CHAPTER 1

INTRODUCTION

1.1 COMPUTER AIDED DIAGNOSIS

The future of healthcare is changing dramatically with revolution in medical treatment technologies. A number of sophisticated techniques are evolved to reduce the risk of a disease and improve quality of life. However, clinical physicians follow conventional diagnosing methods by making use of patient’s medical records, clinical examination reports and relevant symptoms of the disease. Most of the medical practitioners predict the presence of a disease intuitively from their acquired knowledge in learning and experience. Difficulties in reasoning may lead to improper diagnosis or delay in prognosis of disease outcome and its severity level because of human errors. Such imprecise decisions may setback in providing right treatment or even bring loss of life.

Many people will not show readiness in accepting general practitioners approach of prescribing expensive tests, scans and other clinical procedures that are necessary for diagnosing the disease. They could not come to a decision for further treatment as well. Therefore, they may opt for getting opinion from more than one medical expert to arrive at a conclusion. Even after consulting with many specialists, if the patient gets confirmed to know about the risk level of disease at the current stage and if it is in curable state, then they could frame their mind satisfactorily to undergo treatment. Early prognosis of disease may effectively prevent its growth so as to improve life.
expectancy. Therefore, an intelligent Computer Aided Diagnosis system (CADx) or Medical Decision Support System (MDSS) is needed for automatic prediction of disease, confirming its severity level and preventing forthcoming risks based on patient’s medical information as the major motto in healthcare field is “prevention is better than cure”.

CADx is intended for diagnosing the disease by analyzing clinical information and interpreting medical images. The diagnosis of coronary artery disease is done invasively by angiography techniques. However, a reliable non-invasive method or a system is required for prognosis and repeated monitoring of the disease status (Furukawa 2004). The algorithms designed for the systems are highly responsible for early detection of diseases. It also helps the medical professionals in their medical decision-making process. It serves the purpose of an electronic doctor to provide second opinion in detecting abnormalities, describing disease progress and decision-making. It makes use of data processing systems which accepts textual data from patient’s medical records and medical images for predicting the prevalence of disease automatically. On positive prognosis of disease, the patient can undertake prophylactic treatment to prevent its severity. This system is also helpful for the patients to follow up the current status of the disease. The above all reasons kindled the ever-increasing research in the practical implementation of CADx for various kinds of diseases for clinical decision-making.

The design and development of accurate CADx for diagnosing disease has become a challenging research in computational technology. The medical professionals and computer specialists carry out significant experiments over decades in improving the performance of this clinical decision support system day by day. Medical images are used for diagnosing numerous diseases in the patients and giving appropriate treatments to them.
They are highly informative in providing visual representations of anatomical structures of a body for treating the disease by observing the minute changes and abnormalities in them. Best interpretations of information from the medical images require experienced medical professionals. Different medical doctors make diverse analysis leading to different diagnostic measures for the disease. Moreover, for the same set of medical images, clinicians may come up with different results in different time. The great deal of information provided by the medical imaging techniques such as X-rays, MRI scan, CT scan, ultrasound diagnostics are analyzed and evaluated comprehensively within a short span of time by the medical professionals. To obtain more accurate and reliable diagnosis, an efficient and effective computer aided diagnosis system can assist the medical doctors in the best interpretation of medical images and help in providing right diagnosis for the disease at right time. Indeed, it reduces the time taken to infer from the medical images in traditional manner.

Among various diseases, Coronary Artery Disease (CAD) is one of the leading causes of death in the World every year (WHO Statistics 2018). Even though there is a remarkable development in healthcare applications, there is a long way to completely erase this disease from the human history. The development of an efficient computer aided diagnosis system is therefore needed for accurate and automatic diagnosis of the prevalence of CAD.

1.2 HUMAN HEART

Heart is one of the vital organs in humans to pump the blood throughout the body and carrying the vital nutrients needed for survival. When there is a disturbance in the flow of blood to the parts of the heart, it leads to severe or prolonged lack of nutrients and oxygen to the heart muscles. The blood is supplied to the heart through left and right coronary artery. The obstruction in the blood flow to the heart is caused due to the thickening of
inner walls of coronary arteries called atherosclerosis by the build up of plaque composed of fat deposits, cholesterol, and other substances.

The plaque deposits may get ruptured and eventually forms a blood clot. Later on, the blood clot formed within the plaque blocks the blood flow completely (thrombosis) or it may dislodge and get trapped in the arterial pathways (embolism) hindering the blood supply forming a vulnerable plaque. If the blood and oxygen supply to the heart stops for more than a few minutes, then the muscle cells of the heart get damaged and die, developing severe pain in the chest and shoulders called angina. At a critical stage, if it is not treated immediately, then it results in acute Myocardial Infarction (MI) also called as heart attack (Willerson & Holmes 2015, Ambesh et al. 2017). Various stages of coronary artery disease in human heart are depicted in Figure 1.1.
Coronary heart disease is a complex disease that causes abnormal or absent blood flow in the coronary arteries. It is usually a degenerative disease which is uncommon before the age of 30 and common after the age of 60 (Coronary heart disease: Causes, symptoms, and treatment 2018).

1.3 COMORBIDITIES OF HUMAN HEART

Diseases other than heart disease such as brain disease, lung disease and kidney disease are more or less related with improper functioning of the heart (Moe 2016). Majority of the risk factors of these diseases are common to heart disease as well. However, many systems proposed in the existing literature are developed with restrictions of predicting only the presence or absence of disease without depicting the risk severity level. They involve complex computations and incur high computational time for analyzing clinical information and processing medical images to provide disease diagnosis results. Developing CADx with high accuracy and low CPU execution time is still a challenging issue in research.

1.4 GENERAL STEPS CARRIED OUT IN COMPUTER AIDED DIAGNOSIS SYSTEM

The primary goal of a CADx is to increase the detection of diseased area by neglecting false negatives due to observational oversights. The algorithms employed in the CADx are designed to search for the same set of features as a radiologist look for case review (Doi 2007).
There are four general steps carried out in any CADx for automated disease diagnosis as shown in Figure 1.2. Initially, the cardiac image is acquired either employing invasive or non-invasive clinical procedures. The image is then pre-processed for enhancing the image quality. Thirdly, the Region of Interest (ROI) is identified and segmented. Further, the necessary risk factor details and disease features are extracted. Finally, the disease diagnosis results are provided.

**Figure 1.2 Steps followed in CADx for disease diagnosis**

1.4.1 Image Acquisition

The first and foremost step in computer aided diagnosis is to acquire one of the medical images. Various cardiac imaging modalities are explicated as follows.

Coronary angiography or X-Ray Angiography (XRA) is an invasive radiographic imaging technique, the standard test for analyzing the coronary anatomy that reflects the vessel luminal diameter. The coronary
angiography was first performed by Mason Sones in Cleveland Clinic in the year 1959 (Watson & Gorski 2005). The high resolution XRA helps to visualize the presence of stenosis. This method is considered as the golden standard for diagnosing the coronary artery disease (Escolar et al. 2006).

(Source:https://www.mercyangiography.co.nz/Proceucers/CardiacProcedures/CORA.html)

**Figure 1.3 Coronary angiogram of human heart**

During this test, cardiac catheterization is performed by injecting the dye into the coronary arteries through a thin, long hollow tube called catheter. The dye acts as a coloring agent that makes the coronary arteries visible on X-ray pictures. This helps the doctor to identify any blocks present in the arteries. Coronary angiography reveals where the blood vessels originate and branch as shown in the Figure 1.3. The patient needs bed rest for several hours or a day to return to the normal activities. The XRA reveals the two-dimensional (2D) projections of coronary arteries.

An alternate method is to take Computerized Tomography Angiography (CTA) scan or Magnetic Resonance Imaging (MRI) scan which provide images with good resolution, depicting the functional effect in relation to coronary supply and identification of risk areas (Escolar et al. 2006). CTA scan is a painless invasive test that uses an X-ray
machine to take clear and detailed 3D images of the heart. The doctors utilize this study to delineate the presence or absence of coronary stenosis in patients. During this test, the X-ray machine will move around the body in a circular motion. The machine will take a picture of each part of a patient’s heart (Vlodaver et al. 2012). A computer will place the pictures altogether to get a 3D image of the whole heart as shown in Figure 1.4.

![Figure 1.4 CT angiography of human heart](http://ww1.prweb.com/prfiles/2012/02/07/9174141/64slicect.jpg)

More than a decade, Magnetic Resonance Imaging (MRI) has shown to be capable of imaging the heart in 3D form, coronary arteries and demonstrating the affected zones without catheterization (Kohsaka & Makaryus 2008).

The coronary artery plaque can be identified and the coronary artery size can be determined from MRI scan. But, the resolution and image quality of MRI is low. MRI scan machines use strong magnetic fields and radio waves to get the images of heart pertaining to its anatomy to locate any abnormalities as shown in the Figure 1.5. MRI scanners must be handled with at most care and safety precautions because it uses an extremely powerful magnetic field (Joshi et al. 2012).
Intravascular Ultra Sound (IVUS) scan is an invasive percutaneous cardiac imaging technique which uses a specially designed catheter with a small ultrasound probe attached to the distal end of the device. The other end of the device is attached to a computerized ultrasound scan machine. The probe consists of piezoelectric transducer or Capacitive Micro-machined Ultrasonic Transducer (CMUT) to determine the amount of atheromatous plaque built up in the inner wall of the coronary arteries. It transmits and reflects high frequency ultrasound signals to generate 2D cross sectional image of the coronary artery by rotating the Intravascular Ultra Sound catheter (Nissen & Yock 2001). The IVUS method is useful in finding out the degree of stenosis (abnormal narrowing) of the coronary artery (Papadogiorgaki et al. 2008).

The 2D cross-sectional images of vessel wall architecture and plaque morphology can be studied. IVUS scan visualizes the lumen of the coronary arteries and atheroma hidden within the artery wall as shown in Figure 1.6. Intravascular Ultra Sound scan is the widely used strategy in
research to study the behavior of atherosclerosis, plaque composition and coronary stenting (Bourantas et al. 2011).

(Source: https://en.wikipedia.org/wiki/Intravascular_ultrasound)

**Figure 1.6** Intravascular ultra sound image of the coronary artery delineating plaque deposits and lumen

Optical Coherence Tomography (OCT) is a micro-scale resolution invasive cardiac imaging technique that is the optical analog of intravascular ultrasound imaging (Kubo et al. 2011) as shown in Figure 1.7. The resolution of OCT image is ten times higher than that of IVUS image. OCT scan provides detailed structural information of the coronary artery wall (Rathore et al. 2010, Terashima et al. 2012).

(Source: Rathore et al. 2010)

**Figure 1.7** Optical coherence tomography image of the coronary artery
Stress imaging is a nuclear imaging technology without catheterization which depicts the zones with inadequate blood supply by inducing stress to the patient with exercise such as walking or treadmill running to elevate the heart beat to its peak rate. The technique is referred to as stress / rest Myocardial Perfusion Imaging (MPI) scan (Josephson et al. 1982). The Figure 1.8 (a) and Figure 1.8 (b) represent the myocardial perfusion scan image of a patient at rest and stress who suffered from typical chest pain.

![Figure 1.8](http://www.snmmi.org)

**Figure 1.8** (a) MPI scan image at rest showing less perfusion (b) MPI scan image at stress showing good perfusion

It is a non-invasive nuclear imaging study, which produces 3D images called as perfusion images. They depict which areas of heart muscle are perfused or supplied with blood and which areas are blocked with plaque (Loong & Anagnostopoulos 2004). The cost of this test is also less when compared with other radiographic imaging methods (Sun 2013). The amount of blood flow perfused (colored portion) and the plaque deposit (black portion) in the coronary artery is obvious in the above scanned images from which the doctor can come to a conclusion that the patient is risking for getting heart attack in the future (Takx et al. 2015).

Echocardiography, a sub technique of ultrasonography is a non-invasive method of producing ultrasound images of the heart structures.
Figure 1.9 illustrates the echocardiogram, showing the demarcation of heart chambers. It provides the accurate assessment of the amount of blood flows through the heart with the help of a pulsed or continuous wave Doppler ultrasound scanner. It employs standard two-dimensional, three-dimensional and Doppler ultrasound scans to obtain heart images. It is routinely used for the diagnosis and follow-up of the patients, those who suffers from any suspected or known heart diseases (Mädler et al. 2003). The grayscale image quality and poor resolution makes difficult to interpret the wall motion and thickening.

Figure 1.9 Echocardiogram showing the cardiac chambers

Concerning the various cardiac image acquisition methods as discussed above, conventional X-Ray coronary angiogram (XRA) is considered as the benchmark cardiac imaging modality and XRA is the widely used scanning technique for diagnosing CAD. However to provide an accurate interpretation of medical images require a computer aided diagnosis system to support medical professionals for treating the patients with satisfaction (Tsipouras et al. 2008, El-Baz et al. 2011).
1.4.2 Image Preprocessing

The acquired medical image is preprocessed for the reduction and removal of artifacts such as image noise, leveling of image clarity and enhancing the quality of medical image to obtain accurate diagnostic results (Cruz-Aceves et al. 2016). The image pre-processing techniques that are applied to cardiac images include filtering techniques, contrast enhancement, morphological operations, histogram equalization, etc.

1.4.3 Image Segmentation

Image segmentation is the process of delineating the anatomical structures, extracting the diseased portion separately from the medical image to differentiate normal and abnormal regions of interest from medical images for automating the disease diagnosis using computers. Medical image segmentation is a vital part of any CAD system process. The performance of the system depends heavily on the segmentation accuracy. Some of the standard segmentation techniques used for cardiac images includes thresholding technique, edge-based segmentation, region-based segmentation, atlas-based segmentation, deformable model-based segmentation and soft computing segmentation (Foster et al. 2014).

1.4.4 Feature Extraction and Disease Diagnosis

The features needed to diagnose the disease are obtained from the segmented region of the medical image. The features to be extracted differ from different cardiac images taken for study. The most common features that are extracted from the cardiac images include the length of the coronary artery branch, lumen diameter and orientation of the coronary artery, texture features
including the pixel intensity features, gray scale co-occurrence features, plaque morphology, plaque composition, stent position in the case of stent implantation, cardiac chamber features and vascular territories. Disease diagnosis can be provided based on the nature of the features extracted (Jiang et al. 2010).

1.5 PERFORMANCE ANALYSIS OF CADX

Performance analysis of CADx is carried out by evaluating the algorithm for its run-time complexities, determining the efficiency, effectiveness of its usage and also towards the comparative study among systems with similar intended purpose. The precision of evaluation of CADx depends on the factors such as selection of training data sets and test cases, reference standard used for performance assessment, selection of the region of interest of targeted abnormalities and the methods & metrics used for assessing the performance of CADx with that of ideal results prescribed by medical experts (Petrick et al. 2013, Li & Nishikawa 2015).

1.6 PROBLEM FORMULATION

This thesis aims at designing and developing a single ended Medical Decision Support System (MDSS) for prediction and diagnosing the risk level of Coronary Artery Disease (CAD) using MATLAB R2013a version. The objective of this research work is to develop a CAD diagnosis system and evaluate the performance of the system using standard metrics such as sensitivity, specificity, accuracy and precision. The system needs to carry out preliminary CAD risk prediction, risk level classification and then confirm the presence of CAD on positive diagnosis. The system consists of two stages. In the first stage, non-invasive medical diagnosis for CAD risk
prediction is performed. In the presence of CAD risk, the coronary angiogram image is further processed to analyze the severity of CAD and obtain final disease decision in the next stage. The system is designed by combining the features of mathematical modeling, data mining techniques and medical image processing.

Initially, the weights of the risk attributes for CAD diagnosis is computed using a Multiple Criteria Decision Making (MCDM) method namely Analytic Hierarchy Processing (AHP). These attribute weights are used in ANN, ANFIS and in other two MCDM methods for preliminary CAD prediction namely TOPSIS (Technique for Order Preference by Similarity to Ideal Solution) and SAW (Simple Additive Weighting) method.

Secondly, the Artificial Neural Network (ANN) and Adaptive Neuro-Fuzzy Inference System (ANFIS) are the two soft-computing techniques used in the system. Multi Layer Back Propagation Neural Network (MLBPNN) is implemented and trained based on gradient descent approach that adjusts weights to reduce system error and get better system convergence to obtain CAD risk prediction. ANFIS is trained using generalized bell member function (gbellmf) for CAD risk status classification as Type 0 to Type 4 CAD.

Finally, the medical image processing is carried out on coronary angiogram image to confirm the severity of CAD risk on identifying the presence of CAD in the prediction results. Image pre-processing, coronary artery segmentation, stenosis detection and its grading are the four steps carried out to confirm the presence of CAD risk. The system is implemented to provide promising disease decision making similar to the medical experts
by combining the features of MCDM, intelligent techniques and image processing.

1.7 THESIS ORGANIZATION

The design and development of a MDSS for CAD risk prediction and diagnosis is implemented and evaluated. MCDM methods, computational intelligent techniques and medical image processing capabilities are combined together to obtain more accurate disease diagnosis. This thesis is organized with following chapters as,

Chapter 1, “Introduction” presents the research gap in the area of study and the immediate necessity for computer aided diagnosis system for effective heart disease diagnosis. This chapter also gives the aim and objectives of the research and the general steps carried out in computer aided diagnosis system.

Chapter 2, “Literature Survey” discusses the researches being carried out in existing algorithms and techniques used in computer aided diagnosis system for coronary artery disease diagnosis.

Chapter 3, “Coronary artery disease risk prediction using Multi Criteria Decision Making (MCDM) methods” describes the preliminary diagnosis carried out to predict the risk of coronary artery disease. The algorithms for three MCDM methods namely AHP, TOPSIS and SAW methods are used for this purpose. AHP is implemented to determine the attribute weights to be used in TOPSIS and SAW methods for CAD risk prediction.

Chapter 4, “Coronary artery disease risk prediction and disease severity level classification using Neuro-fuzzy techniques” explain the use of
computational intelligent techniques to learn the medical information and predict the CAD risk. ANN and ANFIS are designed and implemented for CAD risk prediction and risk level classification respectively.

**Chapter 5, “Automatic stenosis grading for confirming the risk of coronary artery disease using coronary angiogram”** describes the image processing framework for confirming the presence of CAD. The diameter narrowing of coronary artery (stenosis) is computed and the stenosis grading is assessed to provide computer aided diagnosis results as a second opinion to the medical professionals.

**Chapter 6, “Conclusion”** summarizes the contribution of this thesis with the implementation of CAD risk prediction algorithms in design and development of computer aided diagnosis system for coronary artery disease and their performance evaluation. Suggestions for future work are also included in this chapter.