can be viewed as a two-dimensional image on screen. Ultrasound probes containing more than 100 transducers in sequence form the basis for these most commonly used scanners, which cost about $50,000.

- **M-Mode.** Motion Modulation. A rapid sequence of M-mode scans whose images follow each other in sequence on screen enables doctors to see and measure range of motion, as the organ boundaries that produce reflections move relative to the probe. M mode ultrasound has been put to particular use in studying heart motion.

- **Doppler mode.** Doppler ultrasonography includes the capability of accurately measuring velocities of moving material, such as blood in arteries and veins. The principle is
the same as that used in radar guns that measure the speed of a car on the highway. Doppler capability is most often combined with B-mode scanning to produce images of blood vessels from which blood flow can be directly measured. This technique is used extensively to investigate valve defects, arteriosclerosis and hypertension, particularly in the heart, but also in the abdominal aorta and the portal vein of the liver.

1.5 ORGANISATION OF THE THESIS

Chapter 2 of this thesis reviews those papers presented by physicians in the area of vascular aging. The contribution of technical people in this area is also reviewed. This further discusses the various segmentation algorithms presented by different people working in this area.

Chapter 3 describes the methodology followed in this work. It explains the segmentation and boundary extraction of the vessel lumen and measurement of diameter. This is done by two different methods and a comparison is also done. Measurement of distension of the vessel lumen is discussed. The chapter also includes the description and implementation of back propagation network in evaluating vascular aging.

Chapter 4 discusses the results and draws conclusions of this work.

Chapter 5 discusses the future directions for further research.