

LV Prasad Eye Institute

IMAGING-BASED DECISION-MAKING IN RETINOPATHY OF PREMATUREITY

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❖ I have no financial disclosures.

Non-contact widefield neonatal retinal imaging for ROP using the Clarus 700 high-resolution **true colour** reflectance imaging



ARTICLE



Non-contact widefield neonatal retinal imaging for retinopathy of prematurity using the Clarus 700 high resolution true colour reflectance imaging

Akash Belenje¹, Rakasi Ugandhar Reddy¹, B. Optom¹, Komal Agarwal¹, Deepika C. Parmeswarappa¹ and Subhadra Jalali¹✉

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LVPEI Atlas of Retinopathy of Prematurity and other Neonatal Retinal Diseases

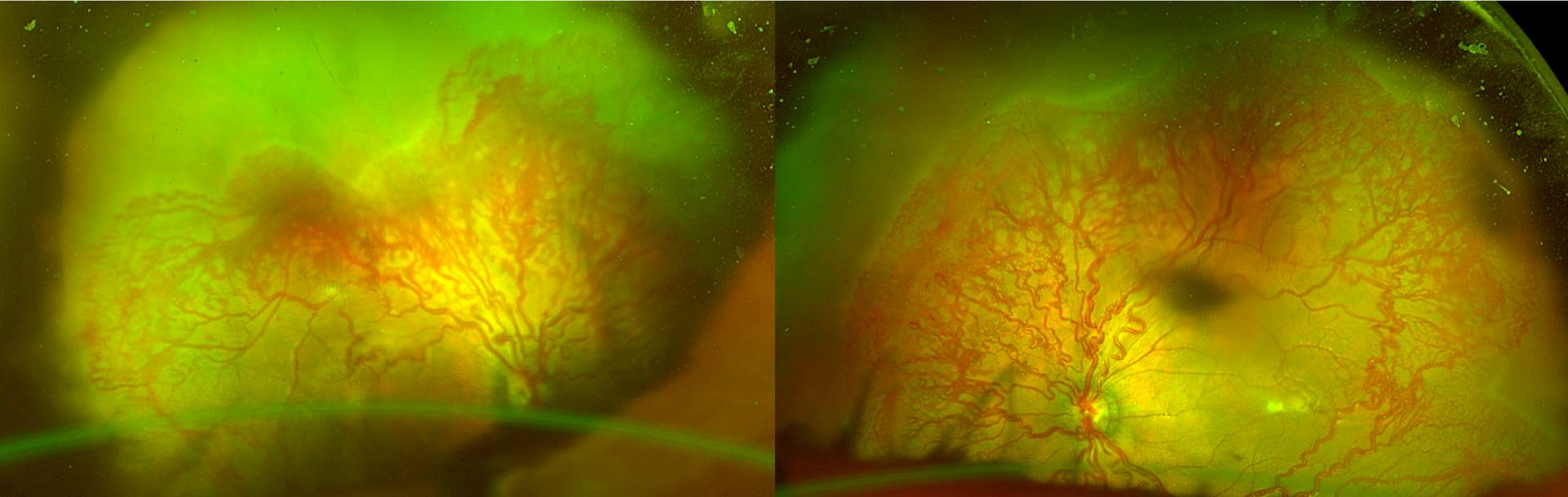
Dr. Akash Belenje &
Mr. R Ugandhar Reddy



Shot on ZEISS CLARUS 700
UWF Fundus Imaging System

Supported by





A-ROP is Highly vascular unpredictable aggressive disease



PROSPECTIVE STUDY : IRB APPROVED



Flying Baby Position

Objective: To illustrate the role of non-contact ultra-widefield swept source optical coherence tomography (**NC-UWF SS-OCT**) **biomarkers** in predicting treatment response to intravitreal injection of anti-vascular endothelial growth factor (anti-VEGF) Bevacizumab, in aggressive retinopathy of prematurity (A-ROP).

Baby with GA 30 weeks, PMA 34 weeks,
Birth weight 1500 grams

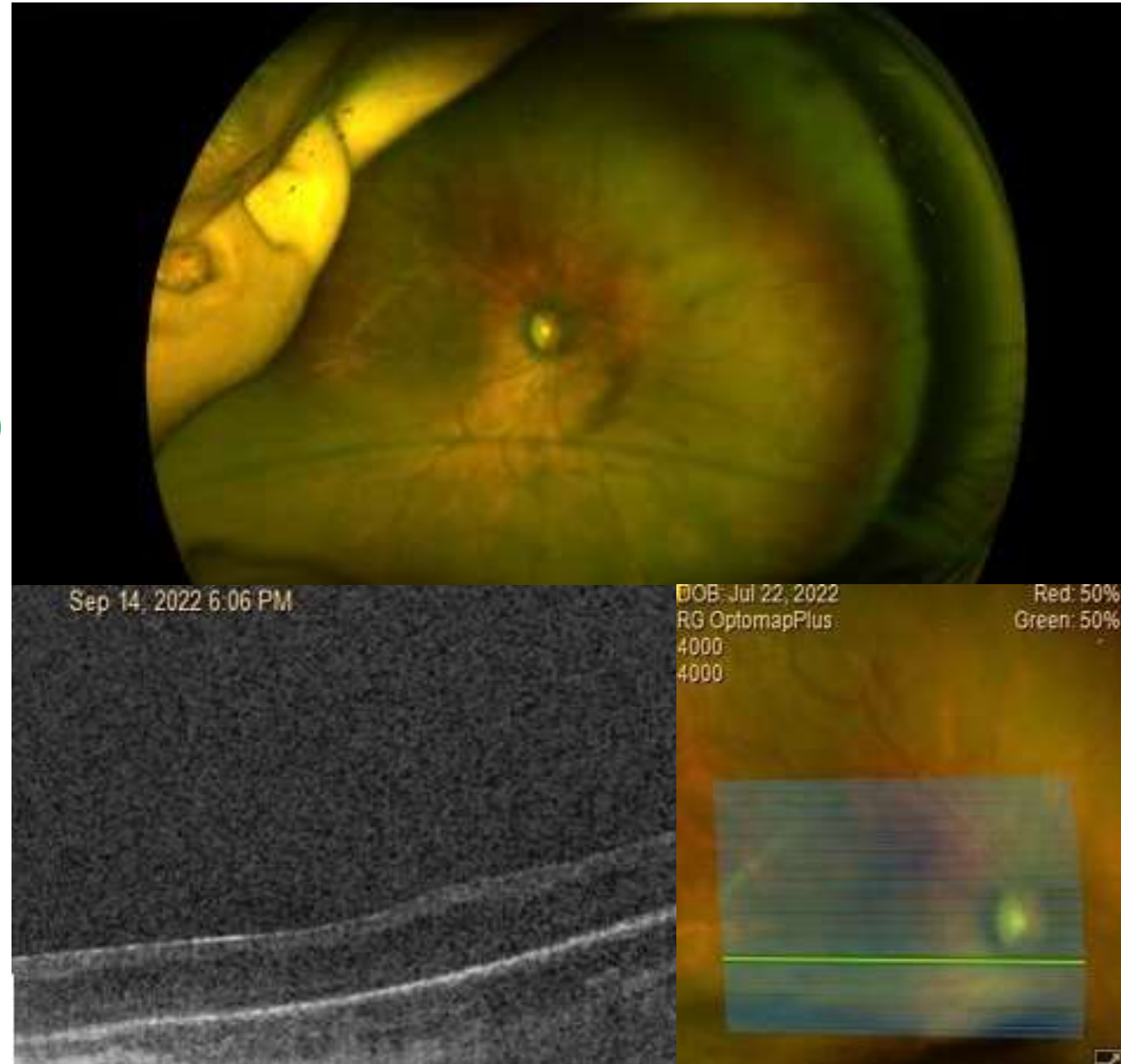
Hypo reflective intraretinal cystic changes at the fovea
Choroidal thickness >300 microns



Faster vascular progression

Complete vascularization
post anti-VEGF monotherapy

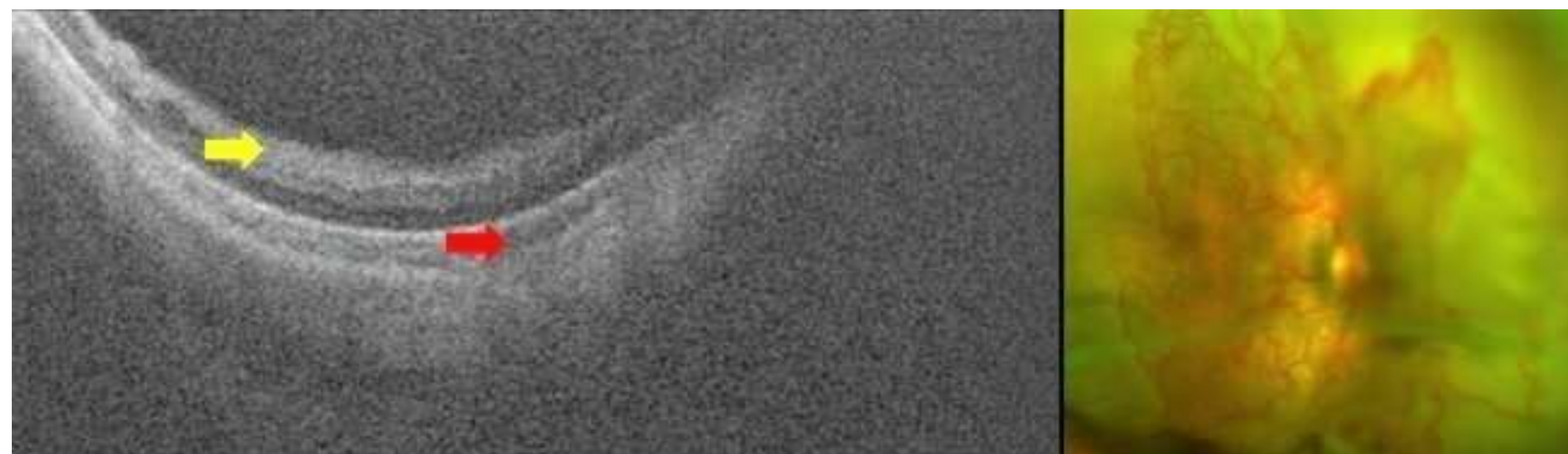
(Group 1 favourable outcomes)



Baby with GA 28
weeks, PMA 32 weeks,
Birth weight 1100
grams

Hyperreflectivity of inner retinal layers

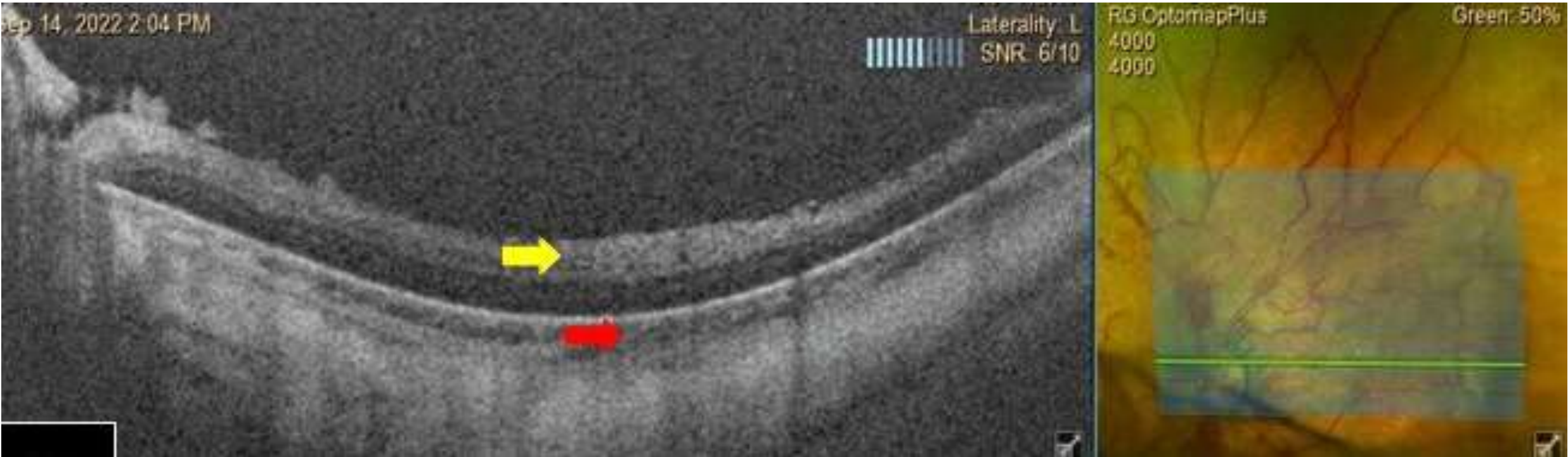
Choroidal Thinning (<250 microns)



Baby with GA 28 weeks, PMA 32 weeks, Birth weight 1200 grams

Hyperreflectivity of inner retinal layers

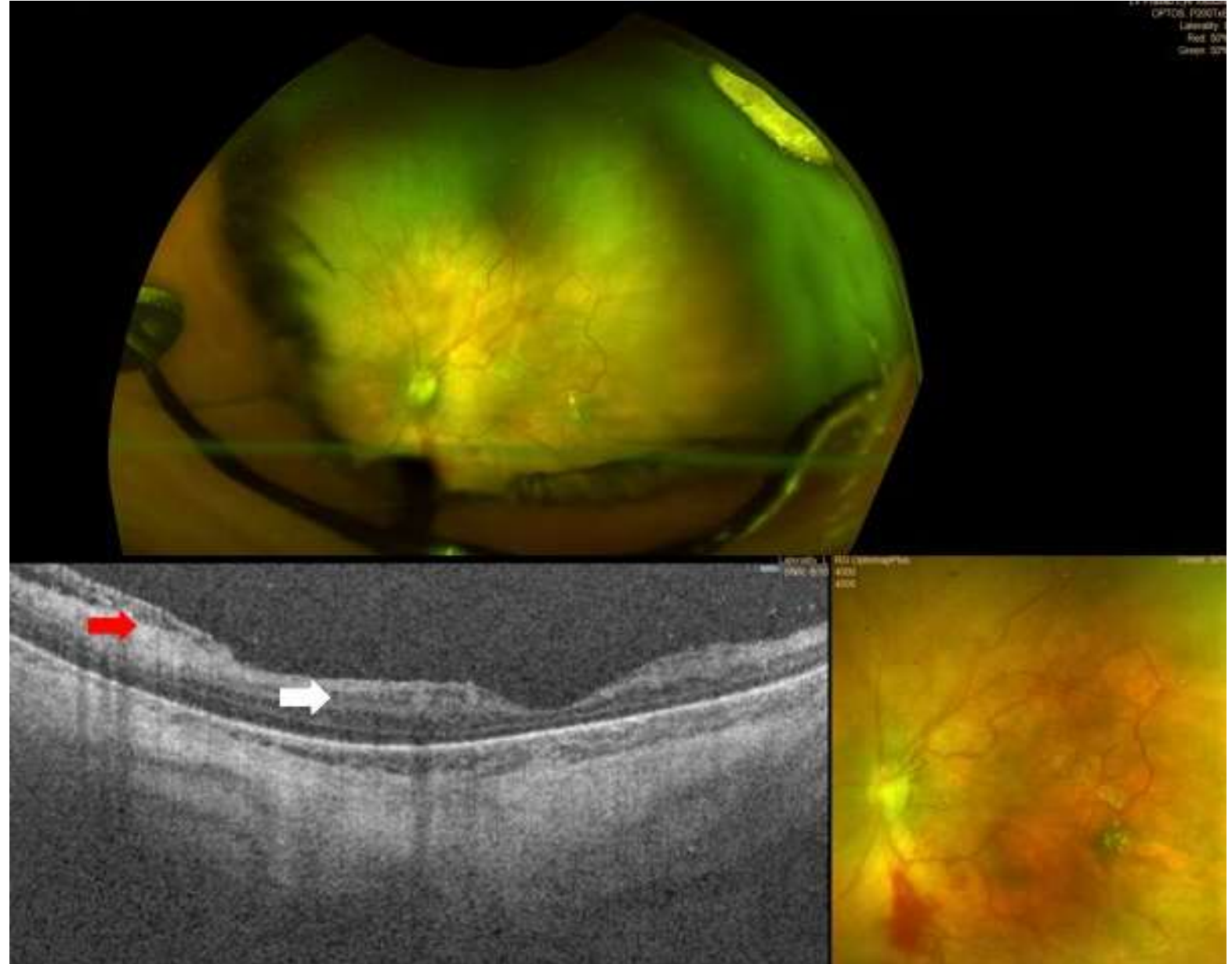
Choroidal Thinning (<250 microns)



Slower vascular progression

Peripheral avascular retina
(PAR) / Reactivation needing
laser

(Group 2 unfavourable
outcomes)



ARTICLE



Evaluation of optical coherence tomography biomarkers to differentiate favourable and unfavourable responders to intravitreal anti-vascular endothelial growth factor treatment in retinopathy of prematurity

Akash Belenje¹, Rakasi Ugandhar Reddy¹, Deepika C. Parmeswarappa¹, Tapas Ranjan Padhi², Bala Subbarao¹ and Subhadra Jalali¹✉

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OBJECTIVE: Evaluation of optical coherence tomography biomarkers in predicting treatment response to intravitreal injection of anti-vascular endothelial growth factor (anti-VEGF) Bevacizumab, in aggressive retinopathy of prematurity (A-ROP).

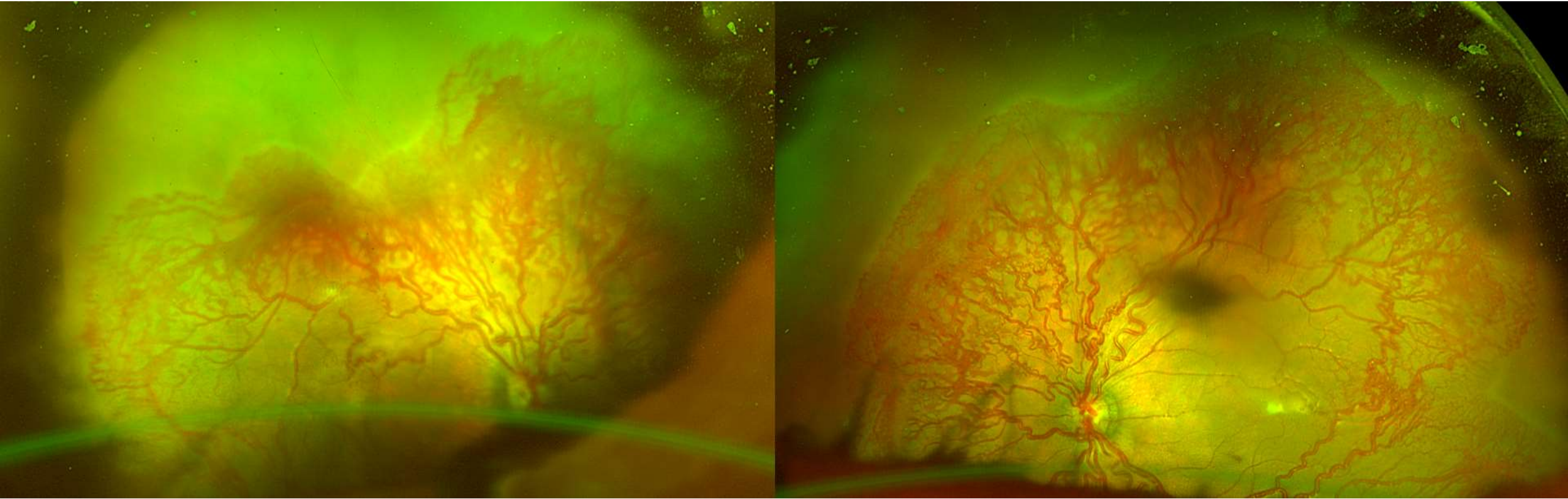
METHODS: Non-contact ultra-widefield (NC-UWF) fundus imaging with integrated UWF guided swept source Optical coherence tomography (SS-OCT) was performed prospectively in preterm babies before and after intravitreal anti-VEGF (Bevacizumab) monotherapy. OCT biomarkers were analysed in eyes that reached complete vascularization versus others.

RESULTS: Eyes with retinal vessels reaching near ora serrata were labelled as regressed ROP and vascularised retina (Group 1). Eyes with reactivation of ROP needing laser or vitreoretinal surgery or eyes with peripheral avascular retina (PAR) at 16th week post-injection were considered as Group 2. Pre-injection baseline OCT showed a hyperreflectivity of inner retinal layers in 12 out of 46 eyes in Group 1 versus 30 out of 34 eyes in Group 2 (p value 0.002). None of the eyes in Group 1 showed choroidal thinning at posterior pole as compared to 14 out of 34 eyes in Group 2 (p value 0.001). Intraretinal hypo reflective Cystic changes at fovea were seen in 16 out of 46 eyes in Group 1 and 2 out of 34 eyes in Group 2 (p value 0.012).

CONCLUSION: Pre-injection swept source OCT biomarkers could predict the treatment outcomes of anti-VEGF (Bevacizumab) monotherapy in A-ROP eyes. Hyperreflectivity of inner retinal layers and choroidal thinning had poorer and unpredictable response to anti-VEGF injection whereas, cystic changes at fovea predicted favourable response.

Eye; <https://doi.org/10.1038/s41433-023-02824-1>

- A-ROP is an epidemic of the 21st century.
- The world has shifted to **anti-VEGF** – Better anatomical and functional outcomes.



Challenges

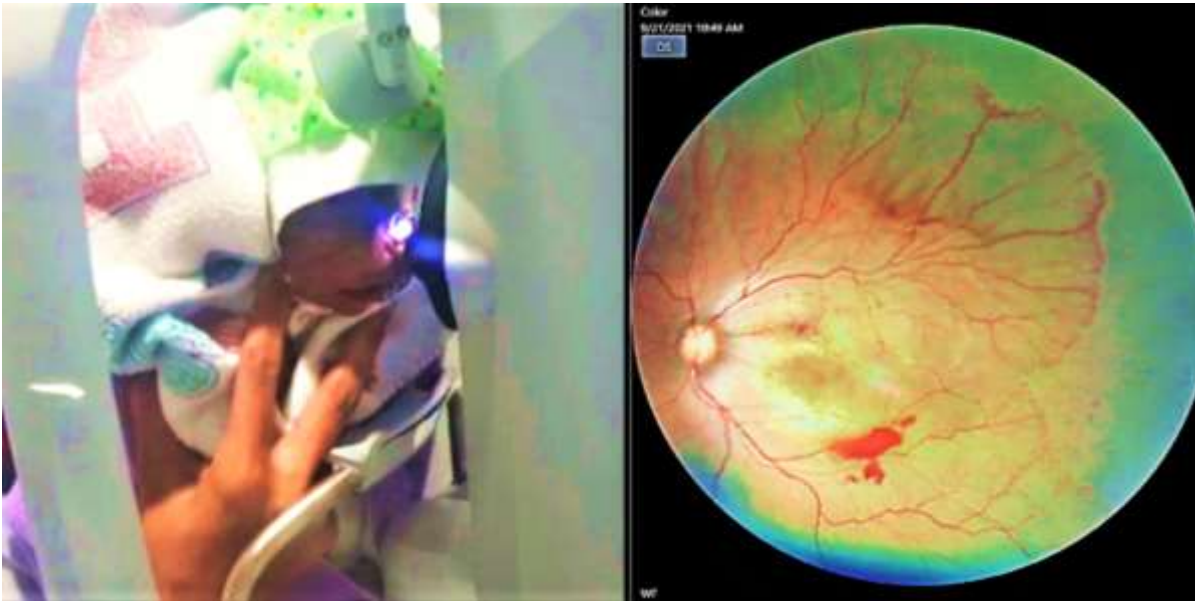


1. Anti-VEGF-injected A-ROP eyes need longer and more frequent follow-ups.
2. Higher chances of **Reactivation** or **persistent avascular retina (PAR)** needing retreatment with laser or repeat anti-VEGF injection.
3. The reactivation rate can be as high as **60 to 90 percent** in eyes treated with anti-VEGF for ROP in the posterior zone I.
4. Reactivation can occur between **6 weeks to 16 weeks** post-anti-VEGF.

Fundus fluorescein angiography (FFA) using intravenous dye injection under general anesthesia seems to be the gold standard for studying active leaks and other aspects of retinal vascular diseases including ROP.



High-resolution, ultra-widefield fundus cameras can quickly capture images of the retina and OCT scans.

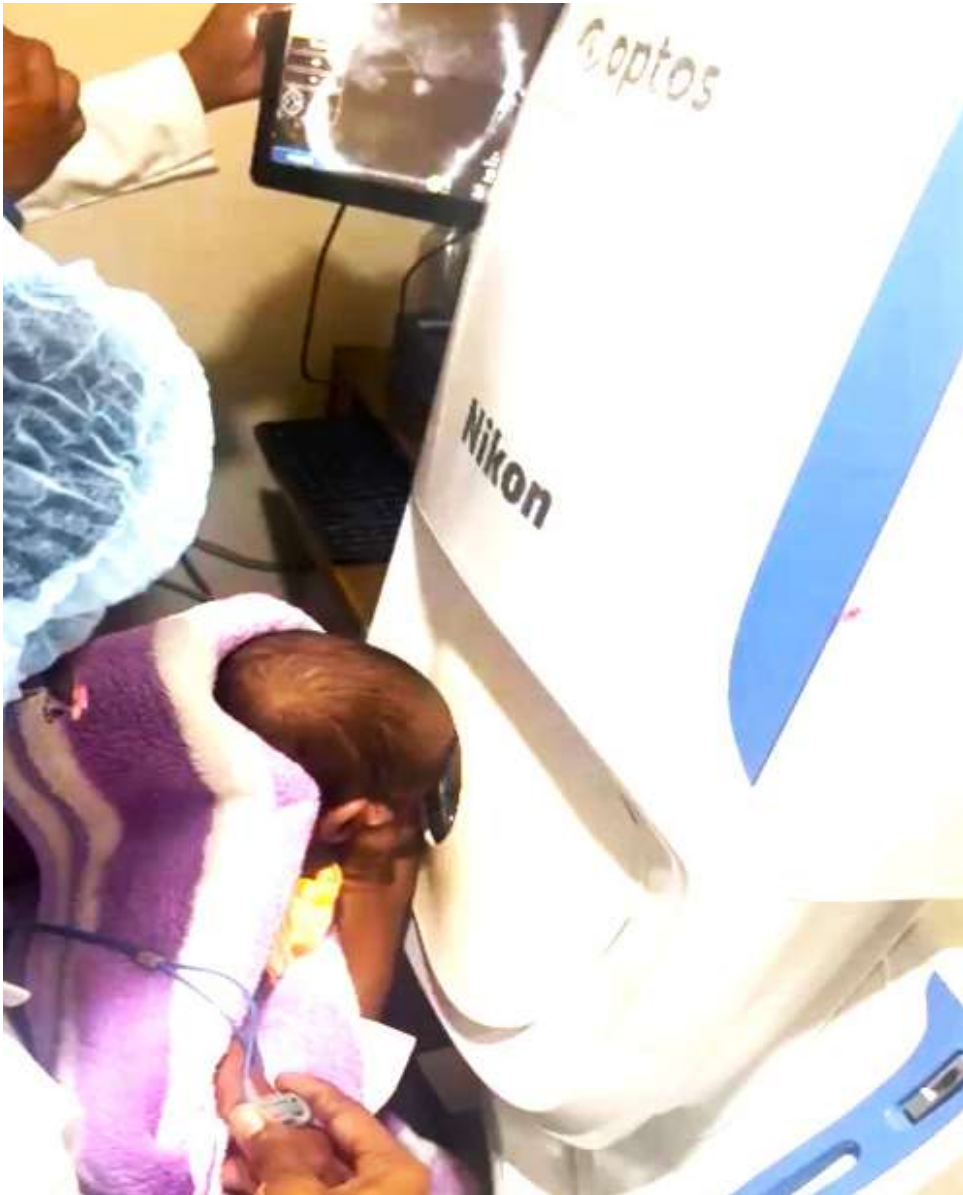


Belenje A, Reddy RU, Optom B, Agarwal K, Parmeswarappa DC, Jalali S. Non-contact widefield neonatal retinal imaging for retinopathy of prematurity using the Clarus 700 high resolution true colour reflectance imaging. *Eye (Lond)*. 2023 Jun;37(9):1904-1909.

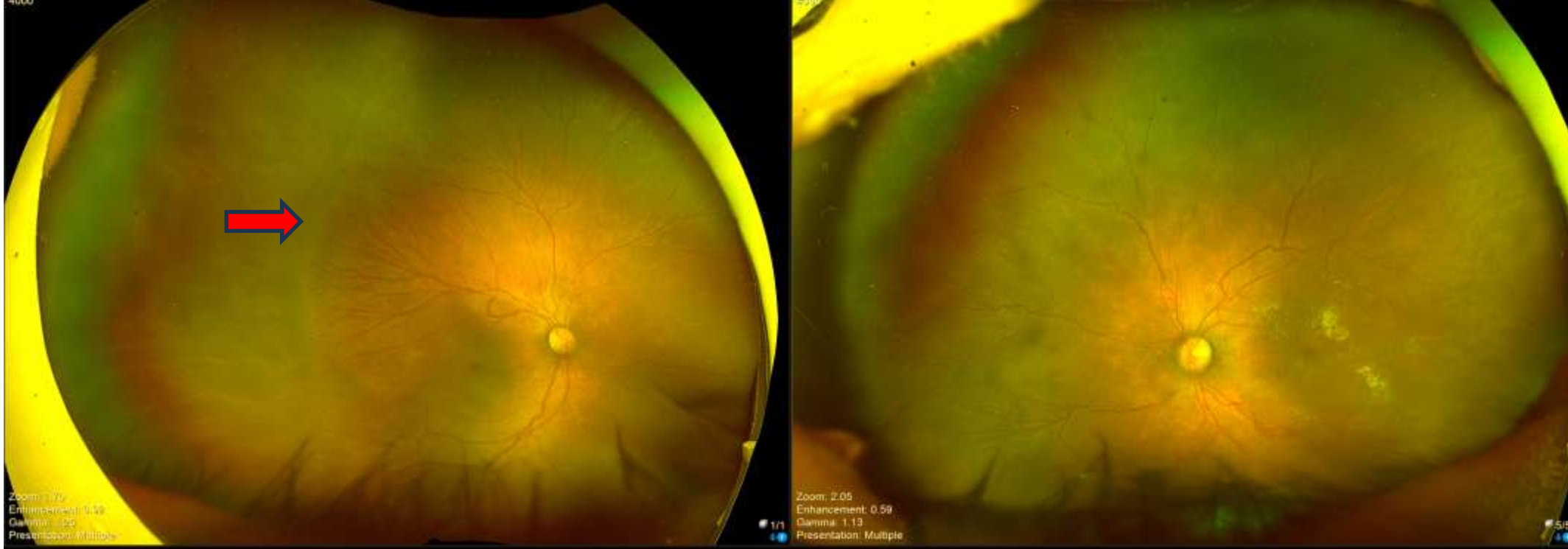
Belenje, A., Reddy, R.U., Parmeswarappa, D.C. *et al*. Evaluation of optical coherence tomography biomarkers to differentiate favourable and unfavourable responders to intravitreal anti-vascular endothelial growth factor treatment in retinopathy of prematurity. *Eye* **38**, 1097–1103 (2024).



OBJECTIVE: Oral Fundus Fluorescein Dye Angiography (OFDA) Detects Reactivation Post Anti-VEGF in Aggressive Retinopathy of Prematurity (A-ROP).



- ❖ We enrolled 36 eyes of 18 babies for FFA imaging who were previously treated with intravitreal anti-VEGF and clinical suspicion of disease reactivation using Indirect Ophthalmoscopy or fundus photography.



The indications for performing oral fundus fluorescein dye angiography (OFDA) are:

- To detect or confirm reactivation in **clinically doubtful cases**.
- Accurate delineation of capillary non-perfusion (CNP) areas including anterior to the ridge, pockets of avascularity at the ridge, and posterior to the ridge. This helps in **judicious targeted laser treatment**.

METHODOLOGY FOR PERFORMING OFDA

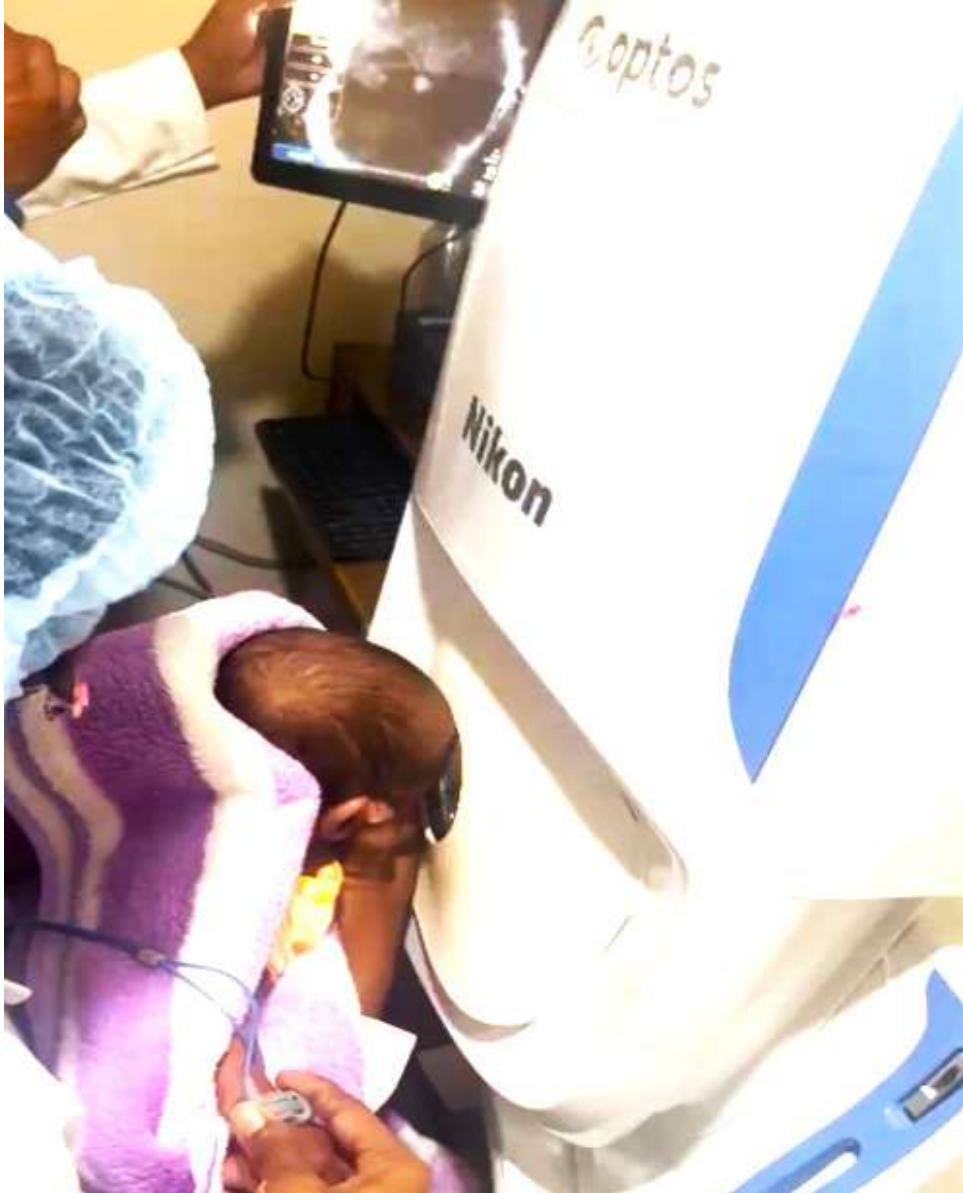


RESUSCITATION	3 KG	4 KG	5 KG
Epinephrine (1:10,000)	0.03 mg (0.3 mL)	0.04 mg (0.4 mL)	0.05 mg (0.5 mL)
Epinephrine ET (1:1,000)	0.3 mg (0.3 mL)	0.4 mg (0.4 mL)	0.5 mg (0.5 mL)
Atropine (0.1 mg/mL)	0.06 mg (0.6 mL)	0.08 mg (0.8 mL)	0.1 mg (1 mL)
Atropine ET (0.4 mg/mL)	0.15 mg (0.38 mL)	0.2 mg (0.5 mL)	0.25 mg (0.63 mL)
Sodium Bicarbonate 4.2%	3 mEq (6 mL)	4 mEq (8 mL)	5 mEq (10 mL)
Lidocaine 2% (20 mg/mL)	3 mg (0.15 mL)	4 mg (0.2 mL)	5 mg (0.25 mL)
Lidocaine ET 2% (20 mg/mL)	6-9 mg (0.3-0.45 mL)	8-12 mg (0.4-0.6 mL)	10-15 mg (0.5-0.75 mL)
1 st Defibrillation	6 J	8 J	10 J
2 nd Defibrillation	12 J	16 J	20 J
3 rd Defibrillation	12 J-30 J	16 J-40 J	20 J-50 J
Cardioversion-1st/2nd Dose	3 J/6 J	4 J/8 J	5 J/10 J
Adenosine (3 mg/mL)			
1 st Dose	0.3 mg (0.1 mL)	0.4 mg (0.13 mL)	0.5 mg (0.17 mL)
2 nd Dose	0.6 mg (0.2 mL)	0.8 mg (0.27 mL)	1 mg (0.33 mL)
Amiodarone (50 mg/mL)	15 mg (0.3 mL)	20 mg (0.4 mL)	25 mg (0.5 mL)
Calcium Chloride (100 mg/mL)	60 mg (0.6 mL)	80 mg (0.8 mL)	100 mg (1 mL)
Procainamide (100 mg/mL)	45 mg (0.45 mL)	60 mg (0.6 mL)	75 mg (0.75 mL)
Procainamide (500 mg/mL)	45 mg (0.09 mL)	60 mg (0.12 mL)	75 mg (0.15 mL)
Magnesium Sulfate (40 mg/mL)	150 mg (3.8 mL)	200 mg (5 mL)	250 mg (6.2 mL)
Magnesium Sulfate (80 mg/mL)	150 mg (1.9 mL)	200 mg (2.5 mL)	250 mg (3.1 mL)



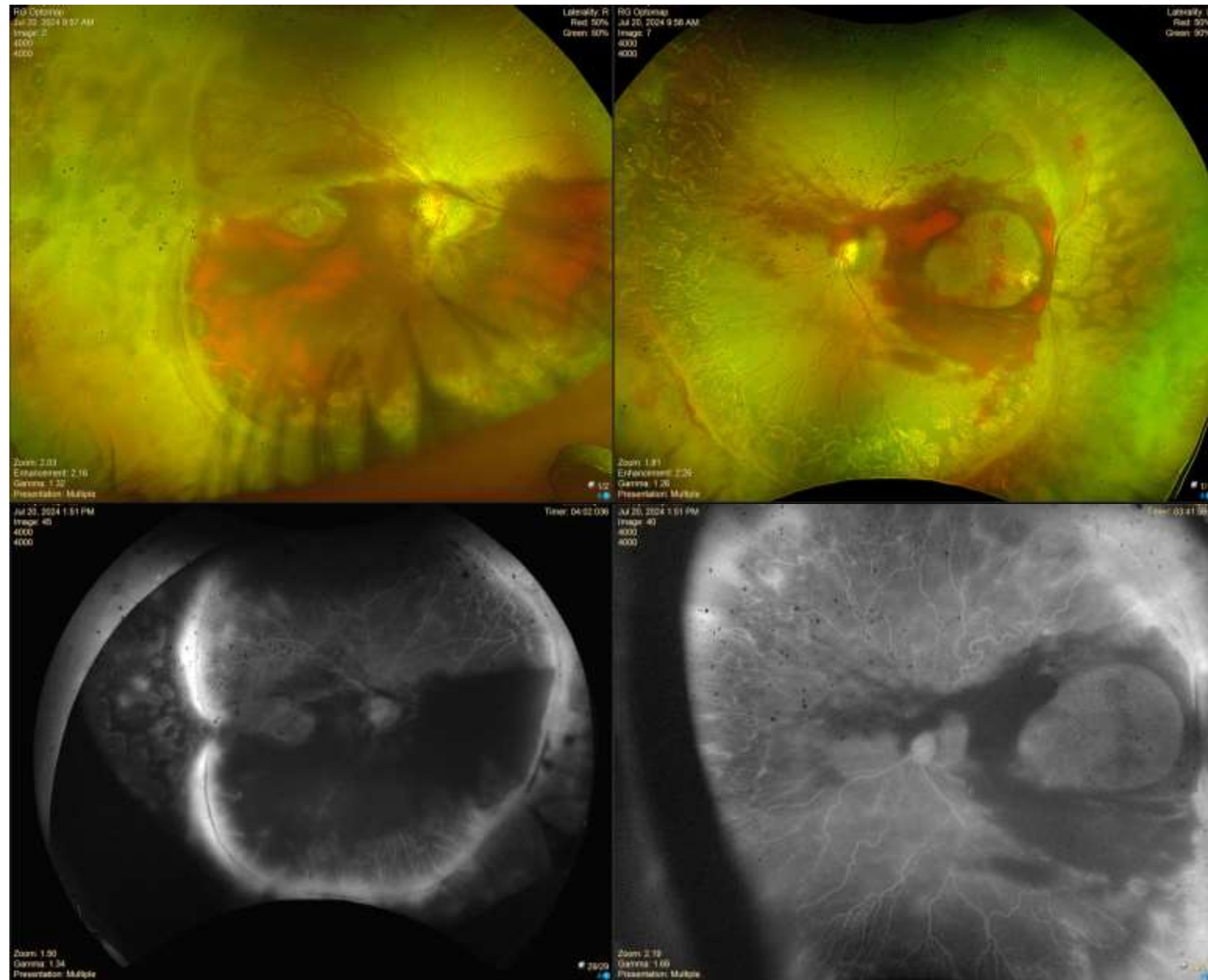
Age of the patient	Dosage	Sodium fluorescein 20%	Sodium fluorescein 10%
Children <18 years old	7.5 mg/kg body weight	0.0375 ml/kg	0.075 ml/kg

Marmoy OR, Henderson RH, Ooi K. Recommended protocol for performing oral fundus fluorescein angiography (FFA) in children. Eye (Lond). 2022 Jan;36(1):234-236. doi: 10.1038/s41433-020-01328-6. Epub 2020 Dec 15. PMID: 33323986; PMCID: PMC8727556.

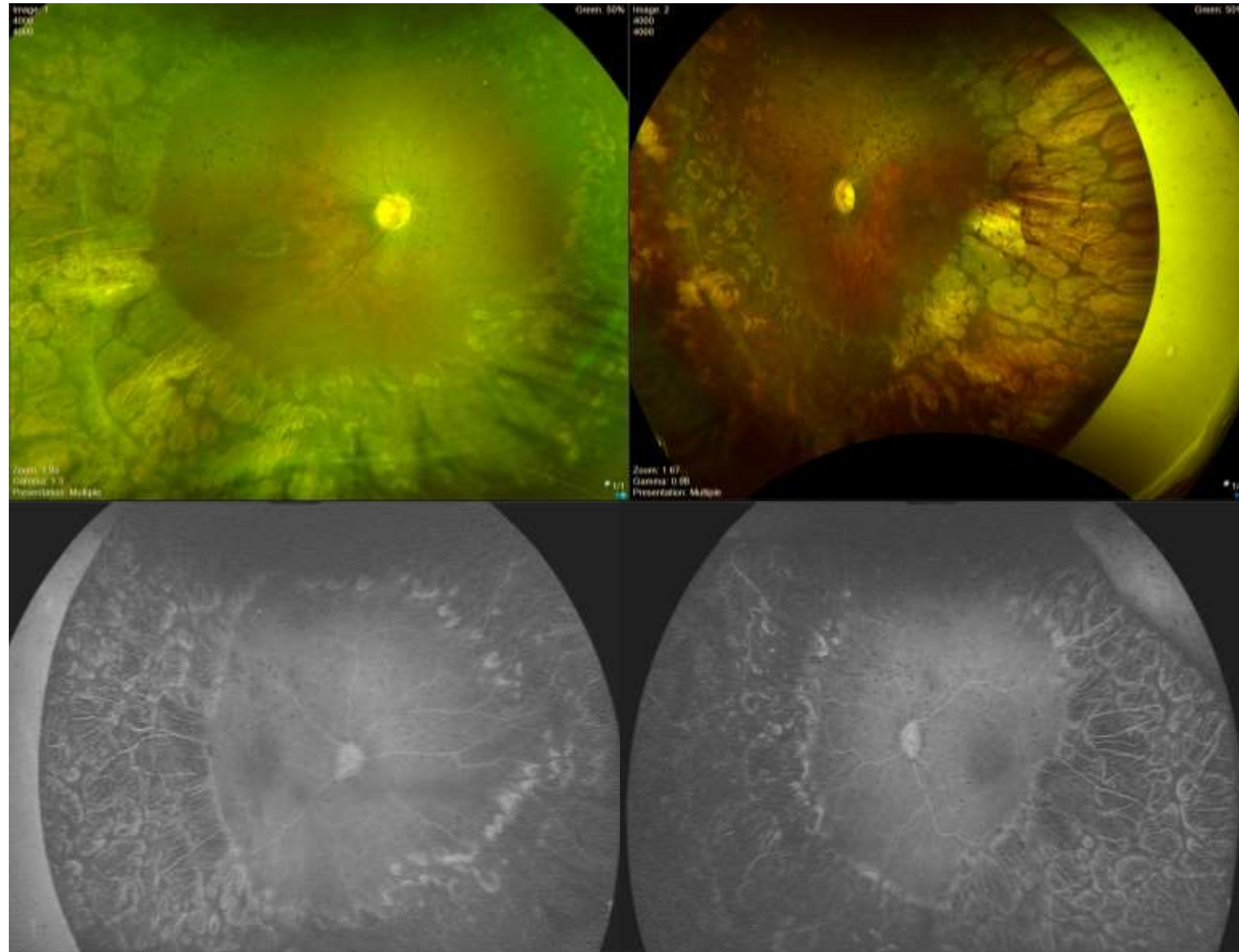


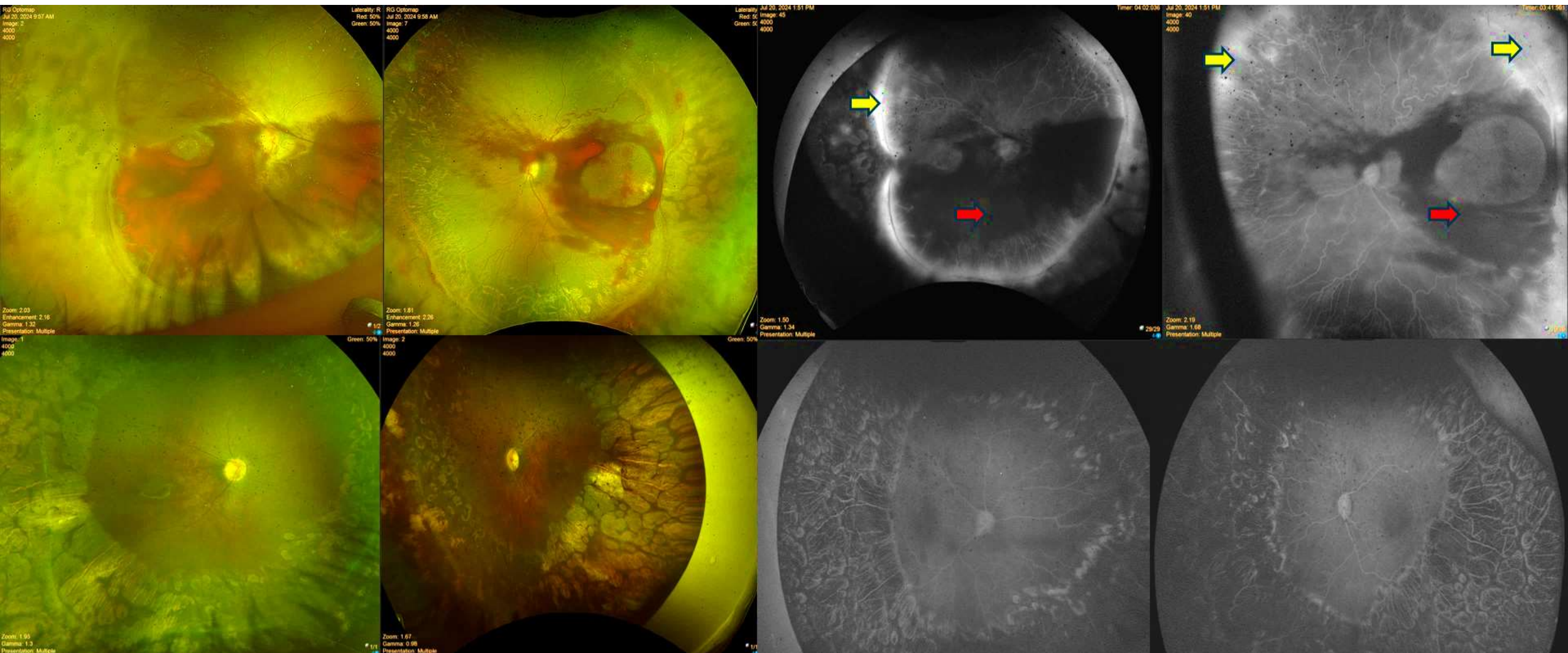
- ❖ The babies were kept **fasting for 1 hour** for better absorption of oral fluorescein dye.
- ❖ The capturing of the **images commenced 5 minutes after the babies were fed** (and burped) with the milk containing the oral fluorescein dye.
- ❖ For the next 2 minutes, serial images of both eyes were taken. We select the eye with more pathology for the OFDA image first and then we switch the OFDA image capturing serially between the two eyes.

Case 1, GA 26 weeks
BW 880 grams
S/P Ranibizumab and s/p LIO

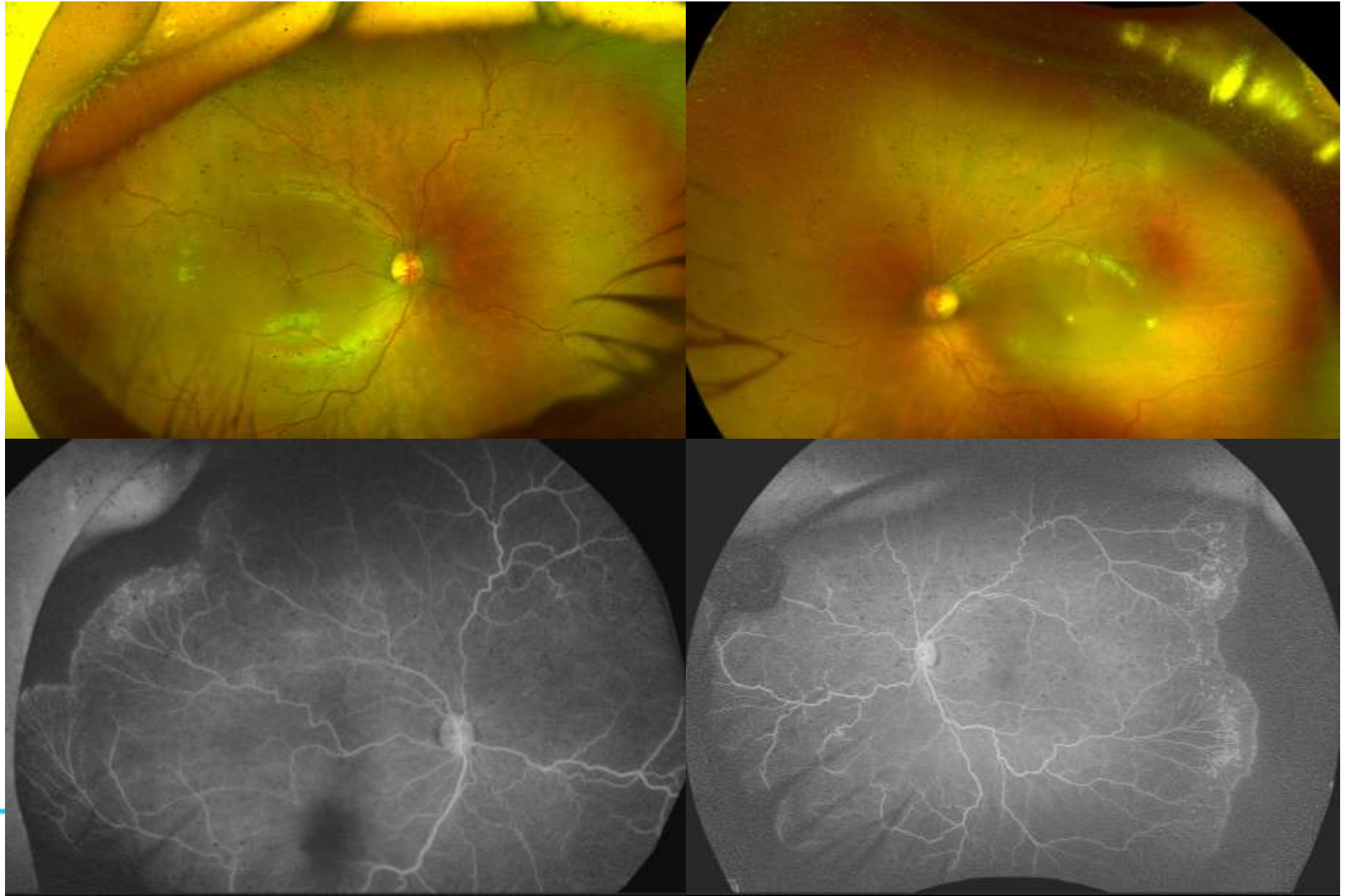


Case 1, GA 26 weeks
S/P Lens Sparing Vitrectomy
and OFDA guided targeted
laser





Case 2, GA 28 weeks
1400 grams BW
S/P Bevacizumab 10
weeks ago.



ARTICLE

 Check for updates

Oral fundus fluorescein angiogram detects reactivation post anti-VEGF in aggressive retinopathy of prematurity

Akash Belenje¹, Rakasi Ugandhar Reddy¹, Tapas Ranjan Padhi² and Subhadra Jalali¹✉

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OBJECTIVE: Utility, safety, and feasibility study of office-based Non-contact Ultra widefield Oral Fundus Fluorescein Dye Angiography (NC-UWF-OFDA) to assess disease reactivation in babies treated with intravitreal anti-vascular endothelial growth factor (anti-VEGF) for Aggressive Retinopathy of Prematurity (A-ROP).

METHODS: Eyes clinically suspected to have a possible or definite reactivation after anti-VEGF injection were included in this pilot study. NC-UWF-OFDA was performed in the office setting. Imaging was done prospectively in preterm babies with A-ROP injected with anti-VEGF. OFDA images were analysed for signs of reactivation.

RESULTS: A total of 20 eyes of 10 preterm babies treated with anti-VEGF underwent NC-UWF-OFDA imaging. The OFDA images were analysed to assess the pattern and dynamics of retinal vasculature with a special focus on detecting the active new vessels through leakage, the pattern of vasculature at the vascular avascular (V-Av) junction, and delineation of the persistent avascular retina (PAR). Seven eyes were confirmed with reactivation of ROP requiring treatment while the rest were followed up. None of the subjects had dye or procedure-related systemic adverse events.

CONCLUSION: NC-UWF-OFDA is safe and effective in the diagnosis of reactivation of ROP following anti-VEGF injections. A better appreciation of retinal vascular dynamics with accurate delineation of the posterior extent of capillary non-perfusion areas, PAR, and early definitive detection of active neovascularization helped in formulating the extent of laser treatment needed including intraoperatively. This helped us avoid unnecessary parenteral injections/general anaesthesia for evaluation of disease reactivation and helped avoid over-treatment of cases having clinical suspicion of reactivation during fundoscopy.

Eye; <https://doi.org/10.1038/s41433-025-03896-x>

Anaemia is a strong systemic risk factor for retinopathy of prematurity (ROP) in neonates,

- ❖ Immature hematopoietic system,
- ❖ Inadequate erythropoietin production
- ❖ Failure to thrive
- ❖ Iatrogenic blood loss during frequent sampling
- ❖ poor antenatal care
- ❖ post-natal infections
- ❖ maternal anaemia.

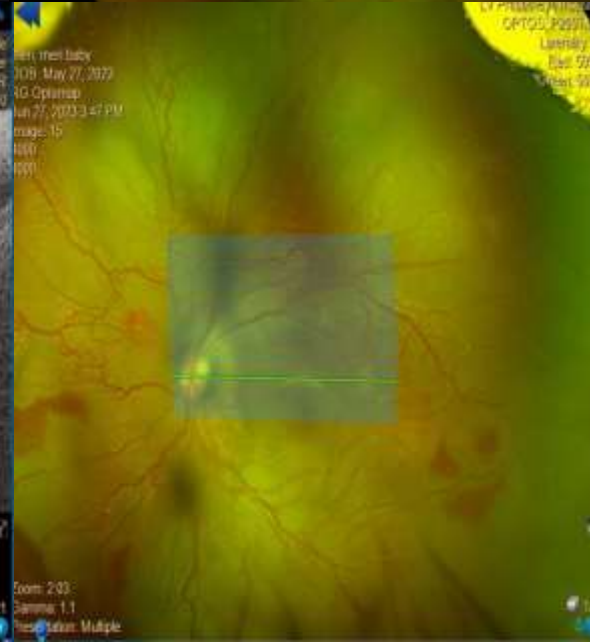
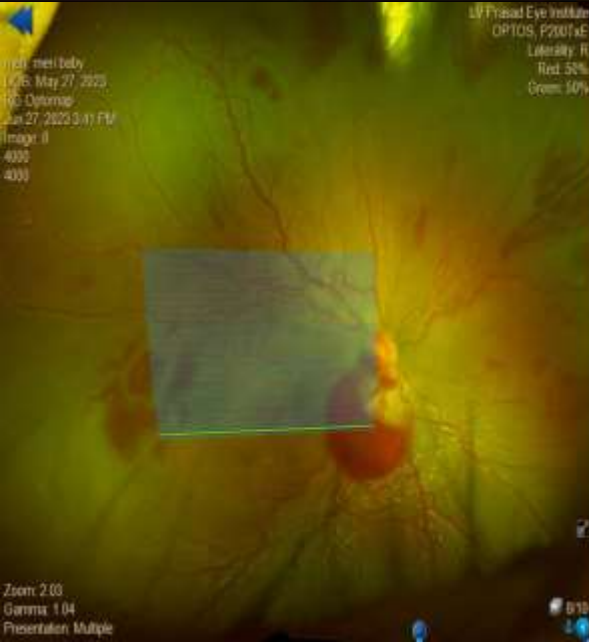
According to world health organization severity of anemia in infants can be classified as

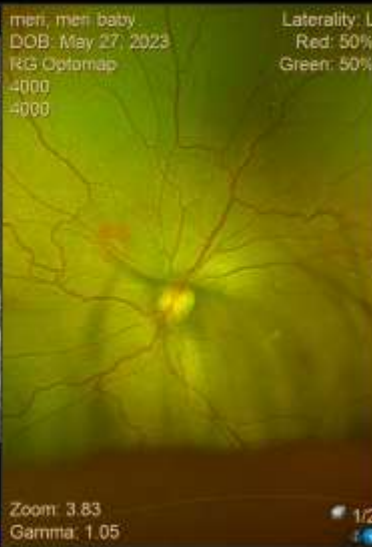
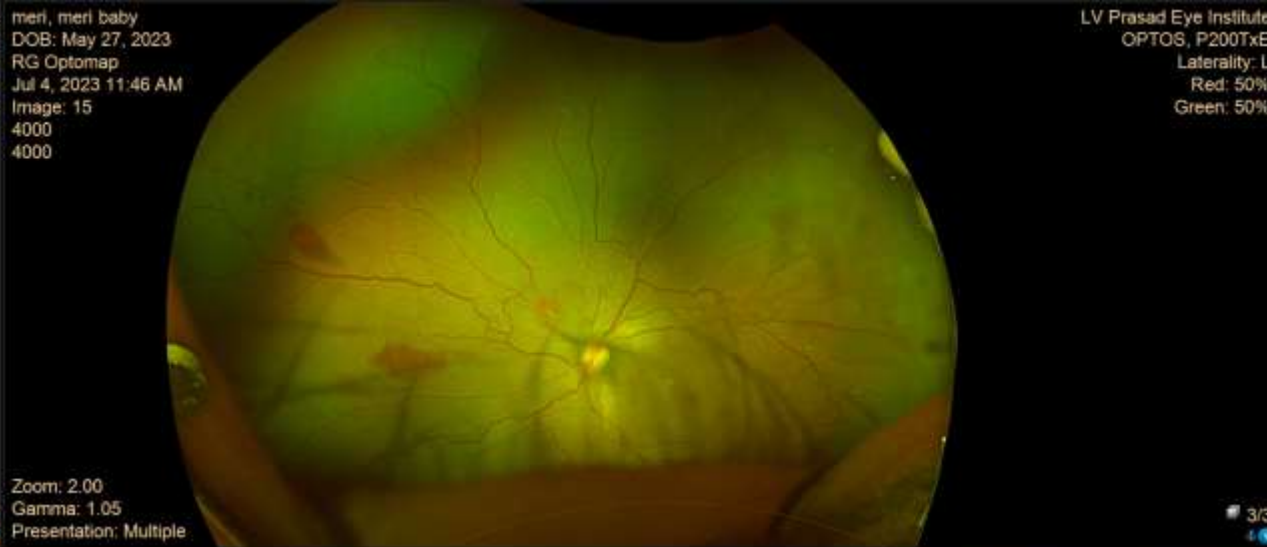
Mild anemia (Hemoglobin 10.0-10.9 g/dl),

Moderate anemia (Hemoglobin 7.0-9.9 g/dl),

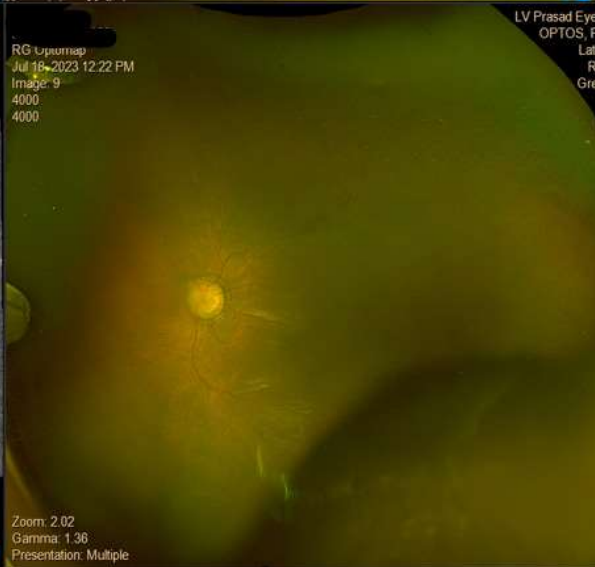
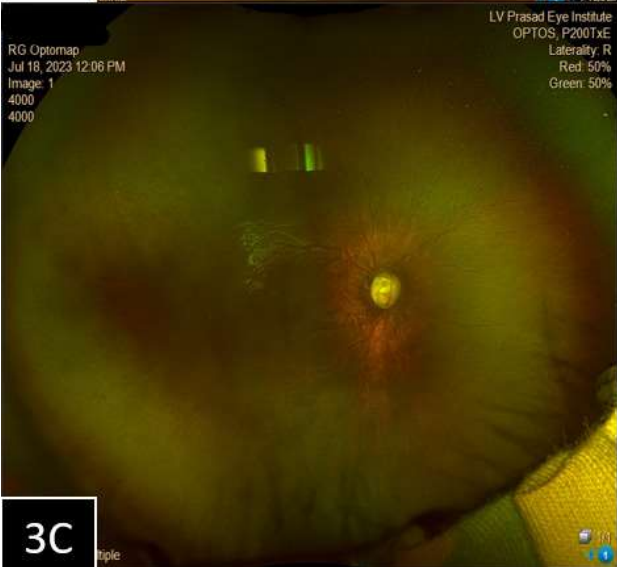
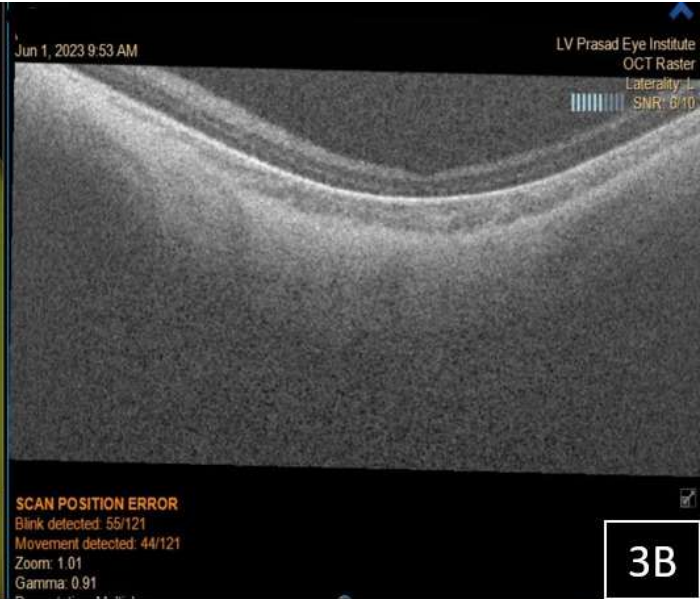
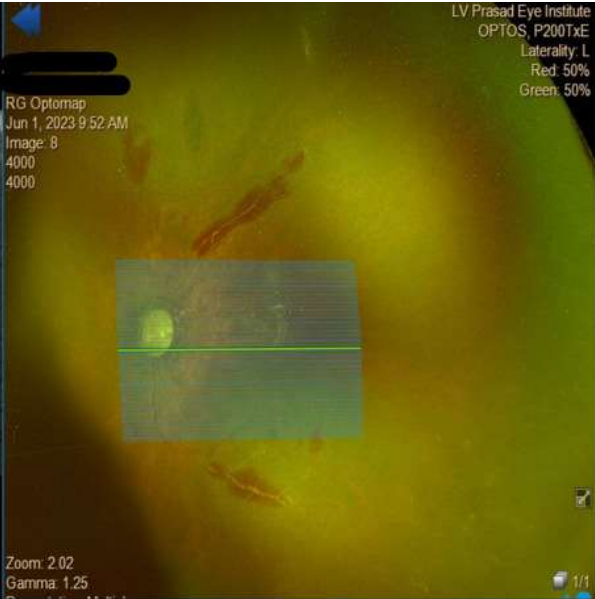
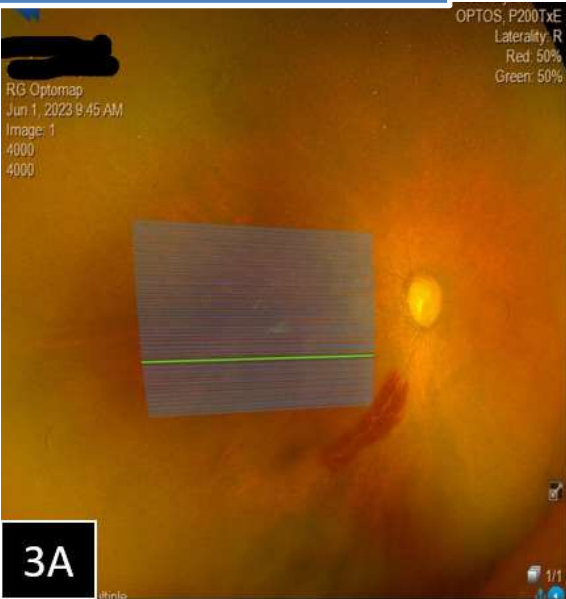
and severe anemia (Hemoglobin <7.0 g/dl).

Baby with GA 28 w,
PMA 32 w, Birth
weight 1000 grams,
Hb 6.6 gm%





Baby with GA 28 w,
PMA 32 w, Birth
weight 1200 grams,
Hb 7.4 gm%



Observations of simultaneous aggressive anemia correction and intravitreal therapy for aggressive retinopathy of prematurity: A multimodal ROP assessment study (MROPAS) report number 2

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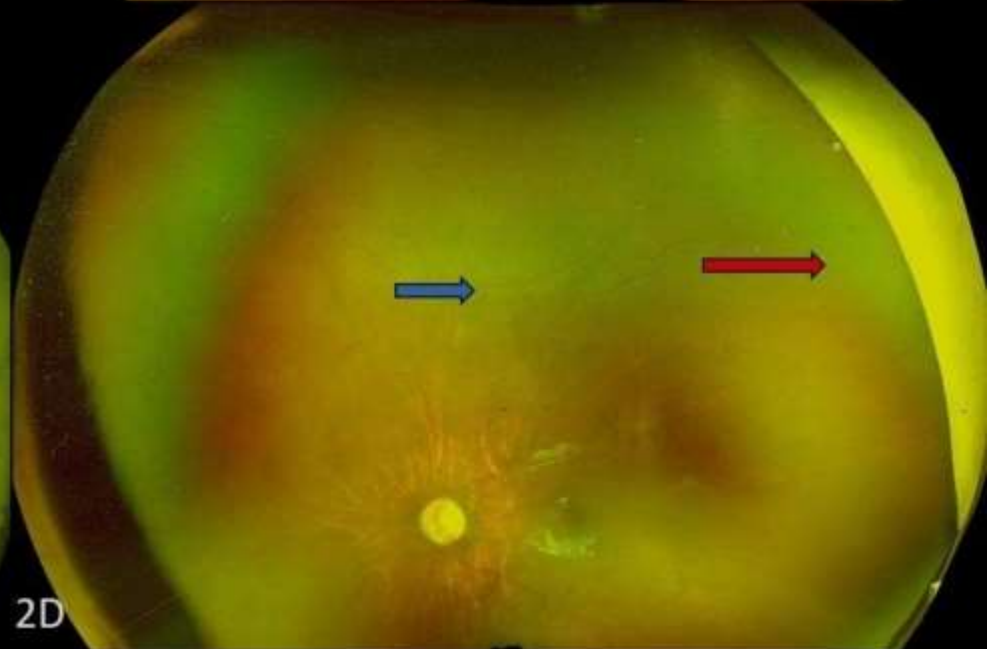
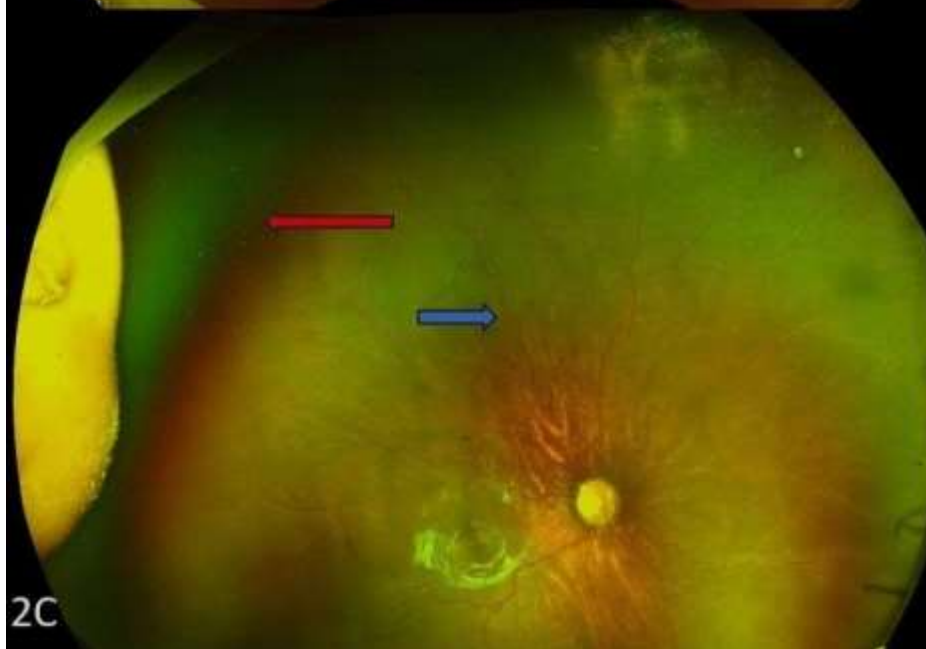
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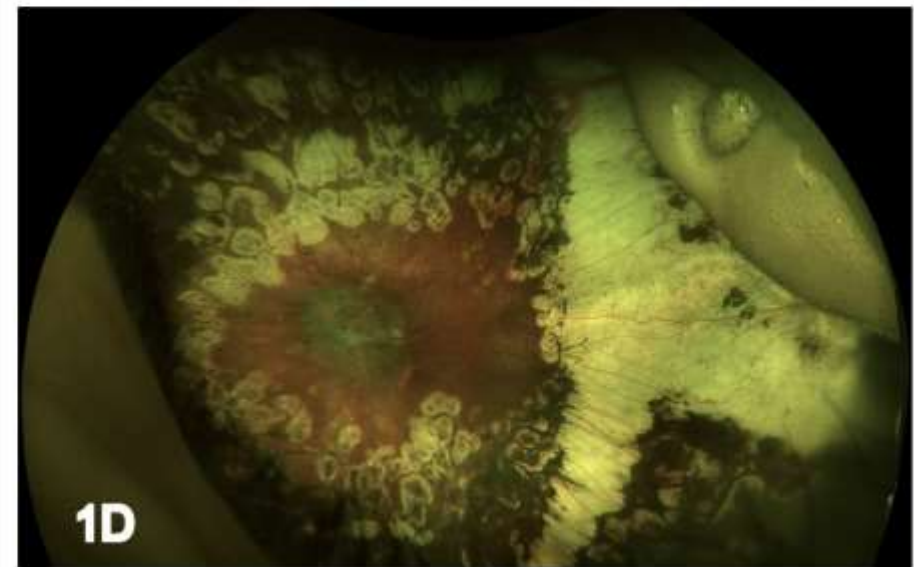
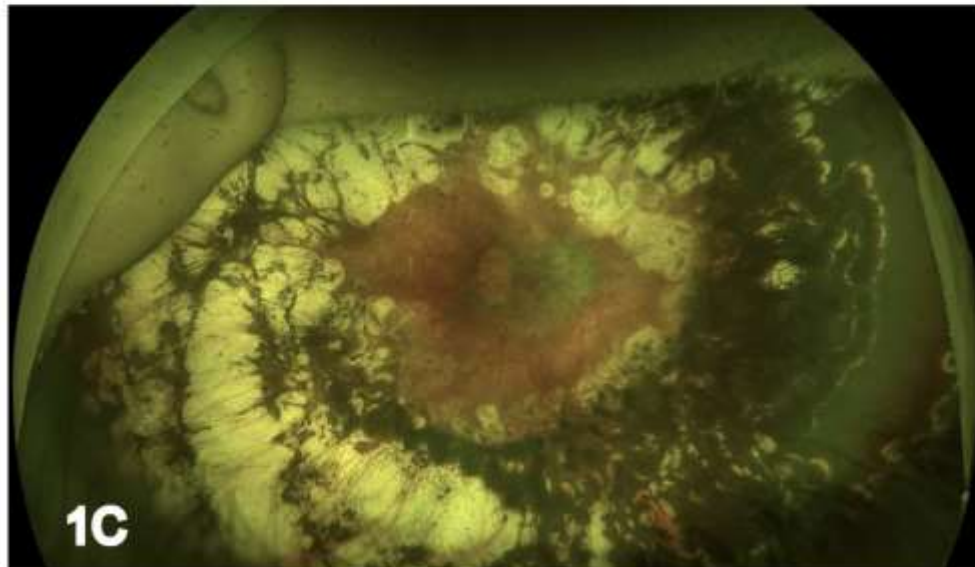
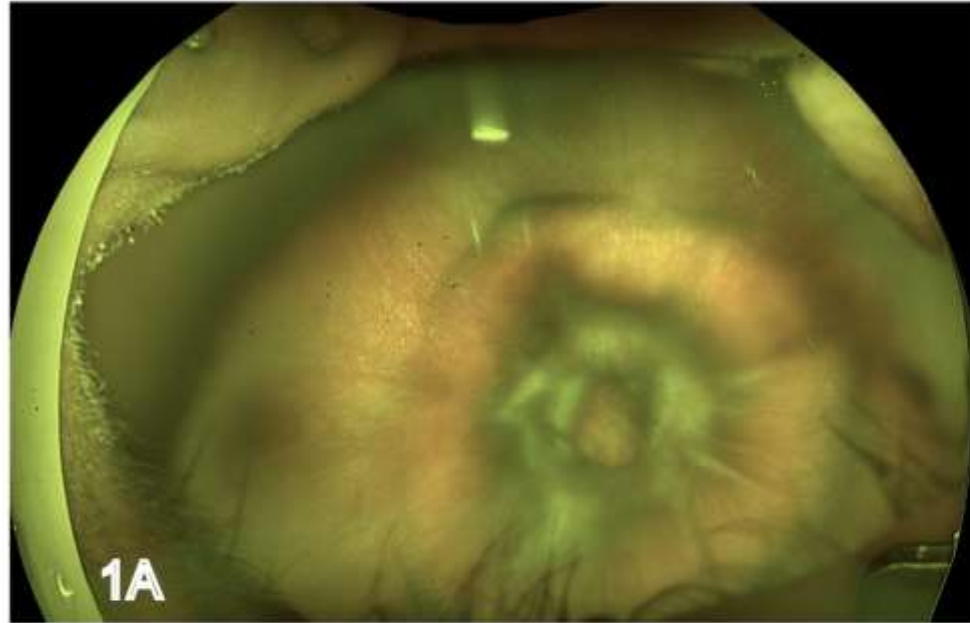
Baby with Hb 6.4
gm%

ATYPICAL 360
DEGREE
SCLEROSIS



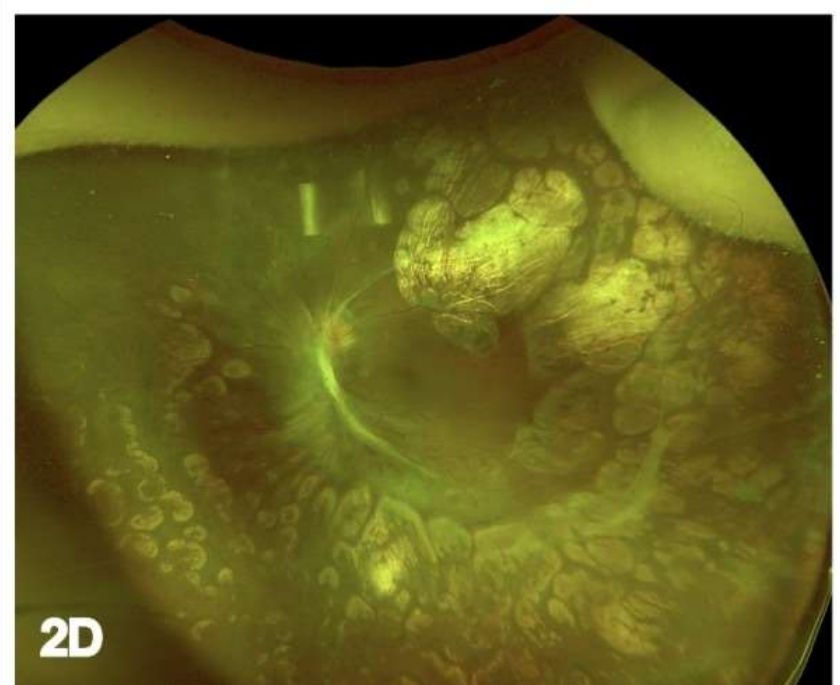
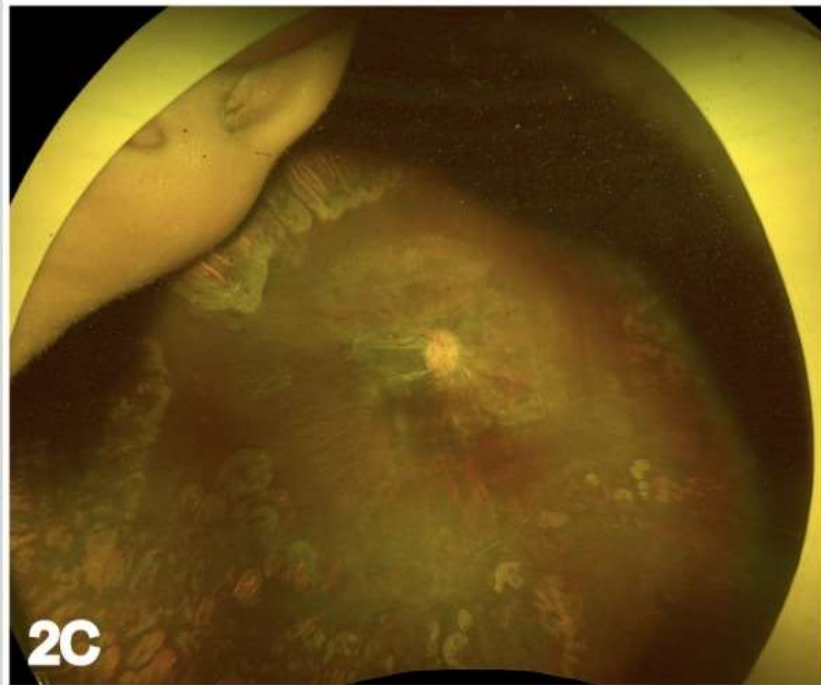
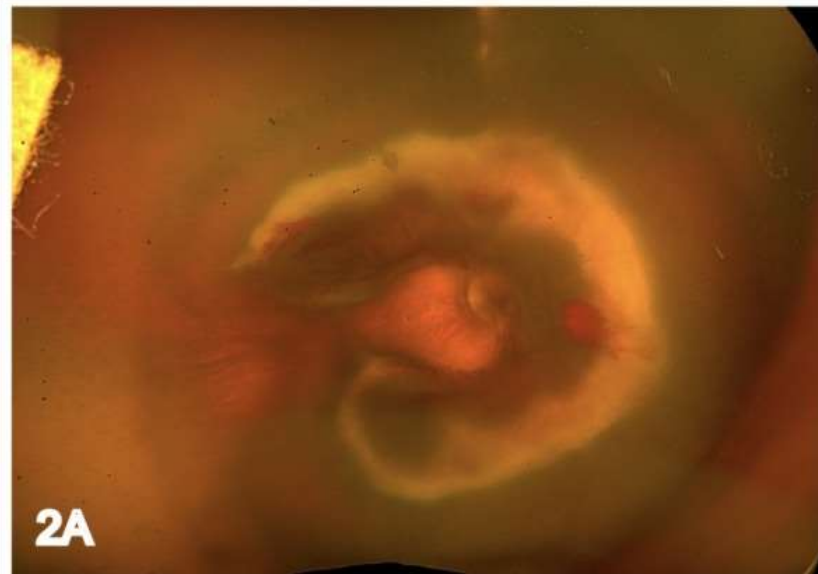
**ATYPICAL BLEB LIKE
ROP WITH POSTERIOR
COMBINED
DETACHMENT**

HB 8.2 GM%

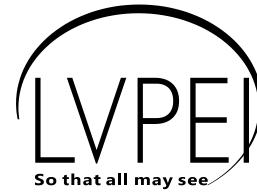


**ATYPICAL BLEB LIKE
ROP WITH POSTERIOR
COMBINED
DETACHMENT**

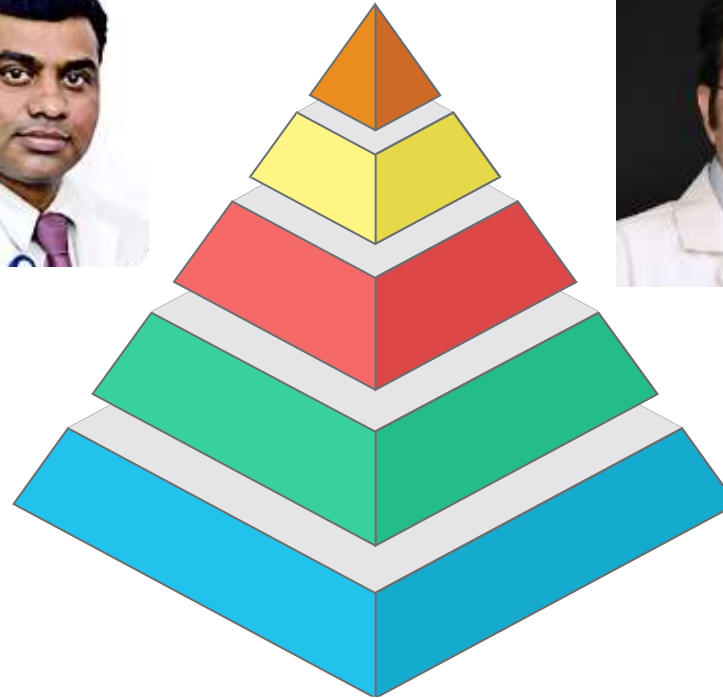
HB 7.6 GM%







LV Prasad Eye Institute



Excellence • Equity • Efficiency

Thank You