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# Classification of Alzheimer Condition using MR Brain Images and Inception-Residual Network Model

**Abstract:** Alzheimer's Disease (AD) is an irreversible progressive neurodegenerative disorder. Magnetic Resonance (MR) imaging based deep learning models with visualization capabilities are essential for the precise diagnosis of AD. In this study, an attempt has been made to categorize AD and Healthy Controls (HC) using structural MR images and an Inception-Residual Network (ResNet) model. For this, T1-weighted MR brain images are acquired from a public database. These images are pre-processed and are applied to a two-layer Inception-ResNet-A model. Additionally, Gradient weighted Class Activation Mapping (Grad-CAM) is employed to visualize the significant regions in MR images identified by the model for AD classification. The network performance is validated using standard evaluation metrics. Results demonstrate that the proposed Inception-ResNet model differentiates AD from HC using MR brain images. The model achieves an average recall and precision of 69%. The Grad-CAM visualization identified lateral ventricles in the mid-axial slice as the most discriminative brain regions for AD classification. Thus, the computer aided diagnosis study could be useful in the visualization and automated analysis of AD diagnosis with minimal medical expertise.

**Keywords:** Alzheimer's Disease, Inception-Residual Network, Visualization, Class Activation Mapping

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## 1 Introduction

Alzheimer's Disease (AD) is the most predominant form of dementia among elderly population over 65 years [1]. It is symptomatically characterized by an impairment in the memory, executive and visuospatial abilities. According to the World Alzheimer's Report, it is estimated that by 2050, the number of world-wide AD patients will reach about 152 million [1]. Structural Magnetic Resonance (sMR) imaging is widely preferred for diagnosis of AD owing to its ability to quantitatively characterize AD biomarkers [2]. Numerous studies have developed computer-aided AD diagnosis systems based on sMR images [2-5].

Recently deep learning models, particularly convolutional neural networks (CNN) are extensively utilized in neuroimaging domain due to its ability to extract highly discriminative features specific to the classification task [3,15]. Residual neural Network (ResNet) has been used to extract features from sagittal view sMR images to differentiate AD from Healthy Controls (HC) [4]. Data augmentation methods has been carried out and an F-measure of 44.45% has been achieved in differentiating AD [4]. An end-to-end AD diagnosis system using a customized CNN and Inception V3 network has achieved an accuracy greater than 60% in classifying AD stages [5]. Differentiation of AD from HC has been performed using a deep CNN model and axial view sMR brain images [6]. Majority of the deep learning models developed for AD diagnosis employ transfer learning techniques [4, 6].

Interpretability of deep learning models is crucial to improve the reliability of the diagnosis system. The filter outputs obtained from initial convolutional layers have been analyzed to identify the feature maps learned by model in AD diagnosis [3]. Gradient weighted Class Activation Mapping (Grad-CAM) and occlusion-based methods have been employed to identify the discriminative behaviour of the model [7].

In this study, a customized Inception-ResNet model is developed to differentiate AD from HC sMR images.

Inception-ResNet is a CNN architecture that incorporates residual connections on an Inception network. Addition of these residual connections have reported to accelerate the training of Inception networks [11]. The performance achieved by model in AD diagnosis is analyzed. Further, Grad-CAM is utilized to visualize the most discriminative brain region identified by the model for differentiating AD from HC.

# 2 Methodology

The images obtained from public database are spatially normalized and skull stripped. Further, 2D slices in axial view are extracted from 3D MR volume. The images are trained and tested using Inception-ResNet model. The classification performance of the proposed model in differentiating AD is evaluated using standard metrics. Visualization of discriminative brain regions identified by model is carried out using Grad-CAM.

## 2.1 Image Database and Pre-processing

The images obtained from Alzheimer's Disease Neuroimaging Initiative (ADNI), a multi-site and multi-scanner database, are used in the study. The three Tesla T1-weighted cross-sectional ADNI Baseline MR brain images of 100 HC and 100 AD subjects are considered. Each 3D MPRAGE volume is gradient unwrapped, intensity normalized, and corrected for B1 non-uniformity and geometric distortions [8].

The sMR images obtained from the database are spatially registered to align with the standard Montreal Neuroimaging Institute template. FMRIB's Linear Image Registration Tool is employed for the affine alignment of brain images to remove linear global differences [9]. The spatially normalized images are skull stripped using FMRIB's Brain Extraction Tool [10] and contrast enhanced. Out of 182 slices, mid-axial slice is considered in the study.

## 2.2 Network Architecture

The pre-processed axial view sMR images are fed into an Inception-ResNet model [11], a combination of Inception and Residual network, for feature extraction and classification. The architecture of the proposed network is shown in Figure 1. The model includes a stem block and two Inception-ResNet-A modules [11], Figure 1(b). The stem block comprises of three Convolutional (Conv) layers with a filter size of three. Each Inception-Resnet module has three branches with varying filter sizes, the outputs of which are concatenated. The residuals are scaled down by a factor of 0.15 before adding the output of previous layer to the concatenated outputs. The Inception-Resnet modules are followed by an Average Pooling (AvgPool) layer of pool size and stride three.

(a)

(b)

Figure 1. Block diagram of proposed model (a) and network architecture of Inception-Resnet-A module (b)

The model is trained for 100 epochs with cross-entropy loss function. Activation function used in this study is rectified linear unit. The batch size is fixed to be 10 and network is optimized using Adam optimizer with a learning rate of 0.001. The parameters of network are fixed empirically. The dataset is randomly split at a ratio of 80:20 for training and testing. Data augmentation is carried out on the training set by rotating the images randomly. The performance of network is evaluated using recall, precision, F-measure and accuracy.

## 2.3 Visualization using Grad-CAM

Inorder to visualize the most discriminative brain regions identified by the network in differentiating AD from HC, Grad-CAM [12] is employed. It creates a spatial heatmap using the gradient input of final convolutional layer of the model. The gradient of classification score for a target class with respect to a particular feature map is computed. Global average pooling of gradients is further carried out to obtain the importance weights of neurons for target class [12]. A coarse localized heatmap is obtained by combining the activation maps.

# 3 Results and Discussion

The T1-weighted representative original MR brain images in axial view of HC and AD subjects are shown in Figure 2(a-b). The corresponding spatially normalized images are represented in Figure 2(c-d). The sMR images of different subjects are aligned with each another such that the brain regions of each image occupy the same voxel. Figure 2(e-f) shows the skull stripped images where the non-brain tissues are removed. It is observed that the sizes and shapes of brain structures varies within AD as well as between AD and HC. These inter and intra subject variability pose challenges in the automated classification of AD and HC.

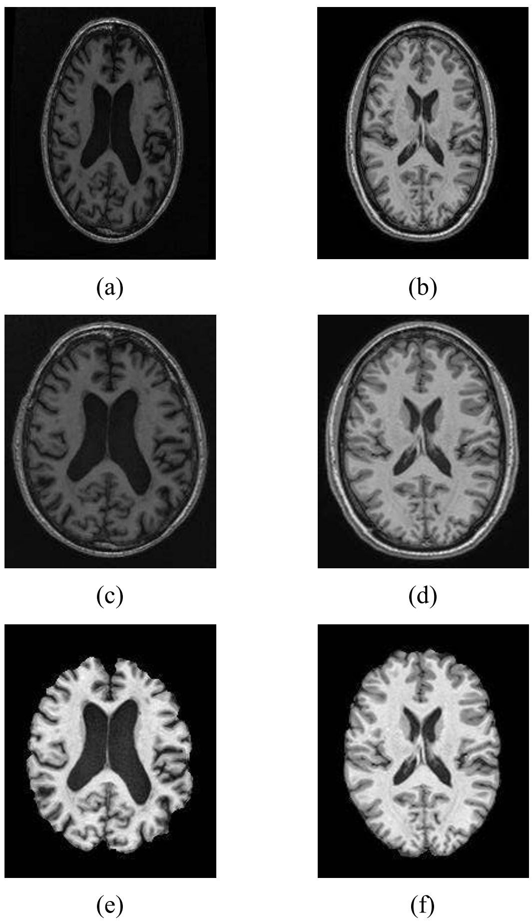


Figure 2. Representative original (a-b), spatially normalized (c-d) and skull-stripped (e-f) axial view MR images of AD (a, c, e) and HC (b, d, f)

The training accuracy of model at varied number of epochs is represented in Figure 3. A maximum training accuracy of 80% is achieved with 100 epochs. The accuracy is found to vary non-linearly with epochs. However, a rise in training performance is observed as epochs increases.

The network attains an average accuracy of 69% in differentiating AD from HC. It is found that the model achieves a recall and precision of 76% in identifying AD subjects. However, it is seen that the network attains 62% F- measure in identifying HC, thereby decreasing the average

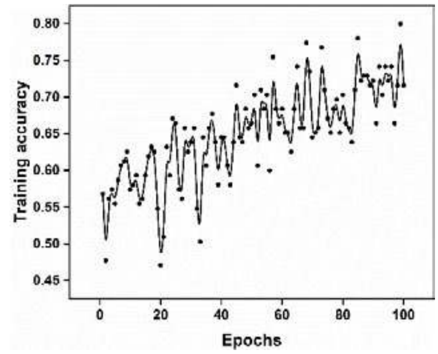


Figure 3. Variation in training accuracy of model with number of epochs for differentiation of AD and HC

performance measures of the model. The network achieves an average recall of 69%.

The overlay of heatmaps obtained using Grad-CAM on original input images and are shown in Figure 4. Figure 4(a, c) depicts the representative AD and HC images. Figure 4(b, d) shows the corresponding heatmaps obtained. Figure 4(a, b) represents correctly classified AD image whereas Figure 4(c, d) represents misclassified HC. The visualization results indicate that the model identifies lateral ventricles as the most discriminative region in classifying AD and HC.

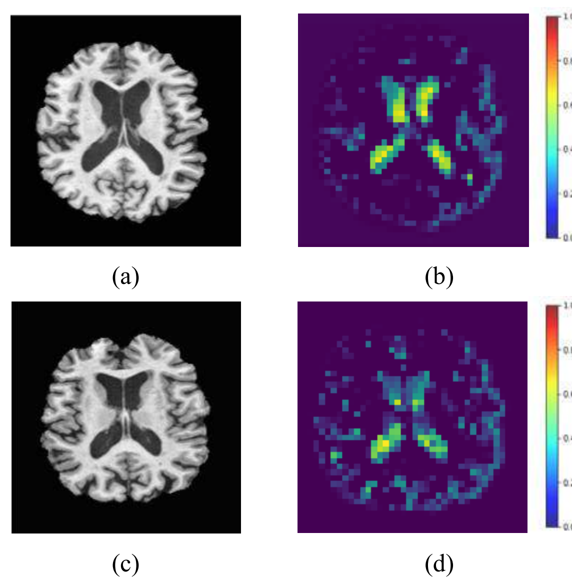


Figure 4. Representative Grad-CAM heatmap overlay (b, d) of correctly classified AD (a) and misclassified HC (c)

In this study, 2D sMR images are considered although it provides less information compared to 3D volume. This is because 2D models require lower computational resources than 3D models. Computation time is a significant factor for the implementation of a computer aided diagnosis system in a clinical setting [13]. Also, the availability of 3D sMR images are limited [13].

Limited availability of images for training deep networks is a major challenge in disease diagnosis [14]. To overcome this, data augmentation is carried out on the training images. This technique reduces overfitting of the model and thereby could enhance the generalization performance of network [14].

The obtained visualization results are in agreement with the existing reports [7] as enlargement of lateral ventricles is a consistently studied AD biomarker [2]. This indicates the reliability of the proposed Inception-ResNet model in differentiating AD from HC.

# 4 Conclusion

Deep learning models are extensively utilized for diagnosis of AD because of its ability to extract task-specific features suitable for classification. An Inception-ResNet model is developed in this study for AD prediction. Visualization using Grad-CAM method indicates the reliability of the model in classifying AD and HC. The lateral ventricles are identified to be the most discriminative region. Since the proposed Inception-ResNet model is capable of differentiating AD and HC MR images, this study could be useful in the visualization and automated analysis of AD diagnosis with minimal medical expertise.

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