Neuroimaging and Machine Learning for Dementia Diagnosis

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***Abstract*—Dementia, a chronic and progressive cognitive declination of brain function due to disease or impairment, is becoming more prevalent due to the aging population. A major challenge in dementia is achieving the accurate and timely diagnosis. In recent years, neuroimaging with computer-aided algorithms have made remarkable advances in addressing this challenge. Much of the success of these approaches can be attributed to the application of machine learning and deep learning techniques for neuroimaging. In this review paper, we present a comprehensive survey of automated diagnostic approaches for dementia using medical image analysis and machine learning algorithms published in the previous five years (2013-2018). Based on the rigorous review of the existing works, we have found that while most of the studies focused on Alzheimer's disease have demonstrated reasonable performance, the identification of other types of dementia remains a major challenge. Hybrid imaging analysis through deep learning approaches may hold promises for early diagnosis of these other types of dementia, and warrant further investigation in the future. The main contributions of this review paper are as follows: 1. Based on the detailed analysis of the existing literature, this paper discusses the most recent neuroimaging procedures for dementia diagnosis, and 2. It systematically explains the machine learning techniques and, in particular, deep learning approaches for early detection of dementia.**

***Index Terms*—Dementia, Neuroimaging, Computer-Aided Diagnosis (CAD), Image Processing, Machine Learning, Deep Learning.**

I. Introduction

OVER the years, the prevalence of infectious diseases and chronic conditions has been increasing due to demographic shifts in the developed nations associated with aging. One severe chronic condition in particular that has garnered significant interest in the mental health research community is dementia, due to (1) its high prevalence among older adults, and (2) its deleterious effects on cognitive skills and abilities required for daily activities [1]–[3]. Dementia is a neurocognitive mental disorder that is a general term covering several diseases causing dependency and disability among older adults worldwide [4]–[6]. According to the World Health Organization (WHO), approximately 47 million people are living with dementia worldwide, and this number is expected to increase to 82 million in 2030 and 150 million by 2050. The underlying causes of dementia can due to neurodegeneration, the weakening of brain interconnects resulting in impaired decision making and memory, and it can also due to non-neurodegenerative mechanisms such as in vascular dementia. The most prevalent types of dementia are depicted in Figure 1, grouped based on whether they can be characterized as neurodegenerative or non-neurodegenerative [7]–[10].

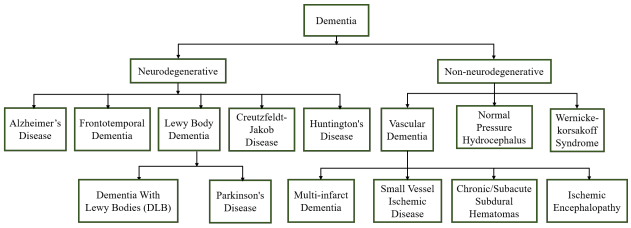


Figure 1: Significant types of Dementia.

Neurodegeneration is the main cause of dementia in the elderly. Alzheimer disease, vascular dementia, dementia with Lewy bodies, frontotemporal lobar degeneration, and Parkinson diseases often appear among older adults can be considered as degenerative dementia [11]–[14]. Examples of non-neurodegenerative dementia include mild cognitive impairment, normal pressure hydrocephalus, chronic alcohol abuse, hypothyroidism, intracranial masses (e.g., subdural hematomas, brain tumors), vitamin deficiencies (e.g., B12, thiamine), traumatic brain injury, psychiatric illness (profound depression/anxiety), chemotherapy-related cognitive dysfunction and infections (e.g., human immunodeficiency virus) [15]–[18].

Due to the rapid growth of dementia population, the worldwide death-factor is increasing day by day. Therefore, the early clinical diagnosis of dementia is essential to detect degenerative histological changes, containing the amyloid plaques, hypo-metabolism, and neurological disorders (atrophy) which indicate biological and pathological processes as a biomarker. Trustworthy biomarkers can help us to differentiate and predict the dementia progression. Over the last few decades, researchers have introduced biomarkers in the form of neuroimaging techniques which is widely used for diagnosis and suggest a specific pathology underlying the clinical dementia syndrome. Neuroimaging techniques such as Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET) and single-photon emission computed tomography (SPECT) are proficient to diagnose the functional and anatomical infor-

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mation about the neurodegeneration. Hereafter, the widespread applications of medical imaging have led to a new direction in early diagnosis and prediction of dementia [19]–[22].

In the past few years, researchers have presented several review papers detailing the technological advancements in biomedical image processing for dementia diagnosis. In [23], structural, functional and molecular imaging techniques are discussed for only four types of dementia in the early stages in 2014. Most recently, authors reviewed MRI and PET brain image analysis techniques focused on assessing synaptic dysfunction and identification of diverse phenotypes [24]–[27]. Since then, many new technological tools for integrated analysis of distinct neuroimaging data have been proposed, and these approaches also include methods beyond MRI / PET; with these more recent approaches, the ability to automatically quantify brain morphology, function, connectivity, and pathology has improved considerably. Certain trade-offs must be made according to the priorities and constraints of each study, and as new technologies are introduced to adapt these trade-offs. This review paper provides a detailed overview of the most recent years' research in dementia diagnosis using biomedical image processing with machine learning and deep learning techniques. Thus, the state of the art in neuroimaging, brain anatomy assessment and neurodegenerative condition diagnosis is presented.

We thoroughly researched leading databases, namely, IEEE Xplore, ScienceDirect, PubMed, ACM Digital Library, Springer and Nature for dementia diagnosis by medical image processing from the year 2013 to 2018. Searching the databases based on keywords, such as, "image processing for dementia diagnosis," myriad of research articles were found, from which approximately 300 were selected after carefully assessing the relevance of the article based on their abstracts. Then, follow by a detailed assessment on the full text of these 300 papers and the total number of papers analyzed in depth was narrowed down to 100 papers, from which 45 papers were selected for discussion in the following sections. The main contributions of this paper are as follows: 1. discuss the most recent neuroimaging procedures in the field of dementia diagnosis for clinical applications and 2. systematically evaluate the machine learning techniques and, in particular, deep learning approaches in early detection of dementia.

This review is organized as follows: Section 2 discusses the medical imaging analysis in dementia care based on clinical and statistical approaches. In Section 3, conventional and recent machine learning approaches to classify dementia are described. Performance measurement is discussed based on the criteria defined in Section 4. Challenges and future prospects of the present research on dementia are outlined in Section 5. In Section 6, the paper is concluded and future research directions are proposed.

II. Clinical/Statistical Analysis of Neuroimaging for Dementia Diagnosis

Early diagnosis, subsequent treatment and support is essential for patients in presymptomatic / predementia stages to slow the deleterious effects and preserve quality of life as long as possible. Biomedical imaging is a means of visualizing degenerative histological changes, which include hypo-metabolism, amyloid plaques, and atrophy. Specifically, imaging can yield quantitative biomarkers suggesting a particular pathology and prognosis for dementia [28], [29]. Figure 2 depicts different imaging modalities available for such biomarker derivation in the form of MRI/PET/SPECT images (datasets are discussed in below) which has advantages to capture the brain anomalies and neural vulnerability factors related to dementia.

There exists several publicly available neuroimaging databases, including Alzheimer's Disease Neuroimaging Initiative (ADNI) established in 2004 [30], Open Access Series of Imaging Studies (OASIS) first released in 2007 [31], The Australian Imaging, Biomarker & Lifestyle Flagship Study of Ageing (AIBL) launched in 2006 [32] and CADDementia, structural brain MRI scans [33]. These databases have been extendedly used in many studies and greatly supported the research in dementia.

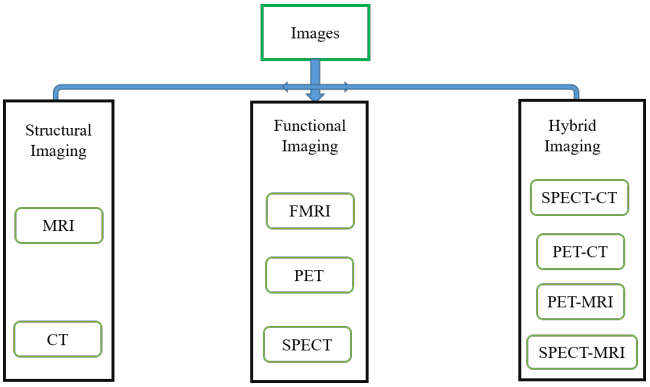
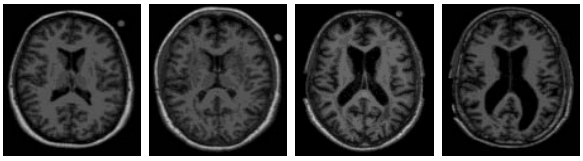


Figure 2: Biomedical imaging modalities.

In this section, we discuss the most salient imaging modalities and analysis algorithms to evaluate the early development, aging and pathological stages of the brain to assist dementia diagnosis based on clinical and statistical approaches.

A. MRI Modalities

A non-invasive procedure, Magnetic Resonance Imaging (MRI) uses powerful magnets to generate magnetic waves to form two- or three-dimensional images of the brain anatomy without radioactive tracers, enabling researchers to study both the functional and structural brain abnormalities including dementia. Patients with neurodegenerative diseases can quickly be assessed safely by this neuroimaging methodology, which permits evaluation of functional neural activity and imaging of cortical regions [34], [35]. The functional connectivity between the right hippocampus and the set of regions such as the medial prefrontal cortex (MPFC), ventral anterior cingulate cortex (vACC), right inferior temporal, precuneus cortex, right superior, left cuneus and middle temporal gyrus and posterior cingulate cortex (PCC), were found to be interrupted in AD [36]. Figure 3 shows some representative examples of MRI scans for dementia diagnosis.



(a) (b) (c) (d)

Figure 3: MRI scans of Healthy Control (a-b) and AD (c-d), [37].

Table 1 summarizes the recent advancements in dementia diagnosis using various forms of MRI scans. It is apparent that many different forms of technical and clinical methods have been developed and utilized for classifying or identifying brain pattern for early diagnosis of dementia.

Arterial spin labeling (ASL) - MRI is a noninvasive emerging technique to measure brain perfusion, and augment routine diagnoses as well as differential diagnoses. ASL can reliably assess the cerebral blood flow (CBF) of a given brain area in patients with dementia [44]. In [43], early diagnosis and differentiation between AD and FTD were assessed by investigating ASL-MRI. CBF and Gray matter (GM) volume with corrected partial volume effects were quantified using 3D pseudo-continuous ASL-MRI data and tissue segmentation methods of SPM8 in the entire supratentorial cortex and ten GM regions. Chi-square test and ANOVA were used to group the patients and their age respectively. MMSE (Mini-Mental State Examination) was used to distinguish between AD and FTD patients and control subjects. Receiver operating characteristic (ROC) analysis was considered to evaluate sensitivity and specificity showing significant CBF differences. The region of interest (ROI) was different compared with the functional definition of ROIs which affect hypoperfusion examination.

In [42], the authors proposed an ASL-fMRI immersive tool based on pairwise ranking and learning techniques for dementia disease diagnosis. Standard regression methods were used for Partial Volume Effects (PVE) correction, including fractional Gray Matter (GM), White Matter (WM), and Cerebro-Spinal Fluid (CSF) tissue volume. Tissue segmentation was performed via the SPM toolbox on the left & right hippocampus, the left & right parahippocampal gyrus, the left & right putamen, and the left & right thalamus of the brain to calculate mean ASL signal. To validate the immersive tool they used continuous and differentiable surrogated Kendall-Tau rank correlation coefficient. The extensive experiments and comprehensive statistical analysis show that the proposed method outperform conventional methods.

White matter hyperintensities (WMH) indicate the presence of cerebrovascular changes: specifically, the loss of vascular integrity of the brain in asymptomatic elderly subjects. The underlying pathology of the WMH signal is heterogeneous and may vary depending on the image intensity [45]. In [40], AD-related pathology was examined among patients with DLB, PDD, and non-demented PD by associating the WMH severity and medial temporal lobe atrophy. Each subject underwent one or more cognitive evaluations, such as the revised Hasegawa's dementia scale (HDS-R) and MMSE. Group comparisons were performed through Student's t-test and the χ^2 test. Fazekas methods were used to semi-quantify the images, and medial temporal lobe atrophy (MTA) score was applied to visualize the MTA. The WMH evaluation shows that DLB and AD have more severe WMH than PDD.

In [38], the differential diagnosis of behavioral-variant frontotemporal dementia (bvFTD) from AD, DLB and subjective memory complaints (SMC) is evaluated using six MRI quantification methods, namely VOL, TBM, VBM, Manifold, grading and WMH. Image quantification was examined based on the utility of the T1-weighted and FLAIR MRI sequences and DSI (Disease State Index) score. The authors also studied the role of the related genetic status in the distinction of the carriers and noncarriers sensitivity. The demographic and the clinical statistical utility were analyzed by applying Student t-tests and Pearson χ^2 tests for measuring sensitivity using IBM-SPSS. Only VBM and VOL were found to be convenient in the differentiation of bvFTD from other diseases. In [46], the researchers also used T1 and FLAIR to identify WMSA.

ADC (Apparent Diffusion Coefficient), a measure of tissue water diffusivity, depends on the interactions between water molecules and the chemical environment. The ROI (Region of Interest) is a method to measure the ADC value using the following sequences diffusion-weighted imaging, axial T2-weighted image (WI) FLAIR, 3D Inversion recovery T1-WI. A total of sixteen ROIs per subject were drawn per side to check the white matter of corona radiate hemispheres: frontal, caudate nuclei and parietal, and lenticular nuclei in [39], to discriminate in periventricular and deep white matter diffusion patterns in patients with AD, sVD, normal aging (NA) and possible iNPH.

Additionally, ventricle enlargement is an essential structural biomarker for the diagnosis of dementia using MRI scans to visualize the brain structures. In [37], modified distance regularized level set methods are used to segment ventricles, and extract geometric features to identify the clinical significance of AD diagnosis based on the OASIS database. Pixel counting approach is another way to analysis the brain tissue. In [41], used MRI head scans to determine caudate and putamen for identifying the existence of brain tissue of Creutzfeldt-Jakob Disease (CJD) with the help of pixel counting approach through analyzing the image block by block, and three stages image segmentation.

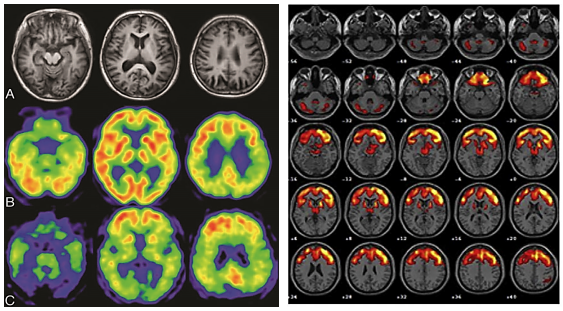
B. PET Modalities

By injecting radio-tracers into the bloodstream, Positron Emission Tomography (PET) measures emissions to produce two- or three-dimensional images of the chemical distribution throughout the brain. The primary benefit of PET imaging is that blood flow, oxygen and glucose metabolism in the working brain tissues are easily visible, thus reflecting brain activity and providing insight into its function. For diagnosing progressive neurodegenerative disease, biomarkers may be able to provide the pathophysiological objective measurement based on the metabolism images obtained from PET scans. In addition, the combination of PET with structural MRI

Table I: Summary of MRI Modalities Employed in Diagnosis of Dementia

Ref.	Year	Methods	Purpose	Datasets	Remarks
[38]	2018	VBM, TBM, VOL, Manifold Learning, Grading, WMH	Identification	bvFTD: 50, AD: 537, FTLD: 154, LBD: 61, SMC: 359	Six quantification methods were used and only VBM and VOL were found useful in identification of bvFTD.
[39]	2018	ROI (Regions Of Interest) Method	ADC Value Discrimination	Patients: 120	ROI analyses of mean ADC values in different periventricular and deep white matter areas.
[40]	2018	Fazekas Method	White Matter Hyperintensities (WHM)	AD: 50, DLB: 50, PDD: 50, PDND: 50, NC: 50	MTA and the severity of WMH correlation is assessed suggesting that WMH reflect AD-related pathology rather than atherosclerotic cerebrovascular changes.
[41]	2017	Pixel Counting Approach	Brain Tissue	—	Three stage image segmentation: pre-processing enhancement and pixel counting.
[42]	2016	Pairwise Ranking and Learning Techniques	Identification	AD: 110, MCI: 120, NCI: 120	5-Fold Cross-Validation is incorporated using Kendall-Tau Rank Correlation coefficient.
[43]	2016	Receiver Operating Characteristic (ROC)	Differentiation	AD: 13, FTD: 19, Age-Matched Older: 25, Younger: 22	Diagnostic performance of ten grey matter region were evaluated showing significant CBF differences between FTD patient groups.
[37]	2015	CED Filter and Level Set Method	Ventricle Segmentation	OASIS: Normal:20, AD:20	Shape-based Geometric features are extracted from the segmented ventricles.

can improve the accuracy of dementia identification [47], [48]. Figure 4 shows some representative scanning patterns of dementia using PET imaging.



(a) (b)

Figure 4: (a) Various PET scans of a patient with Alzheimer's disease at the age of 77, A) Right Hippocampus, B) FDG-PET and C) PiB accumulation [47]. (b) single-subject FDG-PET maps for the two bvFTD variants.

A summary of the typical development of dementia diagnosis using PET scans is presented in Table 2. It illustrates that brain metabolism using PET imaging is useful for early diagnosis of dementia by fusing different types of clinical and statistical approaches.

FDG-PET determines the hypometabolic region which is useful in differentiating between various types of primary dementia. In [49], authors explored FDG-PET abnormalities to differentiate iNPH from common neurodegenerative disorders. Partial volume corrected, and uncorrected, images were reviewed separately using unified segmentation and normalization procedures in SPM12. The FDG-PET pattern of hypometabolism in idiopathic normal pressure hydrocephalus (iNPH) involving the caudate and putamen was reported to understand the pathophysiology clinical features. In [50], [51], the FDG-PET image was optimized using the SPM software to identify typical AD hypometabolism pattern of each subject. ADNI FDG-PET scans were preprocessed using MMSE, ANOVA, and Chi-square test score. SPM statistical comparisons performed with the two different healthy control databases showed a high degree of concordance.

In [58], the ROI-based topological pattern of the metabolic brain network was examined in subjects with MCI, AD, and NC using FDG-PET data and graph theory. Data were analyzed using CDR and MMSE score to evaluate dementia severity and cognitive function of all patients involved. Brodmann atlas divided the whole brain into 82 areas to construct the networks. A three-step statistical analysis was performed to remove the effects of age, gender and the average value of the brain metabolic activity, and the Pearson correlation coefficient was computed to identify the correlation matrix. The leave-one-out (LOO) approach was used to explore the individual contribution to the group-level metabolic network showing that the topological patterns of the metabolic networks were aberrant in patients with MCI and AD.

The performance comparison between FDG-PET and arterial spin labeling (ASL) MRI diagnostic value in identifying the pathological abnormalities of frontotemporal dementia (FTD) is studied in [54]. Twenty subjects are considered to determine the qualitative and quantitative diagnostic utility of ASL and FDG-PET for analyzing the ROI and subjective visual ratings. Visual assessments revealed lower sensitivity, specificity and inter-rater reliability for ASL (66.67%/ 62.12%/0.2) compared to FDG-PET (88.43%/90.91%/0.61). Across all regions, ASL performed lower than FDG-PET in discriminating patients from controls (areas under the receiver operating curve: ASL: 0.75 and FDG-PET: 0.87).

Amyloid imaging for the detection of plaques has high specificity and sensitivity compared with histopathology [60]. [61], demonstrated that amyloid-PET tracer can be used to distinguish AD, DLB, FTLD, VD and non-degenerative pseudodementia. According to [53], the particular and hierarchical implementation of amyloid PET scans is addressed in relation to cerebrospinal fluid analysis in a naturalistic setting at French tertiary memory clinics in patients presenting with mixed dementia symptoms. A total of 205 patients were recruited for high-level diagnosis. Statistical analysis was investigated based on mean, standard deviation, and frequency distributions values while the Wilcoxon sign rank test was reported for comparison of initial and final confidence levels. To test

Table II: Summary of PET Image Modalities in Diagnosis of Dementia.

Ref.	Year	Methods	Purpose	Datasets	Remarks
[52]	2018	Voxel-based SPM	Prediction of AD	MCI: 80	classification and CSF Aβ Significantly predicted the conversion from MCI to AD dementia.
[49]	2018	SPM12, Gaussian Kernel, t-Test	Pattern of Hypometabolism	HC: 21, AD: 14, DLB/PDD: 14, bvFTD: 7, iNPH: 7	Group statistical comparisons of striatum metabolism were performed using a one-way ANOVA test with Tukey HSD post hoc pairwise analysis to compare the iNPH group with others.
[53]	2018	Clinical Study	Cerebrospinal Fluid Analysis	AD: 205	Results are interpreted based on regional cortical tracer uptake assessment.
[54]	2018	Jaccard similarity index (JI)	Pathological Abnormalities	FTD: 10, HC: 10	Regional mean values in thirteen a priori regions of interest (ROI) were analyzed to identify FTD.
[55]	2017	Clinical Assessment	The Propagation Of Tau Pathology	18	Imaging profiles were collected from illustrative patients with baseline diagnoses of prodromal AD, AD dementia and CBS
[56]	2017	optimized SPM	AD conversion	MCI:30	Combining the biomarkers, FDG- and Amyloid-PET improved classification accuracy.
[57]	2017	Clinical Diagnosis	Impact of the amyloid-PET	Patients:211	The clinical diagnosis and visual rating analog scale was assessed to improve the diagnosis.
[58]	2017	Robustness and Leave-One-Out	Metabolic Brain Networks	MCI:86, AD:89, NCs:97	The combination of robustness analysis and LOO approach, shows abnormal organization of the metabolic networks.
[59]	2016	Atlas-based and voxel-based analyses	Pattern Comparison	DLB: 19, AD: 19, NC: 95	Tau and Amyloid PET in DLB with MRI are investigated.
[51]	2014	SPM	Cerebral Glucose Metabolism	AD:36, MCI:12, bvFTD:6, DLB:6	Multiple center images were used to create a dementia specific template and validated by a spatial normalization.

variables, Kruskal-Wallis ANOVA with Dunn's multiple comparisons and Mann- Whitney tests were performed. Frequency comparison was made by Fisher exact test and the Cochran-Armitage test was applied for distinguishing trends. PET findings resulted in enhancing self-confidence in patients.

In [57], the amyloid PET imaging was assessed using flutetamol tracer for early diagnosis of dementia based on atypical clinical symptoms, regarding the diagnosis and patient management plan. Data was analyzed using the MMSE score after a routine diagnosis which was interpreted as amyloid-negative or amyloid-positive based on visual rating. Kruskal–Wallis tests, and Pearson χ^2 tests were assessed among groups and for the patient management plan. Their clinical diagnosis increased the overall diagnostic confidence and altered the patient management plan.

In [56], both FDG-PET and amyloid PET were assessed in a clinical setting to predict AD from MCI using a database of the Karolinska Institutet Stockholm, Sweden. Data were classified according to the diagnosis criteria. Image analysis accuracy was carried out with SPM5 software and Matlab. ROC analysis and AUC were applied to calculate the sensitivity, accuracy, and specificity for both PET biomarkers with SPSS software. The results have shown that the brain glucose metabolism and amyloid load yield a high accuracy for predicting MCI to AD conversion.

Tau pathology with the comparison of an amyloid PET is another suitable way to investigate the cerebrospinal fluid (CSF), lumbar puncture and preclinical spectrum of dementia. A pattern determination was studied in [59] using tau tracer AV-1451, with probable dementia with Lewy bodies, compared to AD, and its relationship to β-amyloid deposition on PET. Multimodal neuroimaging data were collected at the Mayo Clinic Alzheimer's Disease Research Center (ADRC). MMSE, DRS and CDR score was used to quantify dementia severity. Subjective characteristics were compared among the clinical groups with the Fisher's exact test, student's t-test, or variance analysis followed by Tukey Honest Significant Differences test. The area under the receiver operating characteristic curves (AUROC) was calculated to distinguish DLB and CN, and DLB and AD groups using median SUVr of each atlas ROI after combining the left and right hemispheric ROIs. FDG-PET brain metabolism and CSF (tau) classification were used to predict AD and non-AD, in [52]. Data was collected based on neurological and neuropsychological assessments, and clinical follow-up. FDG-PET data were analyzed with a validated voxel-based SPM method.

Neuroinflammation is a significant way to deposition of beta-amyloid plaques and microglia in dementia and can occur in both the gray and white matter due to the heterogeneity. The relationship between tau pathology and glucose metabolism is assessed in [55] to determine the propagation among prodromal and Alzheimer's disease dementia using PET scans with tau deposition, FDG (glucose metabolism) and amyloid-β deposition.

C. SPECT Modalities

Single-Photon Emission Computed Tomography (SPECT) imaging is a functional nuclear imaging technique to evaluate the regional cerebral perfusion of the brain depending on the radioactive tracer or SPECT agent and, two- or three-dimensional images are captured. Figure 5 shows the scanning patterns of SPECT modalities of DLB vs. NC.

Table 3 represents the recent technological advancements of SPECT imaging in dementia diagnosis. It indicates that it is possible to differentiate among various types of dementia by analyzing brain blood flow or perfusion based on SPECT images using clinical approaches as well as statistical methods.

SPECT by using ligands of the presynaptic dopamine transporter (DAT) is a suitable tool for investigating the

Table III: Summary of SPECT Image Modalities in Diagnosis of Dementia.

Ref.	Year	Methods	Purpose	Datasets	Remarks
[63]	2018	3d-SSP Statistical Analysis	Cerebral Blood Flow Study	Patient: 1 (Case Study)	Posterior Associative and Cingulate Cortex is analyzed for the diagnosis of SD.
[62]	2017	VOIs using eZIS software	Brain Perfusion	DLB: 13, AD: 13	Optimization of cingulate island sign (CIS).
[64]	2017	Grober and Buchske, Isaac Set test, visual Discrimination and Wechsler tests	Subcortical in Vivo Studies	DLB: 11, HC: 12	By using Walker and Neuropsychiatric scales, cognitive fluctuations and apathy were assessed.
[65]	2017	Butterworth Filter	Dopamine Transporter Binding Finding	PRD-DLB: 20, CLIN-DLB: 18, AD: 10	Correlations between SBR scores and clinical symptoms are investigated.
[66]	2017	Conventional and DWH SBR methods	SBR	DLB: 50	McNemar's test is used to inspect the proportion of proper VOI definition using DWH compared with conventional method.
[67]	2016	t-test, χ^2-test	Differentiating DLB from AD	AD: 57, DLB: 76	A combination of DAT SPECT and MIBG myocardial scintigraphy is studied.
[68]	2014	Univariate Analysis and Multivariate Analysis	Brain Perfusion and Myocardial Scintigraphy	Probable DLB: 72, Without DLB: 180	AUC values used to assess the indexed diagnostic measurement for the discrimination of dementia with Lewy bodies (DLB).
[69]	2014	SPM	Cerebral Blood Flow	SIVaD:28, HC:33	Cognitive dysfunction Mild Subcortical Ischemic Vascular Dementia may be related to these regional CP arrears.
[70]	2013	Semi-quantitative Circumferential Profile	rCBF	AD:11, WM-VaD:20, NC:17	All subjects underwent both MRI and Tc-99m HMPAO SPECT to analysis rCBF.

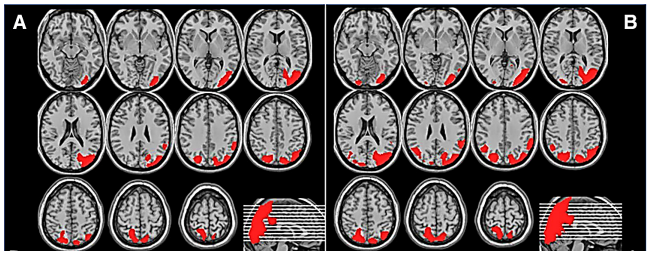


Figure 5: Group analysis of gray matter accumulation between the DLB and Normal Controls using SPECT scans [62].

functional integrity of dopaminergic nigrostriatal, which can be a pathway for dementia diagnosis [71]. In [66], the specific binding ratio (SBR) is an index to measure DAT density from Dopamine transporter single photon emission CT (DAT-SPECT), and distance-weighted histogram (DWH) is used to improve SBR for dementia with Lewy bodies (DLB). Two weeks evaluation of patients was performed enduring brain MRI, DAT-SPECT, and cerebral blood flow SPECT with I-123 IMP. Using scatter correction with a Butterworth filter and a standard filtered back-projection algorithm without attenuation, the cerebral blood flow SPECT data were reconstructed. SBR of the striatum was calculated using conventional and DWH SBR methods. Two experienced nuclear medicine physicians (NM1 and NM2) and brain MRI and CBF SPECT visualization were evaluated based on VOI definition. Also, the validation of inter-observer reproducibility, conventional and DWH SBRs were independently evaluated by NM1 and NM2. McNemar's test examines the VOI definition changing by DWH with the conventional method through visual evaluation. To improve inter- and intra-observer reproducibility of SBR, DWH may be useful. In [65], the limited prodromal stage of dementia with Lewy bodies (DLB) has been addressed by measuring the dopamine transporter binding, and clinical relevance of I-FP-CIT SPECT resulting with the long-term olfactory dysfunction and RBD may indicate more severe degeneration of the nigrostriatal dopaminergic pathway.

MIBG myocardial scintigraphy may be a comprehensive diagnostic tool comparing the differential diagnosis of dementia based on brain perfusion SPECT. In [68], the combination of I-MIBG myocardial scintigraphy and I-IMP brain perfusion SPECT was assessed to discriminate DLB. Data was collected using consecutive both IMP brain perfusion SPECT and I-MIBG myocardial scintigraphy examination in a clinical setup. The relationship between variables and presence or absence of DLB in the groups was analyzed by using univariate analysis while multivariate analysis was performed to obtain a combined index value that forecasts the possibility of DLB. ROC curve with a cutoff value was assessed to calculate the diagnostic value of the index. However, in [62], [67], the use of the combination of DAT-SPECT and MIBG myocardial scintigraphy was assessed for differentiating DLB only from the AD. The sensitivity, specificity, and accuracy of both methods, as well as their combined use, were assessed for differentiating DLB.

In addition, in [69], the mechanism of cognitive dysfunction of subcortical ischemic vascular dementia (SIVaD) was investigated and compared with the distribution of regional cerebral perfusion (CP) changes in the mild forms of SIVaD, using technetium-99m hexamethylproplyeneamineoxime (Tc-99m HMPAO) SPECT analyzed by SPM. Patients were recruited to undergo SPECT imaging for a time duration. Using the SPSS software, all statistical analyses for demographic factors were performed, and independent t-test was used for the comparison of continuous variables, and Pearson's chi-squared analyses were used to compare categorical variables. Whereas in [70], semi-quantitative circumferential-profile was analyzed between Alzheimer's disease (AD) and white matter vascular dementia (WM-VaD). Regional cerebral blood flow

(rCBF) patterns comparison was estimated by underwent MRI, and Tc-99m HMPAO SPECT.

A case study on Semantic Dementia (SD) is done in [63], which is a type of primary progressive aphasia with language dysfunction. They present a finding based on SPECT by showing the involvement of the right inferior parietal area, the posterior cingulate cortex and adjacent precuneus compatible with new hypo-perfused areas have seen in AD. In [80], the in vivo subcortical level in DLB has been evaluated using I-iodobenzovesamicol, a Single Photon Emission Computed Tomography (SPECT) radiotracer of the Vesicular Acetylcholine Transporter (VAChT), in three cholinergic pathways: septohippocampal, innominate-cortical and Ponto-thalamic and the involvement of the cholinergic system in cognitive and neuropsychiatric disorders of DLB patients has been assessed.

III. Machine Learning Approaches for Dementia Diagnosis

Neuroimaging diagnosis for dementia identification is a very complicated process and involves a myriad of factors depending on the imaging modalities. Predicting brain phenotypes and morphology (e.g., white and grey matter tractography) from neuroimaging is still challenging. Machine Learning provides the clinical diagnostic decision by automatically classifying and predicting dementia using computer-aided diagnosis (CAD) techniques. The fundamental step by step computer-aided diagnosis of dementia using Machine Learning approaches is shown in Figure 6. Images were preprocessed using software like SPM or SeeCAT [72] depends on the parameters selection. For feature extractor and relevant feature selection, different statistical methods [73] were used, and cross-validation [74] optimization was used to ensure the generation of the methods. Finally, machine learning approaches, such as SVM, [75] has been applied to classify, predict or distinguish dementia. In this section, the state-of-the-art machine learning methods used in dementia research has been systematically discussed.

A. Conventional Machine Learning Approaches for Dementia Diagnosis

Different types of machine learning approaches with their purposes and accuracy is depicted in Table 4, with different imaging modality. It shows that most of the recent literature used SVM, PCA, ensemble classifier approaches with MRI scans to detect or classify AD type's dementia.

Supervised learning technique SVM, used for classification, regression or other related tasks by drawing a hyperplane or a set of hyperplanes in a high dimensional space [87]. It is one of the most commonly used classifiers which can perform well with limited training samples and yield low generalization error. In multivariate classification and to predict an early diagnosis of dementia, SVM is the most frequently used classifier. In [84], SVM based classification of the AD in early-stage diagnosis using three sections of the brain by referencing OASIS MRI database. The proposed system yields a 90.66% accuracy in the early diagnosis of the AD. In [74], SVMs were trained to classify AD-CN, FTD-CN, AD-FTD,

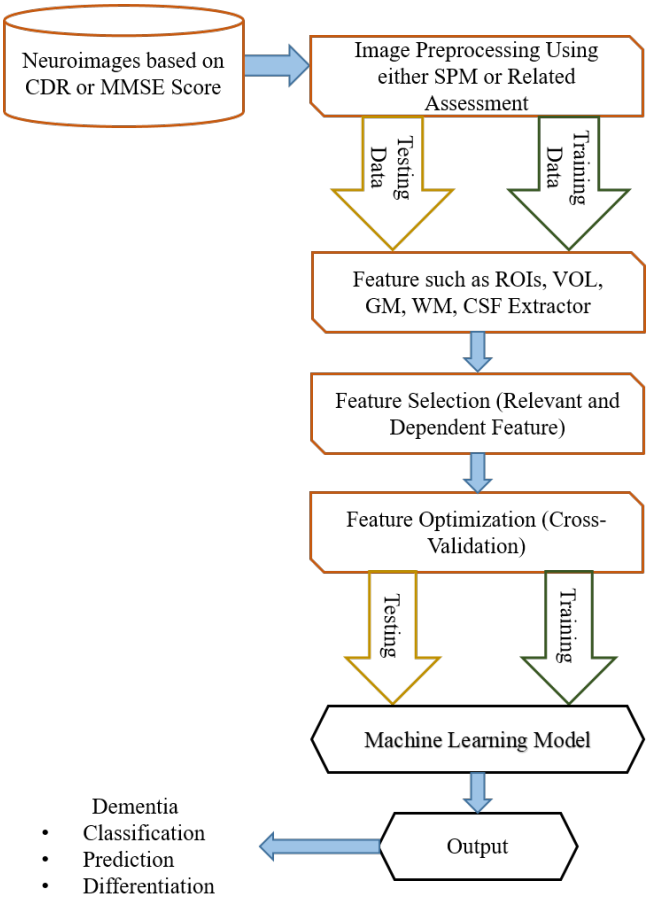


Figure 6: The fundamental step by step computer-aided diagnosis of dementia using Machine Learning approaches.

and AD-FTD-CN, using voxelwise feature maps derived from structural MRI, ASL, and DTI. AUC and SVM significance maps were analyzed for performance validation and regional brain contributions respectively. In [75], using either linear or an RBF kernel selection method to ensemble SVM for multi-class classification of NC, MCI, cMCI and AD based on ADNI MRI features. The ensemble SVM outperformed single SVM with accuracy up to 59.1%. Early detection of the AD in a fully automatic computer-aided diagnosis (CAD) based on SPECT image classification using RBF SVM was assessed in [72]. They found that coronal standard deviation and sagittal correlation parameters are the most effective among all the features using ROIs and improving the accuracy of the system as of 90.38% comparing voxel-as-features (VAF) approach. A personalized diagnostic approach has been proposed using SVM and MRI brain data in [76], where, bvFTD is classified and predicted in a group comparison as well as each subject using brain atrophy from MRI scans across the whole brain and frontotemporal, insular and basal ganglia most affected regions with the whole brain accuracy as of 86.5%. Combination of SVM, GPC, and AdaBoost to classify AD using MLNeCh MRI data feature vectors of high dimensionality was evaluated in [77]. Different techniques of feature selection/reduction are associated to evade the curse-of-dimensionality problem. In [73], comparative study on feature selection method based on

Table IV: Summary of Machine Learning Techniques in Diagnosis of Dementia.

Ref.	Year	Application	Image Modality	Methods	Datasets	Validation System	Number of Feature	Accuracy(%)
[75]	2018	Classification: NC vs. MCI vs. cMCI vs. AD	MRI	Ensemble SVM (Linear+ RBF)	NC: 100, MCI: 100, cMCI: 100, AD: 100	Learning:240, Testing: 160	426	55.6/55.0
[76]	2017	Pattern Classification: bvFTD vs HC	MRI	VBM+SVM	bvFTD: 52, HC: 52	Leave One Out	—-	83
[77]	2017	Classification: AD vs MCI,HC	T1 MRI	SVM+GPC+AdaBoost	HC: 100, AD: 100, MCI: 100, nMCI: 100	Training: 240, Testing: 160 (4-fold cross validation)	More than 400	57.1
[78]	2017	Classification: ND vs VMD vs MD	OASIS-MRI	PSO	ND:135, VMD:70, MD:30	Training: 113, Testing: 112	64 features of an image	77.4
[79]	2017	Discrimination: NC vs MCI vs AD	ADNI-T1 MRI	ELM+RFE-SVM	MCI-NC: 281, MCI-C: 69, NC: 208, AD: 160	10-fold cross validation	323 (80 selected)	92.84
[74]	2017	Classification: AD-CN, FTD-CN, AD-FTD, AD-FTD-CN	ASL/DTI MRI	SVM	AD: 24, FTD: 33, CN: 34	4-fold cross validation	voxel-wise features	84
[80]	2017	Distinguish: AD vs bvFTD	MRI	RF+WM	EOAD: 62, bvFTD:27	—-	Spatial, Temporal Features	82
[81]	2016	Metabolic Patterns	FDG-PET	SPM+PCA	bvFTD: 52	—-	Neuro-psychological Features	—-
[82]	2016	Classification: AD vs DLB vs FTD vs HC	T1-MRI	SVC	AD:101, DLB: 28, FTD: 55, HC: 73	Leave-one out	—-	68–93
[83]	2016	Classification: AD vs NC, MCI vs NC	ADNI MRI	SVM	AD:200, MCI:400, NC:231	10-fold cross-validation	1000	84.6/ 79.7
[84]	2016	Detection: AD vs MCI vs NC	OASIS MRI	SVM	NC: 50, MCI: 17, AD: 8	ROIs	—-	90.66
[73]	2015	Classification: CN vs AD vs MCI vs MCIc vs MCInc	ADNI MRI	SVM	AD: 137, MCIc: 76, MCInc : 134, CN: 162	k-fold (k=100,2)	200	90.0/64.8
[85]	2014	Classification: CN vs AD, PMCI vs SMCI	ADNI MRI	mi-Graph + LSVM	CN: 231, SMCI: 238, PMCI: 167, AD: 198	Leave-One-Out and 10-Fold	—-	89/70
[86]	2013	Classification:CTR vs AD vs FTD	SPECT	PCA+SVM	CTR: 26, AD: 26, FTD: 21	5-fold cross validation	—-	92.66
[72]	2013	Detection: AD	SPECT	SVM	NOR:23, ATD:29	Leave-Five-Out	FDR-based	90.38

SVM weights as a significance map (p-map), SVM weight vector directly, t-statistics and expert knowledge were evaluated using ADNI MRI data for classifying MCI who converted to AD (MCIc), MCI patients who did not convert to AD (MCInc), AD, and cognitively normal controls (CN). In [79], T1 MRI, to discriminate the AD, MCI from normal control (NC) using extreme learning machine (ELM) classifier in combination with linear kernel support vector machine (SVM) is studied. Also employed SVM-based recursive feature elimination (RFE-SVM) algorithm to find the optimal subset of features and the result shows that RFE-SVM with ELM has the superior classification accuracy to that of linear kernel SVM. In [82], Six MRI visual rating scales were exposed to collect T1-weighted images of confirmed dementia with the AD, DLB, and FTD. Voxel-based morphometry feature was used for performance measurement using a support vector classifier (SVC). In [83], two classification problems: AD vs. NC and MCI vs. NC using MRI voxel-based feature was classified by SVM, with or without filter-based feature selection.

Principal component analysis (PCA) based Correlation analyses between neuropsychological is a meaningful way to identify dementia brain dysfunction. In [81], FDG-PET metabolic patterns were retrospectively analyzed to identify probable bvFTD. ROIs based cluster analysis was performed and validated by PCA. They found distinct patterns of brain dysfunction. Both SPECT and PET images were used to diagnosis AD, and FTD in [86], here an extensive and comparative evaluation has been studied using PCA and PLS). Three classification methods comprising elastic-net logistic regression (ENLR), multiple discriminant analysis (MDA), and SVM were used to classify AD, asymptomatic controls (CTR) and FTD participants. In [88], MRI of multi-type dementia is used to reduce the dimensionality of an extract key features using sparse autoencoder (SAE), and PCA approach used to train a LDA and LR classifiers to compare their prediction accuracy.

The combination of structural (cortical thickness [89], [90] and white matter microstructure) with functional MRI has

been explored to distinguish AD and bvFTD using random forest and receiver operator characteristic curve in classifying the two clinical syndromes in [80]. In [85], to detect AD and MCI from ADNI MRI scans using a multiple instance learning (MIL) method is proposed based on leave-one-out cross-validation. OASIS MRI dementia data is used to classify three dementia classes: non-dementia, very mild dementia and mild dementia using particle swarm optimization (PSO) providing automated clinical decisions to diagnose dementia with an accuracy 77.4%, [78].

B. Deep Learning Approaches for Dementia Diagnosis

Another class of machine learning techniques is deep learning which uses multilayer of nonlinear information processing to recognize feature quantities from data like text, image and so on. The main advantage of deep learning is that highly accurate mathematical model from a certain amount of large dataset with improvements in computational power, fast data storage, and parallelization, can easily be obtained without knowing the detailed internal process. Deep learning algorithms have promptly become an emerging methodology to the researchers for analyzing medical images employing image classification, segmentation, registration and other tasks due to its predictive power and ability to generate automatically optimized high-level features and semantic interpretation from the input data [91], [92]. Figure 7 shows a deep learning based biomarker using Softmax as a classifier for early diagnosis of dementia.

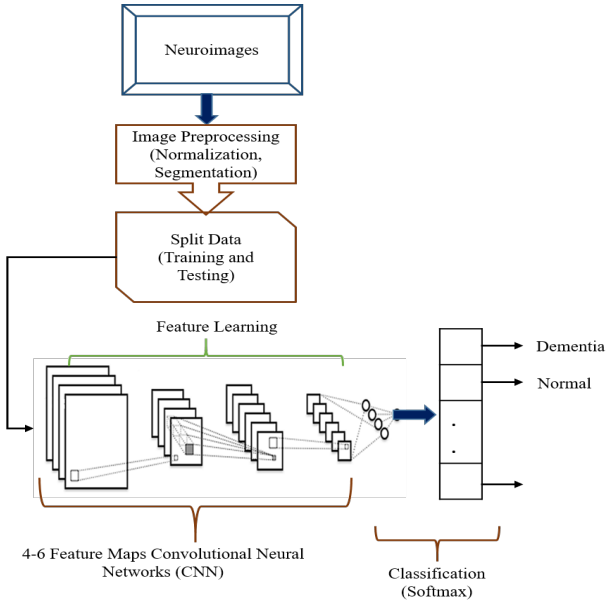


Figure 7: Deep learning CNN based hierarchical feature learning and classification to prognosis dementia using Softmax classifier [88], [92], [93].

Biomedical imaging modalities with deep learning methods in early prediction and detection of dementia are summarized in Table 5, showing that deep neural network depends on the layer, has better accuracy than conventional machine learning methods.

An artificial neural network (ANN) is one of the constructions of deep learning and has been applied for a diversity of tasks comprising medical image processing. In [94], a two-layered feed-forward neural network designed with sigmoid function is trained using the Levenberg-Marquardt supervised algorithm to classify the images as normal or demented. The Two-Threshold Binary Decomposition algorithm breaks down the input grayscale image into binary images. Segmentation based Fractal Texture Analysis (SFTA) technique was used for the extraction of features. In [95], proposed a novel ensemble learning framework to identify neuroimaging abnormalities of brain MRI, PET and PET-MRI scan based on four layered ANN for classifying AD and MCI which solved the feature fusion learning problem as well as the prediction problem simultaneously. Comparing the Baseline methods LR, SVM, LGR and NB they have higher accuracy.

In [96], presented a multi-modal imaging marker using a new deep learning algorithm named randomized denoising autoencoder marker (rDAM) and ADNI MCI data to predict future cognitive and neural decline from FDG-PET, amyloid florbetapir PET, and structural MRI scans. While [97] used only stacked auto-encoder (SAE) deep neural networks (DNN) to classify AD from cognitive normal (CN) and mild cognitive impairment (MCI) in dementia patients.

The prognosis and diagnosis of AD and MCI for clinical decision making using a Deep Ensemble Sparse Regression Network are proposed in [99], where two conceptually different methods of sparse regression and deep learning are combined. They experimented propose model in ADNI cohort by achieving highest diagnostic accuracies in three classification task. However, in [98], Deep Belief Network was analyzed to detect Alzheimer's disease from Structural MRI Classification. They considered a voxel-based morphometric approach for image preprocessing and feature extraction. Their DBN was consisted using 3-hidden layer, fine-tuned three parameters including epoch, momentum and the number of nodes in each layer.

With the comparison of SVM (67.01%), Logistics regression(67.04%) and CNN with softmax layer (61%), the proposed method in [88], [93], combined convolutional neural networks and logistic regression show better performance (74.93%) by training them on MRI scans of the AD. Where they used six convolutional layers, six max-pooling layers, six local normalization layers, three fully connection layers, and two dropout layers in CNN learning. On the other hand in [100], a very deep convolutional network and the Open Access Series of Imaging Studies (OASIS) database was analyzed for multi-Class Alzheimer's disease detection where a stem layer includes several 3 * 3 convolution layers, 1 * 1 convolution layer, and max-pooling layer and seven 3 * 3 convolution layer connected in different stages and two filter expansion layers.

IV. Performance Measurement

Computer-aided diagnosis of dementia depends on different algorithms using neuroimaging modalities have shown high performance in the previous literature, but their performance is varied as data sets, and evaluation methodology is different,

Table V: Summary of Deep Learning Techniques in Diagnosis of Dementia.

Ref.	Year	Purpose	Image Modality	Datasets	Methods	Network Structure	Feature Vector Size	Number of Feature	Accuracy(%)
[94]	2017	Feature Extraction and Classification	OASIS: MRI	NC: 40, MD: 40	SFTA+ feedforward NN	2-layered	80*6	3 for each of the binary image	97.5
[97]	2017	Classification of AD	ADNI: MRI	CN: 171, MCI: 232, AD: 101	SAE+DNN	3-layered	—-	311 with FDCM: 5000	56.6/73.3
[98]	2017	Classification	OASIS: MRI	AD: 49, HC: 49	DBN	3-hidden layered	—-	3635	91.76
[99]	2017	AD vs. NC , MCI vs. NC, pMCI vs. sMCI	ADNI: MRI	AD: 186, MCI: 393, NC: 226	DESRN	5-layered	3*4, 3*1, 2*1	93	90.28
[93]	2017	Differentiating Types of Dementia	MRI	OASIS: 74	CNN	23-layered	176*208	—-	70.97
[100]	2017	Multi-class Classification	OASIS: MRI	416	CNN	7-layered	299*299	—-	73.75
[95]	2016	AD/MCI related classification	ADNI: MRI+PET	AD: 51, MCI:99, NC:52	ANN	4-layered	—-	Binary feature	SPE 96.7/SPE 0.62
[96]	2015	Prediction of Dementia	ADNI2: PET+MRI	AD: 101, HC: 148, MCI: 267	rDA	2-level randomization	—-	—-	NaN

so it is difficult to address their performance comparability, generalizability, and clinical applicability issues. The performance is being reckoned through the calculation of various measures, such as Sensitivity, Specificity, Predictive Values, Accuracy, Precision, Confusion Matrix, and sometimes missing value assumption. Most of the literature showed their methods validation based on either in accuracy or sensitivity or specificity. However, for an acceptable, accurate and suitable tool for dementia diagnosis there need to validate the proposed methods through the calculation of various measures rather than accuracy or sensitivity or specificity as discussed below.

1) Classification Accuracy: The differentiating between patients with dementia and normal controls, the accuracy of the image interpretation is one of the key performance measurement for computer-aided diagnosis of dementia. The percentage of predictions in identifying patients with onset dementia syndromes to the total number of the dataset is given by the equation below.

$$acc = Trp + \frac{Trn}{a+b+c+d}$$

Where $a+b+c+d$ denotes the total number of subjects.

2) Confusion Matrix: The two-dimensional matrix where each column presents a predicted class while each row represents an actual class. In performance measurement of a CAD algorithm to diagnose dementia with known ground truth diagnosis against a test dataset, each matrix cell represents either predict class or actual class in a row-column way.

3) Precision: To get the high-performance computer-aided diagnosis of neuroimaging, the proportion of predict subjects to the total actual subjects is being considered, which is called precision.

4) Sensitivity: The probability of diagnostic assessments to recognize the subjects who have dementia. The CAD sensitivity can be defined by,

$$Sensitivity = \frac{a}{a+c}$$

Where a is the total number of patients having dementia as a positive test and c refers to the total number of dementia people with a negative test. Thus, $a+c$ represents the total number of subjects with dementia.

5) Specificity: The probability of negative test identification among the subjects without dementia. The CAD specificity is given by,

$$Specificity = \frac{d}{d+b}$$

Where, d indicates the patients as not having dementia, b refers the subjects without dementia by negative test and $d+b$ represents the total number of subjects without dementia.

6) Predictive values (PV): It is defined as the added value of correctly identified as people having dementia, i.e., true positive (TrP) and not having dementia, i.e., true negatives (TrN). PV is given by,

$$PV = TrP + TrN$$

7) Missing Values Confiscation: The performance of a model can be different due to the missing value of the training data, it may affect the performance like it is wrong or imprecise predictions. Various methods have been suggested based on clinical dementia rating (CDR), to improve the classification accuracy as well as ignore the performance issue.

The validation of each model proposed in early diagnosis of dementia is signified by investigating the capability of these biomarkers to distinguish between HC and patients with dementia as well as types of dementia. Therefore, in the future research, researchers need to consider these validation criteria for the better diagnosis of dementia patients.

V. Major Challenges and Future Prospects

The concept of assisting radiologists in neuroimaging analysis based on computer-aided diagnosis (CAD) is growing in

acceptance over the recent years, and particularly holds merit for the prediction and earl detection fo dementia.

The state-of-the-art has focused on discriminating Alzheimer's disease multistate mostly, so the diagnosis of various types of dementia is remaining a significant gap. However, the diagnosis of dementia for early detection and prediction is a vast, challenging work according to the human brain irregularities like the cognitive function of the brain, neuroimaging quality, noise and related reasons.

Based on the details discussion of the recent research articles we have found several challenges in dementia diagnosis: 1) Radio-tracer used in image collection which may have some side effects, 2) Large neuroimaging dataset needs a sufficient amount of labeling time to train a machine learning system, 3) Another limiting factor is noise, 4) Data heterogeneity, and 5) Finally, clinical features in medical imaging sometimes defends on physicians collection. Therefore, researcher's need to focus here to discover an indicative biomarker regarding dementia diagnosis that can enhance our understanding of neuroimaging.

In the future, there needs a routine clinical practice of neuroimaging to diagnostic dementia. Deep learning will be more accessible to learn from examples and prior knowledge of more data sources which are playing an essential role in the diagnostic application. Using deep learning architecture recently the visualization and quantification of brain blood flow, and image interpretation like classification task is made successfully [101]. Such as [102], [103], they discriminated AD from MCI using deep learning unsupervised Stacked-autoencoder method to learn the hidden patterns using the segmentation of the gray-matter of MRI and FDG-PET scans, which has higher accuracy compared with SVM and PCA+SVM approaches. In [104], stacked autoencoder and softmax classifier are used to classify AD using R-fMRI data, comparing with LDA, LR, SVM their accuracy increase maximum 18.75% improvement in classification performance. So we forecast that deep learning leveraging technologies have an enormous impact on neuroimaging modalities analysis to diagnose dementia for early detection and prediction.

It is predicted that multi-modal molecular imaging can seizure the corresponding information of a patient in a single scan such as the recent development PET/MRI or SPECT/MRI or PET/CT or SPECT/CT which has the advantages including spatial and temporal resolution, functional anatomical basis, targeting disease biomarkers with high accuracy in brain research. Temporal and spatial registration of simultaneous PET/MRI is assessed in [105], where Arterial Spin Labeling (ASL) is shown to be an alternative of FDG-PET for clinical diagnosis of bvFTD. So based on the recent advancement of medical image modalities along with their analysis technologies in dementia diagnosis, the performance of automatic dementia diagnosis is noticeably improving.

On the supplementary, Electroencephalography (EEG), reflects the unseen brain anomalies which can be employed to determine and distinguish certain brain function conditions. EEG brain signal analysis using computerized methods has revealed the cognitive dysfunction of dementia diagnosis. Therefore EEG can be used as a yardstick to early diagnosis of dementia using deep learning method [106]. According to [107], deep learning CNN was exploited to classify AD from MCI and HC using EEG patterns. EEG data were collected based on the golden standard of 119 dementia patients. Two layered CNN was subjugated where second convolutional layer was generated as of an auto-encoder MLP. The performance result (80%) was satisfying comparing with others conventional methods. In [108], multilayer neural networks (MLP-NN) was assessed to differentiate CJD patients from AD using EEG data with an accuracy of 89%.

Instantaneous detection of dementia can prevent the patients from significant type's severity like stroke, death. Despite neuroimaging and EEG, wearable sensor-based diagnosis for early detection and treatment of dementia are now widely used for continuous sensing the physiological parameters. Behavioral and environmental sensing and intervention (BESI), which can sense behavioral activities using wearable and monitor ambient parameters within the home. With this real-time behavioral data, it is possible to give real-time notifications for early treatment of dementia type patients [109]. Recently in [110], deep learning recurrent neural network (RNN) based on long short-term memory (LSTM, was examined the patterns of the PWD inertial motion data to build a sequential behavior model for inferring physical agitation in dementia.

VI. Conclusion

This review paper augments the existing literature by providing a comprehensive survey of all relevant neuroimaging modalities and associated analysis techniques presented in the past five years for diagnosing dementia. Previous review papers have focused only on a particular imaging modality such as MRI or PET, or on one specific type of dementia only such as AD. We aimed to cover a broader space of imaging and machine learning / deep learning technologies for dementia diagnostics such that researchers in the field could readily identify the state of the art in the domain. Moreover, we emphasize the importance of early detection and prediction of dementia, such that treatment and support can be provided to patients as soon as possible—this would, in turn, slow the degenerative processes and sustain the patient's quality of life for as long as possible. Our review can be divided into two categories: (1) a discussion of the most recent neuroimaging procedures in the field of dementia diagnosis for critical clinical applications, and (2) a systematic description of the machine learning techniques and, in particular, deep learning approaches for early detection of dementia. We summarized the most recent neuroimaging modalities—MRI, PET, and SPECT—and machine learning and deep learning technologies for feature extraction and classification methods in diagnosing various forms of dementia. We concluded based on the performance measures among algorithms in the existing literature that the ability to diagnose AD using MRI scans is promising but substantial progress is needed for diagnosing other types of dementia such as FTD, VD, and PD. We further found that the deep learning approaches for analyzing brain images obtained with state-of-the-art imaging techniques perform better than conventional machine learning and imaging methods—the

field is thus progressing rapidly in the direction of delivering the accurate and early diagnosis of dementia in its various forms. However, more research is needed to perform better classification for diagnosing dementia and, in particular, for providing earlier detection for enabling early onset treatment.

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