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# A Deep Learning Framework for Identifying Zone I in RetCam Images

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**ABSTRACT** Retinopathy of prematurity (ROP) has been one of the worldwide causes of blindness among children. Grading and treatment guidelines of ROP are mainly based on zone, stage, and plus disease. For serious ROP, identifying zone is more important than staging. However, identifying zone I from RetCam fundus images is not accurate and subjective by ophthalmologists. To address it, we develop a new deep learning framework to automatically identify zone I from RetCam images. Specifically, we train a deep convolutional neural network (DCNN) algorithm based on the RetCam images. The disc and macular center in terms of the threshold of intersection over union (IOU) were identified automatically. The algorithm is validated on fundus images and results show that zone I identification accuracy of 91% is achieved when the IOU threshold is 0.8. The obtained promising identification accuracy of zone I from the RetCam images indicates the potential applications in ROP grading, monitoring, and prognosis for infants.

**INDEX TERMS** Retinopathy of prematurity, deep convolutional neural network, optic disc, macular center, zone I.

## I. INTRODUCTION

Retinopathy of prematurity (ROP) is a vascular proliferative, blindness-causing disease, and has become one of the worldwide causes of childhood blindness [1]–[5]. ROP is one of the most dangerous and serious complications of premature infants' eyes [6], which can be better prevented in countries with high or middle income. The International Classification of ROP (ICROP) divides ROP by zoning, staging, and grading of plus disease [7]. The incidence of type 1 ROP is higher in developing countries [4] but lower in developed countries. It is only 6.1% in the United States and Canada [8]. Type 1 ROP is more serious and mostly occurs in zone I. zone I ROP occurs earlier and progresses more rapidly than zone II or III ROP [9], which is commonly found in the tiniest babies. These infants are particularly vulnerable to the severe stage of ROP. With the increasing number of high-risk of tiniest babies, the number of infants with zone I ROP is also increased [10]. This type of ROP may have different mechanism and prognosis from traditional ROP and perform more effectively treatment reaction to intravitreal injection of anti-VEGF agents [1]. Current clinical experience shows that the delay in diagnosis and treatment of zone I ROP may lead to extensive traction retinal detachment [11] and even endanger vision and lead to blindness. Early intervention and frequent follow-up are essential for continued ROP treatment and monitoring, which can significantly improve zone I ROP prognosis of children [12]. Ophthalmologists can determine the severity of ROP by observing whether the ROP symptoms have progressed to zone I [13]. For this reason, identify zone

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I from the retinal images is of vital significance [14] for early assessment and diagnosis of ROP severity.

In fact, the current status of ROP screening in China are as follows: 1) With China's two-children policy and the development of the neonatal intensive care unit, the survival rate of premature infants have been increasing as well as the ROP incidence rate [15]. Accordingly, the number of premature infants requiring screening has been increasing year by year [3], [16], [17]. 2) ROP screening and diagnosis require medical experience and a long training period for the young ophthalmologists. Clinical assessment of ROP mainly depends on the ophthalmologist's subjective interpretation of the symptoms, thus requires professional knowledge and it is too time-consuming. The missing and incorrect screening may lead to serious medical malpractice, which causes the unlikeness of ophthalmologists doing this work [3], [16]. As a result, there is a shortage of professional ophthalmologists in many countries and regions. Current telemedicine technology is under development and still unable to solve this problem [3], [18]. 3) The existing ophthalmologists highly rely on binocular indirect ophthalmoscope and wide-angle digital retinal imaging system (RetCam) in the ROP diagnosis of the premature infants [9]. The ICROP provides only qualitative signs rather than quantitative descriptions [19]. Since each ophthalmologist has his/her unique style of disease diagnosis knowledge and different level of experience, the ROP diagnosis is highly subjective, especially the zoning. To address it, automatic and consistent identification of zone I from the retinal images via the popular deep learning algorithm is highly desirable, which can also overcome the limitation of the traditional methods.

It is known that the deep learning algorithm via DCNN has been used to automatically diagnose cataract [20], glaucoma [21], [22], macular degeneration [23], and diabetic retinopathy [24]. Also, the deep learning algorithm has been used to automatically diagnose the plus disease of ROP and achieves satisfactory performance [16]. However, little relevant literature has been reported on automatic identification of zone I ROP. For this reason, we develop a new deep learning algorithm to identify zone I from RetCam images automatically. Ophthalmologists can identify zone I ROP by observing whether the ROP symptoms are the location inside zone I, which identified by the algorithm. Specifically, we devise a new deep learning algorithm based on the latest techniques. Our algorithm extracts image features via DCNN. Since the target category is shown in each pixel, the category detection, feature extraction, and image segmentation are conducted [1]. Namely, our algorithm contains four main parts: the DCNN, region proposal network (RPN), fully convolution network (FCN), and transfer learning. The DCNN is used to extract the deep features of the images [26]. RPN is employed to generate zone recommendations [27] for the region of interest (ROI) detection. To extract the deep feature map of the image, a deep residual network (ResNet) is adopted. Meanwhile, FCN performs the binary-value segmentation and classifies each pixel in each ROI to achieve target segmentation [28]. Furthermore, transfer learning is also used for model pre-training, which transfers the trained model parameters to the new model for performance boosting [29]. Our algorithm obtains the expression of data layered features via pre-trained models for high-level semantic classification. The low-level semantic features (e.g., edge, color) in the bottom layer of the model are fixed in different classification tasks [30]. Therefore, the learned model parameters can be transferred to a new model in a specific way, which can speed up and optimize the learning efficiency of the model and save time than learning from scratch [31].

We validate our algorithm on the RetCam fundus images from the premature infants screened in the Shenzhen Screening for Retinopathy of Prematurity Cooperative Group. The achieved the promising performance of our algorithm indicates that the automatic identification of zone I from fundus images has potential application in clinical practice to reduce the heavy workload of ROP screening and reduce the rate of blindness caused by misdiagnosis or missed diagnosis [3].

The rest of this paper is organized as follows. Section II describes the general overview of the proposed algorithm and detailed illustration of our dataset. Section III is dedicated to experimental results and comparisons. Finally, Sections IV and V present the discussions and conclusions, respectively.

## II. METHODOLOGY

### A. OVERVIEW

According to the ICROP, zone I consists of a circle, the radius of which extends from the center of the optic disc to twice the distance from the center of the optic disc to the center of the macula [7], [9]. In this study, an algorithm is designed to automatically identify the center of optic disc and macula, and then automatically identify zone I from RetCam images according to the center of the optic disc and the center of the macula. The study protocol was reviewed and approved by the institutional review board of the Shenzhen Eye Hospital, and written informed consent was obtained from the guardians of all participants.

### B. DATA SET

In our experiment, a total of 9800 RetCam images from 490 infants from January 2016 to May 2017 are collected for the training. All the RetCam images are preprocessed first before training. The preprocessing classifier developed in [32] is used to remove the unqualified images. A total of 90 images of highly blurred, dark or bright and non-fundus photographs are excluded for training. Images present only optic disc or macula are also excluded. Finally, we have a total of 2849 images in our experiment. All the remaining images contain both structures of optic disc and macula. A total of 582 images of 97 children had ROP. Of these, 276 Retcam images of 46 children were zone I ROP. The images are then divided into three sets: the training set contains 2394 images, the validation set contains 355 images, and the test

**TABLE 1. Summary of datasets used in our experiments.**

| | Training Dataset | Validation Dataset | Test Dataset | | | |
|---|---|---|---|---|---|---|
| Label category | Expert[a] | Expert | Standard[b] | Expert | Senior[c] | Junior[d] |
| No. of Images | 2394 | 355 | 100 | 100 | 100 | 100 |

[a]Expert indicates that the data set is labeled by an experienced ophthalmologist who has a professional level.
[b]Standard indicates that the data set is labeled by several professional ophthalmologists together, which is regarded as a validation standard.
[c]Senior indicates that the data set is labeled by a senior oculist-in-charge ophthalmologist who has a medium level.
[d]Junior indicates that the data set is labeled by a junior intern ophthalmologist or who has a primary level.

set contains 100 images. The training and validation set are used to train and validate the algorithm, while the test set is used to test the performance of the algorithm, respectively.

Each infant received a standard 10-position photograph (disc-centered images, macular-centered images, nasal images with the optic disc, lateral nasal image with optic disc but close to serrated edge, temporal images with the optic disc, temporal images without the optic disc, top image with the optic disc, top image without the optic disc, bottom image with the optic disc, and bottom image without the optic disc). According to the characteristics of the ICROP, this study can only select images with both disc and macular center. Each image's center of the optic disc and macula in the training set is previously annotated by six ophthalmologists according to the ICROP. All of the annotators have been engaged in ROP diagnosis and treatments for more than 10 years. Two of the annotators are the chief physicians and the remaining four are visiting doctors. In the training set, the 6 ophthalmologists annotated all the images individually. Each expert reviewed all experts' annotation and selected data with inconsistent labels. They discussed and the final result was determined by the most experienced expert. To facilitate the reignition of optic disc center and macular center, a circular frame with fix diameter to match the area of optic disc and macula rather than a point is used for annotating in the labeling system. According to the anatomical size of the optic disc and macula (the diameter of the newborns' optic disc is about 0.6 mm, and the diameter of the macula is slightly larger than that of the optic disc). The optic disc and macula of each image are annotated in the labeling system with fix 120 pixels and 160 pixels of circular frames, respectively. According to the center of the two circular frames, zone I of the fundus images is automatically annotated by the labeling system. The datasets used in this study are summarized in Table 1.

### C. DEEP LEARNING ALGORITHM

For classification problem, deep features can enhance the classification performance by extracting the in-depth and representative feature maps. The deep features can be extracted by the DCNN, where the parameters inside the network are calculated according to the expression of the network features of the upper layer. For example, after feeding an image into the DCNN, the first convolutional layer uses internal parameters to calculate the expression of the input features, such as edges, angles, curves. If the input of the second convolutional layer is the output of the first layer, the convolution of this layer combines low-order features through calculation and outputs high-order features, such as semicircle, quadrangle, etc. Therefore, the increase in network convolutional layers may extract more complex features. Deep learning uses back propagation algorithms to determine how to adjust the internal parameters of these networks and learn the characteristics of different network layers. The increasing network depth enhances the network expression, which has been experimentally demonstrated by Simonyan and Zisserman [33]. However, simply increasing the network depth can lead to the degradation problem. Namely, the increase of network depth will cause the saturation of accuracy, and its further increase will lead to a decrease in accuracy. To address it, we adopt the residual network (ResNet) to solve the problem of decreasing accuracy due to increasing network depth [34]. ResNet scans with 3x3 sliding windows and considers nine possible anchors in each sliding window location, which can extract the feature effectively.

In this study, when a RetCam image is inputted into the model, the deep convolutional layer of the model will extract the deep image features based on the optic disc and macula. According to the extracted features, the RPN network will predict the general position and category (belonging to foreground or background) of optic disc and macula on the feature map. Then, refined learning classifies the optic disc and macula (optic disc, macula or background) [1]. The bounding box regression suggested by fixed anchors obtains the region of interests (ROI). Then, the ROIs of different sizes selected for the ROI alignment operation are put into the full connection layer to judge the target classification and precise position. Meanwhile, FCN will conduct up-sampling on the selected locations of RPN prediction [28], and enlarge the selected area to the corresponding size in the original image, and then classify each pixel (belonging to the optic disc, macula or background), so as to separate optic disc and macula. Finally, a circular frame matching the area of the optic disc and macula was generated. Zone I was thus labeled by the model based on the center of the two circular frames according to ICROP. The transfer learning strategy is also used to enhance the performance, where the weights of the transfer learning are derived from the training results of Microsoft COCO dataset (http://cocodataset.org/). In this study, a multi-task loss function is defined for each sample in a rectangular window (labeled optic disc or macula boundary area). The loss function is composed of classification loss (Lcls), boundary box regression loss (Lbox) and mask

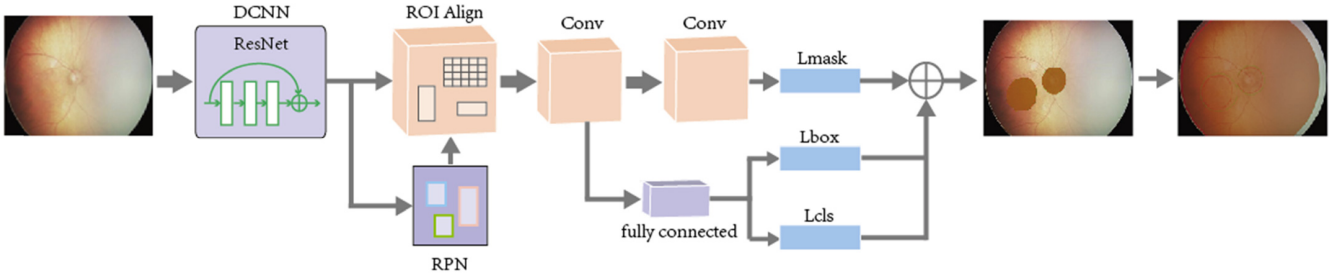



**FIGURE 1.** Block diagram of the proposed method. The position of optic disc and macula is identified firstly, and then the central point of optic disc and macula are calculated. Finally, zone I of images is calculated according to the center of optic disc and macula.

loss (Lmask), which are used to calculate the error between the output result of the model and the ground truth. The process is iteratively repeated until the error is no longer reduced, which means that the model output is closest to the ground truth. Accordingly, the target detection process is completed. After model training, the test set was used to test the prediction effect of the model on the new input data. The block diagram of the proposed method is shown in Fig.1.

### D. PERFORMANCE EVALUATION

In this study, 100 RetCam images were randomly selected to test the model, which were not included in the training set and validation set. Six ophthalmologists independently annotated the optic disc and macula of the fundus images in the labeling system. After that, zone I of the fundus image is annotated automatically in the labeling system according to the ICROP. The results of this study were quantitatively analyzed by calculating the effect of Intersection over Union (IOU). IOU is the coincidence rate of the candidate bound identified by the proposed method and the gold standard bound annotated by the six experts [31], which is formulated as

$$\mathrm{IOU} = \frac{Dectection\ result \cap Ground\ truth}{Dectection\ result \cup Ground\ truth}. \tag{1}$$

when evaluating the identification accuracy of the model, IOU of the optic disc, macula, and zone I were calculated, respectively. The identification accuracy of optic disc, macula, and zone I was calculated under different IOU thresholds. Accuracy is defined as the ratio of the correctly labeled samples to the total samples when the IOU is greater than or equal to a certain threshold. For example, when the IOU threshold is set to be 0.8, the training model is considered as accurate if the calculated IOU of the macula and optic disc is larger than or equal to 0.8, Zone I of RetCam images calculated by the model and expert labeling are defined as circle 1 and circle 0, respectively. IOU is calculated according to the coincidence between circle 1 and circle 0, and the accuracy of model identification in zone I of images was calculated under different IOU thresholds. If lower the IOU requirement, more sample will be identified as correct by the model. In other words, when the requirements for IOU value is low, the accuracy of model annotation improves.

### E. COMPARISON WITH CLINICIANS DIAGNOSIS

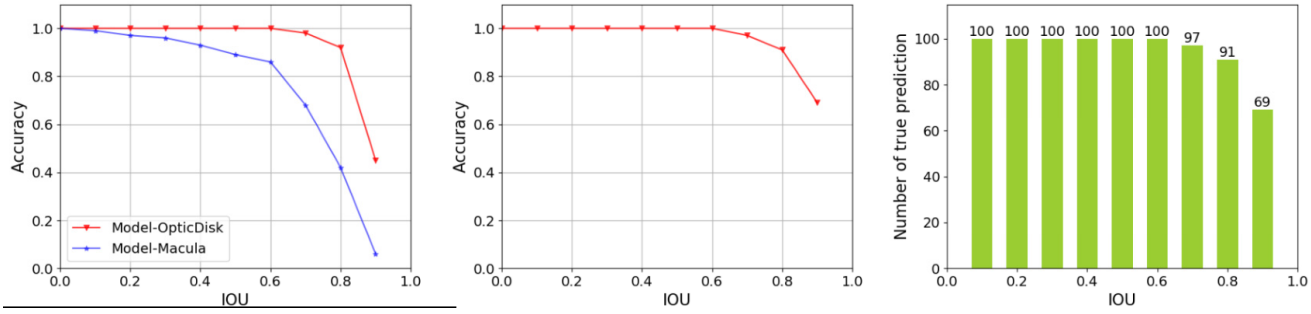
In this study, we divide the model evaluation into four groups: model group, the professional ophthalmologist group with expert experience, senior ophthalmologist group and junior ophthalmologist group. The model group is the one obtained from this study, the professor-level expert group is the chief ophthalmologist with more than 10 years' experience, the senior ophthalmologist group is the experienced retinal specialists, and the junior ophthalmologist group is the ophthalmic trainees. Each group labeled the optic disc and macula of the 100 test set images, and zone I of the fundus images was calculated according to the labeled circle of the optic disc and macula. The accuracy of optic disc and macula labeling in the four groups and the identification rate of zone I of retinal images were compared under different IOU thresholds.

## III. EXPERIMENTAL RESULTS

Six experts who annotate the training set discussed the value of the IOU. They agreed that when IOU of macula, optic disc and zone I is greater than or equal to 0.5, identification of optic disc, macula and zone I of the model is considered accurate, otherwise, it is inaccurate. Therefore, IOU threshold is set to be 0.5 in our experiment. Our algorithm is run on a GTX 1080TI GPU and takes 0.8s for each test image. The identification accuracy is defined as the ratio of the correctly labeled samples to the total samples when the IOU $>$ 0.5. We achieve an accuracy of 100% and 90% for optic disc and macula detection, respectively. Since our ultimate goal of this study is to identify zone I of RetCam images, and the label of the zone I is based on the label of optic disc and macula. To better understand the identification accuracy between them, the identification accuracy of optic disc, macula and zone I of the model were evaluated under different IOU thresholds.

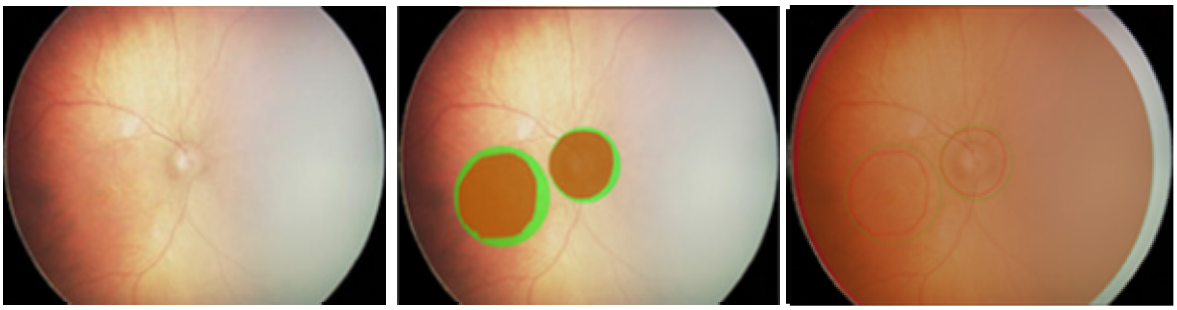
### A. ASSESSMENT FOR OPTIC DISC AND MACULA

Fig. 2 (a) illustrates the accuracy of the optic disc and macula detection under different IOU thresholds. The red solid line represents the accuracy of optic disc, and the blue solid line represents the accuracy of macula. When the IOU threshold is 0.8, the accuracy of optic disc is 90%, while the




(a) (b) (c)

**FIGURE 2.** Performance of different models under different IOU thresholds. (a) The accuracy of optic disc and macula in identification of fundus images under different IOU thresholds. (b) The accuracy of zone I in the identification of funds images under different IOU thresholds. (c) The number of true predictions by the developed model in identifying zone I of fundus images.



(a) (b) (c)

**FIGURE 3.** Output images of different models. (a) the original image; (b) the detection results of the optic disc and macula; (c) the identification results of zone I of retinopathy.

accuracy of macula is only 50%. From the original image, an ophthalmologist can clearly identify the optic disc. Since the development of macula in the newborn is incomplete, the recognition of macula needs professional ophthalmologist with rich experience and medical knowledge to make accurate diagnosis. Since the professional ophthalmologist labeled optic disc and macula according to medical standards and their rich experience, the model achieves promising performance built on the ophthalmologist's knowledge and experience. Therefore, the low accuracy of macula in our model is consistent with the practical clinic application. The accuracy of model detection of macular center is lower than that of optic disc center since the macula is more difficult to detect than the optic center. Zone I of the fundus images is determined by both the label of optic disc and macula. Thus, the IOU of optic disc and macula affects the accuracy to identify zone I of fundus images.

### B. ZONING ASSESSMENT

Fig. 2 (b) shows the accuracy of identifying zone I under different IOU thresholds using the proposed model. The vertical coordinate represents the accuracy, while the horizontal coordinate represents different IOU thresholds. It can be seen that when IOU threshold is 0.8, the identification accuracy of model for zone I is 91%. When IOU threshold is 0.9, the accuracy is 69%. Fig. 2(c) illustrates the number of correct quantities in identifying zone I of RetCam images under different IOU thresholds.

### C. EFFECT OF MODEL OUTPUT

Fig. 3 shows the effect of the model outputs. Fig. 3 (a) is the original image, while Fig. 3 (b) is the result of optic disc and macula detection. The red circular region represents optic disc and macula detected by the model, while the green circular region represents optic disc and macula marked by experts (The macula is on the left and the optic disc is on the right). Fig. 3(c) displays the identified zone I according to the center of optic disc and macula, in which the area within the green line is determined by zone I according to the center of optic disc and macula circular frame labeled by experts, and the area within the red line is the determined by zone I according to the center of optic disc and macula detected by the model.

### D. MODEL COMPARISON

Fig. 4(a) illustrates the accuracy comparisons among the proposed model and the ophthalmologist in recognizing optic disc and macula under different IOU thresholds. The standard refers to the validation set are based on the annotation of 6 ophthalmologists. Red, black, blue and green

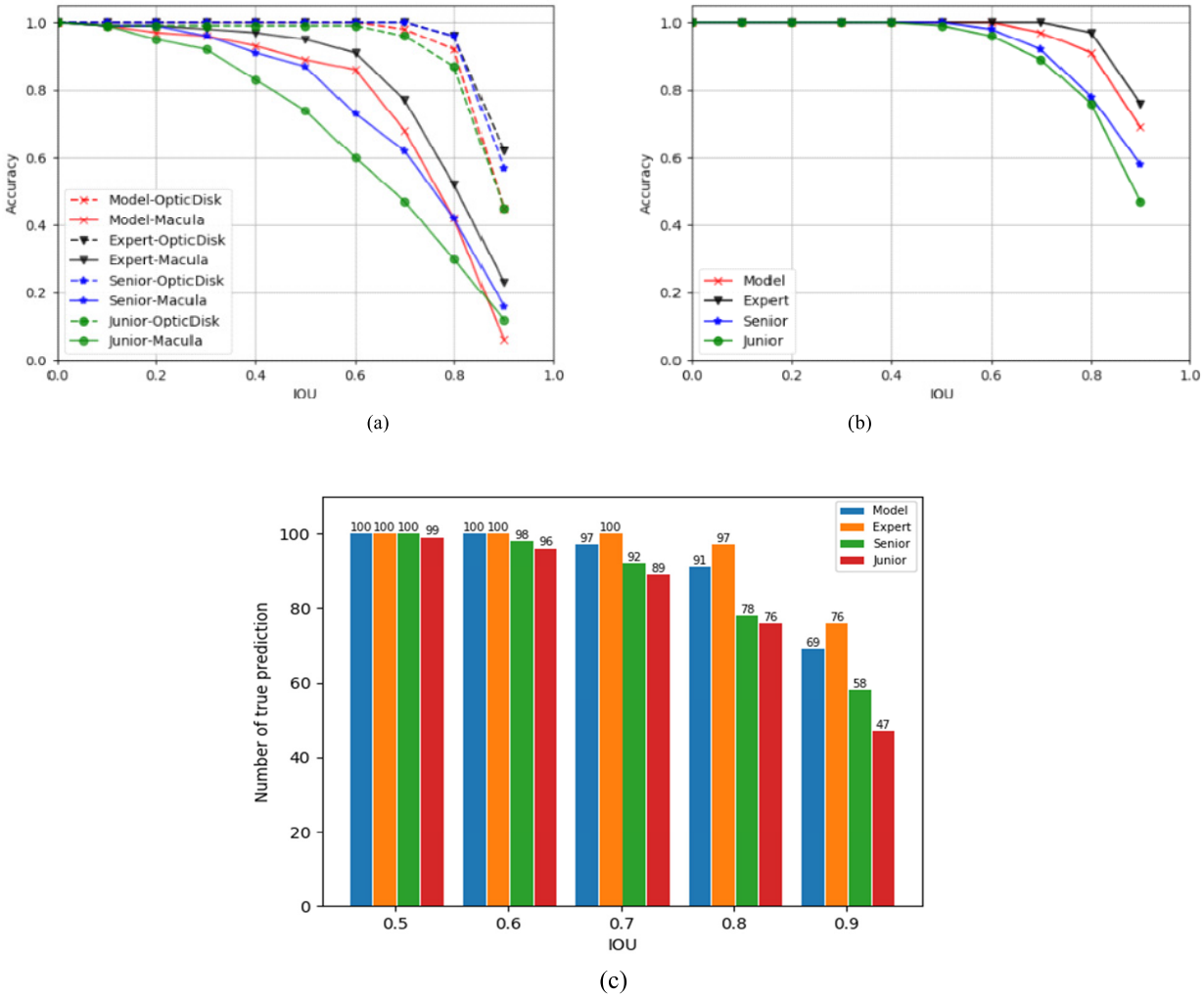



**FIGURE 4.** Results of the ophthalmologist and model using different IOU thresholds. (a) Accuracy of the model and the ophthalmologists to identify optic disc and macula under different IOU. (b) Zone I identification accuracy of the fundus images versus different IOU thresholds. (c) Number of true identification of the zone I samples versus different IOU thresholds.

represent the model, expert-level chief ophthalmologists, senior ophthalmologist, and junior ophthalmologist, respectively. The dotted line represents the optic disc and solid line represents the macula. It can be seen from the comparison results that the accuracy of the four groups for the detection of optic disc is similar. For macula detection, the accuracy of model is lower than the expert level, but it is higher than that of senior ophthalmologists and junior ophthalmologists. Fig. 4 (b) shows the accuracy of the model and the ophthalmologist to identify zone I of images under different IOU thresholds. Fig. 4 (c) shows the number of images when zone I is accurately identified by the model and ophthalmologists under different IOU thresholds. Red, black, blue, and green represent the model, chief ophthalmologists, senior ophthalmologists and junior ophthalmologists, respectively. The three figures show that experts achieve the highest accuracy in identifying zone I, and the accuracy of the model is similar to the expert level but higher than that of senior and junior ophthalmologists.

## IV. DISCUSSIONS AND LIMITATIONS

The ROP prognosis are based on zone I and II in terms of clinical features, which are quite different [35]. Compared with zone II ROP, zone I ROP is more quickly progressive to threshold ROP [9], [12], [17], [36], [37]. Treatment requiring ROP is defined as any stages with plus disease in zone I, stage 3 without plus disease in zone I, and stages 2 or 3 with plus disease in zone II. Most zone I ROP requires treatment. Even the partial zone I ROP does not need immediate treatment, the close follow-up is needed to prevent progression. Therefore, it is quite important to identify zone I from the RetCam images accurately [37].

In our experiment, with the deep learning algorithm, the accuracy to automatically identify zone I of RetCam images has reached the expert level. If we input a RetCam image of an infant into our framework, zone I can be identified automatically in 0.8s, which is achieved without manual segmentation and classification of fundus images. In literature, some researchers strongly recommend that strict

screening guidelines must be followed for prompt ROP treatment before vision-threatening via complications [17].

Our proposed method can identify zone I according to the ICROP, which facilitates an objective assessment of ROP severity for ROP diagnosis, treatment, and prognosis. ROP infants can therefore reduce irreversible visual damage. The popularity of the application is expected to change the way of diagnosing ROP in future and benefit premature infants worldwide.

In future, we will continue to use more data for the algorithm development. More data renders the identification of zone I with higher accuracy. Although some literature has reported that deep learning algorithm can automatically diagnose plus disease of ROP [16], few researches have been focused on accurately identifying zone I. This study utilizes the deep learning algorithm to automatically identify zone I of RetCam images. To the best of our knowledge, this is the first study on automatic identifying zone I. It is also noted that our proposed method can be extended for the diagnosis zone I ROP.

In spite of the achieved promising performance, the current framework still has some limitations. First, identifying zone I from RetCam images in ADS is based on the detection of the disc and the macula [7], [9], [19]. Therefore, the fundus image without the two structures cannot be analyzed. However, each infant is fully photographed in a standard 10 orientations during the screening, and at least three images contain two structures. Therefore, identifying zone I of RetCam images can be judged by the images containing two structures and the images with only the disc or macula can be identified based on the images containing two structures. This study chooses fundus images with 130 degree, which is unilateral bit image and cannot cover the zone I, II, and III, simultaneously. As a result, our method can only accurately identify zone I of RetCam images. zone II and III still need professional ophthalmologist to label. In this study, we identify zone I from RetCam images, rather than zone I ROP. However, we have previous publications regarding the ROP recognition. We can realize to identify zone I ROP based on our method and the Automated Screening System [32].

Second, our proposed method needs to explore the mosaic algorithm for diagnosis application. Images of the standard 10 position fundus images need to be automatically mosaiced and the model identifies zone of the mosaic fundus images. The mosaic panoramic images can be automatically divided into zone I, II, and III by the algorithm. It not only solves the problem that zone I in part of the images with optic disc or macula cannot be identified by our algorithm, but also solves the problem that the unilateral bit image cannot distinguish zone II and III. To improve the accuracy of identifying zone I, we also strive to combine medical knowledge, clinicians' experience, and optical knowledge to further improve model accuracy, which could even outperform the performance of the expert and would be potentially accepted by ophthalmologists, eventually.

Third, in this study, the optic disc and macular center of images were first detected by the algorithm, and then zone I was calculated according to the ICROP based on two structures [7], [9]. Therefore, the identification accuracy of zone I of images depends on the detection accuracy of optic disc and macula. By the annotated data, the algorithm can automatically determine the center of the optic disc and macula. However, the macula of the newborn is not fully developed, ophthalmologists are suffered from the subjectivity when marking fovea centralis. The more accurate annotated data can lead to higher model accuracy. The experts' level determines the model accuracy to some extent [24]. According to the data of training set, the developed model may deviate from the position of macula due to the subjectivity of the experts in macular annotation, which will eventually lead to a certain deviation of zoning results. For this reason, we will apply more RetCam images to train more robust model and reduce the influence of the experts' subjectivity.

Finally, our algorithm still can identify zone I of some images with low accuracy due to the low segmentation accuracy. It is believed that the difference of image clarity, resolution, and focal length will result in the image heterogeneity, which may also have some negative impact on the algorithm accuracy. This study has not explored ROP staging and diagnosing some special categories (e.g., pre-threshold disease, threshold disease, and AP-ROP). Future research and exploration by professional clinicians still need further development.

## V. CONCLUSIONS

A new deep learning framework is successfully developed to automatically identify zone I from RetCam images in infants. The model shows that an accuracy of 91% in zone I identification is achieved when the IOU threshold is 0.8. The promising identification accuracy results show its extensive application, which is expected to reduce the workload of ophthalmologists. However, compared with the existing ophthalmological examination, the efficiency and the algorithm feasibility in real clinical application still needs more in-depth observation and research [24]. Nevertheless, the algorithm provides new opportunities and directions for the grading of ROP. The algorithm can also be applied in the identification and screening of other retinal diseases, which require future exploration and research by clinicians. Our future work will focus on the further development of algorithms and the larger datasets for training, which will eventually push forward the medical reform in the new situation.

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