Detection of Alzheimer Disease in MR Images using Structure Tensor

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Abstract— **Alzheimer's disease (AD) is the most common progressive neurodegenerative disorder. Therefore, early detection and evaluation of prognosis of AD is an important issue in contemporary brain research. Magnetic Resonance Imaging (MRI) provides valuable diagnostic information about AD. In this work, brain tissue is extracted using phase-based level set method. Structure tensor analysis is used to visualize and quantify structural features of the brain from MRI. Further, quantitative measures are derived to classify different stages of AD. Normal and AD subjects were classified up to an accuracy of 88% using these features. It is observed that structural changes in brain can be characterized using this technique and therefore can be helpful in tracking the progression of AD and aid in classification between normal and AD subjects.**

I. Introduction

Alzheimer Disease is a progressive brain disorder that gradually destroys memory and thinking skills and, eventually, the ability to carry out the simplest daily tasks. Definitive diagnosis of AD can be made only through histopathological examination of brain tissue for the presence of neurofibrillary tangles and amyloid plaques, usually at autopsy. Therefore, there is a need for reliable, objective and non-invasive methods for accurate diagnosis of AD during the lifetime of an individual [1].

Recent advancements in imaging techniques have aided in accurate diagnosis of AD and also in identifying its early preclinical stages. Magnetic Resonance Imaging has been the most widely used imaging modality in differentiating AD from other brain related pathologies. MRI based measures of atrophy are regarded as predictive biomarkers of the disease state and its progression [2].

Manual measurements of sub-cortical structures for AD diagnosis from MRI are time consuming and do not capture the full pattern of atrophy. Clinical MRI scans can be made more useful in diagnosis of AD, by employing non-expert dependent, automated methods which perform equally well or better than clinical studies [3]. Recently it has been reported that ultrahigh field MR images can be helpful in the study of textural changes in subcortical structures of the brain [4].

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It has been established that structure tensor features aid in unsupervised recognition of patterns in images [5]. It has also been widely used in object tracking and motion pattern analysis [6]. Lately, analysis of brain tissue of rat using structure tensor has proven that it helps in characterizing the micro structure of brain [7].

The overall goal of this study is to characterize the orientation and structural anisotropy of brain by carrying out texture analysis on MR images. Subsequently, derive quantitative measures to classify different stages of AD. Structure tensor (ST) analysis is used as a texture analysis method on MRI to visualize and quantify the microstructures in brain. Using the metrics derived, the subjects were classified as AD, mild cognitive impairment (MCI) or normal controls.

II. METHOD

A. Data

The images considered for performing the experiments are taken from an open source online database Open Access Series of Imaging Studies (OASIS) [8]. The MRI scans considered for this study are T1-weighted images of resolution 1.0 x 1.0 x 1.25 mm3. Each volume is the post-registration average of 4 independently acquired magnetization prepared rapid gradient-echo (MP-RAGE) scans with repetition time: 9.7 ms, echo time: 4.0 ms, inversion time: 20 ms, delay time: 200 ms and flip angle: 10°, obtained using a 1.5 T Siemens Vision scanner (Erlangen, Germany). All the subjects considered are right handed. The demographics of the subjects considered are given in Table 1.

TABLE I. DEMOGRAPHICS OF SUBJECTS CONSIDERED FOR STUDY

Feature	Normal	MCI	AD
Number of subjects	92	67	45
Age	67.90 ± 13.96	73.87 ± 8.96	76.77 ± 7.13
Gender (M/F)	68/24	44/23	24/21
Clinical Dementia Rating	0	0.5	1
Mini-mental state examination	29.04 ± 1.16	25.87 ± 2.78	21.23 ± 3.28

In order to ensure that voxels in different images refer to the same anatomical positions in the brain, the brain images are preprocessed. The MR images in the OASIS database are gain-field corrected and atlas-registered to the 1988 atlas space of Talairach and Tournoux [8].

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B. Data Analysis

Structure tensor is an image texture analysis technique often used in image processing and computer vision. Structure tensor, J, of an image is a matrix derived from the image partial derivatives [9]. It is defined as,

$$J = \begin{bmatrix} < f_x, f_x >_w & < f_x, f_y >_w \\ < f_x, f_y >_w & < f_y, f_y >_w \end{bmatrix} \quad (1)$$

Where f_x and f_y are the partial derivatives of image f(x,y) along the x and y directions respectively. It is defined for each pixel as a second order symmetric positive matrix. The weighted inner product between two images g and h is defined as

$$< g, h >_w = \iint_{R^2} w(x,y) g(x,y) h(x,y) dxdy \quad (2)$$

where, w(x,y) is a Gaussian weighting function with a specified width (σ) defining the local neighborhood. The eigenvalues λ_1 and λ_2 and the corresponding eigenvectors e_1 and e_2 summarize the distribution of the gradient of the image within the window defined by w.

If an eigenvalue is zero, the grey values in the direction of the corresponding eigenvector do not change. If one eigenvalue is zero and one greater than zero, it represents a simple neighborhood with ideal orientation. An isotropic structure is observed when $\lambda_1 = \lambda_2$.

Local orientation, anisotropy and energy for each pixel can be calculated for the structure tensor matrix [10]. The direction of the largest Eigen vector of the tensor corresponds to the local predominant orientation θ given by

$$\theta = \frac{1}{2} \arctan \left(2 \frac{< f_x, f_y >_w}{< f_y, f_y >_w - < f_x, f_x >_w} \right) \quad (3)$$

The anisotropy measure AI is given as

$$AI = \frac{\left(\sqrt{\left(< f_y, f_y >_w - < f_x, f_x >_w \right)^2 + 4 < f_x, f_y >_w} \right)}{< f_x, f_x >_w + < f_y, f_y >_w} \quad (4)$$

The anisotropy measure gives a relation between the length of the orientation vector to the length of the gradient vector. The values of anisotropy measure vary from 0, indicating isotropic to 1 indicating highly oriented structures.

Energy is given by the trace of the structure tensor J [11]

$$E = Trace\ (J) = < f_x, f_x >_w + < f_y, f_y >_w \quad (5)$$

Higher value of energy indicates highly oriented structures. Energy and anisotropy of the structure tensor can be used for structure analysis. Homogeneous areas in an image cause the energy to be small. In areas around edges, the structure tensor has a large energy as well as a large anisotropy, while corners result in a large energy but small anisotropy. In this work orientation, anisotropy, energy, λ_1 and λ_2 are considered as features. The resulting values are visualized by combining in a composite image where hue, saturation and brightness (HSB) correspond to local orientation, coherency and the original image intensities.

C. Classification methods

Classification algorithms were explored to discriminate between the MRI of patients with varying degree of AD and their age matched control normals. Performance of different classifiers including naive Bayes, support vector machine, random forest and AdaBoost are studied. The performance of the classifiers was analyzed using standard parameters accuracy, specificity and sensitivity using ten 10-fold cross validation runs.

Naïve Bayes classifier is a supervised probabilistic classifier based on Bayes' theorem. This classifier assumes that given a class, its features are independent, i.e. the presence or absence of a feature is not related to the presence or absence of another feature [12].

Support Vector Machine (SVM) is a supervised, multivariate classification system. In this algorithm the feature vectors are linearly mapped to a higher dimension feature space. In this feature space, a linear separation surface called a hyperplane is created to separate the training data by maximizing the distance between the vectors of the two classes [13].

Random forest is a group of regression trees created by using bootstrap samples of the training data and random feature selection in tree generation. Prediction is made by combining the predictions of the group [14].

AdaBoost, short for Adaptive Boosting, is a machine learning algorithm, is used in conjunction with many other learning algorithms to improve their performance. AdaBoost is adaptive in the sense that subsequent classifiers built are tweaked in favor of those instances misclassified by previous classifiers. Here, after each iteration the data is reweighted, where the weight of misclassified examples is increased, while the weight of the correctly labeled samples is decreased. In this work AdaBoost.M1 algorithm has been used [15].

III. RESULTS AND DISCUSSION

Typical MRI images of different stages of AD are shown in the first column of Fig. 1. It can be seen that as AD progresses there is a visible decrease in the brain tissue structure. It can also be seen that due to this atrophy, the size of the ventricle increases as AD advances.

The MR images are first subjected to phase-based level set algorithm to remove the non-cerebral tissues [16]. Fig. 1 shows results of the segmentation for different patients at different level of AD using phase based level set method. The initial contour was defined on the image as shown in the first column of Fig. 1. The algorithm evolved the initialized contour over 80 iterations. At the end of all iterations a mask of the final zeroth level contour was created and multiplied with the original image, to give the segmented output. The advantage of local phase is that the measure is not sensitive to the magnitude of boundaries in the image, so it allows

segmentation along weak or strong boundaries between anatomical structures. The gradient diffusion process helps the contour to stick to the concave area of the region [16].

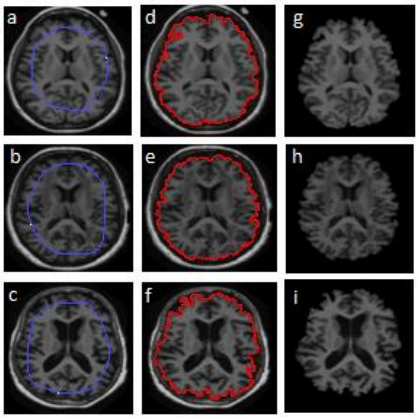

Figure 1. (a-c): initial contour, (d-f): final evolved contour and (g-i): segmented brain of a normal subject, MCI and AD patient

The MRI scan after skull stripping is subjected to structure tensor analysis and features are extracted from all MR images. The features extracted are orientation, anisotropy index, energy, λ_1 and λ_2. The visualization of the resulting scalar values of the features is shown in Fig. 2.

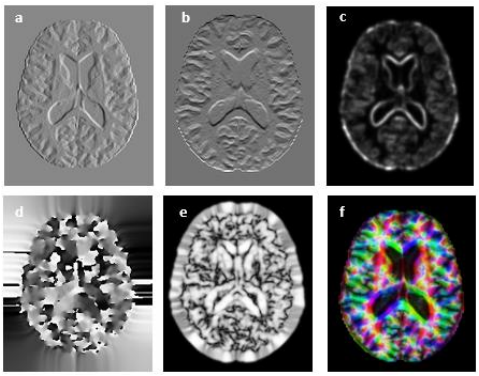

Figure 2. (a) Gradient-X (b) Gradient-Y (c) Energy (d) Orientations (e) Anisotropy index (f) Orientation, anisotropy and original image intensity combined as a HSB image

Fig. 2(a) and (b) show the MRI convolved a Gaussian derivative filter along the x and y direction. Fig. 2(c) shows the representation of the energy feature of the MR image. From Fig. 2(d) it can be seen that there are jumps in the image representing orientation. When orientation, which is a cyclic quantity, is represented using grey scale, unnatural jumps between the smallest angle and the largest one dominate the appearance of the orientation image. For better visualization the orientation is combined with the anisotropy index and is represented as a color image. Fig 2(f) shows the color representation of the structure tensor. As the structure tensor has three independent pieces of information, orientation angle, coherency and the image intensity, it fits well to the three degrees of freedom available to represent color in an image: luminance, hue, and saturation. Here, the squared magnitude of the gradient is mapped onto the intensity, the coherency measure is used as the saturation and the angle of the orientation vector is represented as the hue.

Using features extracted from MRI after structure tensor analysis, different stages of AD are classified. The classification is performed by selecting the most discriminative features using Fischer discriminant ratio criterion.

The five features extracted from the structure tensor analysis of the brain are used to classify the MR images into normal, MCI and AD. The performance of different classifiers for structure tensor features was analyzed. The results of classification between normal, MCI and AD subjects are presented in Tables 2 and 3.

TABLE II. CLASSIFICATION RESULTS USING SVM FOR NORMAL VS AD SUBJECTS

	Accuracy (%)	**Sensitivity (%)**	**Specificity (%)**
Orientation	76.1	71.34	72.43
Anisotropy index	65.76	62.54	59.85
λ1	51.17	48.46	45.32
λ2	87.39	85.56	83.45
Energy	88.67	87.65	84.87

TABLE III. CLASSIFICATION RESULTS USING SVM FOR NORMAL VS MCI SUBJECTS AND MCI VS AD SUBJECTS

	Normal vs MCI subjects			**MCI vs AD subjects**		
Feature	**Acc. (%)**	**Sen. (%)**	**Spec. (%)**	**Acc. (%)**	**Sen. (%)**	**Spec. (%)**
Orientation	65.8	71.3	65.8	66.7	64.3	62.5
Anisotropy index	57.1	55.1	54.8	53.3	52.6	53.3
λ1	47.3	47.1	46.3	43.6	42.5	40.5
λ2	75.8	73.6	74.4	75.2	68.3	70.5
Energy	80.3	76.4	78.3	79.1	74.7	76.7

The accuracy obtained in classifying normal from AD subjects was higher when compared to that between MCI and AD or normal and MCI. This may be due to the increase in severity of the structural changes as the disease progresses. The energy feature gave the highest classification accuracy in all the cases. Due to AD related histological changes the homogeneity of the AD tissue increases. Homogeneous areas in an image cause the energy to be small. This difference in energy captured at the sites of neuronal loss, seems to be useful in differentiating normal from AD subjects. The best classification results in all the cases were obtained with support vector machine as shown in Fig. 3.

The sensitivity of energy feature was high at 87.65% when only normal and AD subjects were classified. When MCI subjects were compared with AD and normal subjects, the sensitivity values decreased to about 74.7%. This may be attributed to very less variation in the structural features during the progression from normal to MCI and from MCI to AD. The specificity also shows similar trend as sensitivity, with a maximum of 84.87% in classifying normal and AD

using SVM. The sensitivity is reduced to around 76% when MCI subjects are introduced in the classification.

From Fig. 3 it can be seen that when compared to other classification techniques, the average predictive accuracy of SVM is slightly higher. Fig. 4 shows the performance of different classifiers in 3-class classification of normal, MCI and AD, using a combination of features. The accuracy obtained using SVM is comparatively higher.

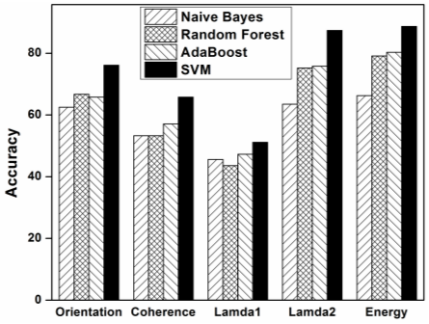

Figure 3. Accuracy of different classifiers in classifying normal and AD subjects

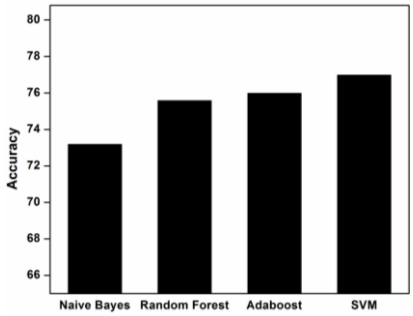

Figure 4. Performance of different classifiers in classification of Normal, MCI and AD subjects using orientation and anisotropy values

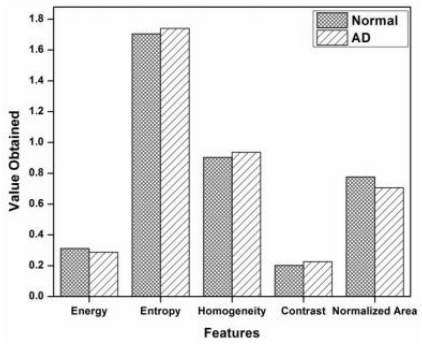

Figure 5. Grey Level Co-occurrence Matrix features

Grey Level Co-occurrence Matrix (GLCM) features have been the most commonly used texture features in brain studies. The GLCM features for the considered data set are shown in fig. 5. The advantage of ST over GLCM is that the Eigen vector decomposition of ST gives a higher consistent representation of orientation of small features [17].

Overall, it is observed that the structure tensor features are able to characterize the structural changes in the human brain tissue, and is in agreement with earlier reports on rat brain [7]. It helps track the progression of AD and aid in classification between normal, MCI and AD condition with acceptable accuracy.

IV. Conclusion

In this study structure tensor is used to identify different stages of AD from MR images. The brain tissue is extracted from MRI using phase-based level set method. It is observed that, leakage of contour at weak boundaries is reduced by using gradient diffusion process and phase information in segmentation. It is observed that structural changes in the brain could be captured using structure tensor analysis and quantitate measures obtained could classify normal and AD subjects up to an accuracy of 88.67% using SVM. Furthermore, the classification accuracy can be improved by considering ultrahigh field MR images as they provide better textural heterogeneity.

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