CHAPTER 1

INTRODUCTION

1.1 MOTIVATION

The report of World Health Organization (WHO), Global atlas on cardiovascular disease prevention and control states that cardiovascular diseases (CVDs) are the leading causes of death and disability in the world. Although a large proportion of CVDs is preventable, they continue to rise mainly because preventive measures are inadequate. It has been estimated that 17.3 million people died from CVDs in 2008, representing 30% of all global deaths. Of these deaths, an estimated 7.3 million were due to coronary heart disease and 6.2 million were due to stroke (Kyriacou et al 2010). By 2030, almost 23.6 million people will die from CVDs, mainly from heart disease and stroke. CVD is projected to remain the single leading cause of death.

Over 80% of the world's deaths from CVDs occur in low- and middle-income countries. People in low- and middle-income countries are more exposed to risk factors leading to CVDs and other noncommunicable diseases. They are less exposed to prevention efforts than people in high-income countries. They have less access to effective and equitable health care services which respond to their needs. As a result, many people in low- and middle-income countries die often in their most productive years.
Lifestyle changes due to urbanization, industrialization and globalization promote heart disease. These risk factors include tobacco use, physical inactivity and unhealthy diet. People are exposed to these risk factors for longer periods as life expectancy in developing countries is rising sharply. It is costly and prolonging to care CVD clinically. As Individuals are affected by CVD in their peak midlife years, it disrupts the future of their families. It also undermines the development of nations by depriving valuable human resources in their most productive years. At macro-economic level, CVDs place a heavy burden on the economies of low- and middle-income countries. It has been estimated that heart disease, stroke and diabetes would reduce GDP between 1% and 5% in low- and middle-income countries. World maps given by WHO, showing the global distribution of CVD mortality rates in males and females are given in Figure 1.1 and 1.2.


**Figure 1.1 Global distribution of CVD mortality rates in males**
The WHO programme on Cardiovascular Diseases works on prevention, management and monitoring of cardiovascular disease globally. It aims to develop global strategies to reduce the incidence, morbidity and mortality of cardiovascular diseases by developing cost effective and equitable health care innovations for management of CVD. Though different methods are investigated for the analysis of CVD, the need still exists for the development of an integrated system enabling automated diagnosis. Hence an effort is made in this work to develop a cost effective system for the diagnosis of CVDs.

1.2 BACKGROUND

The heart is a muscular organ. A normal heart with its blood supply is shown in Figure 1.3. The normal heart beat rate is 70 times per minute for a person at rest. When a person is active or experiences strong emotions, the heart rate increases. Heart muscle receives its own blood supply from a system of coronary arteries. Arteries are blood vessels that carry blood.
between the heart, different tissues and organs of the body. They have ability to expand or contract to allow more blood or control the flow. Hollow center through which blood flows is called lumen. Blood from the heart to the brain is carried by two large vessels that run along either side of the neck. They carry oxygen and nutrients to all parts of the brain. A good blood supply is vital for the normal function of the brain and heart.

Figure 1.3 Normal heart with its blood supply

1.2.1 Cardiovascular Diseases

Cardiovascular diseases are a group of disorders of the heart and blood vessels. Different types of CVDs are listed below.

- Coronary heart disease: It is caused by the disease of the blood vessels supplying blood to heart muscle (e.g. heart attack)

- Cerebrovascular disease: It is caused by the disease of the blood vessels supplying blood to brain (e.g. stroke)
• Peripheral arterial disease – It is caused by the disease of blood vessels supplying blood to arms and legs

• Rheumatic heart disease: It is caused by the damage to the heart muscle and heart valves from rheumatic fever

• Congenital heart disease: It is caused by the malformations of heart structure existing at birth

Heart attacks and strokes are usually acute events. They are mainly caused by a blockage that prevents blood from flowing to the heart or brain. The most common reason for this is a build-up of fatty deposits on the inner walls of the blood vessels that supply the heart or brain. Strokes can also be caused by bleeding from a blood vessel in the brain or from blood clots. The underlying disease process in the blood vessels that results in coronary heart disease and cerebrovascular disease is known as Atherosclerosis.

Atherosclerosis is a complex pathological process in the walls of blood vessels that develops over many years. It is responsible for a large proportion of CVDs. In atherosclerosis, fatty material and cholesterol are deposited inside the lumen of medium- and large-sized blood vessels. These deposits are called as plaques. Narrowing of artery due to plaque is shown in the Figure 1.4.

![Figure 1.4 Normal artery and artery narrowed by atherosclerosis](image_url)
Plaques cause the inner surface of the blood vessels to become irregular and the lumen to become narrow, making it harder for blood to flow through. Atherosclerotic plaques can either cause stable coronary artery stenosis leading to angina pectoris during exercise, or lead to acute coronary or vascular events such as myocardial infarction or stroke when they rupture (Katouzian et al 2008). Blood vessels also become less pliable as a result. Eventually, the plaque can rupture, triggering the formation of a blood clot. If the blood clot develops in a coronary artery, it can cause a heart attack. If it develops in the brain, it can cause a stroke. Different stages of atherosclerosis are shown in the Figure 1.5.

![Figure 1.5 Different stages of atherosclerosis](image)

1.2.2 Common Carotid Artery

Common Carotid Artery (CCA) supplies oxygenated blood to skull, brain, eyeballs, ears and external nose (Wang et al 2009). It is the largest artery in the neck. It is present on the left and right sides of the body. The right common carotid artery originates in the neck from the brachiocephalic trunk. The left common carotid artery originates from the aortic arch in the thorax. These split into the external and internal carotid arteries at the upper border of the thyroid cartilage, at around the level of the fourth cervical
vertebra. The anatomy of the carotid artery is shown in the Figure 1.6 which is given in the literature (Gupta et al 2012).

Figure 1.6 The anatomy of the carotid artery

The internal carotid artery begins at the termination of the CCA opposite the superior margin of the thyroid cartilage, and terminates in the middle fossa of the skull by dividing into the anterior and middle cerebral arteries. The external carotid artery arises from the CCA opposite the upper border of the thyroid cartilage. The great blood vessels of the neck have numerous variations, and their exploration is more than interesting for a better anatomic knowledge of the neck. This knowledge is also very important in choosing the surgical approach and for diagnosis in radiology. Lack of experience regarding possible variations could lead to fatal errors if one blood vessel should be mistaken for another (Zumre et al 2005). The significance of common carotid artery is that the long-term outcome of patients with carotid artery disease rests on modifying risk factors for circulation problems that can also lead to blockage in the heart and leg arteries (Balasundaram & Banu 2006).
1.2.3 Ultrasound Imaging

Among the popular imaging modalities, Ultrasound (US) imaging is widely used for real-time diagnostic situations. Besides the qualitative information for visual interpretation, the quantitative information on the US scans, such as the sizes, edges and positions of anatomical structures, is also of significant interest for computer-aided diagnosis. The accurate detection of organs or objects from US images plays a key role in many applications such as the accurate placement of the needles in biopsy, the assignment of the appropriate therapy in cancer treatment, and the measurement of the prostate gland volume (Xie et al 2006).

Ultrasound imaging of the carotid artery is a common procedure when screening for cardiovascular diseases, as the vessel is particularly prone to Atherosclerosis and easily accessible with ultrasound probes (Swillens et al 2012). It has the advantage that it is noninvasive and does not involve the use of ionizing radiation. It is therefore ideally suited for serial investigations. It is also relatively inexpensive and images are acquired in real time (Barratt et al 2004).

The resolution of diagnostic ultrasound image is significantly limited by speckle noise. It is believed that speckle is a high frequency component of the image. As the texture of speckle often carries useful information, it is not truly a noise in the typical engineering sense. Ultrasound experts with insufficient experience may not often draw useful conclusions from the images due to the presence of speckle (Tsiaparas et al 2011). Ultrasound based estimation of arterial properties can be used to assess arterial stiffness and atherosclerosis. Most studies in vessels have focused on radial strain and only a few have addressed strain in the longitudinal axis of the vessel wall (Larsson et al 2011).
But analysis of Intima-Media Thickness (IMT) and plaque deposit can be done effectively only in the longitudinal view. As ultrasound imaging allows noninvasive assessment of the degrees of stenosis and plaque morphology, it is widely used in the diagnosis of atherosclerosis of the carotid artery. It is also inexpensive and easy to use. Hence, longitudinal B-mode ultrasound images are used in this work. A sample image showing the longitudinal view of CCA is given in Figure 1.7.

![Figure 1.7 Longitudinal view of CCA](image)

The artery wall consists of three layers. The innermost is called intima, the middle media and the outermost adventitia. In longitudinal view, the CCA is seen as a dark region comprised of lumen between the Near Wall (NW) and Far Wall (FW). The intima layer is poorly represented and it is fused with the media layer because of poor difference in the acoustic impedance of the two adjacent layers. The media layer is usually represented by a dark grey area, whereas the adventitia layer is highly echogenic and appears as a bright grey area (Molinari et al 2010a).

IMT is the distance between the Lumen-Intima (LI) and the Media-Adventitia (MA) boundaries. IMT is widely used as an early indicator of atherosclerosis and Cardio Vascular Diseases. It is usually measured by using
ultrasound imaging. Normally, trained sonographer manually measures the IMT from longitudinal projections of the CCA. But these manual measurement methods are time consuming, subjective and tedious.

1.3 OBJECTIVES

Medical diagnosis has become highly attributed with the development of technology lately. Furthermore, computer tools have improved the medical practice implementation to a greater extent. The application of machine learning methods in medical field is the subject of considerable ongoing research. Advancements in machine learning techniques always encourage the researchers to develop Computer Aided Diagnosis (CAD) system to assist doctors in making decisions. Hence an effort is made in this work to develop a classifier to classify normal and abnormal common carotid arteries. The major objectives are

- To take a step forward in the early detection of CVDs.
- To eliminate the need for a trained radiologist for CVD intervention.
- To develop a non invasive system that allows the subjects to take the test comfortably.
- To develop a cost effective system for detecting the abnormalities in CCA using ultrasound images.

1.4 MACHINE LEARNING

The aim of machine learning is to build a model that makes decisions based on evidence in the presence of uncertainty. Many successful approaches to automatic diagnosis rely on classification by supervised –
learning techniques. In supervised learning labelled training data is used to train a classification scheme for the target data. Initially features are extracted from the training and target data, after which a classifier is trained. This classifier can then be used to segment the target data into different classes, based on the extracted features (Opbroek 2015).

The main concept of the medical technology is an inductive engine that learns the decision characteristics of the diseases and can then be used to diagnose future patients with uncertain disease states. Feature selection is an optional stage, whereby the feature vector is reduced in size including only, from the classification viewpoint, what may be considered as the most relevant features required for discrimination (Guler & Ubeyli 2006).

In order to improve the diagnosis of diseased arteries, many CAD systems have been recently developed. Although the clinical roles of CAD systems may still be debatable, the fundamental role should be complementary to the radiologists’ clinical duties, where the pathways of achieving ultimate performance enhancement taken by the machine observer and human observer may not necessarily to be close. For example, CAD systems may attack the tasks that the radiologists cannot perform well or find difficult to perform (Li et al 2001).

A typical CAD tool consists of two main modules, namely the feature selection module, which spares the most clinically useful features from redundant ones, and the classifier, which is trained using the selected subset of features. Selection of features is a crucial step in the CAD design to simplify both the feature vector and the classifier. It is also very important to enhance the computational performance of the CAD system in terms of execution time and memory requirements (Gastounioti et al 2015).
The main objective of this work in the field of automated diagnosis of CVDs is to identify the representative features of CCA by analyzing it both in spatial and transform domain and develop a classifier using the identified features for the classification of normal and abnormal arteries. In this work, four different classifiers are developed using different machine learning methods namely Support Vector Machine (SVM), Multi Layer Perceptron (MLP), Radial Basis Function Network (RBFN) and Learning Vector Quantization (LVQ) for the classification of normal and abnormal CCA. All the classifiers are implemented in MATLAB version 2015a. Performance of the classifiers is compared using accuracy, specificity and sensitivity.

1.5 **SEGMENTATION**

Segmentation subdivides an image into its constituent regions or objects. It is the process of partitioning a digital image into multiple regions and extracting a meaningful region known as the region of interest (ROI). Regions of interest vary with applications. No single universal segmentation algorithm exists for segmenting the ROI in all images. Therefore the user has to try various segmentation algorithms and optimize an algorithm to get the best result for the given problem. Based on user interaction, the segmentation algorithms can be classified into manual, semi automatic, and automatic.

Manual method of extraction is time consuming, highly subjective, prone to human error, and has poor intra-observer reproducibility. Automatic segmentation algorithms are preferred as they segment the structures of the objects without any human intervention. They are preferred if the tasks need to be carried out for a larger number of images. Semi automatic algorithms are combination of automatic and manual algorithms. In these algorithms, human intervention is required in the initial stages.
Based on the properties of pixel intensity values like similarity and discontinuity, segmentation algorithms can be classified as contextual algorithms and non-contextual algorithms. In contextual algorithms, the pixels are grouped based on some similarity that exists between them. These are also known as region-based or global algorithms. Non-contextual algorithms ignore the relationship that exists between the pixels. Instead, they identify the discontinuities that are present in the image such as isolated lines and edges and then group them into a region. These algorithms are also known as edge-based or local algorithms. The performance evaluation of image segmentation results is still a challenging problem as they fail to extract the correct boundaries of objects in noisy images (Somkantha et al. 2011).

One of the major classes of problems commonly addressed in computational processing of medical images is segmentation. A fully segmented or labeled scan allows surgeons to qualitatively visualize the shapes and relative positions of internal structures and more accurately measure their volumes and distances quantitatively. The distance between two structures cannot be measured without knowing the boundary. Due to the noise typically present in medical imagery, similar appearance of different tissues and the complex anatomical structures, boundary extraction is difficult (Jayanthi & Banu 2009).

Formation of plaque on the walls of the artery causes enlargement of the arteries and thickening of the artery walls. The diameter of arteries decreases due to increase in the thickness. This causes a reduction of the lumen with possible vascular problems and alters the arterial properties elasticity and stiffness (Loizou et al. 2011). Precise segmentation of carotid artery allows the computation of various biomechanical and anatomical properties of the artery wall that may be useful to clinicians to follow the evolution of the atherosclerosis diseases (Destrempes et al. 2011). Several
algorithms for the segmentation of carotid artery have been proposed in ultrasound imaging.

Though different algorithms are available for the segmentation of CCA, an algorithm that performs the segmentation based on minimal user interaction is important in the research context. In this work both edge based and region based segmentation algorithms are applied on the longitudinal B mode ultrasound images of CCA for the spatial domain analysis to choose the algorithm that performs the best for the segmentation of the lumen and intima-media regions.

Multiwavelets can simultaneously provide perfect reconstruction, while preserving length, good performance at the boundary and a higher order of approximation. These features are responsible for the better performance of multiwavelets over scalar wavelets in image processing applications. Hardin Marasovich (HM) and Geronimo Hardin Massopust (GHM) multiwavelets are used in this work to analyze the CCA images in transform domain.

1.6 PARAMETER IDENTIFICATION

As the carotid artery supplies oxygenated blood to the brain, it may be very useful to quantify its stiffness information in the early diagnosis and characterization of vascular diseases such as carotid artery atherosclerosis (Luo et al 2012). The intimal thickening of stenotic artery is known as the beginning step of atherosclerosis. Atherosclerosis is a common dangerous disease and a major cause of death in many countries. There are a large number of investigations which have led to the understanding of the flow disorders due to stenosis (Razavi et al 2011).

Arterial stiffness has been reported to be an independent predictor of cardiovascular mortality. Provided there is progressive fibrosis of large
arteries that reduces their elasticity, aging is known to be the dominant process altering arterial stiffness. These changes in stiffness with age are accelerated in hypertension and highly amplified by the association with other cardiovascular diseases and concomitant risk factors (Zakaria et al 2010). Arterial tissue elastic properties and detection of rupture-prone vulnerable plaques, in particular, are one of the most active areas of research in cardiology. The main mechanical properties are radial strain, which is related to plaque type and vulnerability and shear stress, which influences the probability of plaque accumulation (Hernandez-Sabate et al 2009).

Blood flow induces body forces and stresses in the arterial walls due to complex fluid–structure interactions. These forces and stresses play an important role in the onset and progression of many acquired and congenital cardiovascular diseases such as atherosclerosis and aneurysms. Atherosclerosis involves the accumulation of plaque in the intima of the arterial wall, which reduces arterial lumen and increases local arterial stiffness (Al-Jumaily & Lowe 2013).

Moreover, the mechanical quantities stress and strain are known to trigger the onset of several diseases such as atherosclerosis. These facts are some of the reasons why the mechanical properties of arterial wall tissues have received increasing attention in the literature over the past few years (Sommer & Holzapfel 2012). Shear strains in the arteries have been subjects of less interest, in contrast to subjects such as intima-media thickness and or tracking the diameter change in different arteries (Adibi et al 2014).

CCA is an elastic artery. Studies reveal that elastic arteries better suit the purpose than muscular arteries like femoral artery as they are not clearly altered by age. 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. Therefore CCA is a highly
compliant artery for the study of elastic properties like distension (Jayanthi & Banu 2011).

Distension is the change in diameter of the artery from diastole to systole. The distension of an artery during a cardiac cycle depends on the elastic characteristics of the vessel wall. It is evaluated by using the change in diameter obtained from the displacements of near and far walls and by measuring the displacements at multiple points along the axial direction of the artery. By definition, one point measurement of the change in diameter is widely used for the assessment of mechanical properties of the arterial wall (Hasegawa & Kanai 2006).

Recent research is focused on determining early indicators of atherosclerosis. IMT is one of the early indicators. It precedes luminal narrowing due to plaque formation. Since plaque formation starts in the walls of the artery, IMT could be a better indicator than lumen area or blood velocity and positively associated with an incident of stroke. Recently it has been shown that an increased IMT is cross sectionally associated with a higher risk of brain infarction. Clinically, IMT is used as a validated measure for the assessment of atherosclerosis (Cheng & Jiang 2008).

It is clear that monitoring of the arterial characteristics like the vessel lumen diameter, the intima media thickness of the far wall and the morphology of the atherosclerotic plaque are important in order to assess the severity of atherosclerosis and evaluate its progression (Panayides et al 2011). Measurement of lumen diameter helps to characterize the elasticity of the artery and IMT helps to identify plaque deposits and hence stiffness in the wall. Hence these two parameters, lumen diameter and IMT are used in the spatial domain for classifying the CCA tested as normal or abnormal.
Multiwavelets preserve high frequency information in the image i.e edges and give very good performance in the boundaries. As the formation of plaque is in the inner walls of the artery and alters the boundary, the difference between the normal and abnormal CCA is expected to reflect in the subband energy values of approximate and detailed coefficients. Hence these energy values are used for classification of normal and abnormal CCA in the transform domain.

1.7 ORGANIZATION OF THESIS

Chapter 2 of this thesis reviews the research papers in the areas of automated diagnosis of cardiovascular diseases due to the abnormalities in arteries. The contribution of technical people in this area is also reviewed. This further discusses the various algorithms for the segmentation of CCA, application of multiwavelets and different classifiers presented by different people working in this area.

Chapter 3 describes the materials and different methodologies used in this work. It explains the segmentation and boundary extraction of the layers of CCA in spatial domain and measurement of diameter, IMT and other numerical attributes for the characterization of CCA. It also describes mathematical modeling of CCA to describe its behavior during a cardiac cycle. A new approach is proposed for the transform domain analysis of ultrasound CCA images using multiwavelets. The chapter also includes the description and implementation of different classifiers used in this work for the classification of normal and abnormal CCA.

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

Chapter 5 discusses the scope for the future work for further research.