Automatic Detection of Alzheimer Disease from 3D MRI Images using Deep CNNs

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***Abstract*—Alzheimer's disease (AD), also referred to simply as Alzheimer's, is a chronic neurodegenerative disease that usually starts slowly and worsens over time. It is the cause of 60% to 70% of cases of dementia. In 2015, there were approximately 29.8 million people worldwide with AD. It most often begins in people over 65 years of age as it affects about 6% of people 65 years and older, although 4% to 5% of cases are early-onset Alzheimer's which begin before this. In 2015, researchers have figured out that dementia resulted in about 1.9 million deaths. Continuous efforts are made to cure the disease or to delay its progression. Brain imaging is one of the hottest areas in AD research. Techniques like CT, MRI, SPECT, and PET assist in disease detection and help in excluding other probable causes of dementia. Imaging helps to perceive the intended cause of the disease as well as track the disease through its course. This paper applies Image processing and machine learning techniques combined to MRI brain images to help in detection of AD and classify the case either to MDI or Dementia.**

Keywords*—*Alzheimer detection; brain scanning techniques; MRI scanning; image processing; machine learning

I. Introduction

The most common early symptom of AD is the short-term memory loss or in other words the difficulty in remembering recent events. As the disease advances, symptoms can include problems with language, disorientation (easily getting lost), mood swings, loss of motivation, not managing self-care, and behavioral issues [1, 2]. As a person's condition declines, they often withdraw from family and society. Gradually, bodily functions are lost, ultimately leading to death [3]. Although the speed of progression can vary, the average life expectancy following diagnosis is three to nine years [4, 5].

The cause of Alzheimer's disease is poorly understood. About 70% of the risk is believed to be genetic with many genes usually involved [1, 6]. Other risk factors include a history of head injuries, depression, or hypertension. The disease process is associated with plaques and tangles in the brain [6]. A probable diagnosis is based on the history of the illness and cognitive testing with medical imaging and blood tests to rule out other possible causes [7]. Initial symptoms are often mistaken for normal ageing. Examination of brain tissue is needed for a definite diagnosis. Around the world, the current challenge in Alzheimer's disease is to search certain therapeutic technique that can detain or arrest the disease progression. Neuroimaging can act as a good biomarker used extensively in drug trials. Brain imaging is also helps in diagnosis of AD at its early stage. The clinical studies in AD require heavy cost and thousands of patients are generally incorporated for the accuracy of assessment. Both in academic and industrial studies, the prime focus is on the use of significantly fewer subjects exposed to treatment [8]. The computed tomography (CT), magnetic resonance imaging (MRI), Single-photon emission computed tomography (SPECT) and positron emission tomography (PET) scanning techniques are totally non-invasive and rely on the methods offering molecular diagnostics. These techniques are also extensively used in drug trials. Thus, brain imaging offers a robust and efficient tool and is considered as a biomarker for detecting AD in its prodromal stage.

The remaining of this paper is organized as follows: In Section II is discussed a comparison between different brain scanning techniques. In Section III, an overview of AD detection in literature is presented. Section IV presents the theory. Section V demonstrates the proposed approach, whereas Section VI demonstrates the experimental work and the results achieved. Finally, the paper is concluded in Section VII.

II. Brain Scanning Techniques

The neuroimaging is a powerful biomarker for understanding the pathology of Alzheimer's disease and its progression. Following are the main different techniques widely used in this area:

MRI scan in AD detection: Magnetic resonance imaging (MRI) scan stand upon the principle of nuclear magnetic resonance. The nucleus of hydrogen atom (proton), residing inside the brain tissue as water or fat, becomes exited with radio wave pulse in a magnetic field. When the pulse is turned off, the proton emits radiofrequency signal and return to its native energy level. Depending upon a combination of different pulses and gradients, a sequence of signals are made and cumulatively form a tissue specific map of the brain [9].

CT scan in AD detection: Defused cerebral atrophy with enlargement of the cortical sulci and ventricular space are the primary criteria for computed tomography (CT) scan diagnosis of AD. Generally, diameters of third and lateral ventricles as well as the bifrontal and bicaudate diameters are linearly measured to evaluate the extent of atrophy. Research reveals that the volume of third and lateral ventricles is increased in AD than control [10]. Scientist have pinpointed that there is a positive correlation between brain atrophy and cognitive loss [11]. Dilated peri-hippocampal fissure forms hippocampal lucency or hypoattenuation in the temporal area medial to the temporal horn and it is a good radiologic marker for AD detection by CT.

PET Scanning in AD detection: Positron emission tomography (PET) scan is a robust, sensitive, powerful, noninvasive technique quantify cerebral blood flow using metabolic property of brain tissue and binging property of amyloidal beta plaque. This technique is essential for accurate diagnosis, evaluation of disease progression and assessment of drug response [12, 13]. In AD, at baseline, PET scan can show relation with decline in mini mental state examination score [14]. A major limitation of PET is it is very expensive.

SPECT Scanning in AD detection: Single-photon emission computed tomography (SPECT) is a noninvasive technique uses photon emitting property of radio nuclei with half-life of 6 to 12 hours. This scan depicts a clear 3D image of brain indicating regional cerebral blood flow. Number of studies with SPECT reveals a positive correlation between severity of dementia and temporoparietal hypofunction [15, 16]. Bilateral temporoparietal hypoperfusion shows 82% positive predictive value for AD [17]. A major limitation of PET is it is very expensive. Fig. 1 shows the four different brain scanning techniques.

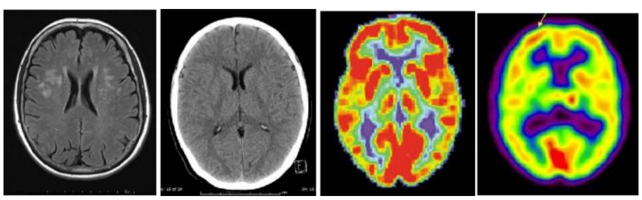

Fig. 1. Different brain scanning techniques, from left to right: MRI scan, CT scan, PET scan, SPECT scan.

III. Literature Review

Many researchers have studied the detection of AD. These studies usually follow two main approaches: the analysis of biomarkers and the examination of patients' decreasing cognitive abilities. The first approach yields reliable results in the detection of AD in its moderate and advanced stages, albeit still performing insufficiently in the early stages of the disease [18]. The second approach has gained more attention in recent years, since, in clinical practice, it has shown promising results in the early detection of AD [19, 20]. Furthermore, when compared to the first approach, the analysis of the decline of cognitive abilities represents an inexpensive and noninvasive alternative. In 2012, Ali El-Zaart and Ali A.Ghosn [21] have proposed a new method for image thresholding (bimodal and multimodal thresholding). Their segmentation method was based on between-class variance and using Gamma distribution. Authors stated that their approach solved the problem of non-symmetric histogram of images by using Gamma rather than Gaussian distribution. They then confirmed that the experimental results obtained by testing their approach showed a good efficiency and satisfying segmentation results, but they mentioned nothing about the accuracy rate or the impact of their segmentation results on the AD automatic detection. Fig. 2 demonstrates the segmented results obtained from that work.

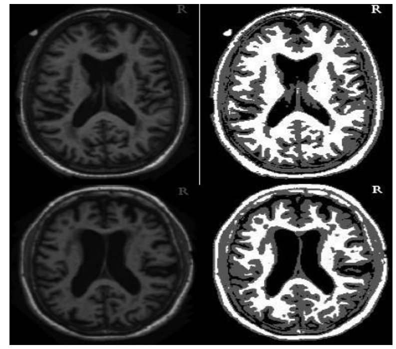

Fig. 2. Original MRI images and segmented Results by El-Zaart and Ghosn approach [21].

Siavash Fashtakeh suggested a research idea in the same year [22]. The idea was based on applying pattern recognition techniques to structural MRI images and then uses automatic classifiers to detect AD in its early stages. ADNI database was used in this study. Brain tissue categorization into white matter (WM), grey matter (GM) and cerebrospinal fluid (CSF) was held first followed by customized tissue probability maps created for bias correction. SVM was used then for feature reduction and feature selection. As a future work, the author mentioned some trials about developing better classifier using Neural Network for automate classification. Although the paper contains detailed explanation of the steps and the dataset used, all the results discussed by Fashtakeh research are expected in future! In 2013, Herrera et al [23] have used Discrete Wavelet Transform (DWT) for feature extraction, then Principal Component Analysis (PCA) for feature reduction. Researchers have confirmed that the experimental study showed that the use of dimensionality reduction in this problem led to a worse classification accuracy. The main conclusion of their study accordingly was that all available information is important to achieve a good classification performance. They also confirmed that due to that fact the computational cost of classifiers training will be very large, but the results would be worthy. They then confirmed that their system using SVM without feature reduction showed promising results, but they did not write a clear accuracy rate. S. K. Aruna and S. Chitra [24] two years later used the OASIS MRI brain dataset to compare different machine learning approaches. The researchers firstly used Gabor filter with four different orientations and GLSM to extract features, then they normalized and fused the features. They then used SVM with different kernels to compare between the effectiveness of features obtained by Gabor, GLCM, and the fused features. Authors finally confirmed that their fused features achieve better accuracy than the features obtained by both Gabor and GLCM; however, nothing about the accuracy rates of AD detection was mentioned in their article. In the same year Moradi et al [25] have used SVM and LDS classifiers to detect AD from MRI brain images, with and without feature selection, and compared all the results obtained in all cases. Authors confirmed that LDS classifier with feature selection led to the best results with accuracy rate of 74.74% which was the highest accuracy rate achieved by their work. Bolurchi et al [26] have published the most recent work conducted in this area in 2018, as they used 3D MRI brain images to improve the accuracy rates of automatic AD detection and they assured that they were successful as they used three different feature extractors (PCA, PDF, and contrast homogeneity) with respect to state-of-art, and they fused the features extracted from the three key slices together. Furthermore, they adopted and compared three different classifiers (decision tree, K-NN, and SVM). Authors finally confirmed that SVM achieved the better detection accuracy rate which reached 88.1%. Fig. 3 demonstrates the MRI preprocessing steps.

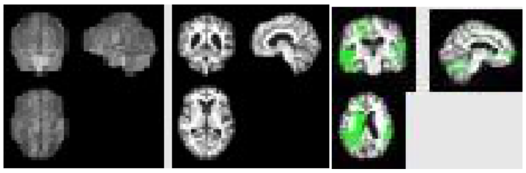

Fig. 3. Preprocessing steps of Bolurchi et al, 3D image (left), key slices (middle), feature detection (right) [26].

IV. Theory

There are mainly three differences between healthy and non-healthy brain images which are: Severely enlarged ventricles often result in changes in the shapes of them, extreme shrinkage of cerebral cortex often results in changes in the outer shape of the brain, and extreme shrinkage of hippocampus [27] (see Fig. 4). Among those three different signs of abnormality this paper limits the automatic detection on the first sign which is the enlargement in ventricles as an obvious abnormality sign that proved to the most promising sign to detect AD automatically from brain MRI images. Two approaches are used here for AD detection: Image thresholding approach and deep learning approach. The following subsections explain the steps of each approach in details.

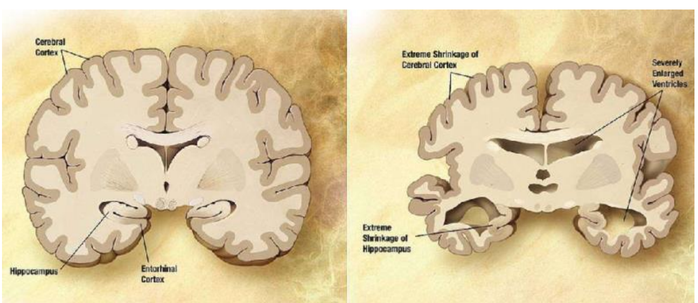

Fig. 4. Comparison of a normal aged brain (left) and the brain of a person with Alzheimer's (right). Characteristics that separate the two are pointed out.

V. Proposed Approach

This work adopts two different approaches to detect Alzheimer form brain MRIs and then combine them together to get a hybrid approach. The following subsections explain the steps of every approach.

A. Image Thresholding

Some image processing steps were conducted to get the MRIs classified to either sick or normal case based on certain threshold. Fig. 6 represents the steps of the image thresholding approach.

The data in ADNI database are stored in dicom files, so firstly the dicom files were converted to normal images. After the dicom file is converted to bng image, this data is an open source which can be found in ADNI website [28]. First, a color space conversion takes place to convert the RGB images to grayscale images. Otsu's threshold [29] is then applied to the grayscale images. Otsu's method is roughly a one-dimensional, discrete analog of Fisher's Discriminant Analysis. It automatically calculates a certain number (Threshold) based on image color analysis. The idea is that it applies color clustering-based image thresholding to convert the image from grayscale image to binary image. The algorithm uses a bi-modal histogram to exhaustively search for the threshold that minimizes the intra-class variance (the variance within the class), defined as a weighted sum of variances of the two classes. Otsu shows that minimizing the intra-class variance is the same as maximizing inter-class variance. Fig. 5 shows a sample dicom file.

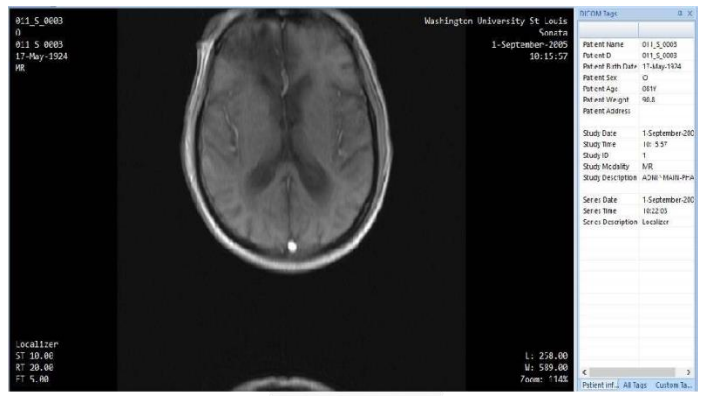

Fig. 5. Sample Dicom file.

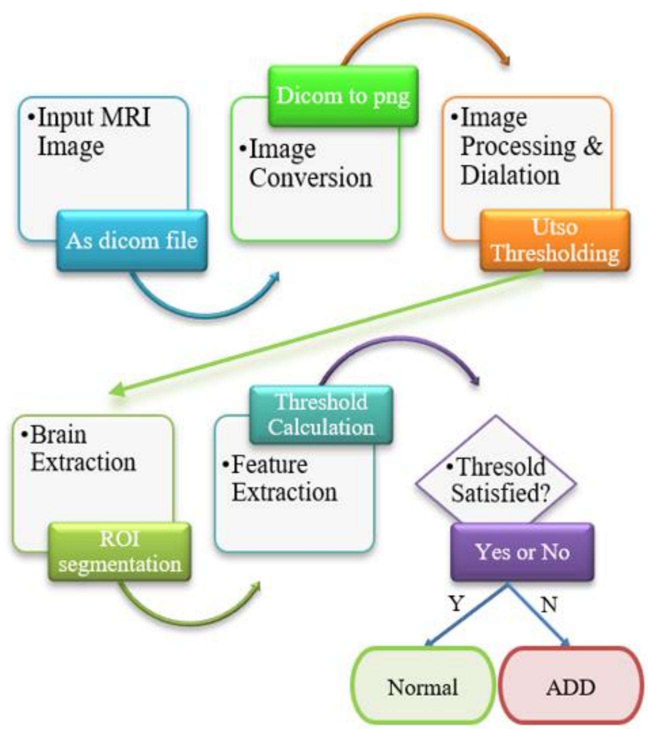

Fig. 6. Image processing phases and steps.

The Algorithm I shows the main steps of the Otsu thresholding method.

Algorithm.1. Otsu Algorithm [29]

1) Compute Histogram and Probabilties of each Intensity Level
2) Set up Initial $\omega_i(0)$ and $\mu_i(0)$
3) Step through all Possible Thresholds t=1, ..., Maximum Intensity
    - Update $\omega_i(0)$ and $\mu_i(0)$
    - Compute $\sigma^2\, b(t)$
4) Desired Threshold corresponds to maximum $\sigma^2\, b(t)$

Fig. 7 shows image before and after applying Otsu Thresholding.

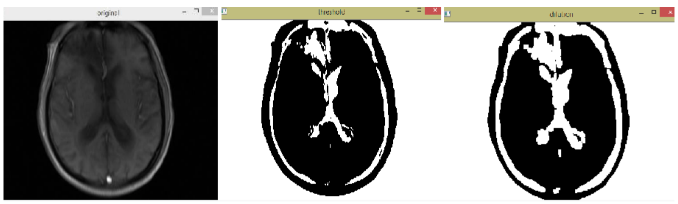

Fig. 7. Axil: The original image (left), the Otsu based threshold image (middle), the dilated image (right).

A morphological image processing is then held to fill the gaps in the ROI (brain ventricles). After wards the brain is then cropped by pixel aggregation. Once the brain image is cropped the ventricles region can be cropped easily as it is in the middle of the image. The ratio of white to black pixels is calculated and the brain is then classified to either normal or sick (with AD).

B. *Deep Learning*

Convolutional Neural Networks (CNN) is then adopted to extract features automatically from the Original MRIs, and then classify the cases. It is mainly composed of five layers: the input layer, the output layer and three layers in between. Where, the first layer contains 16 filters, the second one is composed of 32 filters, then the third layer is composed of 64 filters. Fig. 8 shows the components of the CNN followed by a detailed explanation.

Every layer takes the feature map and enters it to three different components which are Rectified Linear Units (ReLU function), Batch normalization, and Max pooling. ReLU function converts every fraction to 0 and forward the integers as it is to the batch normalization. Batch normalization then normalize the input it received by subtracting the batch mean and dividing it by the batch standard deviation. Max pooling component uses down sampling to reduce the number of features in its input feature map. Following is the Algorithm II of batch normalization transform.

Algorithm.2. Batch normalization transform

Input:
- Values of $\boldsymbol{x}$ over a mini-batch: $\boldsymbol{\beta = \{x_1,\ldots,m\}}$
- Parameters to be learned: $\boldsymbol{\gamma, \beta}$

Output:
- $\boldsymbol{\{y_i = BN_{\gamma,\beta}(xi)\}}$

Mini-batch mean:
- $\boldsymbol{\sigma_B^2 \leftarrow \frac{1}{m}\sum_{i=1}^{m}. (x_i - \mu_B)^2}$

Normalize:
- $\ddot{x} \leftarrow \frac{xi - \mu B}{\sqrt{\sigma_B^2 \;+ €}}$

Scale and shift:
- $\boldsymbol{yi \leftarrow \gamma\, \ddot{x}i + \beta \equiv BN_{\gamma,\beta}(xi)}$

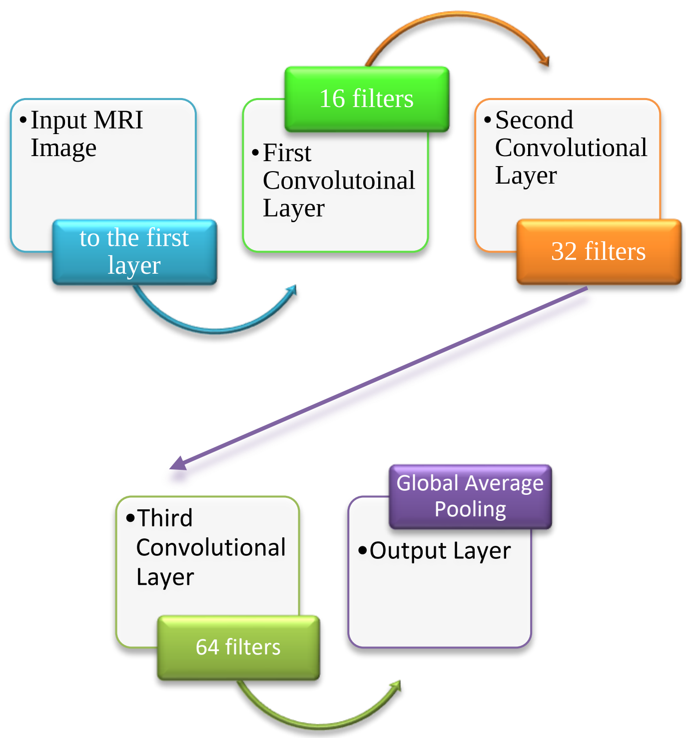

Fig. 8. Layers of CNN.

C. *Hybrid Approach*

In this phase, a combination between Otsu thresholding and CNN approaches was adopted to study the results of a hybrid approach. This time the CNN's input layer takes the output of the Image thresholding approach rather than the original MRI. In other words, the input taken by the CNN is the thresholded binary image of the brain ventricles. This required less computational cost and time as a lot of features are eliminated from the input images entering the input layer of the CNN. Fig. 9 shows the combination flow of the two approaches.

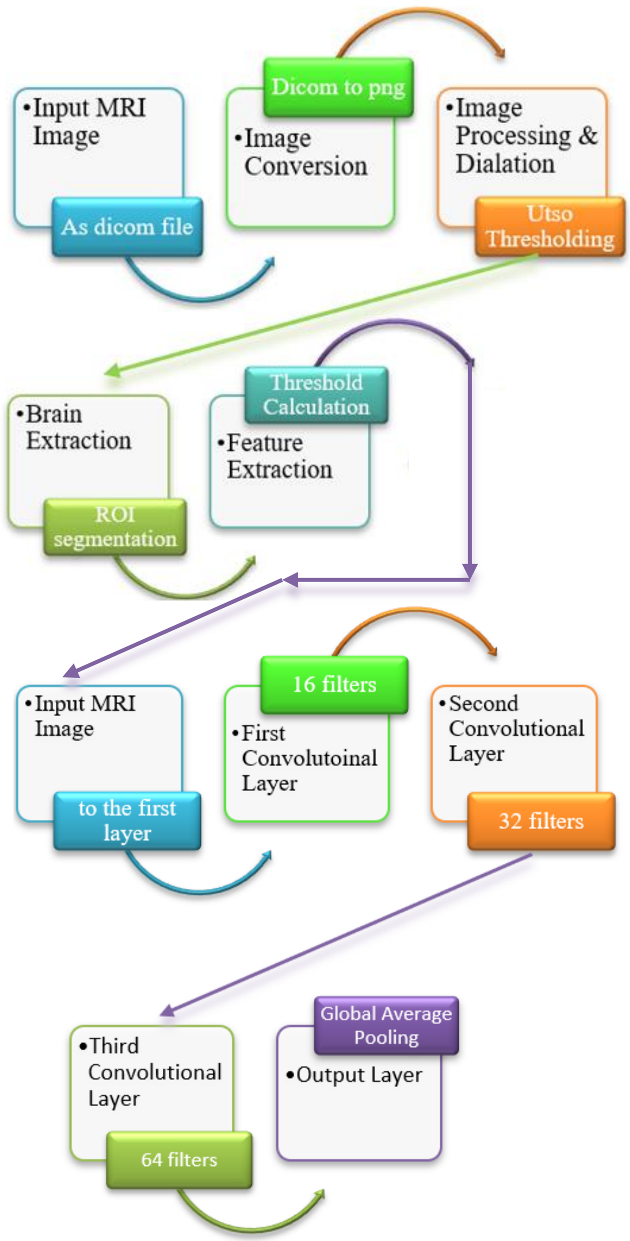

Fig. 9. The hybrid approach (Image Thresholding + CNN).

VI. Experimental Results

ADNI Database was used to test and validate this work. Researchers and collectors of ADNI confirmed that when significant abnormalities are seen on the screening MRI scan, such as a hemispheric infarction, the participant is excluded. Additionally, sites are notified by email if a radiological finding that is not normal for age is identified by the MRI QC team [30].

The following tables show the results obtained by Image thresholding, CNN, and the hybrid approach respectively. The tests were conducted using the 3D MRI images, i.e., Axial, Sagittal, and Coronal.

As it can be observed from Tables I, II, and III, CNN achieved the highest accuracy rate in case of Axial scanning direction. It can also be seen that the Axial direction is the best in AD detection whatever the approach adopted. However, CNN takes more time and computational cost to detect the disease; it outperforms the results of image processing and the hybrid approach concluding that deep learning approaches are much better in such a field. The preceding fact tells that all features are important for automatic AD detection and that feature reduction in not a preferred solution for lowering time and cost. Nevertheless, it must be mentioned that surprisingly the hybrid approach outperforms CNN in case of coronal brain scanning direction.

TABLE I. Results Obtained by Image Thresholding Approach

MRI	Accuracy rate
Axial	76%
Sagittal	68%
Coronal	71%

TABLE II. Results Obtained by CNN Approach

MRI	Accuracy rate
Axial	**90%**
Sagittal	**85%**
Coronal	71%

TABLE III. Results Obtained by the Hybrid Approach

MRI	Accuracy rate
Axial	81%
Sagittal	70%
Coronal	**75%**

VII. Conclusion and Future Work

Three different approaches for automatic AD detection from MRIs were adopted in this work: Otsu thresholding, CNN, and a hybrid approach between them. The three approaches have achieved promising accuracy rates compared to literature. A comparative study was also conducted and proved that CNN outperforms image thresholding and even the hybrid approach in terms of accuracy rates. At the same time, image thresholding methodologies require less time and computational cost. However, by comparing the accuracy rates, CNN worth its computational time and cost. ADNI brain MRI Database was used for the testing process. 3D MRIs were adopted for the validation.

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