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Prediction of Premature Retinopathy Fundus Images Using Dense Network Model for Intelligent Portable Screening Device

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Abstract

Retinopathy of Prematurity (ROP) is a serious retinal condition that affects preterm babies and, if ignored, can result in irreversible blindness. The challenges are related to variability and inconsistency among observers in diagnosing ROP, so the development of an automated system for ROP prediction becomes imperative. While various methods have been explored for automated ROP diagnosis, dedicated models with satisfactory performance have been lacking. This study aims to address these gaps with the objective to construct a multi-channel dense Convolutional Neural Network (MCD-CNN) which is tailored for ROP prediction, suitable for large-scale infant screening. The process involves utilizing CLAHE pre-processing, image labelling, image denoising, making and image generation for retinal vessel prediction in fundus images. The multi-channel CNN uses the feature selection method to extract and choose features from pre-processed pictures. The findings show that the suggested model attains a noteworthy 97.5% accuracy, 98% sensitivity, and 98.5% specificity. Significantly, this outperforms both pre-trained models and deep learning classifiers. Overall, the study contributes to improving ROP diagnosis and fostering accessibility to healthcare, particularly in remote areas.

Keywords: Retinopathy, Premature, Prediction, Deep Learning, Pre-processing, Telemedicine, ROP.

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1 Introduction

Retinopathy of prematurity (ROP) is a condition affecting premature infants, characterized by abnormal development and contraction of cellular membranes in the vitreous cavity and along the sides of the retina. Left untreated, ROP can progress to severe stages causing retinal detachment and permanent blindness (Ju et al., 2013; Kavitha, 2020). Preterm baby survival rates have grown dramatically as a result of advancements in newborn medical treatment consequently raising the prevalence of ROP worldwide. This trend is particularly notable in developing nations like India (Singh et al., 2018). Worldwide, there are around 14.38 million preterm births each year, with 23 per cent occurring in India. ROP caused serious visual impairment in almost 5000 newborns in India in 2010, leaving 2900 infants with visual impairment attributable to ROP. ROP accounts for around 10% of cases of visual impairment worldwide (Honavar, 2019). ROP is more likely to occur in infants born weighing less than 2000 grams or with incubation age of less than 32 weeks. Approximately 5000 of the approximately 490,000 babies born in India with gestational ages < 32 weeks require therapy for recurrent open pneumonia (Razzak et al., 2018; Sakthivel et al., 2019). The prevalence and severity of ROP are significantly influenced by the administration and duration of oxygen treatment, in addition to incubation age and less birth weight (Kulkarni et al., 2018; Mumtaj Begum., 2022).

2 Related Works

Developing an automated approach to predict ROP during baby mass screenings is imperative, given the increasing incidence rate and the considerable variability and inconsistency among observers in ROP diagnosis (Zou et al., 2019; Chatterjee et al., 2024). By using artificial intelligence to estimate retinal pigment epithelial pressure (ROP) from non-invasive fundus pictures of preterm neonates, pediatric ophthalmologists may diagnose preterm infants earlier and with less stress thanks to indirect ophthalmoscopic exams (Arora, 2024; Jelena et al., 2023). Deep Convolutional Neural Networks (DCNNs) have become essential instruments in recent medical advances and have found wide use in automated diagnosis (Bhatkalkar et al., 2020). To classify Retinopathy of Prematurity (ROP) from fundus pictures, Hemelings at al., (2019) constructed a computerized system that used two pre-trained networks, a quicker region-based convolutional neural network and ResNet 101 Even with an astounding accuracy of 90.3%, the Faster-RCNN system's computational load rose as a result of the added parameters. In different research, (Taha et al., 2015) predicted ROP plus illness with a maximum accuracy of 91% using U-Net for vascular segmentation and a pre-trained network trained on Inception Version 1. However, the employed pre-trained network lacked ROP specificity, leaving room for further enhancement (Venugopal, 2023; Choi & Zhang, 2022; Alamer et al., 2023; Bobir et al., 2024).

There are five phases in which ROP might present itself, ranging from first stage (early stage) to final stage 5 leading in permanent blindness (Reid & Eaton, 2019). Three anterior-posterior zones (designated I to III) that are focused on the optic disc and indicate the damaged site are further characteristics of the disorder (Yi et al., 2019; Ahmad et al., 2024). The phrase "plus disease" refers to the aberrant dilatation and twisting of retinal blood vessels that characterize the course of ROP (Rani & Rajkumar, 2016). Management of Type 1 ROP (zone I plus disease at all stages), zone I with third stage ROP, and zone II with 1 or 2 stages are all required according to the Early Treatment of ROP (ET-ROP) protocol (Jelena et al., 2023). On the other hand, Zone I at stages 1 or 2 and Zone III at stage 3 without further illness are required for periodic tests in Type 2 ROP (Litjens et al., 2017; Kutlu et al., 2021). Therapy with laser photocoagulation is advised for stage 3 ROP in zones 1 or 2 since it has been shown to provide better results and cause less discomfort (Hu et al., 2018; Trivedi et al., 2023). In cases of stage 4 and 5 retinal detachments, (Wang et al., 2018) suggested vitrectomy. Even with a successful surgical procedure, newborns may still have poor visual results; the repetition likelihood of retinal objectivity is around 5% in Stage 4 and 22% in Stage 5, respectively (Zhao et al., 2019). According to (Kim et al., 2019), it's critical to diagnose ROP within a 7–10-day window to reduce problems and improve visual acuity by early identification and the best possible treatment. Also, (Pugalendhi et al., 2021) devised a smart camera based for ROP detection.

Significant advancements are made by the article in the following important areas:

1) The study introduces the use of multi-channel CNN for accurate prediction of retinal vessels in fundus images. This method is associated with the existing approaches showcasing its effectiveness in delineating retinal structures.
2) A novel multi-channel network combining CNN architecture with image generation is devised for predicting ROP in photos of an infant's fundus. This model aims to efficiently capture ROP-specific features and deliver accurate predictions.
3) The study conducts a comprehensive performance comparison between the proposed model and several pre-trained networks. This comparison provides insights into the relative efficacy of the developed model against established architectures commonly used in image classification tasks.

Overall, the contributions outlined in the paper encompass advanced segmentation techniques for retinal vessels, the innovation of a specialized hybrid model for ROP prediction, an in-depth analysis of ROP-specific features, and a comprehensive evaluation against prevailing pre-trained networks. The combined goal of these efforts is to improve the precision and comprehension of ROP diagnosis through the use of fundus imaging.

3 Methodology

This study introduces an automated Retinopathy of Prematurity (ROP) screening system employing multi-channel dense CNN (MCD-CNN) models. The primary aim is to enable telemedicine-based ROP screening and improve hospital cooperation. This segment delineates the methodologies employed in constructing the ROP detection datasets, the development and assessment of MCD-CNN models and the creation of automated ROP screening systems. Figure 1 illustrates the proposed model.

Dataset Details

This work considers the HVDROPDB dataset which is composed of temporal and posterior fundus image views of premature infants. The images are captured using RetCam (US and clarity MSI) and Neo (healthcare centre, Bangalore). This camera is employed by many institutes all over the work. It is used for image segmentation/prediction with ground truth values to provide the essential image structure for stage and zone detection. The dataset has 12 subsets and 600 plus samples for prediction.

Pre-processing

The images were subjected to pre-processing using MATLAB 2020a before their input into the CNN. To highlight differences in pigmentation between the avascular and vascular retina, contrast-limited adaptive histogram equalization (CLAHE) was first done to improve picture contrast. Further, to minimize the image input size and enhance the visibility of darker and more pronounced features like vessels and demarcation lines, the green channel was removed from the picture. The picture was subjected to a Wiener filter to remove the distortions caused by CLAHE. All of the photographs were reduced to 1, 1470 pixels before CNN training so that they would match the dimensions of the images in the dataset that was used to train the model. Figure 2 exemplifies these pre-processing stages.

In this study, we utilize the sparse representation-based denoising toolbox developed to reduce noise in the ROP images. For clarity, an example is provided in Figure 2d, where the figure represents the original image and showcases the denoised image. Then masking stage of the denoised picture is denoted by I in this instance, and the binary image that results is 1or 0.

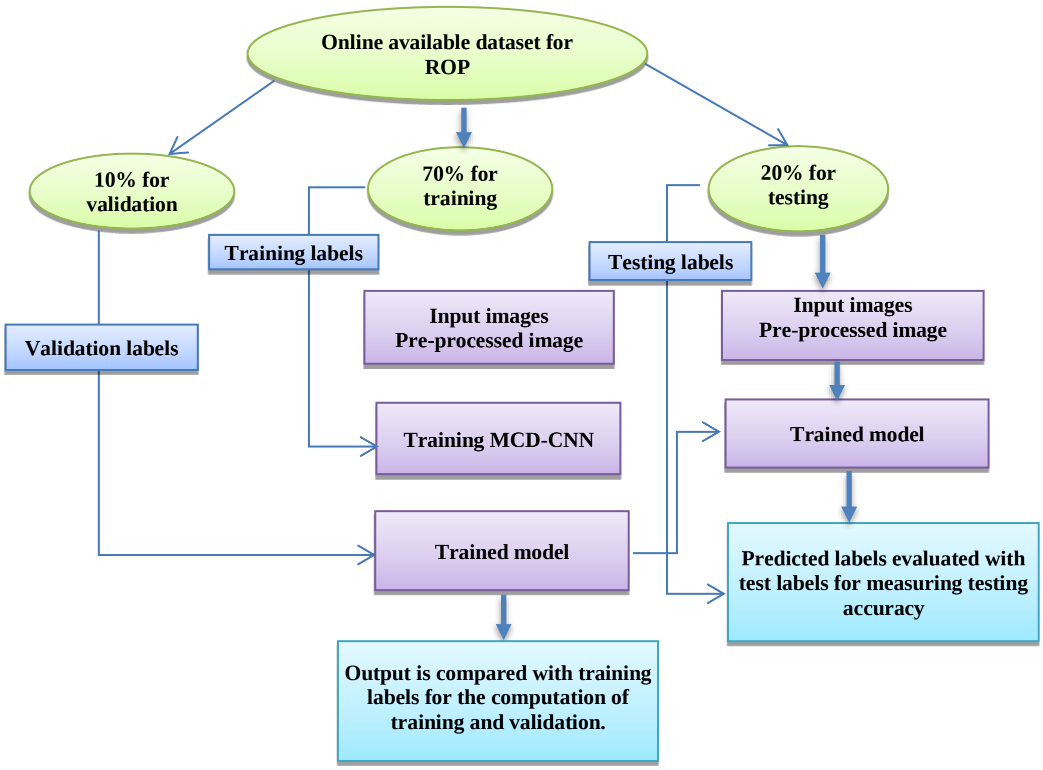

Figure 1: Workflow of the PROPOSED model

Figure 2a: Healthy Image

Figure 2b: Pre-processed Image Using CLAHE Method

Figure 2c: Denoised Image

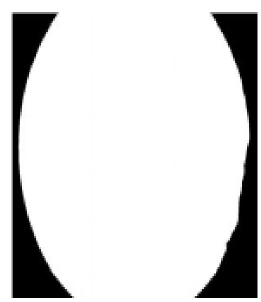

Figure 2d: Image Mask

Multi-channel Dense CNN

Convolutional neural networks (CNNs) are computational models that utilize multiple layers (channels) to learn increasingly abstract representations of data. Convolutional, pooling and fully linked layers make up a standard CNN design. Convolutional layers consist of trainable filters or kernels (denoted as

'k') with associated weights (w). Using these filters to convolve the picture and maybe adding biases (b), convolutional layers produce multiple feature maps each representing the output of a specific filter. Non-linear downsampling is carried out via pooling layers, which keep task-relevant data while eliminating unimportant features. The produced characteristics are mapped to output neurons by fully linked layers, where each neuron represents a judgment class. Figure 3 shows the model design of the MCD-CNN that was employed in this investigation. Gradient descent is a common approach used in MCD-CNN models to learn the parameters (θ = [w,b]). Additionally, various techniques exist to enhance MCD-CNN performance.

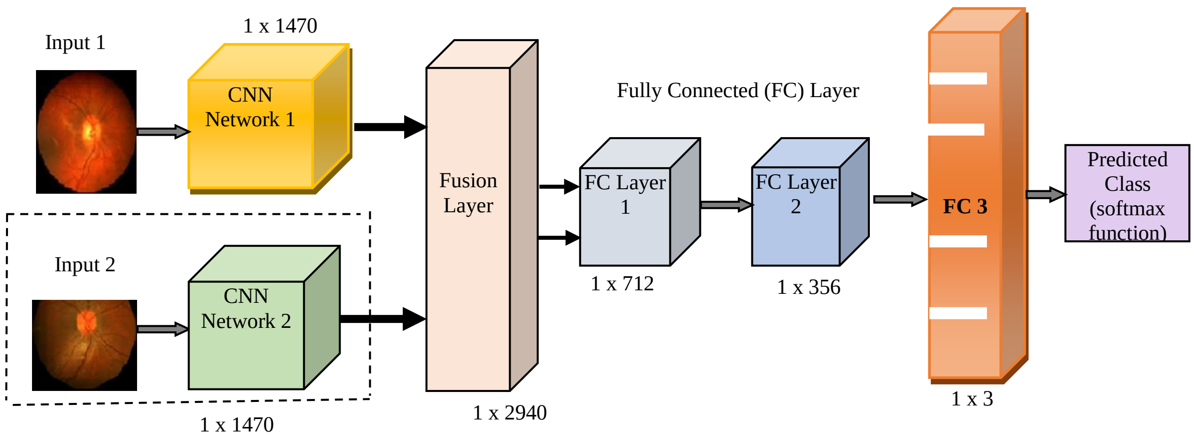

Figure 3: Proposed MCD-CNN Architecture

Among these are ensemble approaches, dropout, batch normalizing, whitening, data augmentation, and contrast normalization. These techniques serve to improve MCD-CNN performance by enhancing its learning capabilities, robustness, and generalization. To train and evaluate the MCD-CNN model, the alternative pictures are subjected to contrast normalization and whitening in this study. Additionally, a multi-channel technique inspired by ensemble methods is employed. Unlike traditional ensemble methods where multiple learners are trained separately and their outputs are combined, Only the MCD-CNN model is trained in this method. On replacement photos of each category, the trained model's outputs are averaged to provide an ensemble-like effect. The formula for this ensemble-like averaging process can be expressed as follows:

$$p(i) = \frac{1}{K}\sum_{j=1}^{K}[L_j = i] \; where \; i = 1,2,..,n \qquad (1)$$

Here's a breakdown of the elements within the equation (1): The number of categories is denoted by n, and the number of test image substitutes is K. The MCD-CNN model's prediction label for the j^th replacement picture is denoted by L_j; the square brackets, [·] indicate an indicator function, meaning that if $L_j = i$ is true, $[L_j = i]$ equals 1; otherwise, it equals 0. In this case, p(i) represents the likelihood that the original picture will be placed in the i^th category. The final result for a particular test picture is calculated by averaging the outputs produced on replacement photos of each category by the trained MCD-CNN model. This averaging technique aggregates the MCD-CNN model's predictions based on the substitute images, simulating an ensemble-like effect without the need for training multiple models. Certainly, the equation provided demonstrates the ensemble-like averaging process applied to obtain the final output from MCD-CNN model predictions on substitute images. The formula uses the average of the MCD-CNN model's predictions on replacement photos from different categories to calculate the final output for a test image. Each prediction is weighed according to how likely it is that the original image will fall into a particular group.

4 Numerical Results and Discussion

This section gives an extensive analysis of various prevailing approaches with the anticipated model:

Discussion

This study investigated the efficacy of CMD-CNN in identifying ROP stages 1-3 in pictures of the retinal fundus. The research findings are summarized as follows: MCD-CNN exhibited a high accuracy in screening for retinal pictures with stages 1-3 ROP when trained and tested within the same population and camera setting (See Figure 4). The MCD-CNN was trained using datasets from online resources. Notably, the dataset represented typical demographics observed in lower-income countries which have distinct characteristics in neonatal care and disease prevalence. When evaluated on outside samples whose attributes were different from those of the initial training dataset, the performance of the trained MCD-CNNs decreased. This study highlights the promising potential of MCD-CNN in accurately screening for stage 1–3 ROP within specific populations and camera settings. However, further investigation and evaluation are required to determine the practical applicability and effectiveness of these AI-based screening systems in real-world ROP screening scenarios.

The second key finding emphasizes the challenges faced by trained MCD-CNNs when examined using outside samples whose properties differ from those of the initial training dataset. The third key finding underscores that combining populations for training can enhance both internal and external performance. The better performance of the combined model indicates that the training data's degree of heterogeneity—which takes into consideration other picture attributes in addition to quantity—may have had a role in improving performance. Notably, the MCD-CNN exhibited robust classification performance for different stages despite learning unique features from each population or camera.

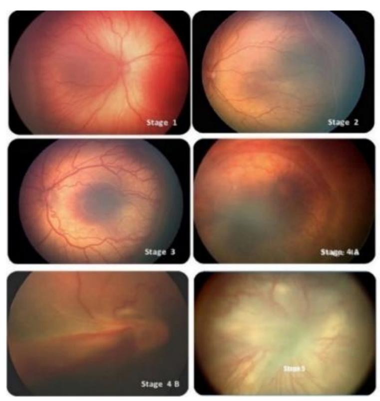

Figure 4: Stages of ROP (1-5)

Evaluation Metrics

It appears you have provided explanations and formulas for several evaluation metrics commonly used in assessing classification models. These metrics are essential for quantifying the performance of deep learning models, particularly in classification tasks like the identification of ROP zones. Here's a breakdown of these metrics:

Accuracy (ACC): calculates the percentage of all samples that were accurately predicted shows in equation (2).

$$Accuracy = \frac{TP+TN}{TP+TN+FN+FP} * 100\% \quad (2)$$

False Positives (FP), False Negatives (FN), True Positives (TP), and True Negatives (TN).

Precision (Prec): shows the percentage of accurately detected positive cases out of all the cases that were expected to be positive shows in equation (3).

$$Precision = \frac{TP}{TP+FP} * 100\% \quad (3)$$

Recall (Sensitivity): calculates the ratio of all actual positive cases to all accurately anticipated positive instances shows in equation (4).

$$Recall = \frac{TP}{TP+FN} * 100\% \quad (4)$$

F1 Score: serves as a balanced indicator of precision and recall by representing the harmonic mean of the two shows in equation (5).

$$F1 - score = \frac{TN}{TN+FP} * 100\% \quad (5)$$

Area Under the Curve (AUC) - Receiver Operating Characteristic (ROC) Curve: It gauges a model's capacity to trade off TP (sensitivity) and FP (1-specificity) to determine how well it separates into groups (like ROP zones) in equation (6). The AUC is between 0 and 1, where higher values indicate better model performance.

$$FPR = \frac{FP}{TN+FP} \quad (6)$$

These indicators offer a thorough assessment of the model's functionality, offering insights into its accuracy, ability to detect positive instances, and trade-offs between true positives and false positives. The ROC curve, along with the AUC, is particularly useful in analyzing the model's discrimination ability across various thresholds as in Figure 5.

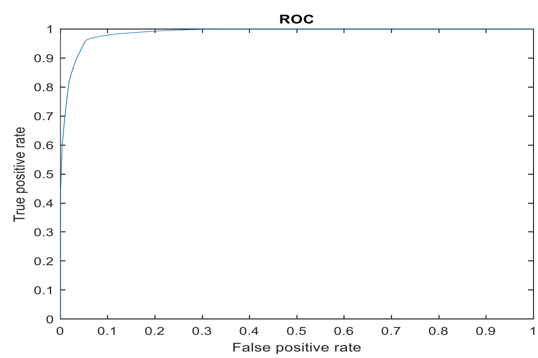

Figure 5: ROC Curve

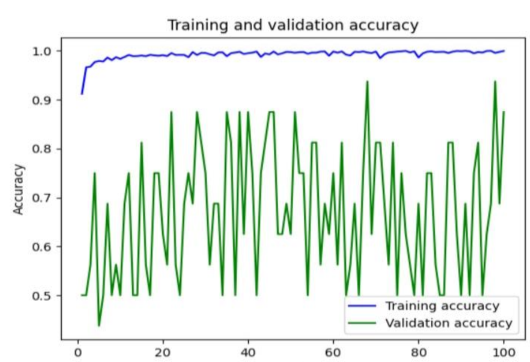

Figure 6: Training and Validation Accuracy

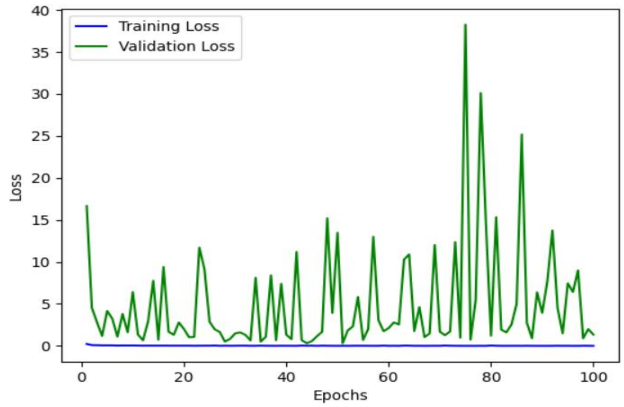

Figure 7: Training and Validation Loss

Results and Discussion

The objective and methodology of the study aimed at identifying ROP zones in preterm newborns using deep learning techniques. Here's an outline of the study's key aspects: 1) The primary goal is to develop models capable of accurately identifying ROP zones in preterm newborns using fundus images; 2) Utilizing datasets trained on MCD-CNN distinct classifiers to predict ROP zones from fundus images. To evaluate the performance and trends in the data, this study uses AUC, precision, recall, and F1 score. Next, the model utilizes a multi-channel classifier to combine the outputs of individual classifiers, providing an overall accuracy result. The execution is done utilizing an Intel Core i7 PC with 2.7 GHz and 8 GB RAM for data processing leveraging an open-source deep learning library, for model development and evaluation. Additionally, this work uses MATLAB 2020a an open-source web tool, for creating and sharing reports that integrate code, graphics, equations, and text. It looks like this strategy entails creating and assessing deep learning models for accurate ROP zone identification in preterm newborns, utilizing appropriate metrics (See Figure 6 and Figure 7) and computational resources.

The methodology and results of the study focused on predicting the severity of ROP using different deep-learning models and other techniques as in Table 1. The study suggests that the anticipated technique, particularly the voting classifier, combining predictions from different DL models, enhances prediction accuracy for ROP severity compared to individual models. The MCD-CNN model exhibited superior performance among individual models. The ROC curves and thorough comparison analysis shed light on how successful the suggested approach is.

Table 1: Performance Evaluation of Various Existing with Proposed Approaches

Models	**Accuracy (%)**	**Recall (%)**	**F1-score (%)**	**Precision (%)**	**AUC**
MCD-CN	**97.5**	**98**	**98.5**	**97**	**98**
VGG-19	96	97	95	95.5	97
VGG-16	88	96	76	94	96
Inception-V3	72	94	40	85	76
DenseNet	76	67	88	66	77
MobileNet	86	86	85	81	87

The stages of ROP has been examined using a variety of statistical techniques to evaluate the outcomes of different texture metrics A Receiver Operating Characteristic (ROC) curve and group mean comparisons using a t-test are included. To compare sample means and show the likelihood of a mean difference, Student's t test is computed.

Using the p-values from the 2-tailed Student's t-test and the AUC value from the ROC curve, the pertinent features are found. The student's t-test is the standard statistical method used to determine the significance of a mean difference. Student's t distribution can be used to estimate the corresponding value of p once the value of t has been established.

Table 2: Student's t-test Pair Wise Comparison Statistical Result Analysis between AUC of the Classifiers

	MCD-CNN vs DenseNET	**VGG19 vs DenseNET**	**MCD-CNN vs VGG19**	**DenseNET vs MobileNET**
MSE Error	0.00954	0.0256	0.0120	0.0102
Significance Level	P<0.05	P<0.05	P<0.05	P = 0.793
Confidence Interval (CI) 95 %	0.0901-0.125	0.0691-0.0162	0.0796-0.0190	-0.0179-0.032
Significance Level	P < .05	P < .05	P < .05	P = 0.793
Difference in AUC curve	0.08	0.03	0.12	0.02

The pairwise comparison in Table 2 between the MCD-CNN vs DenseNET, VGG19 vs DenseNET, the comparison of MCD-CNN and VGG19 reveals that both models' confidence intervals exclude the 0 value at $p < 0.001$, indicating that the AUC difference is statistically significant in both scenarios. Conversely, the pairwise comparison of the AUC values of DenseNET and MobileNET reveals no statistically significant difference, since the Confidence Interval (CI) includes a value of 0 with a non-significant p value of 0.793. Thus, various statistical results significantly prove that the MCD-CNN and VGG -19 classifier has higher classification accuracy. Thus, various statistical findings clearly demonstrate the higher classification accuracy of the MCD-CNN and VGG-19 classifiers.

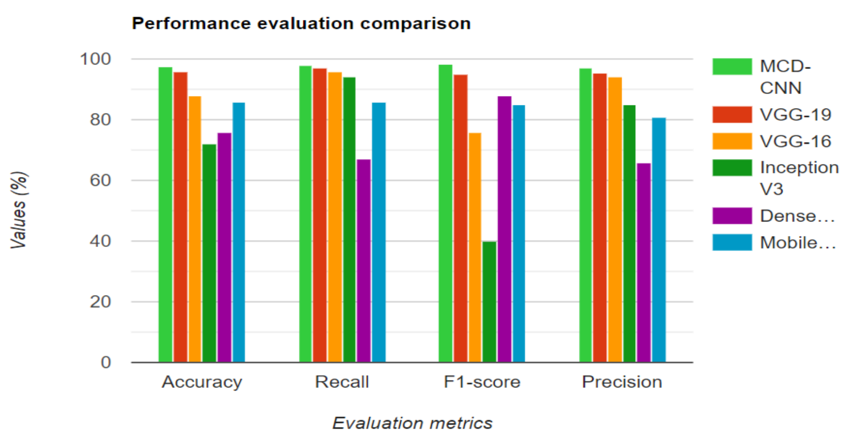

Figure 8: Performance Analysis

The study evaluated accuracy, recall, F1 measure, and AUC as part of the trained module's performance assessment. This work intends to focus on further algorithm development, exploring additional methodologies, and expanding the training dataset to continue improving the accuracy and robustness of the ROP detection system. Overall, the study demonstrates the potential of employing the MCD-CNN classifier to enhance the automatic identification of ROP in newborns, paving the way for potential advancements in medical diagnostics for ROP, particularly in resource-constrained settings Performance Analysis shown in figure 8.

5 Conclusion

It appears that the study focuses on employing MCD-CNN to automatically identify ROP in newborns aiming to address the shortage of ophthalmologists and the need for accurate diagnosis, especially in rural areas with a high prevalence of premature infants. Here's a summary of the key points achieved by the anticipated MCD-CNN: Developing a system for accurate identification of ROP in preterm infants using classifiers trained with dense learning. This work employs a customized CNN to train a dataset specifically for detecting ROP zones with infants in preterm period. An overall accuracy of 88.82% was achieved by employing an MCD-CNN classifier which aggregates predictions from multiple models. The above system thus enhances the prediction of premature retinopathy fundus images using dense network model to be used for intelligent portable screening device.

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