AUTOMATED DETECTION OF ALZHEIMER'S DISEASE USING BRAIN MR IMAGES - A REVIEW

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***Abstract*— Alzheimer's disease (AD) is a progressive multifarious neurodegenerative disorder, it is the leading cause of dementia in late adult life. Detection of AD is significantly and rapidly growing in research field of Medical and Computer Science domain. Early prognosis of AD plays a vital role in improving treatment possibilities and increases the survival rate of the patients. Since the detection of AD in early stage is tough task and hence this survey is helpful to find methods for early detection of AD through segmentation and quantification of different brain tissues in Magnetic Resonance Imaging (MRI). This paper describes an exploratory review of recent literature on the AD detection and quantification using MR brain images.**

Keywords — *Alzheimer's Disease, Magnetic Resonance Imaging, Segmentation, Brain Tissue.*

I. INTRODUCTION

The brain is the part of central nervous system that is protected inside the cavity of the skull in the human head. The most complex part of the human body is a soft mass of supportive tissues and nerve cells, which is connected to the spinal cord. The brain and spinal cord together form the central nervous system which transmits messages to the various parts of the body. The brain consists of four main components: Cerebrum, Cerebellum, Limbic System and Brain Stem. Soreness in the brain can lead to problems such as vision loss, weakness and paralysis. Loss of brain cells leads to stroke which affect human ability to think clearly, Brain tumours can also affect brain function. Some brain diseases are genetic and some of brain diseases have fewer symptoms to identify such as Alzheimer's disease. The major brain disorders are Parkinsons Disease, Multiple Sclerosis (MS) and Schizophrenia. The advances in brain imaging techniques facilitate medical scientists to detect the brain abnormalities and the associated functional losses in the brain. The most commonly used brain imaging technique is Magnetic Resonance Imaging which is a safe and painless test that uses a magnetic field and radio waves to produce detailed images of the brain.

II. OVERVIEW OF ALZHEIMER'S DISEASE

Alzheimer's Disease is a degenerative disorder of the brain that results in memory loss [1]. AD influences 5.3 million people and is the 7th leading cause of death in the US. There are two fundamental varieties of the disease; Familial AD influences human beings more youthful than 65, accounting for almost 500,000 AD instances in the U.S.A[1]. The rest of AD instances arise in adults aged sixty-five and older and are labelled as sporadic AD. The superiority of advert varies among many different factors inclusive of age, co-morbidities, and genetics. There is no complete cure for AD, however promising studies and improvement for early detection and treatment is underway. The following Fig.1 illustrate the changes in human brain before and after the occurrence of AD.

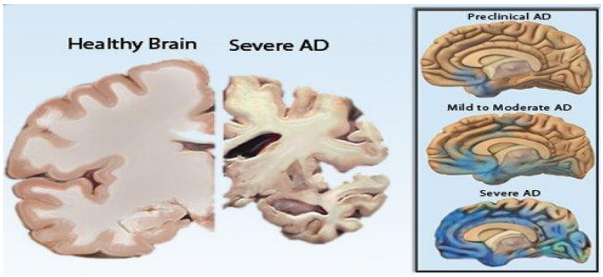


Illustration of Healthy Vs AD affected brain structure [Courtesy: https://www.pinterest.co.uk/pin]

A. HISTORY OF ALZHEIMER'S DISEASE

Alzheimer's disease was identified by Alois Alzheimer in 1906, a German neurologist and psychiatrist [2]. The sickness initially located in a 51 years old female named Auguste D. Circle of relatives delivered her to Dr. Alzheimer in 1901 after noticing changes in her personality and behaviour. The own family mentioned problems with memory, difficulties in talking, and impaired comprehension. Dr. Alzheimer later defined Auguste as having a competitive form of dementia, manifesting in reminiscence, language and behavioural deficits [3]. Dr. Alzheimer cited many unusual signs and symptoms, which includes problem with speech, agitation, and confusion [4]. He followed her to take care for five years, till her death in 1906. Following it, Dr.Alzheimer achieved an autopsy, throughout which he determined dramatic shrinkage of the cerebral cortex, fatty deposits in blood vessels, and atrophied mind cells[2]. He observed neurofibrillary tangles and senile plaques, which have grown to be indicative of AD [4]. The circumstance become first mentioned in clinical literature in 1907 and named after Alzheimer in 1910.

B. *STAGES OF ALZHEIMER'S DISEASE*

a. Early Alzheimer's Ailment

The initial stage, which normally lasts two to four years is regularly when the sickness is first recognized. Common symptoms at this stage includes[2][5].

- Problems in remembering new facts.
- Patients can also begin to have hassle in decision making
- Challenges in dealing with finances or other instrumental sports of daily dwelling.
- Changes in character. The individual may additionally begin to withdraw socially or display lack of motivation.
- Difficulty in expressing feelings.
- Misplacing property or getting misplaced. The affected person might also have trouble navigating in acquainted environment.

b. Mild Alzheimer's Ailment

This is the longest stage of sickness which lasts for 2 to 10 years. The following are the signs and symptoms at this stage [2][5].

- Increasingly bad judgment and confusion. The affected person might also begin to confuse own family members, lose orientation to time and area, and might start wandering, making it dangerous for them to be left by own.
- Problem in finishing complex obligations, such as the various instrumental sports of each day living, consisting of coping with finances, grocery buying, planning, and employer.
- More reminiscence loss. Sufferers may additionally start to overlook details of their private history.
- Great character adjustments. The individual may come to be withdrawn from social interactions and broaden unusually high suspicions of caregivers.

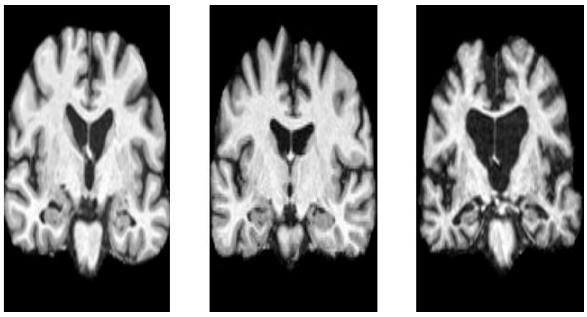
c. Excessive Alzheimer's Ailment

This final stage of the disorder remains from 1 to 3 years. The patient may have the following unusual symptoms of this stage[2][5]

- Loss of potential to speak. The affected person may additionally nonetheless speak brief phrases, but are not able to hold on a coherent conversation.
- Reliance on others for non-public care, inclusive of eating, bathing, dressing etc.
- Incapability to characteristic bodily. The individual may be unable to stroll or sit down independently. Muscle mass can also end up rigid and swallowing can sooner or later be impaired. The following figure Fig.2. illustrates the stages of AD in sample MRI brain images. discussion of machine learning algorithms and conclusion is given in section 5.

d. Diagnostic Standards for Alzheimer's Disease

The criterion for diagnosing mental issues may be determined in the Diagnostic and Statistical manual of mental problems (DSM-III), published by the Yankee Psychiatric affiliation[6]. On this guide, AD falls into the class of primary degenerative dementia. The diagnostic criterion includes



(a) (b) (c)

Stages of AD in sample MRI brain image (a) Controlled Normal (CN) (b)Mild Cognitive Impairment (c) Excessive Alzheimer's Ailment [Courtesy: https://www.nature.com/articles/s41598-018-29295-9]

dementia, insidious onset with modern deterioration, and exclusion of all different types of dementia with the aid of history and bodily examination [7].

An analysis of dementia includes a lack of intellectual abilities severe enough to intervene with social or occupational functioning, reminiscence impairment, and a diffusion of different symptoms. The first step in finding an analysis is acquiring the patient history. In the course of this time, the doctor will determine the signs present with the patient, and the way it improved over time. The family records of contamination are also pertinent. The doctor will perform a physical exam, consisting of blood exams and urinalysis. This may rule out other causes of dementia, along with hormone imbalance, diet deficiency, and urinary tract infections. Brain scans can also be completed to exclude tumors, cerebrovascular injuries, traumatic mind injury and infections. Those scans are also helpful in identifying the characteristic tangles and plaques seen in advert. Structural imaging scans, such as Magnetic Resonance Imaging and Computed Tomography (CT), offers facts about the shape and volume of the brain. Practical imaging permits the physician to decide how effectively the brain cells are running. A practical MRI or Positron Emission Tomography (PET) test can also be used[8]. Moreover, Neuropsychological examinations can also be used to become aware of cognitive symptoms. The maximum typically administered take a look at this Mini-Mental State Exam (MMSE). The physician begins via asking a sequence of questions designed to check the patient's ability to consider and call a list of gadgets, perform simple mathematics, and comply with commands. The affected person is then assigned a scoreout of 30 viable factors, with a rating of much less than 12 indicating intense dementia. AD patient's scores commonly decrease 2 to 4 factors each year[2].

The physician might also use the Alzheimer's sickness Assessment Scale (ADAS) to degree the severity of the sickness. The ADAS evaluates the affected person's orientation, memory, reasoning and language on a scale of 0 to 70. A higher score represents a better degree of cognitive

impairment. The cognitive part of the ADAS is sensitive to a wide array of symptoms and assesses many cognitive capabilities, which includes spoken language ability, bear in mind of instructions, ability to find accurate phrases, following instructions, and orientation to environment and time. In addition to intellectual checks, the health practitioner may additionally perform a neurological exam to evaluate the function of the patient's brain and anxious gadget. This exam will test reflexes, coordination and balance, sensation, muscle electricity, speech and eye function.

III. AD Detection using MR Brain Images

The MRI system generates brain image as 3D volumetric data expressed as stack of two-dimensional slices and it is necessary to use computer-aided tool to explore the information contained in these brain slices for other brain image applications such as volumetric analysis, study of anatomical structure, localization of pathology, diagnosis, treatment planning, surgical planning, computer-integrated surgery, construction of anatomical methods, 3D visualization and research[9]. Magnetic Resonance Imaging strategies, first used in 1977, create two or 3 dimensional photos of the body that may be used to diagnose injury and illness. The important element of the MRI system is the superconducting magnet, which produces a large and solid magnetic field. There are smaller gradient magnets that create weaker magnetic fields. Those magnets allow for exceptional components of the body to be scanned. The human frame is composed of billions of atoms. But it miles the hydrogen atoms which are altered by way of the magnetic field. Every hydrogen atom is randomly spinning round an axis, but in the magnetic area of the MRI, the molecules are lined up with the route of the field, half of the atoms point in the direction of the patient's head, and half of point towards the toes, cancelling every different out. The machine then emits a radio frequency pulse particular to hydrogen, which causes these protons to spin in a unique path. While the spinning ceases, the protons launch energy, that is interpreted by way of the gadget using assessment dye, every form of tissue responds in a different way and appears as a unique coloration of grey when the image is created[10].

IV. Automated Methods for AD Detection

Alzheimer's Disease detection in MRI brain image is a significant process for diagnose and classification. Identifying reduction measures of WM, GM, and CSF by comparing with standard brain images is a way of detecting AD. This section describes the available methods on AD detection and quantification methods in the literature,

Francis et al[11], examines the existing scientific applicability of the original cholinergic hypothesis of Alzheimer's disease by describing the biochemical and histopathological changes of neurotransmitter markers that occur in the brains of patients with Alzheimer's disease both at postmortem and neurosurgical cerebral biopsy and the behavioural consequences of cholinomimetic drugs and cholinergic lesions. The different aspects of pathophysiological mechanisms behind Alzheimer's disease and its management through conventional drug therapy, including modern investigational therapeutic strategies, recently completed and ongoing have discussed by Kumar and Singh[12].The importance of a healthy Blood-brain Barrier Breakdown (BBB) for therapeutic drug delivery and the adverse effects of disease-initiated, pathological BBB breakdown in relation to brain delivery of neuropharmaceuticals are briefly discussed. Finally, future directions, gaps in the field and opportunities to control the course of neurological diseases by targeting the BBB are presented and highlighted in Sweeny et al[13].

Nebel et al[14], highlighted the current state-of-the-science in the AD field on sex and gender differences then addressed the knowledge gaps in assessing sex and gender differences and discussed twelve priority areas that merit further research in this field of study. Normally four stages in AD detection and classification such as removal of noise, extraction of AD portion from brain features related to MRI images and storing for classifier respectively. Thompson et al[15] focused on describing their approaches to map structural changes in the cortex. This method has already been used to reveal the profile of brain anomalies in studies of dementia, epilepsy, depression, childhood and adult-onset schizophrenia, bipolar disorder, attention-deficit/hyperactivity disorder, fetal alcohol syndrome, Tourette syndrome, Williams syndrome, and in methamphetamine abusers. In this work, they described an image analysis pipeline known as cortical pattern matching that helps to compare and pool cortical data over time and across subjects. Statistics were then defined to identify brain structural differences between groups, including localized alterations in cortical thickness, Gray Matter Density (GMD), and asymmetries in cortical organization.

Alzheimer's Association [16][17] examines how the use of biomarkers may influence the AD diagnostic process and estimates of prevalence and incidence of the disease. An estimated 5.5 million Americans have Alzheimer's dementia. This new approach could promote diagnosis at an earlier stage of disease and lead to a more accurate understanding of AD prevalence and incidence. The benefits of diagnosing Alzheimer's earlier in the disease process, in the stage of mild cognitive impairment due to Alzheimer's disease. With the identification of AD biomarkers in recent years, their understanding of the disease has moved from symptoms-based approaches. A new classification technique called Tree Augmented Bayesian Neural Networks (TANNN) used to get high performance compared with some other classification techniques such as Support Vector Machine (SVM), Naïve Bayes, k-Nearest Neighbour (KNN), and Decision Tree(DT) mentioned by Ali et al[18].

Cuingnet et al[19], performed three classification tests namely Elderly Control(CN) vs AD, CN vs Mild Cognitive Impairment converters (MCIc) and MCIc vs Mild Cognitive Impairment non converters (MCInc) on 509 subjects from the ADNI database to obtain an unbiased estimate of the

performance and they evaluated the performances of ten approaches on the same data base (five voxel-based methods, three methods based on cortical thickness and two methods based on the hippocampus). Noticeably the use of feature selection increased the computation times but not the performance. Wolz et al[20], aimed to assess the improvement in classification accuracy that can be achieved by combining features from different structural MRI analysis techniques. Automatically estimated MR features used are hippocampal volume, tensor-based morphometry, cortical thickness and a novel technique based on manifold learning. Baseline MRIs acquired from all 834 subjects (231 Healthy Controls (HC), 238 Stable Mild Cognitive Impairment (SMCI), 167 MCI to AD progressors (P-MCI), 198 AD) from the ADNI database were used for evaluation. They compared the classification accuracy achieved with Linear Discriminant Analysis (LDA) and Support Vector Machines (SVM). The most stable and reliable classification was achieved when combining all available features.

Jedynak et al[21], proposed a widely applicable statistical methodology for creating a Disease Progression Score (DPS), using multiple biomarkers, for subjects with a neurodegenerative disease. The proposed methodology was evaluated for AD using the publicly available ADNI database, yielding an Alzheimer's DPS score for each subject and each time-point in the database. Biju et al[22], provided a software solution for detecting the brain abnormalities for detection of Alzheimer's disease. Their proposed algorithm produced a 3D representation of the brain from the MRI slices. In this method each MRI slices undergone different processes such as de-noising, segmentation, slice-o-matic (3D construction), and calculation of residual volume of brain parts. It used the grey to white matter ratio for determining whether the person is affected by Alzheimer's disease. Kalavathi et al[23] segmented the WM and GM from MRI human head scans to detect Alzheimer's Disease using Spatial Fuzzy Clustering with Level Set Method(SFCM) in two tier process, tier1 proceed with brain portion extraction using skull stripping method and tier2 segments WM and GM using SFCM with level set method, WM and GM are analysed to detect AD by evaluating Jaccard(J) and Dice(D) similarity measures.

Kalavathi et al[24], proposed a method consisting of two processes, in the first process, the skull is removed from the brain image using Contour based brain segmentation method (CBSM), and then they applied clustering technique namely Fast Fuzzy C Means (FFCM) to segment the brain tissue such as WM and GM. In the second step, the segmented WM and GM are analyzed to detect AD in MR brain images by computing the similarity measures such as Jaccard and Dice against the normal brain. A framework proposed for the reproducible evaluation of machine learning approaches in AD is presented in Samper-Gonzalez et al[25], they used images from three public datasets: ADNI, the Australian Imaging Biomarker and Lifestyle study (AIBL) and the Open Access Series of Imaging Studies (OASIS). A modular set of preprocessing pipelines, feature extraction and classification methods, together with an evaluation framework that provided a baseline for benchmarking the different components of brain images. The work was extended by introducing more feature types and more classification algorithms. They also demonstrated the use of the framework for comparison of different classifiers, features and imaging modalities. Zhang et al [26], developed a novel machine learning system that could diagnose AD automatically from brain magnetic resonance images. A predator-prey particle swarm optimization was proposed to train the weights and biases of the classifier. In this method, they used four level decomposition and yielded 13 Stationery Wavelet Entropy (SWE) features. In terms of classification performance, the method performs better than 10 state-of-the-art approaches and the performance of human observers. Therefore, this proposed method found to be effective in the detection of Alzheimer's disease.

A method for the diagnosis of AD proposed by Zeng et al [27], consists of MRI image preprocessing, feature extraction, principal component analysis, and the Support Vector Machine (SVM) model. In particular, a new Switching Delayed Particle Swarm Optimization (SDPSO) algorithm was proposed to optimize the SVM parameters. The developed framework based on the SDPSOSVM model was successfully applied to the classification of AD and MCI using MRI scans from ADNI dataset. The developed algorithm could achieve excellent classification accuracies for 6 typical cases. Furthermore, the experimental results demonstrated that the proposed algorithm outperforms several SVM based models and also two other state-of-art methods with deep learning embedded techniques and, thereby serving as an effective AD diagnosis method. A Whole Brain Hierarchical Network (WBHN) employed by Liu et al[28], based on Automated Anatomical Labelling(AAL) atlas represented each subject into 90,54,14 and 1 regions. Pearson's correlation coefficient used as a Classification feature to compute the connectivity between each pair of regions. Features with higher F-scores selected to reduce the dimensionality of features to conclude they used multiple kernel boosting (KBoost) algorithms to perform the classification. Alzheimer's disease Neuroimaging Initiative (ADNI) database MRI images used to evaluate their proposed methods. The experimental results show that their proposed method achieves an accuracy of 94.65%.

Automated brain tissue segmentation for Magnetic Resonance brain images was proposed by Priya and Kalavathi[29], to reduce time complexity and computational efficiency in diagnosing process, they developed brain tissue segmentation method using Histogram based Swarm Optimization techniques and the proposed method were compared with existing swarm optimization techniques such as Particle Swarm Optimization (PSO), Darwinian Particle Swarm Optimization (DPSO), Fractional Order Darwinian Particle Swarm Optimization(FODPSO) and also Adaptive Maximum a posteriori probability (AMAP), Biased Maximum a Posteriori Probabiltiy(BMAP), Maximum a

posteriori Probability (MAP), Maximum Likelihood (ML), and Tree structure K-Means (TK-Means). This proposed technique was tested with three brain datasets and obtained better results than other proposed techniques.

V. CONCLUSION

This paper describes the overview of an Alzheimer's disease and the computational methods for AD detection and quantification methods using MR brain images. This exploratory review reveals the fact that the development of automated methods for AD detection and classification remains challenging and devising robust and reliable computational methods is still demanding area of research in the medical field.

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Table.1 Summary of AD Detection and Quantification Methods

Author (s) and Year	Title of the Article	Methods Used	Remarks
Thomposon et al, (2004) [15]	Mapping cortical change in Alzheimer's disease, brain development and schizophrenia	Structural Brain Mapping Methods	Revealed the profile of Structural brain defects of dementia
Ali et al, (2010) [18]	Automatic Detection and Classification of Alzheimer's Disease from MRI using Tree Augmented Bayesian Neural Networks	Tree Augmented Bayesian Neural Networks	99.2 Accuracy in Classification
Cuingnet et al, (2011) [19]	Automatic classification of patients with Alzheimer's disease from structural MRI: A comparison of ten methods using the ADNI database	Voxel- Based Segmentation	94% accuracy, 92% sensitivity and 97% specificity
Wolz et al. (2011) [20]	Multi-Method Analysis of MRI Images in EarlyDiagnostics of Alzheimer's Disease	Support vector machines (SVM), Linear Discriminant Analysis (LDA)	95% confidence interval for the classification accuracy
Jedynak et al. (2012) [21]	A computational neurodegenerative disease progression score: method and results with the Alzheimer's disease Neuroimaging Initiative cohort	Statistical Methodology	Computed Alzheimers Disease Progression Score
Biju et al, (2017) [22]	Alzheimer's Detection Based on Segmentation of MRI Image	Wavelet Transform	Software solution for the detection of brain abnormality, specifically the Alzheimer's disease
Kalavathi et al, (2017) [23]	Detection of Alzheimer Disease in Human MRI Head Scans Using Spatial Fuzzy Clustering with Level Set Method	Spatial Fuzzy Clustering with Level Set Method	AD detected using Similarity Measures Jaccard & Dice
Kalavathi et al 2017 [24]	Detection of Alzheimer Disease in MR Brain Images using FFCM Method	Contour based brain segmentation method (CBSM), Fast Fuzzy C Means (FFCM)	AD detected using similarity measures
Samper-Gonzalez et al, (2018) [25]	Reproducible evaluation of Alzheimer's Disease classification from MRI and PET data.	Partial Volume Correction (PVC), Standardized Uptake Value Ratio (SUVR)	Produced better classification results than T1 MRI for all the selected features

Zhang et al, (2018) [26]	Multivariate Approach for Alzheimer's Disease Detection using Stationary Wavelet Entropy and Predator-Prey Particle Swarm Optimization	Stationary Wavelet Entropy (SWE), Predator-Prey Particle Swarm Optimization	The classification yielded an overall accuracy of 92.73±1.03%, a sensitivity of 92.69±1.29%, and a specificity of 92.78±1.51%.
Zeng et al, (2018) [27]	A New Switching-Delayed PSO Based Optimized SVM Algorithm for Diagnosis of Alzheimer's Disease	PSO Optimized SVM Classifier	Accuracies: 93.3% (for AD vs NC)
Liu et al, (2018) [28]	Classification of Alzheimer's Disease using Whole Brain Hierarchical Network	Multiple Kernel Learning (MKL) (MKBoost)	94.5 classification accuracy
Priya and Kalavathi, (2019) [29]	Brain Tissue Segmentation from Magnetic Resonance Brain Images using Histogram Based Swarm Optimization Techniques	Histogram Based Swarm Optimization techniques	WM, GM and CSF are segmented and yields better results.

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