CHAPTER 1
INTRODUCTION

1.1 GENERAL BACKGROUND

Engineering in medicine is one of the blessed contributions to mankind. The engineering technology helps the doctors to see and predict clearly, to analyze, to store and to communicate etc. It has been the goal of researchers to study and provide morphometric and anatomic information about various regions of interest.

Image segmentation is the classification of an image into different regions based on certain characteristic properties [1]. The segmented image makes the analysis easier and the derived regions will attain significance rather than the whole image. Image segmentation in some contexts means extracting the image from the background, or it is separating the contours based on boundary or edges, or extracting particular set of objects distributed throughout the image [2]. The segmented region will vary in intensity, colour and texture. Segmented brain images are widely used in cortical surface mapping, volume measurement, tissue classification and differentiation, functional and morphological adaptation assessment, and the characterization of neurological disorders such as Alzheimer’s disease (AD), stroke and multiple sclerosis [3].

Dementia is a devastating disease largely affecting the elderly population with implications for the whole family and society. It also affects cognitive abilities severe enough to interfere with social functioning. It can result from various diseases that cause damage to brain cells [4]. There are many different types of dementia, each with its own cause and symptoms. Alzheimer's disease is the most common cause of dementia among people aged 60 years and older. It was first discovered in 1906 by Alois Alzheimer. The main clinical feature of AD is increasing memory impairment followed by impairment of other cognitive domains, a characteristic pathological cortical and hippocampal atrophy, histological feature of senile plaques of amyloid deposits and neurofibrillary tangles [5]. The prevalence of AD is expected to increase dramatically as the population around the globe continues to age with increasing life-expectancy at birth. Better understanding of this demanding disease, therefore, is essential, and early diagnosis combined with a comprehensive management strategy initiated early in the course of the cognitive decline will likely be the most effective method of controlling the progression of AD [6]. Mild
Cognitive Impairment (MCI) is a relatively new concept in the area of cognition and dementia. Its importance lies in the fact that it represents the precursor stage of dementia. This MCI provides a window for intervention in the preclinical stages of dementia and therapy for possible prevention of dementia. There is intense ongoing research on the longitudinal course of MCI.

An emphasis in ongoing Alzheimer’s disease research is identifying biomarkers which best predict future cognitive decline, especially at the earliest stages of disease progression. Biomarkers have diagnostic and prognostic value in the early detection of AD [7]. Neuroimaging techniques may be useful for both the early diagnoses as well as preclinical detection of neurodegenerative disease. Magnetic resonance imaging is a neuroimaging technique that provides a noninvasive way to view the structure of the brain. Structural MRI acquires only one scan of each subject with high spatial resolution. It provides a good contrast between different tissues, especially useful for detecting small anatomical changes in the brain [8] [9].

MR brain Image segmentation is an essential tool in medical image processing and it is important that it be of high precision and accuracy [10]. The rapidly growing availability of the 3D reconstruction technique has lead to the development of numerous semi-automatic, and automatic classification techniques to replace manual segmentation, which is a labor-intensive, subjective, and thereby a non reproducible procedure. MR brain image segmentation refers to the pixel by pixel labeling of regions as Gray Matter (GM), White Matter (WM), and Cerebro-Spinal fluid (CSF). At a higher level these regions can be labeled as anatomical structures and then grouped across slice to give three dimensional descriptions of these structures.

In summary, the victims of the AD are people in old age and deprive a man of his memory, results loss of neurons in WM and GM leading to brain tissue atrophy and subsequently the widening of ventricles and sulci filled with CSF and finally shrinking of the brain [11] [12]. The purpose of the research work is to detect such subtle changes in the volume of the brain and to identify the atrophy exists before the onset of dementia or during the MCI stage. The secondary objective is to clarify the differences between cerebral atrophy due to normal aging, MCI and AD. Due to the progressive nature of AD, the longitudinal MRI should be able to detect the progressive structural changes occurring within an individual and improve the
diagnostic accuracy.

1.2 MOTIVATION FOR THE STUDY

Alzheimer’s disease is the most common cause of dementia among people aged 60 years and older. The prevalence of AD ranges from 6.44% in south India [13] to 4.86% in Shanghai [14] China by 3.92% in Sri Lanka for populations above 65 years [15]. With the increasing life expectancy, WHO (World Health Organization) estimates India and China to have the largest population of senior citizens who will be at risk for dementia. The prevalence of AD is expected to increase dramatically as the population around the globe continues to age. Better understanding of this demanding disease, therefore, is essential, and early diagnosis combined with a comprehensive management strategy initiated early in the course of the cognitive decline will likely be the most effective method of controlling the progression of AD. Currently one of the major handicaps towards achieving this is the difficulty in early and definitive diagnosis of AD. Early detection and correct diagnosis can lead to disease retarding therapies which can slow disease progression and reduce patient and caregiver stress and morbidities. The rationale for this is that early and pre-clinical diagnosis will assist in early intervention and perhaps allow for the prevention of AD.

Brain imaging segmentation of magnetic resonance imaging data is an important but time-consuming manual task performed by medical experts. Automating this process is a challenging task among different patients and in many cases similarity with the normal tissues. MR imaging has several advantages over other imaging techniques. The accuracy of the segmentation of brain MRI depends upon the accuracy with which the brain tissues are extracted from the MR images. Brain changes in AD are difficult to distinguish from those in normal ageing, and this has led to the development of powerful computational methods to extract statistical information on the brain changes that are characteristic of AD, mild cognitive impairment and different dementia subtypes [16]. These methods yield insight into the dynamics of AD and MCI, showing where brain changes correlate with cognitive or behavioral changes. Computational methods are powerful enough to track dementia in clinical trials, on the basis of their efficiency and sensitivity to early change, and the detail in the measures they provide.

Most of these neuropsychological and imaging studies are done in
western populations. There are a limited number of Indian studies on the clinical, neuropsychological profile of MCI, its radiological correlates or its conversion rate to AD in the real data set. The proposed study is expected to identify neuropsychological and MRI measures in the Indian population that may serve as potential predictors of cognitive impairment or dementia in the elderly population in India. With the expected rise in the population at risk for dementia in the coming years in the country and the devastating nature of the disease for the patient as well as the family, ability to make early diagnosis or preclinical diagnosis will provide an enormous potential for disease modifying intervention, which is perhaps one of the most intensely researched areas that is making rapid progress.

This work is driven by the motive to provide our clinicians or neurologists an efficient and cost effective tool in diagnosing and treating AD. The clinical manifestation of the disease may be subtle, but early diagnosis is crucial to enable early drug intervention and improved prognosis. The progression of the disease can be generated by early treatment and hence it becomes very crucial to detect the onset of AD early in a patient. The memory impairment and the cognitive loss are very subtle and go unnoticed in the early stage of the disease. The disease manifests wanting attention only at a very late stage. This only makes the rationale of the work more significant, to determine any signs of volume loss or tissue degeneration at a very early stage.

1.3 OBJECTIVES OF THE INVESTIGATION

1. The main aim of this study is to investigate the performance of the VBM and classification algorithmic methods to detect the presence and severity of gray matter atrophy in individuals with mild cognitive impairment and differentiating AD patients and from normal elderly controls.

2. The current study is to investigate the structural changes of certain specific brain regions at baseline and structural changes in the overall time that could serve as an accurate predictor of future development of AD in the MCI subjects with magnetic resonance imaging using voxel-based morphometry as the analysis method.

3. This study also examines the correlation between VBM and classification algorithms to map the progression of GM loss in MCI patients over time and compare converters to non-converters in the real MRI data set.
4. It also intends to look for the correlation of neuropsychological and MRI volumetric parameters that would determine the transition from NCI to MCI and MCI to AD.

1.4 CONTRIBUTION OF THE STUDY

The purpose of this study is to develop and apply methods for volumetric analyses of real magnetic resonance imaging data (2009-2013) for comparisons of patients with AD, MCI and NCI. Brain changes in AD are difficult to distinguish from those in normal ageing, and this has led to the development of powerful computational methods to extract statistical information on the brain changes that are characteristic of AD, MCI, and different dementia subtypes. Segmentation and extraction of brain parts have been explored, but were limited to the GM, WM and CSF in Alzheimer's brains.

Here, the proposed study uses two CAD approaches to map brain deficits in AD: Voxel Based Morphometry and classification algorithms like unsupervised K-means, supervised RBFNN, GRNN, PNN, BPNN, MSVM and BFO tuned ANN classifiers. These methods yield insight into the dynamics of AD and MCI, showing where brain changes correlate with cognitive or behavioral changes. Computational methods are powerful enough to track dementia in clinical trials, on the basis of their efficiency and sensitivity to early change, and the detail in the measures they provide.

The dissertation is divided into two parts. The first part is devoted to the analysis of automated VBM technique for assessing the structural changes in the brain. The VBM with ROI based volumetric technique can provide very important information about regions of atrophy across group wise analysis also by providing anatomical information that can be helpful for differential diagnosis of disease. These studies validate the results of VBM with statistical parametric map method and compare the results to other methods through real data analysis.

The second part covers the analysis of structural changes in the MR imaging of the brain using classification algorithmic approaches. This algorithm provides a detailed map of brain structure, especially useful for detecting small anatomical changes as a result of the disease process. The goal of this structural analysis is to train an automated classifier technique that can identify the patients from healthy controls. The proposed AD detection algorithms are composed of three
stages: Skull stripping based on mathematical morphology, extracting the texture features from the pixels of the preprocessed MR images using 2D Gabor filters. These features are used for segmentation of GM, WM and CSF in MRI using K-Means clustering and supervised classifiers like RBFNN, GRNN, PNN, BPNN, and BFOANN based classifiers for the early diagnosis of AD. In the longitudinal analysis of these classifiers map the progression of GM loss in MCI patients over time and compared progressive MCI to stable MCI subjects. The present results suggest that novel classifier methods of pattern classification reach a clinically relevant accuracy for the a priori prediction of the progression from MCI to AD. The rational for this study is that early and preclinical diagnosis will assist in every intervention and perhaps allow for the prevention of AD.

1.5 ORGANIZATION OF THE THESIS

Introduction: This chapter introduces the general background of AD in several aspects including the cause of the disease, the disease nature as well as how the disease is investigated in clinical practice. The rest of the chapter discusses the motivation for the present work, the major objectives of the investigation and finally discusses the applicability of our contribution for efficient and cost effective tool in the early diagnosis and tracking of AD in the real MR images in a South Indian population.

Review of the Literature: This chapter presents a review of the clinical diagnosis of dementia, AD and the concept of MCI. This chapter also discusses the recent CAD techniques for early diagnosis, classification, and progression, of AD and the different segmentation techniques as applied to brain MRI over the past decades is revisited in this chapter.

Subjects and Materials: This chapter discusses a subject selected for the proposed study and provides the details of the image acquisition parameters we have used to develop our application.

Architecture of Proposed System: In this chapter report on the works have done to evaluate the feasibility of the early detection and tracking the progression of Alzheimer’s disease on the basis of the analysis of real structural MRI brain data using voxel based morphometric analysis and different classifier techniques. This chapter presents preprocessing steps prior to segmentation of the brain tissues and a feature extraction process and finally volumetric analysis uses the
computational classification techniques.

Neuropsychological Evaluation study in AD: This chapter discusses and displays the analysis of different neuropsychological tests for the early diagnosis of AD and the longitudinal and cross sectional analysis result for discriminate the AD patients from controls.

VBM for assessing structural changes in the brain: This chapter discusses the structural brain alterations in AD patient’s comparison to matched healthy elderly using VBM analysis. This cross-sectional study prospectively evaluates the rate of regional atrophy in AD, MCI and healthy elderly controls. Rates of atrophy overtime may be useful for the differential diagnosis and could be used to monitor the disease progression serving as an outcome measure for clinical trials.

Brain imaging segmentation based on unsupervised clustering techniques: Unsupervised K-means clustering algorithm is discussed in this chapter. The K-means classification approach to distinguish brain magnetic resonance images of AD patients from those of elderly normal controls. On the basis of the selected clusters, classification accuracy, sensitivity and specificity and Youden’s index were obtained.

Brain imaging segmentation based on supervised classification Techniques: Six supervised classification methods proposed in this work are discussed in this chapter. In this section we give a detailed study of the use of optimization methods with classification approaches for brain image segmentation and for the discrimination of AD patients from healthy control subjects.

Comparative results and discussion: This chapter discusses and displays the comparative results of segmentation using VBM and different classifier techniques in the longitudinal and cross sectional analysis.

Summary and Conclusions: This chapter discusses the major findings of this proposed study and conclusion.