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ORIGINAL RESEARCH ARTICLE

Catalyzing early intervention: A robust deep learning approach for detecting retinopathy of prematurity and plus diseases in infants

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ABSTRACT

Retinopathy of prematurity (ROP) is a major cause of childhood blindness, requiring precise and prompt diagnosis. This paper presents a new method that uses deep convolutional neural network (DCNN) models—VGG19, ResNet101, and DenseNet169—to identify illnesses in ROP fundus images. 2776 pictures from the Al-Amal Eye Centre were included in the dataset, with an equal number of normal and plus illness cases. The models underwent thorough training and evaluation, with VGG19 emerging as the most accurate, with an impressive 97.07% accuracy. The study emphasizes the potential benefits of using these models to improve ROP screening programs by offering a consistent and effective method of diagnosis that can greatly impact clinical decision-making. This research enhances the field of neonatal ophthalmology and provides vital insights for enhancing patient care in managing ROP.

Keywords: DCNN; ResNet101; DenseNet169; VGG19; retinopathy of prematurity; fundus images; plus disease

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1. Introduction

One of the most common reasons for blindness in children is retinopathy of prematurity (ROP), a vascular proliferative disease[1–4]. In the eyes of premature infants, ROP is among the most life-threatening conditions that can develop[5]. Newborns with a low birth weight and a birth duration of fewer than 32 weeks are at risk for retinopathy of prematurity, or ROP (less than 1.5 kg)[6–8].

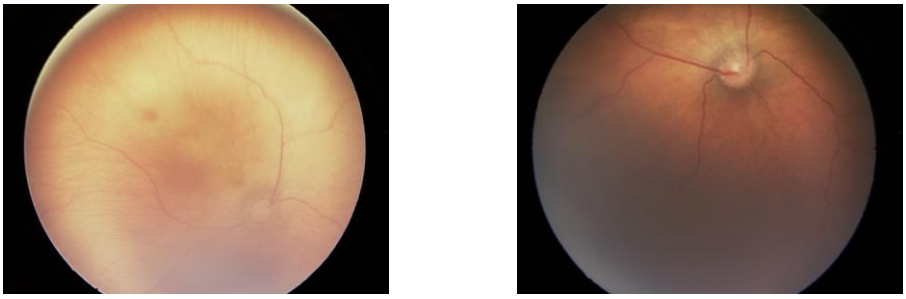
According to the 1984 recommendations put forward by the International Classification of Retinopathy of Prematurity (ICROP)[9], 1987[10], and 2005[11], Based on the presence or absence of the plus illness shown in **Figure 1**, ROP is classified. Stages (1–5) and zones can be assigned to ROP based on where it is found in the body (1–3).

The following is the outline for this paper: Methods using deep learning to diagnose ROP are discussed in Section 2 (plus disease). Section 3 shows examples from our dataset and explains the framework of our proposed most accurate method. Section 4 discusses the contrasts between the algorithms, while Section 5 concludes.

Medical imaging interpretation and triage have been greatly enhanced by artificial intelligence (AI) inspired by the complex

human neurological system, enabling more accurate disease detection and objective patient assessments by less-trained personnel[12]. Deep learning models have enabled substantial progress across various computer vision applications, such as picture categorization, object recognition, image segmentation, and disease detection.

With the advent of deep network architectures and easy access to large amounts of data, artificial intelligence (AI) has been proposed to relieve the burden on medical specialists[13]. Since 2012, deep learning algorithms have used CNNs for image classification, with impressive results in disease detection[14]. CNNs have been successfully used in the diagnosis of skin cancer[15], lung cancer[16], glioma[17], brain tumour[18], pneumonia[19], and breast histopathology[20]. Since 2012, deep learning algorithms have used CNNs for image classification, with impressive results in disease detection[21–23]. The primary challenge in medical image analysis is the lack of large training data sets and annotations for medical pictures.



(a) **(b)**

Figure 1. Retina images of the normal and plus disease of ROP. **(a)** normal; **(b)** plus disease[8].

Diagnosing and treating ROP is complex and presents various obstacles. Conventional diagnostic techniques depend significantly on manual assessments conducted by experienced ophthalmologists, leading to subjectivity and inconsistency in results. This not only creates difficulties in ensuring regular and prompt evaluations but also burdens healthcare resources, particularly in areas with little availability of specialized ophthalmic knowledge[4]. Moreover, the changing comprehension of ROP requires flexible diagnostic methods that can adjust to different presentations and levels of severity.

Given these limitations, emerging technologies, including deep learning models, show promise in tackling the intricacies of ROP diagnosis. By automating the diagnostic process and offering objective assessments, these models could transform ROP screening, enhance diagnostic precision, and enable prompt therapies.

This study seeks to enhance ROP diagnosis by introducing a strong deep learning method for detecting plus illnesses in ROP fundus photos. We aim to improve diagnosis accuracy and establish uniform and efficient screening procedures by utilizing three different DCNN models: VGG19, ResNet101, and DenseNet169. This research has significant significance for pediatric ophthalmology by demonstrating how modern technologies can be used into real-world clinical settings to enhance outcomes for premature newborns susceptible to ROP.

2. Related work

Extensive study has been conducted on retinopathy of prematurity (ROP), utilizing diverse methods for its diagnosis and categorization. This part offers a thorough review of current methodologies and emphasizes the distinctive features of our suggested methodology.

Brown et al.[24], A CNN-based DL approach was developed and evaluated in 2018 to diagnose ROP at three stages: Normal, pre-plus disease, and plus disease. The DCNN was taught using data from 5511 retinal pictures. Three experts agreed on a final image grade for each image, and a single expert provided a clinical diagnosis, yielding a total of four RSDs for each image (i.e., normal, pre-plus disease, or plus disease). The method was tested and validated on 100 photos taken at random using a 5-fold cross-validation procedure.

Pictures were taken at eight different universities as part of the Imaging and Informatics in ROP (i-ROP) cohort study. A panel of eight ROP specialists evaluated the deep learning technique. RSD classified 4535 individuals as normal (82.3%), 805 as having a pre-plus illness (14.6%), and 172 as having a plus condition (3.1%). Images of the retina were included in the 5511. The average (standard deviation; 0.01) area under the receiver operating characteristic curve was 0.94 for normal (versus pre-plus disease or plus illness) diagnosis and 0.98 for plus disease (against normal or pre-plus disease) diagnosis (0.01). The algorithm's performance in detecting Plus disease in a test using 100 retinal pictures was 93% sensitive and 94% specific. One hundred percent sensitivity and 94% specificity were achieved in diagnosing pre-plus sickness or worse. The approach outperformed 6 of 8 domain-specific ROP experts and achieved a quadratic-weighted k value of 0.92, putting it ahead of RSD on the same test set. This fully automated approach successfully diagnosed ROP plus disease with the same or higher accuracy as human experts. Newborns at risk of ROP can benefit from improved diagnosis, monitoring, and prognosis.

In 2019, Redd et al.[25], developed a neural network to rate the severity of retinal vascular anomalies on a scale from 1 to 9, allowing for more precise diagnosis (i-ROP plus score). A reference diagnostic based on a consensus model was used to establish the overall category of ROP disease. A second set of 100 rear photos was collected and analyzed by experts to determine the extent of ROP. They analyzed the 4861 tests taken by 870 kids. One-hundred and fifty-five examinations had a type 1 ROP reference diagnostic consistent with normalcy (3 percent). When identifying cases of type 1 ROP, the area under the receiver operating curve for the i-ROP deep learning (DL) vascular severity score is 0.960. With a cutoff i-ROP DL score of 3, diagnostic performance for type 1 ROP was 94% sensitive, 79% accurate, 13% positive, and 99.7% negative. There was a remarkable correlation between the overall ROP severity and the total ROP severity in the expert rank order. For the i-ROP DL vascular severity score, the Spearman correlation coefficient was 0.93 (p0.0001). After being educated primarily on posterior pole vascular morphology, the i-ROP DL system automatically identifies diagnostic categories and total disease severity.

In 2019, Tan et al.[26], ROP.AI was a deep learning system that can automatically detect retinopathy of prematurity (ROP) plus disease in fundal pictures, according to a recently published study. There are 3487 images in a local database used for the scheme. One ROP professional graded all the photos in the training collection, and another expert graded the test set. To double the number of images, Data augmentation was used to pre-process the images for training. In image recognition and feature focus, CNNs were used. Then the photos were graded and categorized into normal and disease plus. The RMSProp optimizer created this approach to maximize the output by altering the operating points. To show the generality and accuracy of ROP, the researchers included 26 pre-plus pictures in the test set after the system was established. Since the early stages of illness identification, AI can potentially improve prognosis. The technique has shown to be highly accurate in both diagnosis and illness, and it has the potential to be used in quantitative ROP analysis.

In 2020, Mao et al.[27], conducted automatic diagnosis and established quantitative analysis for more diseases. The machine makes a diagnosis choice and quantitatively analyzes the illness's usual features, allowing doctors to evaluate and make their best decisions. The deep study system divided the retinal vessels and the optical disk (OD). Based on the segmentation of the vessel, plus disease, tortuosity, width, fractal dimensions, and vessel density were automatically assessed. With a 97.8 percent specialty in diagnosing plus illness, 95.1 percent was reached by the trained network. The sensitivity and specificity to detect pre-plus or worse were 92.4% and 97.4%.

Huang et al.[28] applied transfer learning to five deep neural network architectures in 2020. The severity of the disease was classified; the VGG19 model showed 98.82 percent accuracy in predicting the severity of the disease with 100 percent and 98.41 percent sensitivity and specificity, respectively. To check the reliability of the VGG19 model, they conducted a 5-fold cross-validation on the datasets and found that the VGG19 model exhibited high accuracy in predicting ROP. These results may help promote computer-aided diagnosis

growth.

Nazar et al.[23] focuses on tackling the obstacles associated with identifying Retinopathy of Prematurity (ROP), a primary cause of permanent pediatric blindness. The current diagnostic method depends on subjective grading, which is time-consuming and susceptible to mistakes. The paper suggests utilizing a deep learning approach with transfer learning models and a fusion classification technique to improve accuracy and efficiency. Three deep convolutional neural network models (ResNet50, Densenet161, and EfficientNetB5) were trained on the photos. The separate models attained accuracy ratings of 69.78%, 80.57%, and 81.29% in their respective categories. The study suggests that the method created has the ability to improve the accuracy and efficiency of ROP diagnosis. Early identification and treatment with this method may decrease the likelihood of childhood vision loss. The results indicate that the suggested deep learning approach, which includes transfer learning and fusion classification, shows potential for enhancing ROP diagnosis and leading to improved outcomes for premature infants.

Originality and contribution of our study

Our study specifically concentrates on detecting positive illnesses in ROP using fundus pictures, unlike other methods. Three unique deep convolutional neural network (DCNN) models, VGG19, ResNet101, and DenseNet169, were trained using a comprehensive dataset from the Al-Amal Eye Centre. These models were selected for their shown efficacy in a range of computer vision tasks.

Our main contribution is the thorough assessment of these models, with VGG19 standing out as the most precise, attaining an astonishing accuracy of 97.07 percent. Our study is distinguished by the thorough training on a large dataset and the in-depth measurement of performance indicators such as sensitivity, specificity, and area under the ROC curve. The confusion matrices offer a detailed perspective on the model's predictions, displaying both accurate classifications and misclassification tendencies.

Our study highlights the particular difficulties presented by ROP and centers on detecting additional disease, a crucial feature of pediatric ophthalmology. Deep learning models, particularly VGG19, show promise in providing precise diagnoses for ROP, which can improve patient care and medical diagnostics.

3. Methodology

3.1. Implementation of DCNN models

Three renowned DCNN models, VGG19, ResNet101, and DenseNet169, were used to detect plus illnesses in retinopathy of prematurity (ROP) fundus pictures. Details regarding the implementation of each model are outlined below:

3.1.1. VGG19 architecture and parameters

VGG19, a 19-layer deep network, was chosen for its established success in picture categorization tasks. The design has several convolutional layers, each succeeded by max-pooling layers. Batch normalization and ReLU activation algorithms were utilized following each convolutional layer to introduce non-linear behavior.

Parameters:

- Input Size: 224 × 224 pixels;
- Convolutional layers: 16 convolutional layers organized in five blocks;
- Fully connected layers: Three dense layers;
- Activation function: ReLU;
- Optimization: Stochastic Gradient Descent (SGD);
- Learning rate: 0.001;
- Loss function: Binary cross-entropy.

3.1.2. ResNet101 architecture and parameters

ResNet101, a variant of the ResNet architecture, is known for its deep structure and skip connections, addressing the vanishing gradient problem. The network comprises 101 layers, and residual connections facilitate the flow of gradients during training.

Parameters:

- Input size: 224 × 224 pixels;
- Residual blocks: 101 layers organized into four blocks;
- Activation function: ReLU;
- Optimization: Adam optimizer;
- Learning rate: 0.0001;
- Loss function: Binary cross-entropy.

3.1.3. DenseNet169 architecture and parameters

DenseNet169, a densely connected convolutional network, fosters feature reuse through dense blocks, promoting efficient parameter utilization. The architecture includes densely connected blocks, transition layers, and a global average pooling layer.

Parameters:

- Input size: 224 × 224 pixels;
- Dense Blocks: Four dense blocks;
- Transition layers: Three transition layers;
- Activation function: ReLU;
- Optimization: Adadelta optimizer;
- Learning rate: 0.001;
- Loss function: Binary cross-entropy.

3.2. Dataset and implementation

3.2.1. Data

The photos were taken at the Al-Amal Eye Center Private Clinic in Baghdad, Iraq. The photographs were captured by skilled professionals using a RetCam3. This specialist facility has been providing ROP screening services for an extended period. 2776 fundus pictures were captured with ROP screening from 2015 to 2020. Various measures were implemented to address potential biases in the dataset. The dataset was preprocessed to standardize image dimensions and resolution, reducing inter-image variations. Data augmentation methods, like random horizontal flipping and rotation, were used to avoid overfitting and enhance the diversity of the training dataset. The dataset for this research was gathered from many sources, comprising images of patients with different ages, genders, and ethnic backgrounds. It is essential to utilize comprehensive and inclusive datasets for medical image analysis. It is crucial to acknowledge and address any potential biases in the dataset when analyzing and interpreting results.

3.2.2. Image labelling

The research involves two senior ophthalmologists who have more than 15 years of experience in treating individuals with ROP. The professionals categorized the fundus photos as either normal or sick. The two ophthalmologists sorted the photos separately and then compared them to identify any inconsistencies in the labeling process to determine if the specialists assigned specific images to different labels. The labels were collaboratively organized after specialists discussed, and the photographs were then labeled.

3.2.3. Dataset partitioning criteria

The dataset was divided into training, testing, and validation sets to aid in model training and thorough

evaluation. **Table 1** illustrates the random allocation of photos among these groups, guaranteeing a fair distribution of both normal and diseased cases. The criteria for partitioning were as follows:

- Training set (70%): The training set, which makes up 70% of the overall dataset, consisted of 915 normal photos and 1027 images showing disease.
- Validation subset (20%): The test set, comprising 20% of the overall dataset, consisted of 262 normal photos and 294 images with the disease, and was used as an independent dataset to evaluate the model.
- Validation set (10%): The validation set, used for fine-tuning and optimization, comprised 10% of the overall dataset, consisting of 131 normal photos and 147 images with disease.

Table 1. ROP datasets.

	Normal	**Plus disease**
Train set (70%)	915	1027
Test set (20%)	262	294
Validationt set (10%)	131	147
Total	1308	1468

This partitioning technique sought to balance training on a big dataset and validating and testing on separate subsets to assure the model's generalization performance.

3.2.4. Cross-Validation approach

We improved the reliability of our model evaluations by using a 5-fold cross-validation technique on the training set. The process entailed partitioning the training set into five equal folds, utilizing four folds for training and one for validation in each iteration. The cross-validation method was iterated five times, with each fold used as a validation set exactly once. The average performance metrics from these folds provide a reliable approximation of our models' capability.

3.2.5. Preprocessing

The fundus images were initially captured at a resolution of 640 × 480 pixels but were resized to 224 × 224 pixels before being fed into our deep learning models. 2220 patient data was used for training, excluding photos that were unclear, blurry, or dark from the study. We examined fundus images displaying multiple stages of retinopathy of prematurity (ROP) in a single infant, ensuring that there was no overlap between the training and test datasets. The dataset was divided into three parts: 20% for testing, 70% for training, and 10% for validation. Choose the optimal model based on its performance on the validation set to prevent overfitting, as indicated in **Table 1**.

3.2.6. Data augmentation

Overfitting may arise during training if the model is trained with inadequate data. Data augmentation is utilized to enhance the current training dataset by adding new retinal fundus images. New datasets were generated through the process of data augmentation. Multiple image improvement techniques were experimented with, such as rotation, width adjustment, height adjustment, zoom, and horizontal flip. Expanding the training dataset by a factor of seven resulted in a substantial 22,178 test samples.

3.2.7. Implementation

Intel CoreTM i7-5500 processor, 2.40 GHz, 16 GB RAM, was used to run the entire algorithm. Windows 10 was used throughout, and Python 3.9.5 was installed.

4. Results and discussion

Three distinct models were used in this investigation; these models were chosen from a larger pool of available categorization models (each of which has a unique number of layers), such as VGG19[29],

ResNet101[30], DenseNet169[31]. Our primary goal was to pick these DNN models to detect ROP disorders. Based on these results, the model with the highest accuracy is (VGG19).

4.1. Model performance metrics

Table 2 presents a summary of different performance measures for each DCNN model, such as accuracy, sensitivity, specificity, precision, recall, F1-score, area under the curve (AUC), and receiver operating characteristic (ROC) values.

Table 2. Performances evaluation of the three deep neural network models.

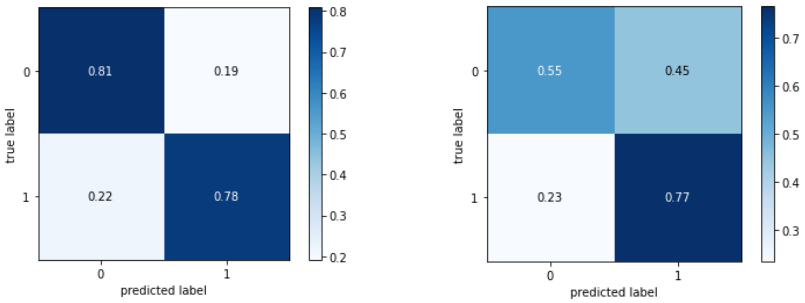
Architecture	VGG19	DenseNet169	ResNet101
Accuracy	97.07	82.21	79.73
Sensitivity	0.99	0.80	0.74
Specificity	0.98	0.82	0.79
Precision	0.98	0.81	0.77
Recall	0.98	0.81	0.77
F1-Score	0.98	0.81	0.77
AUC	0.98	0.81	0.77
ROC	0.98	0.81	0.77

4.2. Comprehensive analysis

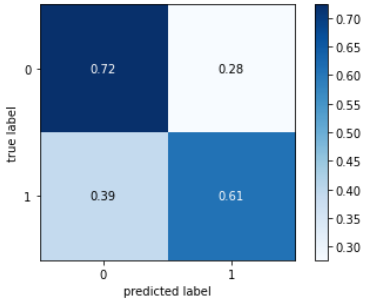
The effectiveness of our model system VGG19 in determining between the plus illness and normal classification of ROP from fundus images was assessed. The outcomes demonstrated that the system had a sensitivity of 0.99, specificity of 0.98, and accuracy of 97.07 percent. AUC and ROC values of 0.98 and F1 scores of 0.98 are also used to rank ROP illnesses (**Table 2**). The system's efficiency was also measured against the outcomes of two additional models (ResNet101, DenseNet169). The accuracy of ResNet101 was 79.73 percent, and that of DenseNet169 was 82.21 percent.

4.3. Confusion matrices and ROC curves

The specific assignments of distinct guesses for each image in three confusion matrices in **Figure 2**. The rows include the anticipated labels for the samples, whereas the columns contain the actual labels. The percentage of photos correctly assigned to each category is displayed along the diagonal of the heat map. Misclassification frequencies and types are displayed in the plots' non-diagonal elements.



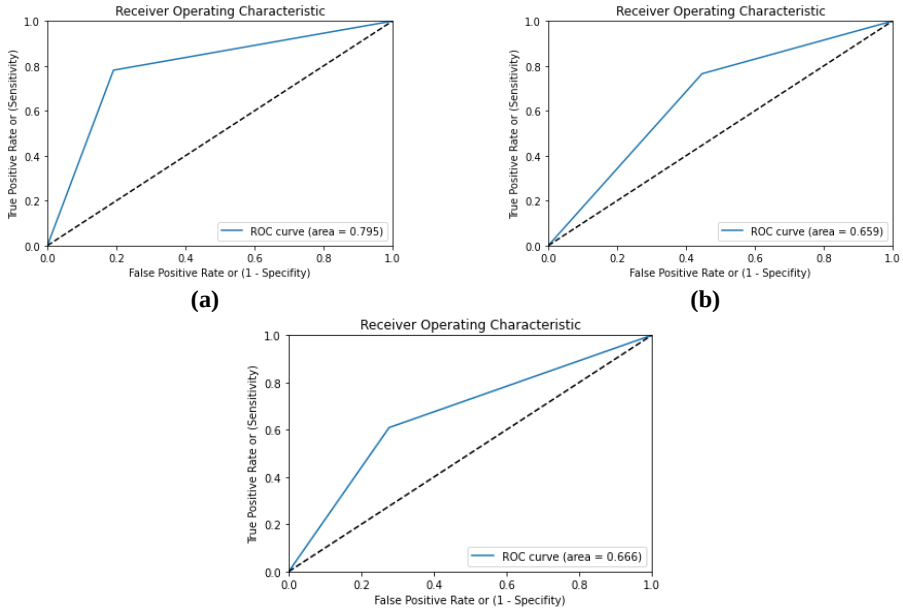
(a) **(b)**



(c)

Figure 2. Confusion matrixes for the three deep neural network models. **(a)** VGG19; **(b)** DenseNet169; **(c)** ResNet101.

Figure 3 shows the ROC curve for the algorithms detecting ROP zones. The ROC for VGG19, DenseNet169, and ResNet101 algorithms were 0.98, 0.81, and 0.77, respectively.



(a) **(b)**

(c)

Figure 3. Receiver operating characteristics (ROC) curves for algorithms detecting diseases of ROP. **(a)** VGG19; **(b)** DenseNet169; **(c)** ResNet101.

4.4. Discussion

VGG19 consistently performs better than DenseNet169 and ResNet101 across several performance parameters, as shown in the full analysis. The excellent sensitivity, specificity, accuracy, recall, and F1-score jointly demonstrate the effectiveness of diagnosing ROP from fundus pictures. The results are consistent with the aim of improving early intervention by precisely detecting diseases.

It is important to recognize possible limitations such differences in image quality and the necessity of a varied dataset for strong model generalization. Future endeavors should prioritize enlarging the dataset, exploring different DCNN structures, and engaging with medical professionals for additional validation.

The study concludes that VGG19 is a good deep convolutional neural network model for diagnosing ROP, showing better performance than other architectures. This study adds to the expanding knowledge base on utilizing deep learning for pediatric ophthalmology and highlights the possibility for improved patient care with precise and objective diagnosis.

5. Conclusion

In summary, using fundus pictures for the detection of ROP illnesses showed significant promise for the

VGG19 DCNN model after training on a solid dataset. In this study, three different deep neural architectures were used to diagnose ROP in premature infants, and the one with the best accuracy was chosen for further study (VGG19). According to our findings, the VGG19 was 97.07 percent accurate in identifying ROP illnesses. To assist push medical reform forward in light of the changing circumstances, we want to devote our future efforts to expanding our training dataset and developing improved algorithms.

5.1. Clinical significance

The importance of our findings is their potential influence on ROP screening programs and the improvement of patient care in neonatal ophthalmology. The VGG19 model has shown great accuracy in detecting diseases, particularly those classified as plus diseases, indicating its promise as an advanced diagnostic tool. This could simplify the screening procedure for clinicians by providing a more objective and efficient way to identify infants at risk for ROP.

5.2. Practical utility in real-world screening programs

The suggested deep learning models have practical value in real-world ROP screening processes, providing numerous benefits. The automated models decrease the need for manual examination, allowing for a quick and consistent evaluation of fundus images. This could be extremely beneficial in fast-paced clinical environments, where prompt and precise diagnosis is crucial.

The VGG19 model's excellent sensitivity and specificity make it a reliable screening tool. Precise recognition of both healthy individuals and those with additional medical conditions is crucial for prompt intervention and personalized treatment strategies. The model's performance, demonstrated by the ROC curve and AUC values, highlights its effectiveness in distinguishing different illness states.

5.3. Impact on clinical decision-making

Incorporating our advanced deep learning algorithms into current ROP screening techniques could transform clinical decision-making. These models could help clinicians identify infants that need closer monitoring or early intervention by offering impartial and reliable evaluations. This could optimize resource allocation to ensure that infants at higher risk receive quick attention.

5.4. Future directions and medical reform

In the future, we will concentrate on enlarging our training dataset and improving the algorithms to boost the accuracy and generalization abilities of the models. These models have the potential to significantly impact medical advancements in neonatal ophthalmology. We aim to enhance the ROP diagnosis process and enhance outcomes for preterm newborns by smoothly incorporating cutting-edge technologies into clinical workflows.

Author contributions

Conceptualization, NS, MK, and NH; methodology, NS, MK, and NH; software, NS; validation, NS, MK, and NH; formal analysis, NS, MK, and NH; investigation, NS, MK, and NH; resources, NH, AA and SA; data curation, NH, AA and SA; writing—original draft preparation, NS; writing—review and editing, NS; visualization, MK, NH and DB; supervision, MK, NH and DB; project administration, MK; funding acquisition, AS. All authors have read and agreed to the published version of the manuscript.

Conflict of interest

The authors declare no conflict of interest.

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