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Treatment and prevention of ROP in Shenzhen , China 2003 - 2018

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Shenzhen Eye Hospital

ROP Cooperative Group Shenzhen , China

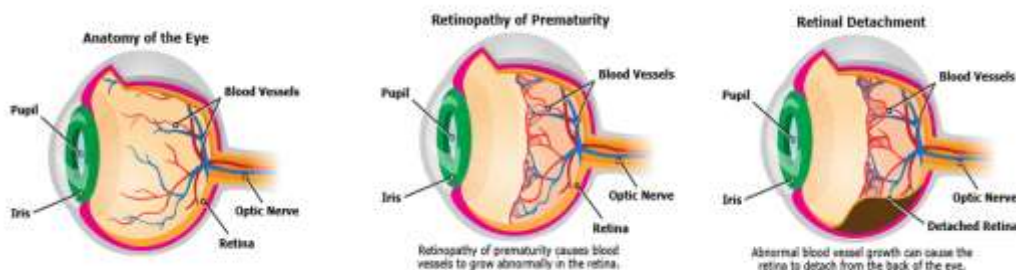
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1. Introduction

- ◆ Premature and low birth weight babies
- ◆ The main cause to lead blindness
- ◆ Timely screening and early treatment can avoid blindness



HARTNETT M E, et al. NEJM, 2012

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1.1 Introduction of worldwide ROP screening



Countries responding to the survey with ROP screening (77):

Countries responding to the survey without ROP screening (15):

Countries that could not be contacted or from which no response was received (102):

Countries with established ROP screening protocols (68):



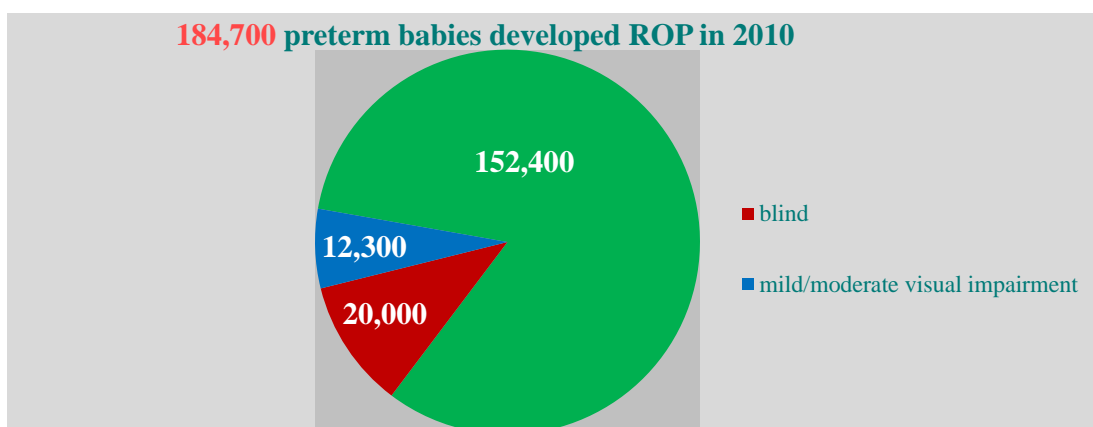
MORA J S, et al. BJO, 2018

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1.2 Worldwide ROP incidence



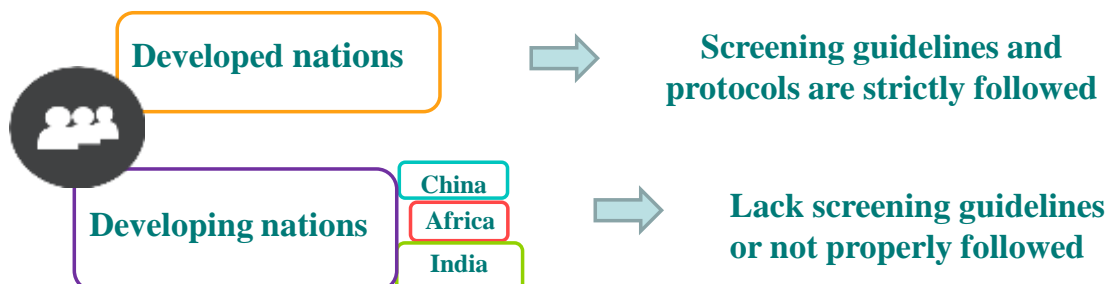
- BLENCOWE H, et al. Pediatric research, 2013
- SHAH P K, et al. World journal of clinical pediatrics, 2016

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- ◆ **65%** visually impaired from ROP were born in **middle-income regions**



- BLENCOWE H, et al. Pediatric research, 2013
- SHAH P K, et al. World journal of clinical pediatrics, 2016

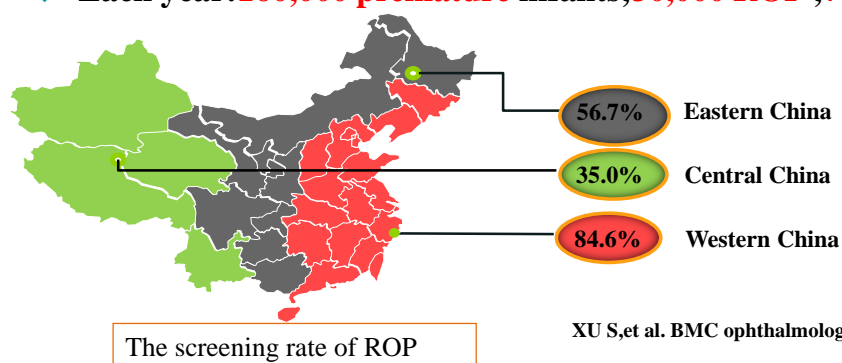
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1.3 ROP in China

- ◆ Economic development , resource **disproportion**
- ◆ ROP screening is in **imbalance**
- ◆ Each year: **160,000** premature infants; **30,000 ROP** ; **7,500 severe ROP**



XU S, et al. BMC ophthalmology, 2018

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1.4 Introduction of ROP prevention in Shenzhen

- ◆ **Major city** in China, bordering Hong Kong to the south
- ◆ In 1980, established as **China's first special economic zone**
- ◆ One of the **fastest-growing cities in the world** in the 1990s and the 2000s



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Ranked second on the list of “**top 10 cities to visit in 2019**” by Lonely Planet



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- ◆ Population: 20 million
- ◆ Newborns: 200,000/yr
- ◆ Prematurity: 10,000/yr
- ◆ ROP: 1500/yr
- ◆ Severe ROP: 50-100/yr



Zhang GM, et al. Chinese Journal of Ocular Fundus Diseases, 2008

2. ROP Screening in Shenzhen, 2003~2018

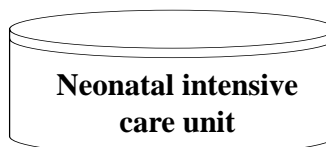
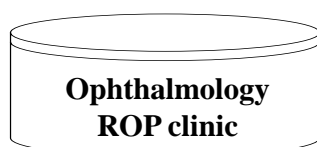
Three Stages		Jul, 2003 ~ Jun, 2005	<ul style="list-style-type: none">• Few screening• Cryotherapy
		Jul, 2005 ~ Dec, 2010	<ul style="list-style-type: none">• Standard screening• Comprehensive therapy
		Jul, 2011 ~	<ul style="list-style-type: none">• Integrated development



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ROP Screening by Cooperative Group

Shenzhen Eye Hospital + **Cooperative hospitals**



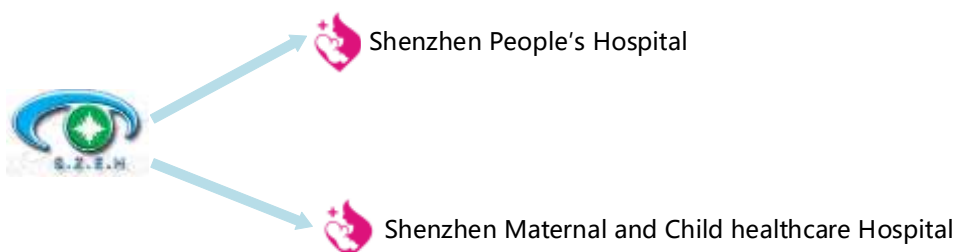
ROP Cooperative Group Shenzhen

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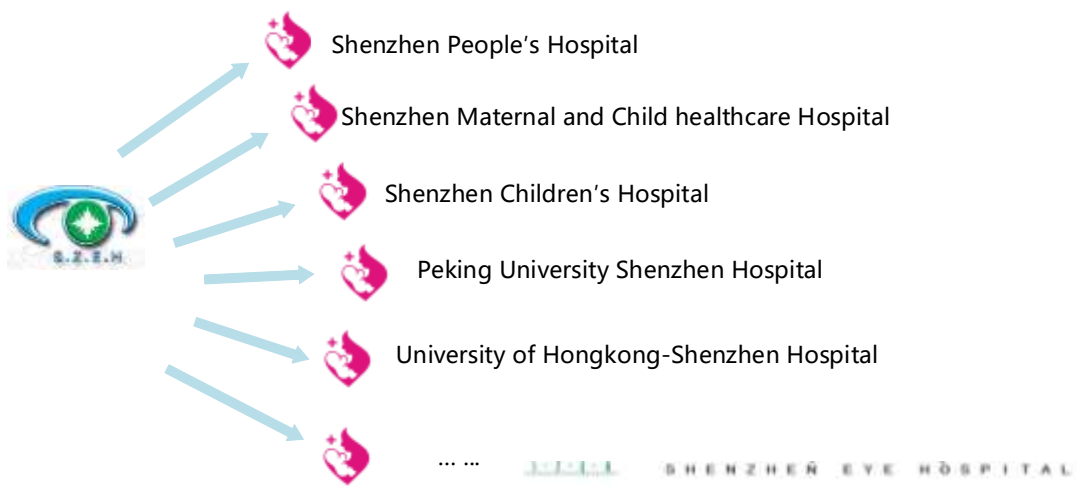
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The first stage: July, 2003 ~ June, 2005 Pattern: **1+2**



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The second stage: July, 2005 ~ Dec, 2010 Pattern: 1+18



The third stage: 2011 ~ Pattern: 1+32



Screening Strategy 1 : BOI combined with RetCam



Binocular indirect ophthalmoscope(BOI)



RetCam

Screening Strategy 2 : Ophthalmology combined with NICU



NICU bedside screening

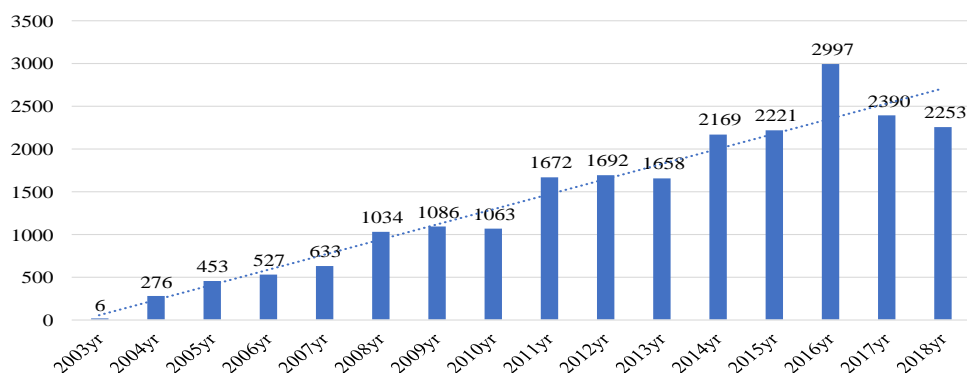


Ophthalmology clinic follow-up



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ROP Screening number per year(2013~2018)



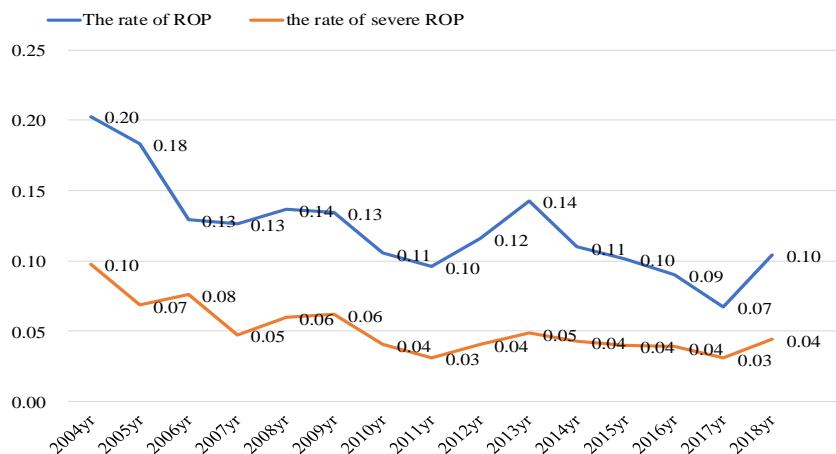
- Total ROP screening infants > **22,000**
- Treatment-required infants > **1,000**

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The rate of ROP and the rate of severe ROP per year



From 2004 to 2018

- ROP incidence decreased:
12% to 9%
- Severe ROP incidence decreased:
5% to 3%

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The earliest severe ROP case in Shenzhen

- ◆ Yuan XX
- ◆ Birth date: 2003/10/26
- ◆ Female
- ◆ Twin
- ◆ GA: 26w
- ◆ BW: 700g

2004/1/15 Cryo therapy



BCVA:

OD: -9.75DS/-4.50DC×4° → 20/20

OS: -8.50DS/-2.50DC×175° → 20/20

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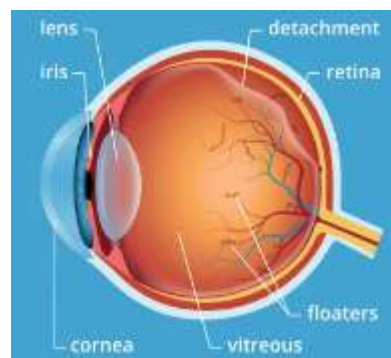
3. ROP treatment in Shenzhen

Main treatments:

1. Laser photocoagulation
2. Intravitreal injection of anti-VEGF agents

Which one is **better** ?

It' s **controversial** !





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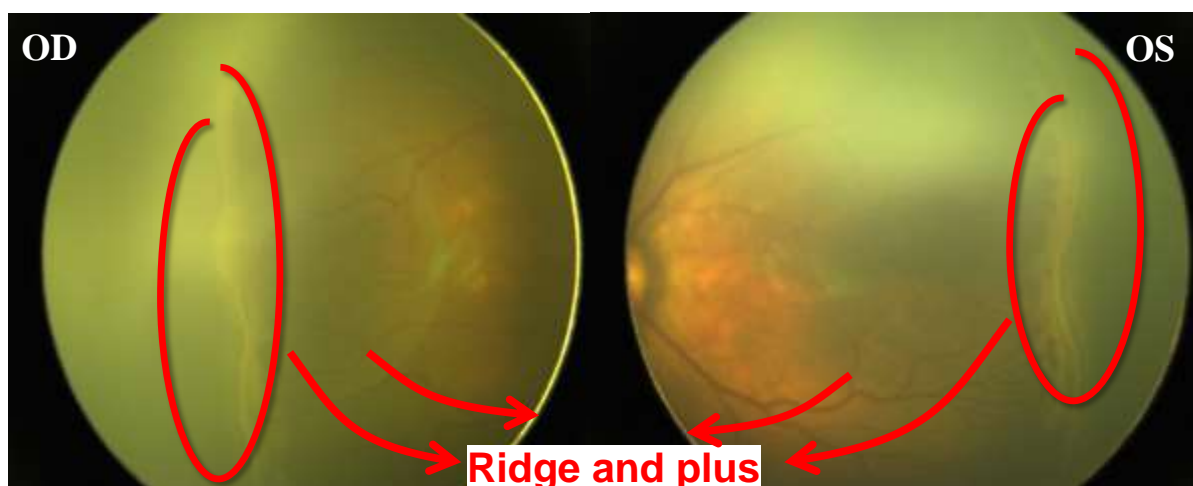
Case 1

- Li XX
- Male
- GA: 24 w
- BW: 670 g
- Natural birth

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Corrected GA 36W, RetCam Images

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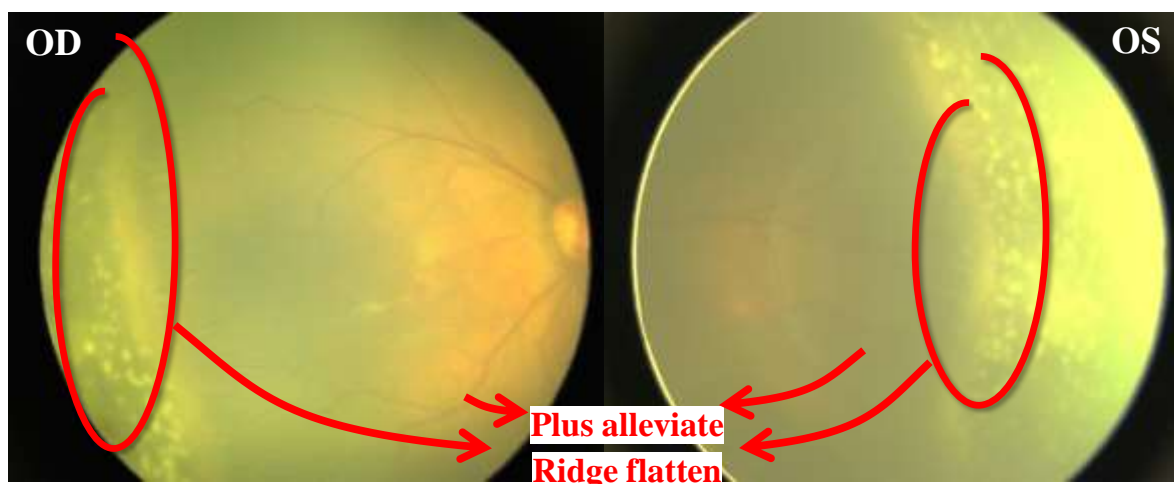
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- ◆ **Diagnosis: Threshold ROP ou**
- ◆ **Treatment: Laser photocoagulation ou**

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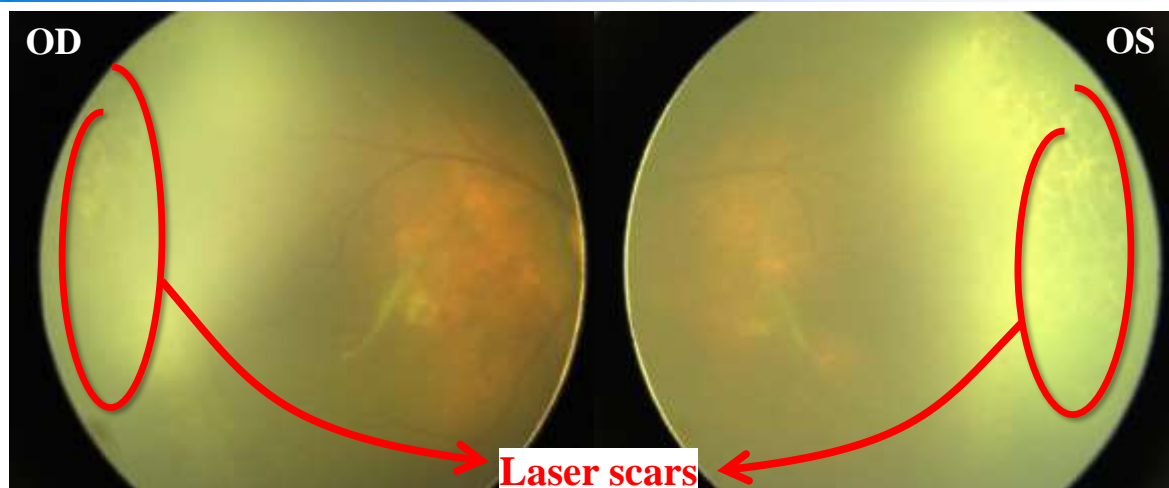


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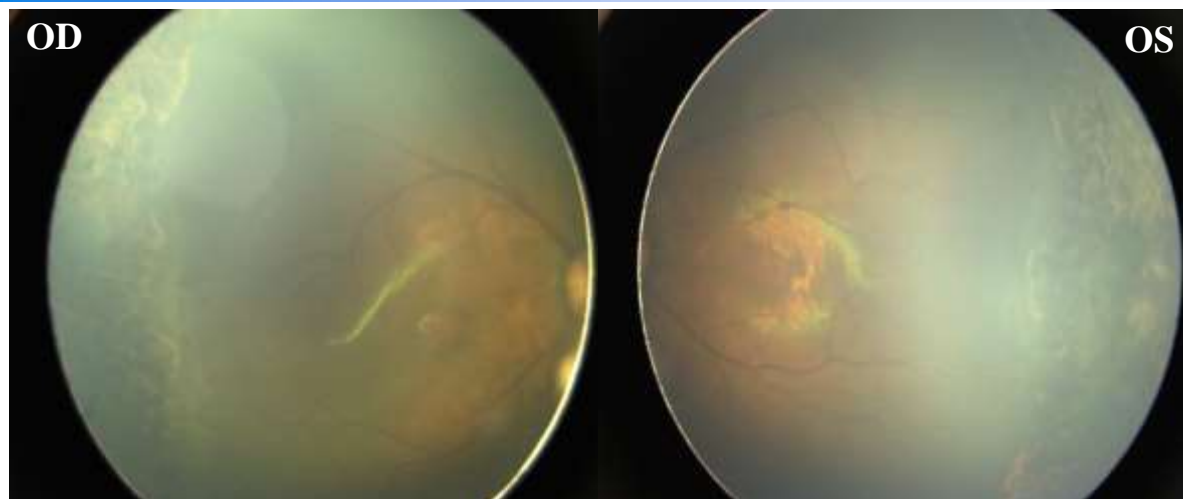


1 week after laser photocoagulation: ROP alleviated

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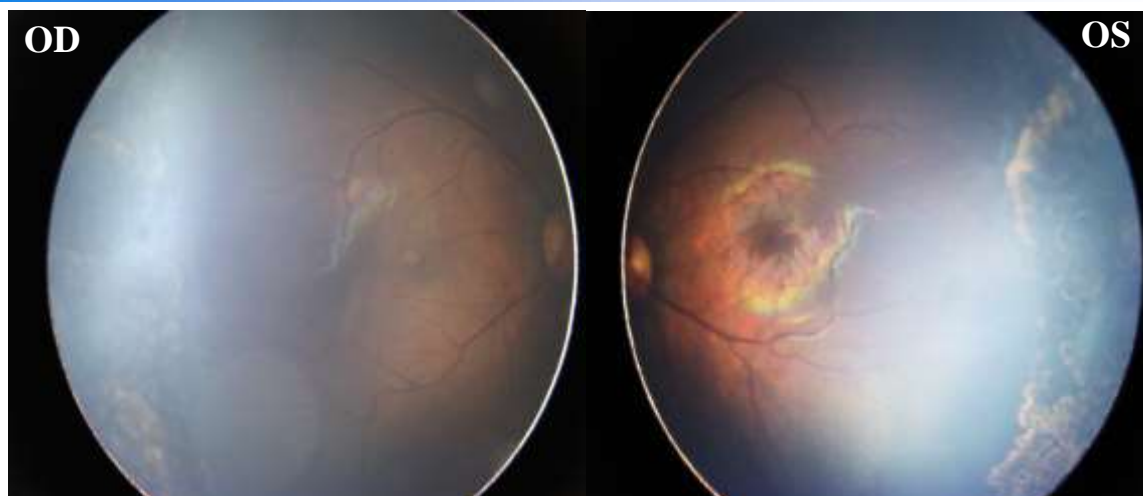
2 week after laser photocoagulation: ROP was controlled



1 mon after laser photocoagulation: fundus were stable



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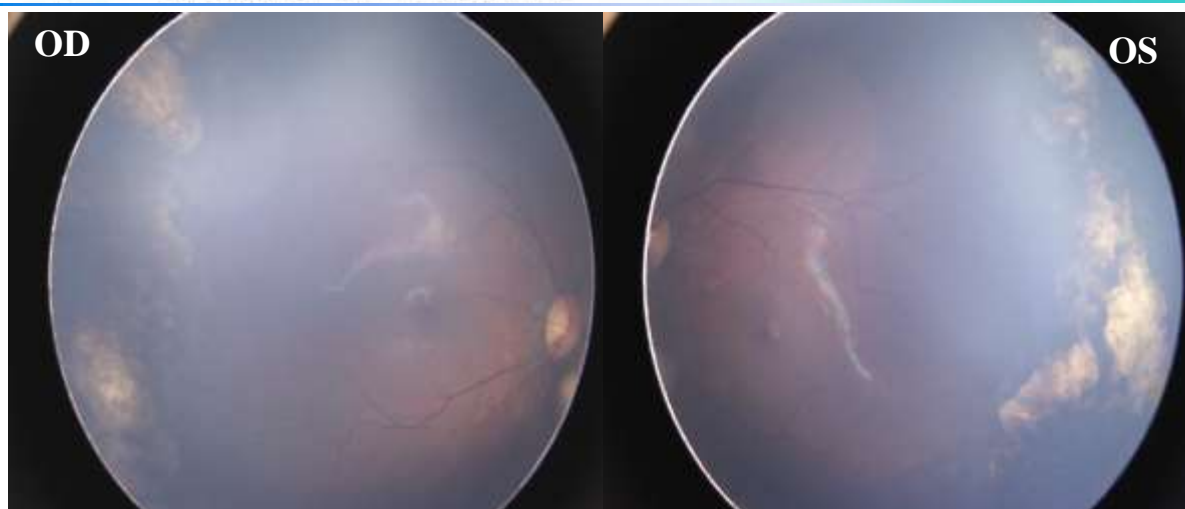


2 mon after laser photocoagulation: fundus were stable

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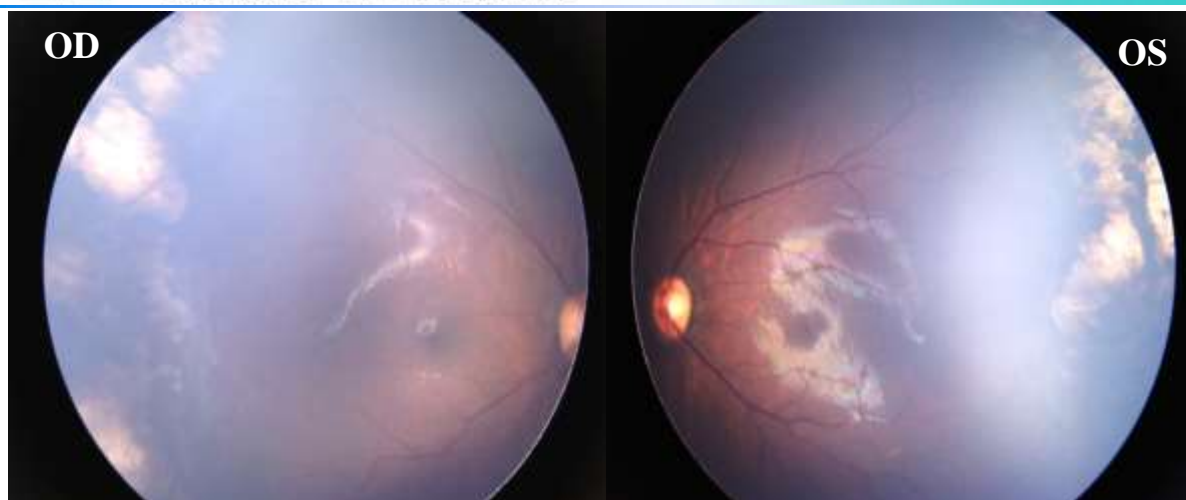


4 mon after laser photocoagulation: fundus were stable

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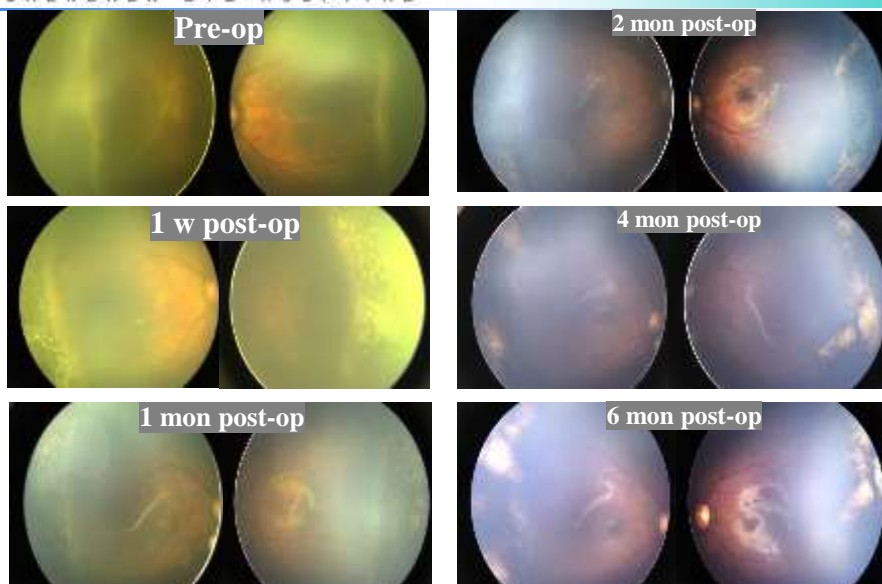


6 mon after laser photocoagulation: fundus were stable

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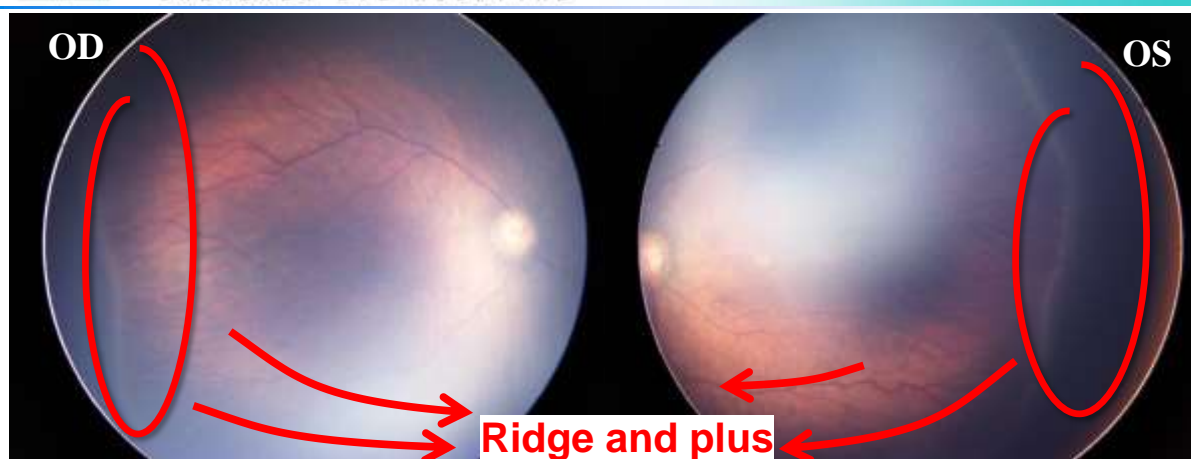
Case 2

- Hong XX
- Male
- GA 24w+2d
- BW 590g
- Cesarean section

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Corrected GA 36W, RetCam Images

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- ◆ **Diagnosis:** Type 1 prethreshold ROP
- ◆ **Treatment:** Intravitreal injection of Ranibizumab (IVR) ou

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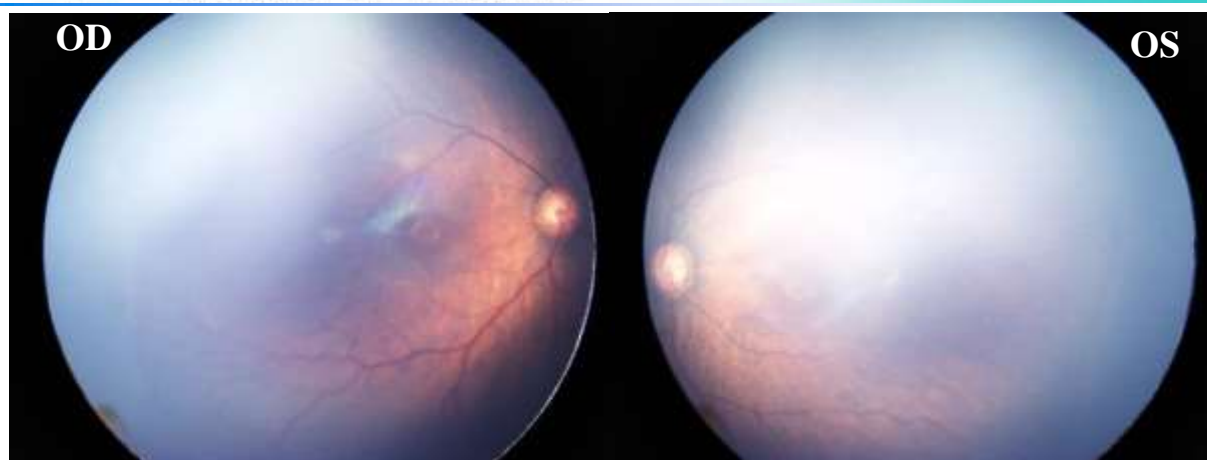


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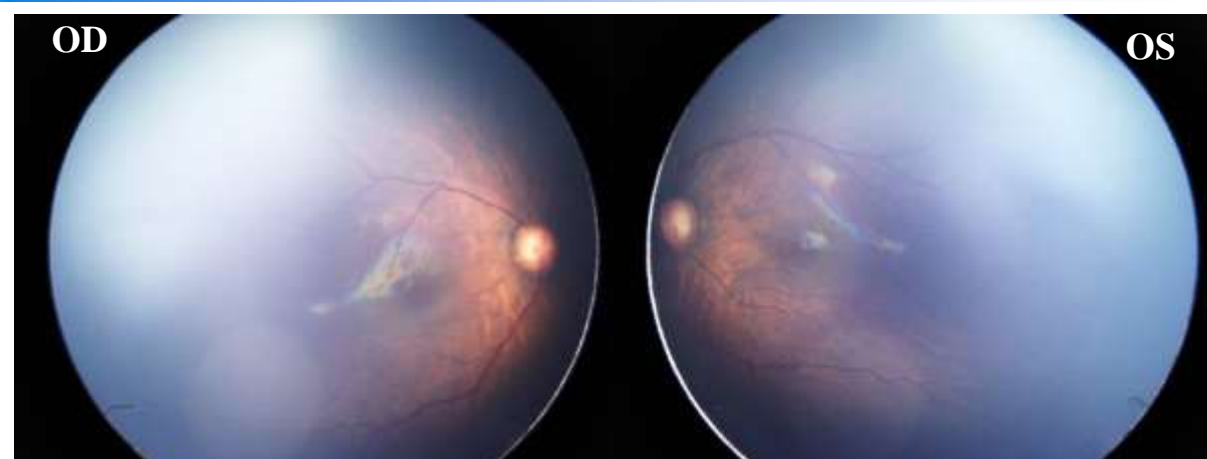


1 week after IVR: ROP were controlled

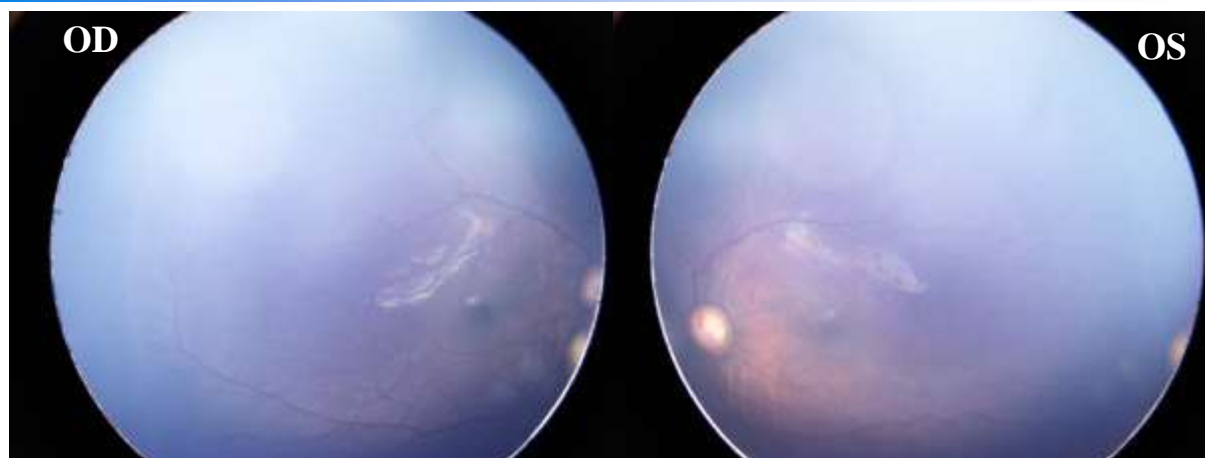
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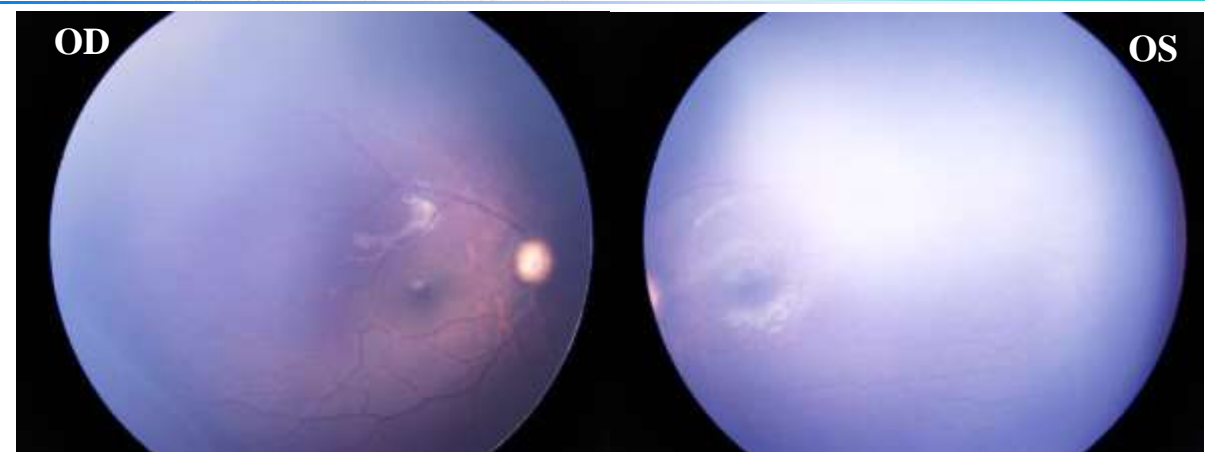
1 mon after IVR: fundus were stable



2 mon after IVR: fundus were stable



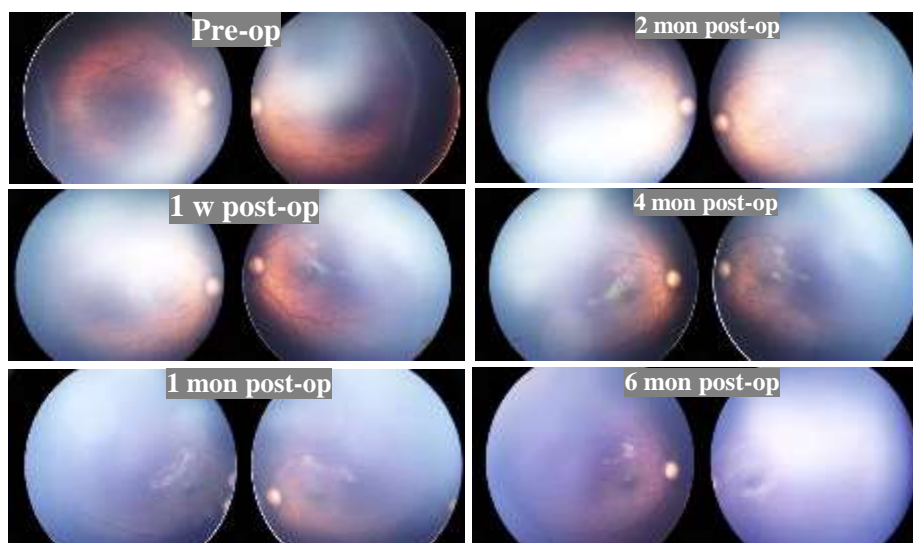
3 mon after IVR: fundus were stable



6 mon after IVR: fundus were stable



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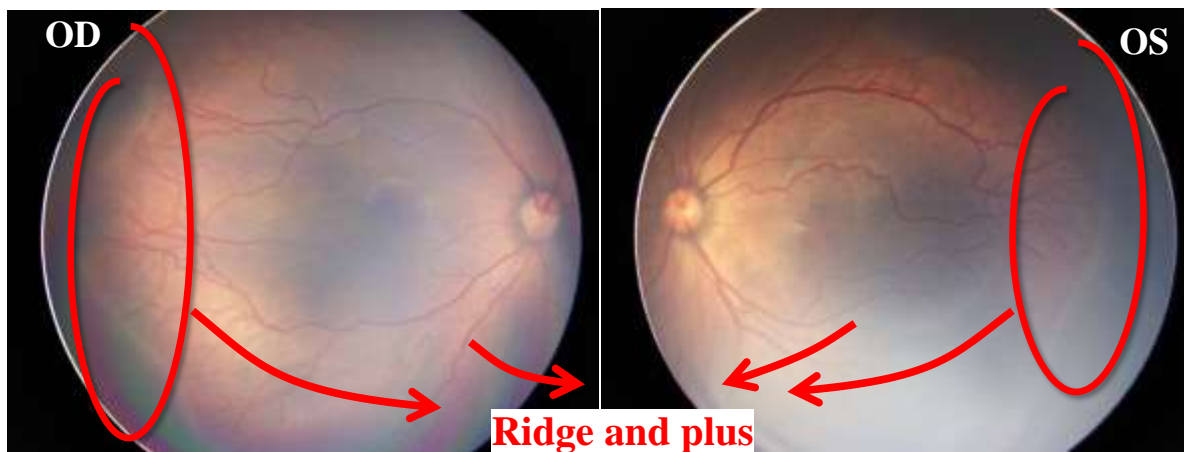
Case 3

- Zhang XX
- Male
- GA 34w+3d
- BW 1220g
- Cesarean section

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Corrected GA 40W, Retcam Images

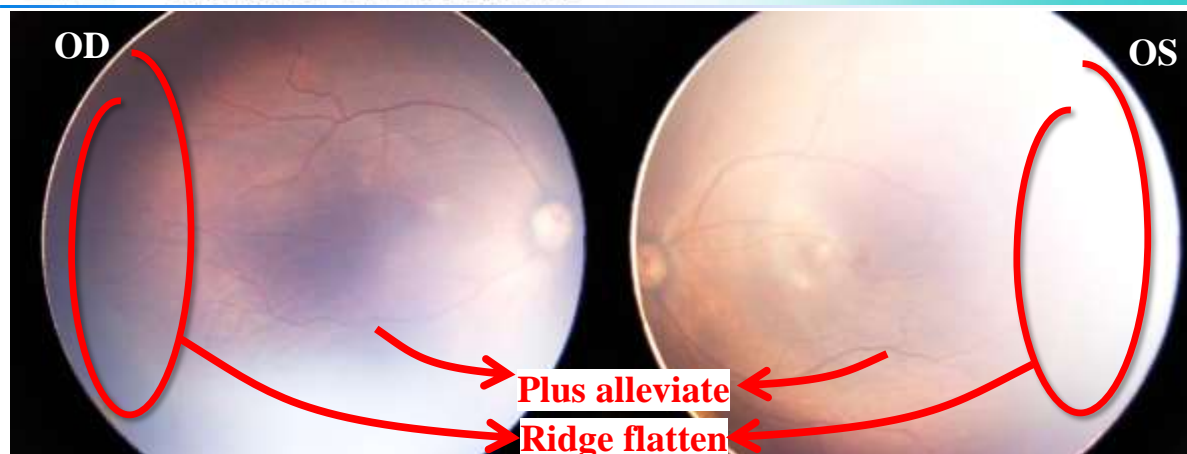
SHENZHEN EYE HOSPITAL



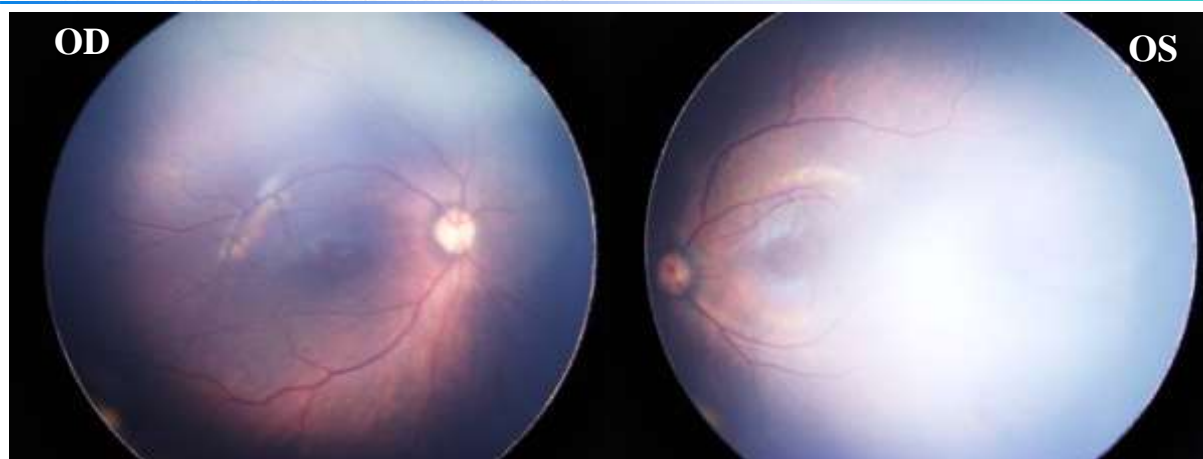
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- ◆ **Diagnosis: Type 1 prethreshold ROP**
- ◆ **Treatment: Intravitreal injection of Conbercept (IVC) ou**

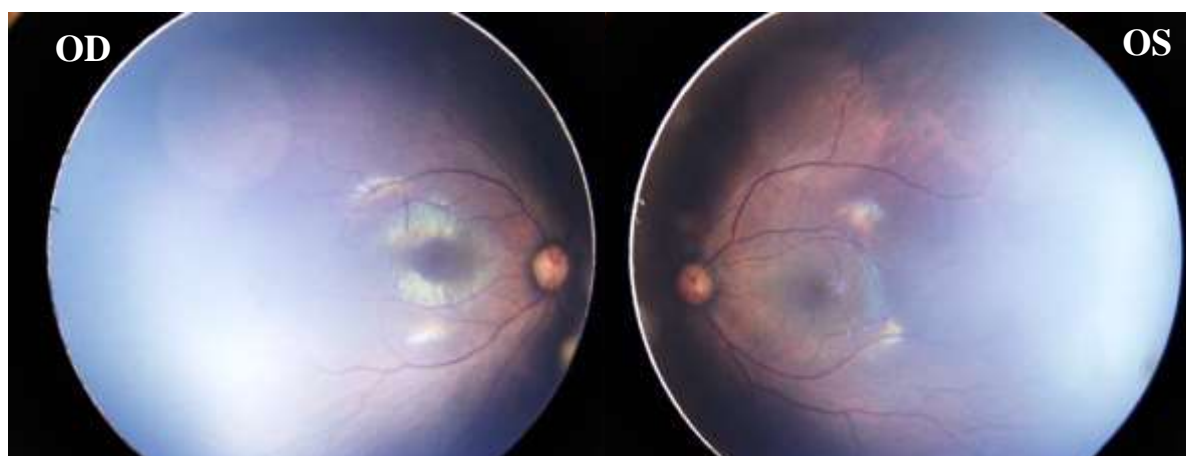
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1 week after IVC: ROP were controlled

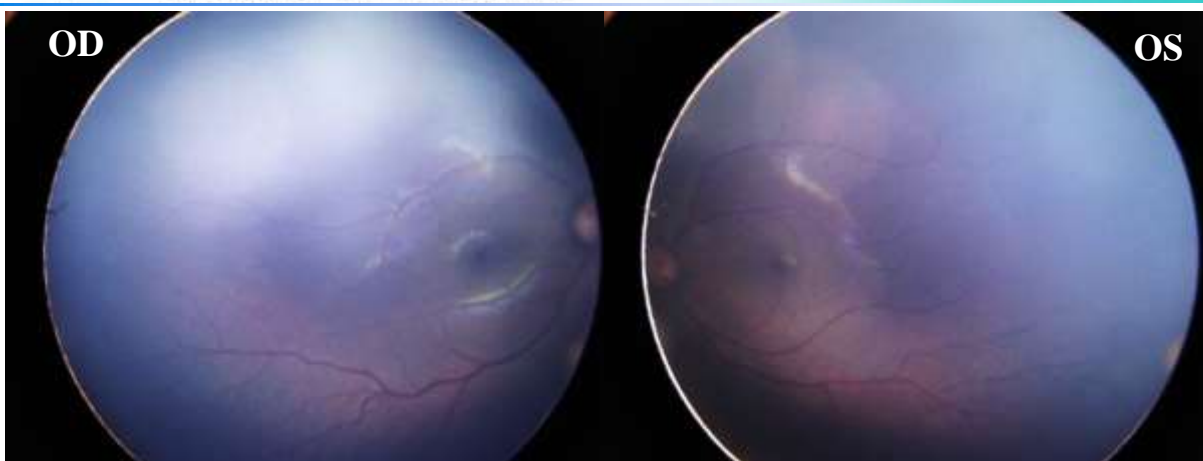


1 mon after IVC: fundus were stable



2 mon after IVC: fundus were stable

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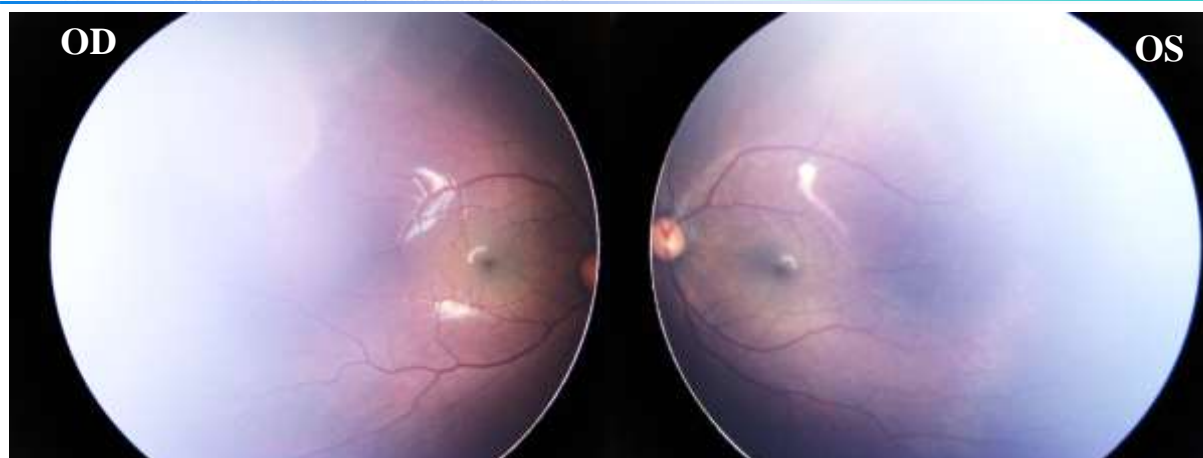


3 mon after IVC: fundus were stable

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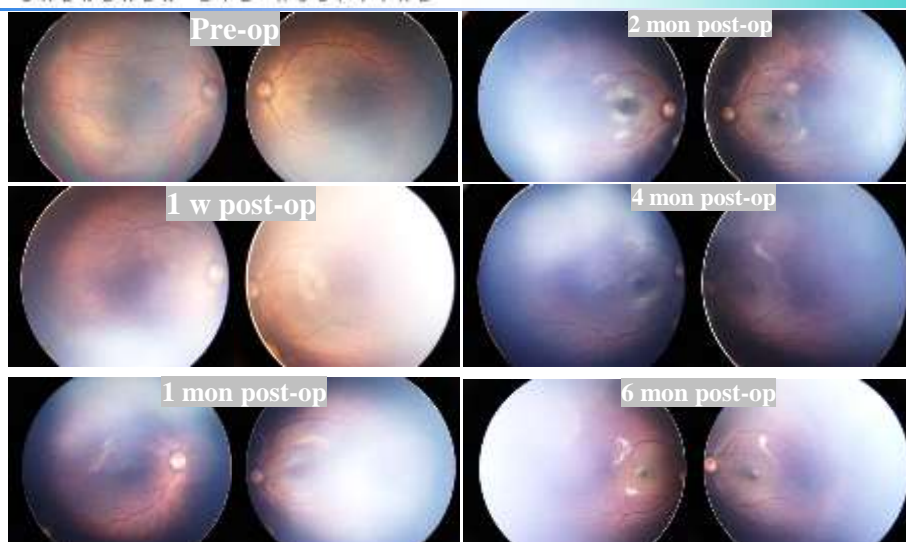


6 mon after IVC: : fundus were stable

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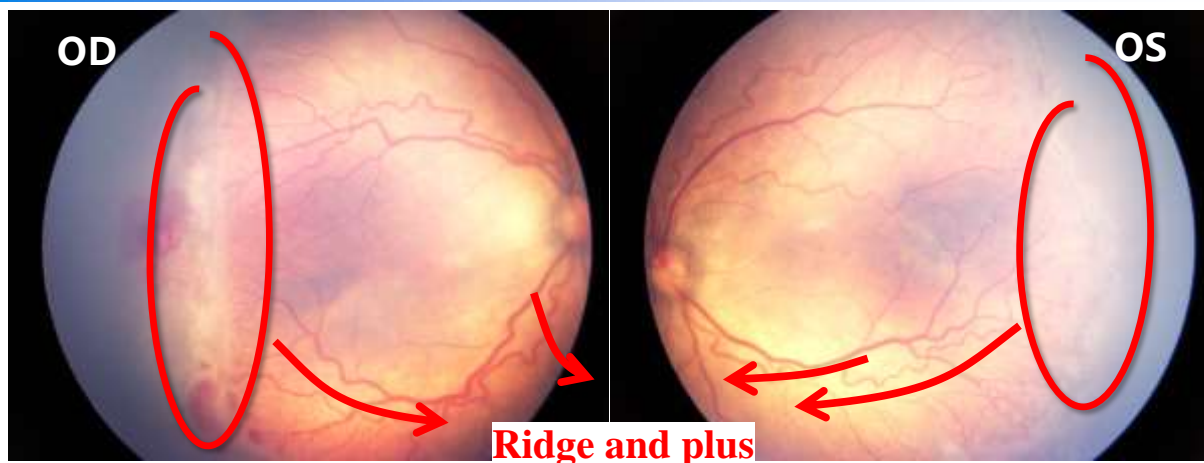
Case 4

- Li XX
- Male
- GA 24w
- BW 640g
- Cesarean section

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Corrected GA 33W, RetCam Images

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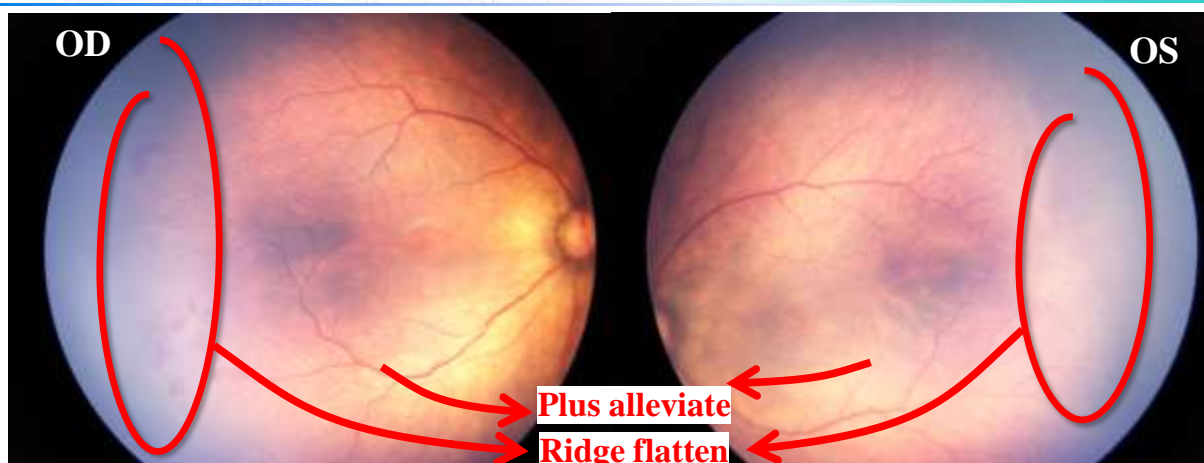
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- ◆ **Diagnosis:** Type 1 prethreshold ROP
- ◆ **Treatment:** Intravitreal injection of ranibizumab (IVR) ou

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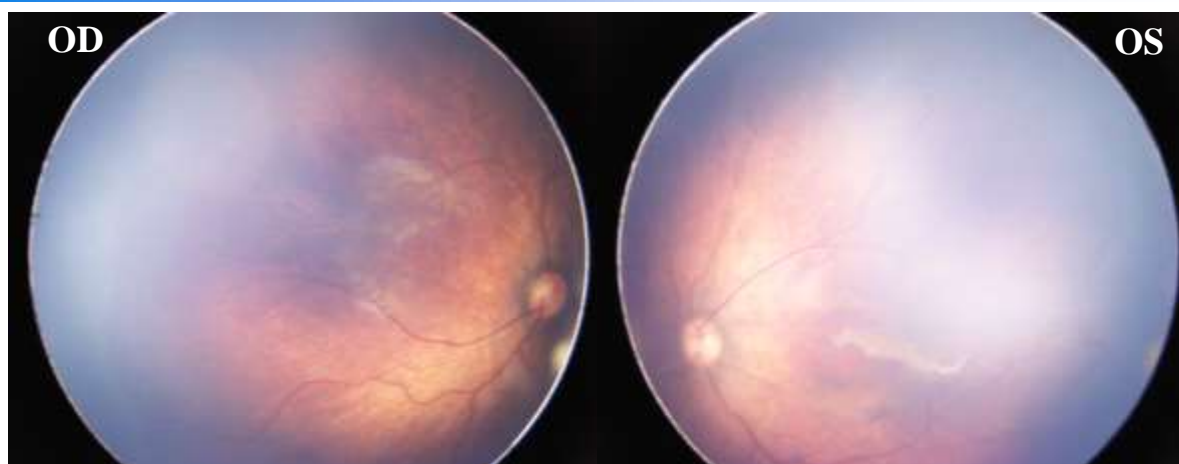


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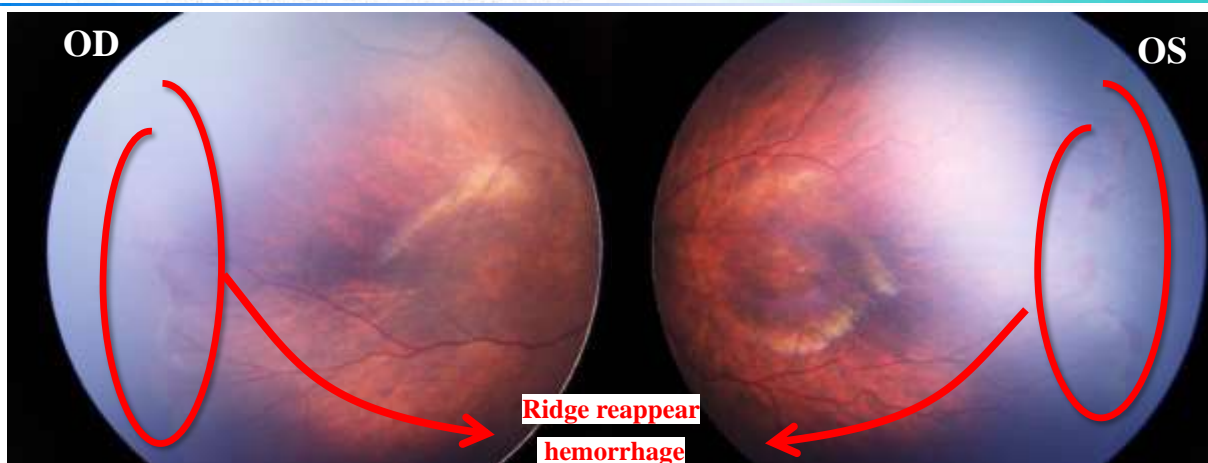


1 week after IVR: ROP were controlled

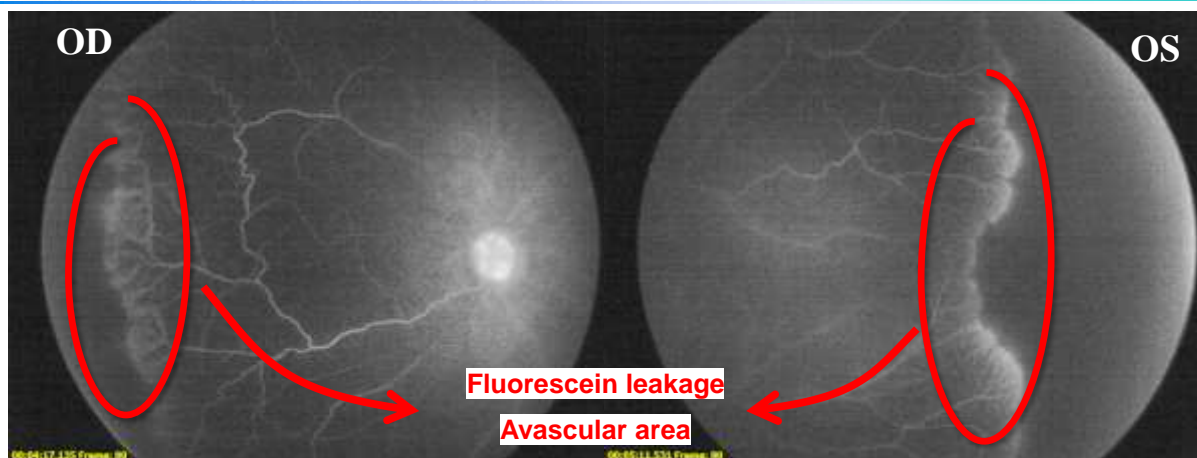
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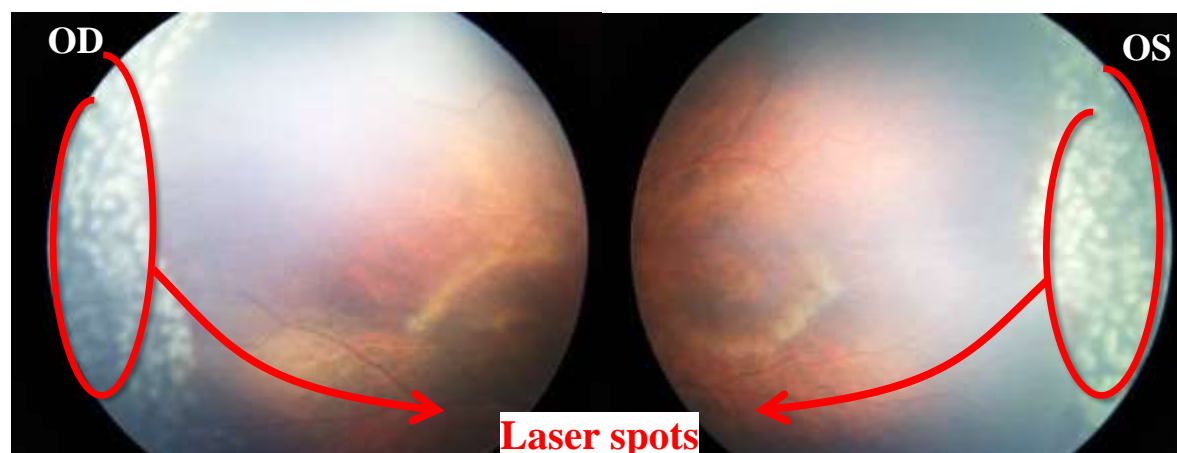
1 mon after IVR: fundus were stable



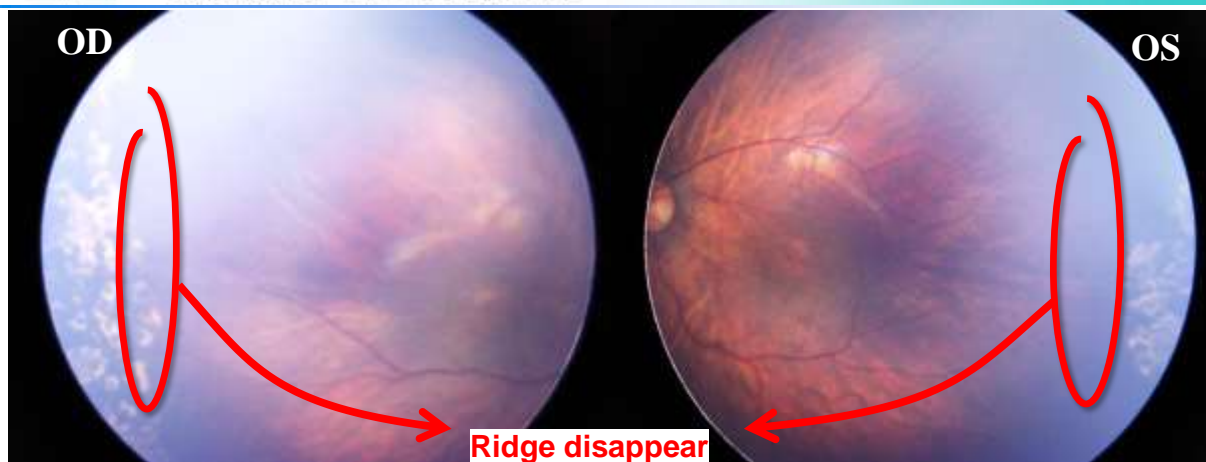
2 mon after IVR: ROP recurred



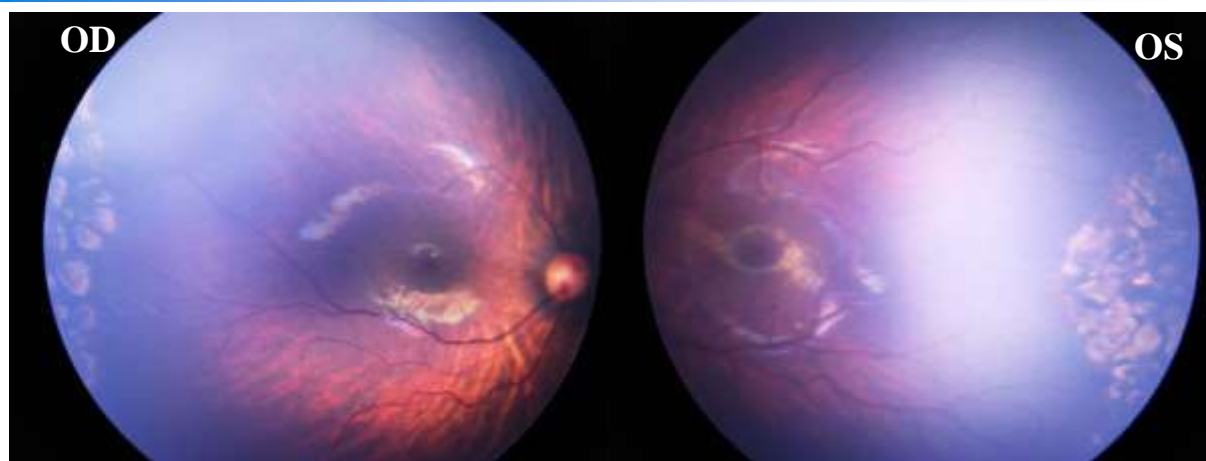
Retcam FA : ROP recurred



Supplement laser photocoagulation on



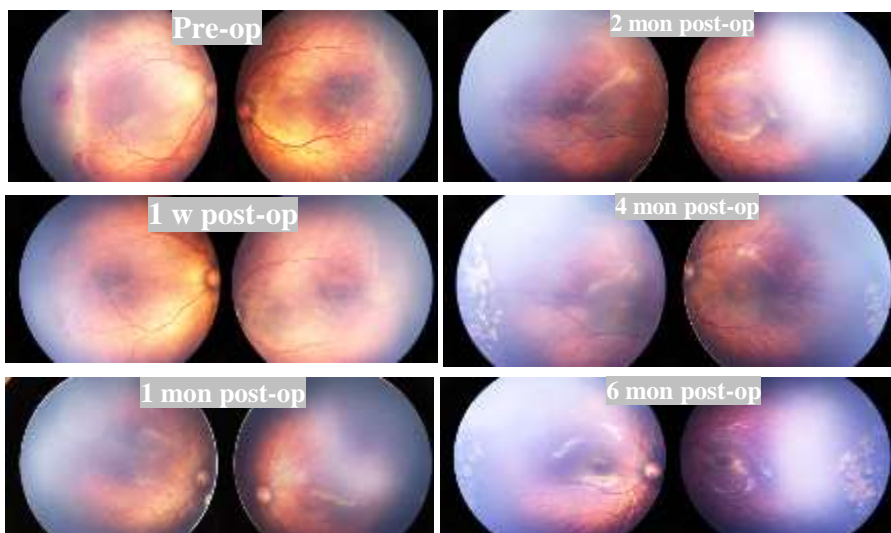
3 mon after IVR: plus alleviate



6 mon after IVR: fundus were stable



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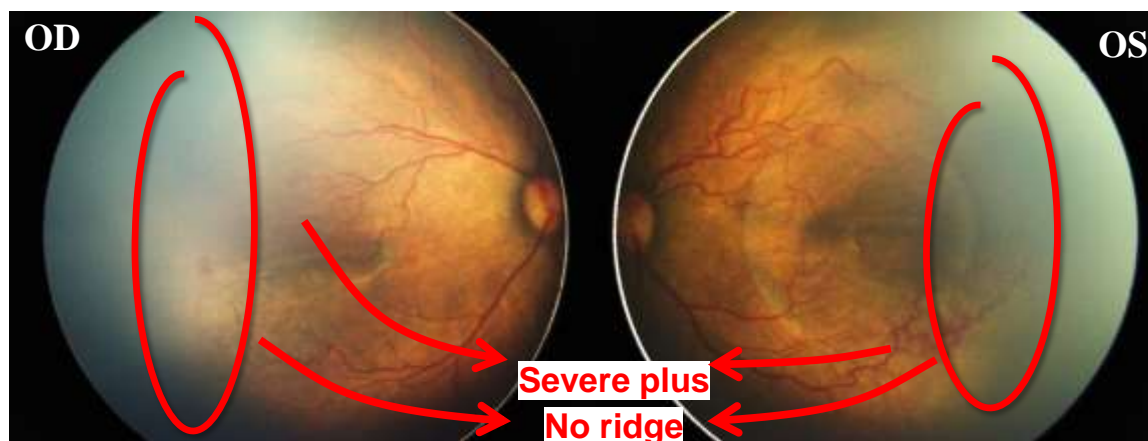
Case 5

- Liu XX
- Male
- GA 29w
- BW 1200g
- Cesarean section

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Corrected GA 36W, RetCam Images



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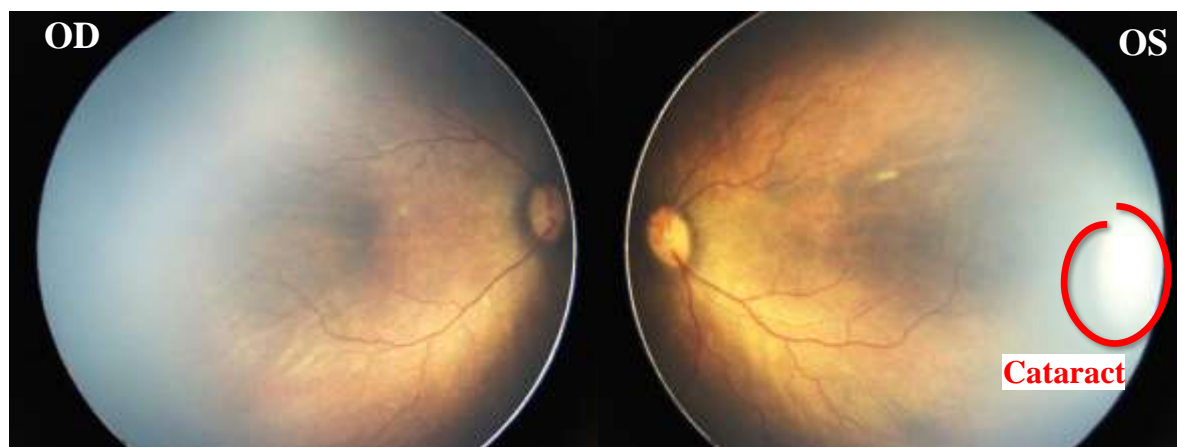


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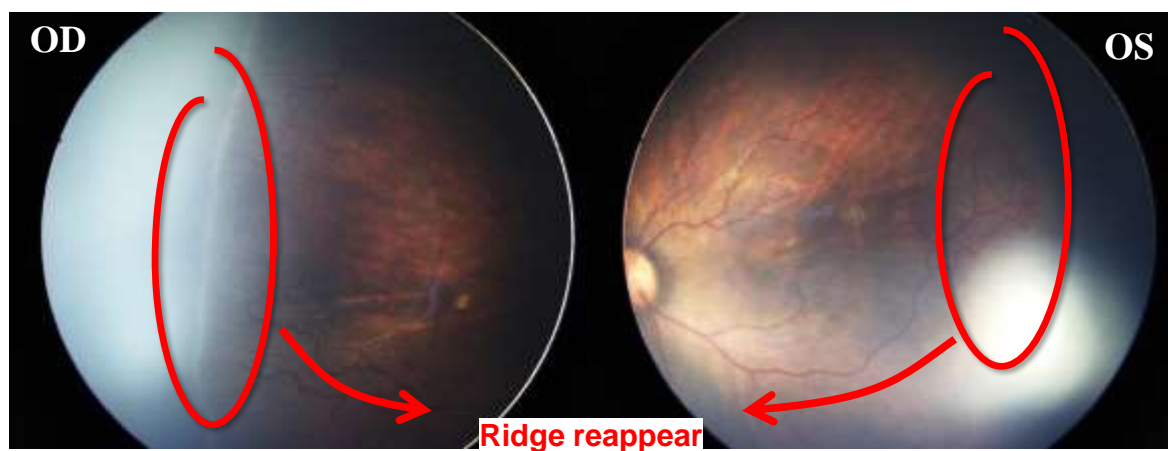
- ◆ **Diagnosis :** AP-ROP ou
- ◆ **Treatment:** Intravitreal injection of Conbercept (IVC) ou



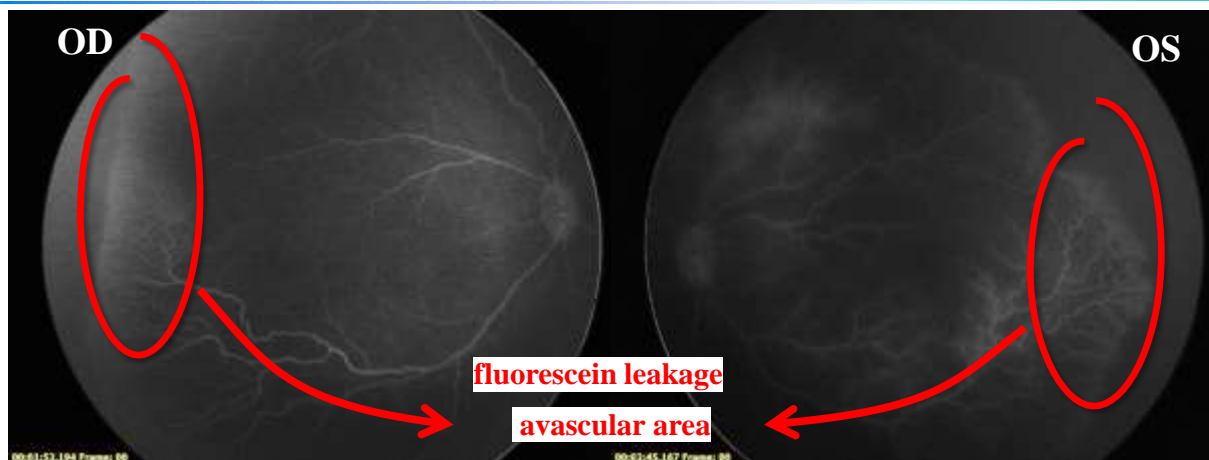
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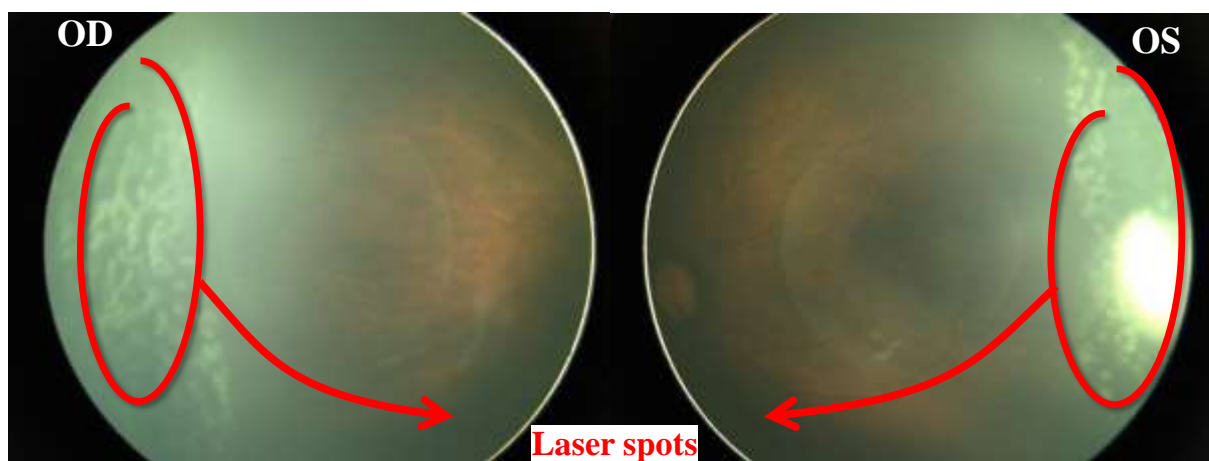
1 week after IVC: plus disease alleviate



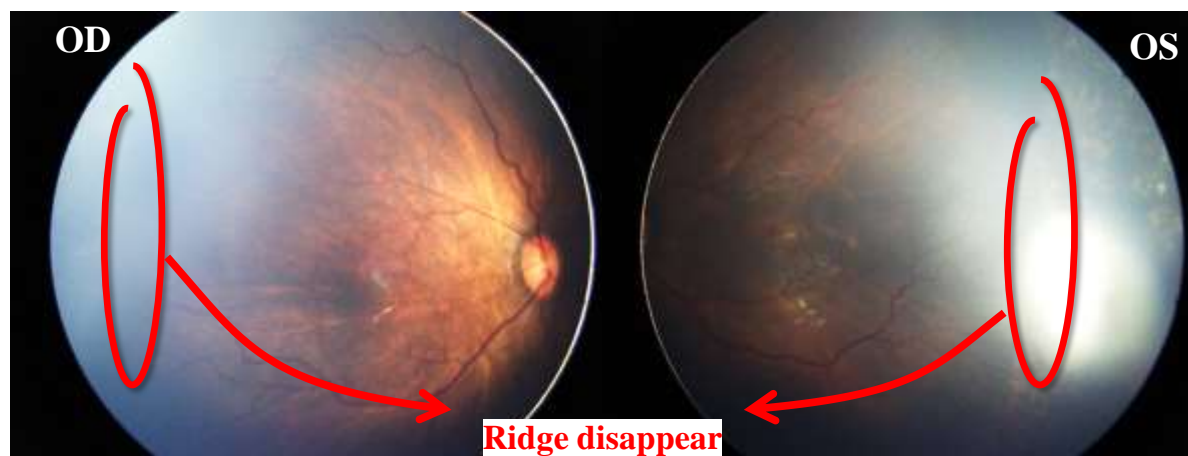
1 mon after IVC: ROP recurred



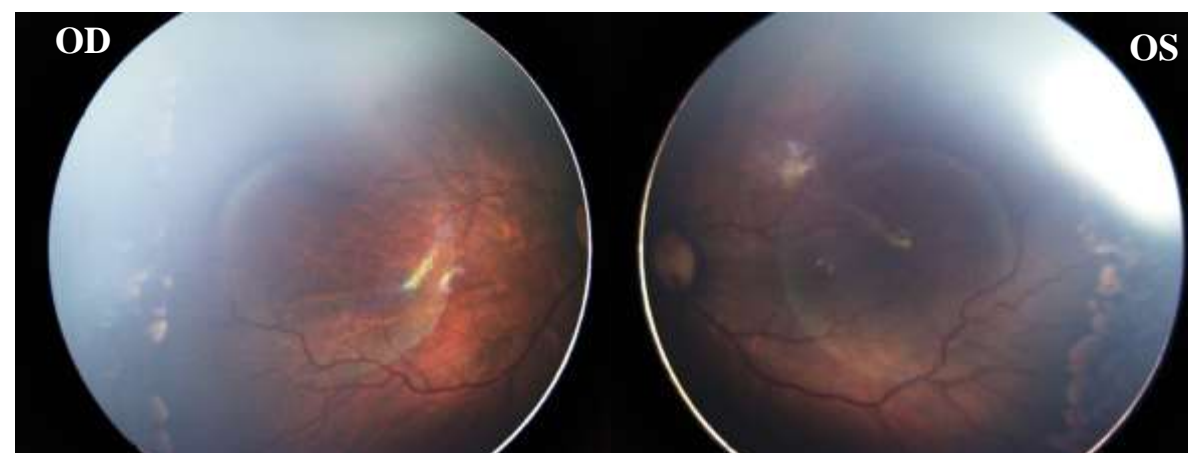
RetCam FFA:ROP recurred



Supplement laser photocoagulation ou



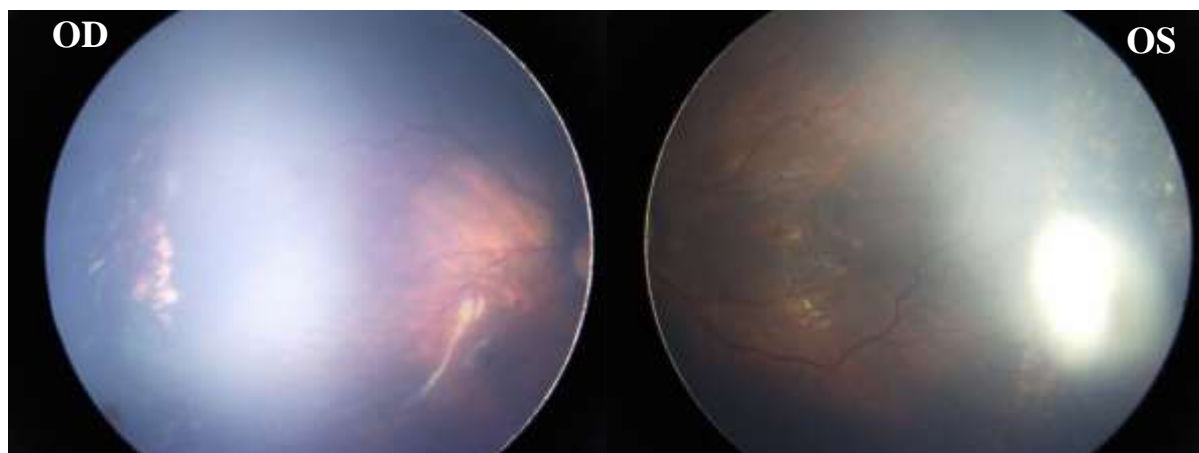
2 mon after IVC: plus alleviate



3 mon after IVC: ROP were controlled



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6 mon after IVC: fundus were stable

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Pre-op



2 mon post-op



1 w post-op



3 mon post-op



1 mon post-op



6 mon post-op

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How to choose the treatment for ROP?

- ◆ Intravitreal injection of anti-VEGF agents :
Zone I、 posterior zone II、 AP-ROP
- ◆ Laser therapy:
Peripheral zone II with vascular proliferation
- ◆ Recurrent IVI:
reinjection or laser therapy

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4. Studies of ROP from our group

4.1 Comparision of IVR versus laser therapy for ROP

- ◆ 25 cases: IVR group
25 cases: laser therapy group
- ◆ Main outcome: recurrence rate
- ◆ Observation time: 6months
- ◆ Conclusion: IVR is not recommended as a monotherapy for zone 2 ROP because of its high recurrence rate



Zhang GM, et al . Retina ,2017

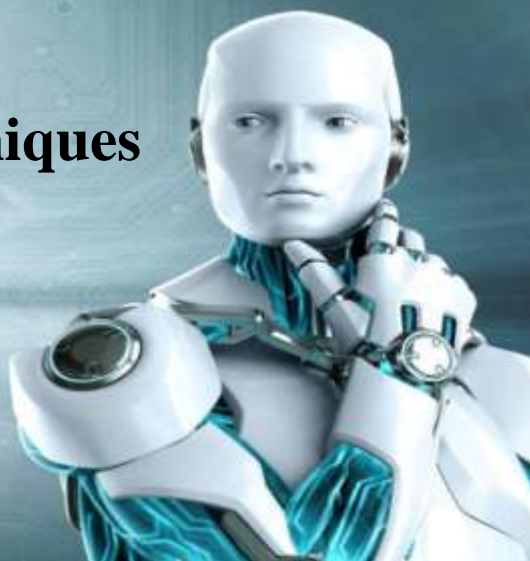
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4.2 To compare the efficacy of Conbercept and Ranibizumab for ROP

- ◆ 30 cases: IVC group
- 30 cases: IVR group
- ◆ Main outcome: recurrence rate
- ◆ Observation time: 6 months
- ◆ Result : the same recurrence rate



4.3 New diagnostic techniques (AI) in ROP



4.3.1 Case Information Management System for ROP

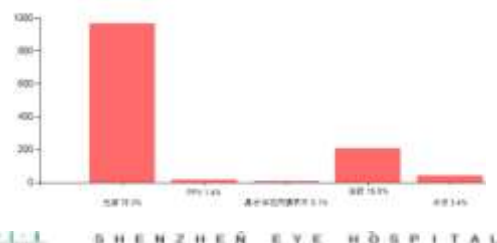
病案号	病历号	母亲	小孩	编辑
	S181114-10		姜习研	编辑
	S181114-9	姜平香	叶俊哲	编辑
	S181114-8	曾均强	卢莹莹	编辑
	S181114-7	杜维娜		编辑
	S181114-6	于蕊娜		编辑
	S181114-5	姜小冬		编辑
	S181114-4	郭晓秀		编辑
	S181114-3	张慧		编辑
	S181114-2	何冰妮		编辑
	S181114-1		钟晓安	编辑

显示第 1 至 10 项，共 27,258 条

◆ Containing all preterm infants' baseline information, RetCam images, follow-up results

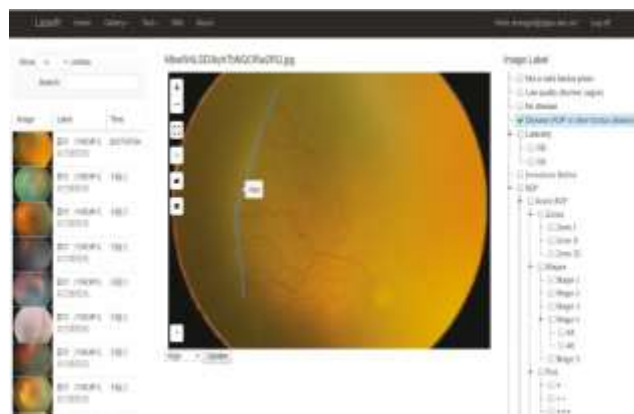
◆ 27,258 preterm infants

◆ 0.4 million images



4.3.2 Establishment of labeling software

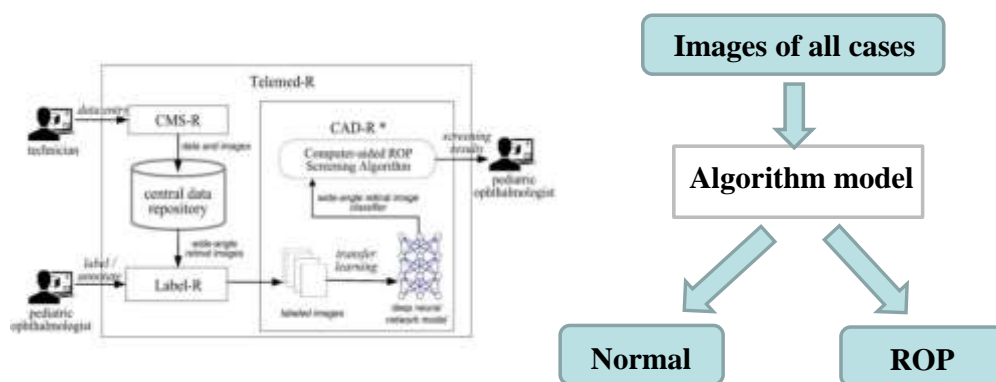
- ◆ Experts labeled lesions of RetCam images by software
- ◆ These labeled images were used as training set to train neural networks for ROP automatic diagnosis



Zhang GM, et al. Journal of Healthcare Engineering, 2018



4.3.3 Automated Screening System for ROP Using a Deep Neural Network



Zhang GM, et al. IEEE Access, 2019

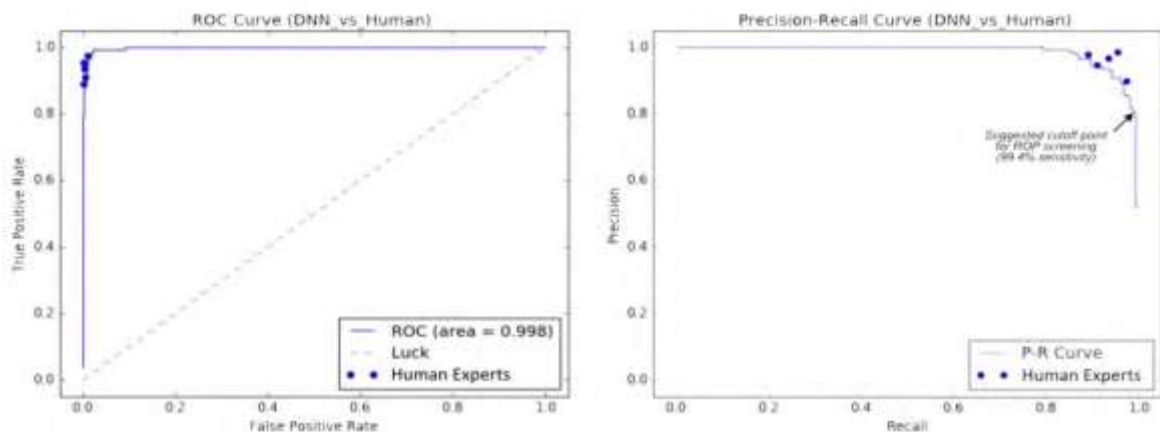


Comparison of ophthalmologist and the the machine

Ophthalmologists and DNN	Accuracy	Sensitivity/ recall	Specificity	Precision	F1 score	Youden index	MCC
Chief 1	99.5%	95.5%	99.8%	98.7%	0.970	0.953	0.968
Chief 2	99.1%	93.5%	93.5%	96.7%	0.951	0.932	0.946
Attending 1	98.8%	89.0%	99.8%	97.9%	0.932	0.888	0.927
Attending 2	98.8%	97.4%	98.9%	89.9%	0.935	0.963	0.929
Resident	98.7%	91.0%	99.5%	94.6%	0.928	0.905	0.921
Median of ophthalmologists	98.8%	93.5%	99.5%	96.7%	0.935	0.932	0.929
DNN cutoff 1	97.8%	99.4%	97.7%	80.6%	0.890	0.970	0.884
DNN cutoff 2	97.9%	98.7%	97.8%	81.8%	0.895	0.966	0.888
DNN cutoff 3	98.8%	96.1%	99.0%	90.9%	0.934	0.951	0.928
DNN cutoff 4	98.8%	94.1%	99.3%	93.0%	0.936	0.935	0.930
DNN cutoff 5	98.8%	93.5%	99.4%	93.5%	0.935	0.929	0.929

MCC = Matthews correlation coefficient; DNN= deep neural network. VGG-16 was selected as the final DNN model.

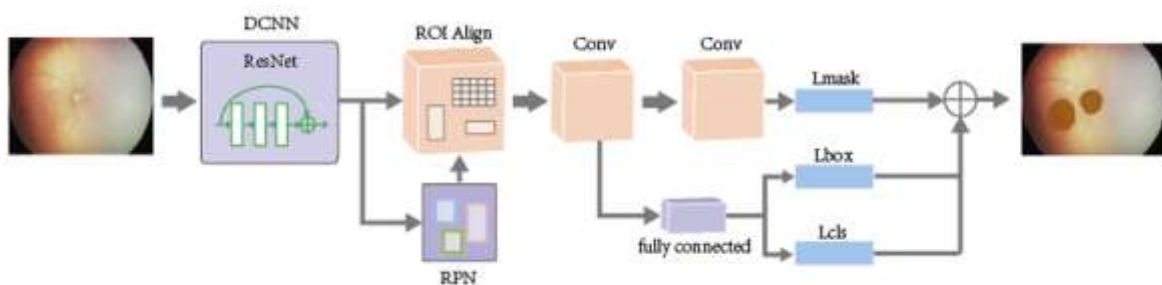
The performance of DNN model identification was comparable to that of experts



Five ophthalmologists were plotted in the ROC curve and P-R curve of the DNN

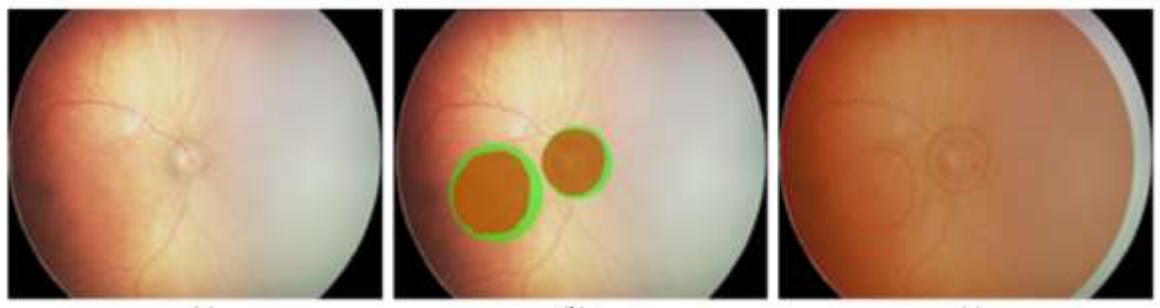
4.3.4 Deep Learning Framework for Identifying Zone I

The training set: 2394; Validation Dataset:355; Test Dataset:100



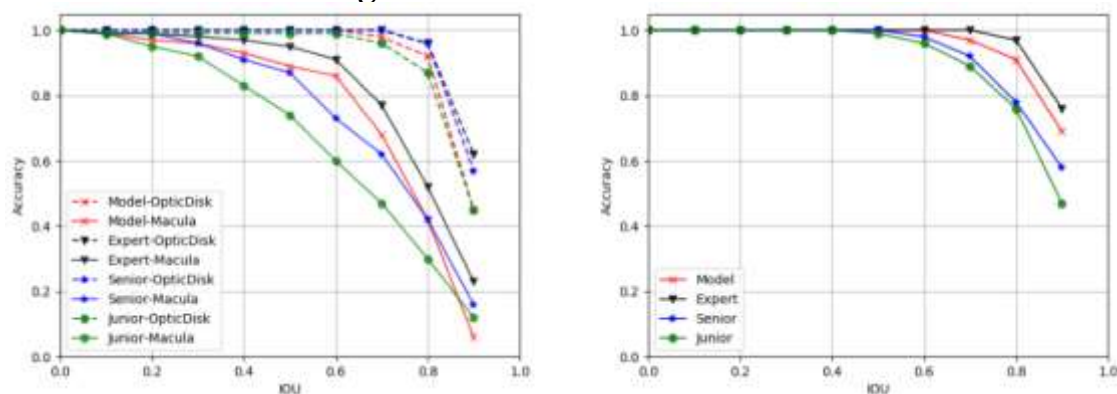
Zhang GM , et al. IEEE Access, 2019

Accuracy rate of model identification for zone I



The zone I identification accuracy of 91% is achieved when the IOU threshold is 0.8

Results of the ophthalmologists and model using different IOU thresholds



IOU=coincidence rate of the model prediction results and gold standard

The performance of model was comparable to that of experts



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4.3.5 The future project

Automatic diagnosis system for ROP:

- ◆ ROP zoning, staging, plus disease and special lesions are automatic diagnosed
- ◆ Treatment-required ROP are automatically diagnosed
- ◆ Be eventually applied to RetCam equipment

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- ◆ The Belt and Road
- ◆ China and Egypt
- ◆ Cooperation in ROP

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