An integrated index to detect the extent of myocardial infarction using echocardiographic texture analysis

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NANYANG
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**AN INTEGRATED INDEX TO DETECT THE EXTENT OF
MYOCARDIAL INFARCTION USING
ECHOCARDIOGRAPHIC TEXTURE ANALYSIS**

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SCHOOL OF MECHANICAL AND AEROSPACE ENGINEERING

2016

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I dedicate this thesis to my beloved son Master Shricharan Bhat, who has enriched my life in ways unfathomable, and who inspired me to pursue PhD.

ABSTRACT

Expansion of infarcted zone after Myocardial Infarction (MI) has serious short and long-term consequences and contributes to increased mortality. Early detection and quantitative assessment of MI will help to prevent further damage of the cardiac muscles. Though two-dimensional (2D) echocardiogram helps to detect MI at early stage, the reading of ultrasound images is subjective due to inter-observer variability and may lead to inconclusive findings which may increase the patient anxiety and cost of treatment. Automated detection of MI and quantification of the extent of MI will enhance the capabilities of diagnosis system. However, little work has been done in the area of computer-based texture analysis for automated detection of extent of MI in general, and existing literature is found to be largely confined only to MI detection. In this thesis, various algorithms have been proposed to identify infarcted myocardium and extent of infarcted myocardium that are categorised into (a) normal myocardium, (b) moderately infarcted myocardium, and (c) severely infarcted myocardium using 2D echocardiogram texture analysis.

The automated identification of normal and infarcted myocardium algorithm is developed first, using Discrete Wavelet Transform (DWT), second order statistics calculated from Gray- Level Co-Occurrence Matrix (GLCM) and Higher-Order Spectra (HOS) texture descriptors. The proposed system is validated using 400 MI and 400 normal ultrasound images, obtained from 80 patients with MI and 80 normal subjects. Among the three techniques presented, DWT yielded the highest classification accuracy.

Another efficient multi-resolution decomposition algorithm is proposed in order to characterize normal and infarcted myocardium by analysing the two cross-sectional views (parasternal short axis mid-left ventricular view at

papillary muscle level and apical four chamber view) of echocardiograms. The Stationary Wavelet Transform (SWT) method is used to extract Relative Wavelet Energy and Entropy (RWE and RWE_{ent}) features from the two cross-sectional views of echocardiography images separately. The proposed method is able to identify MI with an accuracy of 96.80%, sensitivity of 93.70% and specificity of 100% using 16 features extracted from only *two frames* making this a more reliable classification.

An integrated index called ***Myocardial Infarction Index (MII)*** is proposed to discriminate infarcted and normal myocardium using features extracted from apical cross-sectional views of echocardiograms. The cross-sectional view of normal and MI echocardiography images is represented as textons using Maximum Responses (MR8) filter banks from which various features are extracted. Then, combinations of highly ranked features are used in the formulation and development of an integrated ***MII***. This calculated novel MII is used to accurately and quickly detect infarcted myocardium by using one numerical value. This technique is able to characterize MI with an average accuracy of 94.37%, sensitivity of 91.25% and specificity of 97.50% with 8 apical four chambers view features extracted from only *single frame per patient*.

Finally, Curvelet Transform and Local Configuration Pattern (LCP) are employed in this thesis for an automated detection of extent of MI (normal, moderately infarcted and severely infarcted myocardium) using 2D echocardiograms. The methodology extracts the LCP features from curvelet transform coefficients of echocardiograms. The developed algorithm showed an accuracy of 98.99%, sensitivity of 98.48% and specificity of 100% for SVM classifier using only *six* features. Furthermore, an integrated index called ***Myocardial Infarction Risk Index (MIRI)*** is developed to detect the normal, moderately and severely infarcted myocardium using a *single* number.

Thus the proposed systems in this thesis may aid the clinicians in faster identification of MI and extent of infarcted myocardium using texture analysis of 2D echocardiograms. Proposed systems may also aid in identifying the person at risk of developing heart failure based on the extent of infarcted myocardium.

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LIST OF ABBREVIATIONS

2D	Two-Dimensional
ACC	American College of Cardiology
AGT	Angiotensinogen
AHA	American Heart Association
ASE	American Society of Echocardiography
Bior3.7	Biorthogonal 3.7
BMI	Body Mass Index
CABG	Coronary Artery Bypass Grafting
CAD	Computer-Aided Diagnosis
CHD	Coronary Heart Disease
CT	Computed Tomography
DICOM	Digital Imaging and Communications in Medicine
DT	Decision Tree
DWT	Discrete Wavelet Transform
ECG	Electrocardiography
ESC	European Society of Cardiology
FD	Fractal Dimension
FIS	Fuzzy Inference System
FN	False Negative
FP	False Positive
GLCM	Gray-Level Co-Occurrence Matrix

GMM	Gaussian Mixture Model
HOS	Higher-Order Spectra
HRE	Highly Reflectile Echo
IRB	Institutional Review Board
KLD	Kuller-Leiber Divergence
k-NN	K-Nearest Neighbor
KPCA	Kernel PCA
K-S	Kolmogorov-Smirnov
LA	Left Atrium
LBP	Local Binary Pattern
LCP	Local Configuration Pattern
LDA	Linear Discriminant Analysis
LDC	Linear Discriminant Classifier
LPP	Locality Preserving Projection
LSDA	Local Sensitive Discriminant Analysis
LTE	Laws Texture Energy
LV	Left Ventricle
LVEDD	LV End Diastolic Diameter
LVEDV	LV End Diastolic Volume
LVEF	Left Ventricular Ejection Fraction
LVESD	LV End Systolic Diameter
LVESV	LV End Systolic Volume
LVMI	LV Mass Index

MCE	Myocardial Contrast Echocardiography
MFA	Marginal Fisher Analysis
MI	Myocardial Infarction
MIAS	MI in acute stage
MiC	Microscopic Configuration Model
MII	Myocardial Infarction Index
MIRI	Myocardial Infarction Risk Index
MIRS	MI in recovery stage
MISAS	MI in subacute stage
ML	Maximum Likelihood
MPI	Mean Pixel Intensity
MR8	8 Maximum Responses
MRF	Markov Random Field
MRI	Magnetic Resonance Imaging
mRMR	Max-Relevancy and min-Redundancy
NB	Naïve Bayes
NHC	National Heart Centre
NPE	Neighborhood Preserving Embedding
NSTEMI	Non-ST segment elevation
PCA	Principal Component Analysis
PCI	Percutaneous Coronary Intervention
PNN	Probabilistic Neural Network
PPV	Positive Predictive Value

PVCs	Premature Ventricular Contractions
QDA	Quadratic Discriminant Analysis
RA	Right Atrium
RBF	Radial Basis Function
RGB	Red-Green-Blue
ROC	Receiver Operating Characteristics
ROI	Region-Of-Interest
RT	Radon Transform
RV	Right Ventricle
RWE	Relative Wavelet Energy
RWT	Relative Wall Thickness
SD	Standard Deviation
SPECT	Single-Photon Emission Computed Tomography
STEMI	ST segment elevation
SVM	Support Vector Machine
SWT	Stationary Wavelet Transform
TEE	Transesophageal Echocardiography
TN	True Negative
TP	True Positive
TTE	Transthoracic Echocardiography
VA	Ventricular Arrhythmias
VT	Ventricular Tachycardia
WHO	World Health Organization

WMI	Wall Motion Index
WMSI	Wall Motion Score Index
WT	Wavelet Transform

LIST OF NOMENCLATURES

<i>AutCor</i>	Autocorrelation
<i>BS_PhEnt</i>	Bispectrum Phase Entropy
<i>Con</i>	Contrast
<i>Cor</i>	Correlation
<i>DEnt</i>	Difference Entropy
<i>Dis</i>	Dissimilarity
<i>DVar</i>	Difference Variance
<i>E</i>	Energy
<i>Ent</i>	Entropy
<i>FEnt</i>	Fuzzy Entropy
<i>Hom</i>	Homogeneity
<i>InfM1</i>	Information Correlation Measure 1
<i>InfM2</i>	Information Correlation Measure 2
<i>KEnt</i>	Kapur's Entropy
<i>MaxProb</i>	Max Probability
<i>REnt</i>	Renyi's Entropy
<i>RWEnt</i>	Relative Wavelet Entropy
<i>SAver</i>	Sum Average
<i>SEnt</i>	Sum Entropy

<i>Shade</i>	Cluster Shade
<i>ShEnt</i>	Shannon's Entropy
<i>SVar</i>	Sum Variance
<i>Y_Ent</i>	Yager's Entropy

CHAPTER 1. INTRODUCTION

1.1 Background

In 2011, World Health Organisation (WHO) reported that Coronary Heart Disease (CHD) is the main cause of Myocardial Infarction (MI) contributing to 12.5% of global mortality (**WHO 2011**). Each year, an estimated 635000 Americans have new MI and 280000 have recurrent MI. It is also estimated that an additional 150000 silent MI occur each year (**AHA 2012**). The incidence of MI increases with age and the mortality is influenced by the countries' economic conditions and lifestyle. WHO reported a mortality of 6.1% in low-income countries, 13.7% in middle-income countries and 15.6% in high-income countries (**WHO 2011**).

In spite of advances in the diagnosis and treatment of MI, it still continues to be the most common cardiac problem in the modern world mainly because of lack of effective early detection techniques. Cardiac catheterisation is currently the gold standard and most effective diagnostic technique for confirming the presence of coronary artery disease that underlies MI (**Donald 2006**). This invasive technique helps the cardiologist to not only diagnose but treat the problems at the same time, so as to avert potential complications such as heart failure. This diagnostic procedure is invasive, time consuming and also has risk of radiation exposure. On the other hand, non-invasive techniques like electrocardiography (ECG), echocardiography and magnetic resonance imaging (MRI) are preferred for direct visualization of the MI to establish the diagnosis and extent of MI.

The ECG is considered as an essential part of diagnosis and initial evaluation of patients with chest pain (**Thygesan, et al. 2007**). Even though ECG has been an

important diagnostic procedure for MI, it is limited in diagnosis of infero-posterior MI especially during the acute phase (**Izumi, et al. 1995; Martinez, et al. 1970**). Therefore, non-invasive imaging modalities like echocardiography and MRI are used as diagnostic tools due to their advantages. Cardiac MRI is the imaging modality of choice to assess myocardial viability, myocardial ischemia and the extent of infarcted myocardium. Cardiac MRI expertise is uncommon, and the diagnostic test is only available at selected tertiary care institutions as they are expensive (**William, et al. 2001**). In contrast, echocardiography is commonly available and inexpensive, and like cardiac MRI, does not expose patients to ionizing radiation. Echocardiography is used in the assessment of cardiac structure and function, in particular myocardial thickness and motion abnormalities. Advances in echocardiography technique have made the assessment of the endocardial border and myocardial perfusion possible. And also this diagnostic method permits quantification of global and regional function (LV function) (**Flachskampf, et al. 2011**). The ready availability and versatility of echocardiography for assessment of myocardial condition makes this non-invasive method arguably the most significant diagnostic technique for MI diagnosis, and reduces the need for invasive and radiation-based tests.

1.2 Motivation

MI is an irreversible damage of the heart muscles caused by partial or complete blockage in the coronary artery (**Otto 2013**). The clinical presentation and outcome depends on the location of blockages, severity and age of MI. MI progresses with time, highlighting the need for continual monitoring for recognition of established and ongoing Left Ventricular (LV) remodeling and related complications (**ACC/AHA 1996**). Left ventricles with MIs undergo remodeling due to reduced myocardial contractility

(Ghista, et al. 2012), resulting in less curved and more spherical LV in systole as assessed in terms of decreased diastole-to -systole curvedness index. A remodeled LV has increased end-systole wall stress which further amplifies all of these defects. The most important issue in the management of MI patients is to detect myocardial viability for reperfusion treatment, as well as the degree, extent of infarction and LV remodeling (Zhang, et al. 2014). Early reperfusion treatment potentially improves LV function, survival and reversal of LV remodeling (Zhang, et al. 2014); and quantification of infarction and LV remodeling (e.g. using LV shape descriptors) in MI patients shall facilitate prognostication.

Whilst many semi-automated Computer-Aided Diagnosis (CAD) techniques exist in the literature for detecting normal and infarcted myocardium, few studies are focused on animal model (Bauer, et al. 2011; Peng, et al. 2009). Little has been done in the area of automated detection of infarction and extent of infarcted myocardium (normal, moderate and severely infarcted myocardium) using 2D echocardiography images. The 2D echocardiography image contains manifold unique textural information that are not apparent on visual inspection or routine quantitative gray-scale calculations, and which have not been fully exploited for diagnostic applications. Hence texture characteristics and their automated extraction can potentially facilitate accurate and faster diagnosis (Gonzalez, et al. 2002). For example, while visually derived clinical parameters such as wall motion score, LV Ejection Fraction (LVEF), myocardium thinning and thickening may unveil information on myocardial abnormalities related to infarction, its expansion and extent, and non-clinical features like texture characteristics contain exclusive and valid information at a pixel-by-pixel level about infarction and extent of myocardial damage that not be appreciable on visual interpretation. Detecting automatically normal and infarcted myocardium, and the extent of infarction (normal, moderate and severely infarcted myocardium) can therefore aid clinicians significantly in diagnosis

and management decision-making. Detecting the status of the myocardium i.e. normal, moderately infarcted or severely infarcted can aid in appropriate treatment decision in a timely manner thereby preventing the patient from reaching the heart failure stage. Detecting stages of infarction and alerting the clinicians about the severity or extent of condition well in advance can significantly improve survival rate. In order to detect infarction and the extent of infarction, cardiac MRI and Single-photon Emission Computed Tomography (SPECT) offer excellent diagnostic information, but are constrained by expensive costs and the need for radiation exposure in the latter. Hence these modalities are less popular from the patient's point of view. Two dimensional (2D) echocardiography has several advantages such as portability, low cost, widespread availability, freedom from radiation and the need for contrast agents. Given the variety of imaging options, the final selection would depend on the availability, cost and risks involved. Thus, 2D echocardiography-based techniques for detection and extent of infarction may prove to be time- and cost-saving.

1.3 Objectives

The detection of MI needs to be real-time and automated, as it is mainly intended to assist the clinicians (cardiologists) in decision making while treating and managing the cardiac patients. Therefore, developing computationally efficient techniques that can be incorporated into the echocardiography ultrasound machine for automated detection of MI patients is necessary.

Hence the objectives of the thesis are to:

- (i) study and develop an automated CAD system to identify the MI and its different stages of severity (normal, moderate and severe) using echocardiography images and

- (ii) develop an integrated index using clinically significant features to identify different classes of echocardiography images using a single number.

1.4 Scope of the Thesis

MI can be grouped into various stages of severity based on conventional features such as wall motion score index (WMSI), LVEF (LVEF ranging between 30% - 40% denotes infarcted myocardium with moderately impaired function; and LVEF will be less than 30%, severely impaired function), myocardial thinning or thickening.

In this thesis, the algorithms aims to achieve the following scopes of identifying stages of MI based on their WMSI and LVEF parameters.

- Normal myocardium refers to myocardium with no wall motion abnormality (WMSI 1 or less) and LVEF 52%-72%.
- Moderately infarcted myocardium indicates the class of infarction that comprises WMSI > 1 and LVEF of 30% - 40.
- Severely infarcted myocardium refers to the class of infarction with WMSI > 2 and LVEF < 30%.

1.5 Research Contributions

The major contributions of this research work are as follows:

- (a) Study of echocardiography, current method of diagnosing MI and extent of infarction clinically.
- b) Review of existing echocardiography image features extraction methods and their salient characteristics.
- (c) Approval is obtained to collect the data from the Institutional Review Board (IRB).

d) Computationally efficient automated CAD system to detect normal and infarcted myocardium using 2D echocardiography images has been developed. I compared the performance of three texture descriptors - Discrete Wavelet Transform (DWT), Gray-Level Co-occurrence Matrix (GLCM) and Higher-Order Spectra (HOS) – and settled on a proposed method using DWT technique that achieved a high accuracy of 99.5%. The novelty of this proposed method is that it is completely automatic and does not involve any segmentation.

(e) Automated CAD techniques to detect normal and infarcted myocardium using two different cross-sectional views (parasternal short axis mid-left ventricular view at papillary muscle level and apical four chambers view) of 2D echocardiography images are studied using Stationary Wavelet Transform (SWT). One of the key features of the proposed approach is that, it achieved an average specificity of 100% (for designating MI patients) using only 16 features from two different cross-sectional views.

f) An integrated index (Myocardial Infarction Index – MII) to detect normal and infarcted myocardium using unique one number is devised. As a part of this, a novel Texton-based texture analysis method is employed on apical four chambers cross-sectional echocardiography image view captured at the end systole – *single frame per patient* is analyzed to characterize MI.

(g) Data mining technique for identification of extent of infarcted myocardium (normal, moderately infarcted or severely infarcted myocardium) using Curvelet Transform and Local Configuration Pattern (LCP) and 2D echocardiograms is presented. Furthermore, an integrated index called myocardial infarction risk index (MIRI) to detect extent of infarcted myocardium using a single number. The proposed system showed an accuracy of 98.99% in identification of the extent of infarcted myocardium using 2D echocardiogram.

1.5.1 Related Publications

The following papers have been published in or are and submitted to international journals.

Journals

1. **Vidya KS**, Acharya UR, Ng EYK, Chou SM, Tan RS, Ghista DN. Automatic identification of myocardial infarction tissue characterisation using ultrasound images: A Review. *IEEE Reviews in Biomedical Engineering*, 2014; 8: 86-97
2. **Vidya KS**, Ng EYK, Acharya UR, Chou SM, Tan RS, Ghista DN. Computer-Aided diagnosis of myocardial infarction using ultrasound images with Texture, DWT and HOS methods: A Comparative study. *Computers in Biology and Medicine*, 2015; 62: 86-93.
3. **Vidya KS**, Acharya UR, Ng EYK, Tan RS, Chou SM, Ghista DN. An integrated index for automated detection of infarcted myocardium from cross-sectional echocardiograms using texton-based features (Part 1). *Computers in Biology and Medicine* 2016; 71: 231-240.
4. **Vidya KS**, Acharya UR, Ng EYK, Tan RS Chou SM, Ghista DN. Data mining framework for identification of myocardial infarction stages in ultrasound: A hybrid feature extraction paradigm (part 2). *Computers in Biology and Medicine* 2016; 71: 241-251.
5. **Vidya KS**, Ng EYK, Acharya UR, Tan RS, Chou SM, Ghista DN. Infarcted Left Ventricle Classification from Cross-Sectional Echocardiograms Using Relative Wavelet Energy and Entropy Features. *Journal of Mechanics in Medicine and Biology* 2016; 16: 1640009 (19 pages).

1.6 Organization of the Thesis

This thesis is organized into the following 8 chapters:

1. Chapter 1 provides the background, motivation, objectives and major research contributions of the thesis.
2. Chapter 2 provides a review of the existing techniques and methodologies in the area of detection and classification of MI by developing automated CAD systems. Starting with an overview of MI and its detection technologies (invasive and non-invasive) in clinical settings, the feasibility of two-dimensional (2D) echocardiography for MI detection are reviewed. Next, a comprehensive review of various semi-automated and automated (computer-aided) existing techniques for detection of normal and infarcted myocardium is presented. Their strengths and weakness are also outlined. The underlying computational blocks commonly encountered for the development of Computer-Aided Diagnostic (CAD) system based on echocardiographic image texture analysis are discussed. Lastly, the need of automated CAD system in detection of extent of MI (normal, moderately infarcted and / or severely infarcted myocardium) using echocardiography images is discussed.
3. Chapter 3 discusses an automated CAD system to detect normal and infarcted myocardium by comparing the performance of three texture descriptors such as DWT, GLCM and HOS using 2D echocardiography images. 400 MI and 400 normal ultrasound images obtained from 80 MI patients and 80 normal subjects are used in this work. Later, the extracted features are ranked based on t-value and fed to the Support Vector Machine (SVM) classifier to obtain the best performance using minimum number of features.

4. Chapter 4 delineates an automated CAD technique to detect normal and infarcted myocardium using two different cross-sectional views of 2D echocardiography images and texture analysis. Firstly, the Stationary Wavelet Transform (SWT) method is proposed to extract the Relative Wavelet Energy and Entropy (RWE and RWEnt) features from the two cross-sectional views of echocardiography images separately. These features are ranked and subjected to classification in two different steps: (i) the features from each view are separately ranked using entropy, t-test and Wilcoxon ranking tests and fed to the classifier, and (ii) later, the features from both the views are combined and ranked. Finally, these ranked features are subjected to the Support Vector Machine (SVM) classification for the characterization of normal and MI LV ultrasound images using a minimum number of features.
5. An integrated index (Myocardial Infarction Index – MII) to detect normal and infarcted myocardium using unique one number is described in Chapter 5. The cross-sectional view of normal and MI echocardiography images are represented as textons using Maximum Responses (MR8) filter banks. Various features are extracted from proposed textons. These features are ranked using t-test and fuzzy Max-Relevancy and Min-Redundancy (mRMR) ranking methods. Also, the highly ranked features are subjected to classification using different classifiers for the characterization of normal and MI LV ultrasound images using a minimum number of features.
6. Data mining technique for identification of extent of infarcted myocardium (normal, moderately infarcted or severely infarcted myocardium) using Curvelet Transform and Local Configuration Pattern (LCP) and 2D echocardiograms is detailed in Chapter 6. The methodology proposed extracts the LCP features from curvelet transform coefficients of echocardiograms. The obtained features are subjected to Marginal Fisher Analysis (MFA) dimensionality reduction technique

followed by fuzzy entropy based ranking method. Different classifiers are used to differentiate ranked features into three classes normal, moderate and severely infarcted based on the extent of damage to myocardium. Furthermore, I have developed an integrated index called Myocardial Infarction Risk Index (MIRI) to detect the normal, moderately and severely infarcted myocardium using a single number.

7. Chapter 7 presents few possible limitations of the proposed system.
8. Chapter 8 presents the conclusions of the thesis and also recommendations for future work are discussed.

In the next chapter, a detailed literature review of current clinical methods for diagnosing MI and extent of infarction, existing echocardiography image features extraction methods and their salient characteristics are discussed.

CHAPTER 2. LITERATURE REVIEW

2.1 Introduction

The purpose of this chapter is to provide a review of existing techniques and methodologies in the area of detection and classification of normal and infarcted myocardium. Starting with an overview of MI, its detection technologies (invasive and non-invasive) in clinical settings and feasibility of two-dimensional (2D) echocardiography for MI detection is reviewed. Next, a comprehensive survey of various semi-automated and automated (computer-aided) existing techniques for detection of normal and infarcted myocardium is undertaken. Their strengths and weakness are also outlined. The underlying computational blocks commonly encountered for the development of Computer-Aided Diagnostic (CAD) system based on echocardiographic images are discussed. Lastly, the need for automated CAD system in detection of extent of MI (normal, moderately infarcted and / or severely infarcted myocardium) using echocardiography images is discussed.

2.2 Anatomy of Human Heart

Human heart is the vital organ in the whole body, weighing 250-300 grams in females and 300-350 grams in males and is about the size of our fist (**Figure 2.1**) (**Germann, et al. 2002**). Heart is situated on the left side, anterior to the vertebral column and posterior to the sternum. Heart is enclosed by a protective double layered pericardium and composed of three layers. Outer layer is epicardium, middle myocardium and the inner layer endocardium. The heart is divided into 4 chambers,

two superior atria and two inferior ventricles. The Left Atrium (LA), Left Ventricle (LV) and Right Atrium (RA), Right Ventricle (RV) are separated by the inter-atrioventricular septum, dividing the heart into two functionally separate and anatomically distinct units. The heart acts as a pump, controlling the supply of blood required by human body. The RA receives the deoxygenated blood from the body and pumps to RV from there the blood are pumped to lungs for purification. From the lungs oxygenated blood enters the LA and later to LV, from LV blood is pumped to the whole body via aorta. These processes of receiving deoxygenated blood from the body and sending the oxygenated blood to the body are called pulmonary and systemic circulation respectively (**Gray 1918**). The oxygen and nutrients required by body muscles and tissues are provided by the heart, oxygen and nutrients required by the heart muscles (myocardium) are supplied by the coronary circulation. Coronary circulation is the supply of blood to the myocardium through the blood vessels. The vessels that deliver oxygen rich blood to the myocardium are called coronary arteries and those that remove deoxygenated blood from the myocardium are called the coronary veins. Any narrowing of these arteries commonly affected by coronary artery disease (e.g. atherosclerosis) reduces the blood supply causing myocardial ischemia. If disrupted, the atherosclerotic lesions can lead to complete artery blockage causing heart attack (called as MI), and permanent myocardial cell damage.

Figure 2.1: Anatomy of normal human heart.

(<http://www.chw.org/medical-care/herma-heart-center>)

2.3 Myocardial Infarction (MI)

According to European Society of Cardiology (ESC) the term MI should be used when there is evidence of myocardial necrosis (muscle death) (**Figure 2.2**) in a clinical setting consistent with myocardial ischemia (**Thygesan, et al. 2007**). MI is sudden and intense. Generally, it manifests as severe central chest pain, which may also radiate to the left arm, shoulder or jaw. Sweating and feeling faint are common additional symptoms. Women are more likely to develop additional symptoms like shortness of breath, back and jaw pain. However, once affected with MI, it may expand if it is not detected and treated in time. A national survey has found no evidence of important gender difference in the management and outcome of coronary heart disease (**Bowker, et al. 2000**).

Figure 2.2: Heart with myocardial infarction.

(<http://www.medicalwebbook.com/myocardial-infarction/>)

This section describes the pathophysiology behind MI, probable risk factors, MI types, and different ways of staging MI.

2.3.1 MI Pathophysiology

MI is caused by the gradual accumulation of atherosclerotic plaque in coronary artery. This accumulated plaque gets ruptured causing the clot formation which leads to complete blockage of the artery. This artery blockage reduces the blood downstream to the myocardium leading to muscle damage (**Figure 2.3**). If this impaired blood flow to the heart muscle lasts long enough, it triggers a process called ischemic cascade; the heart cells start to die permanently causing the condition called MI. As a result, the patient's heart will be permanently (irreversibly) damaged.

Figure 2.3: Human heart depicting the damaged myocardium due to the blocked artery.

(<http://www.patient.co.uk/health/myocardial-infarction-heart-attack>)

After MI, there is myocardial cell death and thinning (acute loss) of myocardium at the area of infarction. After few hours of cell death, the infarcted myocardium starts to experience coagulation necrosis, a process marked by cell swelling and protein denaturation (**Burke, et al. 2007**). The infarcted myocardium is generally soft in initial days and is therefore susceptible to rupturing. This episode may happen at any time in the first 2 weeks and is commonly fatal and accountable for about 10% of MI mortality (**Aaronson, et al. 2007**). Thus, these thin and weak muscles are unable to bear the haemodynamic pressure and volume load in the same manner as compared to the healthy heart. This abrupt increase in loading conditions induces the pattern of remodeling in the infarcted myocardium area (**Martin, et al. 2000**). Undiagnosed and prolonged infarction gets expanded and further damages LV function, size and shape. Over the course of several months, there is progressive dilation, not only of the infarct zone, but also of healthy myocardium. Infarct expansion puts patients at substantial risk of ventricular arrhythmias, congestive heart failure and free wall rupture (**Burke, et al. 2007**). Once affected with MI, its expansion is exacerbated if it is not detected and

treated in time. Thus, occurrence of MI is the first warning signal for all underlying or forthcoming chain of complications such as LV remodelling and heart failure. The LV remodelling after MI refers to global (entire) and regional changes of LV and is characterised by progressive dilation, hypertrophy, distortion of cavity shape, and deterioration in contractile function (**Martin, et al. 2003**) (**Figure 2.4**). Post-MI LV remodeling has been divided into an early phase and a late phase. The early phase of remodeling involves infarct expansion and extension into adjacent noninfarcted myocardium zone. This results in LV dilation as shown in Figure (**Figure 2.4**). Late phase of remodeling involves the changes in geometry and size of entire LV. The early phase of LV remodeling begins immediately in response to the change in loading condition and can last for months after MI. Left unchecked, LV hypertrophy, dilation and contractile dysfunction may advance and result in progressive decline in ventricular performance (**Marvin, et al. 2011**). The outcome of the treatment after MI depends on the extent of infarction and LV remodeling it caused (**Jaarsma, et al. 1986**).

Figure 2.4: Normal vs. infarcted heart – cross sectional view. The left ventricle has a thick muscular wall, shown in cross-section in (A). After a myocardial infarction (heart attack), heart muscle cells in the left ventricle are deprived of oxygen and die (B), eventually causing the ventricular wall to become thinner (C)
(<http://stemcells.nih.gov/info/scireport/pages/2006Chapter6.aspx>).

2.3.2 Risk Factors of MI

Total of nine risk factors significantly associated with MI in both women and men (Sania, et al. 2008) are abnormal lipids, smoking, high risk diet, physical inactivity, alcohol, diabetes, abnormal obesity, psychological stress, and hypertension. Risk factors more strongly associated with MI in women compared to men included hypertension, diabetes, alcohol intake, and physical inactivity. Many of the risk factors are modifiable namely, smoking, physical inactivity, lipids level, obesity (body mass index, BMI), diabetes, hypertension, and psychological stress and thus MI (heart attack) can be prevented. Non-modifiable risk factors include increasing age, gender, family history and genetic factor (Sadia, et al. 2012)

2.3.3 MI Types and Stages

Clinically, MI can be classified into five types (Thygesan, et al. 2012). **Type 1** is spontaneous MI related to ischaemia caused due to a primary coronary event such as plaque erosion and/or rupture, fissuring, or dissection. **Type 2** is MI secondary to ischemia caused due to either increased oxygen demand or decreased supply. **Type 3** is sudden unexpected cardiac death, including cardiac arrest. **Type 4a** is MI associated with Percutaneous Coronary Intervention (PCI). **Type 4b** is MI associated with stent thrombosis as documented by angiography or at autopsy. **Type 5** is MI associated with Coronary Artery Bypass Grafting (CABG). MI can be sub classified as non-ST segment elevation MI (NSTEMI) and ST segment elevation MI (STEMI). The NSTEMI does not cause any ST elevation changes on an ECG, but echocardiogram and chemical markers

in the blood indicate the damage to the heart muscle. The extent of myocardium damage is relatively minimal due partial or temporary blockage in the artery. The STEMI is caused by completely blocked artery's blood supply. It affects large areas of the heart muscle and can be detected by electrocardiogram (ECG) changes of ST elevation and echocardiogram.

Based on pathology, there are main two types of MI. They are,

Trans-mural MI is associated with atherosclerosis involving a major coronary artery. It can be sub classified into various territories: anterior, posterior, inferior, lateral, or septal. Trans-mural infarcts extend through the whole thickness of the myocardium and are usually result of complete occlusion of the blood supply to the area or region (Reznil 2010).

Sub-endocardial MI involves the sub-endocardial wall of the LV, ventricular septum, or papillary muscles. The sub-endocardial area is particularly susceptible to ischemia (Reznik 2010).

MI may happen even without any symptom. Typically, MI ECG can evolve through 3 stages including (i) MI in acute stage (MIAS, only lasts several minutes to several hours), (ii) MI in subacute stage (MISAS, can last days) and (iii) MI in recovery stage (MIRS). If patients can obtain the thrombolytic therapy or acute percutaneous coronary intervention during MIAS, the heart tissue that is close to death can be saved and continue to survive, otherwise the irreversible heart tissue damage will occur and sometimes even lead to inevitable sudden death in later stages. The various stages of MI are directly related to the size of damaged myocardium supplied by the culprit coronary artery distal to the occlusion (Baxt 2002; Haraldsson, et al. 2004; Acharya, et al. 2007). The outcome of early prognosis depends on the size of damaged myocardium (Matveev, et al. 2006). Consequently the detection of MIAS is more important and significant than that of MISAS and MIRS for patients suffering from CHD in their daily

life. In hospitals, besides MIAS, physicians also need to recognise MISAS for patient's urgent treatment and management.

2.4 MI Diagnosis Techniques

MI can be invasively diagnosed by cardiac catheterisation and non-invasively by Electrocardiogram (ECG) and imaging techniques like X-ray, Magnetic Resonance Imaging (MRI) and echocardiogram. The most popular and established series of invasive and non-invasive MI diagnosis techniques are described below.

2.4.1 Invasive Diagnostic Techniques

a. Cardiac catheterization

It is a combined hemodynamic and angiographic procedure undertaken for diagnostic and often therapeutic purposes. The American College of Cardiology (ACC) and the American Heart Association (AHA) have developed indications for the use of catheterisation and coronary intervention in the management of MI (**ACC/AHA 2004**). The basic principle is that cardiac catheterisation is recommended to confirm the presence of a clinically suspected condition, define its anatomic and physiologic severity and determine the presence or absence of associated conditions. It is most commonly performed to examine the coronary arteries because most of the conditions such as MIs (heart attacks), angina and heart failure originate from these arteries. This procedure allows a comprehensive examination of the heart and surrounding blood vessels. In addition, it also enables the physicians to take angiograms, record blood flow, calculate cardiac output and vascular resistance to evaluate the heart's functional activities. Though it is one of the preferred diagnostic tests, it is categorised as an invasive procedure for assessing the heart, its valves and coronary arteries. It has added

risks involved such as exposure to hazardous radiation, allergic reactions related to contrast agent used and the complications are higher in patients above 60 years of age. In contemporary management of MI, cardiac catheterization is obligatory in all NSTEMI and most STEMI because of the possibility for simultaneous early reperfusion treatment.

2.4.2 Non-invasive Techniques

a. Electrocardiogram (ECG)

It is a non-invasive procedure used to record the electrical activities of the heart (**Chugh 2006**). This test is considered an essential part of the diagnosis, initial evaluation of patients with chest pain and subsequently MI. In a patient with typical symptoms such as presence of ST elevation, especially when accompanied with reciprocal changes, is highly predictive for evolving MI. MI, especially when large, often produces a typical sequence of ST-T changes and abnormal Q waves. The ST-T changes can be divided into two phases: (i) the acute phase, which is marked by ST segment elevations and sometimes tall positive T waves and (ii) the evolving phase, which is characterised by the appearance of deeply inverted T waves. The ST-T changes occur hours or days later during the evolving phase and usually resolve over weeks or months. This information will influence the decision to restore coronary blood flow with thrombolytic agents or direct angioplasty. However, several investigators reported that the sensitivity of ECG for MI may be as low as 50% (**Rude, et al. 1983; Brush, et al. 1985; Lee, et al. 1987**). **Menown, et al. 2000** analysed the efficiency of ECG obtained during admission for diagnosing MI by studying patients with and without chest pain. The study reported sensitivity of 56% and specificity of 94% in detection of MI. **Hedges, et al. 1992** used ECGs performed during admission and 3-4 hours after admission and they found serial ECG changes only in 15% of the patients. As just noted, both the

sensitivity and specificity of ECG in diagnosing MI and extent of infarction are limited. Clinicians need to be aware of these diagnostic limitations. Chest pain, coronary artery disease and mild MI are some important problems that cannot be excluded simply because ECG is normal or shows only non-diagnostic abnormalities.

Most patients with MI show diagnostic ECG changes (i.e., new Q waves and/or ST elevations, hyperacute T waves, ST depressions or T wave inversions). In weeks and months after MI, however, these changes may become less apparent and in some cases, may disappear. Care should be taken to minimise errors in interpreting ECGs. Many mistakes result from the failure to be systematic. Other mistakes result from confusing ECG patterns that are “look-alikes”. Although ECG has definite limitations, it often helps to diagnose MI and sometimes aids in faster evaluation and management of general medical problems.

b. Imaging techniques

Medical imaging techniques can be broadly grouped into (i) ionizing radiation and (ii) non-ionizing radiation. Ionizing radiation group consists of images created by x-rays or gamma rays. Non-ionizing radiation techniques use either ultrasound for echo-ranging imaging or radio-waves combined with high-field magnets in the case of MRI.

Chest X-ray

It is a safe, painless and effective procedure for capturing images of the body's organs and bones (Lacey, et al. 2008). It is used for examining different organs in order to identify the problems associated. This test can even show abnormal heart size and signs of heart failure. It is therefore a good diagnostic method for identifying changes or abnormalities present in the heart and major arteries such as heart failure, congenital heart diseases and pericarditis (inflammation of the heart lining). In addition, this test

can also be used for examining whether complications have arisen from the MI (heart attack), and / or pulmonary oedema (build-up of fluid inside lungs).

Battler, et al. 1980 evaluated the usefulness of radiographic findings on the initial chest x-ray obtained within 24 hours from admission to the coronary care unit in predicting the prognosis of 273 patients with MI. The prognosis of patients with MI depends mainly on the extent of LV dysfunction and extent of infarction (muscle damage). The study concluded that the chest x-ray obtained during first day of admission from MI patients provided significant information about early and late prognosis. In addition, a low-risk group and groups with higher risk of heart failure or death during the first month or year after infarction can be obtained using admission chest x-ray analysis. Chest x-ray is one of the most widely used methods for population screening and patient evaluation in virtually all cardiac diseases (**Ferguson, et al. 2007; Young 2006; Maffessanti, et al. 1998**). However, the value of chest x-ray in detecting LV size and function is limited. It has been suggested that less than half of the patients with LV systolic dysfunction show a cardiothoracic ratio (which aids in the detection of abnormalities) greater than 55% (**Petrie, et al. 2003**). In addition, X-ray imaging involves illuminating the body with a penetrating high energy ionising radiation. The differential absorption of this radiation by various tissues creates an inverse shadow of the body on a film. Thus, this diagnostic method has radiation hazards.

Magnetic Resonance Imaging (MRI)

It is another non-invasive technique with increasing applications in MI for the assessment of function, perfusion and tissue characterisation in a highly reproducible manner during a single examination (**Hundley, et al. 2010**). It provides an accurate and complete assessment of myocardial function in patients with suspected MI. This technique is also able to detect even small areas of sub-endocardial infarction (**Kim, et**

al. 2010; Beek, et al. 2010) and is of value in detecting state of myocardium that can mimic infarction, such as myocarditis (Assomull, et al. 2007).

Cardiac MRI has been traditionally considered a non-invasive imaging tool; however the presence of a magnetic field and contrast administration involves even safety issues that need to be considered. Also the MRI scanner room, with the presence of static and gradient fields may interact with ferromagnetic objects and this may cause electric currents. Finally, the body scanner may transmit radiofrequency waves into the patients. Due to these risk factors patients are screened for implanted cardiovascular devices prior to undergoing MRI (Roguin, et al. 2008). Potential complications of MRI examination in patients with pacemaker include damage or movement of the device, induction of life-threatening arrhythmias, cardiac stimulation and heating of electrode tips (Faris, et al. 2005; Prasad, et al. 2004).

Echocardiography

It is emerged as a readily available non-invasive tool for early assessment of cardiovascular system. Today, M-mode echocardiography is an important part of a complete cardiac examination because of its high temporal resolution, which allows accurate analysis of fast moving structures. At present, M-mode, 2D, pulsed-wave, continuous-wave and colour Doppler flow are all combined in one diagnostic console represent the most comprehensive cardiac diagnostic imaging modality. It provides integrated structural, functional and hemodynamic cardiac information.

The advent of 2D echocardiography has made it possible to detect (i) acute alterations in cardiac topography by serial examination of patients with MI and (ii) presence of regional myocardial dilation and wall thinning due to infarction (Eaton, et al. 1979). It is an inexpensive imaging technique which uses the basic principles of general diagnostic ultrasound. Echocardiography captures the movement of myocardium and does not involve any radioactive hazards or risks. It has small

acquisition time compared to other imaging modalities like Computed Tomography (CT) and MRI. It is a real-time test and is also capable of viewing the heart in multiple planes providing multiple views. It is a fast and simple non-invasive imaging method, and thus represents the preferred imaging tool to quantify the LV remodeling and extent of infarction (**Gheorghe, et al. 2008**).

2.5 Echocardiography of Human Heart

Echocardiography commonly uses ultrasound with frequencies of 2.5 – 10 MHz for normal diagnostic work (**Oh, et al. 1999**). Almost all diagnostic ultrasound machines are based on the principle that ultrasound is reflected by an interface between media of different acoustic impedances. Higher frequency ultrasonic beam has the greater ability to visualize objects or interfaces that are close to each other (**William, et al. 2010**). The essential components of ultrasound machine include the transducer, transmitter, receiver, signal amplifier and the display. The use of echocardiography became widespread with the development of piezoelectric transducers. Echocardiogram image is created by first transmitting sound waves from a transducer into the body and then interpreting the intensity of reflected echoes received by a receiver. The data collected is then processed by a scanner and displayed as a black and white image generally referred to as gray scale. The amplitude of each reflected wave is represented by a dot (pixel), where position of dot represents the depth from which the returning echo is received and brightness of the dot represents the strength of a returning echo. These dots are combined to form a complete image. Quality of images obtained depends on the skill of an operator, as well as the physique of a patient. Dedicated training for competent performance and interpretation of echocardiogram is essential. The ACC and the AHA have recommended a set of minimum knowledge and training requirements for the performance and interpretation of echocardiograms (**Ryan, et al. 2008**). Multiple different viewing angles as recommended by the American Society of

Echocardiography (ASE) are needed to fully visualize all the cardiac structures, because echo view provides only 2D image of the 3D heart. An echocardiographic examination begins with transthoracic 2D scanning from four standard transducer positions: the parasternal, apical, subcostal (subxiphoid), and suprasternal windows (Oh, et al. 1999). From each transducer position, multiple tomographic images of the heart relative to its long and short axes are obtained by manually rotating and angulating the transducer (Table 2.1), hence performing a multiplane examination. The different transducer positions and cardiac views are tabulated in Table 2.1. The long-axis view represents a sagittal or coronal section of the heart, bisecting the heart from the base to the apex. The short-axis view is perpendicular to the long-axis view. The parasternal long-axis view of the LV allows visualization of the aortic root, aortic valve leaflets, the anterior and posterior leaflets of the mitral valve, and their chordal and papillary muscle attachments. In parasternal short-axis view, a cross-section of the LV at the level of the mitral leaflets, a transverse section of the ventricular apex, and a cross-section at the level of papillary muscles are obtained. With the apical transducer position, a four-chamber view of the heart or a right anterior oblique equivalent view of the LV usually is recorded. The apical four-chamber view displays all four chambers of the heart, the ventricular and atrial septa, and the crux of the heart. In addition, this view allows visualization of the emptying of the right and left inferior pulmonary veins into the LA. With the same apical transducer position, the aortic root and valve in addition to the four chambers can be recorded. Figure 2.5 shows the few different views of human heart (Oh, et al. 1999).

Table 2.1: Transducer positions and cardiac views

Transducer position	Cardiac views
Parasternal position	Long-axis view: <ul style="list-style-type: none"> • LV in a sagittal section • RV inflow • LV outflow Short-axis view: <ul style="list-style-type: none"> • LV apex • Papillary muscles (midlevel) • Mitral valve (basal level) • Aortic valve – RV outflow • Pulmonary trunk bifurcation
Apical position	Four-chamber view Five-chamber (or long-axis) view Two-chamber view
Subcostal position	Inferior vena cava and hepatic vein RV and LV inflow LV-aorta RV outflow
Suprasternal notch position	Long-axis aorta-short-axis pulmonary artery Short-axis aorta-long-axis pulmonary artery Long-axis aorta and superior vena cava

Figure 2.5: (a) Parasternal short-axis view at the papillary muscle level, (b) apical four-chamber view, (c) parasternal long-axis view, (d) apical two chambers view (yet to obtain this views).

2.5.1 Role of Echocardiography in MI Detection

Tanaka, et al. 1975, 1978 used high quality diagnostic equipment in the clinical examination of patients with myocardial damage such as cardiomyopathy, MI and myocardial contusion. The intensified abnormal echoes from the damaged myocardial area are frequently detected and analyzed. In clinical settings, detailed structural and functional information of myocardium is required for accurate diagnosis of cardiac abnormalities (**Tanaka 1998**). One of the principal ways of detecting MI is by visual interpretation of features from echocardiogram images.

It is a routine practice for cardiologists to use different cross-sectional planes with various positions of transducer to assess 17 LV wall segments (**Cerqueira, et al. 2002**) and view MI downstream of all three coronary arterial territories (left anterior descending artery: mid anterior, mid anteroseptal, inferoseptal, distal septal and apical walls; circumflex artery: basal anterolateral, mid anterolateral, inferolateral, and distal lateral; right coronary artery: proximal inferoseptal, and mid inferior walls). Using these 17 segments, cardiologists compute the regional wall motion score, wall thinning or thickening and LV functions like Left Ventricular Ejection Fraction (LVEF) to detect the presence of infarct expansion and extent of infarcted myocardium (**Moller, et al. 2006; Carluccio, et al. 2000; Lang, et al. 2015**). Each segment is individually analyzed in multiple views and scored on the basis of its motion and thickening (**Lang, et al. 2015**) (**Kloner, et al. 1987; McKay, et al. 1986; Erlebacher, et al. 1982; Gaudron, et al. 1993; Wilansky, et al. 1991; Pfeffer, et al. 1990**). The parasternal short-axis view at papillary muscle level echocardiography aids the cardiologists in the evaluation of MI patient's LV, RV abnormalities, and papillary muscle rupture. Further, this view also helps to examine LV function (regional and global) and the size of ventricles. Abnormal features in any of the four chambers (LA, LV, RA, and RV) of the heart and wall motion abnormalities can be evaluated from apical four chambers view. In studies with cross-sectional echocardiography, the parasternal (long- short-axis) and apical (two- and four chambers) views of echocardiography are shown to be useful in assessing the severity of wall motion abnormalities in terms of wall motion score in MI patients (**Shen, et al. 1991**). In addition, it has been shown that the apical three chambers and parasternal short axis view at papillary muscle level can be used to evaluate the shortening and thickening of the papillary muscle during systole (**Kisanuki, et al. 1993**). The standard parasternal and apical views 2D echocardiography combined with three apical views (two, three, and four chambers views) of intravenous myocardial contrast echocardiography have been used to assess systolic wall thickening and wall motion to

identify the functional recovery in MI patients immediately after the incident (Swinburn, et al. 2001). A brief description of these visual clinical features is given below (Gaasch, et al. 2011; Greaves 2002; Konstam 2008; Bruyne, et al. 2007; Delewi, et al. 2012).

- Wall motion abnormalities: The LV myocardium will be divided into multiple segments, each of which gets assigned to a number, reflecting the wall motion abnormality. The Wall Motion Score (WMS) equal to 2 indicates hypokinetic (reduced thickening), WMS equal to 3 indicates akinetic (absent or negligible thickening, e.g. scar), WMS equal to 4 represents dyskinetic (systolic thinning or stretching, e.g. aneurysm). The Wall Motion Score Index (WMSI) is the mean WMS of all myocardial wall segments. Details of this parameter are shown in **Table 2.2**.

Table 2.2: Wall motion analysis (Greaves 2002).

Score	Wall Motion	Definition
0	Hyperkinetic	Increased endocardial inward movement and systolic wall thickening
1	Normal	Normal endocardial inward movement and systolic wall thickening
2	Hypokinetic	Reduced endocardial inward movement and systolic wall thickening
3	Akinetic	Absence of endocardial inward movement; no systolic wall thickening
4	Dyskinetic	Outward wall movement in systole with absent wall thickening; often associated with myocardial thinning and fibrosis

- LV size (dimension and volume) (**Lang, et al. 2005**): Quantitative assessment of LV dimension is performed by linear measurements (LV cavity diameters, wall thickness) or calculation of volumes (LV cavity volume). Measurements commonly performed to assess LV dimensions include LV diameter at end diastole (LVEDD) and at end systole (LVESD), LV volume at end diastole (LVEDV) and at end systole (LVESV). Qualitative assessment of LV dimensions will be performed by trained echo technicians in emergency situations. Qualitative assessment of LV size entirely depends on interpreter's skill and may have significant inter-observer variability; therefore, it should be compared with quantitative measurements.
- LV mass and geometry: LV muscle volume is obtained by subtracting the LV cavity volume from LV epicardium volume. This obtained LV muscle volume is then converted to LV mass (**Schiller, et al. 1989**). Different geometric patterns are obtained based the LV mass index (LVMI) and Relative Wall Thickness (RWT). They are normal geometric pattern-normal LVMI and RWT, concentric remodeling – normal LVMI and increased RWT, eccentric hypertrophy increased LVMI and normal RWT, and concentric hypertrophy increased LVMI and RWT (**Gaasch, et al. 2011; Lavie, et al. 2008**).
- LV function (LVEF): It is the most commonly used index of LV systolic function and is the difference between LVEDV and LVESV, divided by the LVEDV (**Marwick, et al. 2003**). LVEFs less than 52% for men and less than 54% for women indicates abnormal LV systolic function. LVEF ranging between 41% - 53% indicates mild abnormal, 30% to 40% denotes moderately abnormal, and for severely abnormal class LVEF will be less than 30% (**Lang, et al. 2015**).

Based on these visual clinical features of echocardiograms, cardiologists will assess the decline in LV function and complications that may arise from the MI to predict the extent of infarction and muscle damage (**Wilansky 1991**).

Thus, echocardiography imaging technique can be useful in the diagnosis of MI because of their ability to detect wall motion abnormalities or loss of viable myocardium. In addition, it provides clues that may aid the assessment of many non-ischemic and ischemic causes of acute chest pain, such as peri-myocarditis, valvular heart disease, cardiomyopathy and pulmonary embolism (**Flachskampf, et al. 2011**). Therefore, it can be concluded that, 2D echocardiography is the imaging technique of choice for detecting MI, including extent of myocardial damage due to infarction.

In case of late presentation after suspected MI, the presence of regional wall motion abnormality, thinning or scar in the absence of non-ischemic causes, provide evidence of past MI. And also after a MI, the chances of having another one or re-infarction are higher than if he/she never had a MI before. The prevention of these depends on the infarct size, extent of LV remodeling (damage), time between injury and treatment of the previous infarction. The non-invasive 2D echocardiography, play a major role in the early identification of myocardial viability, in localisation of muscle damage and also useful for risk stratification after a definitive diagnosis of MI. The detection of residual or remote ischemia and/ or LV dysfunction using echocardiography provides powerful indicators of later outcome.

After an acute phase of MI, cardiac imaging can provide a wealth of valuable details for patient management. Given the variety of imaging options, the final selection would depend on the availability, cost and risks involved. 2D echocardiography possesses several advantages such as portability, low cost, widespread availability, and no need for radiation and contrast agents. The clinical choice therefore differs depending on resources, patient characteristics and, individual experience of the physician.

An echocardiogram obtained as early as possible in the acute phase of MI helps to exclude acute mechanical complications by regional and global LV function

assessment. In case of emergency such as when patients experience sudden deterioration, hypotension, acute heart failure or a new murmur, urgent echocardiography is mandatory (**Flachskampf, et al. 2011**).

Figure 2.6 shows the short axis view echocardiogram of normal and infarcted myocardium. Echocardiography image feature measurements are done manually by the echo-technicians. The manually measured values and various views' images are then visually interpreted by the experienced cardiologists. Echocardiogram textural features of the myocardium would potentially give more information regarding abnormalities present in the heart. Not only does the 2D echocardiography allow direct and adequate visualisation of real time regional wall motion abnormalities during chronic and acute phases of MI, it also allows accurate localisation of infarcted areas. In addition, the WMSI evaluated by 2D echocardiography, an index of LV function, is a good indicator of prognosis in-hospital and after the discharge (**Shen, et al. 1991**).

Figure 2.6: Normal (a) and MI (b) echocardiogram of human heart. The arrow indicates the thinning of myocardium.

2.6 Visual Interpretation Technologies for Normal and Infarcted Myocardium Detection Using Clinical Features

In echocardiogram, analysis of myocardial viability and extent myocardial cell damage is conducted with visual interpretation of the LV functions by experienced echo technician and or cardiologist. Summary of the research studies conducted using visual interpretations of echocardiography image features in the detection of normal and infarcted myocardium are tabulated in **Table 2.3**. In 1980, **Heger, et al.** reported that during MI measuring the extent of LV asynergy using cross sectional echocardiography correlates well with regional wall motion index (WMI). On the contrary, **Lieberman, et al. 1981** reported that the regional wall motion abnormalities do not necessarily define the extent of infarcted zone because of the overlapping of infarcted and adjacent normal

zones. **In 1982, Visser, et al.** studied the MI patients using apex 2D echocardiography and showed that 91% (48/53) patients had LV asynergy which correlated well with peak value of blood enzymes (CK MB) test. **Parisi, et al. 1981** used a quantitative approach for the assessment of regional LV function using wall motion abnormalities and concluded that an area based method provided the best predictive accuracy of 87-95% compared to linear methods which yielded an accuracy of 76-84% in classifying normal and abnormal LV segments. **In 1986, Jaarsma, et al.** showed that the 2D exercise echocardiography was useful shortly after MI in predicting the wall motion abnormalities adjacent to or remote from the region of infarction. The study reported the sensitivity of 77% and specificity of 95% using exercise echocardiography. **In 1997, Karl, et al.** used LV diameter measured from M-mode echocardiography to calculate LVEF, but were hindered by a wide range of error during assessment of LV size, especially for enlarged ventricles. The proposed technique using M-mode integrated with 2D echocardiography yielded good results in assessing LV remodeling. **In 2003, Martin, et al.** investigated the relationship between LV remodeling and ventricular arrhythmias (VA) after MI using echocardiography. It was reported that the Ventricular Tachycardia (VT) and Premature Ventricular Contractions (PVCs) occurred in 20% and 29% of patients respectively a few hours after MI and increased in one year time.

Hickman, et al. 2004 reported that accuracy of tissue harmonic echocardiography was better than the normal echocardiography in the assessment of systolic wall thickening. They reported a sensitivity of 83% and specificity of 55% using tissue harmonic echocardiography and sensitivity of 71% and specificity of 46% using normal echocardiography. **In 2012, Carolina, et al.** performed a characterisation of LV remodeling in a mouse model for quantitative monitoring of cardiac recovery after MI. Their study showed that the LV dilation resulted in marked changes in LVESD from day 1 (2.82 ± 0.24) to 7 days (3.49 ± 0.42) after MI. **In 2012, Steobe, et al.** used normal

and contrast echocardiography to study the quantification of LV volumes and LVEF for analysis of LV remodeling after MI. Their study reported significant differences in LV volumes (LVEDV: 119 ± 16 vs 135 ± 14 and LVESV: 64 ± 10 vs 69 ± 9) and LVEF (46 ± 5 vs 49 ± 4) obtained using normal and contrast echocardiography. It was also reported that the contrast echocardiography was more accurate in assessing the LV remodeling. **Elaine, et al. 2012** studied the clinical characteristics and predictors of LV remodeling after anterior MI in the modern medical therapy. They reported that in patients with anterior MI, despite high percentage of reperfusion and anti-remodeling treatments, LV enlargement was a common event.

In 2013, Diana, et al. studied the impact of echocardiographic features combined with angiotensinogen (AGT) gene on LV remodeling after MI. Echocardiography showed that patients with LV remodeling had anterior wall MI, lower LVEF (49.4 ± 7.9 vs 54.3 ± 7.8), increased LVESV (43.4 ± 14.3 vs 38.5 ± 13.3) and higher WMI (1.65 ± 0.32 vs 1.49 ± 0.30) compared to non LV remodeling group. Results of this study revealed that the anterior wall infarction, reduced LVEF, polymorphism of AGT can be used as predictors of LV remodeling after MI. **In 2013, Silvio, et al.** used the ratio of mitral inflow velocity (E) and peak diastolic annular velocity (e') (E/e'), as the non-invasive marker of elevated LV filling pressures, in detecting LV remodeling after MI. They showed that the group with LV remodeling had higher LV systolic dimension, lower EF, and higher E/e'. They were able to detect patients with and without LV remodeling with a sensitivity of 70% and specificity of 98%.

The various research results suggest that the echocardiography image features are indeed a suitable parameter for normal and abnormal myocardium differentiation. However, the use of it for MI detection is restricted due to the limitations of echocardiography. Ultrasound does not travel well through bone or air-containing lung; thus the examination must be performed with skill to avoid those areas of the chest that will not permit adequate imaging of the heart (**Feigenbaum 1983**). With the diversity in

training and experience of physicians and technicians working with echocardiogram, the quality of images captured varies dramatically. The efficiency of diagnosis depends on the quality of images and the person evaluating the echocardiogram. The image quality is easily affected by speckle noise which interferes with the diagnosis. MI and LV remodeling will produce different types of clinical features, particularly wall motion abnormalities and wall thickness, on an echocardiography images (**Greaves 2002; Falsetti, et al. 1981**). The evaluation of echocardiography image features by the echo technologists or cardiologists is important to diagnose MI, infarct expansion, extent of infarction and damage (LV remodeling). The accurate visual interpretation of image features requires lot of experience and training. However, visual interpretation of features is subjective, time consuming and operator dependent. Hence, the interpretation is always vulnerable to intra and inter-observer variability (**Chetboul, et al. 2003**). There are also obvious limitations in using clinical features in trying to predict infarction size (**Lieberman, et al. 1981**). Non-infarcted and non-ischemic muscles can be influenced by adjacent muscles i.e. tethering effect (**Force, et al. 1986**). Echocardiography tends to overestimate recent MI and underestimate old infarction (**Force, et al. 1986; Buda, et al. 1986**). And also the echocardiography images are limited by the low resolution and artefacts which hinders the visual identification of subtle changes. Therefore, Computer-Aided Diagnosis (CAD) is required in order to assist cardiologists in relatively better objective interpretation of echocardiogram.

Table 2.3: Summary of studies conducted on identification of MI using echocardiography clinical features.

Authors	Features				Results
	Muscle damage				Results obtained in predicting MI, extent of LV remodelling and complications
	Regional LV function	Global LV function			
	wall motion analysis	LV structure		LV function	
		LV mass and area	LV size (dimensions and volume)	LVEF	
Heger et al. (1980) (Human Study)	✓			✓	<ul style="list-style-type: none"> Wall motion index = 3.2 ± 2.4 in uncomplicated MI and 6.7 ± 1.9 in complicated MI.
Parisi et al. (1981)	✓				<ul style="list-style-type: none"> Accuracy = 87 – 95% (area methods) vs 76 – 84% (linear methods).
Lieberman et al. (1981)	✓	✓	✓		<ul style="list-style-type: none"> Systolic thickening indicates <20% extent infarction.
Visser et al. (1982) (Human study)	✓	✓			<ul style="list-style-type: none"> Reported that 91% (48/53) patients had LV asynergy.
Jaarsma et al. (1986)	✓				<ul style="list-style-type: none"> Sensitivity 77% and Specificity 95%
Karl et al. (1997)		✓	✓		<ul style="list-style-type: none"> Reported that for assessing LV remodelling, LV diameters and LV volume should be preferred.

Martin et al. (2003)	✓	✓	✓		<ul style="list-style-type: none"> Reported that quantitative echocardiographic assessment of changes in LV size, LV mass area, and function predict VT after AMI.
Hickman et al. (2004)		✓	✓		<ul style="list-style-type: none"> Echocardiogram: Sensitivity 77%, specificity 43%. Tissue harmonic echo: sensitivity 92%, specificity 48%
Carolina et al. (2012)		✓	✓	✓	<ul style="list-style-type: none"> Reported marked changes in LV functions after AMI. LVSD: 2.82 ± 0.24, LVEDA: 18.98 ± 1.81 at day 1, and LVSD: 3.49 ± 0.42, LVEDA: 22.04 ± 2.11 at 7 days.
Steobe et al. (2012)			✓	✓	<ul style="list-style-type: none"> Reported that the assessment of LV volumes and LVEF is accurate with contrast echocardiography. Obtained LV volume: LVEDV: 119 ± 16 vs 135 ± 14 and LVESV: 64 ± 10 vs 69 ± 9 using normal and contrast echo. LVEF: 46 ± 5 vs 49 ± 4 respectively.
Elaine et al. (2012)		✓	✓	✓	<ul style="list-style-type: none"> Sensitivity of 67.6% and Specificity of 89.3%.
Diana et al. (2013)	✓	✓	✓	✓	<p>Reported that at follow-up,</p> <ul style="list-style-type: none"> Patients with LV remodelling had anterior wall MI, lower LVEF (49.4 ± 7.9 vs 54.3 ± 7.8), increased LVESV (43.4 ± 14.3 vs 38.5 ± 13.3) and higher WMI (1.65 ± 0.32 vs 1.49 ± 0.30) compared to non LV remodelling group.
Silvio et al. (2013)	✓	✓	✓	✓	<ul style="list-style-type: none"> Sensitivity of 70% and specificity of 98% in detecting LV remodelling.

2.7 Computer-Aided Diagnostic (CAD) System

In order to overcome the limitations of manual measurement, visual identification and interpretations of clinical features from echocardiograms, an automated efficient CAD system can be used for accurate and more objective diagnosis. CAD is an emerging concept developed by combining the knowledge of medicine and image processing in clinical settings. To understand the philosophy of CAD, it is necessary to follow a particular protocol. A typical protocol for a CAD system consists of different stages namely (i) image acquisition and pre-processing, (ii) segmentation / region-of-interest (ROI) selection, (iii) image feature extraction and (iv) classification. Previous researchers, **Fujita, et al. 2010 and Ginneken, et al. 2011** have reviewed and summarised the latest development and application of CAD system. The advanced image processing techniques (e.g. DWT, first and second-order statistics and HOS) based CAD approaches in ultrasound images (**Acharya, et al. 2012c; Acharya, et al. 2012a; Agani, et al. 2007; Giachetti, et al. 1995; Bosch, et al. 2005**), including detection of abnormalities, e.g. atherosclerosis, LV dysfunction, coronary plaque and MI (**Maxime, et al. 2007; Acharya, et al. 2011; Acharya, et al. 2013c; Acharya, et al. 2013d; Bosch, et al. 2005**) may aid doctors to expedite screening of large population and facilitate in early treatment. The use of CAD system by a radiologist or cardiologist could be a double reading and an effective means of reducing errors and help in increasing sensitivity in the diagnosis (**Doi 2006, 2007**).

In the development of CAD system, it is necessary to employ image processing and information processing techniques for quantitative analysis of images (**Doi 2006**). In addition, it is necessary to understand the clinically relevant content of images on the basis of non-clinical features (texture characteristics). Therefore, to develop a CAD system for the detection of normal and infarcted myocardium, I have discussed the extraction of different nonclinical features (texture characteristics or echocardiogram

features), feature ranking, and classification using different classifiers. **Figure 2.7** shows the block diagram of a typical CAD system proposed for the detection of normal and MI. The proposed system uses echocardiography images which are preprocessed to remove speckle noise and to improve image contrast. The region of interest (ROI) is selected using different segmentation methods. Various nonclinical features are extracted from the images using different feature extraction algorithms. Then, these extracted features are ranked using ranking methods. The minimum numbers of first few highly ranked features are to be used for classification to yield the highest classification accuracy using various classifiers. Hence, with the development of this CAD system using nonclinical features from echocardiographic images, the detection of MI and extent of infarcted myocardium can be performed by a person without much medical expertise.

Figure 2.7: Block diagram of a typical CAD system.

2.7.1 Methodology of CAD Development

a. Data Collection and Preprocessing

The required echocardiograms can be acquired in Digital Imaging and Communications in Medicine (DICOM) format from a portable ultrasound machine equipped with transducers or probes. Ultrasound probes can be categorized based on their frequency range, low frequency versus high frequency, and the shape of a probe (curved versus linear). Linear array probes are high-frequency probes. High-frequency probes have less tissue penetration, but have good near-field image resolution (**Armstrong, et al. 2005**). Curved array probes are low-frequency probes having greater tissue penetration, but the resolution is compromised (**Armstrong, et al. 2005**). Images obtained can be preprocessed using appropriate filters to improve the contrast of images.

b. ROI Selection (Segmentation)

Medical image segmentation can be used to delineate the anatomical structures and other ROI (**Pham, et al. 2000**). It has various applications in medical imaging such as detection of tissue volumes, study of anatomical structure, diagnosis, and localization of disease, computer-aided surgery, and planning of treatment. Image segmentation methods are categorized into thresholding (**Sahoo, et al. 1988**), region growing (**Haralick, et al. 1985**), clustering (**Coleman, et al. 1979**), (**Jain, et al. 1988**), Markov random field (MRF) models (**Simon, et al. 1998**; **Wang, et al. 2004**; **Hochbaum 2001**), artificial neural networks, deformable models (**Frangi, et al. 2001**), and atlas-guided approaches.

Binary partitioning of the image pixel intensities segments the images in the *Thresholding* approach. When different regions of the image have contrasting intensities, this method may be effective to segment the images (**Sahoo, et al. 1988**). K-means

algorithm (Coleman, et al. 1979) and the fuzzy c-means algorithm (Jain et al. 1988) are commonly used *clustering methods*. MRF (Hochbaum 2001) modeling is a statistical model which is used within segmentation methods to model intensity inhomogeneity's that can occur in textural properties. *Deformable models* (Frangi, et al. 2001) are methods which delineate region boundaries using curves or surfaces which deform due to internal or external forces and have been used to measure the dynamic behavior of LV.

Various methods have been used for deformation recovery based on shape properties (Frangi 1972). In the 2-D deformable contour model, initially LV boundary is segmented in every slice of the image volume. In the next instant, these contours are considered as initial approximation of the LV boundaries in corresponding slices of the image volume, and they are later deformed to obtain new set of LV boundaries (Singh, et al. 1993; Geiger, et al. 1995). The method proposed by Singh *et al.* (60) takes 15 min to segment an image, but the manual segmentation takes 1.5–2 h.

The LV motion was tracked and analyzed using bending energy and surface curvature using a surface model approach proposed by Amini, et al. 1992.

c. Feature Extraction

This is an important step in the development of a CAD system using echocardiographic images. Important nonclinical features may be extracted from echocardiography images using different methods and may be used as an input to the classifier for automated diagnosis.

Nonclinical Features: Texture Features

Textures describe regularity, smoothness, and coarseness of pixels in an image. They represent the neighboring pixel intensity relation (Mirmehdi, et al. 2008; Acharya, et al. 2013a; Acharya, et al. 2012c). There are two common approaches to textural analysis: structural analysis and statistical analysis. The structural approach is complex and

provides elaborate symbolic description of the image (**Mirmehdi, et al. 2008**). Various measures based on gray-level co-occurrence matrix are evaluated in the statistical approach. This approach is simpler and provides more information than the structural method (**Castellano, et al. 2004**). A brief description of different statistical and structural texture-based features extraction methods is given below.

1) Statistical Methods

First-order statistics: These measures are calculated from the gray-level intensities of the images which include average intensity of the ROI, variance, standard deviation, skewness, and kurtosis (**Kerut, et al. 2003**). Skewness describes the shift of the pixel distribution from a symmetrical shape. Skewness is positive (or negative) depending on the tilt of the distribution to the right (or left). The degree of steepness of pixel distribution is given by Kurtosis.

Gray-level co-occurrence matrix (GLCM): The one of the most powerful statistical method in the texture analysis is based on features extracted from the GLCM (**Haralick, et al. 1973**). It is a second-order statistical measure of image variation and gives the joint probability of occurrence of gray levels of two pixels separated spatially by a distance $d = (\Delta x, \Delta y)$. Important statistical features like contrast, entropy, energy, and homogeneity having good discriminating power can be obtained. Homogeneity measures the similarity between the two pixels that are $(\Delta x, \Delta y)$ apart in an image. Contrast indicates the amount of local variations between the pixels in an image, and energy denotes the uniformity of an image. Entropy defines the disorder of an image and it will have maximum value when all of the co-occurrence matrices are equal. These texture features are given as follows:

$$\text{Homogeneity : } Hom = \sum_i \sum_j \frac{p(i, j)}{1 + (i - j)^2} \quad 2.1$$

$$\text{Contrast : } Con = \sum_i \sum_j (i - j)^2 p(i, j) \quad 2.2$$

$$\text{Entropy : } Ent = - \sum_i \sum_j p(i, j) \ln p(i, j) \quad 2.3$$

$$\text{Energy : } E = \sum_i \sum_j (p(i, j))^2 \quad 2.4$$

where $p(i, j)$ is the probability of a pixel with a gray-level value i having a pixel with a gray-level value j at a $(\Delta x, \Delta y)$ distance away in an image.

Laws texture energy (LTE): Another approach to generate texture features is the use of local filters of appropriate sizes to discriminate between different kinds of texture (**Laws 1980**). It is a texture energy approach that measures the amount of variation within a fixed size window. The texture energy map E_k for filter k is given by

$$E_k[r, c] = \sum_{i=c-7}^{c+7} \sum_{j=r-7}^{r+7} |F_k[i, j]| \quad 2.5$$

Where $F_k[i, j]$ is the result of filtering with the k th mask at pixel $[i, j]$. The final energy map image is conceptually a single image with a vector of texture attributes at each pixel. These texture attributes can be used to cluster an image into regions of uniform texture.

2) Structural Methods

Local Binary Pattern (LBP): It is a simple, robust, and efficient texture descriptor (Ojala, et al. 1994; Ojala, et al. 1996; Ojala, et al. 2002). It is an excellent measure of both gray-scale (spatial pattern) and rotation (contrast) invariant image texture. LBP feature vector for gray-scale invariant measure is given by

$$LBP_{P,R}(x) = \begin{cases} \sum s(g_p - g_c) & \text{if } U(x) \leq 2 \\ p+1 & \text{otherwise} \end{cases} \quad 2.6$$

Where, $s(x) = \begin{cases} 1, & x \geq 0 \\ 0, & x < 0 \end{cases}$, LBP feature vector for rotation-invariant measure is given by

local variance,

$$VAR_{P,R} = \frac{1}{P} \sum_{p=0}^{P-1} (g_p - \mu)^2 \text{ where, } \mu = \frac{1}{P} \sum_{p=0}^{P-1} g_p \quad 2.7$$

where P is the number of points on the circumference of a circular neighborhood of radius R . The g_c is the intensity of center pixel and the $g_p, p = 0, 1, \dots, P-1$, the intensity of the P points.

Non-Clinical Features: Discrete wavelet transform (DWT) features

It uses filter banks composed of finite impulse response filters to decompose images into low-pass (approximation coefficients) and high-pass (detail coefficients) components (Mallat 1989; Acharya, et al. 2012a; Acharya, et al. 2012d). Using the high-pass and low-pass filters, the original image is decomposed into four subband images

LL , LH , HL , and HH . The LL coefficients show the similar details of original image, so called approximation and also represents the total energy in the images. The details coefficients HL , LH , and HH contain the vertical, horizontal, and diagonal details of the image, respectively. The LL subband image can be further decomposed in the same way for the second-level subband image. Elements of the individual subbands can be represented as matrices are combined to form a feature. These features are represented as $A2$, $H1$, $H2$, $V1$, $V2$, $D1$, $D2$, where $A2$, $H2$, $V2$, $D2$ are the approximation, horizontal, vertical, and diagonal coefficients obtained at the second-level decomposition, respectively (**Figures 2.8, 2.9**). Similarly, $H1$, $V1$, $D1$ are the coefficients obtained at the first-level decomposition (**Daubechies 1992**). The average amplitude or energy computed on these coefficients can be used as the feature for classification (**Acharya, et al. 2012a**).

Figure 2.8: The one level 2D DWT computation.

Figure 2.9: Illustration of two level 2D DWT sub-band computations.

d. Feature Selection/Feature Ranking

Feature ranking is a process of feature selection, which is used to select appropriate and compact feature subset from extracted features. Feature ranking can reduce the complexity of the classifier without affecting its performance. In order to obtain a quantitative measure of how separable are two classes, a distance measure is required. Feature ranking helps to rank the features according to their discriminating criteria. Feature ranking methods namely Kullback–Leiber divergence (KLD) (**Kullback, et al. 1951**), Kolmogorov–Smirnov test (K-S test) (**Press, et al. 1989**), minimal redundancy- maximal-relevance criterion (mRMR) (**Peng, et al. 2005**), and Bhattacharyya distance (**Fukunaga 1972**) are widely used. A number of measures like Bhattacharyya, Euclidean, KLD, and Fisher was studied for image discrimination (**Kailath 1967**) and was concluded that the Bhattacharyya distance method (**Fukunaga**

1972) is the most effective for classification using texture features. Peng, et al. 2005 proposed mRMR method for feature selection and showed promising improvement in the classification accuracy.

e. Classification

The evaluation of the selected features and assigning them to various classes are the most important part in computer-aided medical diagnosis. Classifiers help in this process of automated classification of features. The main goal is to select the best classifier to perform the automated classification. Tenfold cross validation technique (Duda, et al. 2012) is the most commonly used method to evaluate classifiers. In this technique, the whole set of data will be split into ten equal parts. Nine parts of the data will be used for training the classifier, and the trained classifier will be evaluated using the remaining one part (test). This process will be repeated ten times (folds) using different parts of training and testing dataset. In each fold, the performance (sensitivity, specificity, accuracy, and positive predictive value (PPV)) is evaluated. The average of the ten folds gives the actual performance of the CAD system.

Classifiers:

Various classifiers can be used for the automated diagnosis of normal and MI images. Most commonly used classifiers are: Gaussian mixture model (GMM), support vector machine (SVM), K-nearest neighbor (KNN), probabilistic neural network (PNN), decision tree (DT), AdaBoost, Naïve Bayes, Fuzzy Sugeno, and linear discriminant classifier. They are briefly explained below.

GMM:

It is a parametric model used to evaluate the continuous probability density function in statistical classification systems (**Duda, et al. 2001**). It uses the maximum likelihood (ML) parameter estimation criterion and its parameters are evaluated through training in such a way as to maximize the likelihood of the observations using expectation maximization algorithm (**Bilmes 1998**). It is one of the most statistically developed methods used for clustering and density estimation.

SVM:

It is a supervised learning method which has been used widely in pattern recognition. It constructs a hyperplane or set of hyperplanes in the higher dimension space, which can be used for classification (**Vapnik 1998**). The hyperplane that has the largest distance to the nearest training data point of any class is selected to achieve good separation and low the generalization error.

KNN:

It is very simple classifier which uses minimum distance from the test data to the training data to obtain the KNNs. Then, the majority of these KNNs are used to predict the unknown class (**Larose 2004a**).

PNN:

It is a feedforward neural network and makes use of a Bayesian strategy for classification (**Specht 1990**). The operations are organized into a multilayered feedforward network with four layers: input layer, hidden layer, summation layer, and output layer.

DT:

It generates a tree and rules for various classes. These rules obtained from the tree are used to classify the unknown test data (**Larose 2004b**).

Adaboost classifier:

This is a meta-classifier used for the purpose of improving the performance of weak classifiers (**Freund, et al. 1997**). This classifier uses machine-learning algorithm that feeds the input training set to a weak learner algorithm repeatedly.

Naives Bayes classifier:

This classifier is based on Bayes theorem and assumes that the presence of a particular feature of a class is unrelated or not dependent on the presence of any other feature. Generally, Naives Bayes model estimates parameters using the method of ML (**Han, et al. 2006**).

Fuzzy Sugeno classifier (FSC):

In FSC classification, fuzzy inference system (FIS) is generated using subtractive clustering. FIS contains a set of fuzzy rules based on which a feature space is generated during the training phase. To decide the class of test data, fuzzy inference calculations are performed (**Sugeno 1985**).

Linear discriminant classifier (LDC):

The linear classifier is often used in situations where the speed of classification is an issue, since it is often the fastest classifier. The idea of this classifier is to find a hyperplane in instance space that separates two classes (**Witten 2009**). If the linear sum exceeds zero, the first class is predicted; otherwise, the second is predicted. The data are said to be linearly separable, i.e., these can be separated perfectly using a hyperplane, if the weight vector is greater than zero (**Ganesan, et al. 2013**).

Several image processing and machine learning methods such as DWT, texture and HOS (**Acharya, et al. 2012a; Agani, et al. 2007**) and other techniques (**Giachetti, et al. 1995; Bosch, et al. 2005**) are used in semi-automated and automated CAD system to study the variations of medical (ultrasound/echocardiogram) images.

2.8 Computer-Aided Semi-Automated Technologies for Normal and Abnormal Myocardium Tissue Characterization.

Summary of research studies conducted using computer-aided interpretations of echocardiography image features in semi-automated detection of normal and infarcted myocardium are tabulated in **Table 2.4**. The statistical first order and second order techniques were used in classification of myocardial tissue to detect various abnormalities including myocardial contusion (**Amichi, et al. 2009**), amyloid infiltration (**Pinamonti, et al. 1989**), and myocarditis (**Ferdeghini, et al. 1991**). In 2009, **Amichi, et al.** observed that the texture parameters extracted from gray level histogram (first order statistics) in case of anterior, posterior, lateral and septal wall, were not able to discriminate between normal and contused myocardium. The numbers of discriminant parameters were limited and lacked the discriminating power.

In 1989, **Pinamonti, et al.** used qualitative and quantitative analysis of the myocardial wall and regional image texture in 2D echocardiography to identify amyloid heart disease. There was no significant difference in the mean gray level values and in any of the first order variables (skewness, kurtosis, energy, entropy) of the long axis view of septum. In 2001, **Bae, et al.** used statistical texture methods to classify perfused and non-perfused myocardium of dogs using contrast echocardiographic images obtained using fixed machine settings. Further investigations are required to validate the ability of the statistical features to identify abnormal from normal myocardium, in images with regional differences in gray level, and with altered machine settings. **Lieback, et al. 1996** used average brightness to classify myocarditis and normal myocardium. It was reported that the texture analysis of echocardiograms achieved the sensitivity of 100% in classifying myocarditis from normal myocardium. The capability of first and second order statistical analysis methods were limited by the

small region of interest (ROI) of tissue texture (**Amichi, et al. 2009; Pinamonti, et al. 1989**).

Table 2.4: Summary of studies conducted on echocardiography tissue characterisation.

Authors	Modality/Classification technique	Diagnosis (Disease targeted)	Results obtained in myocardial tissue classification or classifier performance
Studies based on texture features:			
Pinamonti, et al. (1989)	2D echocardiogram/ Statistical classification	Amyloid	Entropy: 6.3 ± 0.3 (amyloid) vs 5.9 ± 0.4 (normal)
Ferdeghini, et al. (1991)	2D echocardiograms/ Statistical classifier	Myocarditis	NA
Lieback, et al. (1994)	2D echocardiography/ Manual classification	Cardiac (myocardium) rejection	Sensitivity = 89% Specificity = 83.6%
Lieback, et al. (1996)	Echocardiography/ Manual classifier	Myocarditis	NA
Amichi, et al. (2009)	2D transesophageal echocardiography/ Statistical classification	Myocardial contusion	Contrast: 6.16 ± 2.66 (normal) vs 9.18 ± 6.15 (contusion).
Bae, et al. (2001)	Myocardial contrast echocardiogram/ Distance classifier	Nonperfused myocardium	Entropy 5.60 ± 0.10 (nonperfused) vs 5.57 ± 0.08 (perfused).

2.9 Computer-Aided Semi-Automated Technologies for Normal and Infarcted Myocardium Detection Using Echocardiographic Texture Characteristics

Using these 17 segments, the cardiologists compute the regional wall motion score, wall thickening or thinning and LV functions like LVEF, LV size or volume and LV geometry to detect the presence of infarct expansion and extent of infarcted myocardium (Moller, et al. 2006; Carluccio, et al. 2000; Lang, et al. 2015). Each segment is individually analyzed in multiple views and scored on the basis of its motion and thickening (Lang, et al. 2015). The WMS equal to 2 indicates hypokinetic (reduced thickening), WMS equal to 3 indicates akinetic (absent or negligible thickening, e.g. scar) and WMS equal to 4 represents dyskinetic (systolic thinning or stretching, e.g. aneurysm). WMSI is the mean WMS of all myocardial wall segments; and is an indicator of the extent of MI. Similarly, heart pump function, as expressed by LVEF may also reflect extent of MI involvement. LVEFs > 52% for men and < 54% for women indicates abnormal LV systolic function. LVEF ranging between 41% - 53% indicates mild abnormal, 30% to 40% denotes moderately abnormal, and for severely abnormal class LVEF will be less than 30% (Lang, et al. 2015).

It is very laborious and time-consuming for cardiologists to go through different views of echocardiogram images continuously to compute these WMSI and LVEF. But this 2D echocardiography is non-invasive imaging tool which provides a complete assessment of MI patients. In addition, 2D echocardiography assists clinicians to detect the amount of damage occurred (e.g. wall motion score, decline of LV function) and helps to test the efficacy of treatment (Colonna, et al. 2005). The precise visual interpretation of these parameters on 2D echocardiography images using various views requires experience and training. Furthermore, the visual interpretation is prone to

inter-observer variability (**Chetboul, et al. 2003**). The CAD system for the analysis of echocardiographic image sequence is promising in identifying clinical features, wall motion abnormalities and the LV area changes, occurring through the cardiac cycle (**Giachetti, et al. 1995**).

Numerous CAD techniques and systems have been proposed and developed for detection and classification of various lesions in chest radiographs (**Abe, et al. 2004**), CT (**Li, et al. 2005; Yoshida, et al. 2004**) and MRI (**Arimura, et al. 2006; Hirai, et al. 2005**) in addition to breast lesions in mammograms (**Freer, et al. 2001; Giger 2004**). The characterisation of myocardial tissue by ultrasound was attempted in (**Wild, et al. 1957**), using excised human heart to distinguish infarcted from normal myocardium. Summary of research studies conducted using computer-aided interpretations of echocardiography image features in automated detection of normal and infarcted myocardium are tabulated in **Table 2.5**. **Anil et al.** described the classification system based on textural patterns of echocardiograms as type I (uniform, low intensity, fine speckle: normal), type IIA (multiple, discrete, 3 to 5mm, bright echoes in all walls), type IIB (one or more, but not all, walls with type IIA pattern), and type IIC (uniform very bright echoes in one wall or region). The study reported that, their approach was useful, but lacked specificity.

Skorton et al. 1983 described the ability of a computer based image analysis to assess early textural changes to classify MI from normal. They detected normal and infarcted myocardium by analyzing regional echo amplitude data and extracting various statistical features from cross-sectional 2D echocardiography images of pre- and post-coronary occlusion. From seven 2D echocardiograms, total of three parameters (gray level distribution, kurtosis and skewness) were analyzed. Among them, the kurtosis feature (infarct regions compared to normal regions (0.27 ± 0.47 vs 2.5 ± 1.0)) showed the ability to identify the infarcted myocardium having early variations with

90% average sensitivity and 70% specificity using manual classification. In another study by **Kamath, et al. 1986**, 9 normal and 6 scarred regions of infarcted myocardium were characterized using echocardiography image pixels gray levels (features: pixel intensities) based on the reflection amplitude. Using the intensity values their study reported clear differentiation between MI and normal regions by identifying highly reflectile echo (HRE) zones which correlate with infarcted myocardium. Similar image statistical feature (mean pixel intensity – MPI) extracted from 17 cross-sectional echocardiograms were used to evaluate the wall motion abnormality by **Tak, et al. 1992** for the classification of normal and infarcted myocardium. The study identified significant variations (increment) of MPI in infarction region (24.3 ± 2.3 to 31.9 ± 3.7) compared to normal myocardium zone (20.4 ± 2.0 to 20.5 ± 1.7) using statistical classification method. The experiment also concluded that early identification of infarction using statistical method aids in application of interventional therapy which can improve the abnormal wall motion (from akinetic to hypokinetic) after 2 weeks of MI. In order to perform the image analysis in small ROI / dimensions, **Mojsilovic, et al. 1997** proposed a new wavelet based approach to calculate the features and differentiated MI from normal with average classification rate of 88.5%.

These studies used first order statistics to analyze the texture characteristics of an echocardiography image. However, these first order statistics do not capture the strong higher order correlations that exist across image pixels. In order to capture these higher-order inter-relationships and subtle changes occurring in an image pixel, **Neskovic, et al. 1998** used wavelet method. They analyzed the apical four and two chambers view echocardiography of 18 patients in early post infarction to detect the viability of myocardium. The study extracted energy features from wavelet coefficients and classified using unsupervised classification method. They reported a sensitivity, specificity and accuracy of (i) 73%, 86% and 78% at week 1, and (ii) 100%, 100%, and 100% at week 3, respectively with the proposed approach. **Ohmori, et al. 2001** extracted

second order statistical texture features of contrast-enhanced images to detect the inhomogeneous opacification pattern in infarcted segments of dogs. In 2005, **Perera, et al.** developed a CAD tool for quantification of intracoronary and intravenous echocardiography by using model-based shape analysis method. The CAD developed showed promising results for automated classification of echocardiograms based on wall motion abnormalities (**Bosch, et al. 2005**). In order to analyze LV regional wall motion quantitatively, a computer-aided boundary detection method was applied as an objective and useful model (**Tsai, et al. 1997**).

Later in 2007, **Agani, et al. 2007** assessed manually extracted ROIs of 17 normal and infarcted myocardium echocardiograms using wavelet and Gray-Level Co-occurrence Matrix (GLCM) methods (second order statistics) for developing an automated diagnostic system. The study extracted various features (energy, entropy, contrast and inverse difference moment) from the wavelet coefficients of the apical cross sectional view echocardiography images. The experiment results reported an accuracy of 91.32% in differentiating normal and infarcted ROI's using Mahalanobis distance classifier. These texture and DWT features showed ability to capture the subtle changes in the pixel intensities. The wavelet methods used are better compared to first-order statistics in studying texture characteristics and in identifying the subtle changes in the image. But, Higher Order Spectra (HOS), a nonlinear method with high signal to noise ratio (**Chua, et al. 2010**), is able to even capture interaction among its frequency components and phase coupling. However, the manual extraction of ROIs makes these algorithm non-automated or semi-automated diagnostic systems.

Table 2.5: Summary of studies conducted for MI detection using echocardiography image analysis techniques.

Authors	Features	Classifiers	No. of Subjects	Results/Performance measure
Skorton et al. (1983)	Gray level distribution, kurtosis, skewness	Manual classification	Animal study involved 7 adult dogs.	Sen = 90% Spe = 70%
Kamath et al. (1986)	Amplitude of the gray levels (Pixel intensity)	Statistical classification		NA
Tak et al. (1992)	Pixel intensity	Statistical classification	17 (5 N, 12 MI)	MPI on 1st day 20.4 ± 2.0 vs 24.3 ± 2.3 and 14th day 20.5 ± 1.7 vs 31.9 ± 3.7
Moldovanu et al. (2011)	First order statistical features (mean gray level, skewness, kurtosis, entropy)		12 (6 N 6 MI)	Entropy: 6.23 ± 0.52 vs 9.95 ± 0.17
Mojsilovic et al. (1997)	Wavelet energy features	Unsupervised classification	15	Highest classification rate: 96%
Neskovic et al. (1998)	Wavelet energy features	Unsupervised classification (Distance classifier)	18	On day 2: Sen 73%, Spe 86%, Acc 78%; On 1 week: Sen 91%, Spe 86%, Acc 89%; On 3 weeks: Sen 100%, Spe 100%, Acc 100%
Agani et al. (2007)	GLCM and DWT features	Mahalanobis distance classifier	17	Acc: 91.32%

Acc = Accuracy; Sen = Sensitivity; Spec = Specificity

2.10 Need of Computer-Aided Automated Technologies for Normal and Infarcted Myocardium Including Extent of Infarction Detection Using Echocardiographic Texture Analysis

Many researchers have worked on semi-automated and automated detection of abnormalities based on DWT, texture, HOS and other techniques to analyse the ultrasound images (Maxime, et al. 2007; Acharya, et al. 2011; Acharya, et al. 2012c, 2012a; Acharya, et al. 2013a). The use of this CAD system in echocardiography specifically for the automated detection of infarcted myocardium is a comparatively new field that has not been studied adequately. Hence, there is a need to explore the application of CAD based on image processing methods to extract the features from echocardiogram images for the automated detection of normal and infarcted myocardium. In the previous section (Section 2.9), I have comprehensively discussed various echocardiography image analysis methods used for the semi-automated identification of MI. There are the few studies (Table 2.5) conducted in echocardiography using texture features and wavelet features to classify MI and normal myocardium (Agani, et al. 2007; Neskovic, et al. 1998; Moldovanu, et al. 2011). These semi-automated classification accuracies can be further increased using combination of other texture descriptors such as HOS, Stationary Wavelet Transform (SWT) etc. (Chua, et al. 2010; Acharya, et al. 2014b) and combined with robust classifiers, the CAD system can be made fully automated for the detection of normal and infarcted myocardium.

Most of the studies that presented semi-automated diagnostic systems eliminated the need for the visual interpretations and manual selection of ROIs by echo technician or cardiologist thereby providing more reliable and objective interpretations. These studies differ in input data format, features extraction, echocardiography modalities and the classification methods used. The objective of these studies is to determine the best combination of imaging modality, features and

the classification methods that presents highest classification accuracy in detecting MI from normal myocardium.

Despite numerous research works in the CAD system using clinical features (Giordano, et al. 1992; Maxime, et al. 2007; Acharya, et al. 2012d) and non-clinical features (Table 2.3 – 2.5) for visual (manual) and semi-automated detection of cardiac abnormalities and MI, development of CAD system specifically for the automated detection of MI and extent of infarction using echocardiography non-clinical features is a comparatively new field that has not been studied adequately. There is a need to develop a CAD system for diagnosis of MI. In addition to the automated non-invasive CAD system for normal and MI classification, there is need to predict the extent of muscle damage caused by infarction and guide in early treatment.

Several echocardiographic methods and technologies have been developed to aid in the evaluation of MI, infarct size (Bauer, et al. 2011; Peng, et al. 2009), wall shear stress values which are used to evaluate wall motion and indirectly assess infarct size (Yuan, et al. 2011). 3D echocardiography has been used to assess LV wall motion abnormalities in a mouse model of MI (Streiff, et al. 2015). Although studies have used available echocardiographic techniques to evaluate infarct size, most of these methods have relied on visual analysis, leading to errors caused by operator subjectivity.

To make these diagnoses of infarcted myocardium faster and accurate, computer-aided techniques have been proposed and developed by many researchers using echocardiography (Table 2.5). CAD system has been proposed to detect the myocardial infarct size and measure the myocardial perfusion using Myocardial Contrast Echocardiography (MCE) (Du, et al. 2015). However, it involves intravenous administration of contrast agent, which can be expensive and is contraindicated in some patients. Many other approaches using echocardiography have been proposed to segment the ventricular cavity (Nandagopalan, et al. 2013; Sigit, et al. 2011), and epicardial boundary (Alessandrini, et al. 2013; Seng, et al.

2011). These methods do not evaluate and assess the extent of infarcted myocardium, though they are useful.

Thus, study of literature reveal that there are only few automated algorithms proposed for detection of infarcted myocardium using 2D echocardiography images. To best of my knowledge, till date, no studies have been reported on automated detection of extent of infarcted myocardium using only 2D echocardiographic images. The purpose of echocardiographic based automated CAD extent of infarction detection system is to achieve a performance comparable to that of current gold standard (expert echocardiographers' interpretation or contrast MRI). To achieve an equivalent or better accuracies using echocardiography images, the key issue is the proper choice of non-clinical features which should be extracted from the echo images without the need of obtaining visual clinical features and manual calculations.

2.11 Summary

After a thorough survey on existing literature on semi-automated and automated detection of MI, the following observations are made:

1. Early expansion of infarcted zone (infarct expansion) after MI has serious short and long-term consequences and contributes for increased mortality. Thus an early identification of acute and severe phases of MI before leading to other catastrophic post-MI medical condition (Heart failure) is most important for aggressive treatment and management.
2. A 2D echocardiography is an efficient non-invasive diagnostic tool in characterizing MI and its various stages of expansion leading to heart failure. Advanced image processing techniques together with robust classifier using echocardiogram images have been used for an automated classification of the extent of infarcted myocardium.

3. It is evident from literature review that, there is no study conducted till date on automated detection of infarcted myocardium stages using 2D echocardiograms. In spite of the extensive literature on MI detection, robust extraction of texture characteristics from echocardiograms of different stages of MI patients is a challenging problem.
4. It is understood that the CAD system based on image processing methods are suitable for my research project because
 - a. In the studies cited in **Table 2.5** MI is diagnosed based on the manually cropped region. Hence, completely automatic without segmentation is the main aim of this research work.
 - b. They are still identifying the MI and normal classes. Hence, my method of identifying the MI and extent of muscle damage automatically will add a value to the echocardiography detection modality.
 - c. They are not yet established a diagnostic system and hence there is room for further enhancement.
5. There is need of an automated CAD system that may aid the clinicians in faster identification of extent of infarcted myocardium using 2D echocardiogram. In addition, it may also aid in identifying the person at risk of developing (having high risk of) heart failure based on the extent of infarcted myocardium.
6. Also there is a need to develop an integrated index for detection of MI and the extent of MI risk using 2D echocardiographic texture characteristics. This proposed index may aid the clinicians in faster characterization of myocardium based on the extent of infarction using a single number.
7. The proposed system should avoid the need for other invasive, radio-hazards and expensive imaging modalities (e.g. MRI, SPECT) in order to identify the extent of muscle damage. The proposed system should be subsequently able to help in identifying the patient at risk of developing heart failure. The proposed diagnostic system may be used as an adjunct tool by the

cardiologists to cross check their diagnosis. Such a system can be employed in the polyclinics and hospitals in the third world countries where there is shortage of cardiologists to diagnose the cardiac health.

In the next chapter, the performances of CAD developed using three texture analysis methods namely DWT, GLCM, and HOS for MI detection in echocardiography images are compared.

CHAPTER 3. COMPUTER-AIDED DIAGNOSIS OF MYOCARDIAL INFARCTION USING ULTRASOUND IMAGES WITH DWT, GLCM AND HOS METHODS: A COMPARATIVE STUDY

3.1 Introduction

It is evident from the literature survey (**Chapter 2**) that MI or AMI is one of the leading causes of death worldwide. Thus, (i) identification of myocardial viability and detection of myocardial damage immediately after MI; and (ii) detection of infarct expansion and the extent of decline in LV function are early requirements for optimal treatment and management. MI diagnosis using 2D echocardiography is prone to inter/intra observer variability in the assessment. Therefore, a computerised scheme based on image processing and artificial intelligent techniques can reduce the workload of clinicians and improve the diagnosis accuracy. A Computer-Aided Diagnosis (CAD) of infarcted and normal ultrasound images will be useful for clinicians. Over the years, investigators have developed various types of CAD systems for identification of lesions and distinctive diagnosis of detected lesions based on classification between malignant and benign lesions (**Horsch, et al. 2006; Dean, et al. 2006**). Among them, few CAD systems for identification of lesions like breast lesions on mammograms are successfully applied in clinical situations (**Karssemeijer, et al. 2006; Ganesan, et al. 2014**). In my previous literature review chapter (**Chapter 2**), I have comprehensively discussed the various echocardiography image analysis methods used for the automated identification of MIs. It is evident that, to date, no significant efforts have been made to employ CAD approaches for diagnosis of normal and infarcted myocardium or extent of infarction (normal, moderate or severely infarcted myocardium) using echocardiography

images. The application of CAD concept in echocardiography for the detection of MI and extent of infarction is a new field that has not been studied adequately and is still in its infancy for potential full application. Hence, there is a need to explore the application of CAD scheme on echocardiogram images for the detection of MI and extent of infarction (MI stages).

I have reviewed a few of the semi-automated CAD systems developed using first-order statistics, such as intensity, skewness, kurtosis and entropy which are computed from pixels and then used to classify normal and MI subjects (Tak, et al. 1992; Moldovanu, et al. 2011; Kamath, et al. 1986). Only a few used the features extracted from the sub bands of DWT for the diagnosis of MI using ultrasound images (Mojsilovic, et al. 1997; Neskovic, et al. 1998). It was found that these features extracted using first or second-order statistics and Discrete Wavelet Transform (DWT) texture descriptors are able to identify the minute changes of patterns in the echocardiography images. Even the Higher-Order Spectra (HOS), a nonlinear method (Chua, et al. 2010) can also capture interaction among its frequency components and phase coupling. Hence, in this proposed chapter the performances of CAD approach using DWT, second order statistics calculated from Gray- Level Co-Occurrence Matrix (GLCM) and HOS texture descriptors are compared.

3.2 Performance Comparison of Different Techniques for Detection of Normal and Infarcted Myocardium

In the proposed chapter work, performances of CAD of MI using echocardiography images with DWT, GLCM and HOS methods are evaluated. These three texture descriptors are used to extract important echocardiography image features for developing an automatic detection of normal and infarcted myocardium – two class classifications. The proposed system is shown in **Figure 3.1**. In this

system, normal and MI echocardiography images are subjected to pre-processing using adaptive histogram equalisation. Following steps are carried out on the pre-processed echocardiography images:

- (a) Features are extracted,
 - (i) using DWT coefficients
 - (ii) based on second-order statistics computed from GLCM and
 - (iii) from bispectrum coefficients of HOS
- (b) These three set of extracted features are ranked separately using t-value.
- (c) The highly ranked features from each method are fed to the classifier support vector machine (SVM) one by one separately, to get the highest classification accuracy using minimum number of features.

Figure 3.1: Block diagram of the proposed three methods for MI detection.

3.2.1 Data Acquisition

The echocardiogram image data required for the research study were collected from National Heart Centre, Singapore using ultrasound scanner (ProSound α 10, ALOKA Hitachi, Japan). For this work, a total of 160 subjects (80 MI and 80 normal) were enrolled. Echocardiography video sequences captured in the parasternal short axis mid-left ventricular view were analysed. The age of the subjects (both male and female) ranged from 21 to 75 years. Among MI subjects, the echocardiography data used were from the subjects' images acquired soon after onset of MI.

Typical temporal frame resolutions were 30 frames/seconds. From each echocardiography video sequence of approximately the same duration, the non-consecutive frames from each patient (having 20 frames) were obtained (i.e. 5 equally spaced frames from each sequence of 20 frames) automatically using algorithm. These 5 frames chosen shall include both end diastolic and end systolic phases (i.e. one cardiac cycle). A total of 800 echocardiography image frames were thus available for analysis (400 non-MI and 400 MI images). All the images were cropped automatically to a resolution of 400 X 500 pixels by retaining only the heart region pixels and stored in JPEG format. For this study, approval has been obtained from the Hospital Institutional Review Board (IRB). I have obtained approval for waiver of consent from IRB as this is a retrospective study which does not involve any intervention. **Figure 3.2** shows the type of data obtained for further analysis.

Figure 3.2: Typical echocardiography image in the parasternal short axis view at the mid-left ventricular at diastole (left) and systole (right) in (a) normal patient; and (b) MI patient. The arrows indicate the thinning of myocardium (area/location of infarction).

3.2.2 Pre-processing

The pre-processing step involves enhancement of image contrast to help in the process of feature extraction. In this work, the red-green-blue (RGB) colour echocardiography heart images are changed into grayscale images. Then the grayscale images contrast is improved by using adaptive histogram equalisation (Gonzalez, et al. 2002). By performing adaptive histogram equalisation, the dynamic range of image histogram gets increased and input image pixels intensity values are assigned in such a way that the output image comprises a uniform intensity distribution.

3.2.3 Feature Extraction

The feature extraction from textural image is one of the important steps in an automated CAD system. The image features can be extracted using texture analysis (Mirmehdi, et al. 2008; Srinivasan, et al. 2008) and other methods. In the present chapter, three texture descriptors (DWT, GLCM and HOS) are used to analyze the echocardiography image features. Brief descriptions of those methods are explained in the following sections.

Discrete wavelet transform (DWT): Wavelets are mathematical functions which first divide the data into components of multiple frequencies, and then perform the study on each component with a resolution of its scale (Amara 1995). Wavelet transform (WT) decomposes a signal into basis functions which are known as wavelets. The WT is calculated separately for different frequencies resulting in multi-resolution analysis. The DWT gives a multi-resolution description of a signal, which is very useful in analysing the signals (Ratnakar, et al. 2009). It decomposes a signal into a ranking of scales which ranges from the roughest scale to the finest one. Hence, this method provides portray of an image at different resolutions, and are useful tools for image feature extraction.

The DWT decomposes 2D image at level i into approximation coefficients (cA_i) and detail coefficients in three orientations (horizontal cH_i , vertical cV_i and diagonal cD_i). The approximation coefficients can be further decomposed in the same way for the second-level. In this chapter, I have performed the image decomposition up to second level and extracted Energy (cA_i_E , cD_i_E , cV_i_E and cH_i_E) and Kapur's entropy (cA_i_Ent , cD_i_Ent , cV_i_Ent and cH_i_Ent) features. **Figure 3.3** shows the decomposition of normal and MI echocardiograms using biorthogonal 3.7 wavelet.

Figure 3.3: Two level decomposition of echocardiograms (a) normal, and (b) MI.

Brief descriptions of these features are explained in the following sections.

Energy parameter is calculated as,

$$E = \sum_i \sum_j p(i, j)^2 \quad 3.1$$

where $p(i, j)$ is the probability of occurrence of gray levels (i, j) and is a normalised histogram designated for a specific region of interest.

Kapur's entropy (Pharwaha, et al. 2009; Gupta, et al. 2010) Consider $f(x, y)$ is the normal or MI image, having N_i ($i = 0, 1, 2, 3, \dots, L-1$) distinct gray levels.

The generalised entropy of Kapur of order α and type β is given as,

$$Ent^K(p) = \frac{1}{\beta - \alpha} \log_2 \left(\frac{\sum_{i=1}^N p_i^\alpha}{\sum_{i=1}^N p_i^\beta} \right) \quad \alpha \neq \beta, \quad \alpha, \beta > 0 \quad 3.2$$

where p_i is the probability of occurrence of gray level i , is a normalised histogram designated for a specific region of interest of size $(M \times N)$ is

$$p_i = \frac{N_i}{M \times N} \quad 3.3$$

Gray-level co-occurrence matrix (GLCM): GLCM (Haralick 1973), one of the texture descriptors, is used to compute the second-order statistical features from normal and MI images. Consider an image I having the size of $M \times N$ with N_g number of distinct gray levels. The variations of texture are calculated by using gray tone spatial dependence matrix $p(i, j)$, where the pixels are separated with a distance d at i^{th} and j^{th} gray level. In this present chapter, four angles (0° , 45° , 90° and 135°) are considered with pixels distance of 1. The second-order statistical features (energy (E), contrast (Con), correlation (Cor), homogeneity (Hom), entropy (Ent), autocorrelation ($AutCor$), dissimilarity (Dis), cluster shade ($Shade$), max probability ($MaxProb$), difference variance ($DVar$), difference entropy ($DEnt$), sum average ($SAver$), sum entropy ($SEnt$), sum variance ($SVar$), information correlation measure 1 ($InfM1$), and information correlation measure 2 ($InfM2$)) are calculated using the GLCM (Acharya, et al. 2014a).

Homogeneity measures the similarity between the two pixels that are $(\Delta x, \Delta y)$ apart in an image. Contrast indicates the amount of local variations between the pixels in an image and energy denotes the uniformity of an image. Entropy defines the disorder of an image and it will have maximum value when all of the co-occurrence matrices are equal. These texture features are given below in **Table 3.1**.

Table 3.1: Descriptions of GLCM texture features

Features	Description
Energy	$E = \sum_i \sum_j p(i, j)^2$
Contrast	$Con = \sum_{n=0}^{N_g-1} n^2 \left\{ \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} p(i, j), i - j = n \right\}$
Correlation	$Cor = \frac{\sum_i \sum_j (i, j) p(i, j) - \mu_x \mu_y}{\sigma_x \sigma_y}$
where μ_x, μ_y, σ_x , and σ_y are the means and standard deviations of p_x and p_y	
Homogeneity	$Hom = \sum_i \sum_j \frac{1}{1 + (i - j)^2} p(i, j)$
Entropy	$Ent = - \sum_i \sum_j p(i, j) \log(p(i, j))$
Autocorrelation	$AutCor = \sum_i \sum_j (i, j) p(i, j)$
Dissimilarity	$Dis = \sum_i \sum_j i - j p(i, j)$
Cluster Shade	$Shade = \sum_i \sum_j \{i + j - \mu_x - \mu_y\}^3 \times p(i, j)$
Max Probability	$Max Pr ob = \sum_i \sum_j \max(p(i, j))$
Sum Average	$SAver = \sum_{i=2}^{2N_g} i p_{x+y}(i)$
Sum Entropy	$SEnt = - \sum_{i=2}^{2N_g} p_{x+y}(i) \log(p_{x+y}(i))$
Sum Variance	$SVar = \sum_{i=2}^{2N_g} (i - SEnt)^2 p_{x+y}(i)$
Difference Variance	$DVar = \sum_{i=0}^{N_g-1} (i - \mu_{x-y})^2 p_{x-y}(i)$
Difference Entropy	$DEnt = - \sum_{i=0}^{N_g-1} p_{x-y}(i) \log\{p_{x-y}(i)\}$

Information Correlation Measure 1

$$InfM1 = \frac{Ent - HXY1}{\max\{HX, HY\}}$$

Information Correlation Measure 2

$$InfM2 = (1 - \exp[-2.0(HXY2 - Ent)])^{\frac{1}{2}}$$

where HX and HY are entropies of p_x and

$$HXY1 = - \sum_i \sum_j p(i, j) \log \{p_x(i) p_y(j)\}$$

p_y and

$$HXY2 = - \sum_i \sum_j p_x(i) p_y(j) \log \{p_x(i) p_y(j)\}$$

Higher Order Spectra (HOS): The HOS method is one of the powerful techniques used for the analysis of non-linear properties of the images (**Acharya, et al. 2008; Nikias, et al. 1993**). HOS is the spectral portrayal of higher order statistics such as third and higher order moments and cumulants. It is a novel method for evaluating non-Gaussian and non-stationary signals. It identifies diversions from Gaussianity and phase correlations among frequency components of the signal (**Chua, et al., 2010**). It is more immune to noise and can retain the actual phase information of the signal.

Radon transformation (RT) is first performed to transform the 2D image into one dimensional signal, before extracting the important features by using the HOS method (**Acharya, et al. 2013c**). In this proposed work, RT is performed for every 10° rotation of whole images.

The Third-order statistics of the image bispectrum is used in this chapter work. The bispectrum displays symmetry and is evaluated in the principal domain region Ω as shown in **Figure 3.4**. (**Chandran, et al. 1993; Chandran, et al. 1991; Chandran, et al. 1992**).

Figure 3.4: Non-redundant region (Ω) and HOS features are evaluated in this region.

The bispectrum phase entropy (BS_PhEnt) is defined as,

$$BS_PhEnt = \sum_n p(\Psi_n) \log p(\Psi_n) \quad 3.4$$

where

$$p(\Psi_n) = \frac{1}{L} \sum_{\Omega} I(\Phi(B(f_1, f_2)) \in \Psi_n)$$

$$\Psi_n = \left\{ \Phi \mid -\pi + 2\pi n / N \leq \Phi < -\pi + 2\pi (n+1) / N \right\}$$

$$n = 0, 1, \dots, N-1$$

where L = the number of points within Ω region, B = Bispectrum,

Φ = the bispectrum phase angle, f_1, f_2 = frequencies and

$I(.)$ = an indicator function. When the phase angle is within the range depicted by Ψ_n in above equation, $I(.) = 1$.

The bispectral entropies – normalised bispectral entropy (*BS_Ent1*) and normalized bispectral squared entropy (*BS_Ent2*) (Chua, et al. 2006; Chua, et al. 2009) are also computed in this algorithm. **Figures 3.5** and **3.6** show the mesh and contour plots of Bispectrum magnitude for normal and MI classes. These plots are unique for each class.

$$BS_Ent1 = \sum_n \alpha_n \log \alpha_n \quad 3.5$$

$$\text{Where } \alpha_n = \frac{|B(f_1, f_2)|}{\sum_{\Omega} |B(f_1, f_2)|}$$

$$BS_Ent2 = - \sum_n \beta_n \log \beta_n \quad 3.6$$

$$\text{Where } \beta_n = \frac{|B(f_1, f_2)|^2}{\sum_{\Omega} |B(f_1, f_2)|^2}$$

(a)

(b)

Figure 3.5: Typical single projection (10^0) HOS Bispectrum magnitude plots of (a) normal and (b) MI.

It is evident from **Figure 3.5** that, more peaks can be observed in bispectrum plot between 0 and 0.5 radians/s in the normal image as compared to MI image. This is because of the inactive myocardium present in MI subjects due to insufficient blood flow in that region as compared to normal myocardium. In addition, peaks are concentrated in the centre of plot in MI subject, where as in normal subjects, the peaks are available all over the plot and scatter entire the frequency spectrum exhibiting the active normal myocardium.

Figure 3.6: Typical single projection (10^0) HOS Bispectrum magnitude contour plots of normal (top) and MI (bottom)

It can be seen from the **Figure 3.6** that, more peaks can be observed in normal myocardium and they are spread throughout the spectrum as compared to the infarcted myocardium. This is due to the active pixels in normal subjects compared to inactive pixels in infarcted myocardium subjects (insufficient blood supply).

3.2.4 Statistical Analysis-Feature ranking

Feature ranking helps to rank the significant features according to their discriminating criteria (**Fukunaga 1972**). In this current chapter, the significant features are ranked using t-values (**Box 1987**) and are fed to the classifier for classification.

3.2.5 Support Vector Machine Classifier

In this current chapter, the support vector machine (SVM) classifier is used for automated classification. SVM classifier is a supervised learning method, which performs the classification by constructing a separating hyper-plane in an n-dimensional space where n is the number of input features. The hyper-plane constructed separates input data classes. Using nonlinear kernel function, such as polynomial function of order 1 (linear), order 2, and order 3, and Radial basis function (RBF), the input data is transformed to a high-dimensional feature space so that the transformed data becomes more separable than the original input data (**Edgar, et al. 1997**).

The Ten-fold cross validation technique is used to evaluate the classifier performance. The original features' dataset is divided into ten equal sets. The first nine sets are used for training the classifier, and the tenth set is used for testing the classifier. This process is repeated ten times using different sets of test data. The average of ten-folds is used to evaluate the performance (accuracy, sensitivity, specificity and positive predictive value (PPV)) of the classifier.

3.3 Results

In this current proposed algorithm (chapter 3), DWT, GLCM and HOS are used to extract features from echocardiography images to identify the differentiation between normal and MI cases. My experiment findings are discussed in the following sections.

3.3.1 Results of DWT, GLCM and HOS Methods

Tables 3.2, 3.3 and 3.4 show the statistical analysis results of various features obtained from DWT coefficients, GLCM (second-order statistics) and HOS using echocardiography images. **Figures 3.7 - 3.9** show the plot of features from three texture descriptors for normal and MI classes. All 16 features extracted from DWT coefficients exhibits clear distinction between normal and MI echocardiography images (**Table 3.2, Figure 3.7**). This method identifies the subtle changes occurring in image pixels in vertical, diagonal and horizontal directions. Similarly, all 16 second-order statistical parameters obtained in **Table 3.3** using GLCM also presents distinct differentiation between normal and MI classes (**Figure 3.8**). Using HOS total of 108 features are extracted from echocardiography images. The first 37 features out of 108 shown in **Table 3.4** and **Figure 3.9** demonstrate the differentiation between two groups of images.

Table 3.2: Results (mean $\pm$ SD) features extracted from DWT coefficients for normal and MI images ($p < 0.05$).

Features	Normal		MI		<i>t</i> -value
	Mean	SD	Mean	SD	
<i>cH1_Ent</i>	5.997	0.293	6.330	0.183	19.256
<i>cV2_Ent</i>	6.121	0.254	6.334	0.230	12.451
<i>cH2_Ent</i>	6.841	0.248	6.988	0.211	9.013
<i>cV1_Ent</i>	5.727	0.254	5.847	0.179	7.713
<i>cA2_Ent</i>	7.555	0.140	7.627	0.177	6.382
<i>cH1_E</i>	13389.550	1862.580	12572.590	2111.570	5.802
<i>cA2_E</i>	1537.890	364.990	1703.170	446.470	5.732
<i>cD1_Ent</i>	5.566	0.381	5.693	0.260	5.487
<i>cD1_E</i>	12305.360	3535.610	13593.250	3512.280	5.168
<i>cD2_E</i>	3767.000	783.620	3534.140	574.340	4.793
<i>cV2_E</i>	3625.460	1094.590	3852.200	377.930	3.916
<i>cD2_Ent</i>	6.245	0.266	6.312	0.262	3.577
<i>cV1_E</i>	14175.530	2094.850	13736.730	1736.650	3.225
<i>cA1_Ent</i>	7.531	0.167	7.556	0.103	2.521
<i>cH2_E</i>	3966.320	512.890	3912.260	563.900	1.418
<i>cA1_E</i>	5743.690	1653.620	5877.060	1333.430	1.255

Figure 3.7: Plot of features from DWT coefficients for normal and MI classes.

Table 3.3: Results (mean $\pm$ SD) of features computed using GLCM for normal and MI images ($p < 0.0001$).

Features	Normal		MI		<i>t</i> -value
	Mean	SD	Mean	SD	
<i>DEnt</i>	0.480	0.104	0.528	0.094	6.729
<i>InfM1</i>	0.621	0.038	0.603	0.036	6.508
<i>Dis</i>	0.175	0.056	0.200	0.055	6.300
<i>Con</i>	0.274	0.093	0.315	0.090	6.234
<i>DVar</i>	0.274	0.093	0.315	0.090	6.234
<i>Hom</i>	0.924	0.023	0.913	0.023	6.138
<i>Ent</i>	1.507	0.361	1.614	0.325	4.397
<i>SVar</i>	18.814	5.233	20.384	5.547	4.116
<i>SEnt</i>	1.332	0.310	1.414	0.276	3.957
<i>AutCor</i>	6.841	2.116	7.449	2.261	3.927
<i>SAver</i>	3.866	0.646	4.045	0.664	3.853
<i>E</i>	0.513	0.121	0.483	0.106	3.790
<i>MaxProb</i>	0.707	0.089	0.685	0.085	3.475
<i>Shade</i>	79.584	15.951	82.844	11.521	3.312
<i>Cor</i>	0.955	0.011	0.953	0.009	2.748
<i>InfM2</i>	0.851	0.053	0.860	0.038	2.654

Figure 3.8: Plot of features computed using GLCM for normal and MI classes.

Table 3.4: Results (mean $\pm$ SD) of features extracted using HOS for normal and MI images.
($p < 0.0001$).

Features	Normal		MI		<i>t</i> -value
	Mean	SD	Mean	SD	
<i>BS_PhEnt_230</i>	0.524	0.263	0.632	0.240	6.093
<i>BS_PhEnt_260</i>	0.610	0.227	0.526	0.215	5.331
<i>BS_Ent1_320</i>	0.501	0.185	0.432	0.191	5.177
<i>BS_PhEnt_50</i>	0.540	0.274	0.633	0.237	5.140
<i>BS_Ent2_320</i>	0.292	0.199	0.228	0.192	4.617
<i>BS_PhEnt_90</i>	0.595	0.258	0.674	0.235	4.544
<i>BS_PhEnt_200</i>	0.504	0.260	0.426	0.238	4.410
<i>BS_Ent1_20</i>	0.487	0.198	0.551	0.210	4.385
<i>BS_PhEnt_20</i>	0.486	0.266	0.408	0.243	4.360
<i>BS_Ent1_140</i>	0.534	0.167	0.480	0.183	4.352
<i>BS_Ent2_20</i>	0.218	0.151	0.266	0.186	4.051
<i>BS_Ent1_10</i>	0.468	0.181	0.515	0.175	3.733
<i>BS_Ent1_190</i>	0.503	0.212	0.552	0.178	3.581
<i>BS_Ent2_40</i>	0.244	0.172	0.293	0.217	3.552
<i>BS_Ent2_220</i>	0.231	0.156	0.277	0.208	3.548
<i>BS_Ent1_280</i>	0.454	0.202	0.502	0.189	3.415
<i>BS_PhEnt_80</i>	0.538	0.254	0.478	0.250	3.334
<i>BS_Ent1_100</i>	0.472	0.218	0.520	0.191	3.298
<i>BS_Ent2_80</i>	0.274	0.201	0.323	0.242	3.113
<i>BS_Ent2_140</i>	0.317	0.202	0.273	0.199	3.108
<i>BS_Ent2_90</i>	0.200	0.170	0.237	0.169	3.091
<i>BS_PhEnt_120</i>	0.580	0.254	0.527	0.243	3.020
<i>BS_PhEnt_70</i>	0.566	0.254	0.518	0.241	2.720
<i>BS_Ent2_170</i>	0.306	0.223	0.267	0.207	2.536
<i>BS_Ent1_110</i>	0.539	0.196	0.571	0.188	2.355
<i>BS_Ent2_100</i>	0.265	0.217	0.303	0.238	2.341
<i>BS_PhEnt_40</i>	0.596	0.246	0.636	0.236	2.339

<i>BS_Ent2_240</i>	0.260	0.170	0.290	0.204	2.286
<i>BS_Ent2_350</i>	0.279	0.208	0.246	0.192	2.265
<i>BS_PhEnt_220</i>	0.591	0.270	0.631	0.237	2.224
<i>BS_Ent1_200</i>	0.476	0.211	0.508	0.198	2.211
<i>BS_Ent1_80</i>	0.493	0.196	0.523	0.198	2.183
<i>BS_PhEnt_10</i>	0.510	0.262	0.473	0.228	2.124
<i>BS_Ent1_310</i>	0.471	0.189	0.443	0.196	2.062
<i>BS_PhEnt_250</i>	0.590	0.248	0.554	0.244	2.051
<i>BS_PhEnt_270</i>	0.613	0.235	0.644	0.196	1.998
<i>BS_Ent2_270</i>	0.245	0.190	0.273	0.204	1.945

Figure 3.9: Plot of features extracted using HOS for normal and MI classes.

It can be seen from the result **Tables 3.2 – 3.4** and **Figures 3.7 – 3.9** that, entropy values are high for normal class compared to MI due to more variations in the pixels in normal echocardiography images. Pixels in images of MI class exhibit less variation. The reason for this is not clear; or could possibly be due to insufficient blood flow to the myocardium. Thus, these MI patients exhibit low WMSI and LVEF in echocardiogram images as compared to normal subject's images. Each set of parameters extracted using three texture descriptors are ranked using t-values. All features of **Tables 3.2, 3.3**, and **Table 3.4** are subjected to classification using SVM classifier.

3.3.2 Classification Results

Tables 3.5, 3.6 and **3.7** show the results of classification using DWT, GLCM and HOS methods respectively. **Table 3.5** shows that the SVM classifier with RBF kernel achieved an accuracy of 99.50%, sensitivity of 99.75% and specificity of 99.25% using 16 features obtained from DWT coefficients. **Table 3.6** shows that the SVM classifier with polynomial of order 3 kernel yielded 85.75% accuracy, 90.25% sensitivity and 81.25% specificity using 16 features computed from GLCM. **Table 3.7** shows that, the SVM classifier with RBF kernel achieved 93.0% accuracy, 94.75% sensitivity and 91.25% specificity using 23 features obtained from HOS. **Figure 3.10** shows the plot of accuracy versus the number of features used for three methods.

Table 3.5: Results of classification of features extracted from DWT coefficients.

Classifier (SVM)	Features	TP	TN	FP	FN	Sen (%)	Spec (%)	Acc (%)
poly_1.00	13	331	339	61	69	82.75	84.75	83.75
poly_2.00	16	393	388	12	7	98.25	97.00	97.63
poly_3.00	11	391	374	26	9	97.75	93.50	95.63
rbf_0.50	7	391	355	45	9	97.75	88.75	93.25
rbf_0.60	7	390	371	29	10	97.50	92.75	95.13
rbf_0.70	8	393	378	22	7	98.25	94.50	96.38
rbf_0.80	11	400	385	15	0	100.00	96.25	98.13
rbf_0.90	12	400	393	7	0	100.00	98.25	99.13
rbf_1.00	13	400	391	9	0	100.00	97.75	98.88
rbf_1.10	14	399	396	4	1	99.75	99.00	99.38
rbf_1.20	16	399	397	3	1	99.75	99.25	99.50
rbf_1.30	16	399	397	3	1	99.75	99.25	99.50
rbf_1.40	16	398	397	3	2	99.50	99.25	99.38
rbf_1.50	16	398	397	3	2	99.50	99.25	99.38

TP = true positive; TN = true negative; FP = false positive; FN = false negative; Sen = sensitivity; Spec = specificity; Acc = accuracy

Table 3.6: Results of classification of features extracted using GLCM.

Classifier (SVM)	Features	TP	TN	FP	FN	Sen (%)	Spec (%)	Acc (%)
poly_1.00	16	294	224	176	106	73.50	56.00	64.75
poly_2.00	16	331	306	94	69	82.75	76.50	79.63
poly_3.00	16	361	325	75	39	90.25	81.25	85.75
rbf_0.80	16	326	300	100	74	81.50	75.00	78.25
rbf_0.90	16	323	296	104	77	80.75	74.00	77.38
rbf_1.00	15	331	291	109	69	82.75	72.75	77.75
rbf_1.10	16	333	292	108	67	83.25	73.00	78.13
rbf_1.20	15	335	289	111	65	83.75	72.25	78.00

Table 3.7: Results of classification of features extracted using HOS.

Classifier (SVM)	features	TP	TN	FP	FN	Sen (%)	Spec (%)	Acc (%)
poly_1.00	27	279	294	106	121	69.75	73.5	71.62
poly_2.00	22	314	322	78	86	78.5	80.5	79.5
poly_3.00	37	365	374	26	35	91.25	93.5	92.37
rbf_0.80	19	380	311	89	20	95.00	77.75	86.38
rbf_0.90	23	369	345	55	31	92.25	86.25	89.25
rbf_1.00	23	378	357	43	22	94.50	89.25	91.88
rbf_1.10	27	385	357	43	15	96.25	89.25	92.75
rbf_1.20	23	379	365	35	21	94.75	91.25	93.00

(a)

(b)

(c)

Figure 3.10: Plot of accuracy versus number of features used for (a) DWT, (b) GLCM and (c) HOS methods.

3.4 Novelty of Proposed Chapter Technique

In this present chapter, the performances of DWT, GLCM and HOS in CAD of MI using echocardiography images are compared. The results obtained clearly show that these three methods are able to pick up minute changes in the echocardiography images effectively and hence yielded high accuracy. DWT helps to quantify sudden changes in the pixels and hence the entropy value is lower for MI compared to normal class. This indicates that the high frequency components are less in MI cases. Entropy computed from the DWT coefficients in the horizontal (*cH1-Ent*, *cH2-Ent*) and vertical (*cV1-Ent* and *cV2-Ent*) directions have provided highest discrimination. Echocardiography images with non-uniform pixels cannot be fully described by second-order statistics (GLCM). Second-order statistics can describe minimum phase system only (Pareek, et al. 2013). Therefore, HOS is used to reveal information of the phase and nonlinearity present in MI cases. Hence HOS-based features are more discriminative than the second-order statistics (GLCM). Moreover, HOS performs better even in noisy conditions and thus is able to capture the nonlinear interaction of the pixels in the frequency domain and also phase coupling (Acharya, et al. 2013e; Pareek, et al. 2013).

Comparison of the current proposed algorithm with previous studies conducted on semi-automated CAD of MI, by using echocardiography images, is presented in **Table 3.7**. It can be seen from the table that few researchers used DWT, GLCM (second-order statistics) and HOS for the detection of normal and infarcted myocardium by developing an automated CAD system.

Compared to the previous studies, in this proposed algorithm (**Chapter 3**), I have obtained more than 92% classification accuracy, sensitivity, and specificity using DWT, and HOS methods. However, I have reported more than 92% accuracy, sensitivity, and specificity using 16 features obtained from DWT coefficients.

The following inferences can be made between the previous literature (summarised in Table 3.7) and the results of my study summarised in **Tables 3.5, 3.6 and 3.7**:

(a) In the previous studies cited in **Table 3.8**, MI was diagnosed based on the manually cropped region. On the other hand, my current proposed method is completely automatic and does not involve any segmentation.

(b) I have used more subjects than the previous studies (**Table 3.8**), and reported more than 92% accuracy, sensitivity and specificity using ten-fold cross validation. Hence my proposed method is more robust.

(c) The method is non-invasive and does not involve using any contrast agent.

(d) It can reduce the workload of clinicians significantly.

In this present chapter work, the algorithms and methods are developed into the prototype system. They are validated using 10-fold cross validation method on in-house database which are acquired from the collaborative hospital. Using this prototype system, the methodology proposed in this chapter provided > 92% of accuracy.

On the other hand, some limitation of this method may be stated as follows:

- a) The proposed system is completely automated and does not require human intervention. So, it may affect human skills in interpretation in the long run.

3.5 Summary

In this chapter, the performances of the CAD approach based on image processing methods to detect normal and infarcted myocardium using echocardiography images are compared. The proposed system is validated using 400 MI and 400 normal ultrasound images, obtained from 80 patients with MI and 80 normal subjects. The features extracted from DWT coefficients obtained an accuracy of 99.50%, sensitivity of 99.75% and specificity of 99.25%; GLCM have achieved an accuracy of 85.75%, sensitivity of 90.25% and specificity of 81.25%; and HOS

obtained an accuracy of 93%, sensitivity of 94.75% and specificity of 91.25%. Among the three techniques presented DWT yielded the highest classification accuracy of 99.50% using only 16 features. The proposed CAD system can be used as an adjunct tool to assist cardiologists in making a more accurate diagnosis on the presence of MI and further complications in hospitals and polyclinics. The proposed method can be further extended to detect the MI using different cross-sectional views of echocardiography and different stages (mild, moderate and chronic) of MI.

In the next chapter, an algorithm for detection of normal and infarcted myocardium using different cross-sectional views of echocardiographic image texture analysis is presented.

Table 3.8: Comparison of proposed work with other studies conducted for MI detection using echocardiography image analysis techniques.

Authors	Features	Classifiers	No. of Subjects	Performance measure
Skorton et al. (1983)	Gray level distribution, kurtosis, skewness	Manual classification	Animal study involved 7 adult dogs.	Sen = 90% Spec = 70%
Kamath et al. (1986)	Amplitude of the gray levels (Pixel intensity)	Statistical classification		Not mentioned
Tak et al. (1992)	Pixel intensity	Statistical classification	17 (5 N, 12 MI)	MPI on 1st day 20.4 ± 2.0 vs 24.3 ± 2.3 and 14th day 20.5 ± 1.7 vs 31.9 ± 3.7
Mojsilovic et al. (1997)	Energy computed from Wavelet coefficients	Unsupervised classification	15	Highest classification rate: 96%
Neskovic et al. (1998)	Energy computed from Wavelet coefficients	Unsupervised classification (Distance classifier)	18	On day 2: Sen 73%, Spec 86%, Acc 78%; On 1 week: Sen 91%, Spec 86%, Acc 89%; On 3 weeks: Sen 100%, Spec 100%, Acc 100%
Agani et al. (2007)	Features computed from GLCM and DWT	Mahalanobis distance classifier	17	Acc: 91.32%
Moldovanu et al. (2011)	First order statistical features (mean gray level,		12 (6 N 6 MI)	Entropy: 6.23 ± 0.52 vs 9.95 ± 0.17

	skewness, kurtosis, entropy)			
This Chapter	Features from DWT coefficients	SVM	160 (80 N, 80 MI)	Acc: 99.50% Sen: 99.75% Spec: 99.25%
	Second order statistical features from GLCM			Acc: 85.75% Sen: 90.25% Spec: 81.25%
	Features from HOS			Acc: 93.00% Sen: 94.75% Spec: 91.25%

N = Normal; Acc = Accuracy; Sen = Sensitivity; Spec = Specificity; MPI = Mean Pixel Intensity.

CHAPTER 4. INFARCTED LEFT VENTRICLE CLASSIFICATION FROM CROSS-SECTIONAL ECHOCARDIOGRAMS USING RELATIVE WAVELET ENERGY AND ENTROPY FEATURES

4.1 Introduction

From the previous chapter experimental results, it is found that the wavelet based methods are efficient to extract the salient characteristics of echocardiograms of normal and MI subjects. Therefore, in this proposed chapter, another multi-resolution decomposition technique (the time-invariant method) Stationary Wavelet Transform (SWT) is employed. The SWT is used to analyze two different cross-sectional echocardiography views (parasternal short-axis and apical four chambers views) images captured during the end systole to characterize normal and infarcted myocardium. Cross-sectional view echocardiography is an efficient non-invasive diagnostic tool for characterizing MI and stages of expansion leading to heart failure (Lang, et al. 2005; Heger, et al. 1979). Parasternal and apical echocardiography images captured from different cross-sectional planes (short-axis and four chambers) convey significant information about the structure and function of the infarcted LV myocardium (Lang, et al. 2006; Heger, et al. 1979).

However, analysis of different cross-sectional echocardiography views of images using manual or visual evaluation approach might not yield complete information necessary for assessing the MI patients in time, as the low resolution and artefacts hinders the visual identification of subtle changes (Chetboul, et al. 2003). In order to overcome this shortcoming of manual evaluation, computer-based image processing techniques for analysis of cross-sectional echocardiography images

is proposed (Fujita, et al. 2010; Ginneken, et al. 2011; Smith, et al. 2011; Acharya, et al. 2013c; Acharya, et al. 2013d). An automated computer-aided technique of cross-sectional echocardiography feature assessment can aid clinicians in early and more reliable detection of MI patients before subsequent catastrophic post-MI medical conditions. Literature survey (**Chapter 2**) showed that researchers worldwide are experimenting with different cross-sectional echocardiography views in order to pick up the fine changes occurring within image pixels. In addition, they are also attempting to identify the unique echocardiogram features associated with MI and its complications (Shen, et al. 1991; Kisanuki, et al. 1993; Vaseyi, et al. 2001; Swinburn, et al. 2001; Flachskampf, et al. 2011). Statistical features such as gray level distribution, kurtosis, and skewness assessed from parasternal short-axis view echocardiography images have been efficiently classified as normal and MI (Skorton, et al. 1983). Pixel intensity parameter evaluated from parasternal-long axis and apical four chambers view of echocardiography images are used to differentiate normal and scarred regions of MI (Kamath, et al. 1986). In addition, mean pixel intensity calculated from parasternal long- short –axis, apical four- and two chamber views of echocardiography have been used to assess wall motion abnormality in MI patients (Tak, et al. 1992). Further, single cross-sectional echocardiography view, apical two or four chambers (Mojsilovic, et al. 1997; Neskovic, et al. 1998; Agani, et al. 2007) or parasternal short-axis have been assessed by using wavelet method, in order to evaluate the energy parameter (Mojsilovic, et al. 1997; Neskovic, et al. 1998), entropy, contrast and inverse difference moment measures (Agani, et al. 2007), for classifying normal myocardium and MI.

Thus, these studies from Chapter 2 highlight the significance of different cross-sectional views of echocardiography images. In addition, the significance of features extracted from these views for MI patient's assessment using computer-based techniques compared to manual analysis of cross-sectional views are assessed.

4.2 Proposed Technique for Detection of Normal and Infarcted Myocardium

This chapter focuses on parasternal and apical views of echocardiography and extraction of features from these views which are efficient in identifying the subtle changes within images, for an automated characterization of normal and infarcted myocardium. A novel SWT based algorithm is used for an automated characterization of normal and infarcted myocardium by using cross-sectional views of echocardiography (parasternal and apical views). Moreover, features from only *two frames per patient* (one frame from each view per patient) are used for automated detection. The block diagram of the proposed method of an automated MI characterization is shown in **Figure 4.1**. In this algorithm, two different cross-sectional views (parasternal short axis mid-left ventricular view at papillary muscle level and apical four chamber view) echocardiography images of normal and MI LVs are pre-processed and subjected to three level decomposition using SWT to obtain the sub-band coefficients having different frequency coefficients. Relative wavelet energy and entropy features are then extracted from the SWT coefficients. Then, all the features extracted from each view are (i) ranked separately, and (ii) combined together and ranked, using Bhattacharyya, Entropy, Fuzzy Max-Relevancy and Min-Redundancy (mRMR), Receiver Operating Characteristics (ROC), t-test, Wilcoxon ranking methods. Highly ranked features from each ranking methods are fed to the Support Vector Machine (SVM) classifier one by one, to obtain the optimum classification using minimum features. Performance of the classifier is then evaluated using ten-fold cross validation method.

Figure 4.1: Block diagram of proposed algorithm.

4.2.1 Data Acquisition

For this proposed chapter, echocardiography data (video sequences) of 160 subjects (80 with MI and 80 non-MI) were obtained from different ultrasound scanners at National Heart Centre Singapore. The echocardiography video sequences of two different views parasternal short axis mid-left ventricular view at papillary muscle level and apical four chambers views (with temporal frame resolutions of 30 frames/seconds) were obtained. From each cross-sectional echocardiography video sequence, a single frame during end-systolic phase of cardiac cycle was extracted automatically. Thus, a total of 160 cross-sectional echocardiograms were available from each view for analysis (160 parasternal short axis view and 160 apical four chambers view echocardiography images). **Figure 4.2** shows the typical two views (parasternal short axis at papillary muscle level view and apical four chambers view) of 2D echocardiography images of normal and MI patients obtained during end systole.

Figure 4.2: Parasternal short axis at papillary muscle level view (left column) and apical four chamber view (right column) at end systole of normal (top row) and MI (bottom row) echocardiography images.

This chapter proposes a new method of automated characterization of normal and infarcted myocardium, in which Relative Wavelet Energy and Entropy features are extracted from the SWT coefficients of two cross-sectional views echocardiography images. The technique comprises of the following steps:

- (i) Two cross-sectional echocardiography images are pre-processed.
- (ii) The pre-processed images from each view are subjected to 3 level decomposition using SWT to obtain the 12 sub-band coefficients of two different views of images.
- (iii) For each view, the relative wavelet energy and entropy features values in 12 sub-band coefficients are computed.
- (iv) Features from each view are separately applied to various ranking methods.
- (v) SVM classifier is used to differentiate the highly ranked features of each view obtained from different ranking methods
- (vi) Features from each view are combined together and subjected to ranking methods for obtaining the best significant features
- (vii) Finally, highly ranked features (of combined two views) obtained from each ranking methods are subjected to classification

A detailed description of the each step used is as follows.

4.2.2 Pre-processing

In this chapter, the Red-Green-Blue (RGB) color cross-sectional views of echocardiography images are changed into grayscale images. Then the grayscale images contrast is improved by using adaptive histogram equalization (**Gonzalez, et al. 2002**).

4.2.3 Feature Extraction

Feature extraction process is one of the most crucial steps in developing an automated diagnostic system. In this step, cross-sectional views echocardiography image texture characteristics are analyzed using SWT method by extracting relative wavelet energy and entropy features from the SWT coefficients. In this proposed algorithm, I have used the biorthogonal wavelet (bior3.7) as the mother wavelet due to its ability of capturing fine changes in the images (Acharya, et al. 2014b).

Stationary Wavelet Transform (SWT)

Stationary wavelet transform (SWT) is a wavelet transform designed to overcome the translation-invariance drawback of the discrete wavelet transform (DWT) (Nason, et al. 1995). In SWT, the process of down-sampling is suppressed by up-sampling the filters using zeros between the filter coefficients (Nason, et al. 1995; Acharya, et al. 2014b). Thus, the SWT method is translation-invariant compared to DWT.

The SWT uses the low pass and high pass filters to obtain the low- and high-pass components. Information about the slow varying signal characteristics is present in the low pass component, whereas the information about sudden changes in the signal is in the high-pass components.

Using the high pass and low pass filters, the original image is decomposed into four sub-band images LL , LH , HL , and HH . The LL coefficients show the similar details of original image, so called approximation (A) and also represents the total energy in the images. The details coefficients HL , LH and HH contain the vertical (V), horizontal (H) and diagonal (D) details of the image respectively. The LL sub-band image can be further decomposed in the same way for the second level sub-band image. The coefficients of the individual sub-bands can be represented as $cA_1, cD_1, cV_1, cH_1, cA_2, cD_2, cV_2, cH_2, cA_3, cD_3, cH_3, cV_3$ obtained at the first,

second and third level decomposition respectively (**Daubechies 1992**). From these coefficients of three levels, features are extracted as explained in the next section.

Relative Wavelet Energy and Entropy features

Energy, also known as uniformity, is used as a measure of information present in the image. Entropy measures the uncertainty associated with randomness. Relative wavelet energy and entropy features provide information associated with different frequency bands present in the image and their corresponding degree of importance (**Giannakakis, et al. 2008**). These features measure the disruption of the myocardial tissue. From each of the 12 SWT subsets of coefficients obtained using three level of decomposition, the following features are evaluated. The formulae for calculation of different energy and entropy features are tabulated in **Appendix I**.

4.2.4 Feature Ranking

Not all the features extracted from the SWT coefficients are useful for differentiation of MI and normal. In addition, it is difficult to identify useful features from the extracted features. Hence, in order to select the significant features, different ranking methods are used. In this chapter work, Bhattacharyya, Entropy, Fuzzy mRMR, ROC, t-test, Wilcoxon rank tests are used to rank the features (**Gonzalez 2007**). *Bhattacharyya algorithm* uses the Bhattacharyya distance, which is a measure of the separability between two populations (**Acharya, et al. 2015c; Kailath 1967**). The ranking of features is performed based on the discrimination ability of features. *Entropy method* ranks the features in descending order of relevance, by finding the entropies after removing each feature one at a time (**Dash, et al. 1999**). The *t-test* identifies whether the two classes are different or not, by calculating the *mean*. This test returns the *p*-value and *t*-value which are used to identify the discrimination between the two classes (normal and abnormal) and to rank the features extracted where high *t*-value indicates the higher ranking. *Wilcoxon test* is a paired test that is suitable for comparing two different measurement sets made on the same data (**Wilcoxon 1945**). In *ROC method*, the

ROC is drawn between sensitivity and 1-specificity, for different values of the threshold. Based on the area under the ROC curve, ranking of the features is performed (Acharya, et al. 2015c; Theodoridis, et al. 2003). The *mRMR method* is considering mutual relevance and redundancy between the features (Peng, et al. 2005; Zhang, et al. 2012). For a given dataset maximum relevance is used to search features where mutual information values between each feature and target class should be maximized. However, two features may have high correlation and provides high discrimination on the target class. It is not suitable to include them on classification process (Zhang, et al. 2012). Hence, minimum redundancy is used to search features without correlation (Zhang, et al. 2012). Combining these two criteria resulted a method is called mRMR (Peng, et al. 2005). To compute the mutual information between features, fuzzy entropy (Khushaba, et al. 2011) based method is used.

4.2.5 Classification

Classification is an important process in the development of an automated detection system. Highly ranked significant features are subjected to SVM classifier for the classification of normal and MI classes in this algorithm (Duda, et al. 2012). And in this chapter, different kernels are used, such as polynomial 1, 2, 3, and radial basis function (RBF). Later, ten-fold cross validation method is used to validate the performance of the classifier.

4.3 Results

This chapter analyses two different cross-sectional views of echocardiography images using SWT method. Relative wavelet energy and entropy features are extracted from SWT coefficients of parasternal short axis view at level of papillary muscles and apical four chambers view of echocardiography images to characterize normal and MI subjects.

A total of 120 relative wavelet energy and entropy features are obtained by three level decomposition of SWT. The features extracted from each cross-sectional view are statistically significant ($p < 0.05$), and present distinct differentiation between MI and normal classes. Firstly, all the 120 features from each of the two cross-sectional views are ranked by using Bhattacharyya, Entropy, Fuzzy mRMR, ROC, t-test, Wilcoxon ranking tests. Secondly, the features of two views are combined and ranked using Bhattacharyya, entropy, Fuzzy mRMR, ROC, t-test, Wilcoxon ranking methods. Among the ranking tests used, the entropy test has yielded the highest classification performance.

Tables 4.1 – 4.3 shows the results (mean $\pm$ SD) of features obtained by using the best ranking method used from SWT coefficients for two cross-sectional views of echocardiography images. **Tables 4.1, 4.2 and 4.3** list the top 22 relative wavelet energy and entropy features of parasternal short axis view, apical four chamber view, and combined two views (parasternal short axis + apical four chambers) of echocardiography images, ranked using entropy-test.

Table 4.1: Results (mean and SD) of top 22 highly ranked features (ranked using entropy) obtained from parasternal short axis view echocardiography images ($p < 0.05$).

Features	Normal		MI		Criterion
	Mean	SD	Mean	SD	
$cV_1 - Eng- V_1$	152.598	10.195	198.007	109.805	67.001
$cD_1 - Eng- V_1$	3.410	0.917	8.192	8.292	53.576
$cD_1 - RWEng- V_1$	0.46E-04	0.14E-04	1.17E-04	1.10E-04	42.953
$cD_1 - PEng- V_1$	1.62E-04	0.51E-04	4.11E-04	3.84E-04	38.456
$cH_1 - RWEng- V_1$	9.54E-04	2.57E-04	15.87E-04	10.38E-04	10.402
$cH_1 - PEng- V_1$	32.31E-04	8.94E-04	53.74E-04	34.83E-04	9.693
$cH_1 - Eng- V_1$	71.220	19.382	108.979	79.606	9.473
$cD_3 - RWEnt- V_1$	0.173	0.001	0.176	0.006	6.945
$cV_1 - RWEng- V_1$	21.04E-04	4.40E-04	29.13E-04	14.09E-04	6.047
$cV_1 - PEng- V_1$	71.26E-04	15.67E-04	98.50E-04	47.37E-04	5.298
$cH_3 - PEnt- V_1$	0.270	0.002	0.274	0.006	4.651
$cH_3 - Ent- V_1$	31.35E-04	1.43E-04	33.47E-04	3.76E-04	3.761
$cH_3 - AvgEnt- V_1$	10.45E-04	0.47E-04	11.16E-04	1.25E-04	3.761
$3 - AvgEnt- V_1$	40.93E-04	1.57E-04	43.13E-04	4.06E-04	3.557
$3 - Ent- V_1$	122.78E-04	4.71E-04	129.38E-04	12.19E-04	3.557
$cD_3 - PEng- V_1$	0.302	0.004	0.309	0.012	3.515
$cD_3 - Ent- V_1$	34.93E-04	1.97E-04	37.52E-04	4.92E-04	3.181
$cD_3 - AvgEnt- V_1$	11.64E-04	0.65E-04	12.51E-04	1.64E-04	3.181
$cV_3 - AvgEnt- V_1$	10.12E-04	0.54E-04	10.81E-04	1.27E-04	2.737
$cV_3 - Ent- V_1$	30.35E-04	1.64E-04	32.43E-04	3.81E-04	2.737
$cV_2 - Eng- V_1$	1089.677	123.358	1071.594	332.032	2.703
$cV_2 - AvgEng- V_1$	544.838	61.678	535.797	166.016	2.703

Table 4.2: Results (mean and SD) of top 22 highly ranked features (ranked using entropy) obtained from apical four chambers view echocardiography images ($p < 0.05$).

Features	Normal		MI		Criterion
	Mean	SD	Mean	SD	
$cV_1 - Eng- V_2$	148.293	8.297	199.639	111.003	107.753
$cD_1 - Eng- V_2$	3.425	0.936	8.734	8.992	61.367
$cD_1 - RWEng- V_2$	0.66E-04	0.17E-04	1.44E-04	1.40E-04	43.227
$cD_1 - Eng- V_2$	2.44E-04	0.67E-04	5.08E-04	5.00E-04	34.876
$cH_1 - RWEng- V_2$	12.76E-04	2.61E-04	18.09E-04	12.58E-04	12.812
$cH_1 - Eng- V_2$	66.310	17.382	108.163	79.248	12.454
$cH_1 - PEng- V_2$	44.99E-04	9.55E-04	61.76E-04	42.37E-04	10.499
$cD_3 - PEnt- V_2$	0.302	0.002	0.307	0.012	10.313
$cD_3 - RWEnt- V_2$	0.171	0.002	0.175	0.006	6.173
$cH_3 - PEnt- V_2$	0.268	0.002	0.273	0.006	4.215
$cH_3 - AvgEnt- V_2$	10.64E-04	0.43E-04	11.05E-04	1.20E-04	3.358
$cH_3 - Ent- V_2$	31.93E-04	1.31E-04	33.16E-04	3.60E-04	3.358
$cD_3 - Ent- V_2$	35.94E-04	1.87E-04	37.24E-04	4.70E-04	2.529
$cD_3 - AvgEnt- V_2$	11.98E-04	0.62E-04	12.41E-04	1.57E-04	2.529
$cH - Eng- V_2$	0.086	0.011	0.069	0.020	2.423
$cH - RWEnt- V_2$	0.264	0.001	0.264	0.004	2.342
$cV_2 - Eng- V_2$	1047.576	130.793	1074.208	329.719	2.280
$cV_2 - AvgEng- V_2$	523.788	65.396	537.103	164.859	2.280
$cH_3 - RWEng- V_2$	0.033	0.004	0.026	0.007	2.183
$3 - Ent- V_2$	0.012	0.001	0.012	0.001	2.081
$3 - AvgEnt- V_2$	41.57E-04	1.67E-04	42.81E-04	3.84E-04	2.081
$cH_3 - RWEnt- V_2$	0.152	0.003	0.156	0.004	1.914

Table 4.3: Results (mean and SD) of top 22 highly ranked features (ranked using entropy) obtained from combined two cross-sectional view echocardiography images ($p < 0.0001$).

Features	Normal		MI		Criterion
	Mean	SD	Mean	SD	
$cV_1 - Eng - V_2$	148.293	8.297	199.639	111.003	107.753
$cV_1 - Eng - V_1$	152.598	10.195	198.007	109.805	67.001
$cD_1 - Eng - V_2$	3.425	0.936	8.734	8.992	61.367
$cD_1 - Eng - V_1$	3.410	0.917	8.192	8.292	53.576
$cD_1 - RWEng - V_2$	0.66E-04	0.17E-04	1.44E-04	1.40E-04	43.227
$cD_1 - RWEng - V_1$	0.46E-04	0.14E-04	1.17E-04	1.10E-04	42.953
$cD_1 - PEng - V_1$	1.62E-04	0.51E-04	4.11E-04	3.84E-04	38.456
$cD_1 - PEng - V_2$	2.44E-04	0.67E-04	5.08E-04	5.06E-04	34.876
$cH_1 - RWEng - V_2$	12.76E-04	2.61E-04	18.09E-04	12.58E-04	12.812
$cH_1 - Eng - V_2$	66.310	17.382	108.163	79.248	12.454
$cH_1 - PEng - V_2$	44.99E-04	9.55E-04	61.76E-04	42.37E-04	10.499
$cH_1 - RWEng - V_1$	9.54E-04	2.57E-04	15.87E-04	10.38E-04	10.402
$cD_3 - PEnt - V_2$	0.302	0.002	0.307	0.012	10.313
$cH_1 - PEng - V_1$	32.31E-04	8.94E-04	53.74E-04	34.83E-04	9.693
$cH_1 - Eng - V_1$	71.220	19.382	108.979	79.606	9.473
$cD_3 - RWEnt - V_1$	0.173	0.001	0.176	0.006	6.945
$cD_3 - RWEnt - V_2$	0.171	0.002	0.175	0.006	6.173
$cV_1 - RWEng - V_1$	21.04E-04	4.40E-04	29.13E-04	14.09E-04	6.047
$cV_1 - PEng - V_1$	71.26E-04	15.67E-04	98.50E-04	47.37E-04	5.298
$cH_3 - PEnt - V_1$	0.270	0.002	0.274	0.006	4.651
$cH_3 - PEnt - V_2$	0.268	0.002	0.273	0.006	4.215
$cH_3 - Ent - V_1$	31.35E-04	1.43E-04	33.47E-04	3.76E-04	3.761

V_1 = view 1, parasternal short axis view; V_2 = view 2, apical four chambers view.

It can be seen from this **Tables 4.1 - 4.3** that, entropy values are high for MI as compared to normal due to more sudden changes in the pixel distributions due to MI. All the features extracted from parasternal short axis view, apical four chambers view and combined two cross-sectional view are subjected to SVM classification one by one according to their ranking, for automated classification.

The SVM classifier is evaluated with all the 120 features extracted from each level of decomposition. It is found that, only 32 and 18 highly ranked features from two cross-sectional views, by using entropy ranking test, have yielded the highest

classification accuracies. The features from combined two views have achieved the best classification accuracy, by using 16 features with entropy ranked method. Several combinations of the highly ranked features (32, 18 and 16) are tested to train the SVM classifier by using ten-fold cross validation. Results of this ten-fold cross validation method are obtained in terms of performance evaluation statistical parameters sensitivity and specificity. These parameters measure the classifier's effectiveness in accurately classifying the images into their respective classes.

Table 4.4 shows the highest classification results obtained for features (ranked using entropy method) from parasternal short axis mid-left ventricular view, apical four chambers view, and combined parasternal short axis and apical four chambers views using SVM classifier with ten-fold cross validation. Tables 4.5 – 4.9 shows the classification results obtained for features ranked using Bhattacharyya, fuzzy mRMR, ROC, t-test and Wilcoxon ranking methods respectively.

It can be seen from **Table 4.4** that the SVM classifier with RBF kernel achieved significantly highest accuracy of 95%, sensitivity of 93.70% and specificity of 96.20% using 32 best features extracted from parasternal short axis view of echocardiography images. It has obtained 96.20% accuracy, 97.50% sensitivity and 95% specificity using only 18 best features of apical four chambers view of echocardiography images, and has yielded an accuracy of 96.80%, sensitivity of 93.70% and specificity of 100% using only 16 features from combined two cross-sectional echocardiography views. Thus, by combining features from two views (parasternal short axis + apical four chambers view), with only 16 features, MI and normal subjects are more significantly differentiated using SVM classifier. Hence, viewing the myocardium in two different cross-sectional views (parasternal short axis + apical four chambers), and extracting features using image processing methods from those two views helps to assess the MI patients accurately.

Table 4.4: Classification results using features (ranked using entropy) obtained from two cross-sectional views echocardiography images.

Classifier	No. of	TP	TN	FP	FN	Accuracy	PPV	Sensitivity	Specificity
SVM RBF	Features								
Features from parasternal short axis view alone									
2	32	75	77	3	5	95%	96.10%	93.70%	96.20%
Features from apical four chambers view alone									
0.9	18	78	76	4	2	96.20%	95.10%	97.50%	95%
Features from parasternal short axis + apical four chambers views									
1.8	16	75	80	0	5	96.80%	100.0%	93.70%	100%

TP = true positive; TN = true negative; FP = false positive; FN = false negative

Table 4.5: Classification results using features (ranked using Bhattacharyya) obtained from two cross-sectional views echocardiography images.

Classifier	No. of	TP	TN	FP	FN	Accuracy	PPV	Sensitivity	Specificity
SVM RBF	Features								
Features from parasternal short axis view alone									
1.6	41	75	73	7	5	92.50%	91.40%	93.70%	91.20%
Features from apical four chambers view alone									
1.7	30	73	77	3	7	93.70%	96%	91.20%	96.20%
Features from parasternal short axis + apical four chambers views									
3.9	33	62	75	5	18	85.60%	92.50%	77.50%	93.70%

Table 4.6: Classification results using features (ranked using fuzzy mRMR) obtained from two cross-sectional views echocardiography images.

Classifier	No. of	TP	TN	FP	FN	Accuracy	PPV	Sensitivity	Specificity
SVM RBF	Features								
Features from parasternal short axis view alone									
2.9	33	72	75	5	8	91.80%	93.50%	90%	93.70%
Features from apical four chambers view alone									
2.6	30	74	77	3	6	94.30%	96.10%	92.50%	96.20%
Features from parasternal short axis + apical four chambers views									
2.5	27	75	77	3	5	95%	96.10%	93.70%	96.20%

Table 4.7: Classification results using features (ranked using ROC) obtained from two cross-sectional views echocardiography images.

Classifier	No. of	TP	TN	FP	FN	Accuracy	PPV	Sensitivity	Specificity
SVM RBF	Features								
Features from parasternal short axis view alone									
3.7	26	67	77	3	13	90%	95.70%	83.70%	96.20%
Features from apical four chambers view alone									
2.8	32	73	75	5	7	92.50%	93.50%	91.20%	93.70%
Features from parasternal short axis + apical four chambers views									
2	23	73	76	4	7	93.10%	94.80%	91.20%	95%

Table 4.8: Classification results using features (ranked using t-test) obtained from two cross-sectional views echocardiography images.

Classifier	No. of	TP	TN	FP	FN	Accuracy	PPV	Sensitivity	Specificity
SVM RBF	Features								
Features from parasternal short axis view alone									
2.2	25	71	76	4	9	91.70%	94.60%	88.70%	95%
Features from apical four chambers view alone									
2	24	74	75	5	6	93.10%	93.60%	92.50%	93.70%
Features from parasternal short axis + apical four chambers views									
2	31	77	76	4	3	95.60%	95%	96.20%	95%

Table 4.9: Classification results using features (ranked using Wilcoxon) obtained from two cross-sectional views echocardiography images.

Classifier	No. of	TP	TN	FP	FN	Accuracy	PPV	Sensitivity	Specificity
SVM RBF	Features								
Features from parasternal short axis view alone									
1.8	35	73	72	8	7	90.60%	90.10%	91.20%	90%
Features from apical four chambers view alone									
2.6	28	75	76	4	5	94.30%	94.90%	93.70%	95%
Features from parasternal short axis + apical four chambers views									
1.7	19	73	75	5	7	92.50%	93.50%	91.20%	93.70%

4.4 Novelty of Proposed Chapter Technique

In my previous chapter 3, the performance of three methods namely Discrete Wavelet Transform (DWT), Gray Level Co-occurrence Matrix (GLCM) and Higher-Order Statistics (HOS) for automated detection of MI is studied. I analyzed the single

parasternal short-axis view at level of papillary muscle echocardiography images by taking four non-consecutive frames per cardiac cycle of MI and normal subjects using three methods. The study reported (i) classification accuracy of 99.50%, sensitivity 99.75% and specificity 99.25% using DWT features; (ii) accuracy of 85.75%, sensitivity 90.25% and specificity 81.25% with GLCM features; and (iii) accuracy of 93%, sensitivity 94.75% and specificity 91.25% with HOS features. The study has shown promising results in characterizing normal and infarcted myocardium using features extracted from parasternal short axis view alone but using multiple frames (*5 non-consecutive frames*) per patient. Furthermore, from the experimental results, it is found that the wavelet based methods are efficient to extract the salient characteristics of echocardiograms of normal and MI subjects. Therefore, in this chapter, another multi-resolution decomposition technique (the time-invariant method) SWT is employed and two cross-sectional echocardiography views (parasternal short-axis and apical four chambers views) images captured during the end systole – *two frames per patient (one frame from each view per patient)* are analyzed to characterize normal and infarcted myocardium. The SWT method is able to decompose a cross-sectional echocardiography image into a series of low and high-frequency coefficients. The main advantage of using this method is that it extracts minute changes in images, by capturing both the spatial and frequency information in the images at different scales. It enables analysis of both local and global features present in the image (Acharya, et al. 2012a). This property of SWT method helps in the analysis of pixel variations in cross-sectional echocardiography images.

The two cross-sectional echocardiography views images are captured during the end systole (one frame from each view per patient) for analysis by using the time-invariant SWT method. The end systolic phase aids clinicians in assessing the end systolic volume or ejection fraction, which helps to predict the survival after MI (White, et al. 1987).

The parasternal mid-left ventricular and apical four chamber views shall cover 11 of the 17 left ventricular wall segments (**Cerqueira, et al. 2002**). Of note, the 11 segments in these two views provide efficient coverage of myocardial infarct downstream of all three coronary arterial territories (left anterior descending artery: mid anterior, mid anteroseptal, inferoseptal, distal septal and apical walls; circumflex artery: basal anterolateral, mid anterolateral, inferolateral, and distal lateral; right coronary artery: proximal inferoseptal, and mid inferior walls). In addition, histological, perfusion and mechanical perturbations extend beyond the core of the myocardial infarct that are evident on echocardiography (**Weiss, et al. 1981**). This implies that comprehensive image analysis of all 17 left ventricular wall segments may not be necessary to ensure detection of changes in either the infarct area or its penumbra.

The proposed method is able to detect minute pixel variations in both cross-sectional views of echocardiography images effectively. The results shows that the features obtained by combining parasternal short axis and apical four chamber views of echocardiography images are efficient in identifying MI as compared to individual cross-sectional echocardiography view. The results also indicate that the combined two views aid the cardiologists to make faster assessments. Comparison of proposed technique with other literature in detection of infarcted myocardium using different cross-sectional echocardiography images is tabulated in **Table 4.10**.

In my previous proposed technique (**Chapter 3**) a specificity of 99.25% is obtained with DWT features using 16 features extracted from a single view using *five frames*. But, the cardiologist will not be able to have other views for assessment of patients. Yet, in this proposed method specificity of 100% is achieved using 16 features extracted from two cross-sectional echocardiography views using only *two frames*. Thus, the cardiologist will have a complete two views assessment for the patient. The highlights of this method can be summarized as follows:

1. To the best of my knowledge, this is the first study which uses two different views of cross-sectional echocardiography images to characterize the normal and infarcted myocardium.
2. It is fast and reliable. The proposed system is completely automated and it takes maximum five minutes for the computation of one patient's images.
3. It uses only *two frames* (one frame of end systole from two views per patient) from both views of cross-sectional echocardiography images. Hence, involves less computation as compared to my previous proposed chapter 3.
4. There is no manual extraction of ROI, and it is completely automated.
5. The results achieved an average specificity of 100% (for designating MI patients). Hence, the clinicians are able to classify all normal subjects as normal (no false positive cases). This will reduce the workload of doctors by 50%.
6. Obtained the highest classification accuracy using only 16 features from combined parasternal short axis and apical four chamber views (**Table 4.10**).

4.5 Summary

Automated assessment of MI by extracting features from various views using CAD-based method will help the cardiologists in the fast and efficient assessment of normal and patients with infarcted myocardium. Thus, in this chapter, a novel automated extraction of features from end-systolic two cross-sectional echocardiography views (parasternal short-axis and apical four chambers) for characterizing normal and infarcted myocardium patients by using the SWT method is proposed. The algorithm is developed using 160 subjects (80 with MI and 80 normal) cross-sectional echocardiography views. The current technique is able to characterize MI with an average accuracy of 95%, sensitivity of 93.70% and specificity of 96.20% using 32 features extracted from parasternal short-axis view; an accuracy of 96.20%, sensitivity of 97.50% and specificity of 95% with 18 apical four

chamber view features. In addition, experiment has achieved an average accuracy of 96.80% with 16 features extracted from combined parasternal short axis view at level of papillary muscles and apical four chambers view (*only two frames*). This proposed method has the potential of being used for more reliable classification of MI patients with the proposed inclusion of software within the echocardiography ultrasound machine. This system can even be employed in the polyclinics and hospitals in the third world countries to reliably and effectively diagnose the cardiac health of patients.

In the next chapter, an integrated index for normal and infarcted myocardium detection using 2D echocardiograms is presented.

Table 4.10: Comparison of proposed technique with other literature in detection of infarcted myocardium using different cross-sectional echocardiography images.

Author (year)	No. of subjects	Image View used	Method and Features	Classification	Performance
		ROI or Image			
Skorton, et al. 1983- Animal study	7 adults dogs	LV short axis view at papillary muscle level	Gray level distribution, kurtosis, skewness	Manual classification	Sensitivity = 90% Specificity = 70%
		ROIs of normal and infarcted			
Kamath, et al. 1986- Paediatric study	15 premature infants (6 with myocardial necrosis and 9 normal myocardium)	Parasternal long axis and four chamber views	Gray levels amplitude (pixel intensity)	Statistical classification	Not mentioned
		Image frames			
Tak, et al. 1992	17 (5 normal and 12 MI)	Parasternal long axis view of LV, parasternal short axis view of LV, apical four- and two-chamber views	Pixel intensity	Statistical classification	Mean pixel intensity on 1 st day = 20.4 ± 2.0 vs 24.3 ± 2.3 and 14 th day = 20.5 ± 1.7 vs 31.9 ± 3.7
		Image frames			

Mojsilovic, et al. 1997	15	Apical two chambers view	Energy computed from wavelet coefficients	Unsupervised classification	Classification rate = 96%
Neskovic, et al. 1998	18	Apical four chambers view	Energy computed from wavelet coefficients	Unsupervised classification – distance classifier	<u>Day 2</u> Accuracy = 78% Sensitivity = 73% Specificity = 86% <u>Week 1</u> Accuracy = 89% Sensitivity = 91%, Specificity = 86% <u>Week 3</u> Accuracy = 100% Sensitivity = 100% Specificity 100%
		ROI of normal and MI			
Agani, et al. 2007	17	Apical views	Wavelet and GLCM	Mahalanobis distance classifier	Accuracy = 91.32%
Moldovanu, et al. 2011	12 (6 normal and 6 MI)	Apical two chambers view	Mean gray level, skewness, kurtosis, entropy		Entropy = 6.23 ± 0.52 vs 9.95 ± 0.17
Vidya, et al. 2015a (Chapter 3)	160 (80 normal and 80 MI)	Parasternal short axis view	DWT, GLCM, HOS	SVM	<u>DWT</u> Accuracy = 99.50% Sensitivity = 99.75% Specificity = 99.25% Using 16 features <u>GLCM</u>

		Image frames (<i>five frames per patient</i>)			Accuracy = 85.75% Sensitivity = 90.25% Specificity = 81.25% Using 16 features <u>HOS</u> Accuracy = 93.00% Sensitivity = 94.75% Specificity = 91.25% Using 23 features
Proposed technique (Chapter 4)	160 (80 MI and 80 non-MI)	Parasternal short axis view at level of papillary muscle and apical four chamber view during end systole	Stationary Wavelet Transform and Relative wavelet energy and entropy	SVM	<u>Parasternal short axis view</u> Accuracy = 95.0% Sensitivity = 93.7% Specificity = 96.2% Using 32 features <u>Apical four chamber view</u> Accuracy = 96.2% Sensitivity = 97.50% Specificity = 95.0% Using 18 features <u>Parasternal short axis + apical four chambers</u> Accuracy = 96.8% Sensitivity = 93.7% Specificity = 100% Using 16 features
		Image frames (<i>two frames per patient</i>)			

CHAPTER 5. AN INTEGRATED INDEX FOR AUTOMATED DETECTION OF INFARCTED MYOCARDIUM FROM CROSS-SECTIONAL ECHOCARDIOGRAMS USING TEXTON-BASED FEATURES

5.1 Introduction

In my previous chapter, I have experimented with two different cross-sectional views (parasternal short-axis and apical four chambers) echocardiograms and results showed that the cross-sectional view echocardiography is an efficient non-invasive diagnostic tool for characterizing myocardium. In addition, an algorithm to differentiate automatically normal and infarcted myocardium has been developed in my previous chapter using texture characteristic analysis of two different cross-sectional view images. Therefore, in this chapter, another technique called textons is employed to analyze the apical echocardiography images captured from four chambers cross-sectional view and thereby to develop an integrated index for automated characterization of normal and infarcted myocardium.

According to literature survey (Chapter 2), researchers have worked on ultrasound image texture characteristics analysis using second-order statistics (Acharya, et al. 2012a; Acharya, et al. 2013a; Acharya, et al. 2013b), LBP and Laws Texture Energy (LTE) (Acharya, et al. 2012c) for the diagnosis of MI (Skorton, et al. 1983; Kamath, et al. 1986; Tak, et al. 1992; Agani, et al. 2007) and other diseases. Statistical features such as gray level distribution, kurtosis, and skewness extracted from echocardiography images showed greater efficiency in analyzing the texture characteristics of normal and infarcted myocardium (Skorton, et al. 1983). Even the pixel intensity parameters computed from texture characteristics of echocardiography images have showed significant in differentiation of normal and

MI scarred regions (**Kamath, et al. 1986**) and has also been used to assess wall motion abnormality in MI patients (**Tak, et al. 1992**). Further, wavelet based texture characteristics analysis by evaluating the energy parameter (**Mojsilovic, et al. 1997; Neskovic, et al. 1998**), entropy, contrast and inverse difference moment parameters (**Agani, et al. 2007**) have resulted in efficient characterization of normal and infarcted myocardium echocardiography images. Analysis of textural characteristics of images using texton-based approach have shown great success by few researchers (**Gangeh, et al. 2013; Varma, et al. 2005; Leung, et al. 2001; Sorensen, et al. 2007; Gangeh, et al. 2010**). Thus, these studies highlight the significance of image (ultrasound or echocardiography) texture characteristics for patient's automated diseases assessment. Texton-based approach is one of the dictionary learning and sparse representation-based methods tailored for texture analysis (**Gangeh, et al. 2013**). This approach is mainly based on Julesz's theory, which expresses the textures by few primitive elements called textons (**Julesz 1981**). Leung et al., 2001 are the first to propose a complete texture classification system based on textons (**Leung, et al. 2001**). The technique is further refined and developed in to a state-of-the-art system for texture classification that outperformed many other approaches in the field by **Varma, et al. 2009**.

5.2 Proposed Technique for Detection of Normal and Infarcted Myocardium

In this chapter, textons are used on apical view echocardiography images and extracted features from these textons are efficient in identifying the subtle changes within images. I have also developed a novel concept called *Myocardial Infarction Index (MII)* for an automated characterization of normal and infarcted myocardium by using cross-sectional view echocardiography images. The block diagram of the proposed method of an automated MI characterization is shown in **Figure 5.1**. In this

algorithm, apical four chamber view echocardiography images of normal and MI LVs are pre-processed and convolved with Maximum Response (MR8) filter banks set to obtain the 8 maximum filter responses i.e. textons having different orientations and scales. Various textural features such as Fractal Dimension (*FD*), Higher-Order Statistics (HOS), Hu's moments, Gabor Transform features, Yager's Entropy (*Y_Ent*), Fuzzy Entropy (*FEnt*), Energy, Local binary Pattern (*LBP*), Renyi's Entropy (*REnt*), Shannon's Entropy (*ShEnt*) and Kapur's Entropy (*KEnt*) are then extracted from these textons (filter responses). Then, all the extracted features are ranked using t-test and fuzzy mRMR methods. Combinations of highly ranked features are then used to formulate and develop an integrated *MII*, a single number for automated classification of normal and infarcted myocardium. Also, highly ranked features from each ranking methods are fed to different classifiers one by one, to obtain the optimum classification using minimum features. Performance of classifiers is evaluated using ten-fold cross validation method.

Figure 5.1: Block diagram of the proposed algorithm.

5.2.1 Data Acquisition

For experiment, a total of 160 subjects (80 normal and 80 MI patients) were collected from ultrasound scanner. I have used the echocardiography video sequences of apical four chambers views and from each video sequence; a single frame during end-systolic phase of cardiac cycle was extracted automatically. Thus, a total of 160 cross-sectional view echocardiograms were used for analysis. **Figure 5.2** shows the typical apical four chambers view of 2D echocardiography images of normal and MI patients obtained during end systole.

Figure 5.2: Apical four chamber view at end systole of normal (left column) and MI (right column) echocardiography images.

Using these data, in this chapter a new integrated index (MII) for automated characterization of normal and infarcted myocardium is developed. Various features are extracted from the textons of cross-sectional views obtained using MR8 filter banks. The technique comprises of the following steps:

- (i) cross-sectional view echocardiography images are pre-processed.
- (ii) pre-processed images are convolved with filter banks using MR8 filter bank sets to obtain the 8 maximum filter responses - Textons images.
- (iii) various features (textons) are computed to analyze the textural characteristics.
- (iv) features are applied to various ranking methods.
- (v) integrated index is formulated from ranked features using different combinations.
- (vi) various classifiers are used to differentiate the highly ranked features obtained from different ranking methods

A detailed description of the each step used is as follows.

5.2.2 Pre-processing

As a pre-processing step, the Red-Green-Blue (RGB) colour cross-sectional echocardiography images are converted to grayscale images. Then the grayscale images are subjected to adaptive histogram equalization (**Gonzalez, et al. 2002**). By performing adaptive histogram equalization, the dynamic range of image histogram gets increased and input image pixels intensity values are assigned in such a way that the output image comprises a uniform intensity distribution.

5.2.3 Creation of Two-Dimensional (2D) Texton

The texton-based approach is a technique used for constructing illustrative pixel-level textural features. Basically, this approach is distinct from other texture-based classifier methods which are compelled by the spatial arrangements of pixel intensities. Textons signify the basic structures in natural images and thus represent the fundamental elements in visual perception (**Zhu, et al. 2002**). These textons characterize various different pixel relationships in a region, which is crucial for image texture analysis. It is also be interpreted as the illustrative responses happening after convolving an image with a set of filters, “filter banks”. In this chapter work, MR8 filters set are used to obtain the response vectors for each pixel (textons) (**Zhu, et al. 2002; Jurie, et al. 2005**).

The MR8 filter bank consists of 38 filters, where filters are implemented at multiple orientations and on multiple scales to achieve rotation invariance. It contains Gaussian and Laplacian of Gaussian filters. Maximum response across all orientations reduces the number of responses from 38 (6 orientations at 3 scales for 2 oriented filters, and 2 isotropic) to 8 (3 scales for 2 filters, and 2 isotropic) (**Varma, et al. 2005**). The MR8 filter bank, which highlights local, rotationally invariant features, has been shown to perform well on synthetic data (**Varma, et al. 2005**). On each scale only the maximal response among the different orientations is kept. The final response at each pixel is an 8-dimension feature vector (**Varma, et al. 2002**). **Figure**

5.3 shows schematic illustration of the creation of textons for normal and MI echocardiography images using MR8 filters bank.

Figure 5.3: Schematic illustration of the creation of textons (8 maximum filter responses) using Maximum Response (MR8) filters bank for normal and MI images.

5.2.4 Feature Extraction

In this step, a cross-sectional view echocardiography image texture characteristic is analyzed using maximum filter responses (textons) method by

extracting various features from the textons (**Figure 5.3**). In this algorithm, the MR8 filters sets are used as the filter banks due to its ability of rotation invariance and also are able to capture the angle of maximum response in the images (**Varma, et al. 2005**).

Fractal Dimension (FD): It is used to estimate the roughness or irregularity of an image surface. The rougher appearances of image surface are indicated by higher FD value (**Mandelbrot 1982; Biswas, et al. 1998**). In this chapter work, algorithm proposed by Higuchi's is used for analysis of echocardiography images. Mathematically, FD is computed using the following equation (**Mandelbrot 1982; Biswas, et al. 1998**),

$$FD = \frac{\log N_r}{\log \left(\frac{1}{r} \right)} \quad 5.1$$

Where, N_r is the union of all distinct non-overlapping pieces with a scale factor of r .

Higher-Order Statistics (HOS): It is used to extract the signal's phase and nonlinearity information (**Nikias, et al. 1997; Chua, et al. 2011; Acharya, et al. 2008; Chua, et al. 2009**). HOS represents the higher order statistics, i.e. moments and cumulants of third and higher order using spectral illustration. The HOS method is one of the powerful techniques used for the analysis of non-linear properties of the images (**Acharya, et al. 2008; Nikias, et al. 1993**). Radon transformation is performed first to convert the 2D image into 1D signal before extracting the important features using HOS method (**Acharya, et al. 2012b**). In this proposed chapter work, Radon transform is performed for every 10° . Later, third-order statistics of the image Bispectrum is used in this work.

The bispectral entropies – normalized bispectral entropy (B_Ent1), normalized bispectral squared entropy (B_Ent2) and bispectral cubed entropy (B_Ent3) (**Chua, et al. 2006; Chua, et al. 2009**) are also computed in this algorithm.

Hu's Moments: A set of moments functions are generally used to characterize the patterns in images (**Hu 1962**). They also provide the information about the different types of geometrical features of an image. Two dimensional moment of an image $f(x, y)$ is given by,

$$m_{pq} = \sum \sum x^p y^q f(x, y) \quad 5.2$$

For $p, q = 0, 1, 2, \dots$ the central moment and is defined as,

$$\mu_{pq} = \sum \sum (x - \bar{x})^p (y - \bar{y})^q f(x, y) \quad 5.3$$

Where $\bar{x} = \frac{m_{10}}{m_{00}}$ and $\bar{y} = \frac{m_{01}}{m_{00}}$ are the centroid of the binary image. The normalized central moment of order $(p+q)$ is defined as,

$$\eta_{pq} = \frac{\mu_{pq}}{\mu'_{00}} \quad 5.4$$

Where, $\gamma = \frac{p+q}{2} + 1$.

For this chapter algorithm, seven moments that are invariant to object scale, position, and orientation proposed by (**Hu 1962**) is used.

Gabor Transform: Gabor features helps to capture subtle deviations in the pixels (**Ma, et al. 1996**). A 2D Gabor function ($g_{l,k}(p, q)$) is obtained as follows,

$$g_{l,k}(p, q) = \left(\frac{1}{2\pi\sigma_p\sigma_q} \right) \exp \left[-\frac{1}{2} \left(\frac{p^2}{\sigma_p^2} + \frac{q^2}{\sigma_q^2} \right) + 2\pi j \omega p \right] \quad 5.6$$

Where ω is the frequency of sinusoid, $\sigma_p = 1/2\pi\sigma_x$ and $\sigma_q = 1/2\pi\sigma_y$ represents the standard deviation (SD) of the Gaussian envelopes (**Manjunath, et al. 1996**). The σ_p and σ_q are the filter parameters.

Let us consider $I(p, q)$ is a given IR image. Gabor transform of $I(p, q)$ is calculated as,

$$G_{l,k}(p, q) = I(p, q) * g_{l,k}(p, q) \quad \text{for } l = 1, 2, \dots, S \text{ and } k = 1, 2, \dots, K$$

5.7

Where, $*$ is convolution operator.

The μ_{lk} (mean) and σ_{lk} (standard deviation) of transform coefficients are used as features (Manjunath, et al. 1996). They are computed as follows,

$$\mu_{l,k} = \frac{1}{P^2} \sum_{p=1}^P \sum_{q=1}^Q |g_{l,k}(p, q)| \quad 5.8$$

$$\sigma_{l,k}(p, q) = \left(\frac{1}{P^2} \sum_{p=1}^P \sum_{q=1}^Q (|g_{l,k}(p, q)| - \mu_{l,k})^2 \right)^{1/2} \quad 5.9$$

For this proposed chapter experiment, I have used $K = 6$ orientations and $S = 4$ scales, obtaining total of 48 features which are denoted as,

$$f = (\mu_1, \sigma_1, \dots, \mu_{48}, \sigma_{48}) \quad 5.10$$

Energy (E): This is also known as uniformity, and is used as a measure of information present in the image.

$$E = \sum_i \sum_j p(i, j)^2 \quad 5.11$$

where $p(i, j)$ is the probability of occurrence of gray levels (i, j) .

Local Binary Pattern (LBP): It is used as a texture descriptor and was proposed by Ojala, et al. 1996. LBP of a pixel with intensity g_p using P points in its circular neighborhood of radius R is calculated as,

$$LBP_{P,R}^{orig} = \sum_{p=0}^{P-1} s(g_p - g_c)$$

5.12

where

$$s(x) = \begin{cases} 1, & x \geq 0 \\ 0, & x < 0 \end{cases}$$

A rotation invariant measure called $LBP_{P,R}$ using the uniformity measure $U \leq 2$ is calculated based on the number of transitions in the neighborhood pattern as,

$$LBP_{P,R}(x) = \begin{cases} \sum_{p=0}^{P-1} s(g_p - g_c) & \text{if } U(x) \leq 2 \\ P + 1 & \text{otherwise} \end{cases}$$

5.13

where

$$s(x) = \begin{cases} 1, & x \geq 0 \\ 0, & x < 0 \end{cases}$$

In this current chapter, I have calculated energy and entropy of the LBP image at different radius, $R = 1, 2$, and 3 and points in circular neighborhood, $P = 8, 16$, and 24 values. Thus, total of six LBP features are obtained.

Entropies: These are extensively used to quantify the uncertainty present in the images. In this chapter work, following different entropies are used to quantify the subtle changes in the image pixel intensities (**Acharya, et al. 2007; Yu, et al. 2013**).

Shannon's Entropy (ShEnt) is the most frequently used measure of order in a dynamical system (**Shannon 1948, Renyi 1961**). Consider $f(x, y)$ is the normal or MI image which having N_i ($i = 0, 1, 2, 3, \dots, L-1$) distinct gray levels. Shannon's entropy is given as,

$$Sh_Ent = - \sum_{i=0}^{L-1} p_i \log_2 p_i$$

5.14

Where p_i is the probability of occurrence of gray level i , is a normalized histogram

Renyi's Entropy (REnt) is a generalized form of Shannon's entropy (**Renyi 1961**). In this chapter, I have used the value of $q = 3$ and determined the R for normal and MI classes using equation (**Renyi 1961**),

$$REnt = \frac{1}{1-q} \log_b \sum_{i=1}^N p_i^q \quad (q \neq 1) \quad 5.15$$

Kapur's Entropy (KEnt) is the generalized entropies of Kapur of order α and type β is given as (Pharwaha, et al. 2009, Gupta, et al. 2010).

$$K_Ent^K(p) = \frac{1}{\beta - \alpha} \log_2 \left(\frac{\sum_{i=1}^N p_i^\alpha}{\sum_{i=1}^N p_i^\beta} \right) \quad \alpha \neq \beta, \quad \alpha, \beta > 0 \quad 5.16$$

Yager's Entropy (Y_Ent): It is computed using,

$$Y_Ent = 1 - \frac{\sum_{i=0}^{L-1} |2p_i - 1|}{|M \times N|} \quad 5.17$$

Fuzzy Entropy (FEnt) represents the information of randomness and is defined as the entropy of fuzzy set whose elements have different degrees of membership (Kosko 1986). It is calculated as,

$$F_Ent[A] = \int_{-\infty}^{\infty} S(C_r\{A \geq t\}) dt \quad 5.18$$

Where A is the fuzzy variable, C_r is the credibility measure.

5.2.5 Feature Ranking

All the features extracted from textons (8 maximum filter responses) are not significant for the differentiation of MI and normal. In addition, it is difficult to identify useful features from the extracted features. Hence, in order to select the significant features and rank them, I have used t-test and fuzzy mRMR ranking methods (Gonzalez 2007). The *t-test* identifies whether the two classes are different or not, by calculating the *mean*. This test returns the *p-value* and *t-value* which are used to discriminate the two classes (normal and abnormal) and to rank the extracted features. *Fuzzy mRMR method* searches the features where the mutual

information between independent feature and target is maximum, similarly minimum redundancy is used to identify the features that are mutually maximally distant (Peng, et al. 2005). These two criteria are combined in mRMR to avoid the correlated and redundant features. Mutual information between the features is computed using fuzzy entropy (Khushaba, et al. 2011). Among these two methods, fuzzy mRMR ranking method performed better in ranking the extracted features.

5.2.6 Myocardial Infarction Index (MII)

It would be difficult to track how much each of the selected features vary from the normal and MI cases, in order to make an accurate diagnosis. Even though classifiers can be used for diagnosis, it is more convenient for clinicians' to use a single number that is distinctly different for the two classes. This concept of integrated index is conceived by Ghista (Ghista 2004; 2009a; 2009b). Accordingly, I have formulated an integrated index called the *MI*, by combining the most distinguishing features in such a way that the integrated index value is distinctly different for normal and subjects with infarcted myocardium.

5.2.7 Classification

In this chapter work, highly ranked significant features are subjected to different classifiers namely Decision tree (DT) (Larose 2004a; Duda, et al. 2012), k-Nearest Neighbor (kNN) (Larose 2004b; Duda, et al. 2012), Probabilistic Neural Network (PNN) (Wasserman 1993; Duda, et al. 2012) and Support Vector Machine (SVM) (Duda, et al. 2012) for the classification of normal and MI classes. For SVM classifier, different kernels are used, such as polynomial 1, 2, 3, and radial basis function (RBF). Ten-fold cross validation method is used to validate the performance of the classifiers.

5.3 Results

This proposed chapter analyses cross-sectional view of echocardiography images texture characteristics using textons (8 maximum filter responses) approach. Various features such as Fractal Dimension (*FD*), Higher-Order Statistics (HOS), Hu's moments, Gabor Transform features, Yager's Entropy (*Y_Ent*), Fuzzy Entropy (*FEnt*), Energy, Local binary Pattern (*LBP*), Renyi's Entropy (*REnt*), Shannon's Entropy (*ShEnt*), and Kapur's Entropy (*KEnt*) are extracted from textons of apical four chambers view of echocardiography images obtained using MR8 filters.

A total of 1138 features are obtained from textons. The features extracted from cross-sectional view are statistically significant ($p < 0.0001$). All the 1138 features from cross-sectional views are ranked by using t-test and fuzzy mRMR ranking tests. Among the two ranking tests used, the fuzzy mRMR method has yielded the highest classification performance. The results are shown in this section.

Tables 5.1 and **5.2** and **Figures 5.4** and **5.5** show the results (mean $\pm$ SD) of features obtained by using the two ranking methods used, from textons (filter responses) for cross-sectional view of echocardiography images. **Tables 5.1** and **5.2** list the top 8 and 15 textural features of apical four chamber views of echocardiography images, ranked using fuzzy mRMR method and t-test respectively.

Table 5.1: Results (mean and SD) of 8 highly ranked features (ranked using fuzzy mRMR) obtained from apical four chambers view echocardiography images ($p<0.0001$).

Features	Normal		MI		Criterion
	Mean	SD	Mean	SD	
5_V1_Gabor32	5.49E-04	2.77E-04	15.11E-04	5.39E-04	609
5_V1_Gabor20	25.13E-04	13.32E-04	67.58E-04	22.07E-04	597
5_V1_Gabor10	22.62E-04	9.69E-04	56.19E-04	17.52E-04	587
5_V1_Gabor9	12.51E-04	5.51E-04	31.87E-04	11.12E-04	586
5_V1_Gabor8	52.61E-04	24.49E-04	97.20E-04	23.45E-04	585
5_V1_Gabor2	25.10E-04	17.45E-04	8.21E-04	4.23E-04	579
4_V1_B_Ent2_10	0.382	0.080	0.207	0.153	517
4_V1_B_Ent2_9	0.407	0.064	0.223	0.147	516

V₁ = view 1, apical four chambers view.

Figure 5.4: Bar graph of features versus mean values of features ranked using fuzzy mRMR method.

Table 5.2: Results (mean and SD) of top 15 highly ranked features (ranked using t-test) obtained from apical four chambers view echocardiography images ($p < 0.0001$).

Features	Normal		MI		t-value
	Mean	SD	Mean	SD	
5_V1_B_Ent3_10	0.292	0.057	0.071	0.110	15.845
5_V1_B_Ent2_10	0.356	0.071	0.108	0.126	15.206
5_V1_Gabor10	22.62E-04	9.69E-04	56.19E-04	17.52E-04	14.990
5_V1_Gabor20	25.13E-04	13.32E-04	67.58E-04	22.07E-04	14.729
5_V1_Gabor22	8.48E-04	3.23E-04	22.26E-04	7.74E-04	14.706
5_V1_B_Ent2_9	0.300	0.051	0.125	0.096	14.439
5_V1_B_Ent3_9	0.236	0.050	0.076	0.087	14.256
5_V1_Gabor32	5.49E-04	2.77E-04	15.11E-04	5.39E-04	14.194
5_V1_Gabor9	12.51E-04	5.51E-04	31.87E-04	11.12E-04	13.952
5_V1_Gabor34	1.06E-04	0.30E-04	2.29E-04	0.73E-04	13.756
5_V1_Gabor4	50.36E-04	12.13E-04	22.52E-04	13.79E-04	13.561
5_V1_B_Ent1_2	0.465	0.071	0.617	0.071	13.484
5_V1_Gabor21	4.94E-04	1.91E-04	12.91E-04	4.92E-04	13.481
5_V1_Gabor31	2.20E-04	1.24E-04	6.85E-04	2.84E-04	13.416
5_V1_Gabor19	14.17E-04	7.37E-04	36.18E-04	12.92E-04	13.241

Figure 5.5: Bar graph of features versus mean values ranked using t-test method.

It can be seen from this **Tables 5.1 - 5.2**, and **Figures 5.4 - 5.5** that, entropy values are high for normal as compared to MI due to more sudden changes in the pixels in normal echocardiogram. Pixels in images of MI class exhibit less variation due to the insufficient blood flow to the myocardium.

5.3.1 Results of Myocardial Infarction Index (MII)

In this proposed chapter work, the MII is developed using the high ranking features from apical four chambers echocardiogram view images. So 5_V₁_Gabor20 and 5_V₁_Gabor10 features (ranked using fuzzy mRMR method) are selected from **Table 5.1**. I have then adroitly combined them to develop the optimally distinguishing index. So the mathematical formulation of this Integrated MI Index is given by,

$$MII = 22.62 \times (5_V_1_Gabor20) - 100 \times (5_V_1_Gabor10) \quad 5.19$$

The above equation (5.19) is developed by trial and error method to get maximum discrimination between the two classes. I have used the highly ranked two features to formulate the MII. The ranges of MII for subjects with infarcted myocardium and normal people are shown in **Table 5.3**. **Figure 5.6** shows the plot of MII for two classes. This MII can be further improved by taking better features and more subjects in each class.

Table 5.3: Ranges of MII for normal and MI subjects.

Normal		MI		<i>p</i> -value
Mean	SD	Mean	SD	
0.263	0.073	0.802	0.127	< 0.001

Figure 5.6: Plot of MII for normal and MI subjects.

5.3.2 Results of Classification

All the features extracted from apical four chambers view are subjected to DT, k-NN, PNN and SVM classification one by one according to their ranking, for automated classification.

The classifiers are evaluated with all the 1138 features extracted from textons – 8 maximum filter responses. It is found that, only 8 highly ranked features from apical four chambers view, by using *fuzzy mRMR* ranking method, have yielded the highest classification accuracies. Several combinations of the highly ranked features (8) are tested to train the classifiers by using ten-fold cross validation.

Tables 5.4 and **5.5** show the classification results of features ranked using fuzzy mRMR and t-test respectively. **Table 5.4** shows the highest classification results obtained for features from apical four chambers view (ranked by fuzzy mRMR) using PNN classifier with ten-fold cross validation. It can be seen from

Table 5.4 that the PNN classifier achieved significantly highest accuracy of 94.37%, sensitivity of 91.25% and specificity of 97.50% using *8 best features* extracted from apical four chambers view of echocardiography images.

Thus, only the 8 features from textons representation of apical four chambers view more significantly differentiated normal and infarcted myocardium using PNN classifier. Hence, viewing the myocardium using textons and extracting features using image processing methods from those textons helps to assess the MI patients accurately.

Table 5.4: Classification results using features (ranked using fuzzy mRMR) obtained from apical four chambers view echocardiography images.

Best Classifier	No. of Features	TP	TN	FP	FN	Accuracy	Sensitivity	Specificity
PNN – 0.02	8	73	78	2	7	94.37%	91.25%	97.50%

TP = true positive; TN = true negative; FP = false positive; FN = false negative

Table 5.5: Classification results using features (ranked using t-test) obtained from apical four chambers view echocardiography images.

Best Classifier	No. of Features	TP	TN	FP	FN	Accuracy	Sensitivity	Specificity
DT	15	70	75	5	10	90.20%	87.50%	93.70%

5.4 Novelty of Proposed Chapter Technique

In the previous chapter 4, multi-resolution decomposition technique (the time-invariant method) SWT is employed and two cross-sectional echocardiography views (parasternal short-axis and apical four chambers views) images captured during the end systole two frames per patient (one frame from each view per patient) are analyzed to characterize normal and infarcted myocardium. The proposed technique of Chapter 4, is able to characterize MI with an average accuracy

of 95.0%, sensitivity of 93.7% and specificity of 96.2% using 32 features extracted from parasternal short-axis view; an accuracy of 96.2%, sensitivity of 97.5% and specificity of 95.0% with 18 apical four chamber view features. In addition, experiment has reported an average accuracy of 96.8% with 16 features extracted from combined parasternal short axis view at level of papillary muscles and apical four chambers view (*only two frames*). The results showed that the features obtained by combining parasternal short axis and apical four chamber views of echocardiography images are efficient in identifying MI. The results also indicate that the texture characteristics analysis of cross-sectional view echocardiography images aid the cardiologists to make faster assessments. Therefore, in this proposed chapter work, texton-based texture analysis method is employed on apical four chambers cross-sectional echocardiography image view captured during the end systole *single frame per patient* and is analyzed to characterize MI. The main advantage of using this method is that it extracts minute changes in images, by capturing different orientations information in the image at different scales (**Zhu, et al. 2005**). This property of texton-based image texture characteristic analysis approach helps to study of pixel variations in cross-sectional echocardiography images. The novelty of this chapter is the formulation and development of *MII*, which differentiates clearly the normal and infarcted myocardial cross-sectional echocardiography images using a single number.

Abnormal features in any of the four chambers (LA, LV, RA, and RV) of the heart and wall motion abnormalities can be evaluated from apical four chambers view. In addition, the end systolic phase of cardiac cycle exhibits significant information about the health of myocardium (**White, et al. 1987**). The cross-sectional view of echocardiography captured during the end systolic phase aids clinicians in assessing the end systolic volume or ejection fraction, which helps to predict the survival after MI (**White, et al. 1987**). Thus, the proposed current algorithm is able to detect minute pixel variations in cross-sectional views of echocardiography images

effectively using a single number (**MII**). Comparison of proposed technique with other literature in detection of infarcted myocardium using different cross-sectional echocardiography images is tabulated in **Table 5.6**.

In my previous proposed algorithm (**Chapter 4**) an accuracy of 96.8% is obtained using 16 features extracted from combined parasternal short axis view at level of papillary muscles and apical four chambers view (*two frames per patient*) . But, in this chapter, **MII** is developed which is able to differentiate normal and infarcted myocardium using a single number; and accuracy of 94.7% is achieved using *only 8 features* extracted from apical four-chamber view echocardiography using only *single frame per patient*. Thus, the cardiologist will have a faster assessment for the patient using the proposed MII. The highlights of this method can be summarized as follows:

1. To the best of my knowledge, this is the first study which uses textons of cross-sectional echocardiography images to characterize the MI. The novel part of this chapter work is the formulation of **MII** using echocardiography image features.
2. It is fast, reliable and completely automated. The proposed system takes maximum five minutes for the computation of one patient's images.
3. It uses *single frame* (one frame of end systole patient) of cross-sectional echocardiography images. Hence, involves less computation as compared to my previous proposed chapter (**Chapter 4**).
4. There is no manual extraction of ROI, and it is completely automated.

5.5 Summary

Currently, cardiologists view the LV myocardium at different cross-sectional planes to manually assess various parameters. This manual and visual evaluation of all the significant features from a pool of different cross-sectional views is tedious,

laborious and time consuming. Automated assessment of MI by extracting the features from various views by using my proposed method will help the cardiologists in efficient and fast assessment of MI patients. Thus, this chapter proposes a novel *MII* formulated using automatically extracted features from end-systolic cross-sectional echocardiography view (apical four chambers) for characterizing MI patients. I have used textons-based approach using MR8 filters to extract the features. My proposed technique in this chapter is able to characterize MI with an average accuracy of 94.37%, sensitivity of 91.25% and specificity of 97.50% with 8 apical four chamber view features extracted from only *single frame per patient* making this a more reliable and accurate classification. The algorithm has achieved an average specificity of 97.5% with 8 features extracted from apical four chambers view (*only single frame per patient*). This proposed MII has the potential to be used as reliable tool for the diagnosis of MI patients. This system can even be employed in the polyclinics and hospitals in the third world countries to reliably and effectively diagnose the cardiac health of patients.

In the next chapter, an algorithm for determining the extent of infarcted myocardium and designating myocardium according to the amount of infarction (normal, moderately infarcted and severely infarcted myocardium) is presented.

Table 5.6: Comparison of proposed technique with other literature in detection of infarcted myocardium using different cross-sectional echocardiography images.

Author (year)	No. of subjects	Image View used	Method and Features	Classification	Performance
		ROI or Image			
Skorton, et al. 1983- Animal study	7 adults dogs	LV short axis view at papillary muscle level	Gray level distribution, kurtosis, skewness	Manual classification	Sensitivity = 90% Specificity = 70%
		ROIs of normal and infarcted			
Kamath, et al. 1986- Paediatric study	15 premature infants (6 with myocardial necrosis and 9 normal myocardium)	Parasternal long axis and four chamber views	Gray levels amplitude (pixel intensity)	Statistical classification	Not mentioned
		Image frames			
Tak, et al. 1992	17 (5 normal and 12 MI)	Parasternal long axis view of LV, parasternal short axis view of LV, apical four- and two-chamber views	Pixel intensity	Statistical classification	Mean pixel intensity on 1 st day = 20.4 ± 2.0 vs 24.3 ± 2.3 and 14 th day = 20.5 ± 1.7 vs 31.9 ± 3.7
		Image frames			

Mojsilovic, et al. 1997	15	Apical two chambers view	Energy computed from wavelet coefficients	Unsupervised classification	Classification rate = 96%
Neskovic, et al. 1998	18	Apical four chambers view	Energy computed from wavelet coefficients	Unsupervised classification – distance classifier	<u>Day 2</u> Accuracy = 78% Sensitivity = 73% Specificity = 86% <u>Week 1</u> Accuracy = 89% Sensitivity = 91%, Specificity = 86% <u>Week 3</u> Accuracy = 100% Sensitivity = 100% Specificity 100%
		ROI of normal and MI			
Agani, et al. 2007	17	Apical views	Wavelet and GLCM	Mahalanobis distance classifier	Accuracy = 91.32%
Moldovanu, et al. 2011	12 (6 normal and 6 MI)	Apical two chambers view	Mean gray level, skewness, kurtosis, entropy		Entropy = 6.23 ± 0.52 vs 9.95 ± 0.17
Vidya, et al. 2015 a (Chapter 3)	160 (80 normal and 80 MI)	Parasternal short axis view	DWT, GLCM, HOS	SVM	<u>DWT</u> Accuracy = 99.50% Sensitivity = 99.75% Specificity = 99.25% Using 16 features <u>GLCM</u>

		Image frames (<i>five frames per patient</i>)			Accuracy = 85.75% Sensitivity = 90.25% Specificity = 81.25% Using 16 features <u>HOS</u> Accuracy = 93.00% Sensitivity = 94.75% Specificity = 91.25% Using 23 features
Vidya, et al. 2015c (Chapter 4)	160 (80 MI and 80 non-MI)	Parasternal short axis view at level of papillary muscle and apical four chamber view during end systole	Stationary Wavelet Transform and Relative wavelet energy and entropy	SVM	<u>Parasternal short axis view</u> Accuracy = 95.0% Sensitivity = 93.7% Specificity = 96.2% Using 32 features <u>Apical four chamber view</u> Accuracy = 96.2% Sensitivity = 97.50% Specificity = 95.0% Using 18 features <u>Parasternal short axis + apical four chambers</u> Accuracy = 96.8% Sensitivity = 93.7% Specificity = 100% Using 16 features
		Image frames (<i>two frames per patient</i>)			
Current method (Chapter 5)	160 (80 MI and 80 non-MI)	Apical four chamber view during end systole	Textons and FD, LBP, Entropies, Hu's moments, Gabor transform, HOS and MII	DT, kNN, SVM and PNN	<u>* MII is developed to differentiate normal and MI using a single number.</u> Accuracy = 94.37% Sensitivity = 91.25% Specificity = 97.50% Using 8 features
		Image frames (<i>single frame per patient</i>)			

CHAPTER 6. DATA MINING FRAMEWORK FOR IDENTIFICATION OF MYOCARDIAL INFARCTION STAGES IN ULTRASOUND: A HYBRID FEATURE EXTRACTION PARADIGM

6.1 Introduction

In the previous chapter, I have formulated an integrated index for the identification of infarcted myocardium using one of the cross-sectional echocardiograms. The results showed that texture analysis technique (textons-based feature analysis) employed to analyze the apical echocardiography images captured from four chambers cross-sectional view is efficient in characterizing the normal and infarcted myocardium. Therefore, in this chapter, I have extended my concept of texture analysis of apical view four chambers cross-sectional echocardiograms for the identification of the extent of infarcted myocardium. In this chapter, another novel algorithm namely Curvelet Transform and Local Configuration Pattern (LCP) are employed (i) for an automated detection of normal, moderately infarcted and severely infarcted myocardium and (ii) to develop an integrated index using cross-sectional view of echocardiography images.

Clinically, it is a routine practice for cardiologists to use different cross-sectional planes with various positions of transducer to assess 17 left ventricular wall segments (Cerqueira, et al. 2002) and view myocardial infarct downstream of all three coronary arterial territories (left anterior descending artery: mid anterior, mid anteroseptal, inferoseptal, distal septal and apical walls; circumflex artery: basal anterolateral, mid

anterolateral, inferolateral, and distal lateral; right coronary artery: proximal inferoseptal, and mid inferior walls). Using these 17 segments, the cardiologists compute the regional wall motion score, wall thinning or thickening and LV functions like Left Ventricular Ejection Fraction (LVEF), LV size or volume and LV geometry to detect the presence of infarct expansion and extent of infarcted myocardium (**Moller, et al. 2006; Carluccio, et al. 2000; Lang, et al., 2015**). Each segment is individually analyzed in multiple views and scored on the basis of its motion and thickening (**Lang, et al. 2015**). The Wall Motion Score Index (WMSI) equal to 2 indicates hypokinetic (reduced thickening), WMSI equal to 3 indicates akinetic (absent or negligible thickening, e.g. scar) and WMSI equal to 4 represents dyskinetic (systolic thinning or stretching, e.g. aneurysm). LVEFs less than 52% for men and less than 54% for women indicates abnormal LV systolic function. LVEF ranging between 41% - 53% indicates mild abnormal, 30% to 40% denotes moderately abnormal, and for severely abnormal class LVEF will be less than 30% (**Lang, et al. 2015**).

According to literature survey (**Chapter 2**), several echocardiographic methods and technologies have been developed to aid in the evaluation of myocardial infarction, infarct size (**Bauer, et al. 2011; Peng, et al. 2009**), wall shear stress values which are used to evaluate wall motion and indirectly assess infarct size (**Yuan, et al. 2011**). 3D echocardiography has been used to assess left ventricular wall motion abnormalities in a mouse model of MI (**Streiff, et al. 2015**). Although studies have used available echocardiographic techniques to evaluate infarct size, most of these methods have relied on visual analysis, leading to errors caused by operator subjectivity.

Computer-aided diagnosis system has been proposed to detect the myocardial infarct size and measure the myocardial perfusion using Myocardial Contrast Echocardiography (MCE) (**Du, et al. 2015**). However, it involves intravenous administration of contrast agent, thus making it an invasive method of diagnosis. Many

other approaches using echocardiography have been proposed to segment the ventricular cavity (Nandagopalan, et al. 2013; Sigit, et al. 2011), and epicardial boundary (Alessandrini, et al. 2013; Seng, et al. 2011). These methods do not evaluate and assess the extent of infarcted myocardium, though they are useful.

Thus, study of literature (**Chapter 2**) reveal that there are only few automated algorithms proposed for detection of infarcted myocardium using 2D echocardiography images. Texture characteristics are computed from 2D cross-sectional echocardiograms using various texture descriptors such as first – order statistics (Skorton, et al. 1983; Kamath, et al. 1986; Tak, et al. 1992), wavelet methods (Mojsilovic, et al. 1997; Neskovic, et al. 1998; Agani, et al. 2007), higher-order statistics and textons (**Chapter 3; Chapter 4**) to detect the normal and infarcted myocardium. Extensive review of these developed methods is reported in **Chapter 2**. To best of my knowledge, till date, no studies have been reported on automated detection of extent of infarcted myocardium using only 2D echocardiographic images.

6.2 Proposed Technique for Detection of Extent of Myocardial Infarction

In this chapter, Curvelet Transform is used on the apical view echocardiography images and LCP features are extracted from these curvelet transform coefficients for an automated detection of extent of infarcted myocardium. Furthermore in this chapter, an integrated index called *Myocardial Infarction Risk Index (MIRI)* is developed to detect the normal, moderately and severely infarcted myocardium using a *single* number. The curvelet transform aids in capturing the low and high frequency information of image pixels, whereas LCP helps to gather the local structural information and microscopic details of image pixels. **Figure 6.1** shows the proposed block diagram for automated detection of extent of infarcted myocardium. In this proposed algorithm,

echocardiography images of normal and infarcted myocardium are pre-processed and subjected to curvelet transform. The LCP features are then extracted from the curvelet transform coefficients. Later, all the extracted features are sent to different dimensionality reduction methods such as Principal Component Analysis (PCA), Kernel PCA (KPCA) with Gaussian, linear, polynomial and poly plus kernel functions, Locality Sensitive Discriminant Analysis (LSDA), Neighborhood Preserving Embedding (NPE), Locality Preserving Projection (LPP) and Marginal Fisher Analysis (MFA) to select the best reduction method. The features after reduction are ranked using fuzzy entropy based Max-Relevancy and Min-Redundancy (mRMR) test. Highly ranked features are then fed to different classifiers namely Decision Tree (DT), Discriminant (linear and quadratic), Fuzzy, k -Nearest Neighbour (k -NN), Näive Bayes (NB), Probabilistic Neural Network (PNN), and Support Vector Machine (SVM (polynomial 1, 2, 3 and Radial Basis Function (RBF))) one by one to obtain the best classification using minimum number of features. Also, an integrated index called *MIRI* is formulated using the highly ranked features extracted from three classes of echocardiography images. The novelty of this proposed method is that, it can differentiate a myocardium based on the extent of infarction as normal, moderately infarcted and severely infarcted myocardium using the 2D cross-sectional echocardiography images.

Figure 6.1: Block diagram of proposed methodology.

6.2.1 Data Acquisition

The normal and MI echocardiograms data required for this chapter experiment were obtained from database available at National Heart Centre (NHC), Singapore. I have collected echocardiography video sequences of 120 subjects: 40 normal and 80 MI (40 with moderate MI and 40 with severe MI) patients aged between 21 to 75 years both male and female were obtained from hospital's database (images from different

ultrasound scanners). For this study, I have collected the apical four chambers view echocardiograms. The echocardiography data used were obtained from the subjects' soon after onset of MI. Based on the clinician's decision and clinical parameters such as WMSI, LV diastolic and systolic function, and LVEF were used to categorize the echocardiography data collected in to normal, moderate MI and severe MI.

From each echocardiography video sequence of approximately same duration, 5 non-consecutive frames from each patient (having total of 20 frames) were obtained (i.e. 5 equally spaced frames from each sequence of 20 frames) automatically. These 5 frames chosen include both end diastolic and end systolic phases (i.e. one cardiac cycle) and also capture the sequence of myocardial wall motion. Total of 600 (200 images in each class) echocardiography images were obtained from 120 subjects. **Figure 6.2** shows normal, moderately infarcted and severely infarcted echocardiographic images of apical four chambers view.

Figure 6.2: Apical four chambers view echocardiography images of :(a) Normal, (b) Moderately infarcted and (c) Severely infarcted myocardium (categorized based on the wall motion score and Left ventricular ejection fraction (LVEF)).

6.2.2 Pre-Processing

In this experiment, obtained images are converted to grayscale and subjected to adaptive histogram equalization in order to improve the contrast (Gonzalez, et al. 2002). By performing this, the output images comprise a uniform distribution of intensity values.

6.2.3 Feature Extraction

In this step of feature extraction, the image texture characteristics are extracted using various texture analysis and image processing methods (Acharya, et al. 2013a; Acharya, et al. 2012b; Acharya, et al. 2013b). In the current chapter work, Curvelet Transform and Local Configuration Pattern (LCP) are used to extract the features from echocardiography images. A brief description of the methodology is given below.

Curvelet Transform

Curvelet transform is multiscale transform and proposed by Candes and Donoho (Candes, et al. 2000; 2002; 2004). The curvelet transform is higher dimensional generalization of the wavelet transform designed to represent images at different scales, orientations and locations.

The curvelet transform of function f can be expressed as,

$$c(j, l, k) := \langle f, \phi_{j, l, k} \rangle \quad 6.1$$

Where $\phi_{j, l, k}$ represents the curvelet and j, l, k denotes the scale, direction, and position parameter, respectively. And parameters are given by,

the scales, $a_j := 2^{-j}, j \geq 0$

the rotation angles, $\theta_{j,l} := \frac{\pi l 2^{-\lceil j/2 \rceil}}{2}$ with $l = 0, 1, \dots, 4 \cdot 2^{\lceil j/2 \rceil} - 1$;

the position, $b_k^{j,l} = b_{k_1, k_2}^{j,l} := R_{\theta_{j,l}}^{-1} \left(\frac{k_1}{2^j}, \frac{k_2}{2^{\lceil j/2 \rceil}} \right)^T$

where k_1, k_2 are spatial location parameters and R_θ denotes the rotation matrix with angle θ .

Take an input two-dimensional image in the form of a Cartesian array $f(x, y)$, where $0 \leq x < M$, $0 \leq y < N$ where M and N are the dimension of the array. Now, the outputs - curvelet coefficients $c^D(j, l, k)$ given as,

$$c^D(j, l, k) := \sum_{0 \leq x < M} \sum_{0 \leq y < N} f[x, y] \phi_{j,l,k}^D[x, y]$$

6.2

where $\phi_{j,l,k}^D$ denotes a digital curvelet transform, D represent digital.

In this chapter work, the curvelet transform is performed at scales = 3 (one coarse, one detailed and one fine) on the original echocardiography image.

Local Configuration Pattern (LCP)

LCP feature extraction method is a combination of local structural and microscopic configuration information. To extract the local structural information (local features), Local Binary Pattern (LBP) descriptor is used, and for microscopic configuration information (microscopic features), a Microscopic Configuration Model (MiC) is developed to capture image configuration and pixel-wise interaction relationships. **Figure 6.3** shows the frame work of LCP feature extraction.

Figure 6.3: Framework of LCP feature extraction.

Local Binary Pattern (LBP) – Based Local Features

LBP's are evaluated using circular neighborhood pixels by comparing center pixels with its neighborhood (Guo, et al. 2011; Acharya, et al. 2012c)

LBP of a pixel with intensity g_p using P points in its circular neighborhood of radius R is calculated as,

$$LBP_{P,R}^{orig} = \sum_{p=0}^{P-1} s(g_p - g_c)$$

6.3

where

$$s(x) = \begin{cases} 1, & x \geq 0 \\ 0, & x < 0 \end{cases}$$

A rotation invariant measure called $LBP_{P,R}$ using the uniformity measure $U \leq 2$ is calculated based on the number of transitions in the neighborhood pattern as,

$$LBP_{P,R}(x) = \begin{cases} \sum_{p=0}^{P-1} s(g_p - g_c) & \text{if } U(x) \leq 2 \\ P + 1 & \text{otherwise} \end{cases}$$

6.4

where

$$s(x) = \begin{cases} 1, & x \geq 0 \\ 0, & x < 0 \end{cases}$$

In this proposed chapter work, I have calculated LBP at different $R = 2, 3$ and 4 and $P = 8, 10$, and 12 values.

Microscopic Configuration Modeling (MiC) – Based Microscopic Features

In this section, a microscopic configuration model is developed to obtain microscopic features from echocardiography images which reflect textural properties. To develop MiC, the optimal weights of the neighboring pixel intensities are estimated which in turn helps to linearly construct central pixel intensity (Roweis, et al. 2000). It is calculated using,

$$E(a_0, \dots, a_{P-1}) = \left| g_c - \sum_{i=0}^{P-1} a_i g_i \right| \quad 6.5$$

Here, g_c and g_i represents the center and neighboring pixel's intensity values respectively. a_i ($i = 0, \dots, P-1$) represents weighting parameters associated with associated with neighboring pixel, and $E(a_0, \dots, a_{P-1})$ is the reconstruction error (Roweis, et al. 2000). Optimal parameters $W_L = (V_L^T V_L)^{-1} V_L^T C_L$ are computed to minimize the reconstruction error. Here, C_L is the least square problem and V_L is the neighboring pixel intensities (Roweis, et al. 2000).

Rotation invariant features $H_L(k)$ are obtained by applying 1D Fourier transform to the W_L . The magnitude of $H_L(k)$ is considered as MiC feature, which is computed as,

$$|H_L| = [|H_L(0)|; |H_L(1)|; \dots; |H_L(P-1)|] \quad 6.6$$

Where, $|H_L|$ encodes the image configuration and pixel-wise interaction relationships of each specific pattern and it together with pattern occurrences of LBPs would construct a final feature – LCP – for both the discrimination of microscopic configuration and local structures

$$\text{Thus, } LCP = [|H_0|; O_0]; [|H_1|; O_1]; \dots; [|H_{q-1}|; O_{q-1}] \quad 6.7$$

O_i represents the occurrence of the i th local pattern of interest (i.e. the LBP) and q denotes total number of patterns of interest.

6.2.4 Feature Reduction

Feature extraction produces enormous data that are difficult to analyze. Dimensionality reduction is one of the better methods to represent the original huge

data in a subspace using few data points (Chitra, et al. 2012; Gu, et al. 2014). In this study, performance of *nine* dimensionality reduction techniques namely PCA, KPCA with Gaussian, linear, polynomial and poly plus kernel functions, LSDA, LPP, MFA and NPE are experimented to select the best method. These methods are briefly explained below.

Principal Component Analysis (PCA): It is an unsupervised dimension reduction method which projects the data in the direction of maximum variability which results in minimum reconstruction error (Duda, et al. 2000). Initially, it extracts covariance matrix and eigenvector of covariance matrix computed in the later stage. Finally, the basic functions are the eigenvectors corresponding to the largest eigenvalues. A nonlinear form of PCA is introduced in (SchoElkopf, et al. 1998), which uses nonlinear kernel function instead of standard dot product. In this proposed chapter, I have used KPCA, using different kernel functions such as, linear, Gaussian, polynomial and poly plus kernels.

Locality Sensitive Discriminant Analysis (LSDA): It represents the given data into their both geometrical and discriminant structure (Cai, et al. 2007). For data samples nearest neighbor graph G is built which models the local geometrical structure of sub manifold. Further, k nearest neighbors of each data points is identified and put an edge between its neighbors. Thus, the weight matrix G can be defined (Cai, et al. 2007)

Later, two graphs are constructed, i.e. within-class graph and between-class graph. Their respective weight matrices W_b and W_w are computed. Finally, these weight matrices are used to optimize within-class and between-class objective functions in order to get good map of given data samples (Cai, et al. 2007).

Locality Preserving Projection (LPP): It is a linear projective map that results by solving a vibrational problem that most effectively maintains the neighborhood

structure of the data set. For the high dimensional data the LPP are computed by detecting the best linear approximations to the Eigen functions of the Laplace Beltrami operator on the manifold (He, et al. 2003).

Neighborhood Preserving Embedding (NPE): It is a linear dimensionality reduction technique with linear approximation to the locally linear embedding (Roweis, et al. 2000) algorithm. Initially, an adjacency graph is constructed and then weights on the edges are computed. Finally projection matrix is computed via a linear transformation (He, et al. 2005).

Marginal Fisher Analysis (MFA): It is a supervised learning algorithm which separates data from different classes by expanding the distances between margin data of different classes (Yan, et al. 2005; 2007). In this chapter work, within-class closeness is calculated as the sum of distances between each sample data and its neighbors within the same class using an intrinsic graph (Xu, et al. 2007).

6.2.5 Feature Ranking

In this chapter work, all the extracted features after reduction methods are subjected to ranking using fuzzy entropy based Max-Relevancy and Min-Redundancy (mRMR) technique (Peng, et al. 2005; Khushaba, et al. 2011).

6.2.6 Classification

DT (Duda 2012), Discriminant Classifier (Linear discriminant Analysis (LDA) and Quadratic Discriminant Analysis (QDA)) (Huang, et al. 2015; Khan, et al. 2011), k-NN (Han, et al. 2005), NB (Han, et al. 2005), PNN (Wasserman 1993) and SVM (Han, et al. 2005) classifiers are used in this chapter experiment.

Performance Measures

I have used ten-fold cross validation method to train and test the classifiers in this proposed chapter. A total of 600 images are split into ten parts (folds) randomly in such a way that, each fold has the equal proportion of images from three classes. In training phase, nine folds having 540 images are used for classifier's training. In the test phase, the trained classifiers are used in order to identify the remaining folds (60 images) classes and to evaluate the performance measures. This procedure is iterated 9 more times using different test sets. Later, the average of the performance measures acquired for each of the 10-folds is computed. The classifier's effectiveness in accurately classifying the images into their respective classes is obtained by the performance evaluation parameters namely accuracy, sensitivity and specificity.

6.3 Results

This proposed chapter analyses apical four chambers view of echocardiography images texture characteristics using CT and LCP approach. LCP features are extracted from CT coefficients of apical four chambers view of echocardiography images.

A total of 46,200 CT coefficients are obtained from 600 two dimensional echocardiograms of 120 subjects (40 normal, 40 moderately infarcted, and 40 severely infarcted). Total of 17,850 LCP features are extracted from 46,200 CT coefficients. The dimension of these computed LCP features are reduced using PCA, KPCA with Gaussian, linear, polynomial and poly plus kernel functions, LSDA, LPP, MFA and NPE reduction methods. Among these *nine* reduction methods used, the MFA method has achieved the highest classification performance. The results are shown in this section.

Using MFA reduction methods, a total of 17,850 LCP features are reduced to 30 MFA coefficients. These 30 MFA coefficients are ranked using fuzzy entropy based

mRMR method and the results (mean and standard deviation (SD) values) of MFA coefficients as shown in **Table 6.1** and **Figure 6.4**.

Table 6.1: Results of MFA coefficients for three classes' ranked using fuzzy entropy based mRMR ($p < 0.0001$).

Coefficients	Normal		Moderate		Severe	
	Mean	SD	Mean	SD	Mean	SD
MFA29	-1120.220	5.32E-06	-1107.550	3.618	-1111.270	0.161
MFA21	1126.451	2.5E-06	1113.868	4.432	1117.981	0.498
MFA14	147.663	4.2E-06	140.780	4.603	146.140	3.190
MFA8	7.629	4.06E-06	9.720	19.723	2.978	21.522
MFA5	320.932	2.03E-06	317.604	31.628	316.862	1.462
MFA1	977.131	5.35E-06	966.251	24.618	932.435	29.713
MFA3	-3021.600	4.82E-06	-2988.100	60.993	-2947.600	32.006
MFA12	381.550	3.96E-06	369.616	1.8250	370.234	3.704
MFA11	-7030.580	5.53E-06	-7039.990	4.442	-7039.570	2.872
MFA2	534.013	3.57E-06	523.807	17.896	530.877	33.402
MFA7	-286.544	5.63E-06	-280.060	18.054	-266.201	29.690
MFA4	755.525	8.79E-06	755.688	32.514	756.823	10.005
MFA9	1433.698	3.45E-06	1443.452	42.023	1456.998	27.134
MFA17	40.284	3.53E-06	56.394	4.304	57.893	0.720
MFA13	-178.893	2.32E-06	-187.098	3.885	-187.629	2.062
MFA6	117.761	3.36E-06	117.633	9.942	108.455	31.804
MFA16	587.915	3.35E-06	587.634	5.304	592.612	1.385
MFA10	1049.915	8.42E-06	1053.885	16.927	1029.404	48.744
MFA18	1965.061	6.24E-06	1960.415	1.831	1961.087	0.028
MFA25	-395.205	2.91E-06	-399.890	3.354	-401.582	2.003
MFA22	610.428	5.35E-06	614.898	3.341	613.570	0.821
MFA19	-1910.730	2.62E-06	-1905.330	3.263	-1904.660	2.357
MFA15	-994.731	3.15E-06	-993.875	4.329	-993.939	0.643

MFA20	-988.990	2.41E-06	-985.146	4.154	-984.071	2.513
MFA24	-2187.940	1.82E-06	-2185.360	1.617	-2185.680	1.519
MFA27	6575.762	3.3E-06	6567.416	7.598	6569.093	1.784
MFA26	-189.026	5.73E-06	-175.947	7.479	-179.348	0.963
MFA23	1105.676	4.32E-06	1099.674	3.034	1099.739	0.626
MFA30	693.641	3.89E-06	697.456	4.949	696.355	0.089
MFA28	406.352	2.2E-06	401.582	2.658	402.425	1.849

Figure 6.4: Bar graph of MFA coefficients versus mean values for LCP features ranked using fuzzy mRMR method

It is evident from **Table 6.1** and **Figure 6.4** that there is a slight separation between the three classes. The *mean* values of LCP features are lower for moderate and severe MI classes as compared to normal images, due to the insufficient blood flow to the myocardium. Thus, these patients exhibit low WMSI and LVEF in echocardiogram images as compared to normal subjects.

6.3.1 Results of classification

The ranked features are fed to the different classifiers one by one to obtain the highest performance using minimum number of features. **Table 6.2** shows the performance of different classifiers in classification of highly ranked (mRMR method) MFA coefficients obtained for LCP features.

Table 6.2: Results of classification using different classifiers.

Classifier	No. of Features	Accuracy	PPV	Sensitivity	Specificity
DT	5	97.31%	100%	95.94%	100%
LDA	13	98.65%	100%	97.97%	100%
QDA	13	86.55%	100%	79.74%	100%
NB	12	86.05%	100%	78.98%	100%
PNN	7	98.82%	100%	98.22%	100%
kNN	11	98.82%	100%	98.22%	100%
SVM Poly 1	17	99.15%	100%	98.73%	100%
SVM Poly 2	7	98.65%	100%	97.97%	100%
SVM Poly 3	6	97.81%	100%	96.70%	100%
SVM RBF	6	98.99%	100%	98.48%	100%

It can be observed from the table that the SVM classifier with RBF kernel achieved highest accuracy of 98.99%, sensitivity 98.48% and specificity 100% using only 6 features ranked by fuzzy mRMR method.

6.3.2 Comparative Results

Tables 6.3 – 6.7 show the results obtained with different reduction methods. **Table 6.3** and **Figure 6.5** show the *mean* and standard deviation values of highly ranked (using fuzzy mRMR method) LSDA coefficients obtained from LCP features.

Table 6.3: Results of LSDA coefficients for three classes' ranked using fuzzy entropy based mRMR ($p < 0.05$)

Coefficients	Normal		Moderate		Severe	
	Mean	SD	Mean	SD	Mean	SD
LSDA27	508.904	15.258	490.602	23.319	493.148	32.112
LSDA22	382.661	3.007	379.517	25.528	376.687	53.750
LSDA8	-1352.680	0.350	-1361.900	33.495	-1343.720	23.451
LSDA5	2253.177	0.195	2245.294	16.705	2263.439	54.232
LSDA6	2436.236	6.776	2421.960	60.957	2430.607	1.990
LSDA1	1318.007	0.070	1318.757	2.197	1315.451	39.674
LSDA3	-491.931	0.034	-495.908	26.731	-489.460	9.097
LSDA2	-497.254	0.874	-497.599	1.012	-494.330	40.295
LSDA7	-713.265	0.090	-724.923	52.715	-702.617	30.340
LSDA4	503.738	1.417	507.617	10.764	496.124	43.177
LSDA11	-731.557	7.198	-717.928	47.768	-727.949	6.751
LSDA9	-864.356	2.207	-876.958	40.547	-856.318	29.737
LSDA25	3678.196	8.859	3696.515	73.936	3686.359	7.735
LSDA20	-1474.960	9.968	-1457.160	60.911	-1467.980	6.283
LSDA12	-1790.710	0.093	-1780.200	55.610	-1800.500	34.600
LSDA21	3552.971	0.226	3538.384	93.702	3562.940	43.342
LSDA15	-49.992	3.098	-47.200	28.690	-62.714	51.262
LSDA10	-1599.210	4.085	-1608.860	48.772	-1602.290	21.951
LSDA13	2655.288	4.227	2657.811	23.780	2646.213	48.864
LSDA17	537.757	1.200	546.709	58.031	532.231	31.959
LSDA14	-1648.490	0.147	-1653.110	46.243	-1643.970	31.473
LSDA29	184.860	0.135	188.150	51.066	177.352	59.102
LSDA16	197.863	8.376	190.975	27.293	189.003	32.175
LSDA24	-1966.390	0.449	-1972.030	34.368	-1960.720	62.356
LSDA23	427.833	1.287	417.939	35.367	432.790	42.155
LSDA19	-112.914	0.720	-116.689	37.438	-105.315	37.459
LSDA18	1661.350	4.610	1666.604	27.103	1653.185	40.667
LSDA26	893.186	0.660	898.995	59.988	887.287	43.803
LSDA30	-290.080	12.956	-168.170	120.560	-163.326	111.196
LSDA28	-879.744	1.046	-880.898	42.665	-881.250	31.416

Figure 6.5: Bar graph of LSDA coefficients versus mean values for LCP features ranked using fuzzy mRMR method

Table 6.4 and Figure 6.6 shows the *mean* and standard deviation values of highly ranked (fuzzy mRMR method) kPCA linear coefficients obtained from LCP features.

Table 6.4: Results of kPCA coefficients for three classes' ranked using fuzzy entropy based mRMR ($p < 0.05$)

k-Principle components	Normal		Moderate		Severe	
	Mean	SD	Mean	SD	Mean	SD
kPC6	41081.620	416.366	40417.260	680.931	40296.940	454.656
kPC2	8304.063	1283.055	7199.519	1456.623	6967.394	1343.286
kPC1	-47792.200	1717.130	-48014.300	4120.521	-47519.900	4281.512
kPC8	-3316.050	29.772	-3340.230	78.379	-3282.170	712.701
kPC3	12042.570	648.980	11753.290	1154.198	12163.480	1323.599
kPC4	16401.270	413.128	16434.810	1173.854	16623.770	901.079
kPC13	3418.398	216.734	3269.325	404.016	3362.900	288.273
kPC7	37930.940	259.271	38245.080	759.710	38224.990	571.920
kPC26	-6849.330	161.791	-6727.960	126.611	-6714.450	131.224
kPC5	-23997.000	303.810	-24090.100	1303.825	-24091.100	686.717

kPC19	7496.313	150.279	7411.586	215.089	7471.019	207.962
kPC12	27775.670	193.757	27881.590	468.961	27874.470	232.649
kPC11	-967.344	607.370	-988.754	64.016	-986.791	50.523
kPC9	19742.370	271.235	19821.940	386.190	19844.180	438.639
kPC21	-2594.510	111.310	-2554.090	161.082	-2533.680	252.258
kPC10	-4726.290	142.422	-4705.570	232.440	-4686.390	577.065
kPC15	-43540.700	185.779	-43588.900	379.761	-43620.700	236.734
kPC27	4484.418	142.542	4543.339	179.860	4514.345	113.181
kPC16	-6952.490	245.912	-7013.570	270.058	-6923.830	288.598
kPC17	-3708.310	77.662	-3685.480	119.004	-3677.650	363.961
kPC14	7385.865	107.857	7392.680	474.996	7363.309	170.987
kPC28	2310.307	201.124	2293.956	121.826	2275.606	77.394
kPC25	-6064.220	136.186	-6061.090	197.014	-6106.100	159.785
kPC24	-2725.360	129.784	-2712.410	219.150	-2741.640	138.453
kPC18	-3363.530	176.253	-3392.390	214.439	-3394.580	242.745
kPC20	-142.561	174.724	-122.416	207.042	-144.073	204.690
kPC22	8771.240	109.832	8755.662	220.306	8770.935	186.858
kPC23	-11230.300	132.238	-11235.300	156.988	-11223.800	228.015
kPC30	-4256.500	145.446	-4270.830	151.772	-4265.870	112.770
kPC29	9948.979	109.365	9937.421	194.096	9936.930	88.035

Figure 6.6: Bar graph of k-principle components versus k-principle coefficients for LCP features ranked using fuzzy mRMR method.

Table 6.5 and **Figure 6.7** shows the *mean* and standard deviation values of highly ranked (fuzzy mRMR method) 30 PCA coefficients obtained from LCP features.

Table 6.5: Results of 30 PCA coefficients for three classes' ranked using fuzzy entropy based mRMR ($p < 0.05$)

Principle Components	Normal		Moderate		Severe	
	Mean	SD	Mean	SD	Mean	SD
PC6	41081.620	416.366	40417.260	680.931	40296.940	454.656
PC2	-8304.060	1283.055	-7199.520	1456.623	-6967.390	1343.286
PC1	-47792.200	1717.130	-48014.300	4120.521	-47519.900	4281.512
PC8	3316.049	29.772	3340.227	78.379	3282.169	712.701
PC3	-12042.600	648.980	-11753.300	1154.198	-12163.500	1323.599
PC4	-16401.300	413.128	-16434.800	1173.854	-16623.800	901.079
PC13	3418.398	216.734	3269.325	404.016	3362.900	288.273
PC7	37930.940	259.271	38245.080	759.710	38224.990	571.920
PC26	6849.326	161.791	6727.960	126.611	6714.448	131.224
PC5	23997.050	303.810	24090.090	1303.825	24091.050	686.717
PC19	-7496.310	150.279	-7411.590	215.089	-7471.020	207.962
PC12	27775.670	193.757	27881.590	468.961	27874.470	232.649
PC11	967.344	607.370	988.754	64.016	986.790	50.523
PC9	-19742.400	271.235	-19821.900	386.190	-19844.200	438.639
PC21	-2594.510	111.310	-2554.090	161.082	-2533.680	252.258
PC10	4726.285	142.422	4705.573	232.440	4686.394	577.065
PC15	-43540.700	185.779	-43588.900	379.761	-43620.700	236.734
PC27	-4484.420	142.542	-4543.340	179.860	-4514.340	113.181
PC16	-6952.490	245.912	-7013.570	270.058	-6923.830	288.598
PC17	3708.305	77.662	3685.478	119.004	3677.648	363.961
PC14	-7385.860	107.857	-7392.680	474.996	-7363.310	170.987
PC28	-2310.310	201.124	-2293.960	121.826	-2275.610	77.394
PC39	1719.945	89.052	1705.333	82.895	1688.237	158.714
PC121	-2082.270	49.562	-2091.470	37.660	-2075.500	40.962
PC79	1015.184	68.205	1027.784	49.709	1006.478	55.398
PC59	4728.853	67.345	4735.395	73.419	4703.064	85.726
PC36	-6091.950	157.311	-6074.810	79.266	-6101.750	110.769
PC25	-6064.220	136.186	-6061.090	197.014	-6106.090	159.785
PC24	2725.360	129.784	2712.407	219.150	2741.635	138.453
PC18	-3363.530	176.253	-3392.390	214.439	-3394.580	242.745

Figure 6.7: Bar graph of PCA coefficients versus principle components for LCP features ranked using fuzzy mRMR method

Table 6.6 and **Figure 6.8** shows the *mean* and standard deviation values of highly ranked (fuzzy mRMR method) LPP coefficients obtained from LCP features.

Table 6.6: Results of LPP coefficients for three classes' ranked using fuzzy entropy based mRMR ($p < 0.05$)

Coefficients	Normal		Moderate		Severe	
	Mean	SD	Mean	SD	Mean	SD
LPP4	945.041	26.772	1026.622	56.335	1049.167	60.818
LPP3	294.407	28.391	349.226	154.819	336.660	165.187
LPP2	-1892.950	1.02E-10	-1813.740	183.058	-1756.740	222.484
LPP1	-1770.440	8.94E-11	-1762.380	53.636	-1753.740	75.861
LPP14	58.423	2.128	66.685	61.138	47.874	47.485
LPP7	1146.297	27.662	1172.587	60.985	1159.422	50.776
LPP5	-597.411	0.011	-590.740	47.759	-603.065	62.553
LPP8	-755.751	36.689	-719.861	51.963	-726.647	46.018
LPP6	1191.165	51.263	1205.715	29.932	1196.338	28.298
LPP16	810.692	0.034	814.669	28.032	806.410	67.416
LPP19	-1650.620	4.908	-1656.110	26.833	-1642.870	54.667
LPP30	-196.630	0.111	-198.349	10.556	-195.754	56.088
LPP24	660.097	40.402	676.758	31.854	668.949	24.542
LPP13	-1317.130	41.141	-1306.040	32.180	-1307.800	29.012
LPP9	-1437.570	57.480	-1453.970	29.331	-1453.830	24.908

LPP10	781.056	7.437	786.730	36.557	782.388	50.385
LPP20	-1685.830	25.024	-1671.800	42.029	-1689.700	31.570
LPP11	-2671.550	42.997	-2664.480	32.377	-2666.140	28.810
LPP22	2561.647	25.066	2554.090	39.949	2545.036	32.410
LPP12	-563.114	37.782	-556.878	32.463	-557.755	32.913
LPP27	-575.966	43.898	-566.448	29.161	-578.697	18.741
LPP15	-331.040	34.121	-329.332	36.344	-326.601	19.017
LPP25	1086.441	24.971	1079.226	35.082	1090.763	39.453
LPP17	1060.075	5.451	1058.062	35.650	1060.251	61.667
LPP28	-450.886	36.859	-452.714	29.781	-442.139	23.073
LPP23	113.700	36.220	108.394	35.094	112.184	20.848
LPP21	216.793	7.046	216.524	31.779	213.095	47.034
LPP18	-1495.750	41.599	-1496.160	36.607	-1495.570	20.689
LPP29	427.413	20.493	426.553	37.727	431.324	37.835
LPP26	-171.860	15.546	-171.480	35.243	-170.085	44.090

Figure 6.8: Bar graph of LPP coefficients versus mean values for LCP features ranked using fuzzy mRMR method

Table 6.7 and **Figure 6.9** shows the *mean* and standard deviation values of highly ranked (fuzzy mRMR method) NPE coefficients obtained from LCP features.

**Table 6.7: Results of NPE coefficients for three classes' ranked using fuzzy entropy based
mRMR ($p < 0.05$)**

Coefficients	Normal		Moderate		Severe	
	Mean	SD	Mean	SD	Mean	SD
NPE17	-194.084	11.759	-275.468	47.262	-272.528	38.1326
NPE16	-499.972	6.194	-452.731	107.150	-441.577	92.688
NPE8	-647.371	0.553	-645.286	43.397	-656.965	33.916
NPE2	-443.205	0.842	-438.900	39.940	-425.712	47.746
NPE1	1758.600	0.903	1766.279	64.791	1781.861	69.569
NPE3	111.551	1.417	104.036	50.506	109.308	31.675
NPE4	1470.656	1.948	1464.513	36.511	1453.924	46.352
NPE5	-1570.460	2.009	-1560.790	52.760	-1555.930	42.648
NPE25	1219.443	6.5E-10	1214.820	29.329	1224.185	46.697
NPE24	-2.557	0.172	-7.866	12.917	3.428	76.636
NPE11	-795.852	0.120	-800.808	36.226	-807.337	33.150
NPE10	-493.035	0.949	-464.559	145.931	-463.974	52.853
NPE7	-1084.700	2.176	-1079.880	39.629	-1077.990	44.312
NPE6	133.203	1.891	131.338	30.065	134.087	51.657
NPE19	-71.657	3.187	-79.275	33.886	-71.029	41.032
NPE15	1792.580	1.077	1794.454	31.394	1797.415	33.238
NPE14	472.277	3.181	468.695	35.665	469.366	37.102
NPE12	-1381.020	7.234	-1377.160	35.015	-1376.780	37.645
NPE9	364.767	3.316	367.311	34.709	361.137	47.406
NPE18	37.904	7.38E-10	34.091	37.094	41.815	60.141
NPE13	-702.184	2.772	-700.664	30.849	-702.826	45.206
NPE29	-0.458	49.613	-14.118	29.675	-9.774	9.571
NPE22	462.136	48.433	453.721	34.789	456.138	25.953
NPE20	842.527	5.404	832.716	64.431	836.124	52.572
NPE27	1174.949	55.987	1168.856	20.711	1172.668	6.531
NPE26	-524.922	2.148	-521.460	29.653	-526.323	59.555
NPE21	2451.421	69.627	2446.390	18.523	2448.206	6.438
NPE23	705.280	30.709	706.640	37.535	707.989	28.620
NPE28	2804.438	48.472	2801.524	30.833	2805.527	7.803
NPE30	-765.204	5.388	-771.233	27.640	-764.593	72.484

Figure 6.9: Bar graph of NPE coefficients versus mean values for LCP features ranked using fuzzy mRMR method

Table 6.8 shows the results obtained using different dimensionality reduction techniques such as KPCA (Gaussian, linear, polynomial, poly plus), NPE, LPP, PCA, LSDA and MFA. Figures 6.10 – 6.18 shows the plot of performance versus the number of features used for the best classifier using MFA reduction method.

Table 6.8: Comparison of performance using different feature reduction methods for automated MI stages detection.

Reduction Methods	Classifier	No. of Features	Accuracy	PPV	Sensitivity	Specificity
KPCA Gaussian	SVM (RBF)	22	53.95%	74.49%	46.58%	68.5%
NPE	SVM (RBF)	30	84.37%	96.04%	79.75%	93.5%
LPP	SVM (RBF)	14	87.05%	98.77%	81.51%	98%

KPCA Poly Plus	PNN	24	93.61%	100%	90.38%	100%
PCA	SVM (RBF)	15	92.44%	99.44%	89.11%	99%
KPCA Polynomial	PNN	26	93.45%	100%	90.13%	100%
KPCA Linear	PNN	17	93.78%	100%	90.63%	100%
LSDA	kNN	11	98.48%	100%	97.72%	100%
MFA	SVM (RBF)	6	98.99%	100%	98.48%	100%

Figure 6.10: Plot of performances versus the number of features for SVM classifier using MFA.

Figure 6.11: Plot of performances versus the number of features for kNN classifier using LSDA.

Figure 6.12: Plot of performances versus the number of features for PNN classifier using kPCA-linear.

Figure 6.13: Plot of performances versus the number of features for PNN classifier using kPCA-polynomial.

Figure 6.15: Plot of performances versus the number of features for PNN classifier using kPCA – poly plus.

Figure 6.16: Plot of performances versus the number of features for SVM classifier using LPP.

Figure 6.17: Plot of performances versus the number of features for SVM classifier using NPE.

Figure 6.18: Plot of performances versus the number of features for SVM classifier using kPCA - Gaussian.

It can be seen from Table 6.8 that the features reduced using MFA technique has achieved highest performance. It can be seen from Figures 6.10 – 6.18 that, I have obtained the highest performance using only *six* ranked features.

6.3.3 Myocardial Infarction Risk Index (MIRI)

In the previous chapter (Chapter 5), the concept of integrated index conceived and developed by Ghista (Ghista 2004; 2009a; 2009b) was further advanced by developing an index called **Myocardial Infarction Index (MII)**. Accordingly, in this - chapter work, I have further extended the concept to formulate an integrated index called *Myocardial Infarction Risk Index (MIRI)* by combining the most distinguishing features to detect the extent of infarcted myocardium. The MIRI is formulated using MFA 8 and MFA 1 features from Table 6.1 as,

$$MIRI = (0.15 \times MFA 8) + (0.3 \times MFA 1) + 2.5 \quad 6.8$$

The equation (6.8) is obtained by trial and error technique which results in maximum discrimination between three classes (normal, moderate and severely infarcted myocardium). The values of MIRI for three classes are shown in Table 6.9 and the plot of MIRI is shown in Figure 6.19.

Table 6.9: Range of MIRI for normal, moderate and severely infarcted myocardium.

Normal Myocardium (n = 40)		Moderately Infarcted Myocardium (n = 40)		Severely Infarcted Myocardium (n = 40)		<i>p</i> -value
Mean	SD	Mean	SD			
6.575	0.066	7.376	0.193	5.876	0.118	< 0.001

Figure 6.19: Plot of MIRI for normal, moderate and severely infarcted myocardium.

6.4 Novelty of Proposed Chapter Technique

In this proposed chapter work, a novel automated algorithm for detection of infarcted myocardium stages (normal, moderate and severely infarcted myocardium) using 2D echocardiogram is developed based on texture features. The proposed method extracts the LCP features from CT coefficients of echocardiograms. This feature captures the variations in the microscopic and local structures. The essence of this CT is its ability to reduce the noise without losing much information contained in an image (**Zhang, et al. 2011**). In addition, it has the ability to capture the curvatures and small intensity components of image pixels (**Zhang, et al. 2011; Shukla, et al. 2013**). The LCP is useful in capturing the fine changes in image pixels and its neighborhood (**Huang, et al. 2011**). These excellent capabilities of CT and LCP methods make it an optimum choice for the

analysis of texture characteristics of echocardiography images. Other techniques such as first, second and higher-order statistics and wavelet transform texture descriptors have been explored by various researchers for the classification of normal and infarcted myocardium (Skorton, et al. 1983; Kamath, et al. 1986; Mojsilovic, et al. 1997; Moldovanu, et al. 2011).

In the previous chapter (**Chapter 5**), a novel index MII is developed for an automated infarcted myocardium characterization using Fractal Dimension (FD), Higher Order Statistics (HOS), Hu's moments, Gabor Transform, Fuzzy Entropy, Energy, Local Binary Pattern (LBP), Renyi's Entropy, Shannon's Entropy, and Kapur's Entropy extracted from Textons. The results showed a classification accuracy of 94.37% in detection of normal and infarcted myocardium using PNN classifier. As an extended work, in this chapter, I am able to effectively detect normal, moderate and severely infarcted myocardium based on texture characteristics of 2D echocardiogram images with an accuracy of 98.99% using only 6 features. Also, I have formulated and developed an integrated index *Myocardial Infarction Risk Index (MIRI)* for an automated differentiation of normal, moderately infarcted and severely infarcted myocardium using features extracted from echocardiograms. Comparison of proposed technique with other literature in detection of extent of infarcted myocardium using echocardiography images is tabulated in **Table 6.10**.

It is evident from below **Table 6.10** that, there is no study conducted till date on automated detection of infarcted myocardium stages using 2D echocardiograms. The proposed method extracts LCP features from CT coefficients of cross-sectional echocardiography images. The main advantage of using this method is that it extracts minute (microscopic) changes in images, by capturing both the spatial and frequency information in the images at different scales.

Generally, the cardiologists examine the heart from various cross-sectional planes with different transducer positions to cover the 17 left ventricular wall segments for the computation of wall motion abnormality score (**Cerqueira, et al. 2002**). Thus, the proposed method reduces the time required for examination; otherwise 17 different segments need to be studied. To best of my knowledge, this study result is the first of its kind to efficiently detect the extent of myocardial infarction using 2D echocardiograms.

The highlights of proposed chapter method are summarized below:

- It is fast, non-invasive and radiation free. The proposed system is completely automated and it takes maximum five minutes for the computation of one patient's images.
- There is no manual extraction of ROI and it is completely automated.
- The novelty of this chapter work is that, it may assist clinicians to locate the expansion of infarction and thereby assist in treatment.
- The proposed method may assist in identifying the person at risk of developing heart failure based on the extent of infarction.
- I have obtained the specificity of 100%, indicating that, all normal class is correctly identified by my proposed method. Thus reduces the work of clinicians by 33.3%.
- MIRI helps to identify the three classes using a single number.

6.5 Summary

It can be seen from **Table 6.10** that, this is the first study conducted to automatically identify different stages of myocardial damage using 2D echocardiograms. In this proposed chapter, a computer-aided diagnostic method is

proposed to analyze echocardiograms using texture characteristics to automatically classify myocardium into normal, moderately infarcted and chronically infarcted myocardium based on the extent of muscle damage. The proposed method is able to detect the three stages with an accuracy of 98.99%, sensitivity 98.48%, and specificity 100% using SVM classifier and only *six* features. In addition, the ***Myocardial Infarction Risk Index (MIRI)*** developed is able to identify the stages of MI based on the extent of infarction using a *single* number. The proposed method is effective, non-invasive, radiation free and economical. This system may subsequently help to identify the patient at risk of developing heart failure and may be employed as a supplemental device by the cardiologists to cross check their diagnosis. Such a system can be employed in the polyclinics and hospitals in the third world countries where there is shortage of cardiologists to diagnose the cardiac health.

Table 6.10: Comparison of studies on detection of infarcted myocardium using 2D echocardiography.

Author (year)	No. of subjects	Views used	Features	No. of Parameters	Classification	Results	Future works or Limitations (if any)
		ROI or images					
Two class classification : normal and infarcted myocardium							
Skorton, et al. (1983)	7 adults dogs	LV short axis view at papillary muscle level	Gray level distribution, kurtosis, skewness	3	Manual Analysis	Sensitivity = 90% Specificity = 70%	<u>Future implication (possibility):</u> To identify correctly areas of myocardial ischemia or infarction.
		ROIs of normal and infarcted					
Kamath, et al. (1986)	15 premature infants (6 with myocardial necrosis and 9 normal myocardium)	Four chambers view and Parasternal long axis view	Gray levels amplitude (pixel intensity)	1	Statistical Analysis	HREs detected in 6 myocardial necrosis patients. Pixel intensities in these HREs were higher than the range of normal tissue.	<u>Future possibility:</u> To explore the myocardial necrosis in survivors of prematurity
		Image frames					

Tak, et al. (1992)	17 (5 normal and 12 MI)	Parasternal long- and short- axis views of LV, apical four- and two-chambers views	Pixel intensity	1	Statistical Analysis	Mean pixel intensity on 1 st day is 20.4 ± 2.0 vs 24.3 ± 2.3 and 14 th day is 20.5 ± 1.7 vs 31.9 ± 3.7	<u>Future work:</u> To validate the usefulness of their developed technique
		Image frames					
Mojsilovic, et al. (1997)	15 MI	Apical two chambers view	Energy computed from wavelet coefficients	Not mentioned	Unsupervised classification	Classification rate = 96%	<u>Future Work:</u> Possible detection and characterization of other changes in myocardial structure (such as myocardial ischemia and cardiomyopathy)
		ROIs of normal and MI areas					
Neskovic, et al. (1998)	18 MI	Apical four chambers view	Energy computed from wavelet coefficients	Not mentioned	Unsupervised classification	<u>Day 2</u> Accuracy = 78% Sensitivity = 73% Specificity = 86%	<u>Limitation:</u> Application of their method in patients suffering from multi-infarct coronary artery disease.
		ROI of normal and MI				<u>Week 1</u> Accuracy = 89% Sensitivity = 91%,	

						Specificity = 86% <u>Week 3</u> Accuracy = 100% Sensitivity = 100% Specificity 100%	
Agani, et al. (2007)	17 MI	Apical views	Wavelet and GLCM (contrast, angular second moment, entropy, and inverse difference moment)	4 parameters from 4 sub-bands = 16	Mahalanobis distance classifier	Accuracy = 91.32%	Not mentioned
		ROIs					
Moldovan u, et al. (2011)	12 (6 normal and 6 MI)	Apical two chambers view of end-diastole and end-systole	Mean gray level, skewness, kurtosis, entropy during end diastole and end-systole	4	Statistical Analysis	Entropy = 6.23 ± 0.52 vs 9.95 ± 0.17	<u>Future work:</u> Not mentioned
		ROIs of normal and MI					

Vidya, et al. (2015a) (Chapter 3)	160 (80 normal and 80 MI)	Parasternal short axis view	DWT, GLCM, HOS	DWT = 16 GLCM = 16 HOS = 23	SVM	<u>DWT</u> Accuracy = 99.50% Sensitivity = 99.75% Specificity = 99.25% Using 16 features	<u>Future work:</u> Detection of normal and infarcted myocardium using different cross-sectional views of echocardiographic image
		Image frames (<i>five frames per patient</i>)					
Vidya, et al. 2015c (Chapter 4)	160 (80 MI and 80 non-MI)	Parasternal short axis view at level of papillary muscle and apical four chamber view during end systole	Stationary Wavelet Transform and Relative wavelet energy and entropy	120 features from each view	SVM	<u>Parasternal short axis view</u> Accuracy = 95.0% Sensitivity = 93.7% Specificity = 96.2% Using 32 features <u>Apical four chamber</u>	<u>Future work:</u> Development of an integrated index for detection of normal and infarcted myocardium

		Image frames (<i>two frames per patient</i>)				<u>view</u> Accuracy = 96.2% Sensitivity = 97.50% Specificity = 95.0% Using 18 features <u>Parasternal short axis + apical four chambers</u> Accuracy = 96.8% Sensitivity = 93.7% Specificity = 100% Using 16 features	
Vidya, et al. (2015b) (Chapter 5)	160 (80 MI and 80 non-MI)	apical four chambers view during end systole	Textons and FD, HOS, Hu's moments, Gabor transform, fuzzy entropy, energy, LBP, Renyi's entropy,	8	DT, SVM and PNN	<u>* MII is developed to differentiate normal and MI using a single number.</u> Accuracy = 94.37% Sensitivity = 91.25% Specificity = 97.50%	<u>Future work:</u> Detection of extent of infarcted myocardium (stages of MI)
		Image frames (<i>one frame per patient</i>)					

			Shannon's entropy, and Kapur's entropy				
Three class classification: normal, moderately and severely infarcted myocardium							
Current method (Chapter 6)	120 (40 normal, 40 moderate MI, 40 chronic MI)	Apical four chambers view Image frames (5 non-consecutive frames per patient)	Curvelet Transform and LCP features	6	DT, LDA, QDA, kNN, NB, PNN and SVM	Accuracy = 98.99% Sensitivity = 98.48% Specificity = 100% using 6 features <i>* MIRI is developed to differentiate normal, moderately and severely infarcted myocardium using a single number.</i>	Future work: Detection of mild, moderate, severe stages of infarcted myocardium, and Localization of infarcted myocardium

CHAPTER 7. LIMITATIONS

The proposed system has many advantages compared to conventional diagnosis method. Advantages of each algorithm proposed are summarized in their respective chapters. On the other hand, some limitations of the proposed system may be stated as follows:

1. The proposed system is completely automated and does not require human intervention. So, it may affect human skills in interpretation in the long run.
2. Extent of MI detection algorithm – MIRI - is developed using 5 non-consecutive frames from each patient (having total of 20 frames) i.e. 5 equally spaced frames from each sequence of videos having total of 20 frames. However, the variations of information might not be much within these 5 captured frames per patient.
3. The echocardiogram features of the different types of abnormalities, both mild and severe MI, have to be researched with the close association of cardiologists. Such a study can throw light on the stages of MI that give rise to further complications such as heart failure.
4. On the clinical side, there are practical concerns on the resolution and quality of the echocardiography images obtained due to the presence of speckle noise. These problems are to be diminished using robust pre-processing techniques.
5. The indices – MII and MIRI – formulated are validated over a relatively small number subjects. These indices are not validated clinically using a huge patient's data and with gold standard (contrast MRI).
6. The proposed system performance and robustness may deteriorate due to the error sources such as noise and artefacts in the images, and images representing calcium deposits in the myocardium, arteries and valves.

CHAPTER 8. CONCLUSIONS AND FUTURE RESEARCH

8.1 Conclusion

Handling the complexity of MI diagnosis, treatment, and prognosis would not have been possible without the currently available imaging systems. Current imaging systems play a major role in primary screening, diagnosis, staging (moderately or severely infarcted myocardium), treatment monitoring, and determine the recurrence of MI. In this research work, a comprehensive review of the presently available MI imaging modalities is done in order to understand the limitations of these imaging devices, and thereby lay out the possible areas that warrant for further research and development. It is evident from this review that there is no single modality that can be used to detect MI, myocardial contractility, LV remodeling, and extent of infarcted myocardium (MI stages) with significant accuracy in patients of all ages. Other limiting factors are cost, test time, radiation exposure, image resolution, test environment conditions, and subjectivity of interpretations of results. It is highly impossible that a single modality can be used for all conditions. Hence, hybrid modalities (multi-modalities approaches) like PET-CT and PET-MRI are being developed. These modalities have presented improved diagnostic capabilities for particular cardiac cases which are difficult to be assessed using a single imaging modality.

Moreover, adjunct modalities, which provide added confidence to the diagnosis made by primary modalities such as Electrocardiography (ECG), are finding their way into the market these days. One such adjunct device is the 2D transthoracic echocardiography (TTE). 2D echocardiography is based on using ultrasound for detection of MI.

One of the key objectives of this research work is to evaluate the efficiency of 2D echocardiogram in the detection of infarction and extent of MI. For this purpose, a retrospective study is designed, patient's data and 2D echocardiograms are collected from National Heart Centre (NHC), Singapore and the results analyzed. In this thesis several computer based texture analysis methods are applied on the collected 2D echocardiograms data to investigate the myocardium. Second-order spatial statistical analysis together with wavelet, Higher-order Spectra (HOS), Stationary Wavelet Transform (SWT), Textons, and Local Configuration Pattern (LCP) are used to extract echocardiogram image textural properties within the myocardium. These methods have been proved to be feasible alternatives that have unveiled further useful details of myocardium compared to previous methodologies such as manual and semi-automated techniques.

Using DWT, GLCM and HOS, a total of 140 textural features are extracted from the echocardiograms, out of which 16 features are derived from DWT and GLCM respectively, and 108 are from HOS. The reported findings showed that these features are effective in delineating the variations in echocardiogram texture among normal and infarcted myocardium groups, and a number of correlations among those features are described. This proposed approach for detecting normal and infarcted myocardium by comparing the three texture descriptors systematically exploits the underlying properties of two groups of echocardiograms to achieve robustness and computational efficiency. It is shown that the subtle variations in pixels can be effectively extracted or picked up by the proposed method especially DWT based analysis in the feature extraction step. Thus, further textural investigations on infarcted myocardial echocardiogram should provide better and deeper understandings of MI expansion and extent of MI.

On the other hand, investigations on myocardium in the cross-sectional views (parasternal short axis mid-left ventricular view at papillary muscle level and apical four chamber view) of echocardiograms texture characteristics have prompted discoveries. The SWT based texture analysis method is able to decompose a cross-sectional echocardiography image into a series of low and high-frequency coefficients. The key significance of this method is that it reveals fine or subtle variations in image pixels, by obtaining both the frequency and spatial details in the images at different scales. It is shown that this method analyzed both local and global parameters present in the image. This property of SWT method helped in the analysis of pixel variations in both cross-sectional views of echocardiography images effectively. The results showed that the SWT-based relative wavelet energy and entropy features obtained by combining parasternal short axis and apical four chamber views of echocardiography images are efficient in identifying MI as compared to individual cross-sectional echocardiography view. The results also indicated that the combined two views can aid the cardiologists to make faster assessments as this approach provided complete two views for the MI patient assessment.

Texton-based feature extraction method proposed led to the discovery of a new integrated index called *Myocardial Infarction Index (MII)* for an automated characterization of infarcted myocardium. *MII* developed is able to differentiate normal and infarcted myocardium using a single number; and specificity of 97.5% is achieved using *only 8 features* extracted from cross-sectional echocardiography view using only *single frame per patient*. The method used *single frame* (one frame of end systole per patient) of cross-sectional echocardiography images; hence, requires less computational time. This proposed MII has the potential to be used as more reliable tool for classification of MI patients. The proposed system can even be employed in the

polyclinics and hospitals in the third world countries to reliably and effectively diagnose the cardiac health of patients.

It is evident from literature survey that, there is no study conducted till date on automated detection of infarcted myocardium stages using 2D echocardiograms. This thesis work is the first study conducted to automatically identify different stages of myocardial damage using 2D echocardiograms. In this thesis, a computer-aided diagnostic method is proposed to analyze echocardiograms using texture characteristics to automatically classify myocardium into normal, moderately infarcted and chronically infarcted myocardium based on the extent of muscle damage. The proposed method extracted the LCP features from CT coefficients of echocardiograms. This feature captured the variations in the microscopic and local structures. The essence of this CT is its ability to reduce the noise without losing much information contained in an image. In addition, it has the ability to capture the curvatures and small intensity components of image pixels. Also, an integrated index *Myocardial Infarction Risk Index (MIRI)* is formulated and developed for an automated differentiation of normal, moderately infarcted and severely infarcted myocardium using features extracted from echocardiograms. In addition, the *MIRI* developed is able to identify the stages of MI based on the extent of infarction using a *single* number. The proposed method is effective, non-invasive, radiation free and economical. This system might subsequently help to identify the patient at risk of developing heart failure and might be employed as a supplemental device by the cardiologists to cross check their diagnosis.

Thus, contributions described in this thesis have led to the development of computer-efficient novel techniques that are capable of detecting normal and infarcted myocardium and extent of MI (normal, moderately infarcted and severely infarcted myocardium) using 2D echocardiography images. To best of my knowledge, this study result is the first of its kind to efficiently detect the extent of myocardial infarction using 2D echocardiograms.

The novelties of proposed algorithms in this thesis are summarized below:

- It is based on echocardiography, a non-invasive and radiation free imaging technique.
- It is fast.
- There is no manual extraction of Region of Interest (ROI) and it is completely automated.
- The system may assist clinicians to locate the expansion of infarction and thereby assist in treatment.
- The proposed method may assist in identifying the person at risk of developing heart failure based on the extent of infarction.
- The proposed system is completely automated and is ready to be installed or incorporated into the ultrasound machine for testing. The system may take maximum five minutes to test one patient's images. Therefore, the system is computationally less burden to the operator.

8.2 Suggestions for Future Research

I recommend the following directions for further research:

- In this thesis, only 80 normal and 80 MI patient's data are analysed using texture analysis methods in order to detect and extent of MI, though the findings are

satisfactory, it is far from complete. It is therefore necessary to obtain more echocardiography data of MI patients in order to evaluate or validate the algorithms developed in this thesis.

- Although the detection and extent of MI algorithms proposed in this thesis yield high accuracy, further investigations must be carried out to perform well even with high speckle noise associated with ultrasound images. It is therefore necessary to develop an efficient algorithm for speckle noise reduction as a pre-processing technique before performing the feature extraction so that severe disturbances due to noise or artefacts can be managed efficiently.
- In this thesis work, algorithm called Myocardial Infarction Risk Index (MIRI) is proposed to detect extent of infarction – normal, moderately infarcted and severely infarcted myocardium using 2D echocardiograms. However, more work is needed to validate the MIRI with gold standard (contrast MRI) data in order to enhance the robustness of the algorithm.
- There is a possibility of exploring the detection of mild stage of infarcted myocardium. In addition, localization of infarct area in patients with MI may help in treatment and improve the survival rate. It is therefore necessary to develop an algorithm using echocardiographic texture analysis methods for (i) identification of infarct zones, (ii) comparison with normal subjects, and (iii) validation with contrast MRI results of acute and chronic MI patients. This algorithm may help to localise the infarct region for optimal treatment without the need of contrast agents which involves time, cost and risk to patients.
- Extent of MI detection algorithm is developed using 5 non-consecutive frames from each patient (having total of 20 frames) i.e. 5 equally spaced frames from each sequence of videos having total of 20 frames. These 5 chosen frames include both end diastolic and end systolic phases (i.e. one cardiac cycle) and also captures the sequence of myocardial wall motion. However, the variations of

information might not be much within these 5 captured frames per patient. It is therefore necessary to have either more echocardiograms of MI patients or the serial echocardiograms data for identifying the MI expansion and extent of MI accurately where only one frame per patient is sufficient to develop an algorithm.

- Throughout the thesis, all pre-processing and feature extractions are carried out on the whole echocardiogram image without segmenting the region of interest (ROI). Therefore, more work is needed to segment the ROI from echocardiograms without losing much of myocardial information.

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APPENDIX I

Calculation of relative wavelet energy and entropy features:

1. Sub band coefficients – Energy: $cK_n - Eng$
2. Sub band coefficients – Entropy: $cK_n - Ent$
3. Total of cK sub band coefficients – Energy: $cK - Eng$
4. Total of cK sub band coefficients – Entropy: $cK - Ent$
5. Total of level n sub band coefficients – Energy: $n - Eng$
6. Total of level n sub band coefficients – Entropy: $n - Ent$
7. Relative wavelet of $cK_n - Eng$:

$$cK_n - RWEng =$$

$$\frac{cK_n - Eng}{\sum_{n=1}^3 cA_n - Eng + \sum_{n=1}^3 cV_n - Eng + \sum_{n=1}^3 cH_n - Eng + \sum_{n=1}^3 cD_n - Eng}$$

8. Relative wavelet of $cK_n - Ent$:

$$cK_n - RWEnt =$$

$$\frac{cK_n - Ent}{\sum_{n=1}^3 cA_n - Ent + \sum_{n=1}^3 cV_n - Ent + \sum_{n=1}^3 cH_n - Ent + \sum_{n=1}^3 cD_n - Ent}$$

9. Relative wavelet of $cK - Eng$:

$$cK - RWEng =$$

$$\frac{\sum_{n=1}^3 cK_n - Eng}{\sum_{n=1}^3 cA_n - Eng + \sum_{n=1}^3 cV_n - Eng + \sum_{n=1}^3 cH_n - Eng + \sum_{n=1}^3 cD_n - Eng}$$

10. Relative wavelet of $cK - Ent$:

$$cK - RWEnt =$$

$$\frac{\sum_{n=1}^3 cK_n - Ent}{\sum_{n=1}^3 cA_n - Ent + \sum_{n=1}^3 cV_n - Ent + \sum_{n=1}^3 cH_n - Ent + \sum_{n=1}^3 cD_n - Ent}$$

11. Relative wavelet of $n - Eng$:

$$n - RWEng =$$

$$\frac{\sum (cA_n - Eng + cV_n - Eng + cH_n - Eng + cD_n - Eng)}{\sum_{n=1}^3 cA_n - Eng + \sum_{n=1}^3 cV_n - Eng + \sum_{n=1}^3 cH_n - Eng + \sum_{n=1}^3 cD_n - Eng}$$

12. Relative wavelet of $n - Ent$:

$$n - RWEnt =$$

$$\frac{\sum (cA_n - Ent + cV_n - Ent + cH_n - Ent + cD_n - Ent)}{\sum_{n=1}^3 cA_n - Ent + \sum_{n=1}^3 cV_n - Ent + \sum_{n=1}^3 cH_n - Ent + \sum_{n=1}^3 cD_n - Ent}$$

13. Average of $cK_n - Eng$:

$$cK_n - AvgEng = \frac{cK_n - Eng}{2}$$

14. Average of $cK_n - Ent$:

$$cK_n - AvgEnt = \frac{cK_n - Ent}{2}$$

15. Average of $n - Eng$:

$$n - AvgEng = \frac{n - Eng}{2}$$

16. Average of $n - Ent$:

$$n - AvgEnt = \frac{n - Ent}{2}$$

17. Probability of $cK_n - Eng$: $cK_n - PEng$

18. Probability of $cK_n - Ent$: $cK_n - PEnt$

Where, $Eng = \sum_{i,j} |cA_n(i,j)|^2$

$$Ent = - \sum_{i,j} cA_n^2(i,j) \log(cA_n^2(i,j))$$

Where cK_n corresponds to coefficients (c) of either horizontal (H), vertical (V), diagonal (D) or approximation (A) sub bands at level n . And (i,j) represents the rows and columns of the image.