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Survey on Machine Learning-Based Prognosis of Early-Stage Alzheimer's Disease

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ABSTRACT

Alzheimer's disease (AD) is a progressively worsening neurological condition that poses an increasing concern to global public health. Timely identification and precise diagnosis of Alzheimer's disease are essential for effective intervention and care. This comprehensive review delves into an extensive examination of methods for detecting Alzheimer's disease (AD), with a specific emphasis on approaches centered around medical imaging. We explore the spectrum of imaging modalities, data acquisition, feature extraction, classification techniques, and the latest advancements in AI-based diagnostic systems. Through a comprehensive review of the literature, we highlight the evolving landscape of AD detection, challenges, and future research directions. This survey aims to serve as a valuable resource for researchers, clinicians, and policymakers in the field of AD detection.

Keywords : Alzheimer's, Machine Learning, AI, Image, MRI

I. INTRODUCTION

Alzheimer's Disease (AD) is a progressive neurodegenerative disease characterized by memory loss and cognitive disabilities. It is the most common cause of dementia, accounting for 60-80% of all dementia cases. AD was first described in 1906 and recognized as a major cause of death after 70 years It is a costly disease, with an estimated projected cost of 47 billion dollars in 2018. Early diagnosis is crucial as it can slow down the progression of the disease and reduce healthcare costs [3]. Alzheimer's disease (AD) is a progressive and debilitating neurodegenerative disorder that primarily affects the elderly population, posing a substantial burden on global healthcare systems. The hallmark of AD is the gradual loss of cognitive abilities, ultimately leading to severe dementia. The prompt identification and precise detection of Alzheimer's disease are critically significant, allowing for timely interventions and tailored care strategies. With the advent of medical imaging and artificial intelligence (AI) technologies, the landscape of AD detection has witnessed significant advancements. Structural MRI has been widely studied as a non-invasive method for detecting brain atrophy in MCI patients, particularly in the hippocampal and entorhinal regions [4]. In this survey, we embark on a journey to explore the state of the art in AD detection, focusing particularly on methods leveraging medical imaging data.

AD is an all-encompassing and persistent neurodegenerative condition marked by the gradual deterioration of cognitive functions, memory decline, and, ultimately, profound dementia. With the aging global population, AD has emerged as a pressing public health challenge, impacting millions of individuals and their families worldwide. The socio- economic and emotional burdens it imposes are substantial, compelling a concerted effort to enhance our understanding of the disease, improve its early detection, and provide better care and treatment. Preclinical changes in the brain associated with Alzheimer's can be observed years before the onset of clinical symptoms, making early diagnosis and intervention possible [2].

The urgency of the situation stems from the fact that interventions and treatments are most effective when administered at an early stage of the disease. Mild Cognitive Impairment (MCI) is a preclinical stage of Alzheimer's Disease (AD). This study investigates the classification of MCI using multimodal data and co-training method [1]. Alzheimer's disease (AD) is an irreversible and progressive neurodegenerative disorder that mainly affects individuals aged 65 and older. Mild cognitive impairment (MCI) is the prodromal state of AD, further classified into progressive MCI (pMCI) and stable MCI (sMCI) [9]. Therefore, early detection is not merely a matter of convenience but a critical determinant of the patient's quality of life and the potential success of therapeutic interventions.

In the quest for early detection and accurate diagnosis, medical imaging has emerged as an Developing a low-cost and easy-to-use AD detection tool [10]. It allows us to visualize and analyze the structural and functional changes occurring in the brain as the disease progresses.

The power of imaging lies in its ability to reveal subtle alterations in brain anatomy, such as the atrophy of specific regions and the deposition of amyloid plaques and neurofibrillary tangles, which are pathological hallmarks of AD.

The field of AD detection has also witnessed a revolution fueled by artificial intelligence and machine learning. Machine learning models for early-stage Alzheimer's disease prediction - Importance of early detection and treatment for AD [13]. These advancements in technology have empowered the creation of advanced algorithms with the capability to analyze extensive sets of medical images. These algorithms can extract intricate patterns and features that might elude the human eye, offering a promising avenue for improving the accuracy and reliability of AD diagnosis.

In this comprehensive survey, we embark on a journey to explore the state of the art in AD detection, with a particular focus on methods leveraging medical imaging data. The paper focuses on accurate identification of Alzheimer's disease (AD) using multi-modal data. - It proposes a relation-induced multi-modal shared representation learning method for AD diagnosis [6]. Machine learning methods have been proposed to aid in the interpretation of clinical data for diagnosis and decision making. However, most current machine learning approaches do not mimic the personalized diagnostic process of real clinical settings [8]. Our goal is to provide an in-depth and up-to-date overview of the landscape of AD detection, its challenges, and the directions it is taking. Through an extensive literature review, we aim to provide researchers, clinicians, and policymakers in the field with a valuable resource that encapsulates the diversity of approaches, the current state of technology, and the future horizons of AD detection. We delve into the various imaging modalities, data acquisition and preprocessing techniques, feature extraction methodologies, and classification algorithms that researchers have employed. Alzheimer's disease (AD) is a chronic neurodegenerative disease that requires long-term progression prediction. Structural Magnetic

Resonance Imaging (sMRI) is used to characterize cortical atrophy in AD and its prodromal stages. Existing methods focus on predicting cognitive scores using morphological features derived from sMRI [5] . Furthermore, we highlight the recent advances in AI-based diagnostic systems, which offer great promise for the early diagnosis of AD. While this survey encapsulates the present knowledge and progress in AD detection, we must acknowledge that substantial challenges lie ahead. Data availability and diversity, the interpretability of AI models, and the generalizability of research findings are persistent obstacles that the field must address. Therefore, we conclude our introduction by emphasizing the importance of this survey, which not only summarizes the current state of the field but also sets the stage for the ongoing and vital work of improving the early detection and management of this formidable disease.

II. RELATED WORK

The pursuit of effective Alzheimer's disease detection methods has driven extensive research in the field of medical imaging and machine learning. A comprehensive review of related work reveals the diverse approaches and techniques that researchers have employed. Imaging modalities such as Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET), and Computed Tomography (CT) have been harnessed to capture structural and functional brain changes associated with AD. Data preprocessing methods, encompassing image registration, denoising, and normalization, play a crucial role in ensuring the quality of imaging data. Feature extraction, covering a spectrum from voxel-based measures to advanced texture and morphological features, contributes to the discrimination between AD and healthy controls. Furthermore, an array of classification algorithms, including Support Vector Machines (SVM), Convolutional Neural Networks (CNNs), and ensemble methods, have been employed to distinguish between AD and non-AD subjects. Emerging AI-based diagnostic systems, leveraging deep learning and multimodal data fusion, exhibit promising results. The literature review provides valuable insights into the past and current state of AD detection, laying the foundation for future research directions.

1) A paper published by Shaoxun Yuan and team of researchers focuses on investigating the potential of using both labeled and unlabeled samples from the ADNI cohort to classify Mild Cognitive Impairment (MCI) through the multimodal co- training method. Utilizing structural magnetic resonance imaging (sMRI) data and genotype data to build initial classifiers on labeled MCI samples, and implementing the co-training method to obtain new labeled samples from unlabeled MCI samples.Using the random forest algorithm to obtain a combined classifier for MCI classification in the independent ADNI-2 dataset. Demonstrating that the proposed framework achieves an accuracy of 85.50% and an AUC of 0.825 for MCI classification, indicating that the combined utilization of sMRI and SNP data through the co-training method significantly improves the performance of MCI classification [1].

2) A paper published by Asif Hassan Syed and team of researchers focuses on a method using a novel combination of Cerebrospinal Fluid (CSF) protein biomarkers to predict AD's earlier stages with greater accuracy than existing biomarkers.Use of two feature selection methods, Recursive Feature Elimination (RFE) and L1 regularization, to identify the most important subset of features for building a classification model using the Mild Cognitive Impairment (MCI) dataset.Screening of a novel combination of three biomarkers (Cystatin C, Matrix metalloproteinases (MMP10), and tau protein) using linear Support Vector Machine (SVM) and Logistic Regression (LR) classifiers.Creation of an ensemble model using a weighted average of the two best performing classifiers (LR and Linear SVM) based on the three most informative features.Demonstration of the significantly better performance of the proposed

ensemble model compared to LR and Linear SVM base classifiers, as evidenced by Receiver Operating Characteristic Curve (ROC_AUC) and Area under Precision-Recall values (AUPR) [2].

3) A paper published by Xin Hong and team of researchers focuses onpredicting model based on Long Short-Term Memory (LSTM), a special kind of recurrent neural network, to predict the possible development of Alzheimer's Disease (AD) by encoding the temporal relation between features and the next stage of the disease. The model outperforms most existing models in terms of prediction accuracy.The authors consider the impact of time series data on prediction and use time step data obtained through a data preprocessing pipeline. They also evaluate the stability of their algorithm in different data sizes and its sensitivity to different features.The paper compares the efficiency of their algorithm with recent state-of-the-art algorithms and demonstrates its stability in different data sizes.The authors highlight the importance of capturing time-sensitive features for predicting the future stage of the disease, which their proposed method successfully achieves.The paper contributes to the field of digital health by addressing the need for early diagnosis of AD, which can significantly decrease the risk of further deterioration [3].

4) The paper published by Fusun Er and team of researchers presents a deep learning-based computer-aided diagnosis (CAD) system to forecast the transition from Mild Cognitive Impairment (MCI) to Alzheimer's Disease (AD) using longitudinal non-invasive structural MRI data from baseline and a 12-month follow-up. Employing an array of methodologies such as an autoencoder, convolutional neural network (CNN), and support vector machines (SVM) classifier, the system achieves an accuracy of 87.2% in distinguishing progressing MCI patients from stable ones. Notably, the CAD system sidesteps invasive methods or cognitive tests, offering a less burdensome prediction strategy. However, limitations include the exclusive focus on MCI patients without a healthy control group for comparison, reliance on longitudinal MRI data, potentially limiting broader clinical applicability, and the absence of comparative analysis with other existing prediction methods, leaving room for further performance assessment and improvement [4].

5) A paper published by Yan Zhao and team of researchers focused on predicting the cognitive scores at future time-points using morphological features derived from sMRI .Very few works consider predicting an individual brain MRI image at future time-points .The proposed framework in this paper comprises a 3D multi- information generative adversarial network (mi- GAN) to predict what one's whole brain will look like with an interval, and a 3D DenseNet based multi-class classification network optimized with a focal loss to determine the clinical stage of the estimated brain .The mi-GAN can generate high- quality individual 3D brain MRI images conditioning on the individual 3D brain sMRI and multi-information at the baseline time-point. The mi-GAN shows state-of-the-art performance with a structural similarity index (SSIM) of 0.943 between the real MRI images at the fourth year and the generated ones .The pMCI vs. sMCI accuracy achieves a 6.04% improvement compared to conditional GAN and cross entropy loss when using mi-GAN and focal loss [5].

6) A paper published by Zhenyuan Ning and team of researchers focussed on relation-induced multi-modal shared representation learning framework for Alzheimer's disease (AD) diagnosis. It integrates representation learning, dimension reduction, and classifier modeling into a unified framework .The framework obtains multi-modal shared representations by learning a bi-directional mapping between the original space and shared space, utilizing relational regularizers and auxiliary regularizers to encourage learning underlying associations in multi-modal data and alleviate overfitting.The proposed method outperforms several state-of-the-art methods in terms of accuracy and performance, as demonstrated

through extensive experiments on two independent datasets (ADNI-1 and ADNI-2) [6].

7) A paper published by Rongrong Li and team of researchers focuses on improved method of measuring technology similarity in the medical field based on the subject-action-object (SAO) semantic structure. The SAO semantic structures are extracted and cleaned using the semantic network of the Unified Medical Language System (UMLS) .The similarity between the SAO semantic structures is evaluated using the Metathesaurus of UMLS .The feature weights of the SAO semantic structure are introduced to represent the importance of the patentees' technology features .Each patentee's vector is constructed using the SAO and weight information to measure the technology complementarity between different patentees. The proposed method is compared with traditional methods that measure technology similarity based on IPC codes and keywords .The traditional method of measuring technology similarity based on keywords involves constructing vectors using keyword frequency and characterizing the similarity between patents using Euclidean distance between vectors .The TF-IDF weighting technique is used to calculate the importance of words in documents [7].

8) A paper published by Javier Escudero and team of researchers focuses on machine learning approach for personalized and cost-effective diagnosis of Alzheimer's disease (AD) using locally weighted learning to tailor a classifier model to each patient and compute the sequence of biomarkers most informative or cost-effective for diagnosis. Potential use of the approach to support personalized diagnosis processes and reduce the number or cost of biomarkers needed for diagnosis.Extension of the framework to other biomarkers and diseases.Use of accuracy and AUC as appropriate metrics for selecting

9) AD and HC subjects.Presenting the first application of Kinect V.2 camera and machine learning to provide a comprehensive and and F- score for classifying quantitative analysis of the TUG test for detecting AD patients from HC. Demonstrating the potential of this approach as a new quantitative complementary tool for detecting AD among older adults [10].

10) A paper published by C. Kavitha and team of researchers focussed several techniques such as Decision Tree, Random Forest, Support Vector Machine, Gradient Boosting, and Voting classifiers have been employed to identify the best parameters for Alzheimer's disease prediction .The paper also references recent work on the prediction of Alzheimer's disease, which includes the use of SVM, Decision Tree, NN, and Naive-Bayes models .Additionally, the paper mentions the use of feature selection methods such as Correlation coefficient, Information gain, and Chi-Square in the prediction of Alzheimer's disease .The paper discusses the use of the Open Access Series of Imaging Studies (OASIS) dataset for predictions of Alzheimer's disease. The paper highlights the importance of early diagnosis of Alzheimer's disease and the potential features, with performance improvement tending to decrease monotonically from the first to the last iterations.Funding support from the National Institute for Health Research (NIHR) and the Alzheimer's Disease Neuroimaging Initiative (ADNI). Use of data from the ADNI database to test the approach [8].

A paper published by CHIYU FENG and team of researchers focused on novel deep learning framework for Alzheimer's disease (AD) diagnosis using 3D-CNN and fully stacked bidirectional LSTM (FSBi-LSTM) .The framework combines the virtues of 3D-CNN and FSBi-LSTM to derive deep feature representation from both MRI and PET data, improving the performance of AD diagnosis .The proposed method achieves high accuracies for differentiating AD from normal control, pMCI from NC, and sMCI from NC, outperforming related algorithms in the literature .The framework addresses the challenge of limited availability of imaging data by effectively utilizing CNNs for AD diagnosis .The use of FSBi-LSTM helps to capture hidden spatial information from deep feature maps, further enhancing the performance of the framework. The method is validated on the AD neuroimaging initiative (ADNI) dataset, demonstrating its effectiveness in AD diagnosis [9].

III. LITERATURE SURVEY

Sr.	Reference no.	Dataset	Techniques	Limitations
1.	[11]	OASIS data	Machine Learning techniques (Decision Tree, Random Forest, Support Vector Machine, Gradient Boosting, Voting classifiers) - Feature selection methods (Correlation coefficient, Informationgain, Chi-Square)	The paper mentions the use of various machinelearning models such as Decision Tree, RandomForest, Support Vector Machine, Gradient Boosting, and Voting classifiers, but it does not provide detailed information on the specific parameters or configurations used for these models. The paper does not provide informationon the sample size or demographic characteristics of the participants included in thestudy, which may impact the generalizability of the results.
2.	[5]	ADNI (Alzheimer's DiseaseNeuroimaging Initiative) dataset, specifically ADNI- GO and ADNI-2	3D multi-information generative adversarial network (mi-GAN) - 3D DenseNet based multi-class classificationnetwork	Existing GAN-based models use 2D-MRI slicesinstead of 3D brain images. The models do not consider non-imaging factors that impact AD progression.
3.	[6]	DNI-1 and ADNI-2	Relation-induced multi- modal shared representation learning method. Integration of representation learning, dimension reduction, and classifier modeling	The fusion of multi-modal data and the incorporation of various techniques, such as representation learning, dimension reduction, and relational regularizes, may result in a computationally intensive process. The complexity of the proposed unified framework might limit its scalability and practical application in real-world clinical settings where computational resources may be constrained. The use of advanced techniques, including bi-directional mapping and shared representations, could make the model less interpretable. Understanding the reasoning behind the model's decisions is crucial for gaining trust from clinicians and stakeholders, and complex models might pose challenges in this regard.

4.	[9]	(ADNI) dataset	3D-CNN for feature extraction from MRI andPET inputs- FSBi-LSTMfor extracting high-level semantic and spatial information	The study does not utilize longitudinal MRI data, which could provide complementary information about disease evolution.
5.	[7]	-------------	Cosine measure based onIPC of patent portfolios - SAO semantic structureand professional vocabulary	. The paper does not discuss the potential impact of the chosen feature weights for representing the importance of technology features and whether they may introduce biases or limitationsin the measurement of technology similarity.
6.	[3]	Longitudinal MRI	Long short-term memory(LSTM) network - Deep neural network (DNN) with PCA-LASSO	The paper does not provide a detailed discussion on the specific features or data used in the LSTM model for predicting the development of Alzheimer's Disease. It would be helpful to understand the selection and relevance of these features in the prediction process.
7.	[1]	Labeled and unlabeled samples from the ADNI cohort	Cosine measure based onIPC of patent portfolios - SAO semantic structureand professional vocabulary	The classification performance of the proposed framework was evaluated using the ADNI-2 dataset, but it would be beneficial to validate the results on additional independent datasets to further assess the robustness of the approach.
8.	[8] .	ADNI database	Machine learning approach for personalizeddiagnosis of AD is Locally weighted learningfor tailoring classifier model	Other classifiers can be tested as base learners. "Modified cost" can be developed for biomarkerselection. An independent validation set shouldbe used to optimize the selection of biomarkers and determine clinically acceptable values,which was not done in this study.

9.	[2]	Mild Cognitive Impairment(MCI) dataset	Recursive Feature Elimination (RFE) L1 regularization method	The feature selection methods used in the study, Recursive Feature Elimination (RFE) and L1 regularization, may have limitations in terms of their ability to identify the most informative features for prediction.
10.	[10]	47 healthy control (HC) subjects and 38 Alzheimer'sdisease (AD)	Signal processing and statistical analysis Machine learning with support vector machineclassifier	The data processing step rejected some participants' data due to excessive noise or the presence of outliers, which may have affected the representativeness of the sample.
11.	[4]	ADNI (Alzheimer's DiseaseNeuroimaging Initiative)	Autoencoder, CNN, SVMclassifier used for prediction - Longitudinal data andMRI images used for analysis	The accuracy of the CAD system is reported to be 87.2%, which means there is still room for improvement in terms of prediction performance

IV. DATA COLLECTION

Data collection for Alzheimer's disease detection encompasses a comprehensive approach to gather relevant information from various sources, including clinical assessments, neuroimaging, genetic testing, and Physical analysis. These data points collectively contribute to a holistic understanding of the disease and aid in the development of effective diagnostic and therapeutic strategies. Clinical assessments involve neuropsychological evaluations that measure cognitive function, memory, and language skills.

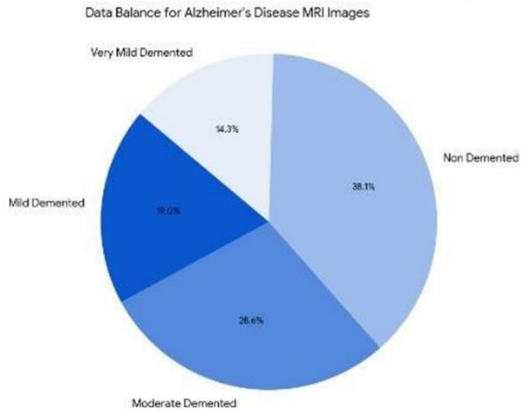
Neuroimaging techniques, such as MRI and PET scans, provide insights into structural and functional brain changes associated with Alzheimer's disease. Genetic testing identifies individuals with predisposing genetic variants, while biomarker analysis detects specific molecules in the blood or cerebrospinal fluid that signal disease progression. By integrating data from these diverse sources, researchers can refine diagnostic criteria, identify potential therapeutic targets, and track the disease's course over time.

Link for the Dataset:
https://www.kaggle.com/datasets/tourist55/alzheimers- dataset-4-class-of-images
The data consists of MRI images. The data has four classes of images both in training as well as a testing set: Mild Demented Moderate Demented Non-Demented Very Mild Demented

V. OBJECTIVE

Designing an in-depth analysis framework for Alzheimer's Disease by examining MRI image datasets to comprehend data characteristics and patterns thoroughly.

Designing and deploying a resilient and precise algorithm for early detection and diagnosis of Alzheimer's Disease. This involves utilizing cutting-edge machine learning and image analysis techniques.



Exploring the integration of optimization techniques in the design of MRI image processing. This design is specifically customized to improve feature extraction, denoising, and segmentation through methods such as L0 Smoothing, Super pixel, and KNN.

VI. PROPOSED SYSTEM ARCHITECTURE

1. The process of research work is to be carried out in the following sequence to achieve the Research Objectives.
2. Image acquisition: Input of MRI image database for pre-processing data.
3. Preprocessing: The obtained image is then pre-processed for improvement that surpasses unwanted distortions and enhances some features important for further processing. Also, the image which is given as the input may not be of standard size. So it is necessary to obtain the required image size. Smoothing will also perform for better edge detection
4. Segmentation: In this phase segmentation will perform using Genetic Algorithm to find out Region of Interest (ROI).
5. Feature Extraction: In this process an initial set of raw variables is reduced to more manageable features for processing, while still accurately and completely describing the original data set of acne images.
6. Classification: Feature will classify for developing Training & Testing System. So system will be evaluate on selected parameter.

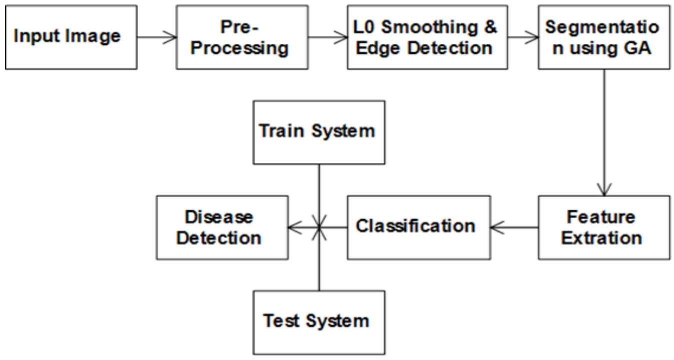
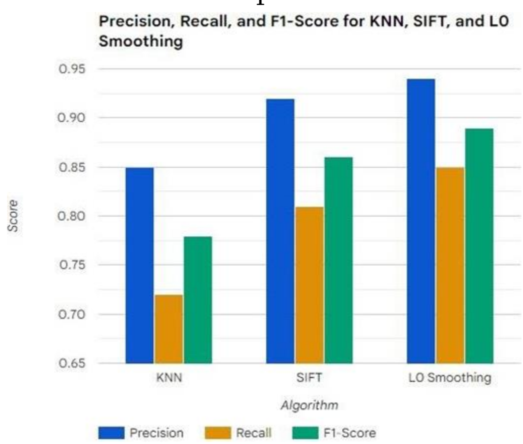


Fig. 1 Simplified Block Diagram

VII. RESULT AND ANALYSIS

Various machine learning (ML) approaches have been employed for Alzheimer's disease (AD) classification, and this study involves a comparative analysis of some of these techniques. Table 2 presents a comprehensive overview of how each ML method performed relative to the others.

In examining different deep learning (DL) techniques for AD classification, notable findings emerged. The DNN technique, specifically Lenet with the ADNI dataset, exhibited an impressive accuracy of 96.64%. On the other hand, a variant DNN with 20 hidden layers using the OASIS dataset achieved an accuracy of 91.00%, and the Feed Forward DNN with the ADNI dataset showed a respectable 79.3% accuracy.



Precision: Precision is the ratio of true positive predictions to the total number of instances predicted as positive by the model. It measures the accuracy of positive predictions.

$$\text{Precision} = \frac{\text{True Positives}}{\text{True Positives} + \text{False Positives}}$$

Recall (Sensitivity): Recall is the ratio of true positive predictions to the total number of actual positive instances in the dataset. It measures the model's ability to identify all positive instances.

$$\text{Recall} = \frac{\text{True Positives}}{\text{True Positives} + \text{False Negatives}}$$

Accuracy: Accuracy is the ratio of correct predictions to the total number of predictions made by the model. It measures the overall correctness of the model's predictions across all classes.

$$\text{Accuracy} = \frac{\text{True Positives} + \text{True Negatives}}{\text{Total Predictions}}$$

VIII. CONCLUSION

In conclusion, this survey paper offers a comprehensive exploration of Alzheimer's disease (AD) detection, with a particular focus on the intersection of medical imaging and artificial intelligence. Early detection of AD remains a critical goal in the field, and advances in imaging modalities, data preprocessing, feature extraction, and classification techniques have propelled the development of increasingly accurate diagnostic models. The progress made in AI-based diagnostic systems, especially those harnessing deep learning and multimodal data, holds promise for improved sensitivity and specificity in AD detection. Nonetheless, challenges persist, including data availability, interpretability, and generalizability. Future research directions encompass the development of more interpretable models, robustness against diverse populations, and further advancements in multimodal fusion. This survey serves as a valuable resource for researchers, clinicians, and policymakers in the realm of AD detection, offering insights into the current landscape and setting the stage for continued progress in the early diagnosis and management of this devastating disease.

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