A Novel Approach for the Prediction of Conversion from Mild Cognitive Impairment to Alzheimer's disease using MRI Images

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***Abstract*—The main objective of our research is to introduce an approach that uses noninvasive MRI images to predict the conversion from mild cognitive impairment to Alzheimer's disease at an early stage. It detects normal controls that are likely to develop Alzheimer's disease and mild cognitive impairment patients that are likely to establish Alzheimer's disease within two years or, contrarily, their stage remains same. The proposed approach uses two types of features i.e. volumetric features and textural features. Volumetric features consist of volume of grey matter, volume of white matter and volume of cerebrospinal fluid. A total of 364 textural features have been calculated. To avoid the curse of dimensionality, textural features are reduced to 15 features using gain ratio, a ranking based search algorithm. All features are tested against four classifiers i.e. AODEsr, VFI, RBF and LBR. Leave-One-Out cross validation strategy is used for the evaluation of proposed approach. Results show accuracy of 98.33% with volumetric features and 100% with textural features using VFI and LBR. Our approach is innovative because of its higher accuracy results as compared to existing approaches yet with a smaller feature set.**

***Index Terms*—computer aided diagnosis, feature extraction, image analysis, image classification, pattern recognition.**

I. Introduction

Alzheimer's disease (AD) is a threat of the 21st century that affects individual's mental and social wellbeing by damaging the structural and functional parts of brain resulting in cognitive decline and eventually death. The impact of AD comes with individuals of above 65 years age and risk of being affected duplicates at intervals of 5 years. Other risk factors include environment and genetics that plays a crucial role in onset and advancement of the disease. Deaths from heart disease have reduced by 16%, breast cancer by 2%, prostate tumor by 8%, stroke by 23% and HIV by 42%, though deaths by AD expanded 68% since year 2000 [1]. Current estimation of Alzheimer's patients is 36 million and with expansion in future this figure will shoot up to more than 115 million individuals by the year 2050 [2].

The diagnosis of AD incorporates examining subject's history, incident history from connections and clinical perceptions. Mini-Mental State Examination (MMSE) and Clinical Dementia Rate (CDR) are used to assess and track a subject's intellectual decline but these methods are tedious and cannot catch the prior changes in brain that can be a pointer for the advancement of AD. Development of automated methods for early diagnosis of AD are crucial as these might help specialists to endorse prescriptions that can at any rate graduate down the advancement of the disease.

In recent years, there has been a greater focus on research relating to identification of AD in early stages [3]. Most of these techniques use machine learning algorithms for prediction of AD and mild cognitive impairment (MCI) [4, 5] and are based on single [6] or multiple biomarkers [7, 8] for the classification task. Among these biomarkers, neuroimages are latest addition which proves to be most efficient and reliable for identification of AD and MCI subject [9, 10]. Although use of multiple modalities is seen in recent studies [11] but collection of data for same subjects is not feasible in most cases, resulting in reduced number of subjects for the study.

Despite the tremendous research done in the field of automatic classification of AD or MCI from normal controls (NC), less work has been done toward the prediction of conversion from MCI to AD [8, 12]. Timely prediction of conversion to AD from MCI is crucial for diagnosing the disease and for devising more effective methods of treatment. Previous studies are either using voxel-based morphometry (VBM) [13, 14], or performs analysis on regions of interest (ROI) by means of some discriminant function [15]. High dimensional pattern classification studies are overcoming the limitations of VBM and ROI based techniques [7, 16]. Although these studies are effective but are based on extraction of a large number of features resulting in increased computational time. Selection of most discriminating features may enhance the effectiveness of our proposed approach with a smaller feature set and eventually reduced computational time.

The proposed approach performs classification between two groups of subjects i.e. AD vs. NC and MCInc (MCI-NonConvertors) vs. MCIc (MCI-Convertors). The focus is to compare MCI patients who had converted to AD within 12 months and MCI patients who had not converted to AD within 12 months. This is required to predict whether MCI patient will develop the disease in future or not. Once preprocessing is performed on MRI images, volumetric and textural features are extracted from it. Volumetric features help in prior identification of AD since densities of grey matter, white matter and cerebrospinal fluid are considered to reduce due to death of brain cells. A total of 306 textural features are extracted from MRI images. The feature set is then reduced to 25 features using gain ratio algorithm. The experimentation is performed using each type of features individually. It is found that reduced feature set performs better as compared to complete feature set, resulting in reduced computational cost.

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Rest of the paper is organized as follows: A comprehensive literature review is presented in section II. Proposed layout of our research work is provided in section III. Results and discussions are presented in Section IV and the paper concludes in section V.

II. Literature Review

MCI is a transitional stage between normal aging with cognitive decline and development of AD [17]. It is considered as prodromal phase of AD because MCI patients are at higher risk of converting to AD. Since not all MCI subjects convert to AD, it is important to identify subjects who will convert to AD from those remaining stable or even improving within next years.

Recent studies have tried to solve this problem with the help of biological markers [18], clinical and neuropsychological assessments [19] and various neuroimaging techniques by measuring the progression of MCI and probable AD. Latest neuroimaging techniques have facilitated analysts to estimate and evaluate various brain functionalities and structures that are useful in tracking down MCI and AD [3, 9]. A number of risk free and recognized techniques for brain imaging exist that are beneficial for the assessment of anatomical, physiological and pathological brain features with satisfactory outcomes. An extensive literature review of these techniques and machine learning based pattern recognition methods with possible advantages and limitations are presented in Table I. It shows dataset used in the research, preprocessing operations, type of features extracted and classifiers used for different groups of AD, MCI and NC along with achieved results including accuracy, specificity and sensitivity. The reported results can be compared to the results of proposed approach showing an obvious improvement.

Early techniques utilized for AD detection make use of volumetric estimations and depended on manual extraction of ROIs [20, 21]. Pattern recognition based techniques are also used for regional feature extraction [7]. Region based features are initially extracted from brain displaying noteworthy group contrasts analyzed by two-example Hotelling's T-square measurement of tissue density and then neighborhood groups are framed utilizing a watershed-based locale developing procedure. Adaptive regional feature extraction and reduction method along with multivariable Support Vector Machine (SVM) classification technique is used for training the sample set. Automated techniques for extraction of ROIs or specific regional volumes are developed recently that performs with similar reliability as manual ROIs in MCI and AD [22].

The problem with such region based strategies is that they do not indicate high affectability and specificity in classification of MCI and AD [23]. Such constraints are overcome by the utilization of VBM, which is a powerful technique for analysis of high resolution MRI data [14]. This technique allows analysis of different tissue types in an unbiased and automated way [24]. A VBM technique is presented by [25] that investigate NC with MCI, and AD patients, utilizing brain atlas warping methodology to produce tissue density maps that mirror the distribution of brain tissues. Tissue density maps are analyzed to distinguish group differences between AD, MCI and NC for cross sectional as well as longitudinal studies [26-28]. Although VBM is used to accurately classify NC and AD patients, and to predict conversion from MCI to AD [27, 29], however, small sample size in longitudinal studies prevents VBM to be used for prediction of MCI to AD conversion. VBM based statistical approach is used for group comparisons, that involves voxel wise t-tests.

The limitations of the ROI, voxel of interest and VBM based techniques are overcome by multivariate methodologies which takes entire image for analysis. A high-dimensional pattern classification technique that inspects spatial patterns of brain atrophy, rather than applying separate segment by segment brain assessments is used by [30]. Hence it is proven to be helpful for detection of prodromal Alzheimer s' disease.

In the field of medical imaging, there has been a growing interest in machine learning and computer aided diagnosis techniques. A machine learning algorithm can be trained to classify a subject as AD, MCI or NC based on a number of features like tissue density, voxel intensity or shape features. These techniques are either ROI based [31, 32] or whole brain based methods [6]. ROI based methods do not use complete information available in the brain image and requires a priori knowledge regarding which brain regions to asses.

A pattern recognition based high dimensional classification method is presented in [23] that measures atrophic spatial patterns of brain using baseline and longitudinal scans to predict MCI to AD conversion. The idea is to predict future MCI to AD transformation with the help of baseline and longitudinal scans of regional brain tissues [33]. A medical image classification technique is presented by [34], that utilizes machine learning and deformation based morphometry. A morphological representation of the anatomical system of interest is initially acquired utilizing high dimensional template warping and the classification features are separated utilizing a watershed division. An SVM Recursive Feature Elimination (RFE) strategy is then used to rank figured elements from the separated areas. Finally, SVM is applied utilizing the best arrangement of features.

The fundamental principle to pattern recognition based approaches for AD is feature extraction from various brain imaging techniques. Although a wide variety of features exist that can be used for this purpose, we have explored textural and volumetric features for prediction of probable conversion of MCI to AD. A number of textural and volumetric features, along with their mathematical models, for classification of MCI and AD are presented in Table II. A substantial number of strategies exist in literature for feature extraction and classification with good accuracy. MRI, because of its non-invasiveness is widely used in AD detection [35-37]. Pattern recognition and machine leaning algorithms have shown high precision in detecting Alzheimer disease [38, 39]. Although these procedures perform well, high dimensionality of the feature vector and label uncertainty emerges as real problems in medical imaging. The proposed approach is based on the reduction of feature set without compromising accuracy.

TABLE I. COMPARISON OF RECENT STUDIES INVESTIGATING POTENTIAL OF MRI TECHNIQUE FOR CLASSIFICATION OF NC, MCI AND AD

Reference	Database	Classifier		Preprocessing					Features			Results		
		Name	Group	Alignment	Image warping	Registration	Segmentation	Normalization	Extraction Technique	Feature Type	Reduction	Accuracy	Specificity	Sensitivity
[35]	ADNI	k-means	NC			√	√	√	PCA	PBVC	DA	83.3	93.3	73.3
		FCM	AD									83.3	93.3	73.3
		SVM										90.0	93.3	86.7
[36]	ADNI	SVM linear	NC- AD			√	√	√	PLS	Volumetric	PLS	88.49	85.11	91.27
			NC-MCI									81.89	81.62	82.16
			MCI-AD									85.41	83.78	87.03
		SVM RBF	NC- AD									88.49	86.17	90.39
			NC-MCI									80.27	82.70	73.51
			MCI-AD									85.41	84.86	85.95
[40]	ADNI	LVQ –SVM	NC			√	√	√	LVQ	Histogram	PCA	91	81	71
		PCA-SVM	AD									88	66	66
		VAF-SVM										90	76	76
[41]	ADNI	Embedding+LapSVM	MCIc						RAVENS	Morphological features	ISOMAP algorithm	56.1	40.8	94.1
		Embedding+SVM	MCInc									55.3	42	88.2
		COMPARE+SVM										52.3	37	89.8
[8]	ADNI	Linear SVM	MCIc	√	√	√	√	√	-	SPARE-AD	-	-	-	-
			MCInc							Cerebrospinal fluid				
[7]	BLSA	Linear SVM	MCI	√	√	√	√	√	Adaptive Regional feature extraction technique	Regional features	ODC	90	-	-
			NC											
[30]	BLSA	Non-linear SVM	MCI	√	√	√	√	√	-	Brain regions	RFE	90	-	-
			NC											
[23]	ADNI	SVM	AD- NC	√	√	√	√	√	t-test	Brain regions	-	94.3	-	-
			MCIc-MCInc									81.5		
[25]	ADNI	SVM	AD-NC	√	√	√	√	√	Atlas warping	VBM	-	82	-	-
			MCI-NC									76.0		
			AD-MCI									58.3		
[42]	ADNI	SVM	MCIc	√	√	√	√	√	-	-	SVM-RFE	82.9	85.71	79.63
			MCIns											
[6]	-	Linear SVM	AD-NC		√	√	√	√	-	-	-	-	95.0	95.0
			MILD AD- NC									-	91.2	75.8
			AD- FTLD									-	83.3	94.7
[43]	OASIS	kSVM-DT	AD-MCI-NC		√	√		√	ALS-PCA	Genetically Features	PCA	80	-	-
[44]	ADNI	SVM	AD- NC	√		√		√	AAL	Wavelet ROI	Deep Sparse learning	-	-	-
			MCIc-MCInc											
[12]	ADNI	SVM	pMCI						RLR	Voxel based	-	90.06	-	-
		LDS	sMCI											
[31]	-	SVM	AD-NC							SPHARM	Bagging Strategy	94	92	96
			MCI-NC									83	84	83
[16]	ADNI	Non Linear SVM	AD-FTD	√	√	√	√	√	ROI	Region by Region	PCA	82	70	70.9

TABLE II. VARIOUS TYPES OF FEATURES AND ASSOCIATED MATHEMATICAL MODELS USED FOR AD, MCI AND NC CLASSIFICATION

Feature Type and Name				Mathematical Model
Textural Features	Statistical Features	**Histogram Features** *r(j)* is normalized vector and *n* is intensity levels	Mean	$\sum_{j=0}^{n} jr(j)$
			Variance	$\sum_{j=0}^{n}(j-1)^2 r(j)$
			Skewness	$(variance)^{-3}\sum_{j=0}^{n}(j-mean)^3 r(j)$
			Kurtosis	$(variance)^{-4}\sum_{j=0}^{n}(j-mean)^4 r(j)$
		Gradient Maps *N* is total number of pixels in an ROI	Gradient Mean	$(1/N_{k,l\in roi})\Sigma g(k,l)$
			Gradient Variance	$(1/N_{k,l\in roi})\Sigma(g(k,l)-GrM)^2$
			Gradient Kurtosis	$(1/\sqrt{GrV^4})(1/N_{k,l\in roi})\Sigma(g(k,l)-GrM)^4-3$
			Gradient Skewness	$(1/\sqrt{GrV^3})(1/N_{k,l\in roi})\Sigma(g(k,l)-GrM)^3$
		Co-occurrence Matrix *q(j,k)* indictates marginal distributions and *x,y* are the rows and columns	Sngular Second Moment	$\sum_{j=1}^{L^x}\sum_{k=1}^{L^x} q(j,k)^2$
			Contrast	$\sum_{x=0}^{L^x-1} m^2 \sum_{j-1}^{L^x}\sum_{k-1}^{L^x} q(j,k)$
			Sum of Squares	$\sum_{j-1}^{L^x}\sum_{k-1}^{L^x}(j-mean_x)q(j,k)$
			Entrpy	$\sum_{j-1}^{L^x}\sum_{k-1}^{L^x}(j-mean_x)q(j,k)$
			Correlation	$\sum_{j-1}^{L^x}\sum_{k-1}^{L^x} jkq(j,k)-(mean_x)(mean_y)$
		Run Length Matrix *q(j,k)* is count of pixels of length *k* and intensity *j*. n^r is the total count of pixels and n^g is the count of grey levels	Run Length Non-uniformity	$(\sum_{k-1}^{n^r}(\sum_{j-1}^{n^g} q(j,k)^2))/D$
			Short Run Emphasis Inverse Moment	$(\sum_{j-1}^{n^g}\sum_{k-1}^{n^r} q(j,k/k^2))/D$
			Grey Level Non-uniformity	$(\sum_{j-1}^{n^g}(\sum_{k-1}^{n^r} q(j,k)^2))/D$
			Fraction	$\sum_{j-1}^{n^g}\sum_{k-1}^{n^r} q(j,k)/\sum_{j-1}^{n^g}\sum_{k-1}^{n^r} kq(j,k)$
			Long Run Emphasis Moment	$(\sum_{j-1}^{n^g}\sum_{k-1}^{n^r} k^2 q(j,k))/D$
	Model based Features	**Regressive Model** g_s represents image intensity at site 's' and, n_r and θ represent image noise		$\sum_{s\epsilon n_r}\theta g_S + r$
	Image Transforms	**Haar Wavelet** b_k and c_k are wavelet coefficients and *t[m]* and *s[m]* are coefficients of low and high pass filter		$b_{k+1[q]}=\sum_{m-\infty}^{\infty} t[s-2q]b_{k[m]}$ $c_{k+1[q]}=\sum_{m-\infty}^{\infty} u[m-2q]b_{k[m]}$
Volumetric Features	**Volume of White Matter**			$\sum_{s=1}^{N}\sum_{u=1}^{x}\sum_{v=1}^{y} l(u,v)>T$
	Volume of Grey Matter			$\sum_{s=1}^{N}\sum_{u=1}^{x}\sum_{v=1}^{y} l(u,v)==T$
	Volume of Cerebrospinal Fluid			$\sum_{s=1}^{N}\sum_{u=1}^{x}\sum_{v=1}^{y} l(u,v)<T$

III. MATERIALS AND METHOD

Dataset: Data used in this research work are obtained from ADNI (Alzheimer's disease Neuroimaging Initiative) database. The primary goal of ADNI is to inspect biological, clinical and neuropsychological assessments for finding the effects in advancement of MCI and pre-AD. The dataset includes T1 weighted MRI images obtained through 3-plane localizer protocol that includes 120 subjects with their baseline, 6 months, 12 months and 24 months scans.

This includes 30 NC, 30 AD patients, and 60 MCI patients of which 30 patients are considered as MCIc based on their MMSE and CDR scores. The rest 30 of MCI patients are considered as MCInc. The dataset is divided into two groups each with 60 individuals. First group is used for classification between NC and AD subjects whereas second group is used for classification between MCInc and MCIc. Table III presents dataset details including number of subjects in each group, sex, age, CDR and MMSE scores.

TABLE III. DEMOGRAPHIC DATA OF SUBJECTS USED IN THE RESEARCH

Group	NC	MCInc	MCIc	AD
No of subjects	30	30	30	30
Sex(M/F)	12/18	18/12	18/12	15/15
Age	77.61±5.33	76.46±7.90	76.48±7.89	76.45±7.95
CDR	0.022±0.18	0.544±0.325	0.547±0.32	0.907±0.476
MMSE	28.95±1.24	25.79±3.47	25.7±3.49	21.70±4.382

Proposed Approach: The proposed approach includes four stages as shown in Fig. 1. In first stage MRI images are preprocessed for further study and analysis. In second stage, textural and volumetric features are extracted from preprocessed MRI images. Third stage reduces textural feature set to minimize the curse of dimensionality. In fourth and final stage, MRI images are classified.

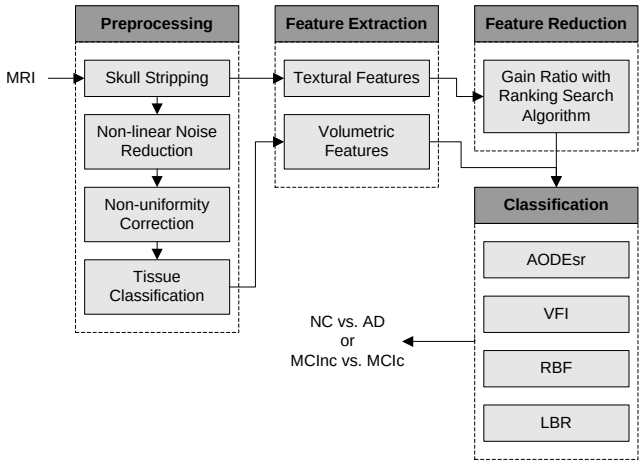

Figure 1. Detailed work flow of the proposed approach

Stage 1: Image Preprocessing: During image acquisition certain noise and inhomogeneity distortions are possible. To overcome such artifacts and to increase the quality of images certain image preprocessing steps are vital. For our proposed approach, preprocessing stage includes skull stripping, non-linear noise reduction, non-uniformity correction and tissue classification (see Section IV, Fig. 2 for details).

1. Skull Stripping: The existence of non-brain voxels may decrease the reliability and accuracy of concerned brain regions. To avoid this, skull stripping algorithm is required that best separates the brain voxels from non-brain voxels, e.g. skull bones. We perform skull stripping using brain surface extractor (BSE) algorithm [45].

2. Non-linear Noise Reduction: Non-linear noise reduction is required to minimize noise and inhomogeneity distortions present in MRI image while preserving edges and corners by averaging a voxel with its neighboring voxels that have uniform intensity [46].

3. Non-uniformity Correction: Structural MRI images often involve problems like non-uniformity in intensity or biasness due to the magnetic field disparity or a fault in the coils of the used system. Non-uniformity correction is performed using bias field correction (BFC) [45].

4. Tissue Classification: Tissue classification is performed by partial volume classifier (PVC) [47], where each voxel is assigned an integer label. These integer labels correspond to different tissue types of the brain e.g. grey matter, white matter, cerebrospinal fluid and background voxels.

Stage 2: Feature Extraction: According to recent studies different types of features, like ROI based, wavelet based and voxel based have been extracted from MR images for AD identification and recognition. In this research work, two types of features have been extracted from T1 weighted MR images namely textural features and volumetric features (see Section II, Table II for details).

1. Textural features: For neuroimaging, texture image analysis is a vital task because it portrays inside patterns of human tissues and organs. Three types of features, categorized as statistical features, model based features and image transforms are extracted from MRI. The first category includes histogram features, gradient maps, co-occurrence matrix, and run length matrix features. Whereas second and third category includes auto-regressive model and haar wavelet features respectively.

2. Volumetric features: Various studies have reported that change in volumes of different tissue types in entire brain, or at specific regions of the brain exhibits the severity of AD. Volumes of three types of brain tissues i.e. grey matter, white matter and cerebrospinal fluid have been extracted using PVC algorithm [47] for tissue classification.

Stage 3: Feature Reduction: The textural feature extraction stage returns 364 features. In order to estimate the discriminating power of individual features and to use most discerning features, feature selection/reduction is performed. The target of feature selection/reduction is to reduce the dimensionality of feature vector, which ultimately results in lower computational cost. Feature reduction method applied here is gain ratio, which uses ranking based search algorithm. Gain ratio is used to solve the multi class problem by settling down information gain. It is designed to classify the reliability of features by calculating the gain ratio of each involved class with the information gain value. Top 15 ranked features are selected for both groups of subjects.

Stage 4: Classification: For classification, publicly available data mining tool weka [48] has been used. The classifiers selected are Averaged One-Dependence Estimators with subsumption resolution (AODEsr), Voting Feature Interval (VFI), Radial Basis Function (RBF) and Lazy Bayesian Rule (LBR). Each of the classifiers is selected from a different algorithmic paradigm to evaluate the reliability of the proposed approach. AODEsr is a Bayesian method that works by identifying specializations between two attribute values at the time of classification and ignores the generalization attribute value. VFI is one of the miscellaneous classifier which is simple, fast and generates intervals between each class and classifies test cases using voting mechanism. RBF is a popular type of feedforward network that comprises of two layers; one covered up and one yield layer. LBR uses lazy learning method to ignore the small disjoint problem by constructing a rule for each test using unique method.

IV. RESULTS AND DISCUSSION

In this research work, MRI images have been used for prediction of conversion or non-conversion from MCI to AD within one year time. The images are preprocessed,

features are extracted, most discriminating features are selected and classification is performed. All preprocessing operations on sample NC, AD, MCInc and MCIc images are shown in Fig. 2. Four different types of classifiers i.e. AODEsr, VFI, RBF and LBR are used to evaluate the performance of our proposed approach. Leave-one-out (LOO) cross-validation strategy is applied for the performance evaluation of different classifiers. The purpose of using LOO strategy is that it works best for linear model classifiers such as RBF network.

The experimentation is performed in three phases. In phase 1, classification is performed individually on each of the seven textural feature sets, i.e. Auto Regression (AR), Geometrical Features (GF), Histogram Features (HF), Run-Length Matrix (RLM), Haar Wavelet (HW), Co-occurrence Matrix (COM) and Gradient Map (GM). This classification is done for both groups of subjects i.e. NC vs. AD and MCInc vs. MCIc. In phase 2, all seven textural feature sets are combined resulting in 364 features. The combined feature set is then reduced using gain ratio and first 15 features from reduced feature set (RFS) are used for classification task. The classification task in phase 2 is applied on both groups of subjects i.e. NC vs. AD and MCInc vs. MCIc as is done in phase 1.

The results of phase 1 and phase 2 for group 1 i.e. NC vs. AD and for group 2 i.e. MCInc vs. MCI are presented in Table IV and Table V respectively. The results are reported as accuracy, sensitivity and specificity and are expressed as percentage values. The graphical presentation of accuracy, sensitivity and specificity for group 1 are provided in Fig. 3, Fig. 4 and Fig. 5 respectively, whereas for group 2, these are provided in Fig. 6, Fig. 7 and Fig. 8 respectively.

Receiver operating characteristic (ROC) values for group 1 and group 2 for all textural feature sets as well as RFS are provided in Table VI and Table VII respectively. The graphical presentation is provided in Fig. 9 and Fig. 10 for group 1 and group 2 respectively.

In the third phase, volumetric feature set is considered which consists of grey matter, white matter and cerebrospinal fluid values and their ratios. Again the classification task is performed on both groups as is done in phase 1 and phase 2. The results reporting accuracy, sensitivity, specificity and ROC for group 1 are presented in Table VIII whereas the same results for group 2 are provided in Table IX.

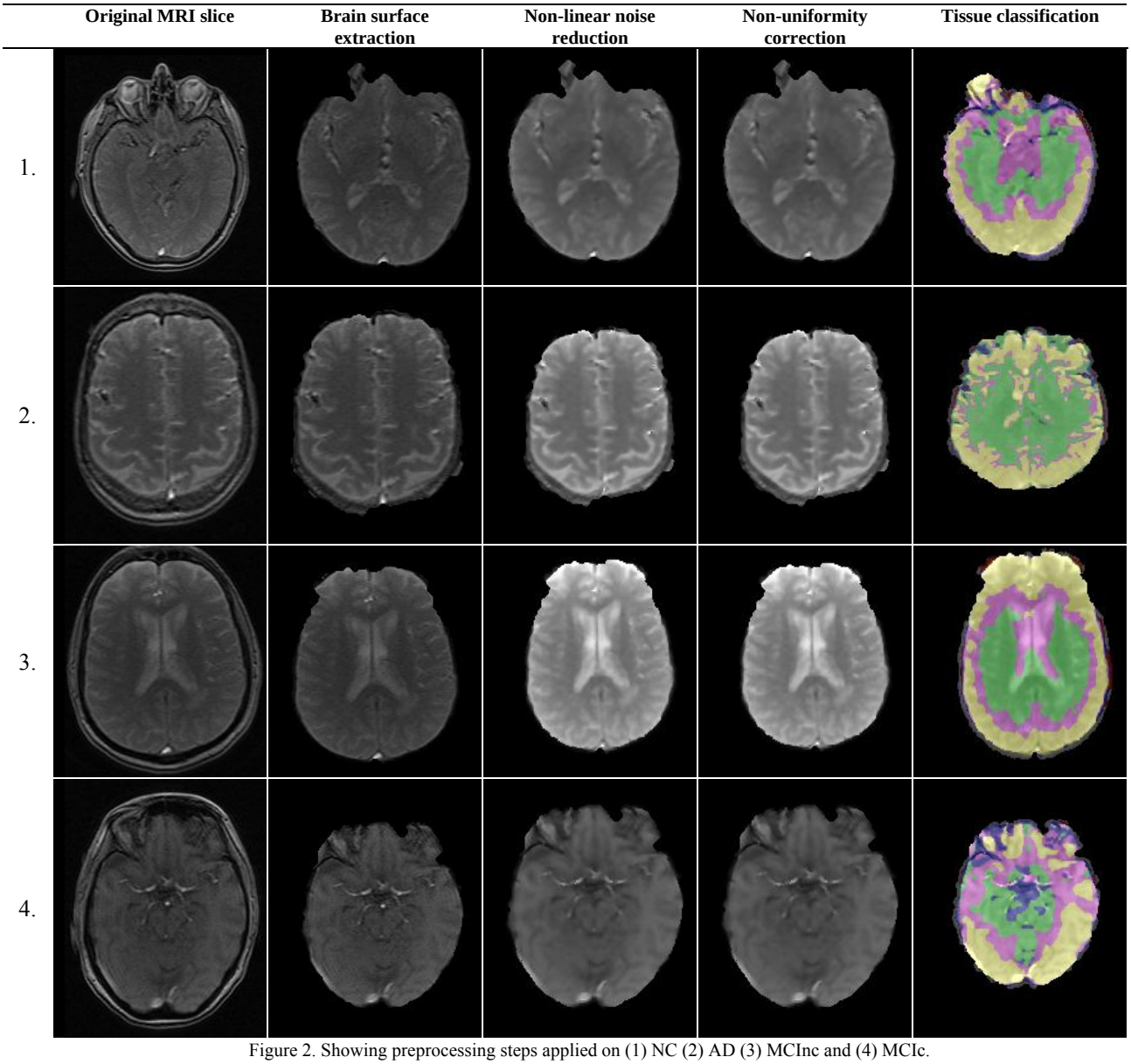

Figure 2. Showing preprocessing steps applied on (1) NC (2) AD (3) MCInc and (4) MCIc.

The graphical presentations of accuracy, sensitivity, specificity and ROC for group 1 (NC vs. AD) are shown in Fig. 11, whereas graphical presentations for same measures for group 2 (MCInc vs. MCIc) are shown in Fig. 12.

For the first group of subjects (NC vs. AD), using textural features it can be observed that AODEsr presented best results on RLM features (100%). On average, HF produced better results on all four classifiers. The results produced by RBF using HW and GM are not of satisfactory level (<60%). When the textural feature set is reduced, VFI and LBR remained good classifiers with an accuracy of 98.33%. Similarly when volumetric features are considered, an accuracy of 98.33% is achieved with AODEsr, VFI and LBR classifiers.

For the second group of subjects (MCInc vs. MCIc), considering the results using textural features, AR and HF remained the best feature sets producing an accuracy of 98.33% with all classifiers. The results produced using GM are not up to the mark. When textural features are reduced, a substantial improvement in results can be observed with VFI and LBR classifier (100%). When volumetric features are used, an accuracy of 98.33% is achieved with all classifiers.

Overall analysis of results shows that VFI and LBR perform better than other classifiers in most cases. Among seven textural features sets AR, GF, HF and RLM performed good as well as volumetric features. It can also be observed that GM alone does not produce satisfactory results. By reducing textural features, it is observed that VFI and LBR still are better than other classifiers. From these results, it can be concluded that LBR and VFI are good options for overall classification between MCI to AD and NC to AD due to its higher accuracy rates. Similarly it can be witnessed that the proposed approach is equally effective for the classification between MCInc and MCIc, which can eventually help in early identification of MCI subjects that are at risk of developing AD. A comparison of existing approaches with designed approach is presented in Table X.

TABLE IV. TEXTURAL FEATURES BASED CLASSIFICATION RESULTS FOR NC VS. AD

Classifier	Results	AR	GF	HF	RLM	HW	COM	GM	RFS
AODEsr	Accuracy	98.33	95.00	98.33	100.00	98.33	85.00	81.67	80.00
	Sensitivity	98.40	95.10	98.40	100.00	98.40	85.00	81.70	80.00
	Specificity	98.30	95.00	98.30	100.00	98.30	85.00	81.70	80.00
VFI	Accuracy	98.33	85.00	98.33	96.67	98.33	91.67	81.67	98.33
	Sensitivity	98.40	85.00	98.40	96.67	98.40	91.70	81.70	98.00
	Specificity	98.30	85.00	98.30	96.67	98.30	91.70	81.70	98.00
RBF	Accuracy	95.00	83.33	98.33	91.67	50.00	78.33	56.67	83.33
	Sensitivity	95.10	83.35	98.40	92.10	50.00	78.33	56.70	85.00
	Specificity	95.00	83.30	98.30	91.70	50.00	78.60	56.70	83.00
LBR	Accuracy	98.33	85.00	98.33	96.67	98.33	85.00	81.67	98.33
	Sensitivity	98.40	85.00	98.40	96.67	98.40	85.00	81.70	98.00
	Specificity	98.30	85.00	98.30	96.67	98.30	86.00	81.70	98.00

TABLE V. TEXTURAL FEATURES BASED CLASSIFICATION RESULTS FOR MCINC VS. MCIC

Classifier	Results	AR	GF	HF	RLM	HW	COM	GM	RFS
AODEsr	Accuracy	98.33	88.33	98.33	86.67	91.67	91.67	30.00	78.33
	Sensitivity	98.40	89.40	98.40	87.30	92.10	91.70	30.00	80.00
	Specificity	98.03	88.33	98.30	86.70	91.70	91.70	30.00	78.00
VFI	Accuracy	98.33	95.00	98.33	73.33	91.67	98.33	30.00	100.00
	Sensitivity	98.40	95.10	98.40	73.33	92.10	98.30	30.00	100.00
	Specificity	98.30	95.00	98.30	73.33	91.70	98.40	30.00	100.00
RBF	Accuracy	98.33	91.67	98.33	66.67	55.00	70.00	51.67	90.00
	Sensitivity	98.40	91.70	98.40	67.00	56.70	90.00	51.70	90.00
	Specificity	98.30	91.70	98.30	66.70	55.00	90.02	51.70	90.00
LBR	Accuracy	98.33	95.00	98.33	73.33	91.67	98.33	30.00	100.00
	Sensitivity	98.40	95.10	98.40	73.30	92.10	98.30	30.00	100.00
	Specificity	98.30	95.00	98.30	73.30	91.70	98.40	30.00	100.00

TABLE VI. TEXTURAL FEATURES BASED ROC VALUES FOR NC VS. AD

Classifier	AR	GF	HF	RLM	HW	COM	GM	RFS
AODEsr	99	94	99	100	96	86	96	66
VFI	99	77	99	94	96	89	72	99
RBF	92	76	99	88	32	74	51	83
LBR	99	77	99	94	96	75	69	99

TABLE VII. TEXTURAL FEATURES BASED ROC VALUES FOR MCINC VS. MCIC

Classifier	AR	GF	HF	RLM	HW	COM	GM	RFS
AODEsr	99	80	99	79	86	87	48	65
VFI	99	93	99	59	86	99	47	100
RBF	99	88	99	56	61	86	46	89
LBR	99	93	99	59	86	99	90	100

TABLE VIII. VOLUMETRIC FEATURES CLASSIFICATION FOR NC VS. AD

Classifier	Accuracy	Sensitivity	Specificity	ROC
AODEsr	98.33	98.00	98.00	100.00
VFI	98.33	98.00	98.00	100.00
RBF	60.00	78.00	60.00	100.00
LBR	98.33	98.00	98.00	100.00

TABLE IX. VOLUMETRIC FEATURES CLASSIFICATION FOR MCINC VS. MCIC

Classifier	Accuracy	Sensitivity	Specificity	ROC
AODEsr	98.33	98.00	98.00	99.00
VFI	98.33	98.00	98.00	99.00
RBF	98.33	98.00	98.00	99.00
LBR	98.33	98.00	98.00	99.00

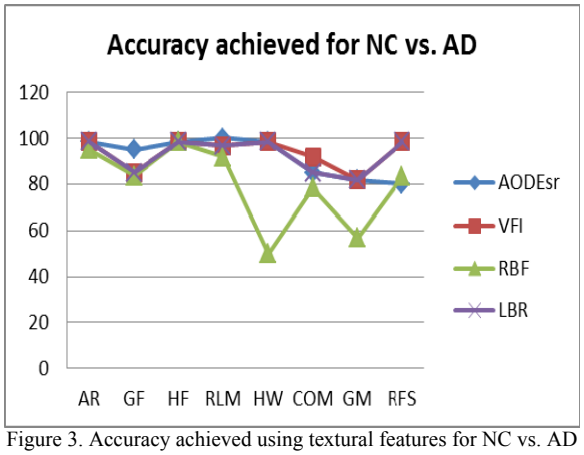

Figure 3. Accuracy achieved using textural features for NC vs. AD

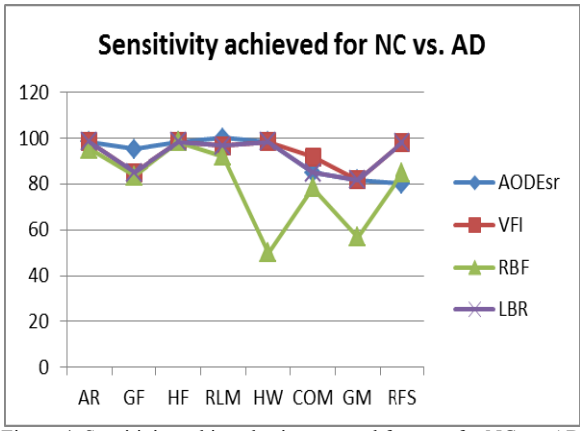

Figure 4. Sensitivity achieved using textural features for NC vs. AD

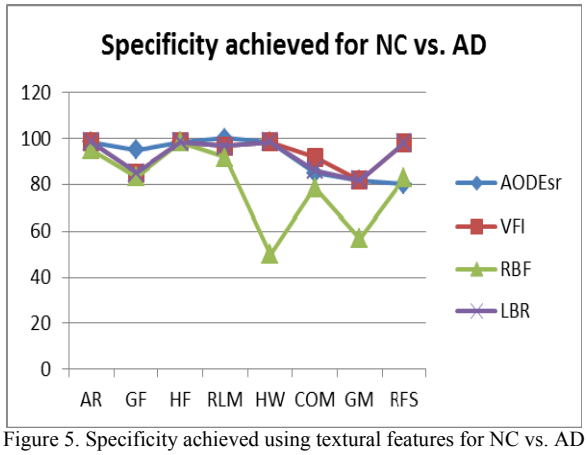

Figure 5. Specificity achieved using textural features for NC vs. AD

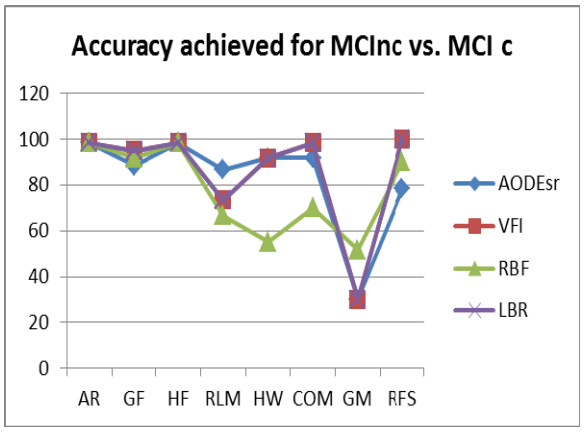

Figure 6. Accuracy achieved using textural features for MCInc vs. MCIc

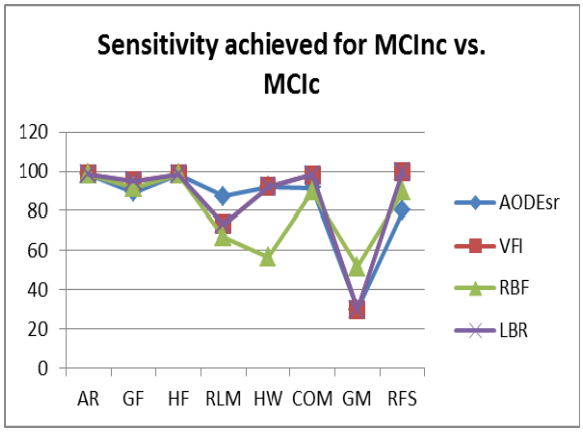

Figure 7. Sensitivity achieved using textural features for MCInc vs. MCIc

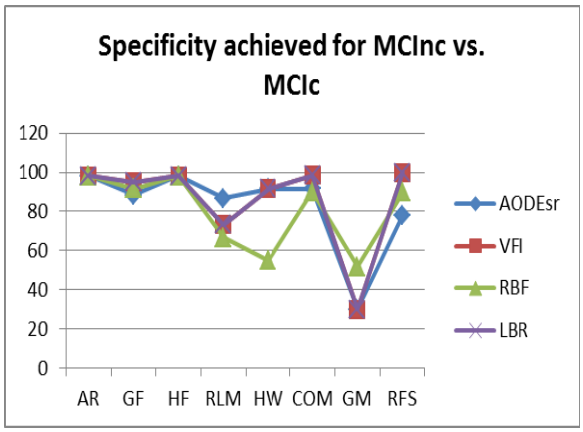

Figure 8. Specificity achieved using textural features for MCInc vs. MCIc

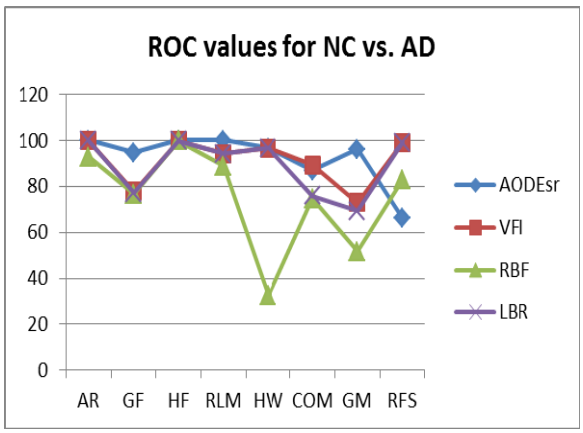

Figure 9. ROC values using textural features for NC vs. AD

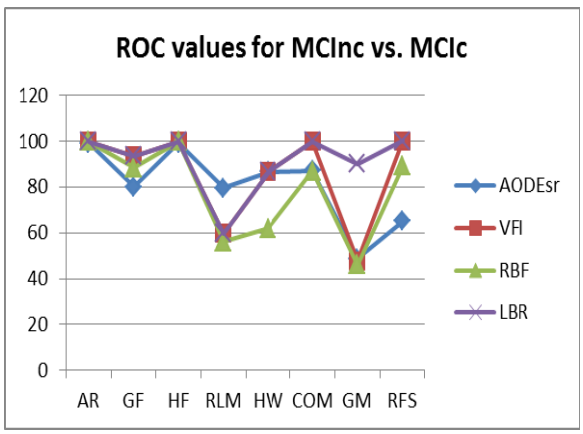

Figure 10. ROC values using textural features for MCInc vs. MCIc

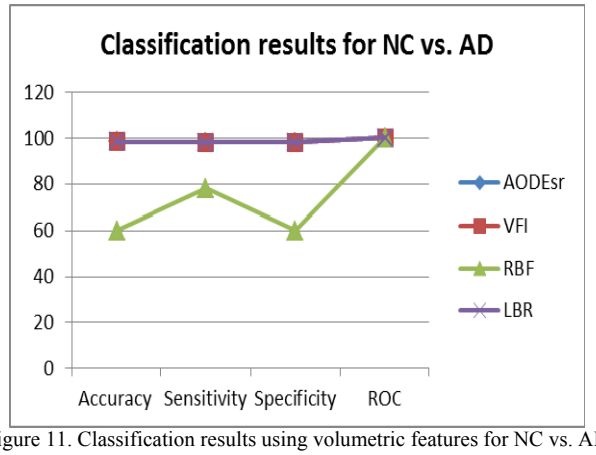

Figure 11. Classification results using volumetric features for NC vs. AD

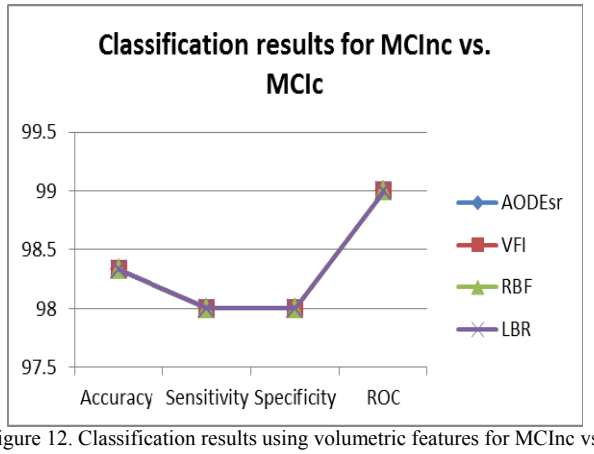

Figure 12. Classification results using volumetric features for MCInc vs. MCIc

TABLE X. COMPARISON OF PROPOSED APPROACH WITH EXISTING APPROACHES

Approach	Features	Group	Classifier	Accuracy
[49]	Volumetric, intensity and cortical thickness	NC vs. AD	Random Forrest	83.00
		MCI vs. AD		68.00
		HC vs. MCI		67.00
		HC vs. MCI vs. AD		54.00
[50]	Textural	AD vs.NC	1-NN	89.70
			ANN	98.50
[51]	Textural	AD vs. NC	L-SVM	80.76
[52]	Volumetric and shape	AD vs. NC	SVM	84.00
Proposed Approach	Textural	MCIc vs. MCInc	AODEsr	78.33
		AD vs. NC		80.00
		MCIc vs. MCInc	VFI	100.00
		AD vs. NC		90.00
		MCIc vs. MCInc	RBF	98.33
		AD vs. NC		83.33
		MCIc vs. MCInc	LBR	100.00
		AD vs. NC		98.33
	Volumetric	MCIc vs. MCInc	AODEsr	98.33
		AD vs. NC		98.33
		MCIc vs. MCInc	VFI	98.33
		AD vs. NC		60.00
		MCIc vs. MCInc	RBF	98.33
		AD vs. NC		98.33
		MCIc vs. MCInc	LBR	98.33
		AD vs. NC		98.33

V. CONCLUSION

In this research work, we have introduced a pattern recognition based MRI classification approach for the prediction of NC that are likely to develop AD and MCI patients that are likely to establish AD within two years or, contrarily, their stage remain same. It is based on extraction of textural and volumetric features from MRI which will help specialists in early detection and diagnosis of AD. Leave-One-Out cross validation strategy is used to evaluate the performance of our designed approach. Machine leaning algorithms are used to classify images as NC, MCInc, MCIc and AD. Both type features are tested using four different classifiers i.e. AODEsr, VFI, RBF and LBR. It is concluded that textural and volumetric features can be equally used for prediction of conversion from NC/MCI to AD. Comparison of our results with existing approaches shows the accuracy and effectiveness of our designed approach.

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