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# Decision Support System for Age-Related Macular Degeneration Using Convolutional Neural Networks

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ABSTRACT

***Introduction***: Age-related macular degeneration (AMD) is one of the major causes of visual loss among the elderly. It causes degeneration of cells in the macula. Early diagnosis can be helpful in preventing blindness. Drusen are the initial symptoms of AMD. Since drusen have a wide variety, locating them in screening images is difficult and time-consuming. An automated digital fundus photography-based screening system help overcome such drawbacks. The main objective of this study was to suggest a novel method to classify AMD and normal retinal fundus images.

***Materials and Methods:*** The suggested system was developed using convolutional neural networks. Several methods were adopted for increasing data such as horizontal reflection, random crop, as well as transfer and combination of such methods. The suggested system was evaluated using images obtained from STARE database and a local dataset.

***Results:*** The local dataset contained 3195 images (2070 images of AMD suspects and 1125 images of healthy retina) and the STARE dataset comprised of 201 images (105 images of AMD suspects and 96 images of healthy retina). According to the results, the accuracies of the local and standard datasets were 0.95 and 0.81, respectively.

***Conclusion:*** Diagnosis and screening of AMD is a time-consuming task for specialists. To overcome this limitation, we attempted to design an intelligent decision support system for the diagnosis of AMD fundus using retina images. The proposed system is an important step toward providing a reliable tool for supervising patients. Early diagnosis of AMD can lead to timely access to treatment.

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## Introduction

Age-related macular degeneration (AMD) is a prevalent retinal disorder caused by destruction of macula cells. It is the major cause of irreversible blindness in the developed countries and the third leading cause of blindness all over the world [1-2]. This disease is one the leading causes of visual loss in people aged 60 or higher. According to the World Health Organization (WHO), at least 8 million people have lost their eyesight due to this disease [3].

AMD is classified into two main types of dry and wet. The dry AMD is considered the most common type, which involves 80% of the patients. However, the wet type causes 90% of vision loss cases [4]. Currently, there is no certain cure for macular degeneration [1]; however, relevant diagnostic techniques and idealistic therapeutic methods can be adopted to prevent disease progression and improve vision [5]. Early signs of AMD are related to drusen, which include changes in shape, size, texture, and color of drusen, and makes it difficult for ophthalmologists to detect the disorder [6]. Signs and symptoms of this disease can be observed in retinal fundus images before serious damages to patient's vision [7]. Regular screening in the early stages of the disease is an important strategy for detecting AMD [8]. However, manual detection of AMD is time-consuming and labor-intensive. More importantly, it depends on the ophthalmologist's experience, therefore, it can lead to inaccurate detection [8].

Computer diagnostic software has great potential in large-scale screening programs and could be helpful for early detection of diseases [9-12]. In the recent years, symptoms of diseases have been identified in patient's retinal images. A large number of patients and images increase the need for skilled labor and cost of screening and undermine quality of disease diagnosis, and in turn, patient satisfaction. An automated screening system can address the mentioned drawbacks [9 ،13-14]. Image processing and machine learning techniques are used in such systems to assess the symptoms of the disease.

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Therefore, decision support systems or classification algorithms are required to detect AMD using retinal images.

A wide range of studies were conducted on the diagnosis of AMD, which used different techniques based on the main stages of image analysis such as texture analysis, thresholding, clustering, as well as edge and template matching [7].

Texture-based methods: Texture is description of surfaces, measured through image intensities. When proper texture analysis methods are applied, drusen respond differently towards the background because they are brighter than retinal surface [7 ،15-16]. Thus, numerous methods have been proposed based on wavelet transform in order to extract texture features of drusen [17-23]. Prasath used grayscale concurrence matrix to extract the static features of texture [24], while Mokia et al. used empirical mode decomposition to extract features and classify normal and AMD images using support vector machine [25]. In another study, Mokia used local configuration template to extract features and classify normal and AMD images [26]. Admixture of amplitude and frequency modulations was used in two studies to extract the multi-scale features for classifying pathological structures [27-28]. In addition, statistical features of texture were used to segment normal parts of the retina and show the reversed image of unhealthy region of the macula [29-30]. Independent component analysis is used for feature extraction in different spatial scales [31].

Thresholding-based methods: Thresholding is an image segmentation method. A binary image is achieved by applying a thresholding method on a gray scale image, which specifies the boundary of present objects in the image with proper accuracy. There are several methods for image thresholding [32-33]. In the previous studies, segmentation of drusen was performed using Otsu thresholding method. This method is applied for image segmentation based on T optimized threshold, and it divides the image into two different classes (black and white). The aim of optimal threshold is to find the T value, which creates the maximum uniformity in intensity function in both classes and minimizes the variance of intensity distribution in pixels between the two classes [34-36]. Rani firstly removed optic disc pixels because of intensity similarities of optic disc and drusen. Then, drusen were detected through image thresholding [37]. Thresholding based on edge and morphological dilation is another method of drusen diagnosis [38]. In other studies, local adaptive thresholding based on the intensity of brightness and probability was used to identify drusen [36 ،39-40].

Clustering-based methods: Clustering or cluster analysis is an unsupervised learning method in machine-learning context. In this method, samples are divided into different classes called clusters with high similarity between members inside each one. Therefore, cluster is a collection of similar objects that are different from the objects existing in other clusters. A few studies were performed focusing on construction of feature vector, spatial histogram, and distribution of brightness intensity [41-43].

Edge and template matching-based methods: Edge is the border between an object and its background. In other words, edge is the change of two gray surfaces that occurs at a particular spot of the image. Edge detection is easy if surface variation is high. Template-matching methods consider a part of or the whole image as a pattern to match it with the area or intended image [44].

All the mentioned methods are based on manual extraction of low-level visual features. The process of machine learning is highly dependent on selection of proper features. Inability in terms of extraction and organization of distinctive features could be due to shortcomings of the current learning algorithms [45]. One of the most critical obstacles in machine learning is feature extraction. Detection of proper features from dataset can help reduce dimension of the input space and the cost of computation of pattern recognition problems such as classification. However, feature extraction is carried out manually, and automatic feature engineering is a significant development in machine learning, which makes feature extraction possible without human interference. Although a number of studies employed data mining techniques instead of machine learning methods, there is a scarcity of studies using automatic feature extraction [5 ،46]. Deep learning algorithm was used in this study to classify normal and AMD images of retina fundus.

## Materials and Methods

Herein, we aimed to classify normal and AMD fundus images using convolution neural networks (CNN) to diagnose AMD patients. In doing so, two datasets were applied including 3195 images of retina fundus (2070 normal and 1125 AMD images) gathered from Ophthalmic Research Center, Iran University of Medical Sciences. The images were taken by TOPCON fundus camera (TOPCON Medical System Inc) with the resolution of 1451×1451 pixels in JPEG format, and 83 images obtained from STARE dataset (36 normal and 47 AMD images) that were taken by TOPCON fundus camera with the resolution of 700×605 pixels (available at: http://www.ces.clemson.edu/~ahoover/stare/). Examples of healthy and unhealthy images are presented in figures 1 and 2.

Since training of deep networks requires a huge number of images, it is recommended to use data increasing methods for enhance performance if the number of primary images in the collected dataset is limited. Several methods are adopted for increasing data such as horizontal reflection, random crop, as well as transfer and combination of such methods [47]. Since more images were required, the number of standard images was increased from 83 to 201 images using data increasing methods such as random crop and transfer.

(a) (b)

**Figure 1.** Example of a) healthy and b) unhealthy images of local data set

(a) (b)

**Figure 2.** Example of a) healthy and b) unhealthy images of standard data set

### *Deep learning*

Deep learning is a collection of machine-learning algorithms that are normally based on artificial neural networks and try to model high-level abstractions existing in data [48]. Deep learning algorithms can be perfectly beneficial when learning is performed with a great amount of unsupervised data [49]. Deep learning has been widely used in the field of computer vision, therefore, a large number of related methods were proposed. CNN, Restricted Boltzmann Machine, Autoencoder, and Sparse coding are the major deep learning methods [49].

### *Convolutional neural networks*

CNN are the most important deep learning method, in which several layers are trained using a powerful method [50]. It has been proven that CNN are very successful in resolving image classification problems, it is also used for analyzing medical images [51]. Normal methods of image classification consist of two steps including feature extraction and classification. CNN are formed out of convolution, pooling, and fully connected layers, with each layer does different tasks. CNN are a hierarchy of neural networks, convolution layers of which are alternate to pooling and fully connected layers [49].

- Convolutional layers

In the convolutional layers, CNN utilize various kernels to convolve the whole image as well as the intermediate feature maps, generating various feature maps as shown in Figure 1 [48].

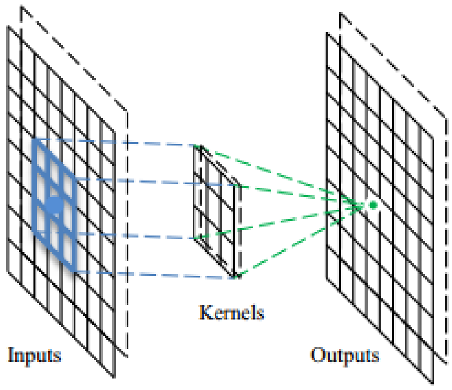


**Figure 3.** The operation of the convolutional layer

- **Pooling layer**

Pooling is an important concept of CNN, which is a form of non-linear down-sampling. However, there are several non-linear functions and max pooling is the most common of them. This function partitions the input image into a set of non-overlapping rectangles and outputs the maximum for each such sub-region. The pooling layer serves to progressively reduce the spatial size of the representation, reduce the number of parameters and amount of computation in the network, and control overfitting. The pooling operation provides a form of translation invariance [52].

- **ReLU layer**

Rectified Linear Units (ReLU) is a layer of neurons that applies the non-saturating activation function. It increases the nonlinear properties of the decision function and the overall network without affecting the receptive fields of the convolution layer. Compared to the other functions, the usage of ReLU is preferable since it results in the neural network training several times faster without making a significant difference in generalization accuracy [52].

- **Fully connected layer**

Finally, after several convolutional and max pooling layers, the high-level reasoning in the neural network is performed via fully connected layers. In a fully connected layer, neurons have full connections to all activations in the previous layer, as seen in regular neural networks.

In each CNN, there are feed forward and backpropagation phases for training. In the first phase, input image is fed to the network. This action is nothing until the convolution between the input and parameters of each neuron and eventually applying the convolutional operation to each layer.

**Table 1.** Network configuration

| Layer Type | input | conv | mpool | relu | conv | relu | Apool | conv | relu | apool | conv | relu | conv | softmxl |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Support | - | 5 | 3 | 1 | 5 | 1 | 3 | 5 | 1 | 3 | 4 | 1 | 1 | 1 |
| Filter diminution | - | 3 | - | - | 32 | - | - | 32 | - | - | 64 | - | 64 | - |
| Number filters | - | 32 | - | - | 32 | - | - | 64 | - | - | 64 | - | 2 | - |
| Stride | - | 1 | 2 | 1 | 1 | 1 | 2 | 1 | 1 | 2 | 1 | 1 | 1 | 1 |
| Pad | - | 2 | 0,1,0,1 | 0 | 2 | 0 | 0,1,0,1 | 2 | 0 | 0,1,0,1 | 0 | 0 | 0 | 0 |

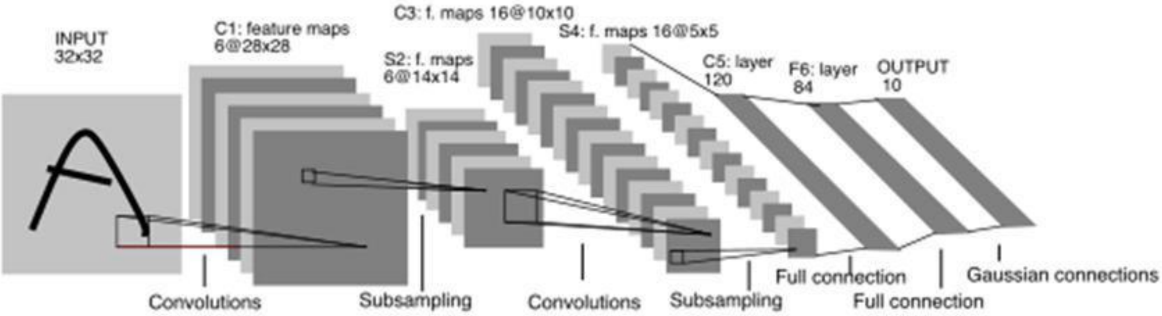


**Figure 1.** The structure of Lenet Network

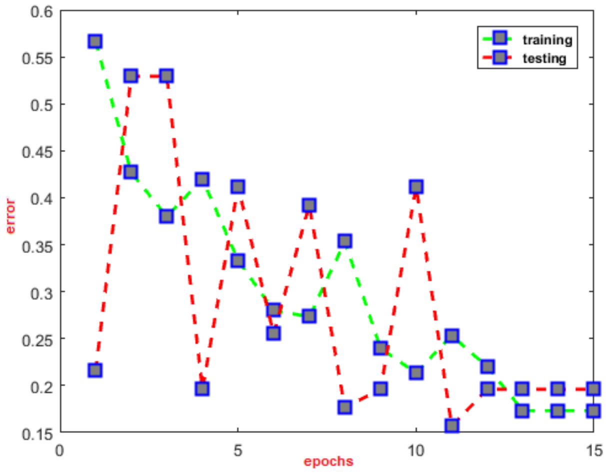


**Figure 2.** Progress of training and test error rate (STARE dataset)

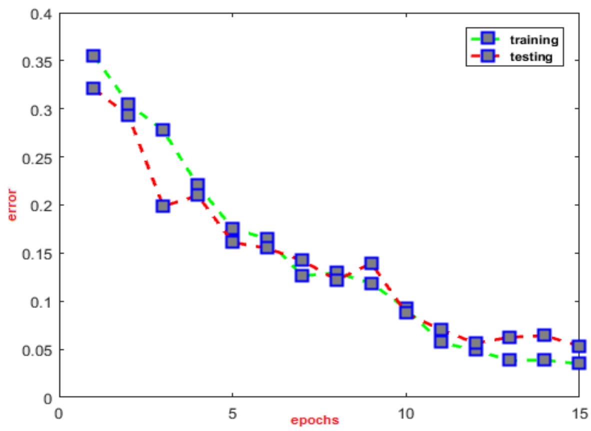


**Figure 3.** Progress of training and test error rate (local dataset)

Then, output of the network is computed. For network training, output is used to compute the rate of network's error. In doing so, network output should be computed with the correct response using a loss function. Backpropagation is in the next phase based on the computed error rate. In this phase, gradient of each parameter would be computed according to chain rule and all parameters change according to their effect on the error. In the next phase, feed forward begins after updating the parameters. Network training and configuration would be stopped after sufficient repetition of the above-mentioned phases [49].

### *Convolutional neural network architecture*

With the recent developments of CNN in computer vision, several CNN models have been created, the most common of which include Lenet, GoogLeNet, VGGNet, Clarifai, and AlexNet.

In the current study, Lenet model was employed since the LeNet architecture, with CONV-RELU-POOLs stacked with fully connected layers at the end, was found to perform well on many classification problems such as ImageNet, notably shown by Krizhevsky et al. in 2012 [53].

The network structure includes repetition of blocks. Each block contains a convolution layer followed by a pooling layer. Each block is finished by ReLU layer. The network uses equivalent blocks without pooling layer. The network is finished by a fully connected layer and a soft max layer. Structure of Lenet network is clearly presented in Figure 4.

Fine-tuning is a very important phase for pure models and specific tasks. Accurate adjustment generally needs class tags for new training dataset, which is loss function for computing. In this case, all layers of the new model are initialized based on the pre-training model (e.g., Lenet) [53], except for the output layer that depends on class tags of the new dataset [49]. Network configuration is presented in Table 1. Spatial resolution layers are not obvious since output resolution was not directly specified. Instead, it was derived from the input image resolution and the filter widths, padding, and strides of the previous layers. For better understanding, MatConvNet provides a visualization function with a simple display.

### *Training*

Since the LeNet architecture was used on 32×32 images [50], the images were at first resized to 32×32×3 for being sent to the network. In general, 20% of the images were employed for testing and the rest for training. A full pass through the whole dataset is called an epoch. The maximum number of epochs to run the training for is also a parameter that can be specified. The default value is 30, but a limited number of epochs can be chosen for small networks or for fine-tuning. The network was trained based on 2556 images of the local dataset and 150 images of the standard dataset after 15 epochs. For the first 10 epochs, we determined the learning rate as 0.05, and for the rest epochs as 0.005. We set weight decay parameter at $5\times10^{-6}$ and the batch size parameter equal to 10 for training and testing.

## Results

For CNN implementation, we used MATLAB MatConvNet toolbox, which allows CNN training using pre-training models [54]. Local and standard datasets were applied separately to compare results of these datasets. Standard and local datasets were validated with errors of 0.19% and 0.05%, respectively. Training results obtained from standard and local datasets are shown in figures 5 and 6, respectively. In these figures, evolution of training and validation errors can be observed through different epochs.

CNN were trained in 15 epochs. It means the processes of forward computing and error propagation were repeated 15 times with all the training images. As presented in figures 5 and 6, training and test errors are showed in green and red colors respectively. Generally, the test error decreases alongside training error but locally has vibrant movement. Each spot is related to particular network training which is not necessarily superior to the previous ones. Therefore, the strategy should be defined after cessation of temporal training, so that a specific training is chosen for CNN. This decision must be made based on minimizing test error. The whole network training with 15 epochs took almost 300 s for local dataset and 38 s for STARE standard dataset using a laptop with Intel Core i5 (2nd Gen) 2410M / 2.3 GHz CPU and 4 GB RAM. Since no need to repeat the training process, the time spent for this process is acceptable. Once the training process is finished, network would be able to classify images into two categories. Image classification is not time-consuming, thus, the suggested system would be very fast after training.

## Discussion

Some of the mentioned methods for drusen segmentation are based on thresholding, which relies on pixels' brightness intensity. Thresholding is a challenging task due to lesions, optic disks, and noises similar to drusen in terms of contrast [5]. In previous studies, local dataset [6 ،18 ،20-21 ،23-24 ، 27-31 ،35-36 ،38 ،41 ،55-57] was used to evaluate algorithm, while others solely used standard dataset [22 ،34 ،58-59]. It should be noted that in this study both local and standard datasets were used separately.

Due to the nature of medical images, machine-learning methods are normally used for image classification based on the definition of particular features. In the studies based on texture, different methods are used for feature extraction. A total of 639 images of local dataset and 51 images of standard dataset were used for testing. The accuracy values for local and standard datasets were 0.95 and 0.81, respectively.

The present study yielded acceptable results in comparison with the studies performed by Cheng et al. [18] and Kose et al. [29]. It should be noted that the obtained results from this study were more satisfactory than the previous studies even though our datasets were not as large as those used in the mentioned studies [30 ،55]. Removing optic disks was used in the studies carried out by Prasath et al. [24], Waseem et al. [22], Kose et al. [30], and Rani [37] to obtain better results. However, it could be time-consuming and imprecise, especially when there is not appreciated lighting through the image. In all the previous studies, feature extraction was performed manually, while in the present study features were extracted automatically, which promoted precision and classification speed.

Classification of 3000 images per minute is one of the benefits of trained CNN, which makes image processing possible immediately after receiving the image. Trained CNN facilitate fast diagnosis and immediate response.

## Conclusion

Deep learning could be helpful in diagnosis and classification of some diseases. In this study, CNN were used to classify normal fundus images and AMD. The proposed method is an important step toward provision of a reliable diagnosis tool for supervising patients. Such systems decrease the risk of misdiagnosis and facilitate early diagnosis. It should be noted that this field is yet open for more research since there is no system is flawless.

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