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RESEARCH ARTICLE

A DEEP TRANSFER LEARNING FRAMEWORK for the STAGING of DIABETIC RETINOPATHY

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ABSTRACT

Diabetes is a highly prevalent and increasingly common health disorder, resulting in health complications such as vision loss. Diabetic retinopathy (DR) is the most common form of diabetes-caused eye disease. Early diagnosis and treatment are crucial to prevent vision loss. DR is a progressive disease composed of five stages. The accurate diagnosis of DR stages is highly important in guiding the treatment process. In this study, we propose a deep transfer learning framework for automatic detection of DR stages. We examine our proposed model by comparing different convolutional neural networks architectures: VGGNet19, DenseNet201, and ResNet152. Our results demonstrate better accuracy after applying transfer learning and hyper-parameter tuning to classify the fundus images. When the general test accuracy and the performance evaluations are compared, the DenseNet201 model is observed with the highest test accuracy of 82.7%. Among the classification algorithms, the highest AUC value is 94.1% obtained with RestNet152.

Keywords: *Convolutional neural networks, CNNs, Deep learning, Diabetic retinopathy, Transfer learning.*

1. INTRODUCTION

Diabetes is a major public health concern, estimated to affect around half a billion people worldwide [1]. It can lead to a variety of complications, such as heart attack, stroke, and vision loss. Among various types of eye diseases that occur due to diabetes, the most common type is diabetic retinopathy (DR). Changes in the vessels as a result of the disease's damage to the light-perceiving retina layer cause vision loss [2]. DR occurs in several stages. The early stage of DR is non-proliferative diabetic retinopathy (NPDR), being the first indicator of abnormal changes in the eye [3]. In this stage, there are three important levels: mild, moderate, and advanced. The veins start abnormally leaking out substances that cause fluid accumulation. Consequently, the nutrition of the retina begins to deteriorate, and if not treated, the disease will slowly continue to progress [4]. In the later stages, or the proliferative diabetic retinopathy (PDR) stage, new vessel formation along the retinal surface and disruptions in tissue nutrition are observed. The thinness of these new vessel formations causes

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intraocular bleeding. With intense bleeding, retinal layer deterioration occurs, and vision loss becomes inevitable [5]. Therefore, accurate detection of DR stages is very vital for treatment. In the diagnosis of DR-induced diseases, devices such as optical coherence tomography (OCT), fundus fluorescein angiography (FFA), and eye ultrasonography (USG) are used. The use of artificial intelligence algorithms in medical image synthesis facilitates the interpretation of medical images and helps medical professionals in the treatment process by obtaining quantitative measurements from the images [6, 7].

There are many different studies for the detection of DR disease stage using retinal fundus images with machine learning methods in the literature [8-11]. Many recent studies have focused on the diagnosis of retinal diseases with deep learning algorithms [7, 12-15], such as the definition of retinal regions with hemorrhage using FFA images [16], determination and classification of retinal images [17], mathematical morphology and template matching assisted retinal hemorrhage detection [18]. In studies, it is seen that for images the preprocessing step is very important to remove the noise. In medical imaging, wavelet transformation has also been applied to fundus images with high-band filters. Rehman et al. [19] obtain an accuracy of 97.85% using the support vector machines algorithm with two classes. Jiang et al. [20] classify 8626 images using the CNNs model as DR and no DR with an accuracy of 75.70%. Gao et al. [21] study with four classes and resize the fundus images to 600x600 pixels and then divide them into 300x300 pixels. Then they transfer these parts to a single vector with four different InceptionNetV3 models. They achieve an accuracy of 88.72% in classifying DR stages in four classes.

Sarki et al. [15] use the ImageNet dataset as a transfer learning model. They have experimented with different CNNs models such as ResNet50, DenseNet, Xception, and VGGNet. Among these models, they obtain the highest accuracy of 86% using ResNet50. Wang et al. [14] examine a transfer learning model by comparing different CNNs models including AlexNet, VGG16, and InceptionNetV3 on the Kaggle dataset. They crop the images to different sizes for each model to classify them into five classes accurately. They obtain the highest accuracy of 63.2% using the InceptionNetV3 model. Another study [17] investigates performances of transfer learning by using three CNNs architectures, namely AlexNet, ResNet, GoogleNet, and VGG on the Kaggle dataset. They obtain the best classification accuracy of 95.68% with the VGG-s model. Sugeno et al. [7] use EfficientNet-B3 which is a transfer learning CNNs model on APTOS 2019 Kaggle dataset. They crop the images to 416x416 pixels. They compare their model EfficientNet-B3 against ResNet50 and VGG16 and obtain sensitivity and specificity values greater than 0.98. On the other hand, morphological procedures performed to clarify retinal blood vessels are widely used in different studies [33-36]. These processes positively increase the accuracy of DR detection. For this reason, morphological processes are applied to the fundus images to highlight the retinal blood vessels.

In this paper, we propose a new deep neural network architecture that is a deep transfer learning-based image detection and classification model to accurately diagnose the five stages of DR. For this purpose, experiments are conducted to classify in five stages: one stage of no DR and four levels of DR lesions. In the preprocessing step, color space transformation, noise removal, segmentation mask determination of the relevant region, and cropping from the mask coordinates are applied in the fundus images. For DR stage detection, cropped images are clarified by the contrast limited adaptive histogram equalisation (CLAHE) method. DR stage is diagnosed more accurately using our proposed model. The contributions of the research to the literature are as follows:

- In the study, data augmentation is applied only to the training set, and the test set consists of independent data.
- Fundus images are classified at 5 different levels.
- CLAHE is used to highlight the eye vessels.
- Well-known CNN architectures are used for feature extraction, classification, and their performances are compared.
- The results obtained are presented in a table based on class.

This paper is organized as follows, in this section we introduce the study and summarise the previous studies. Section 2 explains the methods we used. Section 3 presents and discusses our experimental results. Finally, Section 4 provides our conclusions.

2. MATERIALS AND METHODS

2.1. Dataset

Different procedures can be performed for the detection of blood vessels on the retina, determination of the optic disc and macular region, staging of DR, and detection of lesions. In this study, the classification process of fundus images is run on the open-source Kaggle APTOS 2019 dataset, which has been used in many recent studies with deep learning models. This dataset is introduced by the Asia Pacific Tele-Ophthalmology Society [22]. DR is classified into five stages according to the disease state. In this dataset, these five stages of DR are defined as follows:

- normal: patients without diabetic retinopathy.
- mild non-proliferative retinopathy stage: mild swelling occurs in the blood vessels of the retina.
- moderate non-proliferative retinopathy stage: the blood vessels are swollen and complex and blood carrying capacity is low.
- severe non-proliferative retinopathy stage: the blood vessel is clogged and the blood circulation around the retina slows down.
- proliferative diabetic retinopathy stage: the blood vessels are more fragile, and the fluid of the eye is in gel consistency. Detachment formation is seen in the retina.

Fig. 1 presents the data distribution of images among the DR stages for the APTOS 2019 dataset. The image samples of DR stages can be shown in Fig. 2.

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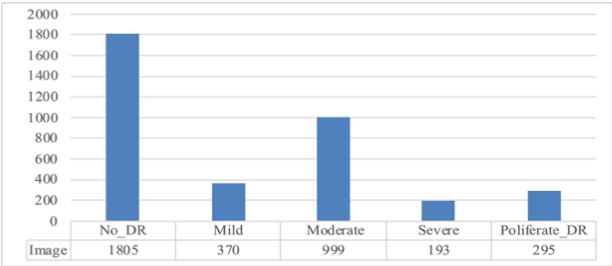

Figure 1. Distribution of images in the dataset according to their classes.

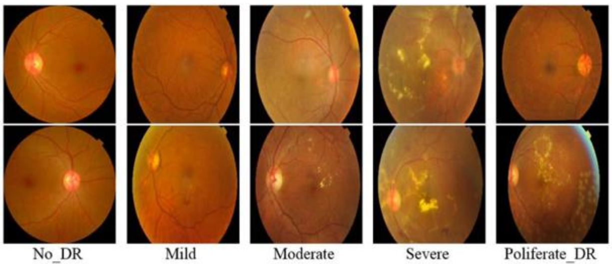

Figure 2. Image samples of DR lesion stages.

2.2. Model

We develop a computer-based system that analyses colored fundus images of the stages of DR and detects the stage of retinal lesions, considered as clinical signs of the disease. In the proposed system, gaussian smoothing is applied by converting fundus images to gray-level color space.

Then, the masks of the images are obtained with the threshold method. The contours of the unmasked images are extracted and cropping is applied to the images. In the final stage, well-known CNN architectures are used for feature extraction and classification. The detected lesions are classified using optimization techniques and deep learning algorithms. The structure of our proposed model is presented in Fig. 3.

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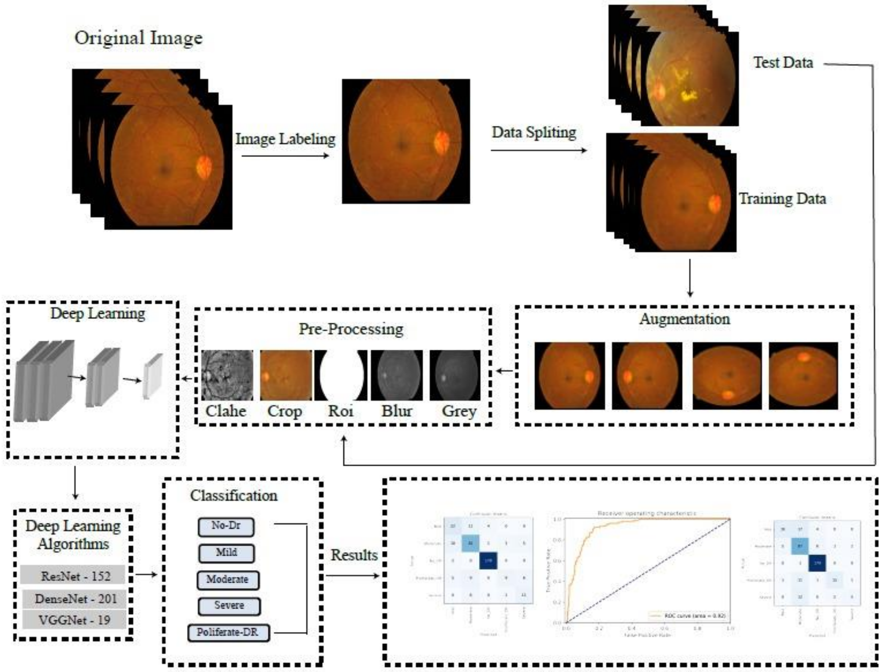

Figure 3. The structure of the proposed model.

2.3. Preprocessing

Preprocessing techniques have been applied to fundus images in the dataset to increase classification accuracy. As can be observed in Fig. 4, the pre-processing involves five steps. In the first step, the images are converted from RGB color space to grayscale. Then, a Gaussian smoothing filter is applied to the images to eliminate the noise from the images. The threshold used for the segmentation process of the Gaussian filter applied images. The mask of the fundus images is obtained with this procedure. By using the contour finding method on the masks, the matrix giving the boundaries in the 2-dimensional plane is extracted for cropping the images. From this matrix, endpoints on the x and y axis are determined, and a standard deviation value is added. Following this step, cropping is performed, and all the cropped images are rescaled to 224x224. The cropping step aims to enable CNNs architectures to focus on the bleeding regions in the fundus images during the feature extraction process. In the last step, the CLAHE method is applied to the cropped images. The purpose of this method is to improve the discrimination ability of the model by making the bleeding vessels in the fundus images apparent.

Fig. 4 shows the visualization of the images after performing the five preprocessing steps. Color fundus images compose groups of pixels with different brightness levels and the contrasts of the fundus image can be quite different. These differences significantly affect the performance of DR stage detection.

Contrast enhancement and image segmentation are important preprocessing steps for the fundus images. The CLAHE method is used to make vessels distinct by increasing the background contrast of

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the fundus images. The number of sub-images and image boundaries affect the results of the CLAHE method [29]. Thus, the noise and contrast condensation barriers are removed and the problem of oversaturation in similar regions is prevented. As shown in Fig. 4b, the fundus images are converted from RGB colour to grayscale. In the second step, the Gaussian filter is applied to the grayscale fundus images to detect the boundaries (Fig. 4c). Also, a threshold value is applied to do segmentation to obtain the mask of the images. In the third step, the matrix that gives the boundaries is extracted using the contour findings method on the masks (Fig. 4d). In the fourth step, the cropping process is performed to classify the images effectively (Fig. 4e). In the last step, the CLAHE method is applied to better distinguish the stages of DR lesions and to improve the discrimination ability of the model (Fig. 4f).

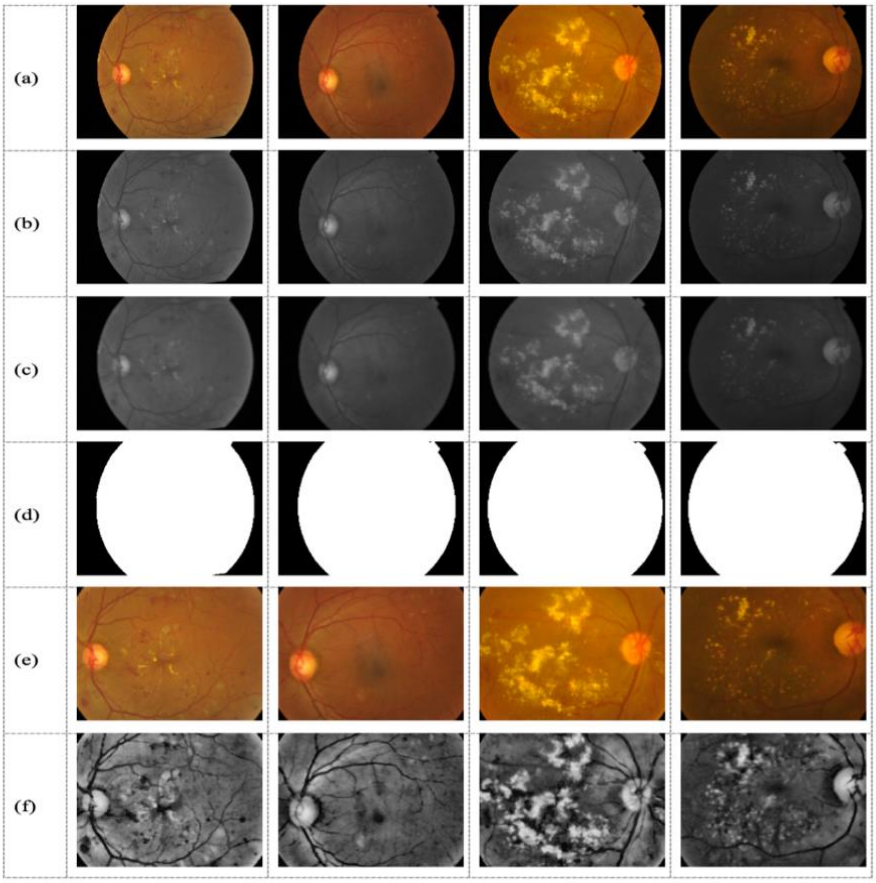

Figure 4. Preprocessing steps applied to fundus images (a) original image (b) grayscale image (c) Gaussian blur applied image (d) image mask (e) cropped image (f) CLAHE applied image.

Data augmentation is an important process that prevents overfitting and increases the performance of the deep learning model [23]. In recent studies that employ CNNs methods, the success of the network depends largely on the amount of data, otherwise training the CNNs with fewer data creates some problems such as overfitting. Data augmentation techniques such as horizontal and vertical shift, brightness change, angular change, zoom, and horizontal and vertical rotation are applied to the fundus images, and then classification performance is improved. Transfer learning is known as a machine learning method for using to train a new model from a previously trained model. Some information such as features or weights is imported from the model that was trained on a larger dataset. We use a transfer learning approach to detect DR in the fundus images using the features of CNNs pre-trained on ImageNet [24] and train a new model on these features.

2.4. Convolutional Neural Networks Architecture Used

Deep Learning algorithms can be considered as the more complex form of artificial neural networks. The increasing abundance of data and accessing more relevant information from this data require optimization regarding the feature estimates. Artificial neural network-based systems can produce solutions to solve problems of image classification. Convolutional Neural Networks (CNNs) have become a model that solves the computational difficulties created by the connections between neurons and layers and the learned parameters experienced in the classical artificial neural network models [25].

The convolution layer is the first layer to process the image in CNNs algorithms. The number of filters and the filter size are hyper-parameters of the convolutional layer, and these are determined individually for each algorithm. In addition, by sharing the parameters, the number of parameters is reduced, and simpler decision limits can be learned. With this process, more accurate predictions can be made with less training data. The pooling layer is a sampling process that is implemented with some spatial invariance. After the convolutional layer, activation functions are determined for the pooling layer. Since linear activation functions are weaker in learning complex properties, nonlinear activation functions are generally preferred in the algorithms. The FC layer is usually the last layer of the CNNs architecture and can be used to optimize class scores. After extracting basic parameters with a 2x2 local image matrix, the low-dimensional images are transferred to the fully connected layer.

ResNet152[26], DenseNet201[27], and VGGNet19[28] architectures can use for feature extraction and classification steps to diagnose DR stage. The ResNet152 achieved a lower error value than the human vision error rate in the ImageNet competition in 2015. Although this architecture uses residual blocks with multiple layers to decrease the training error, it also solves the over-compliance problem of multi-layer networks. In residual blocks, input information from the convolution layer is added to the information after the activation process and transmitted to the next layer.

DenseNet201 was introduced because of attempts to deepen CNN architectures in 2016. Traditional CNN architectures pass the information from the convolution layer to the next layer with n connections. In DenseNet architecture, the information coming out of the convolution layer is sent as input to all layers after it and this process continues towards the last layer with $n(n+1)/2$ connections. DenseNet minimizes the vanishing-gradient problem and strengthens feature propagation. VGGNet19 was first introduced at the ImageNet competition in 2014. VGGNet architecture focuses on deepening the network rather than increasing its layers to improve performance. VGGNet19 architecture has sixteen convolutional and three fully connected layers. Convolution layers have a maximum pooling and ReLU activation function.

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3. EXPERIMENTS AND RESULTS

We examine our proposed model by comparing VGGNet19, DenseNet201, and ResNet152 CNN architectures on the Kaggle APTOS 2019 dataset for DR stage detection. The dataset is divided into 70% for training, 20% for validation, and 10% for testing. Data augmentation has been applied to increase the performance of the model and to prevent overfitting on the training set. It is applied only to the train data and not to validation and test sets. In this way, excessive learning and manipulation are prevented. All experiments are carried out on the K80 Tesla graphics card. Adam optimization algorithm is used for the optimization of CNN architectures, and ReLU activation is used in convolution layers. The batch size is determined as 64 and the epoch number as 50 in the experiments. Five performance evaluation metrics are used in the experiments: accuracy, area under the curve (AUC), precision, recall, and F-Score. The results of the experiments are shown in Table 1 for each CNNs model in these metrics.

Table 1. Classification Performances of CNNs architectures.

	Accuracy	AUC	Precision	Recall	F-score
ResNet152	0.824	0.941	0.820	0.820	0.820
DenseNet201	0.827	0.923	0.830	0.830	0.810
VGGNet19	0.824	0.938	0.810	0.810	0.810

In the experiments, 82.4% accuracy and 82% F-score value were obtained using the ResNet152 architecture. Using DenseNet201 architecture, 82.7% accuracy and 81% F-score value were found. The results of VGGNet19 architecture are seen as 82.4% accuracy and 81% F-score. Although DenseNet201 architecture obtained the best accuracy value, ResNet152 architecture found the best F-score value. However, the findings of the 3 architectures are close to each other. Table 2 shows the weighted average performance values of CNNs architectures for all classes in precision, recall, and F-score values. The ResNet152, DenseNet201, and VGGNet19 architectures predicted the No_DR class with an F-score of 97% and above. The best estimate for the Mild class was the ResNet152 architecture with an F-score of 58%.

Table 2. Comparative analysis of CNN architectures and DR classes.

	Class	Precision	Recall	F-score
ResNet152	Mild	0.56	0.59	0.58
	Moderate	0.76	0.81	0.78
	NoDR	0.97	0.99	0.98
	Severe	0.50	0.58	0.54
	PoliferateDR	0.64	0.31	0.42
DenseNet201	Mild	0.73	0.43	0.54
	Moderate	0.76	0.81	0.78
	NoDR	0.94	0.99	0.97
	Severe	0.71	0.26	0.38
	PoliferateDR	0.83	0.52	0.64
VGGNet19	Mild	0.59	0.46	0.52

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Moderate	0.75	0.77	0.76
NoDR	0.94	0.99	0.97
Severe	0.67	0.74	0.70
PoliferateDR	0.61	0.48	0.54

Fig. 5 presents the complexity matrix showing the predictions and real values obtained by the proposed CNNs model because of 50 epochs.

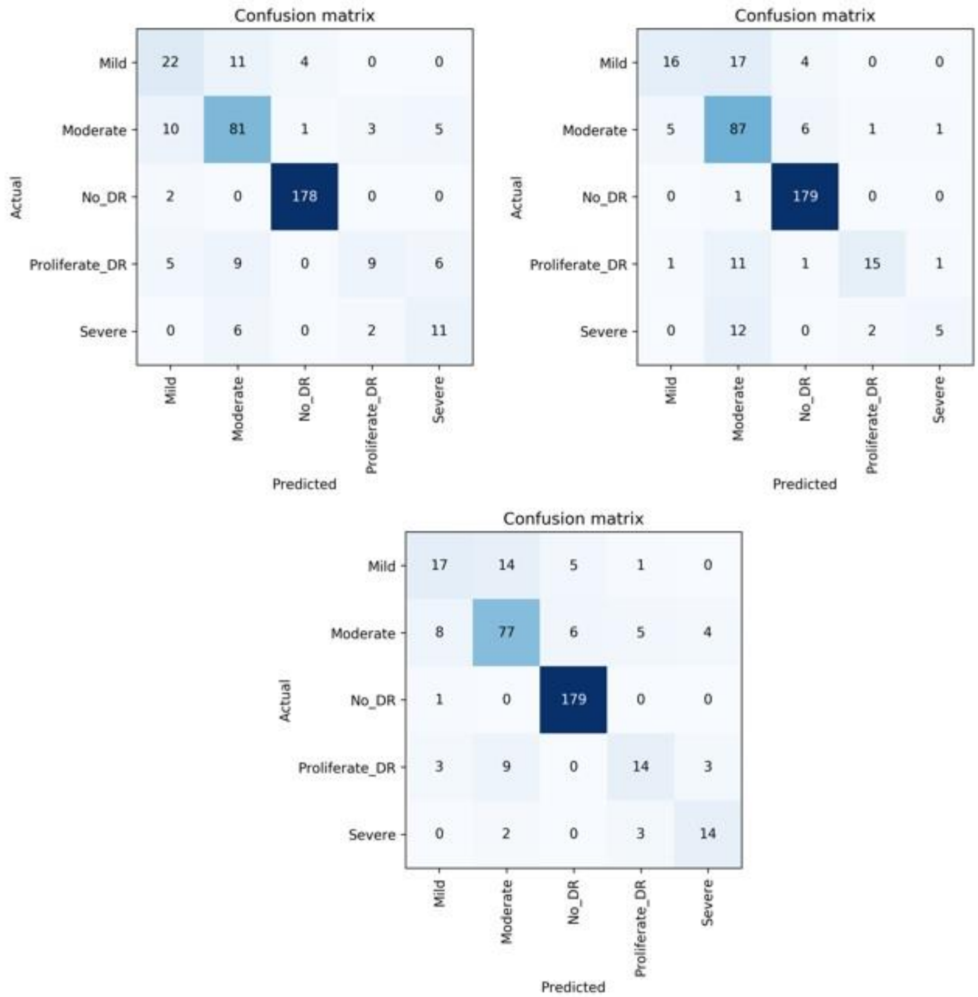

Figure 5. Confusion matrices, (Left Top) ResNet152, (Right Top) DenseNet201, (Bottom) VGGNet19.

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As can be observed, Fig. 6 presents the ROC curve showing the discrimination capability of classification models. The x-axis of the ROC curve gives the false-positive rate, and the y-axis gives the correct positive rate. The area under the curve shows the AUC score. AUC gives the classification model's ability to distinguish.

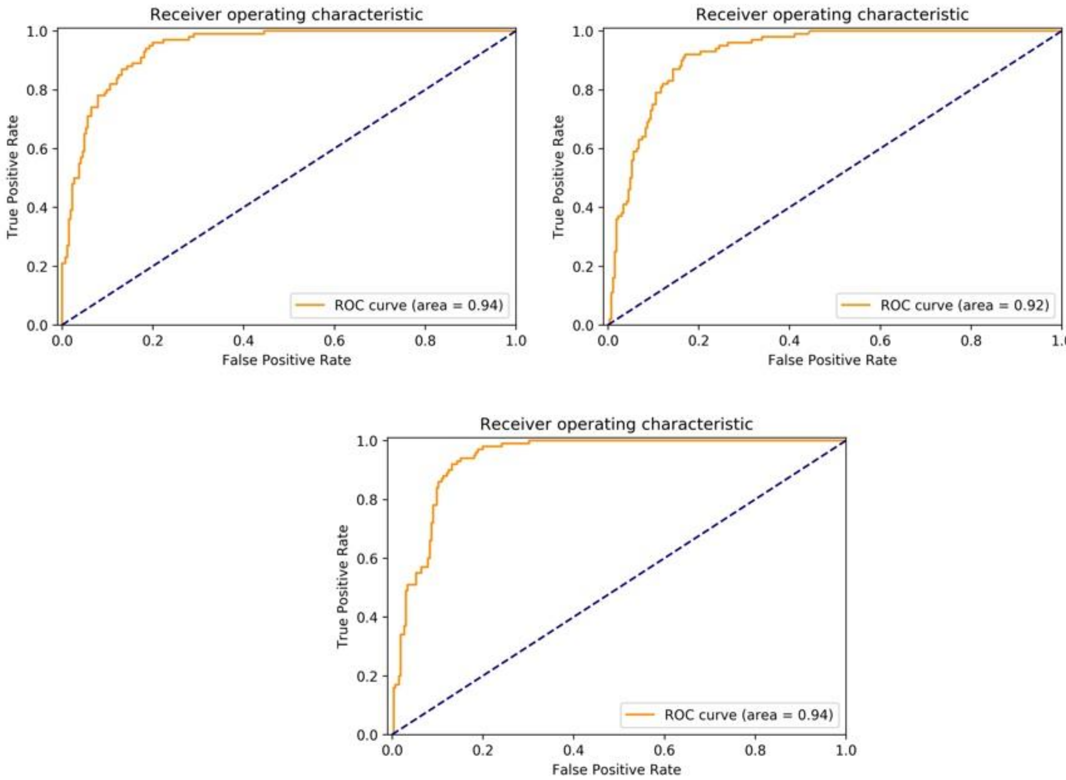

Figure 6. Roc Curves (Left), ResNet152 (Right), DenseNet201 (Bottom), VGGNet19.

Unlike other studies, we do not use the enhanced data in the test set. In this way, the effect of memorized images on learning is minimized. Khalifa et al. [30] achieve 80% accuracy with the SqueezeNet algorithm as a result of the data augmentation process they perform without considering this situation. Lam et al. [31] test their work with the deep learning model in which they apply the accuracy value in three classes; no DR, Mild and Severe. Transfer learning in the pre-trained GoogLeNet and AlexNet models in ImageNet, they find the highest test set accuracy as 74.5% in two classes, 68,8% in the three classes, and 57.2% in four classes. Pratt et al. [23] use CNNs to classify DR stages from fundus images and obtain 75% accuracy with five-fold cross-validation using 5000 images.

We obtain an accuracy of 82.7% using the DenseNet201 algorithm for the classification performance of DR stages. When the AUC values are examined, the ResNet152 algorithm gives the best result with 94.1%. The proposed model stands out with both its accuracy results and classification performance success. Most of the studies in the literature classify two classes as no DR and DR. Kumar et al. [32] find a test accuracy of 80.59% in their study using a mixed dataset for two classes. In this study, VGGNet19, DenseNet201, and ResNet152 algorithms classify the no DR images in four stages with accuracies of 94%, 94%, and 97%, respectively.

4. CONCLUSIONS

Diabetic retinopathy is an important disease that occurs due to diabetes mellitus. With this disease, deteriorations such as microaneurysms, hemorrhages, exudates and new vessel formation occur in the retina of the eye. The computer-aided system has been developed to assist specialist physicians in an effective diagnosis of the disease. The stages of DR lesions have been tried to be determined from color retinal images by deep learning algorithms. We examine our proposed model by comparing VGGNet19, DenseNet201, and ResNet152 CNN architectures on the Kaggle APTOS 2019 dataset for DR stage detection. When the overall test accuracy and performance metrics are examined, it seems the DenseNet201 model reaches the best test accuracy with 82.7%. The highest AUC value is obtained using the ResNet152 model with 94.1%. For future studies, the features of well-known CNN architectures can be combined and the ensemble learning method can be applied for classification. This can increase the accuracy of DR classes that are predicted particularly unsuccessfully.

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