CHAPTER 1

INTRODUCTION

1.4 BACKGROUND

Research to discover new techniques to diagnose diseases has been going on worldwide to improve the life of the people as new diseases emerge day after day for reasons well known. The aim of any similar research is to diagnose the disease accurately, quickly and economically. In present work a new, fast and accurate automatic diagnostic system to identify the Alzheimer’s disease is proposed. Alzheimer's is a brain disease that causes problems with memory, thought and behavior. Symptoms usually develop slowly and become worse as time passes by gradually becoming serious enough to hinder normal physical activities. Alzheimer's is the most common form of dementia, a general term for loss of memory and other intellectual abilities serious enough to interfere with daily life. Alzheimer's disease accounts for 50 to 70 percent of dementia cases. It is not a normal part of aging, although the greatest known risk factor is increasing age, and the majority of people with Alzheimer's are 65 and older. But Alzheimer's is not just a disease of old age. Up to 5 percent of people with the disease have early onset of Alzheimer's (also known as younger-onset), which often appears when someone is in their 40’s or 50’s. Alzheimer's worsens over time. It is a degenerative disease, where symptoms gradually worsen over a number of years. In its early stages, memory loss is mild, but at a later stage, individuals lose the ability to carry on a conversation and respond to their environment. The development of biomarker is necessary for the early diagnosis of Alzheimer’s disease.
Conventional Biomarkers (Lovestone 2009) to identify Alzheimer’s disease depend on the skill of the doctor, the case history of the patient given to the doctor and the ability of the patient to respond to the doctor. No single test can detect Alzheimer’s. The medical workup is designed to evaluate overall health and identify any conditions that could affect the mind and how well it works. Experts believe that a skilled physician can diagnose Alzheimer’s with more than 90 percent accuracy. Thanks to an increasing number of test developers, health care and marketing facilities, dementia screening tests reach the people directly. The Alzheimer's Association believes that home screening tests cannot and should not be used as a substitute for a thorough examination by a skilled doctor. There is an established diagnostic criterion that physicians adhere to when diagnosing someone for Alzheimer's disease. Although dementia screening tests do not claim to offer 100% accurate diagnosis, any test that is conducted may cause great psychological distress to the test taker. Some of the other tests usually conducted by the doctors are reviewing medical history, in which doctors interview the person being examined or family members to gather information about the current and past illnesses; Mental status testing which gives the doctor a general idea of whether the person is aware of his problem or he feels that nothing is wrong; and he knows the date, time and where he is and can remember a short list of words and follow instructions and do simple calculations etc. The Mini-Mental State Examination (MMSE) is one of the tests most commonly used to assess mental function. In the MMSE, a health professional asks the patient a series of questions designed to test a range of everyday mental skills. The maximum MMSE score is 30 points. A score of 20 - 24 suggests mild dementia, 13 - 20 suggests moderate dementia, and less than 12 indicates severe dementia. On an average, the MMSE score of a person with Alzheimer’s declines by 2 - 4 points each year. All these tests require the patient’s cooperation and the doctor’s skill.
New imaging technologies have revolutionized the understanding of the structure and function of the live brain. Currently, a standard medical workup for Alzheimer’s disease often includes structural imaging with Magnetic Resonance Image (MRI) or, less frequently, Computed Tomography (CT). These images are used primarily to detect tumors, evidence of small or large strokes, and damage from severe head trauma or a buildup of fluid. Researchers do intensively try to find whether the use of MRI and other imaging methods may be expanded to play a more direct role in diagnosing Alzheimer’s. Many research findings have shown that the brains of people with Alzheimer’s shrink significantly as the disease worsens (Stefan Kloppel 2008). Research has also shown that shrinkage in specific brain regions, particularly the hippocampus, may be an early sign of Alzheimer’s. The hippocampus is a major component of the brains of humans and other mammals. It belongs to the limbic system and plays important roles in long-term memory and spatial navigation. However, scientists have not yet agreed upon standardized values that would establish the significance of a specific amount of shrinkage in any person at a single point in time. Due to the deposition of amyloid-beta and tau on the hippocampus of the AD patients, the texture features can be utilized to identify the AD.

The research work undertaken is focused on developing a biomarker to detect the Alzheimer’s disease from Hippocampus MRI texture features, which is automatic, accurate and fast.

1.5 MOTIVATION

It is estimated that there are currently about 18 million people worldwide with Alzheimer’s disease. This figure is likely double by 2025 to 34 million (Ferri 2005). Much of this increase will occur in developing countries, and will be due to aging. Currently, more than 50% of people with Alzheimer’s disease live in developing countries and by 2025, this will be over 70%. Recent
research in India suggests that the risk of Alzheimer’s disease is possibly higher in urban than in rural areas. There is an accelerating worldwide effort under way to find better ways to treat the disease, delay its onset, or prevent it from becoming serious. Early diagnosis of AD patients is important because it allows early treatment with cholinesterase inhibitors, which have been shown to delay institutionalization, improve or stabilize cognition and behavioural symptoms (Ritchie 2004, Whitehead 2004). As therapeutic interventions become available, there is a need for developing methodologies that will serve as an in vivo surrogate for these pathologic changes, and thus, accurately identify those cognitively impaired individuals who are in the earliest stages of Alzheimer’s disease.

1.6 OBJECTIVES

The present research intends to find out the most suitable pre-processing technique among the available ones and a new one based on wave atoms shrinkage, which is a multi-resolution technique and is not yet used for medical image de-noising. Also a new algorithm is developed to segment the hippocampus after pre-processing with good accuracy. The whole system will be used to diagnose the Alzheimer’s disease at the early stage. This can be used as a biomarker to detect memory related diseases. Since it is automatic, it is user friendly and accurate.

After pre-processing the MRI with different techniques, the performance is analyzed by calculating the Peak Signal to Noise Ratio (PSNR). To segment the hippocampus, initially lateral ventricle is segmented with the well tested algorithm, based on this geometrical location a new technique is used to search the location of hippocampus. The performance is analyzed by calculating the coefficient of similarity and spatial overlap. The texture features are taken from the hippocampus by different methods, and using either singular
value decomposition or principal component analysis, the number of features for classification is reduced. The support vector machine is used to classify the disease. The classifier is validated by calculating precision, sensitivity, specificity, and accuracy.

1.5 ORGANIZATION OF THESIS

Literature survey pertaining to the area of Alzheimer’s disease, Pre-processing, Segmentation, Feature extraction, Feature Selection and classification methods are detailed in chapter 2. Implementation of pre-processing step using wave atoms shrinkage is explained in chapter 3. Implementation of knowledge based automatic hippocampus segmentation is explained in chapter 4. Feature extraction and selection methods used in this work are explained in chapter 5. The method used to detect the Alzheimer’s disease is given in chapter 6. The contributions of the research, possible extensions for future research are listed in chapter 7. The thesis concludes with the list of publications based on this research work. The overall block diagram of the proposed system is given in Figure 1.1.

![Figure 1.1 Structure of proposed system](image-url)