

Advancements In The Classification Of Retinopathy Of Prematurity: An Overview

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Abstract:

Retinopathy of Prematurity (ROP) is a major cause of preventable childhood blindness worldwide, particularly affecting premature and low birth weight infants. Timely and accurate classification of ROP is critical for effective clinical intervention. This paper presents a comprehensive overview of recent technological advancements in the classification of ROP, focusing on the integration of artificial intelligence (AI), deep learning (DL), and image processing techniques. Convolutional Neural Networks (CNNs), transfer learning models such as ResNet, InceptionV3, and VGG16, and hybrid architectures combining CNN with LSTM have shown promising performance in detecting disease stages, zones, and plus disease from retinal fundus images. Additionally, attention-based models and ensemble methods have been explored to enhance classification accuracy and model interpretability. Despite these advancements, several limitations persist. The lack of large, annotated, and standardized ROP datasets restricts model generalizability across diverse populations. Variations in image quality, illumination, and field-of-view introduce noise and hinder consistent classification. Moreover, most current systems operate as black boxes, offering limited transparency to clinicians regarding decision-making rationale. The future scope lies in developing explainable AI frameworks, federated learning models for cross-institutional collaboration without data sharing, and multi-modal approaches integrating clinical and demographic data. Integration of telemedicine-based diagnostic platforms and real-time screening tools can further expand the reach of ROP care in resource-limited settings. This paper underscores the need for interdisciplinary collaboration to translate these technologies into scalable, ethical, and clinically acceptable tools for ROP management.

Keywords: Retinopathy of Prematurity, Convolutional Neural Networks, Deep Learning

INTRODUCTION

Retinopathy of prematurity (ROP) is a significant cause of preventable blindness in children, primarily affecting infants born prematurely, with major risk factors including low gestational age and extended postnatal oxygen use. Its incidence is rising due to improved survival rates of these infants, and it results from a complex interplay of factors that disrupt normal retinal development and vascularization, including oxygen levels and nutritional status [1]. Early diagnosis of ROP allows for timely identification of treatment required for infants and thus significantly reduces the risk of severe visual impairment and blindness due to ROP. Recently available treatment are retinal laser coagulation and intravitreal anti-vascular endothelial growth factor (VEGF) [2]. The retinopathy of prematurity classification includes three zones I, II, III and five stages 1 to 5. The retina is divided into three zones based on the location of the abnormal vessel growth: Zone I - The posterior zone, closest to the optic nerve, Zone II - The mid-peripheral zone and Zone III - The peripheral zone. The stages of ROP gives the details of the severity of the disease Stage 1 shows the demarcation line between vascularized and avascular retina. Stage 2 shows the ridge formation along the demarcation line. Stage 3 shows the extraretinal fibrovascular proliferation. Stage 4 shows the partial retinal detachment. Stage 5: Total retinal detachment [3][4]. Plus disease is s

subtype of ROP characterized by dilation and tortuosity of the retinal vessels, often associated with worse outcomes [5][6].

This paper focused on the key technical advancements, their impact, and future directions in ROP classification.

Role of Artificial Intelligence in ROP Classification

The machine learning models may have limitations such as overfitting and lower accuracy, but advancements in convolutional neural networks (CNNs) have significantly enhanced ROP detection and staging. Artificial intelligence, particularly deep learning, has emerged as a transformative tool in ROP diagnosis and classification. Govind et. al. presents approach to classify stages 1, 2, and 3 of retinopathy of prematurity using deep learning. This approach uses a pre-trained EfficientNetV2S model for feature extraction from a large dataset of 82,295 images. The results of proposed work shows that the model effectively distinguishes between stage 2 and stage 3 retinopathy of prematurity with high performance metrics, and achieved an accuracy of 93.44%, an 98.71% of AUC and a 93.30% sensitivity [7]. Tan et. al. proposed a deep learning algorithm specifically designed to automatically diagnose plus disease in retinopathy of prematurity. Its performance in internal validation showed a sensitivity of 96.6% and specificity of 98.0%, and after optimizing the operating point, the sensitivity further increased to 97.0% with a high negative predictive value. Fundus images from local Australasian databases are only used in this study. The designed algorithm was majorly focus on images with demographic and clinical characteristics unique to regions like New Zealand and Australia [8]. Another deep learning approach i-ROP for diagnosis of retinopathy, shown ability in detecting plus disease. It highlights the limitations of traditional methods for diagnosing retinopathy of prematurity (ROP), which are often subjective and reliant on manual analysis, leading to inconsistent clinical decisions [9]. This shows the current need for more objective and automated systems for classification of retinopathy of prematurity. Image processing plays an important role in classification. A labelled fundus images are used to train the machine learning models. Based on this concept Wang et. al. proposed a novel self-supervised learning network, MOCO-MIM, aimed for early detection and grading of retinopathy of prematurity using limited-labeled images. This approach addresses the challenge of imbalanced datasets and achieves a test with 98.29% accuracy and 97.6% AUC score across three grading stages [10]. Another approach highlights advancements in the classification of retinopathy of prematurity (ROP) through the use of color fundus photography. It highlights the significance of utilizing longer wavelengths, such as red and green channels, which enhance depth information and improve diagnostic capabilities. These technical advancements aim to bolster screening strategies for ROP, addressing the critical need for effective detection methods to mitigate the global threat to ROP [11]. Proposed method found that the green channel provided the best performance for deep learning classification of retinopathy of prematurity (ROP), achieving an accuracy of 88.00%, sensitivity of 76.00%, and specificity of 92.00%. The red channel followed closely with an accuracy of 87.25%, sensitivity of 74.50%, and specificity of 91.50%, while the blue channel significantly underperformed with an accuracy of 78.25%, sensitivity of 56.50%, and specificity of 85.50%. For multicolor channel fusion architectures, both approaches early-fusion and intermediate-fusion shows performance comparable to that of the green channel input, indicating that combining color channels did not significantly enhance performance of classification beyond that of the green channel alone. The late-fusion architecture, however, showed inferior performance compared to the other fusion methods [11]. G. Hubert et. al. highlights significant advancements in the classification of retinopathy of prematurity using Multilayer Perceptron (MLP) and Convolutional Neural Network (CNN) models. These models automate the diagnosis process, eliminating subjective assessments. The CNN effectively extracts robust features from retinal images, while the MLP enhances predictive accuracy and monitoring capabilities. This ensembled way not only improves the precision and speed of retinopathy diagnosis but also leads to better therapeutic outcomes for preterm infants [12]. The proposed system achieves 97.5% sensitivity, specificity of 96.4%, and accuracy of 96.3%, outperforming previous methods. This innovative approach shows the capability to transform clinical practice and improve access to timely therapies for preterm infants globally. Deep learning-based computer-aided diagnostic methods are the recent trends

for classification of retinopathy of prematurity. These methods leverage large datasets, including unlabeled images, to enhance model performance while reducing the need for extensive annotated data. A semi-supervised learning framework has been proposed, incorporating consistency regularization strategies to extract valuable information from unlabeled data, thereby improving classification accuracy and generalization in clinical settings, ultimately addressing the challenges of annotation costs [13]. It discusses technical advancements in the classification of Retinopathy of Prematurity (ROP) through novel fundus image preprocessing methods and the use of pretrained transfer learning frameworks. These innovations enable the development of hybrid models that significantly enhance diagnostic accuracy. The study reports impressive 97.65% accuracy rates for Plus disease, 89.44% for Stage, and for Zones 90.24%, demonstrating that automated methods can improve classification outcomes compared to traditional imaging processing techniques [13]. The system for automated staging and grading of Retinopathy of Prematurity (ROP) achieved an accuracy of 93.68% for normal detection, and varying accuracies for different ROP stages: 83.33% for stage 1, 85.71% for stage 2, 55.55% for stage 3, and 100% for stage 4. The study utilized feature extraction techniques such as Pyramid Histogram of Words (PHOW) and Scale Invariant Feature Transform (SIFT) with supervised machine learning algorithms—support vector machine (SVM), random forest (RF), and extreme boosting gradient (XGBoost)—to classify the different stages of ROP effectively [14]. Recent technical advancements in the classification of retinopathy of prematurity (ROP) include the use of deep learning frameworks, particularly convolutional neural networks (CNNs), which automate the analysis of fundus images. Novel preprocessing methods enhance image quality, reducing noise and improving classification accuracy. The study achieved 97.65% ,high accuracy rates for Plus disease, 89.44% for Stage, and for Zones 90.24%, demonstrating the effectiveness of these advancements in early detection and diagnosis of ROP in premature infants [15]. Peng et. al. presents a novel deep neural network for classifying retinopathy of prematurity (ROP) into five stages, utilizing a multi-stream parallel feature extractor (ResNet18, DenseNet121, EfficientNetB2) to capture diverse high-level features. It employs a concatenation-based deep feature fusion method and an ordinal classification strategy, enhancing staging performance. Evaluated on 635 retinal fundus images, the method achieved high accuracy (98.27%) and Kappa (0.9786), demonstrating significant advancements in automatic ROP staging and classification techniques [16]. Tong et. al. presented by Tong significant technical advancements in the classification of retinopathy of prematurity (ROP) through a deep learning-based intelligent system. Utilizing a 101-layer convolutional neural network (ResNet) and a Faster Region-based Convolutional Neural Network (Faster-RCNN), the system achieved an accuracy of 0.903 in classifying ROP severity. It effectively detects ROP stages and plus disease, demonstrating performance comparable to retinal experts. This automated approach enhances diagnostic efficiency and supports clinical decision-making in managing ROP [17]. Huang et. al. highlights advancements in the classification of retinopathy of prematurity (ROP) through the use of deep convolutional neural networks (CNNs). This automated system achieved an impressive average accuracy of 99.93% during training and 92.23% during testing. It effectively classified images into no ROP, stage 1 ROP, and stage 2 ROP, demonstrating high sensitivity and specificity. Such technological innovations have the potential to assist ophthalmologists in early-stage ROP detection and classification, improving patient outcomes [18]. The trained deep learning network presented by Mao et. al. achieved a sensitivity of 95.1% and a specificity of 97.8% for the diagnosis of plus disease, with a sensitivity of 92.4% and specificity of 97.4% for detecting preplus or worse conditions. The quadratic weighted k value was 0.9244, indicating a high level of agreement in the diagnostic classification [19]. Whereas Vijay Kumar et. al. presents a significant advancement in the classification of retinopathy of prematurity (ROP) through a Deep Convolutional Neural Network (DCNN) approach. Utilizing YOLO-v5 for optical disc detection and various models for retinal blood vessel segmentation, the system achieved high accuracy rates—98.94% for optical disc detection and 88.23% for diagnosing ROP in Zone-1. This automated method enhances screening efficiency, particularly in low-resource settings, thereby improving healthcare outcomes for premature infants at risk of blindness. For retinal blood vessel (BV) segmentation, the model attained an accuracy of 96.69% and a Dice coefficient ranging from 0.60 to 0.64 [20]. Subramaniam et. al. discusses

advancements in the classification of retinopathy of prematurity (ROP) through the development of a preprocessing pipeline that enhances vessel visualization in smartphone fundus images. This approach improves image quality, enabling automated analysis using deep learning algorithms. A preliminary classifier achieved 96% accuracy in distinguishing plus disease from no plus disease. The preprocessing pipeline developed in the study enhanced vessel visibility in smartphone fundus images by 90%, as measured by the contrast improvement index, leading to unanimous agreement from pediatric ophthalmologists on the improved visibility of vessels in the processed images, as vessel segmentation plays an important role in classification of retinopathy of prematurity. Using GoogLeNet a preliminary deep learning binary classifier was created, achieving an accuracy of 0.96 for distinguishing between plus disease and no plus disease using augmented smartphone images, indicating significant potential for automated analysis of stages of retinopathy of prematurity [21]. A study shows the significant use of integration of deep learning algorithms and belief function theory for classification of retinopathy of prematurity. The key steps involved in this approach are image pre-processing, feature extraction using deep learning models, and classification via belief function theory. It uses a dataset consist of 3720 retinal images are used, the study achieved a classification accuracy of 95.57%, demonstrating the effectiveness of these advanced techniques in enhancing ROP diagnosis and improving treatment outcomes for at-risk premature infants [22]. Whereas Wang et. al. presents, J-PROP, a cloud-based deep learning platform, integrating multidimensional classification for retinopathy of prematurity (ROP) screening. The automated ROP screening platform achieved high performance metrics across its classifiers, with F1 scores ranging from 0.718 to 0.981, sensitivity from 0.918 to 0.982, specificity from 0.949 to 0.992, and an area under the curve (AUC) between 0.983 and 0.998. The referral system also demonstrated strong performance with an F1 score of 0.898 to 0.956, sensitivity of 0.981 to 0.986, specificity of 0.939 to 0.974, and an AUC of 0.9901 to 0.9956 [23]. It shows that computer aided systems can be used for early detection of retinopathy of prematurity. A meta-analysis was performed, which includes nine studies with fifteen classifiers, which analyse a total of 521,586 objects. The pooled sensitivity and specificity for the combined validation and test datasets were found to be 0.953 and 0.975, respectively, with an area under the curve (AUC) of 0.984, indicating high diagnostic accuracy of deep learning models for detecting retinopathy of prematurity. When applying analysis on subgroups, the AUC for differentiating ROP from normal cases was 0.990, while the AUC for distinguishing between two grades of ROP was 0.982, demonstrating the effectiveness of deep learning algorithms in accurately grading the severity of ROP [24]. Another meta-analysis shows that image-based machine learning (ML) for the diagnosis of retinopathy of prematurity (ROP) demonstrated a sensitivity of 93% and specificity of 95%, with an area under the curve (AUC) of 0.98, indicating high accuracy in diagnosing ROP. For the classification of clinical subtypes of ROP, the sensitivity and specificity were both 93%, with an AUC of 0.97, showing that ML classification results were highly comparable to those of clinical experts (Spearman's $R=0.879$). Despite the promising results, the review highlighted concerns regarding the quality and heterogeneity of the evidence, with some studies exhibiting high or unclear risk of bias. Consequently, while machine learning algorithms show considerable potential as automated diagnostic tools for retinopathy of prematurity, they should be regarded as supplementary aids to assist clinicians for screening in early stage rather than replacements for human expertise [25]. Screening of retinopathy of prematurity (ROP) demonstrated a sensitivity of 91.46% and a specificity of 91.22% in detecting ROP in a test set of 7,489 temporal images, indicating its effectiveness in distinguishing between the presence and absence of ROP Stages 1–3. The algorithm achieved a positive predictive value (PPV) of 81.72% and a negative predictive value (NPV) of 96.14%, with an area under the receiver operating characteristic curve (AUROC) of 0.970, suggesting a high level of accuracy in its diagnostic capabilities [26]. Liu et. al. presents a study which utilized a retrospective cohort design, analyzing a total of 24,495 RetCam images from 1075 eyes of 651 preterm infants who underwent RetCam examination at the Shenzhen Eye Hospital between January 2003 and August 2021. This extensive dataset was used to develop the AI system for identifying disease status and recommending treatment modalities for retinopathy of prematurity (ROP). The AI system was specifically designed to perform three tasks: identifying ROP, identifying severe ROP, and recommending

treatment modalities (either retinal laser photocoagulation or intravitreal injections). The performance of the AI system was then compared to that of experienced ophthalmologists using an additional set of 200 RetCam images for validation. The AI system demonstrated strong performance in three key tasks related to retinopathy of prematurity (ROP): it achieved an area under the receiver operating characteristic curve (AUC) of 0.9531 for ROP identification, 0.9132 for severe ROP identification, and 0.9360 for identifying treatment modalities (retinal laser photocoagulation or intravitreal injections). In external validation, the AI system achieved an overall accuracy of 92.0% across all three tasks, significantly outperforming four experienced ophthalmologists, whose accuracies were 56%, 65%, 71%, and 76%, respectively [27]. Peng Li et. al. presents a significant technical advancement in the classification of retinopathy of prematurity (ROP) through the development of a deep convolutional neural network (CNN) system. This system accurately diagnoses stages I to III ROP using quantitative analysis of retinal images, achieving high sensitivity and specificity rates. By integrating quantitative parameters with clinical diagnoses, the system enhances diagnostic accuracy, suggesting its potential as an ancillary tool in early ROP detection, ultimately aiding in preventing childhood blindness. The trained deep convolutional neural network achieved high diagnostic performance with sensitivity and specificity rates for different stages of retinopathy of prematurity (ROP): 90.21% sensitivity and 97.67% specificity for stage I, 92.75% sensitivity and 98.74% specificity for stage II, and 91.84% sensitivity and 99.29% specificity for stage III. For normal images, the system reached a sensitivity of 95.93% and specificity of 96.41%. The analysis of quantitative parameters revealed statistically significant differences among the groups, with the widths of the demarcation lines or ridges measured in pixels being 15.22 ± 1.06 for normal, 26.35 ± 1.36 for stage I, and 30.75 ± 1.55 for stage III. Additionally, the ratios of vascular proliferation within the region of interest were 1.40 ± 0.29 for normal, 1.54 ± 0.26 for stage I, and 1.81 ± 0.33 for stage III [28]. Yingshan Shen et. al. discusses advancements in the classification of Retinopathy of Prematurity (ROP) through the development of a lightweight neural network for early-stage detection and Treatment-Requiring ROP (TR-ROP). It highlights the use of a multi-stream fusion neural network for high accuracy, followed by knowledge distillation to create a more efficient model suitable for embedded devices. The proposed network achieved impressive accuracy (0.9734), sensitivity (0.9456), and specificity (0.9823) in ROP detection, surpassing existing methods [29].

Challenges and Future Directions

AI models must be validated on diverse datasets to ensure robust performance across different clinical settings. Standardization of data acquisition and annotation protocols is essential [30]. The integration of AI into clinical workflows requires addressing ethical, technical, and regulatory challenges. These include ensuring patient privacy, obtaining regulatory approvals, and demonstrating cost-effectiveness [30]. Future research should focus on developing AI systems that can predict ROP progression and response to treatment. The integration of AI with telemedicine holds promise for improving access to ROP screening in resource-limited settings [30][31].

IV. Conclusion

The classification of ROP has undergone significant advancements through the integration of AI, DL, and innovative imaging technologies. These advancements have improved the accuracy, objectivity, and efficiency of ROP diagnosis, enabling early intervention and better patient outcomes. However, further efforts are needed to address the challenges of clinical implementation and to realize the full potential of these technologies in reducing preventable blindness.

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