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Detection of Multi-Class Retinal Diseases Using Artificial Intelligence: An Expeditious Learning Using Deep CNN with Minimal Data

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The health-related complications such as diabetes, macular degeneration, inflammatory conditions, ageing and fungal infections may cause damages to the retina and the macula of the eye, leading to permanent vision loss. The major diseases associated with retina are Arteriosclerotic retinopathy (AR), Central retinal vein occlusion (CRVO), Branch retinal artery occlusion (BRAO), Coat's disease (CD) and Hemi-Central Retinal Vein Occlusion (HRVO). The symptomatic variations among these disorders are relatively confusing so that a systematic diagnostic strategy is difficult to set in. Therefore, an early detection device is required that is capable of differentiating the various ophthalmic complications and thereby helping in providing the right treatment to the patient at the right time.In this research work, 'Deep Convolution Neural Networks (Deep CNN) based machine learning approach has been used for the detection of the twelve major retinal complications from the minimal set of fundus images. The model was further cross-validated with real-time fundus images. The model is found to be superior in its efficiency, specificity and ability to minimize the misclassification. The "multi-class retinal disease" model on further cross-validation with real-time fundus image of the gave an accuracy of 95.63 %, validation accuracy of 92.99 % and F1 score of 91.96 %. The multi-class modelis found to be a theranostic clinical support system for the ophthalmologist for diagnosing different kinds of retinal problems, especially BRAO, BRVO, CRAO, CD, DR, HRVO, HP, HR, and CN.

Keywords: Deep CNN; fundus image; multi-class retinal diseases;theranostic tool.

There are a number of retinal diseases reported so far such as Arteriosclerotic retinopathy (AR), Central retinal vein occlusion (CRVO), Central retinal artery occlusion (CRAO), Branch retinal vein occlusion (BRVO), Branch retinal artery occlusion (BRAO), Coat's disease (CD), Hemi-Central Retinal Vein Occlusion (HRVO), Histoplasmosis (HP), Hypertensive retinopathy

(HR), Choroidal neovascularization (CNV) and diabetic retinopathy (DR), which may even lead to permanent vision loss. Out of these, age-related macular degeneration (AMD) and diabetic retinopathy have been identified as the most significant.[1, 2]

The restrictions of the human eye and inadequacy of the conventional techniques to diagnose the various types of retinal diseases accurately and early in advance are the major challenges faced by the present-day ophthalmologists in the correct treatment of the patients.[2-4] At present, highly sophisticated and dependable diagnostic imaging techniques such as 'Fluorescent Retinal Angiography (FRA) and Optical Coherence Tomography (OCT) etc. are very popular. A countless number of machine learning approaches such as the artificial neural network (ANN), K-nearest neighbor algorithm, support vector machine (SVM) and Naive Bayes classifier (NBC) are incorporated to improve the prediction accuracy towards the detection of retinal diseases from the fundus images. It has been reported that 'ANN basedalgorithms' are efficient in predicting glaucoma from fundus images.[5-8]

Traditional classification approaches depend on feature extraction and feature classification techniques designed for the specific problem based on the available knowledge of the field. Most of the algorithms used in this area encounter the challenge of having the only insufficient number of datasets for training the model through conventional machine learning techniques.[9]The launching of 'deep learning CNN' based algorithms makes evolutionary changes in the approach by directly identifying features from the training data without the categorical elaboration on feature extraction and classification. However, deep learning-based models are found to improve their efficiency on vigorous training using a large number of datasets.[10] The availability of medical images will be highly limited in most cases, causing difficulties in using deep learning-based algorithms in the field of healthcare.[8, 9] A number of open platforms and databases have been developed to store healthcare related medical images around the world. The techniques based on 'deep extraction of information from the available images' such as 'affine transformation' and 'rotation of the images' have been introduced to improve the efficiency of deep learning-based algorithms.[7- 10]

The deep learning based prediction strategy can be extensively used in diabetic retinopathy (DR).[9] An unconventional and evolutionary deep learning prediction model for diagnosing DR by an automatic feature extraction learning method has been developed by Google, which helps even to grade and classify the intensity of nuclear cataract among the patients.[7-10] Similarly, many deep learning approaches have been introduced in the prediction of 'Retinopathy of prematurity (ROP)' and AMD. Recent studies on fundus images using deep learning algorithms establish the possibility of predicting cardiovascular risk factors, suggesting these images as potential predictive models. Due to the lack of the accessible patient database, most of the predictive models designed so far have been set only for binary classification or to identify the presence of only diabetic retinopathy.[9-11]

The possibility of using fundus images for the design of 'multi categorical predictive model' covering various retinal diseases has been tried in the present work. The designed model is used to diagnose and differentiate retinal diseases such as arteriosclerotic retinopathy, branch retinal vein occlusion, etc.

METHODS

Data collection

The fundus images corresponding to different retinal disease were acquired from three standard online databases namely, 'DIARETDB0, HRF Image Database and STARE' for the primary training of the model. Similarly, 91 real-time images were acquired and clinically diagnosed and categorized by practising ophthalmologists, for training and cross-validation.

A total of 130 images were acquired from DIARETDB0, (110 are of diabetic retinopathy - haemorrhages, soft exudates, hard exudates, neovascularization and micro aneurysm] and 20 are from normal healthy people.[12]From 'High-Resolution Fundus (HRF) Image Database' 15 images (normal, DR and glaucoma) were obtained.[13] The images have been collected for the twelve major classes of diseases such as AR, CRVO, CRAO, BRVO, BRAO, CD, HRVO, HP,

HR, CN, DR and normal retina. Additionally, the prediction models have been trained efficiently with minimal retinal images and have been cross-validated using real-time fundus image of patients from the hospital.

Similarly, from the 'Structured Analysis of the Retina (STARE) online database, 14 categories of 397 images including 'Background Diabetic Retinopathy (BDR)', 'Proliferative Diabetic Retinopathy (PDR)', retinitis, emboli, CRAO, CRVO, BRAO, etc. were collected.[14]

The images were collected from various databases to improve the availability of various classes for analysis. The images were rotated to different angles and the corresponding data were also included in the samples to be tested leading to an increase in the effective number of images to 2484. Out of these images, 80% has been used for training and the remaining 20% for testing. The images were then resized to 224 x 224 pixels for optimum image resolution[15-18] the detailed information regarding data collection and dataset preparation has been included in Table 1.

Deep learning architecture

The deep predictive model has been designed based on a pre-trained model, which was developed by Oxford Visual Geometry Group [VGG] known as VGG19. The VGG pre-trained model is built on a 3×3 convolutional layers stacked up together to increase the depth, followed by a max-pooling layer to reduce the volume size. After convolution, these features are more readily learned by a fully connected neural network of 4,096 nodes.[19]The learning weights have been

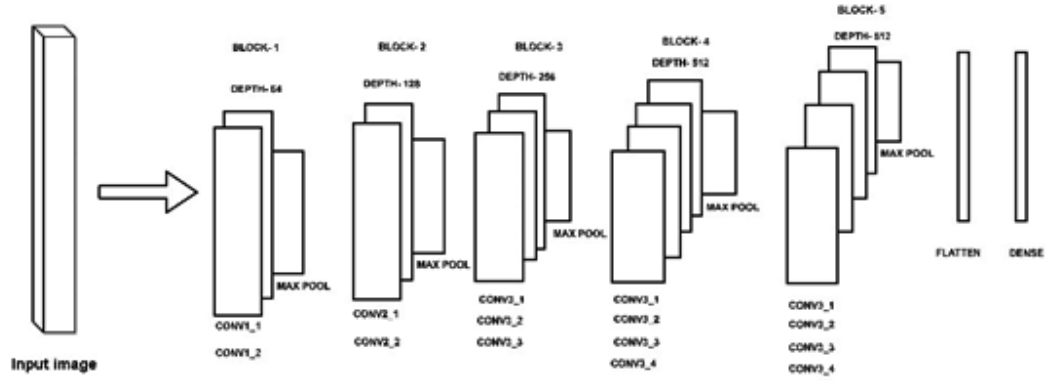

Fig. 1. Deep CNN architecture

Table 1. Detailed Information Regarding Data Collection

Sl. No	Name of the disease	DIRETDB0	HRF retinal database	STARE	Real time images
1	Arteriosclerotic retinopathy [AR]	0	0	20	0
2	Central retinal vein occlusion [CRVO]	0	0	25	14
3	Central retinal artery occlusion [CRAO]	0	0	8	9
4	Branch retinal vein occlusion [BRVO]	0	0	10	25
5	Branch retinal artery occlusion [BRAO]	0	0	5	0
6	Coat's disease [CD]	0	0	10	0
7	Hemi-Central Retinal Vein Occlusion [HRVO]	0	0	10	0
8	Histoplasmosis [HP]	0	0	10	0
9	Hypertensive retinopathy [HR]	0	0	20	16
10	Choroidal neovascularization [CN]	0	0	50	27
11	diabetic retinopathy[DR]	110	15	75	0
12	Normal	20	15	36	0

optimized to achieve maximum accuracy. The model architecture used for the research has been shown in [Fig. 1].

Model optimization

Initially, the number of the epoch was optimized as 50 to provide proper convergence and maximum accuracy. A loss function or scoring function permits the system to compute the efficiency of the classification. In addition, a categorical cross entropy loss function has been used for the evaluation of the VGG19-softmax model by predicting the accuracy and validation accuracy.[20-22] Besides computing accuracy, sensitivity, specificity, and precision have been taken into account and a confusion matrix has been generated for calculating the true positive rate (TPR) and false positive rate (FPR), which reflect the detailed performance information of the classifier.[21-25]

RESULTS AND DISCUSSION

The prediction model gave an accuracy of 95.63 % and validation accuracy of 92.99 %,

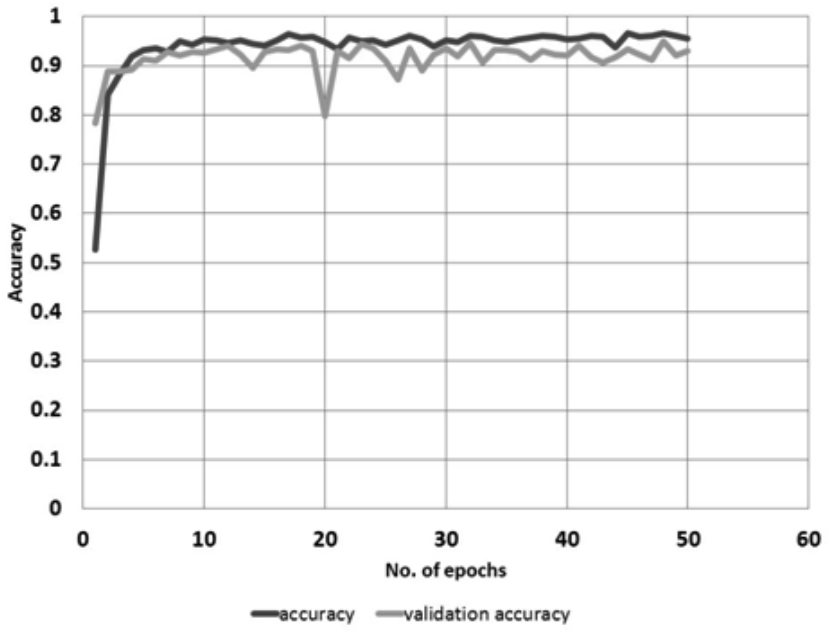

Fig. 2. Results of overall accuracy vs validation accuracy

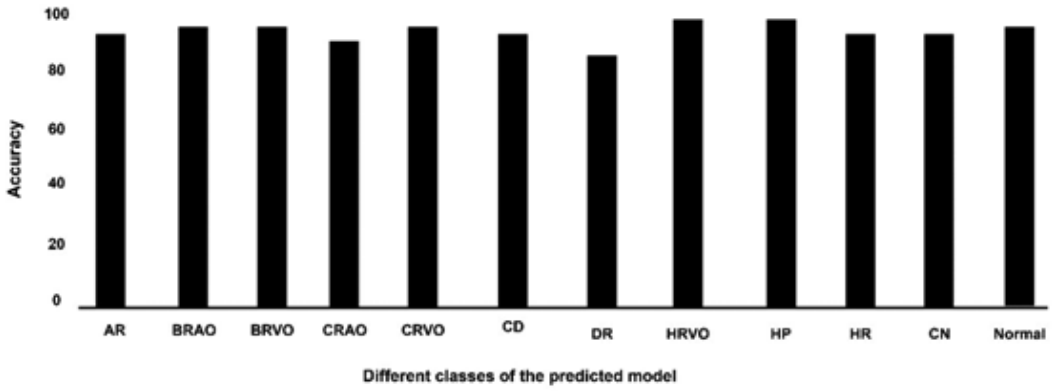

Fig. 3. Accuracy results of all the categories value of our VGG19-softmax model

supporting its effectiveness in the prediction from the image samples [Fig. 2].

A confusion matrix has been computed for further evaluation of the classifiers [Table 2]. It has been found that the model predicts most of the diseases accurately especially, BRAO, BRVO, CRAO, CD, DR, HRVO, HP, HR, and CN. However, the prediction accuracy of the model to the diseases AR and CRVO from the fundus images collected was very low [Fig. 3].

The true positive rate (TPR), a measure of sensitivity has been plotted out of the confusion matrix as shown in [Fig. 4].

The sensitivity score of all the diseases was found to be high, excepting AR. In a few cases such as BRVO, HR, HRVO, HP and Normal, the sensitivity was 100%. Moreover, the false positive rate of these classes is zero [Fig. 5].

The precision values of these classes are found to be high [Fig. 6] suggesting a low level of misclassification. The specificity, which is a measure of the percentage of negatives that have been correctly identified, for the "multi-class retinal disease prediction model" has been found to be greater than 95%, supporting minimum misclassification [Fig. 7]. F1-score of the classes has been shown in [Fig. 8].

All the parameters characterizing the prediction model are included in [Table 3]. The designed prediction tool is found to be a 'potential multi-class retinal disease prediction model' from fundus images.

With recent advancements in the field of medical image processing using machine learning algorithms and data mining techniques, the computer-aided medical diagnostics has become

Table 2. Confusion Matrix Result Of Our Model

N=499	AR	BRAO	BRVO	CRAO	CRVO	CD	DR	HRVO	HP	HR	CN	Normal	
AR	15	3	0	0	0	0	0	0	0	0	0	0	18
BRAO	0	35	0	0	0	0	0	0	0	0	0	0	35
BRVO	0	0	34	0	0	0	1	0	0	0	0	0	35
CRAO	7	0	0	32	0	0	1	0	0	0	0	0	40
CRVO	0	0	0	0	41	0	0	0	0	0	0	0	41
CD	0	0	0	0	0	33	0	0	0	0	0	0	33
DR	5	0	0	1	0	0	54	0	0	0	1	0	61
HRVO	0	0	0	0	0	0	0	40	0	0	0	0	40
HP	0	0	0	0	0	0	0	0	40	0	0	0	40
HR	4	0	0	1	0	0	0	0	0	56	1	0	62
CN	0	0	0	2	0	3	0	0	0	0	48	0	53
Normal	4	0	0	0	1	0	0	0	0	0	0	36	41
	35	38	34	36	42	36	56	40	40	56	50	36	

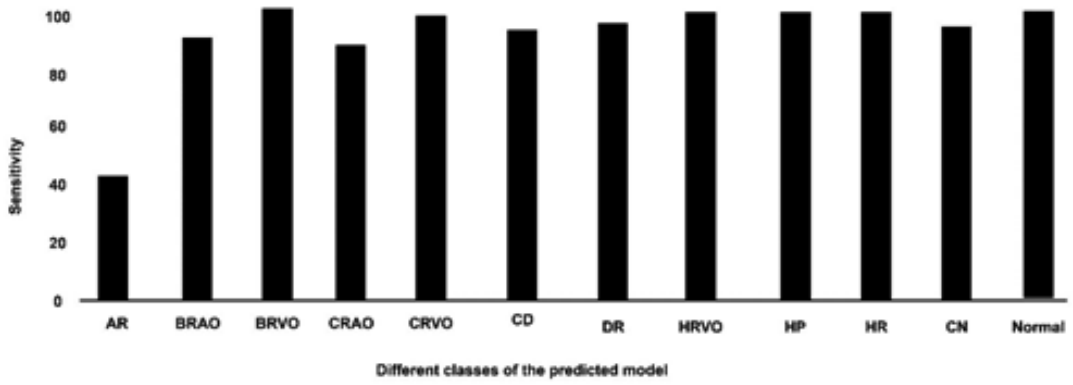

Fig. 4. TPR results of all the categories value of our VGG19-softmax model

an inevitable part of healthcare. In deep learning platform, the binary class-based classifiers have shown better accuracy and performance than multiclass classifiers. The most common drawback faced by multiclass classifiers is the chance for over fitting. For the designed model, the validation accuracy is in close proximity to the training data, therefore the chances of the model to over fit is

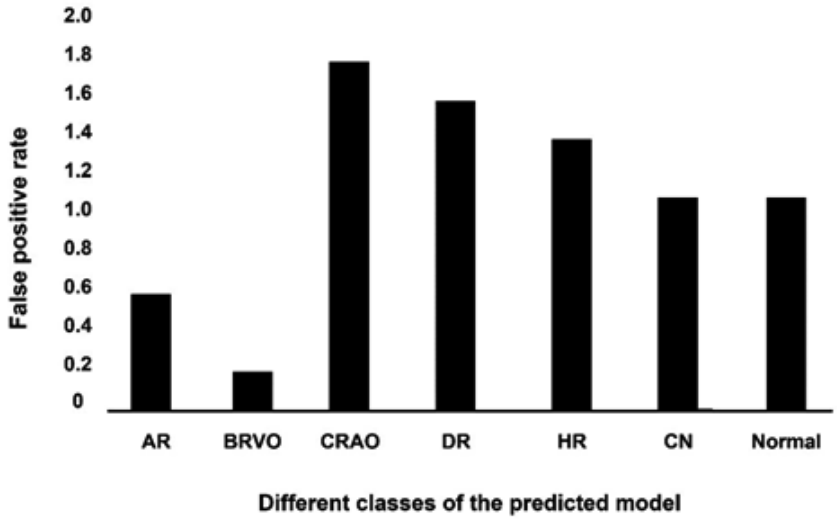

Fig. 5. FPR results of all the categories value of our VGG19-softmax model

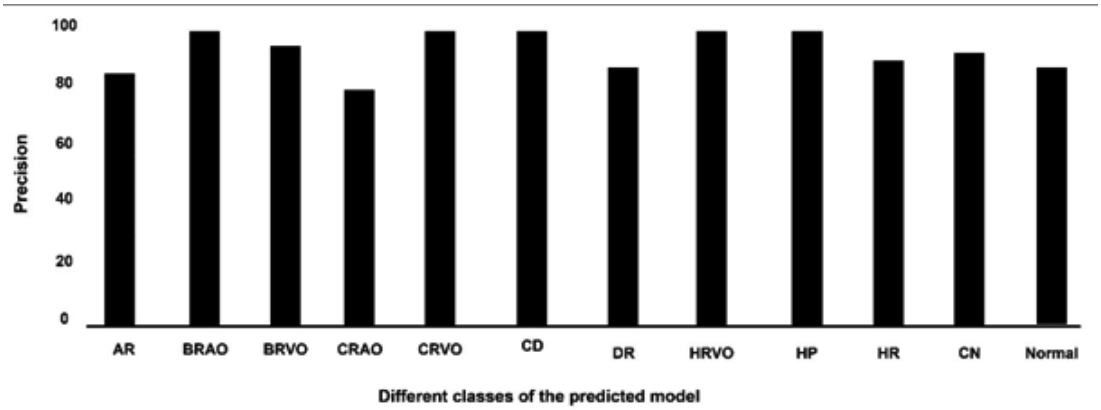

Fig. 6. Precision results of all the categories value of our VGG19-softmax model for multi class retinal diseases

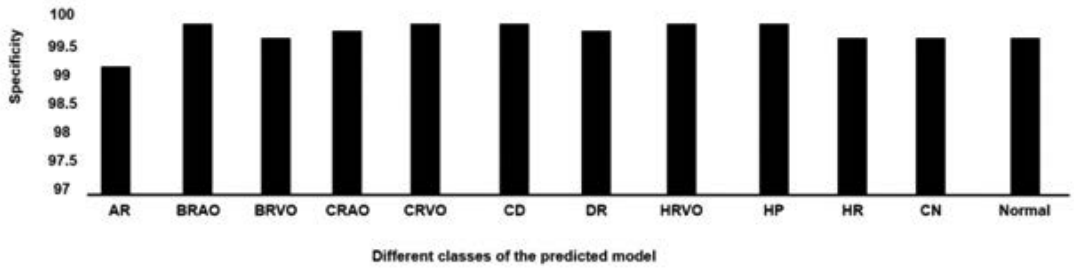

Fig. 7. Results of specificity value of our VGG19-softmax model for multi-class retinal diseases classification problems

Table 3. Results of all the parameters from confusion matrix

Name of the classes	Accuracy	Precision	TPR	Specificity	FPR	F1-score
AR	95.28	83.33	42.86	99.34	0.66	56.60
BRAO	99.36	100.00	92.11	100.00	0.00	95.89
BRVO	99.78	97.14	100.00	99.77	0.23	98.55
CRAO	97.48	80.00	88.89	98.18	1.82	84.21
CRVO	99.78	100.00	97.62	100.00	0.00	98.80
CD	99.36	100.00	91.67	100.00	0.00	95.65
DR	98.10	88.52	96.43	98.32	1.68	92.31
HRVO	100.00	100.00	100.00	100.00	0.00	100.00
HP	100.00	100.00	100.00	100.00	0.00	100.00
HR	98.72	90.32	100.00	98.55	1.45	94.92
CN	98.51	90.57	96.00	98.81	1.19	93.20
Normal	98.93	87.80	100.00	98.85	1.15	93.51

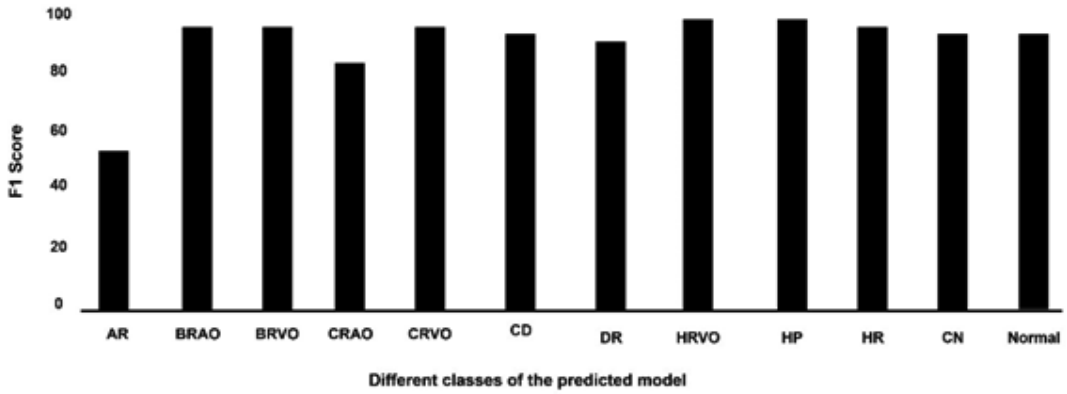

Fig. 8. Results of F1-score of the "VGG19-softmax" model for multiclass retinal diseases classification problems

negligibly small. The lower values of FPR, the higher values of precision and specificity ensure the model to be more dependable with minimum chances for Misclassification.

CONCLUSION

The 'multi-class retinal disease prediction model' is found to be a potential device in predicting retinal diseases from the fundus images. The overall efficiency of the model is found to be 92%. This study supports the possibility of exploiting the opportunities of pre-trained models with different medical applications using deep learning techniques. The model seems to predict the diseases BRAO, BRVO, CRAO, CD, DR, HRVO, HP, HR, and CN.

The model could further be used to make individual variations associated with the images and various mutations corresponding to retinal diseases thereby making fundus image as a potential biomarker for various associated diseases like cardiovascular complications, Alzheimer's disease, hypoxic conditions and etc.

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