Review on Detection of Alzheimer's Disease Using Image Processing at Early Stage

T.Sangeetha Devi[1], Dr.V. Raghavendran[2], Dr.M.Rahimabheevi[3]

[1] T.Sangeetha Devi, *Research Scholar, Department of Computer Science, VISTAS, Chennai,*

[2] Dr.V. Raghavendran, *assistant professor Department of Computer Science, VISTAS, Chennai,*

[3]*Dr.M.RahimaBheevi, HOD, PG Department of Computer Science, MSCAS, Chennai*

Abstract: **Personal lifestyle, genetics, and other environmental factors lead to Alzheimer's disease (AD), which is an irretrievable disease that demolishes the brain's memory cells gradually. Early detection of AD, which is a significant challenge, is essential for solidifying the patient's quality of life and establishing efficient care along with the targeted medicine. Recently, in predicting AD, Artificial Intelligence (AI)-centric approaches, namely Machine Learning (ML) and Deep Learning (DL) have exhibited great promise. In recent days, for medical staff, there is an inevitable trend for detecting AD in disparate phases by the combination of functional Magnetic Resonance Imaging (fMRI) and AI approaches like DL. The DL algorithm's human-level performance has been efficiently displayed in disparate disciplines. Hence, this work explains AD, the detection of AD utilizing Image Processing (IP) at an early stage, types of IP modalities utilized for the earlier detection of AD, AI approaches utilized in AD detection at an early stage, and performance comparison of AI approaches utilized in AD detection at an earlier stage.**

Keywords: ***Alzheimer's disease, Image processing, Artificial intelligence, Machine learning and Deep learning***

1. INTRODUCTION

Ageing of the global population leads to an increasing number of people with mental illness. As per recent studies, 50 million people are living with mental illness among which 60 to 70 % have AD [1]. The most general stage of dementia that needs wide medical care is AD. AD prediction's early and accurate study is essential for clinical progress initiation along with effective patient treatment. A progressive, chronic, and irretrievable neurodegenerative disease that is clinically apparent by cognitive dysfunction, amnesia, and gradual loss of numerous other brain functions and everyday living independence is termed as AD [2]. A few symptoms, namely loss of mental functions and memory, mood and personality changes, along with difficulty in performing everyday activities, writing, routine tasks, understanding what people are talking about, speaking, and reading [3]. The 3 phases of the disease are very mild, mild, and moderate. In the early phase, the treatments have the most impact. It is estimated that by 2030, the worldwide disease burden of AD will attain $2 trillion, which requires early detection [4]. Hence, early diagnosis has an essential part in patient care along with future treatment for delaying its progression [5]. To slow down the abnormal degeneration of the brain's neurons, researchers are continuing early detection of AD. In addition, it produced emotional and financial benefits for the patient's family [6]. AD can be detected early and for predicting the possibility of disease, it can be diagnosed by IP of Magnetic Resonance Imaging (MRI) scans [7]. The conventional procedure for AD detection is described in Figure 1.

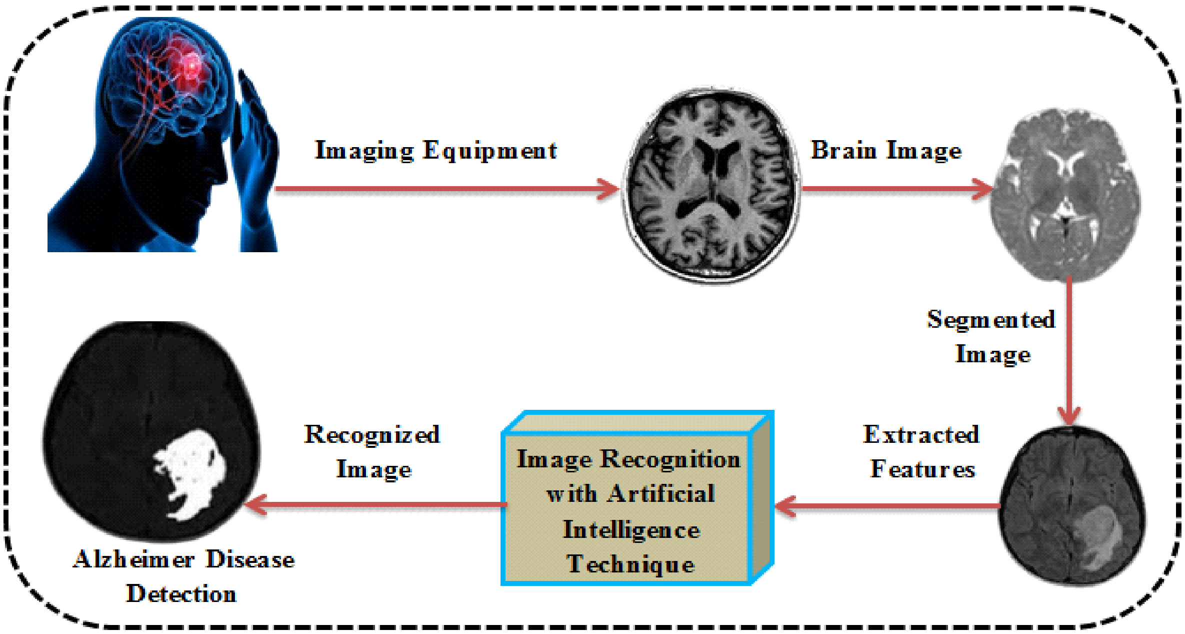

Figure 1: Conventional procedure for AD detection

For detecting Alzheimer's risk with over 90% accuracy, researchers utilized another approach called AI, which could transform how medicine is practiced. Huge breakthroughs in Alzheimer's research could be led by advances in AI and ML [8]. In analyzing brain images for diagnosing brain diseases, a few DL approaches, such as Multilayer Perceptrons (MLPs), Convolutional Neural Networks (CNNs), Generative Adversarial Networks (GANs), and so on are involved [9].

- CNNs: For detecting Alzheimer-affected persons' active MRI scanned sheets, CNNs are utilized. It is performed in data collection, preprocessing and fine-tuning, and classification and evaluation phases.
- MLPs: High-resolution visualizations of AD risk that can be used for precise predictions of AD status are generated by MLPs [10].
- GANs: By providing IP support, encompassing quality improvement for low-dose Positron Emission Tomography (PET) images, GANs have displayed application value in diagnosing AD.

The brain shape is not deformed constantly owing to disease. The brain transforms its shape via a natural process present [11]. Differentiating the deformation of the shape of the brain owing to pathological reasons was difficult in IP even though it has benefits in diagnosing AD early [12].

The survey work is described as: the survey on AD detection utilizing IP at an early phase is described in section 2, the analysis is depicted in section 3, along with that section 4 deduces the work.

2. LITERATURE REVIEW

The IP's use for early diagnosis of AD proved to be successful. Utilizing picture segmentation, vascular enlargement together with the brain atrophy identification of enlarged Vascular is attained. Whether the patient is healthy in the initial stage, in the second stage, in the third stage of AD, or else in the mild phase of cognitive impairment is determined by the enlargement's size. In this work, AD is defined in section 2.1, the detection of AD utilizing IP at an early phase is illustrated in section 2.2, and the AI approaches utilized in AD detection at an early phase are described in section 2.3.

2.1. ALZHEIMERS DISEASE

A brain disorder that gets worse eventually is called AD. Variations in the brain that cause deposits of specific proteins characterize AD. It engenders the brain to shrink as well as brain cells to die eventually [13, 14]. Forgetting recent events or else conversations is included in the disease's earlier signs. Eventually, serious memory issues and loss of the ability for performing daily tasks are progressed [15].

Jessica, et al. [16] built the retinal biomarkers for the earliest phases of AD. The accumulation of cerebral amyloid absence characterized the earliest phase of AD pathogens. As per the analysis, elevated macular Retinal Nerve Fiber Layer (mRNFL) thickness was linked with superior diffusion tensor MRI values particular to AD, and the mRNFL thinning's utility was potentially exhibited as a biomarker for functional cerebral alterations. But, whole-mount specimens studied lacked.

Qiuting, et al. [17] described the matter alterations in early-phase AD as tract-specific work. From 100 participants, Multishell Diffusion MRI data were acquired. As per the analysis, in the thalamic radiation, cingulum, along with the major of participants with MCI, lower Diffusion Tensor Imaging (DTI) fractional anisotropy and the topmost radial diffusivity were perceived. However, a preclinical cerebrovascular disease, which affects white matter along with the modest group sample sizes, was included.

Mate Gyurkovics, et al. [18] explicated the mind-wandering in healthy aging along with early-stage AD. This applied 3 huge cohorts completing the Sustained Attention to Response Task (SART) approach. As per the analysis, mind-wandering self-reports during the SART diminished as a function of age, and the AD group was diminished more. Previous to No-Go errors, the entire 3 groups produced faster responses on trials. Behavioral indices' importance was overrated.

Oliver, et al. [19] expounded the periodontal pathogens along with the related intrathecal antibodies in the AD's early phases. It recorded the clinical periodontal indices. It examined Cerebrospinal Fluid (CSF) for total tau protein (T-tau) along with the amyloid-β (A $\beta_{1\text{-}42}$). As per the analysis, patients' periodontal destruction together with the inflammation was ubiquitous with no dissimilarity betwixt groups. Treponema, T. forsythia, and P.gingivalis species were detected in more than 50% of subgingival biofilm instances, however, neither in serum nor in the CSF.

Ai Kimura, et al. [20] explained malnutrition with Behavioral and Psychiatric Symptoms of Dementia (BPSD) in grown-up women with mild cognitive impairment along with early-phase AD. Utilizing the Dementia Behavior Disturbance (DBD) scale along with the Mini Nutritional Assessment Short-Form (MNA-SF), nutritional status and BPSD were evaluated. The result showed that as per the covariance adjusting analysis, nutritional status was considerably linked with particular BPSD, encompassing "verbal aggressiveness/emotional disinhibition" ($F = 5.87$, $p = 0.016$) along with the "apathy/memory impairment" ($F = 15.38$, $p < 0.001$).

2.2. DETECTION OF ALZHEIMER'S DISEASE USING IMAGE PROCESSING AT THE EARLY STAGE

The clinical diagnosis of mental illness and AD can be supported by structural imaging, whose value is investigated as a marker for disease evolution together with the outcome measures for disease-modifying treatments by several trials [21]. For the extraction of features centered on the parameters, namely corpus callosum, hippocampus shape, and cortex thickness, IP is applied and contrasted [22].

Alina, et al. [23] described AD at an early phase utilizing IP. For diagnosis, evaluation analyses were performed with the chosen image, as well as the essential digital processing approaches were made on them. As per the analysis, whether the image was AD positive and AD negative was predicted early relying upon the value acquired. However, the approaches for the phase of the respective patient should be exhibited, but it wasn't stated.

Fernando, et al. [24] examined Alzheimer's early detection utilizing digital IP via Iridology. It applied the Iridology approach and an automated diagnosis was generated via disparate diagnoses. The evaluation outcomes exhibited that the applied approach acquired superior results with a 47.62% chance that a healthy person is identified as not having the estimated medical condition, a 74.00% that a sick patient acquires a diagnosis with a positive outcome, along with a 61.96% of correct diagnoses.

Shrikant, et al. [25] explained the AD's early detection utilizing IP. For processing the brain's MRI from the sagittal plane, axial plane, along with coronal plane, an IP approach was applied. As per the analysis, the AD's early detection utilizing IP exhibited an accuracy, misclassification Error rate, and true positive rate value of 0.91666, 0.0833, and 0.91666, respectively. The procedure exhibited that the applied approach had the capacity of detecting 1 image at a time.

Yash, et al. [26] explored the detection of AD utilizing IP. The outcome of digital images' medical study, such as magnetization resonance of brain's image scan was provided. The findings displayed that there was elevated vascular and cerebral atrophy, along with that proved that the brain cavity's atrophy was analyzed successfully by the image gradient. However, distinguishing the distortion from the brain's structure as natural or not was challenging.

Chetan, et al. [27] explicated the AD's early detection utilizing IP on MRI scans. Evaluating the IP's utility on MRI scans together with estimating the likelihood of AD's early detection was the goal. As per the study, it could help the analysis for detecting AD together with correlation with the psychiatric outcomes, and hence, could assist the doctors in detecting AD at an earlier phase. However, owing to age, differentiating betwixt atrophy would be challenging.

Dr. D.J. Samatha, et al. [28] examined the AD's earlier detection utilizing IP. For assisting in AD detection along with monitoring the disease's progression, an automated approach was required. The findings exhibited that by estimating the measures in accuracy, the applied graph theory approach was efficient along with that differentiated the brain network's aspects. But, only a limited amount of information could be depicted by the applied approach.

2.2.1. Types of image processing modalities utilized for the early detection of Alzheimer's disease

For AD's early detection, several IP modalities types have been utilized. Computed Tomography (CT), functional MRI, structural MRI, along with PET are encompassed in these modalities [29]. The selection of modality relies on the particular research question together with the available sources. The early detection's accuracy can be enhanced by merging several modalities, namely fMRI along with structural MRI [30, 31]. The IP modalities types utilized for AD's early detection along with their findings and limitations are described in Table 1.

Table 1: Types of image processing modalities used for the early detection of AD with its findings and limitations

AUTHOR NAME	IMAGE PROCESSING MODALITIES	FINDINGS	LIMITATIONS
Safura, et al. [32]	CT	Findings show that for Aβ plaques' early detection in the AD patients' brains, radiopeptide was proved as the best potential CT imaging agent	Imaging agents' broad applications have been limited by the manufacturing process
Jiaming, et al. [33]	PET	Preliminary results from PET Net displayed that graph-centric representation offered a more flexible and computationally inexpensive technique for AD analysis	In natural images, the functional properties were less evidential
Gemma, et al. [34]	MRI	As per the analysis, 1341 (34%) out of 3935 participants progressed to AD dementia and 2594 (66%) did not.	The needful information in the index test wasn't rendered by 24 studies
Uttam, et al. [35]	fMRI	As per the acquired outcomes, other techniques' accuracy in diagnosing AD was elevated by the combination of the hippocampal subfield together with the brain networks with rs-fMRI's numerous measures.	It limited the model size, which may damage the robustness of the group's statistical investigation
Xiaoke, et al. [36]	MRI and PET	As per the experimental results, the applied method of MRI and PRT had superior performance in diagnosing AD and found characteristics	The performance on the multi-class issue wasn't tested by the two-category issue
Subin, et al. [37]	MRI	Results displayed that when contrasted with hippocampal volume in both, composite texture depicted a superior AUC for conversion to AD earlier (0.817 v. 0.726, p = 0.027)	The absence of histological data limited the work, along with that the pathology reflected by the texture measures stays to be authenticated

Lorenzo, et al. [38] identified the AD brain via X-ray Phase Contrast Tomography (XPCT). A highly developed non-destructive 3D multi-scale direct imaging from the cell via the entire brain is termed

XPCT. Aβ plaques' disparate typologies and internal structures along with their communication with patho/physiological cellular and neuro-vascular microenvironments were exhibited by the findings. For the first time, XPCT facilitates amyloid-angiopathy's complete visualization at the capillary level, which was not possible to attain with supplementary techniques.

Szu, et al. [39] described the plasma amyloid test as a pre-screening tool for amyloid PET imaging in early-phase AD. As per the study, amongst clinically assume MCI along with mild dementia patients, the success rate for detecting amyloid PET+ patients efficiently elevated from 42.3 to 70.4%. Nevertheless, amyloid PET scans were costly, along with that the amyloid PET availability was limited.

2.3. ARTIFICIAL INTELLIGENCE TECHNIQUES USED IN ALZHEIMER'S DISEASE DETECTION AT EARLY STAGE

For AD's early detection, AI approaches have emerged as promising tools. For examining medical data together with identifying patterns that are disease's indicative, these approaches utilize advanced algorithms [40, 41]. DL and ML are a few generally utilized AI approaches in AD detection. For detecting AD at an early phase, these approaches can render precise and effective approaches, which is vital for efficient treatment along with care [42]. The AI approaches used in AD detection at an early phase with their findings together with the limitations are described in Table 2.

Table 2: Artificial intelligence techniques utilized in AD detection at an early stage with its findings and limitations

AUTHOR NAME	TECHNIQUES	FINDINGS	LIMITATIONS
Anza, et al. [43]	Long Short-Term Memory (LSTM)	Analysis displayed that the applied approach acquired 88.24% accuracy in predicting early AD and proved superior to the other mentioned techniques	Some extensive follow-up was not utilized; thus, more improvement in the approaches was restricted
Ruoxuan, et al. [44]	Recurrent Neural Network (RNN)	For AD vs. NC, the RNN method acquired 91.33% classification accuracy and demonstrated promising performance for longitudinal MRI analysis.	It didn't consider major imaging features, namely structural along with the functional connectivity networks
ABOL, et al. [45]	CNN and Deep Neural Network (DNN)	Findings indicated that for the left and right hippocampi, the applied methods attained AUC values of 92:54% and 90:62%, respectively, and outperformed well in predicting AD	The applied approach was verified on a comparatively little private dataset.
Ahmad, et al. [46]	CNN	Results exhibited that the CNN system performed well with 99% classification accuracy in predicting early AD	Training data provided for CNN seemed to be less effective
Dilek, et al. [47]	DNN	As per the DNN, the accuracy acquired was about 67% for predicting early AD	Computationally expensive
Sylvester, et al. [48]	Deep NeuralNetworks Language Models (DNNLM)	As per the results on the Dementia Bank language transcript clinical dataset, for the AD prediction, D2NNLM adequately proved and exhibited a better outcome	The dataset was with limited size
Ekin, et al. [49]	2D CNN	Findings indicated that regarding diagnosis accuracy, 2D CNN architectures like VGG16 along with the ResNet50 surpassed. VGG16 system attained 64.3% while ResNet50 acquired 67.1%.	It didn't examine significant volumetric latent representation in the system
Halebeedu, et al. [50]	DNN	Experimental results revealed that in AD recognition, the Histogram of Oriented Gradients DNN (HOG-DNN) with the corrected Adam optimizer attained superior performance along with that exhibited a 16% improvement in classification accuracy	Training data was less efficient
Wanyun, et al. [51]	3D Reversible GAN (RevGAN)	Analysis specified that by utilizing the RevGAN approach, AD diagnosis conversion prediction's performance could be considerably enhanced	Due to the two networks in a GAN, namely the generator along with the discriminator, training will be unstable and slow sometimes

Qi Wang, et al. [52] described the DL-centric brain transcriptomic signatures linked to the neuropathological together with the AD's clinical severity. A DL technique was used for examining the RNA-seq data as of 1114 brain donors. Results collectively propounded that the intrinsic molecular variations are constituted at the cellular stage linked with AD's progression by the transcriptomic signatures recognized by the DL approach.

Parisa, et al. [53] analyzed the DBN for early diagnosis of AD with many features. The findings displayed that with an unprecedented accuracy of about 84.0%, the approach can classify the cognitively normal control group from the early AD detection. However, a limitation was present in the duration of development.

Changhee, et al. [54] expounded the GAN-centric numerous adjacent brain MRI slice reconstruction for unsupervised AD diagnosis. For detecting AD at several phases, a two-step approach utilizing GAN-centric numerous adjacent brain MRI slice reconstruction was applied. As per the study, this system consistently detected AD at a very early phase with an Area Under the Curve (AUC) of 0:780, whilst detecting AD at the delayed phase was much more precise with 0:917 AUC. But, if one network learns too rapidly, then the other network may fail to learn.

2.3.1. Performance comparison of artificial intelligence techniques used in Alzheimer's disease detection at the early stage

For analogizing the AI approaches used in AD diagnosis, the performance comparison is significant [55]. There is a purpose for enhancing the ML or DL approaches' performance as it could identify which approaches performed better when contrasted with all AI approaches [56, 57]. The performance comparison of AI approaches used in AD diagnosis with its findings and limitations is explicated in Table 3.

Table 3: Performance comparison of artificial intelligence techniques utilized in the AD diagnosis with its findings and limitations

AUTHOR NAME	TECHNIQUES	PERFORMANCE COMPARISON	LIMITATIONS
Donghyeon, et al. [58]	DNN	Performance analysis displayed that in predicting early AD detection, the applied DNN approach surpassed with better accuracy and proved to be high	The dataset applied by the approach in the study was small
Fan Li, et al. [59]	RNN	As per the study, for AD versus the normal control, the AUC area under the ROC curve achieved by the RNN approach was 91.0%, 75.8%, and 74.6%	For understanding brain abnormalities, learned features have no adequate clinical information
Petrosian, et al. [60]	RNN	Analysis depicted that the applied RNN executed well and out of 7 AD patients, 5 patients identified the better chance performance with 80% sensitivity	An efficient and universal training approach lacks here.
CHIYU, et al. [61]	3D CNN and FSBI-LSTM	For discriminating AD from Normal Control (NC), FSBi-LSTM achieved average accuracies of 94.82%, 86.36%, along with the 65.35%	Due to the cascade, the brain lesion structure can't be identified directly by up-sampling or else deconvolution
Aparna, et al. [62]	Bidirectional Encoder Representations from Transformer (BERT)-	As per the performance analysis, the linguistics' comparative significance in cognitive impairment detection was rendered by fine-tuned BERT systems, which surpassed other DL techniques on the AD detection task.	A mismatch betwixt pre-training and fine-tuning was created
KR Kruthikaa, et al. [63]	CNN with 3Dautoencoder	As per the outcomes, in AD classification, the applied CNN with 3D autoencoder approach was 98.42% accurate	The analysis needed a large dataset
Shaker, et al. [64]	Stacked CNN and Bidirectional LSTM	The outcomes indicated that regression tasks' performance was reliable. The data's positive role on the performance together with the applied system's superiority was confirmed by the DL system's both classification and regression outcomes.	It examined the relationship betwixt AD progression and the patient's comorbidities partially only

Hoo-Chang, et al. [65] examined the performance analysis of GAN together with Discriminator-Adaptive Loss Fine-tuning (GANDALF) for AD diagnosis as of MRI. For attaining the greatest AD classification performance, GAN was applied. As per the analysis, the applied GANDALF approach achieved the greatest performance in predicting early AD diagnosis with 37.0% accuracy, along with a 0.39 precision rate and 0.40 recall rate. However, the applied approach suffered from generating samples with a little illustration of the population.

Wei Li, et al. [66] established AD centered on 4D fMRI under the DL approach's performance. To extract special features, the C3d-LSTM approach was merged with a sequence of 3D CNNs. As per the analysis, the Gated Recurrent Unit (GRU)'s structure was simpler along with that the tensor operation was less contrasted to LSTM, hence it takes less time for training. But, the applied LSTM approach was too slow.

3. RESULTS AND DISCUSSION

The accuracies acquired by diverse CNNs for earlier prediction of AD along with the comparative study of AI approaches utilized for early AD detection are examined in this part. DL is regarded as a capable tool for performing automatic early detection of AD as of MRI data. Centered on extra traditional features, namely thicknesses along with the ROI volumes, DL helped for outperforming the system clearly [67]. The graphical illustration of disparate CNNs accuracies for AD at an early phase is described in Figure 2.

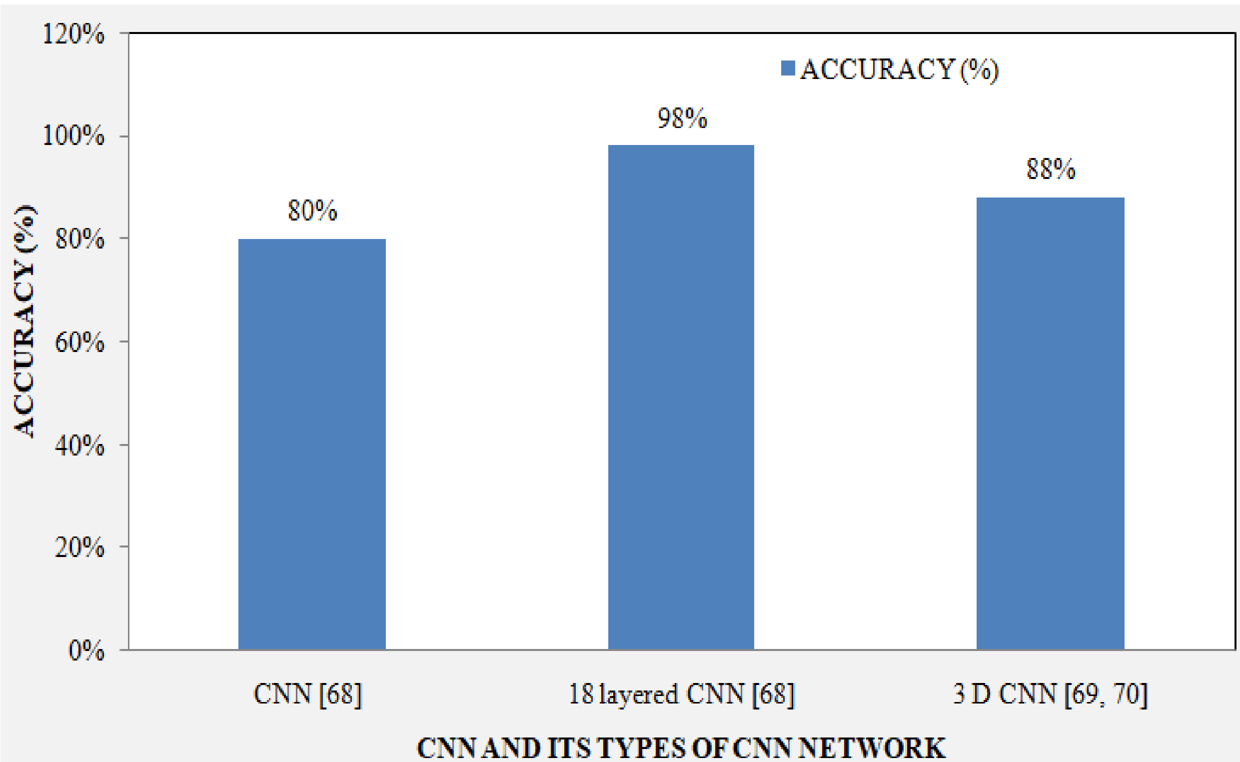

Figure 2: Graphical representation of different CNNs accuracies for AD at the early stage

Figure 2 indicates that for the study, CNN together with its types, such as 18 layered CNN [68] and 3 D CNN [69, 70] was taken. 18-layered CNN and 3D CNN are the 2 most significant DL algorithms, which are utilized for detecting AD's preliminary periods as well as employed on MRI and CT scans along with the brain monitoring modalities. Figure 2 exhibits that 18-layered CNN takes over the other 2 values with high accuracy (98%) in AD at an early phase.

In addition, analysis had been done on performance comparison of AI approaches utilized for early AD detection. In various real-life head care models, the AI approach has achieved better success [71]. The graphical representation of a comparison of AI approaches via metrics utilized for early AD detection is expounded in Figure 3.

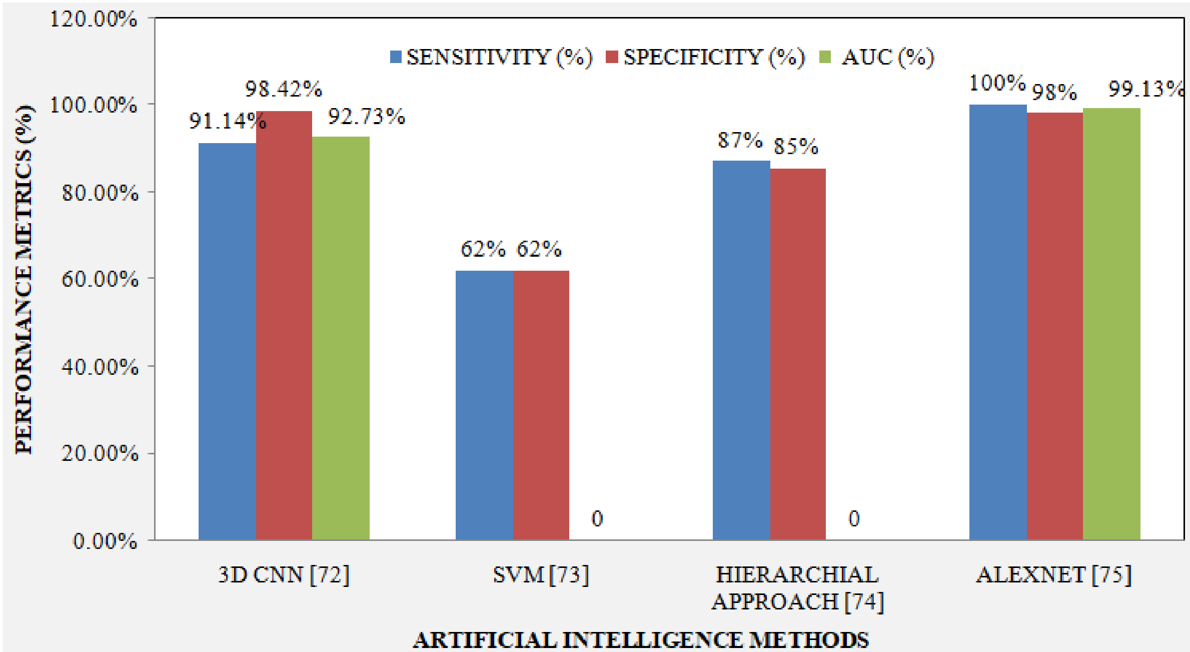

Figure 3: Comparison of artificial intelligence techniques through metrics used for the early AD detection

Figure 3 indicates that the analysis was performed centered on performance metrics, such as sensitivity, specificity, along with the AUC utilizing AI approaches for early AD detection. For the AD diagnosis analysis, 3D CNN [72], SVM [73], HIERARCHIAL APPROACH [74], and ALEXNET [75] approaches were used. Among these, ALEXNET [75] approaches displayed superior results in identifying AD with 100% sensitivity, 98% specificity, and 99.13% AUC.

Summary: In recent years, many systematic works associated with the ophthalmological field, particularly the eye have been done by alternative medicine. The opportunity for analyzing neuronal diseases associated with specific alterations that take place in the iris like Alzheimer's was propounded by various studies; similarly, centered on the images' digital processing, an alternative approach was formed for Alzheimer's early detection. For detecting changes in brain structure along with the function linked to AD, IP approaches, specifically PET, functional and structural MRI, and CT have been utilized. It would be a simpler and more useful efficient end product that could help doctors in their diagnosis by using an IP idea. Recently, in predicting AD, AI-centric approaches, namely ML along with the DL have displayed great promise. The review had been discussed deeply for identifying the pros and cons of the approaches applied from IP for AD diagnosis. The researchers can further move widely to the IP concepts by regarding the limitation identified in this study. Thus, the solutions for the limitations of approaches in the survey like limited sample size, absence of histological data, the small dataset used for the study, et cetera can be identified.

4. CONCLUSION

In conclusion, for establishing efficient care along with targeted medicine, AD's early detection is vital; however, it remains to be a difficult task. In AD's early detection from medical imaging data, namely CT and MRI scans, digital IP approaches along with AI algorithms have displayed to have great potential. Particularly, in detecting AD at an early phase, DL algorithms like 18-layered CNN along with the 3D CNN have demonstrated promising outcomes. Also, for examining the accuracy of diverse AI approaches, including 3D CNN, SVM, Hierarchical approach, and AlexNet in identifying AD, performance metrics, namely AUC, specificity, along with sensitivity have been used. In detecting AD with high AUC, specificity, along with sensitivity values, AlexNet was found to have superior performance. Future work in this region could focus on merging functional MRI and AI approaches for enhancing the accuracy of early

AD detection, leading to earlier intervention and enhanced patient outcomes.

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