# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>ABSTRACT</th>
<th>i</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACKNOWLEDGEMENT</td>
<td>iii</td>
</tr>
<tr>
<td>TABLE OF CONTENTS</td>
<td>iv</td>
</tr>
<tr>
<td>LIST OF TABLES</td>
<td>x</td>
</tr>
<tr>
<td>LIST OF FIGURES</td>
<td>xii</td>
</tr>
<tr>
<td>LIST OF SYMBOLS AND ABBREVIATIONS</td>
<td>xvii</td>
</tr>
</tbody>
</table>

## 1. INTRODUCTION

1.1 GENERAL BACKGROUND                       | 1  |
1.2 MOTIVATION FOR THE STUDY                 | 3  |
1.3 OBJECTIVES OF THE INVESTIGATION          | 4  |
1.4 CONTRIBUTION OF THE STUDY                | 5  |
1.5 ORGANIZATION OF THE THESIS               | 6  |

## 2. REVIEW OF THE LITERATURE

2.1 ALZHEIMER’S DISEASE                     | 8  |
2.1.1 Mild Cognitive Impairment              | 10 |
2.1.2 Diagnostic Criteria for AD             | 10 |
2.1.3 Approaches of Biomarker Studies for Early Detection of AD | 11 |
2.2 COMPUTER AIDED DIAGNOSIS (CAD) OF ALZHEIMER’S DISEASE | 11 |
2.2.1 Voxel Based Morphometry studies in AD  | 15 |
2.2.2 Literature survey on classification Algorithms | 17 |
2.3 IMPROVING COMPUTER AIDED DIAGNOSIS OF ALZHEIMER’S DISEASE WITH PROPOSED CLASSIFICATION ALGORITHMS | 21 |
2.4 SUMMARY                                 | 22 |
3. SUBJECTS AND MATERIALS 24
   3.1 SUBJECTS 24
      3.1.1 Inclusion and Exclusion Criteria 25
      3.1.2 Criteria and Definition 26
   3.2 NEUROPSYCHOLOGICAL ANALYSIS 26
   3.3 MAGNETIC RESONANCE IMAGING 26
      3.3.1 Working Principle 27
   3.4 IMAGING PROTOCOL 28
   3.5 MR IMAGE FORMAT 28
      3.5.1 DICOM files to Analyze Standards 29
   3.6 SUMMARY 29

4. ARCHITECTURE OF THE PROPOSED SEGMENTATION ALGORITHM 30
   4.1 SUMMARIZED DESCRIPTION OF THE PROCESS 31
   4.2 PRE-PROCESSING 39
   4.3 FEATURE EXTRACTION 42
      4.3.1 Texture feature extraction using Gabor features 46
   4.4 CLASSIFICATION 48
      4.4.1 CAD system based on Voxel Based Morphometry 48
      4.4.2 CAD System based on Classification algorithms 49
   4.5 VOLUME CALCULATION AND MANUAL VALIDATION 52
   4.6 SUMMARY 56

5. NEUROPSYCHOLOGICAL PROFILE OF AD 57
   5.1 GENERAL BACKGROUND 57
   5.2 NEUROPSYCHOLOGICAL EVALUATION 57
   5.3 LONGITUDINAL AND CROSS-SECTIONAL ANALYSIS 59
<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.3.1 Demographic Clinical Features and Neuropsychological Performance</td>
<td>59</td>
</tr>
<tr>
<td>5.3.2 Neuropsychological Prediction of Conversion to AD in Patients with MCI</td>
<td>60</td>
</tr>
<tr>
<td>5.4 DISCUSSION</td>
<td>62</td>
</tr>
<tr>
<td>5.5 SUMMARY</td>
<td>63</td>
</tr>
<tr>
<td>6. VBM FOR ASSESSING STRUCTURAL CHANGES IN THE BRAIN</td>
<td>64</td>
</tr>
<tr>
<td>6.1 GENERAL BACKGROUND</td>
<td>64</td>
</tr>
<tr>
<td>6.2 OVERVIEW OF THE VBM</td>
<td>65</td>
</tr>
<tr>
<td>6.2.1 VBM Methods</td>
<td>67</td>
</tr>
<tr>
<td>6.3 STATISTICAL ANALYSIS OF VBM RESULTS</td>
<td>72</td>
</tr>
<tr>
<td>6.3.1 ROI-Based Volumetry in Cross-Sectional Study Groups</td>
<td>73</td>
</tr>
<tr>
<td>6.3.2 ROI-based Volumetry in Longitudinal Study Groups</td>
<td>77</td>
</tr>
<tr>
<td>6.3.3 Pattern of GM Loss in Cross-Sectional Study Groups</td>
<td>84</td>
</tr>
<tr>
<td>6.3.4 Pattern of GM loss in Longitudinal Study Groups</td>
<td>93</td>
</tr>
<tr>
<td>6.4 VBM ROI BASED VOLUMETRY AND SPM ANALYZING GM DIFFERENCES IN ALZHEIMERS DISEASE</td>
<td>98</td>
</tr>
<tr>
<td>6.5 CORRELATION OF VBM AND NEUROPSYCHOLOGICAL RESULTS</td>
<td>103</td>
</tr>
<tr>
<td>6.6 SUMMARY</td>
<td>105</td>
</tr>
<tr>
<td>7. BRAIN IMAGE SEGMENTATION BASED ON UNSUPERVISED CLUSTERING TECHNIQUES</td>
<td>106</td>
</tr>
<tr>
<td>7.1 GENERAL BACKGROUND</td>
<td>106</td>
</tr>
<tr>
<td>7.2 OVERVIEW ABOUT THE CLUSTERING TECHNIQUES</td>
<td>106</td>
</tr>
<tr>
<td>7.2.1 K-means Clustering Techniques</td>
<td>107</td>
</tr>
<tr>
<td>7.2.2 K-means Algorithm</td>
<td>109</td>
</tr>
<tr>
<td>7.2.3 Flow chart for K-means Clustering Algorithm</td>
<td>109</td>
</tr>
</tbody>
</table>
7.2.4 K-means Clustering Based Segmentation of Textures using Gabor Filters

7.3 K-MEANS SEGMENTATION ALGORITHM

7.4 EXPERIMENTAL RESULTS USING K-MEANS CLASSIFIER

7.4.1 Longitudinal Study in NCI Subjects

7.4.2 Longitudinal Study in MCI Subjects

7.4.3 Discriminative study

7.5 DISCUSSION

7.6 SUMMARY

8. BRAIN IMAGING SEGMENTATION BASED ON SUPERVISED CLASSIFICATION TECHNIQUE

8.1 OVERVIEW OF THE ARTIFICIAL NEURAL NETWORK

8.1.1 Neural Network Architecture

8.1.2 Learning Methods in Neural Network

8.1.3 Back Propagation Learning Algorithm

8.1.4 Training by Back Propagation Algorithm

8.2 AD DIAGNOSIS BASED ON RADIAL BASIS FUNCTION NEURAL NETWORK

8.2.1 Overview of the Radial Basis Function Neural Network

8.2.2 Experimental framework for AD detection using RBFNN Classifier

8.3 AD DIAGNOSIS BASED ON GENERALIZED REGRESSION NEURAL NETWORKS

8.3.1 Overview about the Generalized Regression Neural Networks

8.3.2 Experimental framework for AD detection using GRNN classifier
# 8.4 AD DIAGNOSIS BASED ON PROBABILISTIC NEURAL NETWORKS

## 8.4.1 Overview of the Probabilistic Neural Networks

## 8.4.2 Experimental framework for AD detection using PNN

# 8.5 AD DIAGNOSIS BASED ON BACK PROPAGATION NEURAL NETWORKS

## 8.5.1 Overview of the Back Propagation Neural Networks

## 8.5.2 Experimental framework for AD detection using BPNN

# 8.6 AD DIAGNOSIS BASED ON MULTI SUPPORT VECTOR MACHINE

## 8.6.1 Overview about the Multi Support Vector Machine

## 8.6.2 Experimental Framework for AD Detection using MSVM Classifier

# 8.7 AD DIAGNOSIS BASED ON BACTERIAL FORAGING OPTIMIZATION TUNED ANN BASED CLASSIFIER

## 8.7.1 Bacterial Foraging Algorithm: An Overview

## 8.7.2 Experimental Framework for AD Detection using BFO Tuned ANN Classifier

# 8.8 EXPERIMENTAL RESULTS AND DISCUSSION

## 8.8.1 Experimental Results using RBFNN based classifier

## 8.8.2 Experimental Results using GRNN based classifier

## 8.8.3 Experimental Results using PNN based classifier

## 8.8.4 Experimental Results Using BPNN based classifier

## 8.8.5 Experimental Results using MSVM based classifier

## 8.8.6 Experimental Results using BFOANN classifier

# 8.9 DISCUSSION

# 8.10 SUMMARY
9. COMPARATIVE RESULTS AND DISCUSSION 192

9.1 DESCRIPTIVE CHARACTERISTICS 192

9.2 COMPARATIVE PERFORMANCE MEASURES OF THE VBM AND CLASSIFICATION ALGORITHMS 193

9.3 COMPARATIVE PERFORMANCE MEASURES OF THE CLASSIFICATION ALGORITHMS 197

9.3.1 Comparative Performance Measures of Brain Atrophy Using Classification Algorithms 199

9.3.2 Correlation of Classification Algorithm and Neuropsychological Results 201

9.4 DISCUSSION 207

9.5 LIMITATIONS OF THE STUDY 211

10. SUMMARY AND CONCLUSIONS 213

10.1 MAJOR FINDINGS 213

10.2 CONCLUSION 215

10.3 FUTURE DIRECTIONS 216

REFERENCES 217

LIST OF PUBLICATIONS 232

APPENDIX 233